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GUIDELINES

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JCS/JHRS 2019 guideline on non-pharmacotherapy of cardiac arrhythmias

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Abbreviations: AF, atrial fibrillation; AFL, atrial flutter; APC, atriopulmonary connection; ARVC, arrhythmogenic right ventricular cardiomyopathy; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reciprocating tachycardia; CFAE, complex fractionated atrial electrogram; CIED, cardiac implantable electronic device; CLBBB, complete left bundle branch block; CP, common pathway; CPVA, circumferential pulmonary vein ablation; CPVI, circumferential pulmonary vein isolation; CPVT, catecholaminergic polymorphic ventricular tachycardia; CRT, cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy defibrillator; CRT-P, cardiac resynchronization therapy pacemaker; CTI, cavotricuspid isthmus; DOAC, direct-acting oral anticoagulant; ER, early repolarization; ERS, early repolarization syndrome; GP, ganglionated plexus; HOCM, hypertrophic obstructive cardiomyopathy; I. I., image intensifier; ICD, implantable cardioverter-defibrillator; ICM, implantable cardiac monitor; IVF, idiopathic ventricular fibrillation; LAAC, left atrial appendage closure; LAO, left anterior oblique; LAVA, local abnormal ventricular activity; LVA, low-voltage area; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MINDS, Medical Information Network Distribution Service; NSVT, nonsustained ventricular tachycardia; PAC, premature atrial contraction; PPI, postpacing interval; PVC, premature ventricular contraction; PVI, pulmonary vein isolation; QOL, quality of life; RCT, randomized controlled trial; S-ICD, subcutaneous implantable cardioverter-defibrillator; SQTS, short QT syndrome; TCPC, total cavopulmonary connection; TdP, torsade de pointes; TEE, transesophageal echocardiography; TIA, transient ischemic attack; VATS, video-assisted thoracoscopic surgery; VF, ventricular fibrillation; VT, ventricular tachycardia; VTCL, ventricular tachycardia cycle length; WCD, wearable cardioverter-defibrillator; WPW, Wolff-Parkinson-White.

This document is an English version of 2018 JCS/JHRS Guideline on Non-Pharmacotherapy of Cardiac Arrhythmias reported at the Japanese Circulation Society Joint Working Group published in 2019 (https://www.j-circ.or.jp/cms/wp-content/uploads/2018/07/JCS1028_kurita_nogami.pdf).

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Joint Working Group: Japanese Circulation Society, Japanese Heart Rhythm Society, Japanese Association for Thoracic Surgery, Japanese Society of Pediatric Cardiology and Cardiac Surgery, Japanese Association of Cardiovascular Intervention and Therapeutics, Japanese Society for Artificial Organs, Japanese Society for Cardiovascular Surgery, Japanese College of Cardiology, Japanese Heart Failure Society.

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PREAMBLE

The original guideline for non-pharmacological treatments (cardiac implantable electronic device, catheter ablation, and arrhythmia surgery) of arrhythmias (Japanese Circulation Society [JCS] Guideline on Non-pharmacotherapy of Cardiac Arrhythmias) was first published in 2001, and there have been two revisions thereafter (2006 and 2011). The "JCS Guideline on Indications and Procedures for Catheter Ablation" was published in 2012 to cover the rapid development and expansion of catheter ablation techniques. Advances in non-pharmacological treatment of arrhythmia have further accelerated since then, with the succeeding emergence of new functions, usefulness, and evidence. Against the background of these remarkable developments, the guidelines needed to undergo many changes and revisions. Therefore, the format has been revised again to include cardiac implantable electronic devices and catheter ablation therapies.

Since 2011, there has been a succession of innovative devices and treatment methods, such as (1) implantable cardiac monitoring, (2) subcutaneous implantable cardioverter-defibrillators, (3) wearable cardioverter-defibrillators, (4) remote monitoring, (5) magnetic resonance imaging-compatible devices, (6) leadless pacemakers, (7) balloon technology for pulmonary vein isolation, (8) percutaneous lead extraction, and (9) left atrial appendage closure devices. Thus, this revision needed to add new sections to accommodate these developments. In addition, new content on existing treatment methods has been added as much as possible, including hardware improvements, new evidence, and the challenge of reducing radiation exposure. Selecting and summarizing suitable information from the vast amount of available data within a limited space could have been a daunting task for all team members; however, our efforts have culminated in this guideline revision containing carefully selected and essential information, thanks to everyone who collaborated on this project.

Two related guidelines (JCS Guideline on Treatment of Acute and Chronic Heart Failure, and JCS Guideline on Treatment of Genetic Arrhythmia) were each revised in 2018.[1,2] Some working group members participated in the revision of both guidelines, as team members or observers, thus ensuring consistency between the guidelines. Non-pharmacotherapy in the broad sense includes external cardioversion for atrial fibrillation and sustained ventricular tachyarrhythmias, temporary intravenous pacing, and percutaneous pacing. However, for details of these therapies, refer to the JCS Guidelines on Pharmacotherapy of Atrial Fibrillation[3] and the Japan Resuscitation Council Guidelines.[4]

I | INTRODUCTION

1 | Current status of non-pharmacotherapies in Japan

Pacemaker treatment for bradyarrhythmia was first approved for national health insurance coverage in Japan in 1974, and its use rapidly became widespread thereafter. Approximately 40 years later, in 2017, the number of patients treated with this technology has increased to 60 137 (41 895 new cases and approximately 18 242 replacements).[5] Capsule-shaped leadless pacemaker also became available in 2016, and this technology is being established as a new option.

Non-pharmacological treatment of tachy-arrhythmia began in 1969 from when Will C. Sealy performed surgery in patients with Wolff-Parkinson-White (WPW) syndrome (Figure 1). Since then, the application of surgical treatment has expanded to conditions such as ventricular tachycardia (VT) and atrial fibrillation (AF), and surgery has been the pioneer of radical therapy for tachyarrhythmias. At the present time, many surgical methods have been replaced by

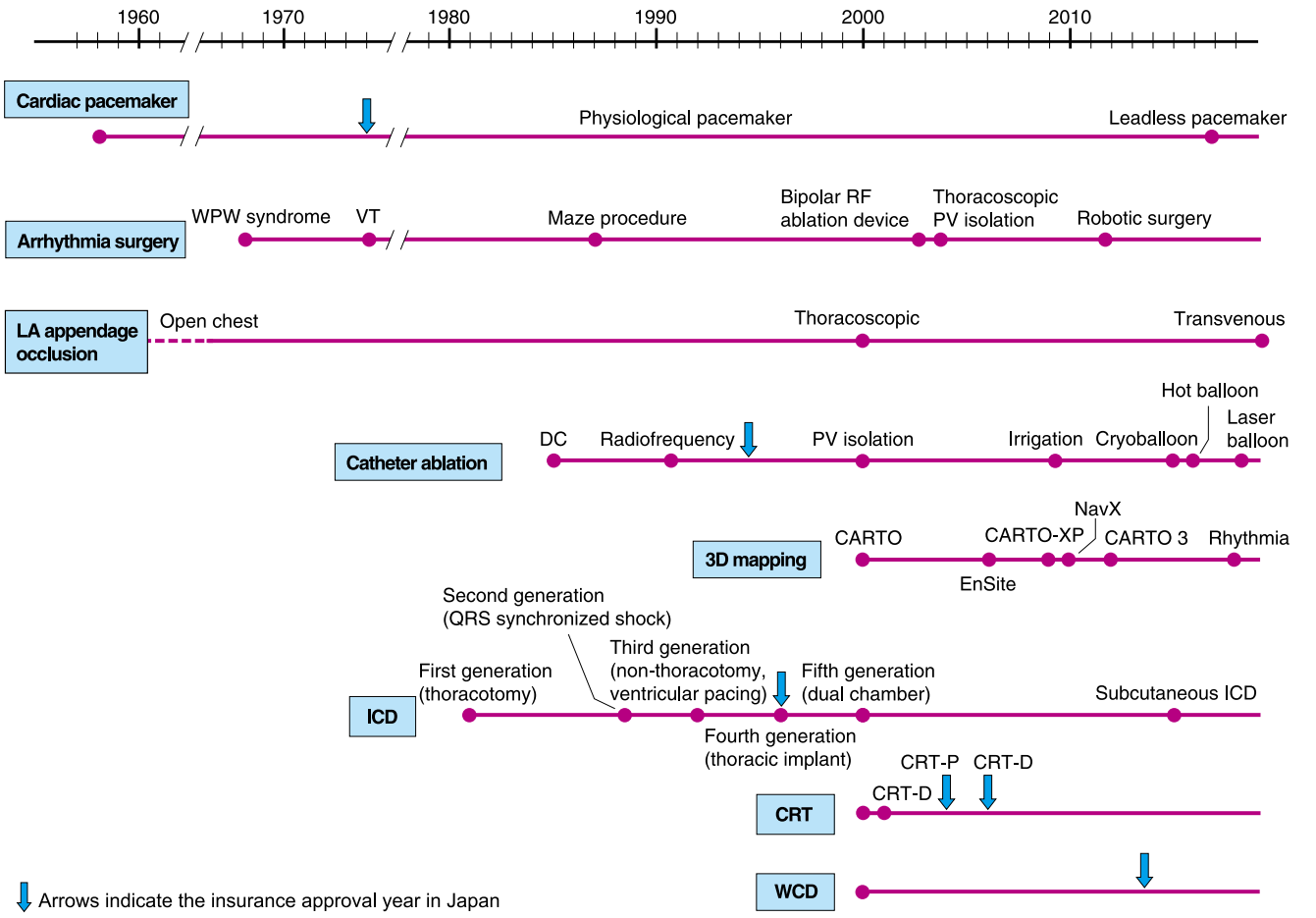


FIGURE 1 History of non-pharmacotherapy of cardiac arrhythmia

catheter ablation; however, surgical treatment still remains an indispensable option for patients with a tachycardia resistant to other medical treatments.

As with surgical treatment, catheter ablation was initially performed for supraventricular tachycardias such as WPW syndrome. However, the revolutionary discovery of pulmonary vein isolation (PVI) for AF and the advent of three-dimensional (3D) navigation systems have subsequently resulted in a tremendous increase in the number of cases treated with catheter ablation. In 2016, >74 000 catheter ablation procedures were performed in Japan, of which >45 000 were implemented for AF.[6] In 2015, a PVI method using cryoballoon ablation was introduced in Japan. Later, new techniques such as hot balloon or laser balloon (endoscopic systems using laser irradiation) ablation technologies entered the market, and safer and easier treatment methods are currently being established. In addition, prevention of systemic embolism using a left atrial appendage closure (LAAC) device is being established as a breakthrough treatment for AF patients who have difficulty in continuing anticoagulation therapy.

Because early implantable cardioverter-defibrillators (ICDs) were highly invasive owing to the requirement for a thoracotomy, the indications for this treatment were highly limited. However, the development of transvenous leads, the discovery of the biphasic shock method, and a reduction in both the size and weight of the generator have now enabled implantation using the same technique as for pacemakers, which has contributed to expanding the application of ICDs to primary prevention. In 2017, approximately 6691 devices (4288 new cases, 2403 replacements) were implanted in Japan.[5] The subcutaneous implantable cardioverter-defibrillator (S-ICD) was developed in 2015, and its clinical usage is progressing.

In 2004, cardiac resynchronization therapy (CRT) became available for patients with impaired cardiac function, and the usefulness of this treatment has been verified. especially in heart failure patients with complete left bundle branch block in Japan. Because patients with heart failure have a high risk of sudden death, an ICD with a biventricular pacing function (CRT defibrillator [CRT-D]) was also developed and approved in 2006. In 2017, CRT was newly administered in 3321 patients in Japan, 2399 of whom (72%) received the CRT-D, demonstrating that the treatment has been actively applied to prevent sudden death.[5] A wearable cardioverter-defibrillator (WCD) was introduced in Japan in 2015, which can be used for candidates for ICD therapy as a bridge treatment until application of an ICD is possible. Many devices are also equipped with a remote monitoring function, which sends most of the biological information and device data to the medical facility while the patient is staying at home by enabling the early detection of abnormal findings.

As described above, there have been remarkable developments in the non-pharmacotherapy of arrhythmias. However, problems still remain, including (1) the risk of complications associated with aging of patients, (2) the requirement for high-quality training of specialists and medical staff to enable them to handle the expanding indications and diversifying treatment methods, (3) the overflow of information and increasing complexity of management because of the sophisticated and multiple functionalities of the devices, and (4) the impact of the expanding indications of expensive devices in the setting of limited medical resources. In the future, it will be necessary to formulate evidence unique to Japan on the extent to which cutting-edge non-pharmacological treatments for arrhythmias improve the prognosis of patients.

2 | Necessity and aim of the guideline

This guideline recommends indications for non-pharmacotherapy of arrhythmia based on the latest findings and evidence. There is an increasing variety of non-pharmacotherapies, and extensive progress is being made in this field. This guideline contains information on conventional cardiac implantable electronic devices (CIEDs), such as pacemakers, ICDs, and ICDs with biventricular pacing function, as well as new information on remote monitoring, magnetic resonance imaging-conditional CIEDs, leadless pacemakers, percutaneous lead extraction, implantable monitors, S-ICDs, and WCDs. Information on catheter ablation includes radiation exposure, new 3D mapping systems, balloon ablation for AF, bipolar ablation, and chemical ablation. In addition, this guideline discusses the LAAC device for the first time, which is not a treatment for arrhythmia itself but for preventing thromboembolism – a serious problem associated with AF.

Non-pharmacotherapy of arrhythmia is expected to increase in the future, so there is a need to standardize all non-pharmacotherapy processes, including not only treatment indications but also their theoretical background, recommended procedures, necessary equipment and implementation system, and precautions that have to be taken before and after the procedure.

The indications of non-pharmacological treatments of tachyarrhythmia in children differ from those in adults, so there are many cautionary points to note. Therefore, CIEDs and catheter ablation for children are described under independent chapters, as in previous guidelines. The information on surgical treatment for arrhythmia mainly focuses on surgical treatment for AF and VT. Surgery for supraventricular tachycardia has been omitted from this guideline because the number of surgical procedures has dramatically decreased in recent years. Nevertheless, surgery is still indicated for some patients with supraventricular tachycardias, including those with unsuccessful ablation.

The aim of this guideline is to clarify the indications, results, and complications of non-pharmacological treatments for arrhythmias such as bradyarrhythmia, supraventricular tachycardia, AF, premature ventricular contractions, VT, and ventricular fibrillation, as well as treatment for the associated heart failure and thromboembolism. We are striving for standardized treatment by explicitly describing the procedures. Specific information on the procedures is also included, such as the knowledge, equipment, and doctor/facility conditions required to perform the procedure. The guideline has been created based on evidence and consensus at the time of publication and should be updated over time. This guideline describes the recommended indications and procedures as of 2018. Future technological advances will further expand the indications for non-pharmacotherapy of arrhythmia and make the procedures more reliable and convenient.

This guideline is designed to be used as a reference by doctors diagnosing and treating diseases in clinical practice, and the final decision should be made by the attending physicians after ascertaining the patient's condition. Even when selecting a diagnosis or treatment that does not follow the guideline, the decision of the attending physicians should be prioritized in consideration of the individual patient's situation. In actual clinical settings, it is most important for the attending physicians to make the judgment after fully considering the clinical background and social situation of each patient while complying with the guideline.

3 | Classes of recommendation and levels of evidence

For this guideline, we first surveyed materials based on evidence from the USA and Europe, then further critically examined the level of evidence, collected information available in Japan, and examined all materials based on the experiences and opinions of members and collaborators in the joint working group. The recommendation classes and evidence levels used in this guideline conform to those of the American Heart Association (AHA), American College of Cardiology (ACC), and Heart Rhythm Society (HRS) guidelines.[7] The recommendation class of indications for each diagnosis and treatment method is classified as I, IIa, IIb, and III, and the level of evidence is classified into levels A, B, and C (Tables 1,2).

The guideline also states the class of recommendation and level of evidence based on the "MINDS Handbook for Clinical

TABLE 1 Class of recommendation

Class I	Evidence and/or general agreement that a given procedure or treatment is useful and effective
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given procedure or treatment
Class IIa	Weight of evidence/opinion is in favor of usefulness/efficacy
Class IIb	Usefulness/efficacy is less well established by evidence/opinion
Class III	Evidence or general agreement that the given procedure or treatment is not useful/effective, and in some cases may be harmful

TABLE 2 Level of evidence

Level A	**Data derived from multiple randomized clinical trials or meta-analyses**
Level B	Data derived from a single randomized clinical trial or large-scale non-randomized studies
Level C	Consensus of opinion of the experts and/or small-size clinical studies, retrospective studies, and registries

TABLE 3 MINDS grades of recommendation

Grade A	**Strongly recommended and supported by strong evidence**
Grade B	Recommended with moderately strong supporting evidence
Grade C1	Recommended despite no strong supporting evidence
Grade C2	Not recommended because of the absence of strong supporting evidence
Grade D	Not recommended as evidence indicates that the treatment is ineffective or even harmful

The grade of recommendation is determined based on a comprehensive assessment of the level and quantity of evidence, variation of conclusion, extent of effectiveness, applicability to the clinical setting, and evidence on harms and costs. (From MINDS Treatment Guidelines Selection Committee, 2007.[8])

TABLE 4 MINDS levels of evidence (in literature on treatment)

I	Systematic review/meta-analysis of randomized controlled trials
II	One or more randomized controlled trials
III	Non-randomized controlled trials
IVa	Analytical epidemiological studies (cohort studies)
IVb	Analytical epidemiological studies (case-control studies and cross-sectional studies)
V	Descriptive studies (case reports and case series)
VI	Not based on patient data, or based on opinions from a specialist committee or individual specialists

(From MINDS Treatment Guidelines Selection Committee, 2007.[8])

Practice Guideline Development 2007",[8] published by the Medical Information Network Distribution Service (MINDS) Evidence-based Medicine dissemination promotion project as a guideline preparation method (Tables 3,4). The MINDS grades of recommendation are comprehensively determined, taking into account the following factors: (1) level of evidence, (2) amount and variation of evidence, (3) extent of clinical effectiveness, (4) clinical applicability (physician ability, regional characteristics, medical resources, insurance system, etc), and (5) evidence on harm and cost.

The MINDS level of evidence (levels of evidence in literature on treatment) is a classification based on research design, and the highest level was adopted when multiple papers were considered. This guideline describes both the conventional AHA/ACC/HRS guideline classifications and the MINDS classification, whenever possible, for the content of each diagnosis and treatment. However, the MINDS grade of recommendation and level of evidence should be used only as a reference, as this system regards the evidence level in a fundamentally different manner.

This revision adds new knowledge acquired from advances in diagnostic techniques and treatment methods, or recently reported important evidence, while considering consistency with each of the previously reported guidelines published by the JCS Joint Working Group.

II | CARDIAC IMPLANTABLE ELECTRONIC DEVICES (CIEDS)

1 | Overview

1.1 | History and transitions

Pacemaker therapy for bradyarrhythmia became covered by insurance in Japan in 1974. Initially, pacemakers only had ventricular pacing function; however, at present, pacemakers with functions such as maintaining atrioventricular synchrony with dual-chamber pacing modes, as well as monitoring atrioventricular conductivity to suppress right ventricular pacing, have been developed, which has contributed to improving patients' prognosis. In 2017, a capsule-type leadless pacemaker appeared on the market, and its clinical application is progressing.

An implantable cardioverter-defibrillator (ICD) was introduced in Japan in 1996 to treat fatal arrhythmias (ventricular tachycardia [VT]/ventricular fibrillation [VF]). Early ICDs were a highly invasive treatment requiring a thoracotomy, severely limiting their indications. However, the subsequent development of transvenous leads, discovery of the biphasic shock method, and reduction in the size and weight of the generator enabled use of the same technique as that for pacemaker implantation, which has greatly contributed to the expansion of indications for improving life prognosis and for primary prevention. The year 2000 saw the appearance of the dual-chamber ICD, which contributed to a dramatic improvement in pacing function during bradycardia, equivalent to that of a pacemaker for bradycardia, and a diagnostic algorithm based on atrial signal detection. Furthermore, the subcutaneous ICD (S-ICD) was introduced in 2015 and has been actively used for patients without venous access and/or those who do not require pacing functions.

In 2004, biventricular pacing, or cardiac resynchronized therapy (CRT), became available for patients with impaired cardiac function, and its utility has been confirmed, especially in patients with heart failure who have desynchronous contractions due to complete left bundle branch block (CLBBB). As patients with heart failure are at a high risk of sudden death, an ICD with a biventricular pacing function (CRT-D) was developed and approved in 2006. Improved pacing-site selectivity with quadrupolar left ventricular leads, functions utilizing self-right bundle conduction, and multipoint left ventricular pacing have been applied in clinical practice and may reduce the number of non-responders. As of 2017, CRT-D has been indicated for 72% of

new cardiac resynchronization therapy (CRT) cases in Japan; thus, aggressive prevention of sudden death is ongoing.[5]

ICDs have limited effectiveness after an acute myocardial infarction and at the early stage after the diagnosis of heart failure. In 2015, wearable cardioverter-defibrillators (WCDs) came into use to prevent sudden death during the waiting period while the indications for ICD are being determined. WCD is also used as a bridging treatment until the next implantation for patients whose ICD has been removed because of infection or other reasons.

Many devices are equipped with a remote monitoring function, which now enables the early detection of abnormal findings related to device functions and biological characteristics. Furthermore, although their use is conditional, magnetic resonance imaging (MRI)-compatible devices has become to be recognized as ordinary function, which is particularly useful in Japan where the rate of installation and using MRI are high.

1.2 | Required knowledge, facility standards, and standards for implementing physicians

Non-pharmacological treatment of arrhythmia requires advanced medical technology, and progress is rapid in this field. Physician and facility requirements are extremely important for the application of this guideline. This section describes the current facility standards and practitioner standards; however, as these may be revised in the future, refer to the Japanese Circulation Society or Japanese Heart Rhythm Society (HRS) websites to obtain the latest information.

Doctors involved in cardiac implantable electronic device (CIED) implantation must satisfy the following requirements.

1. Sufficiently knowledgeable and experienced in clinical cardiac electrophysiology studies.
2. Sufficiently knowledgeable and experienced in pharmacotherapy for arrhythmia and heart failure.
3. Sufficiently knowledgeable and skilled with respect to pacemakers, ICDs, CRT-P/CRT-D, and surgical procedures as non-pharmacotherapy, and able to deal with various complications.

Each non-pharmacotherapy must be applied effectively and safely, and a system for responding to emergencies (human resource development, establishment of a team medical system, use of fully maintained equipment) is required.

1.2.1 | Pacemakers

a. | Implantation and replacement using transvenous leads. The following facility standards for special medical fees are specified as conditions for applying for insurance (based on the 2015 Medical Fee Points Table).

1. There should be one or more physicians with at least 5 years' experience in cardiovascular medicine or cardiovascular surgery. In addition, notification should also be possible in the insurance medical institution (ie, the clinic).
2. Although not a facility standard, it is desirable for the facility to have a system that can perform cardiac electrophysiology studies, an outpatient pacemaker clinic, etc.

b. | Leadless pacemakers. The following institutional standards and practitioner standards were proposed by the Japanese HRS in 2017, considering the novelty of the leadless pacemaker and that this procedure requires cardiac access via the femoral vein using a large sheath[9] (see "**3.7 Leadless pacemakers**" in this chapter).

Facility standards

1. The facility standards for pacemaker implantation and pacemaker replacement using transvenous leads should be satisfied, and there should be full-time doctors with experience in performing the pacemaker implantation or replacement of at least 10 cases per year.
2. There should be a system capable of emergency cardiovascular surgery. However, this does not apply to facilities that maintain cooperation with a neighboring insurance medical institution that performs emergency cardiovascular surgery.

Practitioner standards

1. Practitioners should have sufficient specialist knowledge on CIED therapy.
2. Practitioners should have undergone training conducted by marketing authorization holders and supervised by relevant academic societies.

1.2.2 | ICD, CRT-P/CRT-D, and wearable cardioverter-defibrillator (WCD)

The following facility standards for special medical fees have been established as a condition of insurance application for ICD and cardiac resynchronization therapy pacemaker (CRT-P)/cardiac resynchronization therapy defibrillator (CRT-D) (based on the 2015 Medical Fee Points Table).

1. The hospital advocates cardiology and cardiovascular surgery.
2. At least 50 patients undergo cardiac electrophysiology studies per year, and ≥ 5 cases should be ventricular tachyarrhythmia.
3. At least 30 patients undergo open-heart surgery or coronary artery or bypass grafting per year, and at least 10 pacemaker implantations are performed per year.
4. At least 2 full-time cardiologists and cardiovascular surgeons are appointed, and ≥ 2 of them have completed the prescribed training.
5. Necessary equipment should be available so that the tests listed below, which are required for performing the procedure, can be conducted at any time within the insurance medical institution.
   (i) Blood tests
   (ii) Biochemical tests
   (iii) Imaging diagnostics
   Item (6) below is for CRT-P only.

6. The facility staff should be sufficiently experienced in treating severe heart failure using a ventricular assist device including external systems.

The following practitioner standards were proposed by the Japanese HRS in 2016 for S-ICD implantation.[11]

Practitioner standards

1. Practitioners must have undergone training conducted by marketing authorization holders and supervised by relevant academic societies.
2. At least the first 2 cases of implantation are performed under the guidance of a physician who has completed both the above training and a program for trainers conducted by the marketing authorization holder. Alternatively, the practitioner must have observed at least 1 implantation procedure before performing the first case of implantation, and thereafter must have performed at least 2 other implantations under the guidance of a surgeon.

Clinical use of a WCD requires appropriate selection of cases and understanding of the equipment, and the following practitioner standards were proposed by the Japanese HRS in 2017.[12]

Practitioner standards

1. Practitioners must have undergone training on WCD prescription qualifications supervised by relevant academic societies.
2. Medical personnel (doctors and medical staff) involved in WCD must undergo training conducted by marketing authorization holders.

1.2.3 | Implantable cardiac monitors (ICMs)

ICMs may be implanted in any facility that satisfies the facility standards for pacemakers, ICD, or CRT-P/CRT-D as a condition for insurance application (based on the 2015 Medical Fee Points Table).

1.3 | Informed consent

When deciding on the indications for treatments that require advanced medical technology such as CIEDs, it is essential that the patient provides voluntary consent after receiving sufficient information. The information should be provided using words that the patient can understand, pursuant to the provisions of Chapter 1, Article 1-4, paragraph 2 of the Medical Care Act: "In the delivery of medical care, a physician, dentist, pharmacist, nurse, or other medical care professional shall give appropriate explanations and endeavor to foster understanding in the recipients of medical care."

The content of the explanation is based on the judgment according to the knowledge and experience of each doctor; however, it is necessary to provide the following information to the patient: (1) information on the disease (type and severity of arrhythmia, underlying heart disease, etc); (2) aim and details of the treatment (including device model and manufacturer name), therapeutic effect and success rate, complications (types, severity, and incidence) during the acute phase and during long-term follow-up (requires not only general information but also information on the performance in the facility in question), and the reason for selecting the treatment; (3) treatments other than the treatment in question (pharmacotherapies, other non-pharmacotherapies [including treatment available at other facilities]) and the therapeutic effect of those treatments; (4) expected results with monitoring alone without the treatment in question (predicted outcome and probability thereof); (5) positioning of the treatment in question for various arrythmias and possible unexpected complications (short-term and long-term); (6) cost of the treatment (including the cost of this treatment and other treatments); and (7) assurance that consent can be withdrawn before and during treatment.

After the provision of the above information, if the patient requests opinions from other doctors or medical institutions (second opinion), then it is essential to respond to the request. The patient is the main person in the decision-making process, and the right of self-determination of the patient is the most important factor when deciding on indications for non-pharmacotherapy. Basically, the consent of the patient and/or the family is required, based on their understanding of the explanation provided by the medical staff involved in testing and treatment. If the patient is unable to express their intention or is a minor, a family representative or legal representative will act on their behalf. Ultimately, the signatures of all attendees, including the medical staff, are obtained. Normally, 2 copies of the information sheet are prepared. The original copy is generally kept in the patient's medical record and another copy is given to the patient.

Physicians must be fully cognizant that informed consent is an important opportunity for the patients to compare and consider the benefits and disadvantages of the treatment, and to enable selection of treatment that is truly beneficial for them. The information must also be specific and easy to understand for the patients and their families.

1.4 | Complications and measures

Complications with CIED implantation are due to the device itself (generators and/or leads), or the implantation procedure. Generator complications include malfunctions such as recalls and resets due to electromagnetic interference. Lead complications include malfunctions such as recalls, lead dislodgement and aging, elevated pacing and sensing threshold,[13] venous occlusion,[14,15] and tricuspid insufficiency.[16-18]

Appropriate implantation techniques can reduce complications (eg, infection, pneumothorax, lead fracture, lead insulation break, and perforation resulting from lead insertion technique). There are differences in the incidence of CIED infection among facilities, which is reported to range from 0.2% to 7%.[19] Expansion of the ICD and CRT-D indications has resulted in increased implantation of the devices in high-risk patients (ie, elderly patients; patients with heart failure, renal failure, or diabetes; and patients taking steroids and/or antithrombotic agents), as well as an increased number of replacement operations due to long-term survival, which increases the incidence of infection.[19-21]

It is important to remember that implantation of a CIED is essentially a surgical operation; thus, it is necessary to fully understand the cause of infection and adopt preventive measures (maintaining the operating room environment,[22,23] hand washing, differentiating clean and unclean, surgical instrument disinfection and sterilization, surgical field disinfection, double gloving,[24,25] and use of antibiotics[26]). The Japanese Society of Chemotherapy and the Japan Society for Surgical Infection have proposed "Practical Guidelines for Proper Use of Antibiotics for Prevention of Postoperative Infection",[26] particularly with respect to the use of antibiotics. As hematoma formation is also an infection risk, intraoperative complete hemostasis is required.[19]

The depth of the pocket holding the CIED unit is also important. The pocket is created directly above the fascia of the pectoralis major muscle, not in the subcutaneous fat, to prevent compression necrosis of the skin.[27] If the subcutaneous tissue containing the subcutaneous fat is thin, it is recommended to create a pocket under the pectoralis major muscle.[27]

Puncture for lead insertion can cause complications such as pneumothorax,[28,29] and arterial puncture. Therefore, methods such as angiography before puncture[30] and ultrasound-guided puncture[31] have been recommended to mitigate complications. Axillary vein puncture is prefer over subclavian vein puncture to prevent lead compression fracture by the subclavian muscle and costoclavicular ligament.[32,33]

Meanwhile, the incision method is recommended not only to reduce the aforementioned complications but also to prevent lead fracture, prevent damage to the covering, and improve lead durability.[34] When inserting the lead, care should be taken to avoid perforation of the venous wall and myocardial wall. The perforation rate is reported to be 0.4%–0.64%,[28,29] and perforation is caused by the use of hard stylets, excessive pressure on the lead, rotation of the lead body after lead placement, and lead traction. It is also important to understand the characteristics of the lead tip shape (passive or active).

1.5 | Postoperative management

Before discharge, items including the wound's condition (dehiscence, signs of infection), position of the implanted lead, pacing threshold, and sensory potential amplitude should be checked.

As an early postoperative complication, hematoma has a relatively high incidence. Patients who are taking anticoagulants or antiplatelet drugs due to atrial fibrillation (AF), mechanical valve replacement or arteriosclerotic disease are considered a high-risk group, and postoperative wound observation is particularly important in these patients. Hematoma not only causes postoperative pain but can also cause device infection at a remote phase because it leads to incision dehiscence and compression necrosis. When hematoma is discovered, it is important to determine the necessity of reoperation. If there is no discoloration of the skin surface and no sign of skin necrosis or infection, the hematoma is almost always reabsorbed and can be dealt with using recompression. However, hematoma removal and hemostasis should be considered if the pain intensifies because of hematoma distension or if wound dehiscence occurs. Removal of hematoma by puncture is never performed because it increases the risk of infection.

There is no fixed trend in the onset of device infection, and risk factors include diabetes, renal impairment, heart failure, steroid use, nonuse of preoperative antibiotics, postoperative hematoma and other wound complications, dialysis, chronic obstructive pulmonary disease, cerebrovascular disorders, external pacemaker placement, device replacement, and early reoperation.[35,36] Once device infection has occurred, it is necessary to remove the entire system, which poses a great risk. Careful consideration is required before, during, and after surgery.

Chest X-ray (frontal and left lateral view) to check lead position abnormalities and movement, and simultaneous ECG monitoring to detect early pacing/sensing failure are also important. The intraoperative threshold and peak value of the intracardiac potential may change significantly after surgery. It is necessary to check the pacing threshold and the detected peak value of the intracardiac potential before discharge, and readjust the values as necessary. It is also recommended to conduct optimization before discharge of patients who underwent CRT.

Guidance on daily life after discharge should also be provided. Electromagnetic interference can cause electrical noise, which can trigger pacing inhibition in pacemakers and inappropriate therapy in ICDs. A detailed list of electromagnetic interference sources has been published by the Japan Arrhythmia Device Industry Association.[37] Household appliances can generally be used if the switch is not frequently turned on and off; however, patients must be instructed to maintain a distance of 50 cm from electromagnetic induction-heating rice cookers and 15 cm from mobile phones. Other than home appliances, use of low-frequency therapy equipment, powerful magnets, electric baths, etc, is prohibited. Caution is needed when using electric vehicle chargers (especially rapid chargers), wireless cards (contactless IC cards), electronic article surveillance equipment, and electronic tags (ie, RFID). The patient should be instructed to move away from the location if they experience dizziness, lightheadedness, palpitations, etc.

X-ray and CT have been reported to have an effect, and medical care may be required to prevent interference. There are conditions to be satisfied for MRI, and patients with ICD/CRT-D are required by law to have a restricted driver's license (see **Chapter VI, 1.2.1 Driving restrictions [particularly for patients with an ICD]**). The recent emergence of new devices has made management more complicated. There is also a concern that the degree of understanding of device functions will decline as patients become older. It is important to provide thorough patient education using pamphlets and to offer information on appropriate measures for possible problems.

1.6 | CIED follow-up and remote monitoring

CIED outpatient management is basically performed with device interrogation using the obtained parameters. It is necessary to ascertain not only the mechanical information of the device but also the general condition of the patient using various parameters. Specific information includes: (1) battery status; (2) lead information; (3) pacing

settings; (4) intracardiac electrogram sensing and pacing threshold; (5) arrhythmia detection and treatment status; and (6) heart rate histogram and physical activity biometric information, etc The patient guidance management fee is calculated by looking at this information.

In recent years, it has become possible to perform remote monitoring in most CIEDs. Remote monitoring has been shown to be as safe as conventional face-to-face examinations, and to enable the earlier diagnosis of arrhythmia and lead/device failures.[38-41] Furthermore, shortened hospital stays,[42,43] and improved life prognosis have also been reported.[44,45]

Therefore, remote monitoring for patients with CIEDs is highly useful, and it is recommended to introduce it as a standard management method; however, there are concerns about increased workload for hospital staff. There has been an increase in the number of patients implanted with CIEDs and in the aging population; therefore, efficiently providing outpatient services to patients with CIEDs is required. Doctors, clinical engineers, and nurses need to share roles and create hospital workflow as a team.

Table 5 is a proposed recommendation for CIED outpatient management and remote monitoring in Japan, referencing the consensus report on remote monitoring of patients with CIEDs, published by the HRS.

1.7 | MRI-conditional CIEDs

MRI-conditional pacemakers were first used in Japan in October 2012. Later, the same function was installed in ICDs and CRT-Ds. Initially, only 1.5-Tesla (T) was compatible, but recently a 3.0-T-compatible CIED has come on the market. Although the appearance of MRI-compatible CIEDs has provided benefits to patients, it has also created confusion in medical practice owing to the concurrent use of conventional non-MRI-compatible CIEDs and the different imaging conditions depending on the manufacturer. Even with MRI-compatible models, imaging is possible only when certain conditions are met on both the patient side and the device side. For the patient side, the conditions are that >6 weeks should have passed since implantation; both the lead and the generator are MRI-compatible; and there are no disconnected or residual leads implanted in the chest. The conditions on the device side are that there should be sufficient remaining battery power, and the lead resistance value and threshold value should be within the fixed ranges.

MRI can be performed only in facilities that meet the following criteria.

1. Advocates radiology and cardiovascular medicine or cardiovascular surgery.
2. Allows the test to be performed under the conditions described in the instruction manual for MRI-conditional CIEDs.
3. Appoints an MRI specialist or equivalent personnel to manage the precision and safety of the MRI equipment.
4. Has specialists with sufficient medical experience with CIEDs and able to manage the equipment.
5. Has specialists and staff who have completed the prescribed training supervised by the relevant academic society and held by the marketing authorization holder with respect to appropriate and safe use of the equipment.

Accredited facilities can be confirmed on the MRI examination information website[46] for patients with arrhythmia devices.

The expected events when MRI is performed for patients with non-MRI-compatible CIEDs include: (1) increased threshold owing to heating of the lead tip and myocardial damage, (2) unnecessary myocardial stimulation,[47] (3) improper pacing inhibition, (4) change of the setting mode, (5) battery consumption, and (6) integrated circuit (IC) damage.

MRI for non-MRI-conditional CIEDs is currently contraindicated in Japan; however, reports have shown that there are few adverse effects when imaging is performed with 1.5-T MRI, providing that imaging is mainly of sites other than the chest.[48,49]

Even in patients with non-MRI-compatible CIEDs, if the need for imaging is very high and the benefits to be gained are considered to clearly outweigh the risks, it is recommended to prepare for imaging by providing sufficient explanation to the patient and consulting with radiologists about countermeasures in the event of complications.

MRI is not a 100% safe examination.[50,51] It should be ensured that unnecessary imaging is avoided. The actual procedure is described below.

TABLE 5 Recommendations and evidence levels for CIED follow-up and remote monitoring

	COR	LOE	GOR (MINDS)	LOE (MINDS)
It is recommended that all patients with CIEDs should visit the outpatient clinic annually and be interrogated with programmer	I	A	B	II
It is recommended to offer remote CIED monitoring and interrogation according to the workflow organized by the staff in each hospital	I	B	B	II
Remote monitoring should be considered to all patients with CIEDs as part of the standard follow-up management strategy	IIa	A	C1	III

Abbreviations: CIED, cardiac implantable electronic device; COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence.

TABLE 6 Recommendations and evidence levels for MRI of patients with MRI-conditional CIEDs

	COR	LOE	GOR (MINDS)	LOE (MINDS)
MRI should be considered only in patients implanted with MRI-conditional devices according to the determined procedures in consideration of minimum necessary requirement	IIa	C	C1	V

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence; MRI, magnetic resonance imaging.

1. Check for MRI-compatible CIEDs.
   For this purpose, the CIED notebook, MRI-conditional card, or programmer should be used, or the manufacturing model should be confirmed on a radiograph.
2. MRI model and imaging conditions.
   The required conditions include that the MRI equipment must be a 1.5- or 3.0-T cylindrical bore (tunnel MRI) system, and the maximum gradient slew rate must be ≤200 T/m/s. There are other detailed restrictions depending on the manufacturer or imaging location. When new devices are released in the future, the details should be confirmed on the website of each manufacturer or on the MRI examination information website for patients with arrhythmia devices.[46]
3. Check lead resistance, pacing threshold, and sensing threshold.
   The pacing threshold should be ≤2.0-2.5 V/0.4 ms, and there should be no diaphragm stimulation at 5.0 V.
4. Check the imaging mode (self-pulse).
   If there is no self-pulse, the VOO or DOO mode should be set. If there is a self-pulse, pacing should be set to off. Tachycardia therapy for ICD and CRT-D should be turned off.
5. View the monitor during imaging.
   During imaging, the heart rate must be continuously monitored using a pulse oximeter or an ECG monitor.
6. Prepare for unexpected situations.
   It should be ensured that the room is equipped with an electrical defibrillator to be used in an emergency, if necessary. A hospital manual for handling unexpected situations should be established.

In addition, it should be kept in mind that the threshold and lead resistance need to be re-measured after imaging and the mode needs to be returned to the original setting.

Recommendations are shown in Table 6.

2 | Electrophysiological studies

Introduction

Since the recording of the His bundle electrogram by Scherlag et al in 1969, cardiac electrophysiology studies, including atrial and ventricular potential recording, electrical stimulation, and drug loading have become widespread. Electrophysiology studies play an auxiliary role in the diagnosis and treatment of conditions such as bradyarrhythmia, tachyarrhythmia, and syncope.

Bradyarrhythmia is mainly diagnosed using non-invasive tests such as standard 12-lead ECG, Holter ECG, and exercise ECG, but cardiac electrophysiology studies are performed for auxiliary purposes.

The role of cardiac electrophysiology studies in tachyarrhythmia has significantly changed with the development of non-pharmacotherapy. Currently, cardiac electrophysiology studies are generally performed at the same time as catheter ablation for the treatment of tachycardia, and are used to identify ablation sites. Because the prognosis of fatal ventricular arrhythmias has been clearly improved by implantation of ICDs, induction of VT/VF during cardiac electrophysiology studies is sometimes performed to stratify the risk for sudden death, and primary prevention for ICDs.

The mechanism of syncope can now be elucidated with a relatively high degree of specificity by recording the ECG over a long period (≥1 week), as well as with the development of portable and implantable ECG, and the widespread use of head-up tilt-table tests. Cardiac electrophysiology assists these tests and is useful for examining the relationship between induced arrhythmias and subjective symptoms (syncope, dizziness, palpitations, etc).

2.1 | Bradyarrhythmia

Sinus node function is assessed using methods of recording the sinus node recovery time, sinoatrial conduction time, sinus node potential, etc.[52-55] In patients with atrioventricular block or ventricular conduction disorder, the His bundle–ventricle (H-V) time is measured, the appearance of the block is confirmed with high-frequency atrial stimulation, and the relationship with subjective symptoms is examined.[56-58] In patients with syncope, the presence of a bundle block or bi- to trifascicular -blocks on resting ECG suggests that the symptoms are caused by paroxysmal atrioventricular block; thus, atrioventricular conduction is assessed with cardiac electrophysiology studies.[59,60] However, in patients with fainting symptoms who do not have any abnormal findings on ECG or echocardiography, and who are considered unlikely to have cardiogenic cause, cardiac electrophysiology has little significance.[60-63] As the usefulness of cardiac electrophysiology is low in reflex syncope, such as carotid sinus syndrome and vasovagal syncope, tests such as the carotid sinus massage test and head-up tilt-table test are prioritized.[61-63]

Preoperative assessment of sinus node function and atrioventricular conduction in patients with pacemaker indications is considered

useful for selecting the pacemaker model.[57] However, recent pacemakers are equipped with functions that prioritize sinus rhythm and atrioventricular conduction, enabling real-time optimization based on the dynamic condition after implantation. Therefore, cardiac electrophysiology has limited significance for model selection.[53]

Although there is no active indication for drug stress test in cardiac electrophysiology for bradyarrhythmia, the test may be performed if the symptoms produced by cardiac electrophysiology studies do not match the subjective symptoms. Class Ia (procainamide or disopyramide) and Class IV (verapamil) drugs are intravenously administered to evaluate the function of the sinus node, atrioventricular node, and His–Purkinje system.[64,65]

The causes of sinus dysfunction include (1) intrinsic causes, (2) autonomic dysfunction, and (3) drug-induced causes, and diagnosing these conditions is important for selecting the optimal treatment. Pharmacological autonomic nerve blockade should be performed to exclude the effect of the autonomic nervous system, and 0.04 mg/kg atropine sulfate and 0.2 mg/kg propranolol should be intravenously administered for evaluation.[55] If the drugs seem to affect the cause of bradycardia, evaluation should be performed after discontinuing the drug administration and the relationship with the subjective symptoms should be reevaluated.

2.2 | Tachyarrhythmia

Symptomatic tachyarrhythmias that are not cardiogenic, such as cases associated with hyperthyroidism and anemia, may be subjected to cardiac electrophysiology studies. When tachycardia can be induced with programmed electrical stimulation in persistent narrow QRS (<120 ms) tachycardia,[66-68] and in wide QRS tachycardia, including VT,[69,70] the mechanism is highly likely to be reentrant tachycardia, and it may be possible to perform mapping of the tachycardia and to identify the arrhythmia substrate with stimulation.[71] An accurate diagnosis of tachycardia increases the possibility of a cure with catheter ablation.[68,72] Wolff-Parkinson-White (WPW) syndrome with syncope and dizziness (12-lead ECG with delta waves at rest) can result in sudden death. High-risk groups are identified by inducing tachycardia and measuring the refractory period of the accessory pathway.[73,74] and cure is attempted with one-stage catheter ablation. Cardiac electrophysiology studies are planned for patients with unexplained syncope or dizziness suspected to be caused by tachycardia, relying on a diagnosis of an underlying heart disease (see **Chapter III, "2. Electrophysiological study"** for information on cardiac electrophysiology in catheter ablation).

Evaluation of the efficacy of antiarrhythmic drugs using programmed electrical stimulation is called electrophysiology-guided therapy.[75-78] However, in the ESVEM (Electrophysiologic Study Versus Electrocardiographic Monitoring) trial, there was no difference in the efficacy assessment using cardiac electrophysiology-guided therapy and Holter ECG.[79,80] Moreover, electrophysiology-guided therapy is not essential for evaluating the effect of amiodarone.[77-83] In addition, subsequently published large-scale clinical trials, such as AVID (Antiarrhythmics Versus Implantable Defibrillators),[84] showed the superior effect of ICD compared with antiarrhythmic drug treatment. Electrophysiology-guided therapy has little significance at the present time when an ICD is the first-line treatment for sustained VT and VF.

Patients in whom electrophysiology studies should be considered to assess the risk of sudden cardiac death include the following: (1) those who received cardiopulmonary resuscitation and in whom arrhythmia cannot be ruled out as the cause; (2) those with structural heart disease and an unexplained syncope attack or non-sustained VT (NSVT); (3) those with NSVT due to underlying heart disease and positive ventricular late potential on signal-averaged ECG; (4) those with asymptomatic WPW syndrome (12-lead ECG with delta wave at rest) and a high-risk occupation; and (5) those with asymptomatic Brugada syndrome with other considerations, such as spontaneous type 1 ECG and unexplained syncope or spontaneous type 1 ECG with clinical history, family history, other abnormal ECG findings, genetic mutations, etc.

Electrophysiological risk assessment of sudden death is based on the possibility of inducing a lethal arrhythmia; however, it is not always easy to identify high-risk patients. Cases are comprehensively determined using evaluation based on findings from Holter ECG, exercise test, signal-averaged ECG, and T-wave alternans tests.

Sudden death is highly likely to be caused by VT or VF, and risk assessment has been conventionally performed using electrophysiology-guided studies. Risk assessment with electrophysiology studies is useful when NSVT is recorded or the signal-averaged ECG is positive in patients with reduced left ventricular ejection fraction (LVEF) (<40%) due to ischemic heart disease and heart failure of New York Heart Association (NYHA) class II or higher.[85-88]

Extrastimuli are mainly used to induce ventricular arrhythmia (programmed electrical stimulation) when reentry is the mechanism of tachycardia, usually with 2 different basic cycle lengths from 2 different locations in the right ventricle. When a physician places high priority on specificity, extrastimuli are applied up to 2-3 times in succession, and the coupling interval is evaluated at ≥180 ms Isoproterenol loading is added as needed. The diagnostic specificity falls with ≥4 successive extrastimuli or short-coupled stimuli.[89] When non-ischemic heart disease is the underlying disease, the diagnosis is less reliable than with underlying ischemic heart disease.[90]

For patients with asymptomatic WPW syndrome (12-lead ECG with delta wave at rest) and a high-risk occupation, it is desirable to treat the condition with catheter ablation.[74]

Electrophysiological study for risk stratification in asymptomatic cases of Brugada syndrome is still controversial[2] because there are several inconsistent results for the induction of VT/VF.[91-107] Even among the reports indicating a positive significance of VT/VF induction, some emphasize induction with up to 2 extrastimuli.[101,102]

The clinical significance of induced arrhythmia depends on the underlying heart disease, type of arrhythmia, and induction protocol. Electrophysiology studies are considered less useful in patients with frequent premature ventricular contraction (PVCs) without structural heart disease.

3 | Pacemakers

Introduction

Since being put into practical use in the 1960s, there has been rapid progress in both the hardware and software of implantable pacemakers, and they are now able to reproduce physiological heartbeats. Models compatible with MRI,[108] which was previously contraindicated with pacemakers, and new category models,[109] such as leadless pacemakers, have also emerged. Permanent pacemaker implantation is the only established treatment for bradyarrhythmia, contributing to improved survival and QOL. However, ethical and economic problems due to excessive expansion of indications are currently being pointed out. More strict guidelines for pacemaker implantation are needed to cope with this situation. In 2011, the Japanese Circulation Society took the lead in revising its guidelines for non-pharmacotherapy for arrhythmia. There is no change in the severity of symptoms and patient background in terms of medical indications; however, the current revisions to the guideline have been made considering recent technological advances.

(Refer to other guidelines for artificial pacing indications for atrioventricular block associated with acute myocardial infarction.[110])

3.1 | Atrioventricular block

The treatment indications are determined according to the location, severity, and symptoms of the atrioventricular block (AVB).[58,111-113] The most important factor is the presence of symptoms caused by bradycardia associated with AVB. Therefore, treatment is not indicated for asymptomatic 1st-degree AVB. Pacemaker therapy is also indicated for high-grade or 3rd-degree AVB caused by indispensable drugs or surgery,[114] which is irreversible after ablation or the patient has marked bradycardia or prolonged cardiac arrest,[115] irrespective of the location. It is difficult to assign specific values to the severity of bradycardia or cardiac arrest in these cases; however, as proposed in the 2013 AHA/ACC Guidelines,[116] ventricular rate <40 beats/min and ventricular arrest >3 s are used as reference values.[117,118] The recommendations are shown in Table 7.[111-123]

3.2 | Bifascicular and trifascicular block

In determining the indication for implantation, it is important to determine the danger of causing high-grade atrioventricular block,[124,125] and to evaluate the His–Purkinje system conduction function with electrophysiology studies.[126,127] The reference findings for abnormal conduction below the bundle of His are as follows: (1) marked prolongation of the H-V interval (>100 ms), (2) induction of a block within or below the bundle of His with atrial pacing (≤150 beats/min), and (3) induction of a block within or below the bundle of His with intravenous Class Ia antiarrhythmic drugs. A rare phenotype of trifascicular block can present as an alternating bundle branch block with alternating right branch and left branch blocks. This phenomenon is seen because of a similar level of conduction disturbance in both branches; however, because the possibility that this condition will progress to complete atrioventricular block is very

TABLE 7 Recommendations and evidence levels for pacemaker indication for atrioventricular block

	COR	LOE	GOR (MINDS)	LOE (MINDS)
Permanent pacemaker implantation is recommended for 2nd-degree, advanced, or 3rd-degree AVB with symptoms caused by bradycardia	I	C	B	V
Permanent pacemaker implantation is recommended for patients with advanced or 3rd-degree AVB with any of following conditions: 1. Medical conditions requiring drug therapy that causes symptomatic bradycardia 2. Postoperative AVB that is not expected to resolve after cardiac surgery 3. After catheter ablation of the AV junction 4. Progressive neuromuscular diseases with AVB 5. Obvious bradycardia or long ventricular pause while awake	I	C	B	V
Permanent pacemaker implantation is reasonable for patients with asymptomatic 3rd-degree AVB	IIa	C	C1	V
Permanent pacemaker implantation should be considered for patients with asymptomatic 2nd-degree or advanced AVB and with any of following conditions: 1. Intra- or infra-His levels found on electrophysiological studies 2. Progressive cardiomegaly due to persistent bradycardia 3. Deterioration of AV conduction by exercise or atropine sulfate infusion	IIa	C	C1	V
Permanent pacemaker implantation should be considered for patients with 1st-degree AVB and symptoms probably due to bradycardia, if intra-His or infra-His block is provoked by electrophysiological studies	IIa	C	C1	V
Permanent pacemaker implantation may be considered for patients with 1st-degree AVB and heart failure in whom adjustment of optimal atrioventricular delay is expected to improve hemodynamic conditions	IIb	C	C1	V

Abbreviations: AV, atrioventricular; AVB, atrioventricular block; COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence.

high, it is an indication for implantation.[128] The recommendations are shown in Table 8.

3.3 | Sick sinus syndrome

Although pacemaker implantation is not indicated for asymptomatic sinus bradycardia, syncope may result in injuries such as fractures. It is important to ascertain the symptoms that occur because of bradycardia, sinoatrial block, sinus arrest, or impaired heart rate response during exercise due to a decline in the primary function of the sinus node (syncope, convulsions, blacking out, dizziness, shortness of breath, fatigue, heart failure, etc).[119,120,129-135] Primary sinus node dysfunction is associated with essential reduction in sinus node function. Secondary sinus node dysfunction involves no abnormality in the sinus node itself. Rather, it is defined as a decline in sinus function from causes other than sinus node abnormalities, such as autonomic nervous system disorders, electrolyte abnormalities, and/or thyroid function disorders. Treatment may be indicated for cases caused by long-term administration of essential drugs, such as antiarrhythmic or psychotropic drugs, but not for cases that clearly have reversible causes. Electrophysiology studies have a low sensitivity for the assessment of sinus node function, but atrioventricular conduction assessment may be used to determine the pacing mode.[136] The recommendations are shown in Table 9.

3.4 | Atrial fibrillation (AF) with bradycardia

Pacemaker implantation is not indicated for asymptomatic AF with bradycardia. It is important to confirm that symptoms such as syncope, convulsions, blacking out, dizziness, shortness of breath, and fatigue, as well as symptoms of heart failure, are due to bradycardia or ventricular arrest.[137,138] Treatment may be indicated for cases caused by long-term administration of essential drugs, but not for cases that clearly have reversible causes. If the association between bradycardia and the symptoms is unclear, the severity of bradycardia or ventricular arrest (reference values: awake ventricular rate <40 beats/min or ventricular arrest >3 s) is considered; however, it is necessary to repeatedly investigate the relevance of both factors. Some experts believe that pacemakers are indicated for ventricular arrest of ≥5 s.[116] The recommendations are shown in Table 10.

3.5 | Carotid sinus hypersensitivity and vasovagal syncope

Previous reports have indicated that pacemaker therapy for reflex syncope (vasovagal syncope) inhibits syncope in approximately 50% of cardioinhibitory cases.[139-143] However, in double-blind studies, the success rate was as low as 17%; thus, its effectiveness is not determined.[144] The recent widespread use of external or internal loop ECGs has increased the chance of detecting the paroxysmal cardioinhibitory type of syncope. Recent findings have shown that pacing treatment has little effect on preventing syncope recurrence in patients with a positive tilt test (with a hypotensive response), even if paroxysmal cardioinhibitory syncope is detected.[145] Even when a long cardiac pause (>3 s with symptoms or >6 s without symptoms) is demonstrated on ECG, pacing therapy should be considered only for patients aged 40 years and older, when other therapies (physical counterpressure maneuvers and orthostatic adjustment self-training) are ineffective and the tilt test is negative.[60] However, reflex syncope, especially vasovagal syncope, is often of the vasodepressor type, and prevention is possible in most patients primarily

TABLE 8 Recommendations and evidence levels for pacemaker indication for chronic bifascicular or trifascicular block

	COR	LOE	GOR (MINDS)	LOE (MINDS)
Permanent pacemaker implantation is recommended for patients with chronic bifascicular of trifascicular block, with documentation of 2nd-degree (Mobitz type II), advanced, or 3rd-degree AVB, or alternating bundle branch block	I	B	A	IVa
Pacemaker implantation is recommended for patients with alternate bundle branch block	I	B	B	IVa
Permanent pacemaker implantation is recommended for patients with chronic bifascicular of trifascicular block which may be advanced to AVB by essential drugs for a medical condition.	I	C	B	V
Permanent pacemaker implantation is recommended for patients with syncope and chronic bifascicular of trifascicular block combined with Wenckebach-type 2nd-degree AVB in whom advanced AVB is suspected as cause of syncope	I	C	B	V
Permanent pacemaker implantation should be considered for patients with chronic bifascicular of trifascicular block and with unknown cause of syncope	IIa	C	C1	V
Permanent pacemaker implantation should be considered for patients with chronic bifascicular of trifascicular block and with organic heart disease, if infra-His block is proved by an electrophysiological study	IIa	C	C1	V
Permanent pacemaker implantation may be considered for patients with chronic bifascicular of trifascicular block without organic heart disease, if infra-His block is proved by an electrophysiological study	IIb	C	C1	V

Abbreviations: AVB, atrioventricular block; COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence.

TABLE 9 Recommendations and evidence levels for pacemaker indication for sick sinus syndrome

	COR	LOE	GOR (MINDS)	LOE (MINDS)
Permanent pacemaker implantation is recommended for patients with symptoms such as syncope, convulsions, blacking out, dizziness, shortness of breath and easy fatigability, or heart failure that has been confirmed to be due to bradycardia, sinoatrial block, or sinus arrest associated with primary sinus node dysfunction or heart rate insufficiency during exercise, including patients whose symptoms are caused by long-term treatment with drug(s) that cannot be discontinued	I	C	A	V
1. Permanent pacemaker implantation should be considered for patients with the above mentioned symptoms as well as bradycardia and/or ventricular arrest, but the relationships among those symptoms are unclear 2. Patients with bradycardia–tachycardia syndrome in whom drugs for controlling tachycardia exacerbate bradycardia	IIa	C	B	V
Permanent pacemaker implantation may be considered for asymptomatic patients with sinoatrial block or sinus arrest	IIb	C	C2	V

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence.

TABLE 10 Recommendations and evidence levels for pacemaker indication for atrial fibrillation with bradycardia

	COR	LOE	GOR (MINDS)	LOE (MINDS)
Permanent pacemaker implantation is recommended for patients with symptoms such as syncope, convulsion, blacking out, dizziness, shortness of breath and easy fatigability, or heart failure that have been confirmed to be due to bradycardia or ventricular arrest, including patients whose symptoms are caused by long-term treatment with drug(s) that cannot be discontinued	I	C	A	V
Permanent pacemaker implantation should be considered for patients with the abovementioned symptoms as well as bradycardia and/or ventricular arrest, but the relationships among those symptoms are unclear	IIa	C	B	V

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence.

with lifestyle modifications, including physical counterpressure maneuvers and orthostatic self-training.

There is currently no evidence for the long-term efficacy of pacemaker treatment for cardioinhibitory vasovagal syncope in young persons (<40 years old). However, in elderly patients with vasovagal syncope, pacing therapy may be considered if spontaneous syncope due to cardiac arrest is demonstrated by ECG and is associated with symptoms.[146]

Symptom improvement can be expected with pacemaker therapy in patients with hypersensitive carotid sinus syndrome, if it is clearly the cardioinhibitory type.[147-149] DDD pacemakers should be selected to treat reflex syncope. The recommendations are shown in Table 11.

3.6 | Hypertrophic obstructive cardiomyopathy (HOCM)

Atrial synchronous ventricular pacemaker therapy for HOCM is widely recognized as a treatment in drug-resistant cases.[150-152] Dual-chamber (DDD) pacing was considered effective in improving symptoms caused by left ventricular outflow tract obstruction; however, a placebo effect was observed even in AAI mode, and the superiority of DDD was not demonstrated.[153] However, its effectiveness has been reported in long-term follow-up studies, and there are also reports on efficacy of implantation techniques and post-implantation optimization, as well as on the combined effects with pharmacotherapy.[154-158] Therefore, pacemakers or ICDs should be considered an option for patients with drug-resistant symptomatic HOCM. Assessment of pressure gradient reduction with preoperative atrioventricular pacing can help determine the treatment indications. The recommendations are shown in Table 12.

3.7 | Leadless pacemakers

Many complications of transvenous pacemakers are related to the leads and subcutaneous pockets, and the incidence of complications has been reported to be 8% and 11%, respectively, at 5 years after

TABLE 11 Recommendations and evidence levels for pacemaker indication for carotid sinus syndrome/vasovagal syncope

	COR	LOE	GOR (MINDS)	LOE (MINDS)
Dual-chamber cardiac pacing is reasonable for patients with carotid sinus syndrome that is cardioinhibitory or mixed type	IIa	B	B	II
Dual-chamber cardiac pacing may be considered in a select population of patients aged 40 years or older with recurrent vasovagal syncope and prolonged spontaneous pauses (>3 s with symptoms, >6 s without symptoms) when other therapies have failed	IIb	B	B	II
Cardiac pacing may be considered in patients with vasodepressor-type carotid sinus syndrome and with recurrent syncopal attacks	IIb	B	B	II
Pacemaker therapy is potentially harmful in a select population of patients aged 40 years or younger with recurrent vasovagal syncope, and in patients aged 40 years or older without documentation of spontaneous pauses or a positive head-up tilt test	III	C	D	IVb

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence.

TABLE 12 Recommendations and evidence levels for pacemaker indication for HOCM

	COR	LOE	GOR (MINDS)	LOE (MINDS)
Permanent pacemaker implantation is recommended for patients with significant left ventricular outflow pressure gradient that causes symptoms, combined with other conditions (eg, sinus node dysfunction or AVB) that require cardiac pacing (including drug-induced bradycardia)	I	B	A	IVa
Permanent pacemaker implantation should be considered for patients with significant left ventricular outflow pressure gradient associated with QOL deterioration, in whom drug therapy is refractory or intolerable, or other therapies are inappropriate	IIa	B	B	IVa

Abbreviations: AVB, atrioventricular block; COR, class of recommendation; GOR, grade of recommendation; HOCM, hypertrophic obstructive cardiomyopathy; LOE, level of evidence; QOL, quality of life.

implantation.[29] Leadless pacemakers were developed to overcome this problem.

As of May 2018, the leadless pacemakers approved in Japan are fixed to the myocardium with tines made of shape-memory alloy. A sheath is inserted from the femoral vein, and a delivery catheter equipped with a leadless pacemaker is inserted into the right ventricle to position the pacemaker in place. The placement is completed once it is confirmed that at least 2 of the 4 tines of the generator are fixed to the myocardium. The battery life is ≈12 years, and it has both a rate response function and a capture management function. It is compatible with 1.5- and 3-Tesla MRI,[159] as well as remote monitoring systems. Theoretically, it is possible to implant up to 3 units in the heart.[160]

The safety and efficacy of leadless pacemakers were examined in a multicenter prospective study.[161] A total of 725 patients underwent device implantation in 19 countries, including Japan, and 719 cases were successful. Major complications (death, permanent loss of device function, hospitalization, prolonged hospital stay ≥48 hours, system replacement) were avoided in 96% of the patients at the 6-month follow-up. This result was significantly better than that with a normal pacemaker (hazard ratio [HR] 0.49). Efficacy was confirmed for 98.3% of cases (threshold at implantation was ≤2 V at a pulse width of 0.24 ms, and there was no increase in pacing threshold exceeding 1.5 V during the 6-month follow-up). Furthermore, it was shown that both safety (HR 0.52) and efficacy were good even after 1 year.[162] The rate of complications was 4%, that of inguinal (femoral) access-related complications was 0.7%, and that of pericardial effusion was 4%. It has been reported that leadless pacemakers are equally safe and effective in Japan.[163] In post-marketing surveillance, the incidence of major complications decreased to 1.56%, that of access-related complications decreased to 0.59%, and that of pericardial effusion decreased to 0.37%.[164]

The Japanese Heart Rhythm Society has issued a statement about the standards, including usage conditions, for leadless pacemakers.[9] In the 2008 AHA/ACC/HRS guidelines,[165] patients eligible

for VVI pacing have class I and II pacemaker indications. However, because Japanese people are small-framed and there are many elderly patients in Japan, it is necessary to take sufficient care not only with the procedure but also when determining the indications for implantation.

3.8 | Bundle of his pacing

Right ventricular pacing induces left ventricular asynchronous contraction due to iatrogenic left branch block pattern, which may lead to systolic dysfunction.[166,167] A small number of randomized controlled trials (RCTs), a relatively large number of prospective enrollment trials, and meta-analyses of those trials have reported that selecting the bundle of His as an alternative pacing site maintains normal intraventricular conduction and reduces the adverse effects of right ventricular pacing. [168-176] It has been indicated that bundle of His pacing is effective as an option when biventricular pacing is unsuccessful or impossible.[177]

However, problems with this treatment include unsuccessful implantation, high pacing threshold, low amplitude of ventricular electrograms, atrial wave oversensing, and induction of atrioventricular conduction disturbance.[177,178] Therefore, it is necessary to accumulate more evidence and develop equipment that can perform bundle of His pacing effectively and safely.

4 | Implantable cardioverter-defibrillators (ICDs)

Introduction

ICD implantation is one of the most effective and well-established treatments to prevent sudden cardiac death from fatal tachyarrhythmia and to improve prognosis, regardless of the type of heart disease. ICDs began to be covered by insurance in Japan in 1996; however, since then, advances in electronics have resulted in the ICD generator becoming smaller, lighter, and multifunctional. Further, remote monitoring systems have been developed, making postoperative management easier. As a result, the number of implantations is increasing (Figure 2). S-ICDs and WCDs have also been developed since the last guideline revision in 2011.

Many of the clinical trials on ICD indications have been conducted overseas.[165,179] Those guidelines have comprehensively formulated recommendation classes that consider aspects that are difficult to apply to the actual situation in Japan (Figure 3),[179] owing to the different patient background characteristics. Nevertheless, patients have complex backgrounds and not all patients meet the described indications. The final judgment should be made considering the relationship between treatment and the clinical and social background (age, dementia, frailty), mean life expectancy, and predictive probability of arrhythmia death in individual patients. Therefore, treatment strategies determined on the basis of adequate communication between the attending physician and the patient or the patient's family should take precedence over the recommendations in this guideline.

Evaluation of cardiac function is very important for ICD indication, and many assessments depend on the left ventricular ejection fraction (LVEF). However, the numeric value depends on the inspection method and there is no golden rule. It is also necessary to take account of LVEF variations caused by both progression of disease and treatment.

Secondary prevention is indicated for patients with a history of cardiopulmonary arrest, sustained VT, and VF, and primary prevention is indicated for patients with NSVT only, those who have syncope without ECG records, and those without ECG records but are at a high risk of sudden death or arrhythmia death.

The ICD indications described in this section are applicable to patients with some type of structural heart disease or a primary electrical abnormality, such as Brugada syndrome or idiopathic VF. An ICD is not indicated for pathological conditions that are not associated with structural heart disease, such as idiopathic VT, because these have a very low risk of sudden death and a high possibility of being cured by catheter ablation (class of recommendation III for ICD).

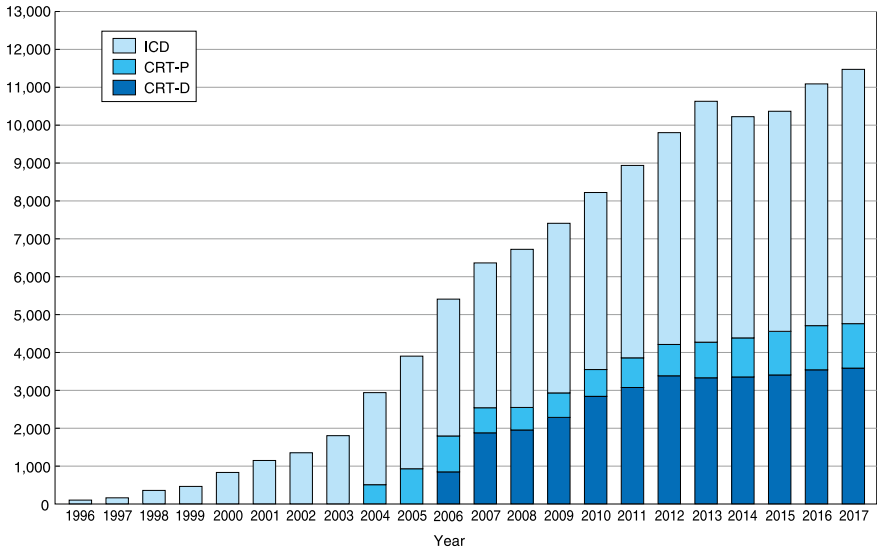


FIGURE 2 Transition in the number of implanted cardioverter-defibrillators (ICD) and cardiac resynchronization therapies (CRT-P/CRT-D) in Japan

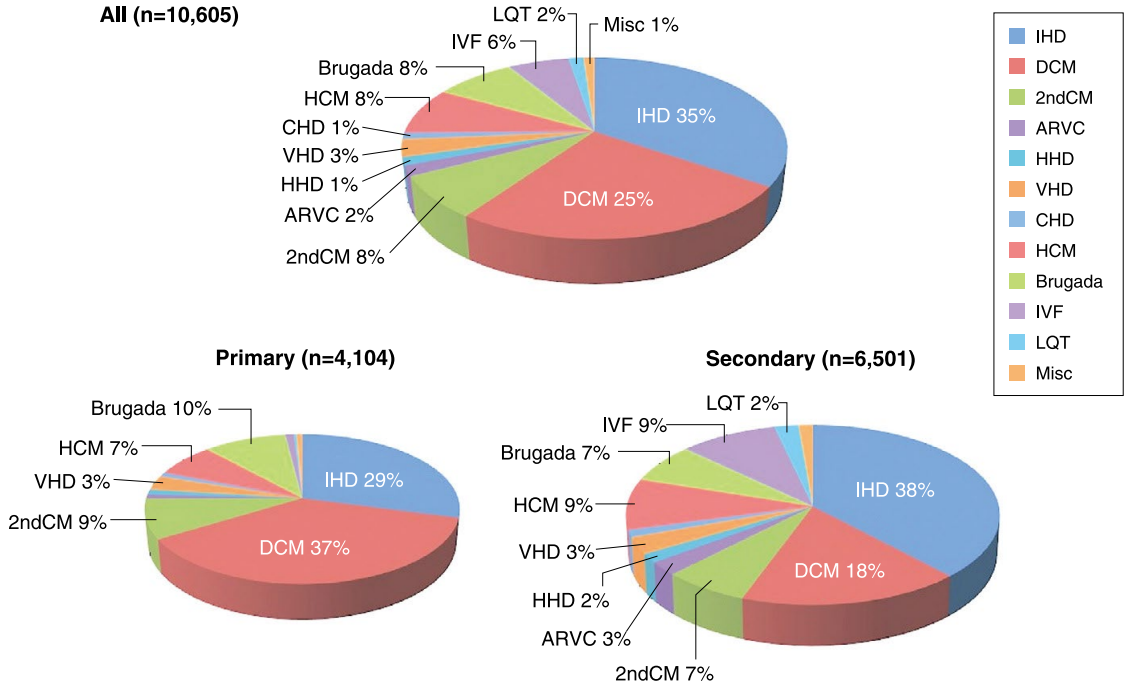


FIGURE 3 Distribution of underlying heart disease in ICD primary and secondary prevention cases in Japan. (From Shimizu et al, 2012[179] with permission.) ARVC, arrhythmogenic right ventricular cardiomyopathy; Brugada, Brugada syndrome; CHD, congenital heart disease; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; HHD, hypertensive heart disease; IHD, ischemic heart disease; IVF, idiopathic ventricular fibrillation; LQT, long QT syndrome; Misc., miscellaneous 2ndCM, secondary cardiomyopathy; VHD, valvular heart disease

4.1 | Secondary prevention for patients with underlying heart disease

4.1.1 | Sustained VT and VF with coronary artery disease

Coronary artery disease (CAD) as addressed in this section refers to conditions other than those caused by the acute phase (within 48 hours) of acute coronary syndrome. The details of conditions with coronary spasm are described later.

In AVID,[84] CASH (Cardiac Arrest Study Hamburg),[180] and CIDS (Canadian Implantable Defibrillator Study),[181] 70%–80% of patients had CAD. ICD clearly has a high secondary prevention effect on fatal arrhythmias associated with CAD.[84,180,181] The mean LVEF of patients in those trials was 32%–45%, and a higher effect can be particularly expected in patients with LVEF ≤35%. In Nippon Storm, a prospective observational study after ICD implantation in Japan (including 38% CAD cases and 27% idiopathic dilated cardiomyopathy cases), secondary prevention implantation was a risk factor for severe electrical storms (hazard ratio 2.698). Thus, ICD implantation is important for secondary prevention.[182]

Catheter ablation to eliminate VT is more preferably attempted in patients with CAD than in those with non-ischemic cardiomyopathy, because a dense scar creating a reentrant circuit tends to exist on the endocardial surface especially in monomorphic sustained VT[183-187] However, ablation does not remove all arrhythmic substrates; thus, ICD indication should be considered even if the ablation procedure is deemed successful.[183,188]

Patients with an old myocardial infarction are considered to have ventricular arrhythmia substrates chronically, and a therapeutic strategy from a long-term perspective is needed for these patients. Further, given that active myocardial ischemia modifies the arrhythmia substrate and leads to higher arrhythmogenicity, it is important to relieve ischemia with coronary revascularization.[189] Sustained VT and VF that appear in the acute phase of acute coronary syndrome (within 48 hours of onset) are unlikely to recur, owing to the relief of ischemia and the subsequent stabilization of the arrhythmia substrate, and are therefore not necessarily indicated for ICD.[190]

Conversely, sustained VT and VF that appear 48 hours after the onset of myocardial infarction, even at an early stage of onset, have a risk for later recurrence.[190] The indications for ICD should be considered according to the extent of cardiac function, presence of residual ischemia, and presence of reversible factors such as electrolyte abnormalities. However, patients registered in a large-scale clinical trial showing the effectiveness of ICD for myocardial infarction demonstrated the development of sustained VT and VF at 3-5 days after myocardial infarction. Therefore, the effectiveness of ICD in patients who develop symptoms earlier has not been proven. In addition, meta-analysis of the AVID, CASH, and CIDS studies found no difference in the prognosis between the ICD group and the amiodarone group in patients with LVEF >35%, and ICD was judged to be highly useful in patients with reduced cardiac function.[184]

Although the prognosis of vasospastic angina is generally good, it is also known to cause acute myocardial infarction and sudden death. Although correction of lifestyle habits (eg, smoking cessation and use of calcium-channel blockers and nitrates) is effective, some reports indicate that patients who are resistant to these medical treatments or who

have a history of out-of-hospital cardiac arrest may have a poor prognosis.[191] Although both the effects and limitations of ICD treatment have been reported,[192] it is considered appropriate to classify this treatment as class IIa for patients with a history of VT/VF, including out-of-hospital cardiopulmonary arrest, if they are resistant to medical treatment, and as class IIb even if medical treatment is effective (Table 13, Figure 4). WCD should also be considered during the acute phase in patients who have had an out-of-hospital cardiopulmonary arrest.[193]

4.1.2 | *Sustained VT and VF with non-ischemic cardiomyopathy*

In previous prospective clinical trials, ICD implantation provided a greater improvement of life prognosis than antiarrhythmic drugs, and the effect was considered equivalent to that in patients with coronary artery disease.[84,180,181]

However, in the countries where the clinical trials were conducted, the prevalence of sustained VT and VF with the underlying disease of non-ischemic cardiomyopathy is lower than that in coronary artery disease, and statistical improvement of life prognosis with an ICD was not proven.

The results of a meta-analysis of 256 cases of nonischemic cardiomyopathy in the CIDS and AVID studies were reported in 2004. Although ICD implantation improved mortality by 31%, there was no significant difference (P=0.22).[194] These results are considered to be related to the small number of cases. Conversely, in Nippon Storm, a prospective observational study after ICD implantation in Japan (including 38% coronary artery disease cases and 27% idiopathic dilated cardiomyopathy cases), secondary prevention implantation was a risk factor for severe electrical storms (HR 2.698).[182] Therefore, ICD is effective for the secondary prevention of non-ischemic cardiomyopathy. WCD should also be considered during the acute phase for the treatment of coexisting heart failure.[195]

In catheter ablation for sustained VT associated with non-ischemic cardiomyopathy, the arrhythmia substrates are more often present in the deep layers of the myocardium or on the epicardial side than in

TABLE 13 Recommendations and evidence Levels for ICD for sustained VT/VF patients with coronary artery disease

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients with prior MI with either a history of VF or OHA requiring electrical shock, not due to reversible causes (eg, treatable ischemia or electrolyte abnormality)	I	A	A	I
ICD is recommended for patients with prior MI or sustained VT not due to reversible causes (eg, treatable ischemia or electrolyte abnormality) under the following conditions: 1. LVEF ≤35% 2. Syncope during VT 3. BP ≤80 mmHg and/or symptoms of brain ischemia and/or chest pain during VT 4. Polymorphic VT 5. Hemodynamically stable, sustained VT but refractory to medication or the efficacy of medication is unknown, and/or catheter ablation is ineffective or impossible	I	A	A	I
ICD should be considered for patients with sustained VT not induced after catheter ablation	IIa	B	B	III
ICD implantation should be considered for patients with sustained VT responsive to antiarrhythmic drugs	IIa	B	B	I
ICD should be considered for patients with a history of VF, sustained VT, or OHA due to coronary artery spasm in whom medical therapy is ineffective or not tolerated	IIa	B	C1	IVa
ICD may be considered for patients with a history of VF, sustained VT, or OHA due to coronary artery spasm in whom medical therapy is effective	IIb	C	C1	IVa
ICD may be considered for patients with VT/VF due to reversible acute causes (eg, acute ischemia within 48 h, except coronary artery spasm, electrolyte abnormality, or drugs), but whose possibility of re-exposure to the same conditions is high	IIb	C	C1	IVa
ICD is not recommended for patients with body function restriction due to chronic disease	III	C	C2	VI
ICD is not recommended with a predicted life expectancy ≤12 months	III	C	C2	VI
ICD is not recommended without consent or cooperation for ICD therapy because of a psychiatric disorder or other reasons	III	C	C2	VI
ICD is not recommended with VT/VF due to reversible acute causes (eg, acute ischemia, except coronary artery spasm, electrolyte abnormality, or drugs), and in whom VT/VF will be prevented after removal of those causes	III	C	C2	VI
ICD is not recommended with a repeat episode of VT/VF refractory or unresponsive to antiarrhythmic drugs and/or catheter ablation	III	C	C2	VI
ICD is not recommended with NYHA class IV with medication-refractory HF who are also not candidates for cardiac transplantation, CRT, or LVAD insertion	III	C	C2	VI

Abbreviations: BP, blood pressure; CIED, cardiac implantable electronic device; COR, class of recommendation; CRT, cardiac resynchronization therapy; GOR, grade of recommendation; HF, heart failure; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; OHA, out-of-hospital cardiac arrest; QOL, quality of life; VF, ventricular fibrillation; VT, ventricular tachycardia.

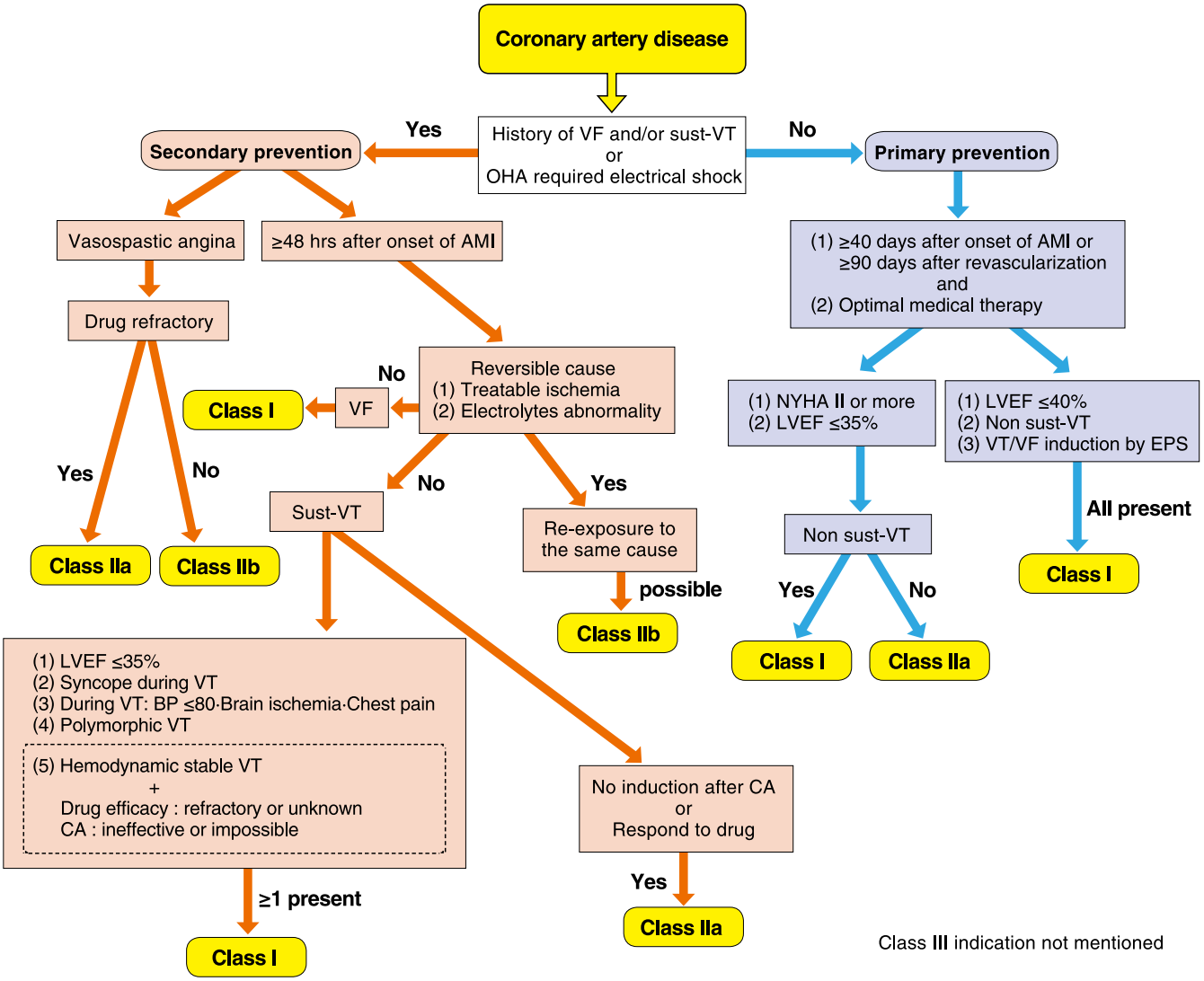


FIGURE 4 ICD indications for coronary artery disease. AMI, acute myocardial infarction; BP, blood pressure; CA, catheter ablation; EPS, electrophysiological study; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association class; OHA, out-of-hospital cardiac arrest; Sust-VT, sustained VT; VF, ventricular fibrillation; VT, ventricular tachycardia

[Correction added on 22 June, after first online publication: Under 'Primary prevention', ≥48 days after onset of AMI or ...' has been replaced with ≥40 days after onset of AMI or ...]

coronary artery disease, and the success rate of this treatment is not high.[196] Not all arrhythmia substrates are removed by catheter ablation; however, considering that the disease is progressive, ICD should be actively indicated even if catheter ablation is judged successful. The recommendations are shown in Table 14 and Figure 5.

4.2 | Primary prevention in patients with underlying heart disease

Numerous previous reports have demonstrated the usefulness of ICDs in patients with low cardiac function or heart failure (HF) who have underlying heart disease. Nevertheless, individual conditions, such as comorbidities, should be fully evaluated for ICD indication. The usefulness of ICDs has not been established in patients with severe HF (such as heart transplantation, CRT, and NYHA class IV drug-resistant severe congestive HF) not indicated for left ventricular assist device (LVAD). Therefore, ICD implantation is not indicated for these conditions (class of recommendation III) (Table 14).

4.2.1 | Primary prevention for patients with coronary artery disease

MADIT-I (Multicenter Automatic Defibrillator Implantation Trial I) was a clinical trial in patients with Q-wave myocardial infarction (MI), non-sustained VT (NSVT), and LVEF ≤35% for which procainamide was ineffective for induced sustained VT/VF based on electrophysiology studies.[197] ICD reduced mortality by 54% compared with conventional pharmacotherapy. MADIT-II removed NSVT and induction with electrophysiology methods as inclusion criteria, and instead examined patients with reduced cardiac function (LVEF <30%).[198] The study found a significant decrease in mortality as a result of ICD implantation (31%) over a mean observation period of 20 months.

TABLE 14 Recommendations and evidence levels for ICD for sustained VT/VF patients with non-ischemic cardiomyopathy

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients with VF or OHA requiring electrical shock, not due to reversible causes (eg, electrolyte abnormality)	I	A	A	I
ICD is recommended for patients with sustained VT not due to reversible causes, such as electrolyte abnormality, under the following conditions: 1. Syncope during VT 2. BP ≤80 mmHg and/or symptoms of brain ischemia and/or chest pain during VT 3. Polymorphic VT 4. Hemodynamically stable, sustained VT refractory to medication or the efficacy of medication is unknown, and/or catheter ablation is ineffective or impossible	I	C	A	VI
ICD should be considered for patients with sustained VT not induced after catheter ablation	IIa	B	B	III
ICD should be considered for patients with sustained VT responsive to antiarrhythmic drugs	IIa	B	B	VI
ICD may be considered for patients with VT/VF due to reversible acute causes (eg, HF, electrolyte abnormality, or drugs), but whose possibility of re-exposure to the same conditions is high	IIb	C	C1	VI
ICD is not recommended for patients with a predicted life expectancy ≤12 months	III	C	C2	VI
ICD is not recommended for patients without consent or cooperation for ICD therapy because of a psychiatric disorder or other reasons	III	C	C2	VI
ICD is not recommended for patients with VT/VF due to reversible acute causes (eg, acute ischemia, electrolyte abnormality, or drugs), and in whom VT/VF will be prevented after removal of those causes	III	C	C2	VI
ICD is not recommended for patients with a repeat episode of VT/VF, refractory or unresponsive to antiarrhythmic drugs and/or catheter ablation	III	C	C2	VI
ICD is not recommended for patients with NYHA class IV with medication-refractory HF who are also not candidates for cardiac transplantation, CRT, or LVAD insertion	III	C	C2	VI

Abbreviations: BP, blood pressure; COR, class of recommendation; CRT, cardiac resynchronization therapy; GOR, grade of recommendation; HF, heart failure; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; LVAD, left ventricular assist device; MI, myocardial infarction; NYHA, New York Heart Association; OHA, out-of-hospital cardiac arrest; VF, ventricular fibrillation; VT, ventricular tachycardia.

The incidence of sudden death in the control group was approximately 5% per year. Furthermore, the results of a long-term follow-up survey over an 8-year period showed that the effectiveness of ICD increased over the long term.[199]

SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial) is the largest prospective RCT on primary prevention, enrolling both patients with ischemic and non-ischemic heart failure (HF).[200] The main registration criteria were: (1) history of HF for ≥3 months, (2) receiving treatment for HF with angiotensin-converting enzyme inhibitors and beta-blockers, (3) LVEF ≤35%, and (4) NYHA class II–III. However, conditions such as NSVT and frequent PVC were excluded. Coronary artery disease accounted for 52% of the total cases, and the ICD group had approximately 20% reduction in mortality compared with the placebo and amiodarone groups. The results of these clinical trials, conducted mainly in North America, support the proactive indication of ICD implantation in patients with coronary artery disease with reduced LVEF.

Conversely, several cohort studies that observed the prognosis of patients with coronary artery disease in Japan showed relatively good life prognosis. In HIJAMI-II (Heart Institute of Japan Acute Myocardial Infarction-II), a prospective observational study of 4,133 patients with MI, the rate of sudden death during the mean observation period of 4.1 years was 1.2% and the rate of sudden death in patients with LVEF <30% (4.8% of the total), a registration criterion of MADIT-II, was only 5.1% in 5 years.[201] Tanno et al reported that only 2 sudden deaths occurred in 90 patients who met the MADIT registration criteria during the 30-month follow-up period.[202] CHART-2 (Chronic Heart Failure Analysis and Registry in the Tohoku District 2) examined the prognosis of 185 patients with LVEF <30%, including those with ischemic and non-ischemic heart disease, and found that the rate of sudden death was 4.9% over a mean observation period of 2.7 years.[203] Considering that approximately half the deaths in MADIT-II were sudden deaths,[204] the ICD indication criteria of MADIT-II may not be very cost-effective in Japan. Therefore, it is recommended to use the results of effective examinations for risk stratification of patients with coronary artery disease, such as electrophysiology studies, as shown in MADIT-I and MUSTT (Multicenter Unsustained Tachycardia Trial).[205] MUSTT showed that ICD implantation increased survival when VT/VF was induced with electrophysiology tests in patients with ischemic heart disease with NSVT and LVEF ≤40%. On the other hand, in CHART-2, the complication of AF and a left ventricular end-diastolic diameter ≥65 mm were independent risk factors for sudden death. Therefore, these should be considered when examining the ICD indications.

It is believed that the arrhythmia substrate after MI is more unstable in the acute phase, and there is a higher risk of sudden death. According to this logic, earlier ICD implantation after the onset of MI would be more effective.

DINAMIT (Defibrillator in Acute Myocardial Infarction Trial) examined the effectiveness of ICD in patients with low cardiac function (LVEF ≤35%) in the early stage (6-40 days) after MI.[206] Arrhythmic death was significantly lower in the ICD group than in the non-ICD

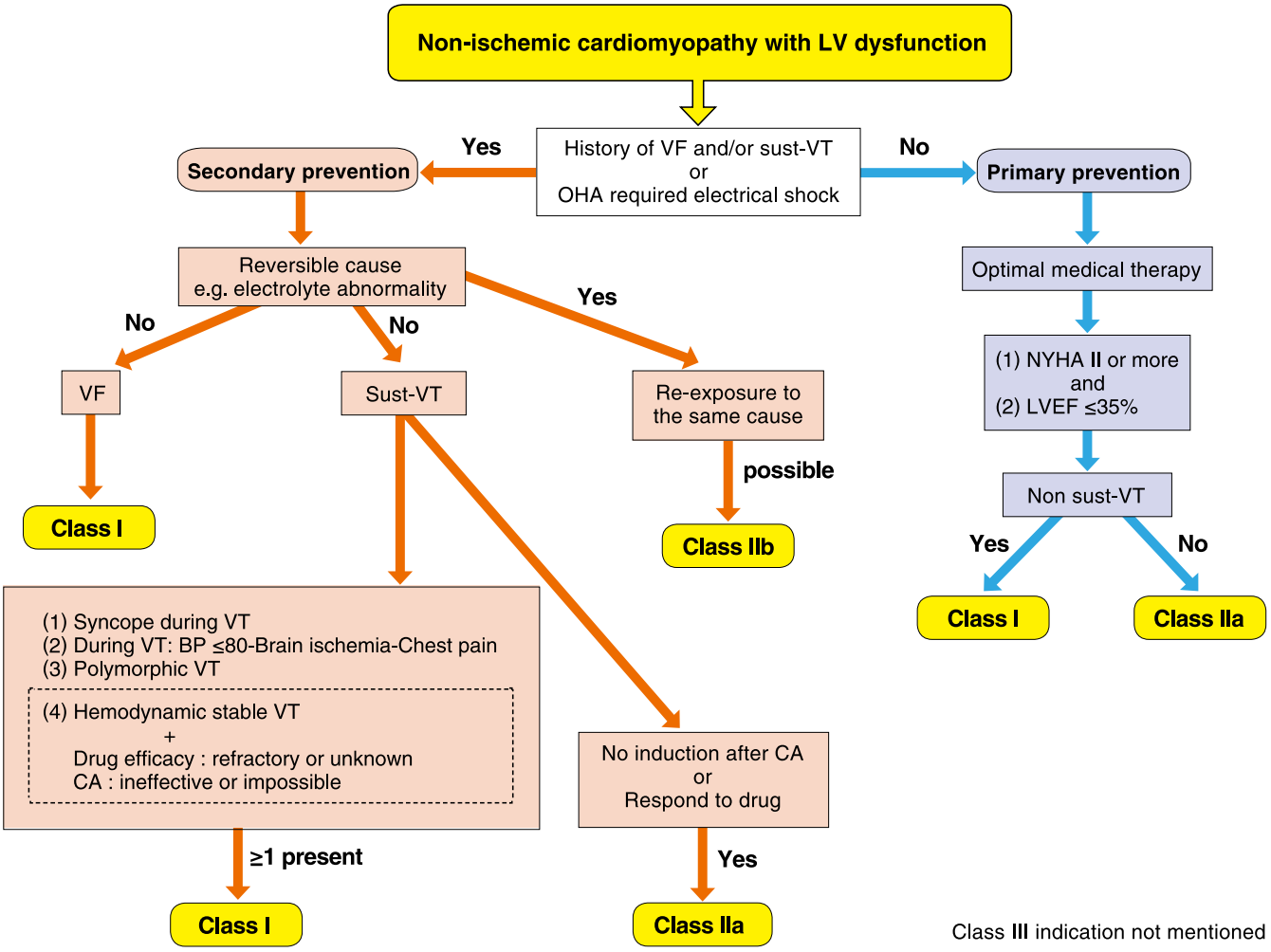


FIGURE 5 ICD indications for non-ischemic cardiomyopathy with left ventricular dysfunction. BP, blood pressure; CA, catheter ablation; EPS, electrophysiological study; LVEF, left ventricular ejection fraction; NYHA, NYHA functional class; OHA, out-of-hospital cardiac arrest; Sust-VT, sustained VT; VF, ventricular fibrillation; VT, ventricular tachycardia
[Correction added on 29 June, after first online publication: '(1) LVEF ≤35%' has been removed and renumbered in the box at the bottom-left.]

group. However, cardiac deaths other than from arrhythmia were significantly higher. Thus, there was no difference in the total number of deaths between the 2 groups. In a subanalysis of MADIT-II, ICD implantation had no superiority in terms of total mortality in patients within 18 months after the onset of MI compared with that in patients at later than 18 months after onset. According to a subanalysis of VALIANT (Valsartan in Acute Myocardial Infarction Trial), which examined the effectiveness of valsartan in patients after acute MI, deaths from non-arrhythmias such as heart failure and cardiac rupture occurred frequently within 1 month after onset, whereas death from arrhythmia tended to increase after 1-3 months.[207]

When considering ICD implantation as a primary prevention after MI, we should pay attentions that reinfarction and pump failure can arise even if patients are saved from sudden death, and conversely, revascularization in the acute phase is predicted to improve cardiac function based on reverse remodeling. Therefore, primary ICD indication should be discussed for patients who have survived at least 40 days after MI. The recommendations are shown in Table 15 and Figure 4.

Reports have demonstrated the usefulness of WCDs during the period when ICDs are not yet indicated for high-risk cases after acute MI and after coronary revascularization (<40 days after acute MI, <3 months after coronary revascularization, <3 months after starting pharmacotherapy). WCDs are considered a bridging treatment until ICD is indicated and implanted.[208-211]

4.2.2 | Primary prevention in patients with non-ischemic cardiomyopathy

The highest risk factor for sudden cardiac death in non-ischemic cardiomyopathy is the degree of cardiac dysfunction and HF, as is seen in ischemic heart disease. DEFINITE (Defibrillators in Non-ischemic Cardiomyopathy Treatment Evaluation) examined patients with non-ischemic cardiomyopathy with LVEF ≤35% who had PVC (≥10/h) or NSVT on Holter ECG. Although the total mortality was reduced by 35% in the ICD group compared with the pharmacotherapy only group, it was not a significant reduction ($P = .08$).[212] SCD-HeFT included 48% non-ischemic HF cases, and ICD demonstrated superiority in the overall patients. However, in the placebo group, the

TABLE 15 Recommendations and evidence levels for ICD as primary prevention of sudden death in patients with coronary artery disease

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients who meet all of the following criteria: 1. CAD (≥40 days after MI and at least 90 days after revascularization) 2. Receiving optimal medical therapy 3. NYHA class II or greater symptoms 4. LVEF ≤35% 5. Non-sustained VT	I	A	B	II
ICD is recommended for patients who meet all of the following criteria: 1. Coronary artery disease (at least 40 days after myocardial infarction and at least 90 days after revascularization) 2. Receiving optimal medical therapy 3. LVEF ≤40% 4. Non-sustained ventricular tachycardia 5. Inducible sustained VT or VF on an electrophysiological study	I	B	B	II
ICD should be considered for patients who meet all of the following criteria: 1. CAD (≥40 days after MI and at least 90 days after revascularization) 2. Receiving optimal medical therapy 3. NYHA class II or greater symptoms 4. LVEF ≤35%	IIa	B	B	II
ICD is not recommended for patients who meet any 1 of the following criteria: 1. Limited physical activity due to chronic diseases 2. Predicted life expectancy ≤12 months 3. NYHA class IV with medication-refractory HF and also not a candidate for cardiac transplantation, LVAD insertion, or implantation of a CRT defibrillator with both pacing and defibrillation capabilities	III	C	C2	VI

Abbreviations: CAD, coronary artery disease; COR, class of recommendation; GOR, grade of recommendation; HF, heart failure; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; VF, ventricular fibrillation; VT, ventricular tachycardia.

total mortality of non-ischemic HF was less than that of ischemic HF (non-ischemic: 27%/5 years vs. ischemic: 43%/5 years). Moreover, although the ICD group had reduced total mortality, by 27%, compared with the placebo group, the difference was not significant ($P = .06$).[200]

The most recent RCT study, DANISH (Danish Study to Assess the Efficacy of ICDs in Patients with Non-ischemic Systolic Heart Failure on Mortality),[213] included patients who met the following criteria: (1) systolic HF (LVEF ≤35%), (2) symptomatic HF (NYHA class II, III or IV scheduled for CRT), (3) N-terminal pro-B-type natriuretic peptide >200 pg/mL, and (4) receiving standard HF treatment, and randomly assigned to the ICD and non-ICD groups. During a median follow-up of 68 months, the primary endpoint (overall mortality rate) was not significantly different between the ICD and non-ICD groups (hazard ratio 0.87, 95% confidence interval 0.68-1.12, $P = .28$).

Meanwhile, a meta-analysis of the effect of ICD on non-ischemic cardiomyopathy, including 5 RCTs (DEFINITE[212]), SCD-HeFT[200]), CAT [Cardiomyopathy Trial][214]), AMIOVIRT [Amiodarone vs. Implantable Defibrillator][215]), and COMPANION [Comparison of Medical, Pacing, and Defibrillation Therapies in Heart Failure][216]), n = 1854), was reported in 2004.[194] ICD implantation significantly reduced the relative mortality (31%, $P = .002$). Similar results were found in a recent meta-analysis of 6 trials, with the addition of DANISH[213] (non-ischemic cardiomyopathy, n = 2970),[217] indicating that ICD implantation significantly reduced the relative mortality (23%). Additionally in a separate analysis of the trials that assessed ICD versus optimal medical therapy (after exclusion of trials that involved patients with CRT defibrillator), a statistically significant 24% reduction in all-cause mortality with ICD was observed. When the 2 trials (COMPANION and DANISH-CRT subgroup) were compared with CRT plus ICD versus CRT alone, there was a trend toward benefit in terms of all-cause mortality in the ICD group. A meta-analysis including 2,573 patients with the addition of DANISH[213] instead of COMPANION[216] also found that relative mortality was significantly reduced by ICD (21%, $P < .001$).[218] These findings suggest that an ICD is useful for preventing sudden death in non-ischemic cardiomyopathy in patients with reduced cardiac function and with HF symptoms, as seen in ischemic heart disease.

There are few data showing sudden death rates in patients with non-ischemic HF in Japan. However, in a cohort study that observed the prognosis of patients with chronic HF, 70% of Japanese patients had non-ischemic HF and the total mortality was reported to be 20%–30% in 3 years.[219] According to CHART (a Japanese prospective observational study), 15% of HF patients with LVEF <30% experience sudden cardiac death within 3 years.[220] Therefore, the prognosis of HF and the incidence of sudden death in non-ischemic cardiomyopathy are considered similar to those seen overseas, and it is worth considering the ICD indications as equivalent. In the CHART-2 study,[203] which prospectively enrolled HF patients with NYHA class II–III and LVEF ≤35% (including 20% with a non-ischemic etiology), the presence of NSVT may increase the risk of developing VT/VF.

TABLE 16 Recommendations and evidence levels for ICD as primary prevention of sudden death in patients with non-ischemic cardiomyopathy

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients who meet all the following criteria: 1. Non-ischemic cardiomyopathy 2. Receiving optimal medical therapy 3. NYHA class II or greater symptoms 4. LVEF ≤35% 5. Non-sustained VT	I	A	B	II
ICD should be considered for patients who meet all the following criteria: 1. Non-ischemic cardiomyopathy 2. Receiving optimal medical therapy 3. NYHA class II or greater symptoms 4. LVEF ≤35%	IIa	B	B	II
ICD is not recommended for patients who meet either of the following criteria: 1. Limited physical activity due to chronic disease 2. Expected life expectancy ≤12 months 3. NYHA class IV with medication-refractory HF and also not a candidate for cardiac transplantation, LVAD, or a CRT defibrillator that incorporates both pacing and defibrillation capabilities	III	C	C2	VI

Abbreviations: COR, class of recommendation; CRT, cardiac resynchronization therapy; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; VT, ventricular tachycardia.

Reports have demonstrated the usefulness of WCDs during the period when an ICD is not yet indicated for high-risk cases immediately after the introduction of pharmacotherapy for acute HF (<3 months after starting pharmacotherapy). WCDs are considered as a bridging treatment during the period until an ICD is indicated and implanted.[208-211] The recommendations are shown in Table 16 and Figure 5.

4.2.3 | Summary of ICD indications for coronary artery disease and non-ischemic cardiomyopathy

Figures 4 and 5 respectively show the flowcharts for the applicable classes and conditions for the above mentioned diseases.

4.3 | Syncope with uncertain diagnosis

Various pathologies cause syncope, but the common pathophysiology is "transient hypoperfusion of the entire brain". Here, the event that occurs as a result of transient hypoperfusion of the entire brain is managed as syncope. Cardiac electrophysiology studies are performed when reflex syncope is ruled out as the cause of the syncope based on medical history, physical examination, and various tests, and when the syncope is suspected to be caused by arrhythmia because there are high-risk factors for cardiogenic syncope (Table 17).[146]

An ICD is indicated when syncope due to VT or VF is the most likely cause. It has been reported that non-arrhythmic syncope can happen in patients with an ICD or CRT-D; thus, a detailed investigation of the cause is essential.[221] Patients with coronary artery disease or non-ischemic cardiomyopathy who have a marked decline in cardiac function (LVEF ≤ 35%), and with NYHA class II or III who develop syncope are a high-risk group for sudden death; an ICD is recommended for these patients.[200] It is also recommended for patients with structural heart disease when syncope was suspected to be caused by tachyarrhythmia, and hemodynamically intolerable VT or VF was induced during electrophysiology studies.[60,181,222,223] An ICD should be recommended for patients with non-ischemic cardiomyopathy, LVEF ≤35%, and syncope regardless of NYHA class.[116,224,225] It is also necessary to differentiate syncope associated with coronary spastic angina. If coronary spasm is induced by coronary angiography, refer to the section in this chapter (**4.1.1 Sustained VT and VF with coronary artery disease**).

Conversely, an ICD is contraindicated when cardiac function is normal and if conditions such as hypertrophic cardiomyopathy, long QT syndrome, Brugada syndrome (including drug-induced Brugada ECG), preexcitation syndrome, and short QT syndrome are ruled out. The recommendations are shown in Table 18 and Figure 6 with reference to the European Society of Cardiology guidelines.[146]

4.4 | Specific heart diseases

4.4.1 | Hypertrophic cardiomyopathy

The incidence of sudden death associated with hypertrophic cardiomyopathy (HCM) has been reported to be ≤1% per year;[226-228] however, it is the most common cardiac cause of death among patients

TABLE 17 Clinical features that can suggest a diagnosis of syncope on initial evaluation

Reflex syncope
- Long history of recurrent syncope, in particular occurring before the age of 40 years
- After unpleasant sight, sound, smell, or pain
- Prolonged standing
- During meal
- Being in crowded and/or hot places
- Autonomic activation before syncope: pallor, sweating, and/or nausea/vomiting
- With head rotation or pressure on carotid sinus (as in tumours, shaving, tight collars)
- Absence of heart disease

Syncope due to orthostatic hypotension
- While or after standing
- Prolonged standing
- Standing after exertion
- Post-prandial hypotension
- Temporal relationship with start or changes of dosage of vasodepressive drugs or diuretics leading to hypotension
- Presence of autonomic neuropathy or Parkinsonism

Cardiac syncope
- During exertion or when supine
- Sudden onset palpitation immediately followed by syncope
- Family history of unexplained sudden death at young age
- Presence of structural heart disease or coronary artery disease
- ECG findings suggesting arrhythmic syncope:
  - Bi-fascicular block (defined as either left or right BBB combined with left anterior or left posterior fascicular block)
  - Other intraventricular conduction abnormalities (QRS duration ≥ 0.12 s)
  - Mobitz I second-degree AV block and first degree AV block with markedly prolonged PR interval
  - Asymptomatic mild inappropriate sinus bradycardia (40-50 bpm) or slow atrial fibrillation (40-50 bpm) in the absence of negatively chronotropic medications
  - Non-sustained VT
  - Pre-excited QRS complexes
  - Long or short QT intervals
  - Early repolarization
  - ST-segment elevation with type 1 morphology in leads V1 – V3 (Brugada pattern)
  - Negative T waves in right precordial leads, epsilon waves suggestive of ARVC
  - Left ventricular hypertrophy suggesting hypertrophic cardiomyopathy

Abbreviations: ARVC, arrhythmogenic right ventricular cardiomyopathy; AV, atrioventricular; BBB, bundle branch block; VT, ventricular tachycardia. (From Brignole et al 2018.[146] with permission.)

with this disease. The risk of sudden death is particularly high in people younger than 30 years, and sudden death often occurs during exercise in this population.[229]

The high-risk factors for sudden death include cardiac arrest, and resuscitation from VF or sustained VT. Because of the relatively high recurrence rate (≈10% annually),[230-233] ICD implantation is recommended as secondary prevention.[230-232,234-237]

The following 5 major risk factors related to primary prevention[230,238] have been known for a long time: (1) family history of sudden death associated with HCM; sudden death in a 1st-degree relative <40 years old with or without a diagnosis of HCM, or in a 1st-degree relative diagnosed with HCM regardless of age), (2) cardiogenic or unexplained syncope, (3) marked left ventricular hypertrophy (>30 mm), (4) NSVT (≥3 in succession and ≥120 beats/min) on Holter ECG, and (5) abnormal blood pressure (BP) response during exercise (systolic BP during maximum effort is not elevated by ≥20 mmHg over resting BP, or decreased by ≥20 mmHg during exercise).[238-246]

ICD implantation should be considered for patients with any of these conditions. However, in general, the negative predictive value of these major risk factors can be as high as 85%–95%, but the positive predictive value is reported to be low at around 10%–20%. In addition, although the risk of sudden death is reported to increase as the number of risk factors increases,[243] there is also a report from Europe and the USA showing no significant correlation between the number of risk factors and the incidence of appropriate ICD therapy.[230] Therefore, it is difficult to predict the risk of sudden death through a simple addition of risk factors.

NSVT alone is classified as IIb, although there is a report indicating that the risk of sudden death is high even in young HCM patients (age <30 years) with NSVT alone.[247] Abnormal blood pressure response during exercise or a family history of sudden death only is designated as IIb, and cases with other major risk factors or modifiers are designated as IIa in this guideline (Table 19).

The European Society of Cardiology guidelines recommend risk stratification based on a sudden death prediction model[248] used in a Web-based calculation formula (HCM Risk-SCD model) that includes 7 risk factors based on a cohort study. A 5-year risk of sudden death of ≥6% is reported for class IIa, 4% to <6% for class IIb, and <4% for class III, and a risk stratification has been proposed accordingly.[236] Reports indicate that the predictability of sudden death is higher than with conventional risk stratification, based on data from the same European population as well as from other populations in Europe, USA, and Asia including Japan.[249,250] As it is useful to predict the 5-year risk of sudden death in the high-risk group, class IIa is determined to be the "high-risk" class according to the HCM Risk-SCD model.[251] On the other hand, a meta-analysis has reported that HCM patients with ICD experience a relatively high incidence of both inappropriate therapies and ICD complications.[252]

At present, ICD implantation should be considered comprehensively for HCM patients who have any of the 5 conventional major risk factors after providing information for consent to patients and their families, taking into account the patient's age, the weight of risk factors, and the risk/benefit assessment of ICD therapy.

In addition to the 5 conventional major risk factors, the end-stage phase, apical aneurysm formation in the left ventricle (including those associated with left midventricular narrowing), left ventricular outflow tract obstruction, and extensive late gadolinium enhancement on cardiac MRI have also been suggested as potential risk factors of sudden death (risk modifiers),[238,253-255] and further studies are needed. Conversely, factors such as AF, inducibility of sustained VT/VF in electrophysiological study, and gene mutation have limited application for the prediction of sudden death.[238,256,257]

TABLE 18 Recommendations and evidence levels for ICD for patients with uncertain diagnosis of syncope

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients with coronary artery diseases or non-ischemic cardiomyopathy, and with symptomatic heart failure (NYHA class II-III) and LVEF ≤35% after optimal medical therapy	I	A	A	II
ICD is recommended for patients with structural heart diseases and inducible hemodynamicallyintolerable VT or VF	I	B	B	II
ICD should be considered for patients with non-ischemic cardiomyopathy and LVEF ≤35% after optimal medical therapy (regardless of NYHA class)	IIa	C	C1	VI
ICD is not recommended for patients without any of following conditions: (1) reduced systolic cardiac function; (2) lethal arrhythmic disease such as hypertrophic cardiomyopathy, arrthmogenic rightventricular cardiomyopathy, Brugada syndrome (including drug-induced Brugada ECG), early repolarization syndrome, or short QT syndrome; and (3) inducible VT or VF	III	C	C2	VI

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; VF, ventricular fibrillation; VT, ventricular tachycardia.

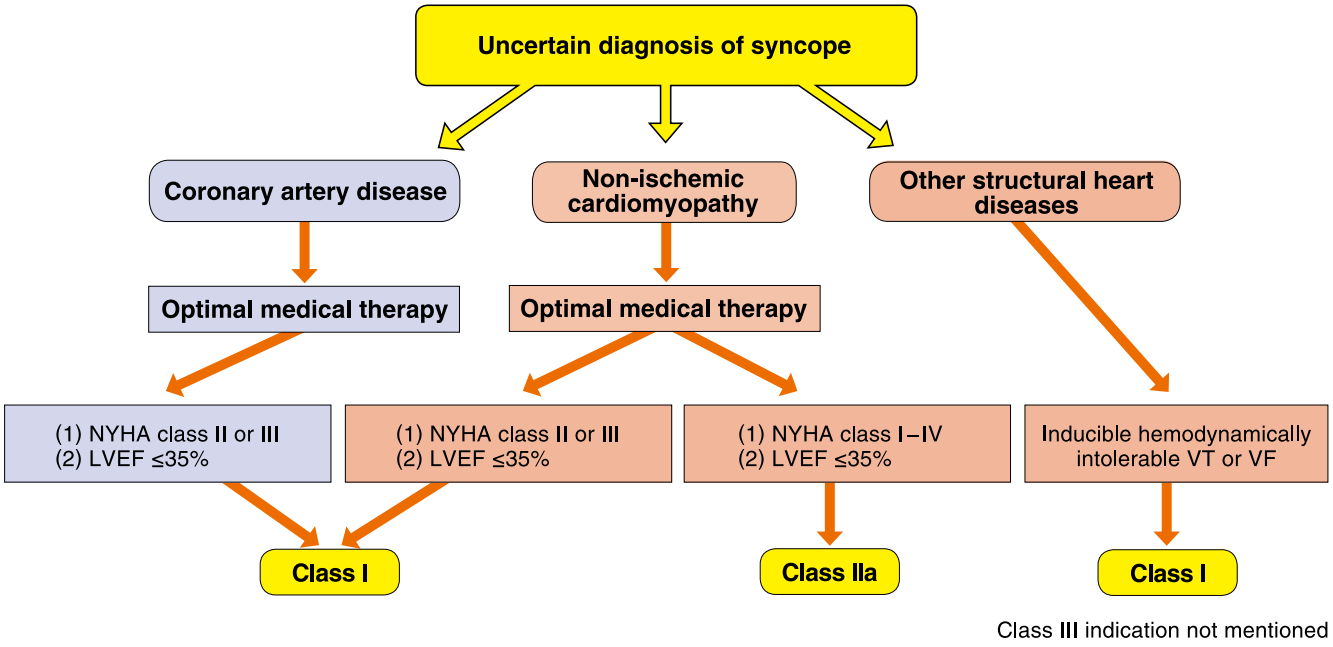


FIGURE 6 ICD indication for patients with uncertain diagnosis of syncope. LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; VF, ventricular fibrillation; VT, ventricular tachycardia
[Correction added on 29 June, after first online publication: '(1) NYHA class I or IV' has been amended to '(1) NYHA class I–IV' in the box above 'Class IIa'.]

4.4.2 | Arrhythmogenic right ventricular cardiomyopathy (ARVC)

ARVC is known to be a major underlying heart disease in cases of sudden cardiac death in young people.[258-264] Fatty degeneration and fibrofatty replacement of the right ventricular myocardium are the main causes of the disease, and ARVC is generally classified as a hereditary cardiomyopathy. However, given the remarkable genetic diversity and low penetrance, involvement of non-genetic factors has also been suggested. Although the etiology remains unknown, the progression of this condition leads to right or bilateral heart failure due to myocardial injury in the right and left ventricles.

The cause of sudden death in ARVC is mainly cardiac arrest due to sustained VT or VF, and in young people the first cardiac accident may be sudden death.[262,263] However, the predictors of sudden death are not well defined. Reports from Japan have suggested that patients with high scores based on the 2010 Task Force Criteria for ARVC[264] and those with a history of hospitalization for heart failure have an increased risk of developing sustained VT or VF.[265,266] However, there are few data that would enable full evaluation from Japan alone. In this guideline, ICD recommendations and levels of evidence were prepared based on the consensus statement issued in 2015[267] (Table 20).

A history of sustained VT or VF is reported to be associated with a recurrence rate of life-threatening arrhythmia of ≥10% per year, making these high-risk cases; thus, ICD is important as secondary prevention.[267-269] A cohort study of 132 ARVC patients treated with ICD

TABLE 19 Recommendations and evidence levels for ICD for hypertrophic cardiomyopathy

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients with prior cardiac arrest or sustained VT/VF	I	B	A	IVa
ICD should be considered for patients with recent cardiogenic or unexplained syncope (<6 months), maximum LV wall thickness ≥30 mm, or with high risk of SCD (an estimated 5-year risk of sudden death ≥6%) using the HCM Risk-SCD model (2014 ESC guidelines)	IIa	C	B	IVa
ICD should be considered for patients with family history of SCD, and with other SCD major risk factors or modifiers	IIa	C	B	IVa
ICD should be considered for patients with non-sustained VT, and with other SCD major risk factors or modifiers	IIa	C	B	IVa
ICD should be considered for patients with abnormal blood pressure response to exercise, and with other SCD major risk factors or modifiers	IIa	C	B	IVa
ICD may be considered for patients with family history of SCD, but without other SCD major risk factors or modifiers	IIb	C	C2	VI
ICD may be considered for patients with non-sustained VT, but without other SCD major risk factors or modifiers	IIb	C	C2	VI
ICD may be considered for patients with abnormal blood pressure response to exercise, but without other SCD major risk factors or modifiers	IIb	C	C2	VI

Major risk factors: prior cardiac arrest or sustained VT/VF, family history of SCD, unexplained syncope, non-sustained VT, maximum LV wall thickness ≥30 mm, abnormal blood pressure response with exercise.

Modifiers: LV outflow obstruction, extensive LGE on CMR imaging, LV apical aneurysm, impaired systolic function (LVEF <50%, end-stage phase).

Abbreviations: CMR, cardiovascular magnetic resonance; COR, class of recommendation; GOR, grade of recommendation; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator; LGE, late gadolinium enhancement; LOE, level of evidence; LV, left ventricular: SCD, sudden cardiac death; VF, ventricular fibrillation; VT, ventricular tachycardia.

TABLE 20 Recommendations and evidence levels for ICD for ARVC

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients with prior cardiac arrest, VF or hemodynamically unstable, sustained VT	I	B	A	IVa
ICD is recommended for patients with severely systolic dysfunction of the RV, LV, or both	I	C	B	IVa
ICD should be considered for patients with hemodynamically stable, sustained VT	IIa	C	C1	IVa
ICD should be considered for patients with cardiogenic or unexplained syncope, and with minor risk factors	IIa	C	C1	IVa
ICD should be considered for patients with non-sustained VT, and with minor risk factors	IIa	C	C1	IVa
ICD should be considered for patients with moderately systolic dysfunction of the RV, LV, or both, and with minor risk factors	IIa	C	C1	IVa
ICD may be considered for patients with minor risk factors	IIb	C	C2	VI

Minor risk factors: younger age, male sex, desmosomal-gene mutations, sustained VT/VF inducible in electrophysiological study, T-wave inversion in inferior leads, T-wave inversion in V4 and beyond, PVCs ≥ 1,000/24 h.

Abbreviations: ARVC, arrhythmogenic right ventricular cardiomyopathy; COR, class of recommendation; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; LV, left ventricular; RV, right ventricular; VF, ventricular fibrillation; VT, ventricular tachycardia.

(including cardiac arrest [n = 13] and sustained VT [n = 82]) also found that a history of cardiac arrest and a history of hemodynamically unstable sustained VT were significant factors associated with appropriate ICD therapies, with the rate reported to be 10% per year.[268]

The most important high-risk factors for primary prevention are severe right ventricular dysfunction (right ventricular fractional area change ≤17%, right ventricular ejection fraction [RVEF] ≤35%) and LVEF ≤35%.[267,268,270-273]

In addition, the consensus statement revealed that unexplained syncope,[267,271,274,275] NSVT on Holter ECG (≥3 times in succession and >100 times/min)[267,274,275] and moderate RV dilatation/dysfunction (RV fractional area change 17%–24%, RVEF 36%–40%) and left ventricular dilation/dysfunction (LVEF 36%–45%)[267,268,270-273] are considered high-risk factors. The rate of appropriate ICD therapies in these high-risk cases has been reported to be 48%–78% over 2-7 years of observation.[267] The North American ARVC Registry also reported that young age (33 ± 15 years) was a risk factor for life-threatening arrhythmia.[269] In these high-risk cases, ICD implantation is recommended as primary prevention to improve the prognosis of patients with ARVC. The consensus statement indicates that ARVC patients with ≥1 risk factors of arrhythmia (syncope, NSVT, moderate RV and/or LV dysfunction) have an intermediate risk.[267] Patients in this category are expected to have an estimated life-threatening arrhythmia rate of 1%–10% per year,[267,274,275] and should be considered for ICD implantation.

Other factors conventionally indicated as risk factors, namely young age at diagnosis, male sex, desmosomal-gene abnormalities, sustained VT or VF inducible in electrophysiological study, T-wave inversion in inferior leads, and T-wave inversion in precordial leads exceeding V4, are considered to be minor risks because they lack sufficient weight as risk factors.[267] Further, some facilities have indicated that frequent occurrence of PVCs (>1,000/day) on Holter ECG is a risk factor.[275] ICD implantation as primary prevention may be considered for patients with ARVC in this category when they have >1 factor; however, it is not strongly recommended. The incidence of ICD complications is 3.7% per year, and that of inappropriate therapies is 4.4% per year in ARVC patients with an ICD.[269] The indication of ICD implantation in ARVC patients should be determined comprehensively after providing information for consent to patients and their families, taking into account the patient's age, the weight of risk factors, and the risk/benefit assessment of ICD therapy.

4.4.3 | *Brugada syndrome*

Brugada syndrome (BrS) is characterized by the presence of a characteristic ST elevation in the right precordial lead of a 12-lead ECG, and VF, causing sudden death mainly during nighttime sleep or at rest.[276] Spontaneous coved-type ST-segment elevation (type I ECG) with elevation of the J-point by ≥2 mm (0.2 mV), or type I ECG after drug challenge test with a sodium-channel blocker, in the right precordial leads, including high intercostal recording up to the second intercostal space, is an essential condition for the ECG diagnosis of BrS.[277]

The diagnosis is based on definitive findings, major findings (ECG, clinical history), and minor findings (clinical history, family history, genetic test results), as shown in Table 21.[2] A diagnosis of symptomatic BrS is made when 1 item in the ECG findings and 1 of the major clinical findings (2A–2D; Table 21) are satisfied. Meanwhile, asymptomatic BrS is diagnosed when there is only 1 ECG finding and no clinical history findings. The minor findings of clinical history 3A and family history 3B–3D (Table 21), and *SCN5A* mutations in genetic testing, are reference findings for risk assessment.[278]

ICD implantation is the only treatment that has been proven effective in preventing sudden death in patients with BrS.[279,280]

TABLE 21 Diagnosis of Brugada syndrome

1. Definitive findings
ECG (12-Lead/Ambulatory)
A. Spontaneous type 1 Brugada ECG pattern at nominal or high leads
B. Fever-induced type 1 Brugada ECG pattern at nominal or high leads
C. Type 2 or 3 Brugada ECG pattern that converts into type 1 Brugada ECG pattern with provocative drug challenge
2. Major findings
Clinical History
A. Unexplained cardiac arrest or documented VF/polymorphic VT
B. Nocturnal agonal respiration
C. Suspected arrhythmic syncope
D. Syncope of unknown mechanism/unknown etiology
3. Minor findings
Clinical History
A. Atrial flutter/fibrillation in patients under 31 years without alternative etiology
Family History
B. Definite Brugada syndrome
C. Suspicious SCD (fever, nocturnal, Brugada aggravating drugs)
D. Unexplained SCD under 46 years with negative autopsy
Genetic Testing (no reimbursement)
E. Probable pathogenic mutation in Brugada syndrome susceptibility gene

Symptomatic BrS: 1 ECG finding and 1 major clinical finding 2A–2D are satisfied.

Asymptomatic BrS: only 1 ECG finding and no clinical history of major findings.

Minor findings 3A (clinical history), 3B–3D (family history), and 3E (*SCN5A* mutation) are used for risk assessment of asymptomatic BrS. When a patient has non-type 1 (type 2 or type 3) ECG alone, BrS is not diagnosed; however, type 1 ECG may appear over time, so it is necessary to monitor patients over time (patients should be examined especially when major findings appear).

Abbreviations: SCD, sudden cardiac death; VF, ventricular fibrillation; VT, ventricular tachycardia.

(From Japanese Circulation Society 2018[2].)

Patients with a history of cardiopulmonary arrest and resuscitation or a history of VF (secondary prevention) in addition to type 1 ECG have a class I recommendation for ICD implantation (Figure 7). There have been various discussions on the ICD indication for primary prevention. In previous guidelines issued by the JCS, a class IIa recommendation was defined as having type 1 ECG and satisfying ≥2 of the following conditions: (1) history of syncope, (2) family history of sudden death, and (3) VF induction with electrophysiology methods. These 3 risk factors had equal importance. Additional data on these 3 risks have been reported in recent years.

Syncope is a high-risk sign and is a presymptomatic event in approximately 20% of patients with a history of cardiac arrest and VF.[281,282] Many prospective studies have demonstrated that syncope is associated with VF (hazard ratio (HR) 1.48-4.2),[104,106,283]

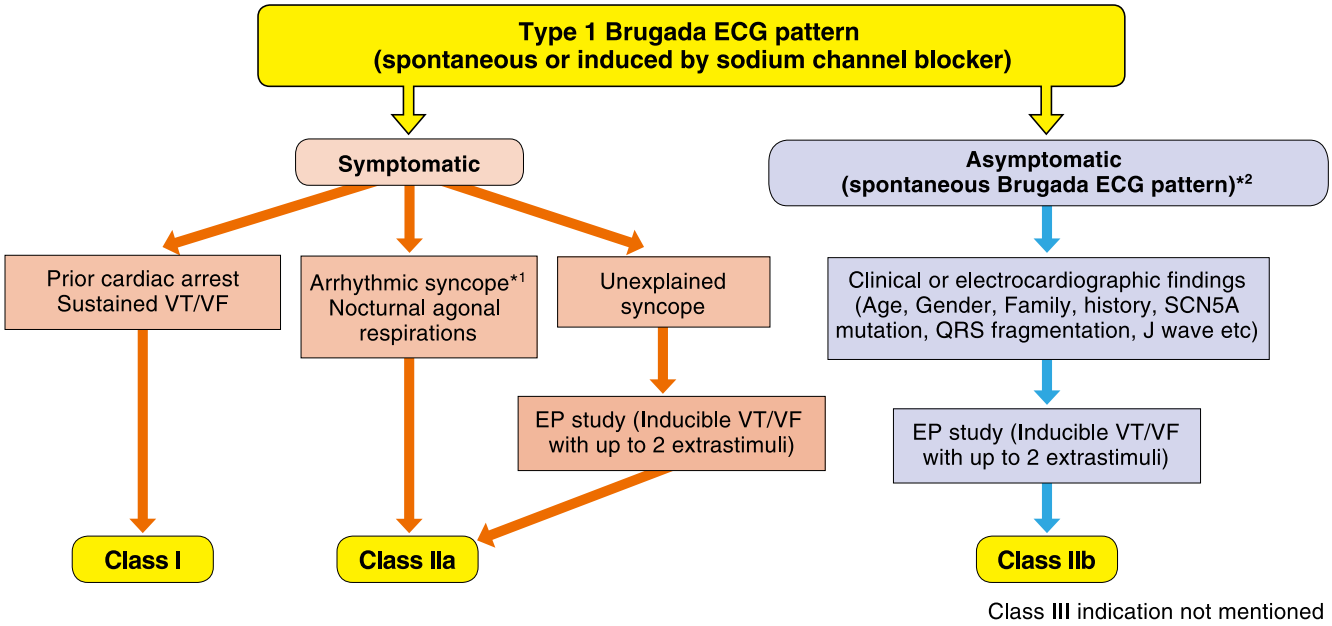


FIGURE 7 ICD indication for patients with Brugada syndrome. *1Arrhythmic syncope: In comparison with non-arrhythmic syncope, there is a great frequency among middle-aged men. Incontinence is frequently observed. Syncope is not driven by a crowded environment, pain, mental stress, and orthostatic body position. *2Close follow-up is recommended in patients with Brugada ECG pattern induced by sodium channel blocker. ICD, implantable cardioverter-defibrillator; VF, ventricular fibrillation; VT, ventricular tachycardia

and ICD should be considered in cases of type 1 ECG and syncope. However, BrS has a high rate of a positive tilt test,[284,285] and to ascertain if the syncope is arrhythmogenic, it is important to distinguish between syncope and loss of consciousness with other causes such as neurally mediated syncope or epilepsy.

There is a report from a registered study in Japan that a family history of sudden death is a high-risk factor (HR 3.3) in patients with BrS who have a family history of sudden death before the age of 45 years;[105] however, the usefulness of this finding in risk stratification is unclear.

The usefulness of risk stratification with VF induction with programmed ventricular stimulation in electrophysiology studies has been inconsistently reported.[95,96,99,100] The reasons include differences in patient background, number of extrastimuli, positive criterion for induction, and the observation period among studies, as well as the effects of sedation and the autonomic nervous system. In Japan, multicenter studies in 2007 and 2009 found no association between VF induction and the occurrence of cardiac accidents;[105,107] however, a single-center study in 2012 reported that induction of ≤2 consecutive extrastimuli may be a predictor.[101] In addition, a pooled analysis from the USA and Europe in 2016 reported that the risk could be high if VF induction with ≤2 consecutive stimuli is applied.

Recent multicenter collaborative studies in Japan[286] have shown that the *SCN5A* mutation is a predictor of arrhythmia events (HR 1.96), and the prognosis tends to be poor, especially when the mutation is located in the central pore region of the sodium channel.

On the basis of the above information, this guideline emphasizes the risk in the order of "syncope" "electrophysiological study" "family history". ICD is indicated for cases of type 1 ECG with unexplained syncope, if the electrophysiological study is positive and the class of recommendation is IIa. In asymptomatic patients with spontaneous type 1 ECG, if some of the clinical findings (age, sex, family history, *SCN5A* mutation, etc) or ECG findings (QRS fragmentation, J-wave, etc) are positive and the electrophysiological study is positive, ICD is assigned a class IIb recommendation (Table 22). Further investigation is necessary to determine the validity of these indications.

S-ICD has recently become available as an alternative to conventional ICD. Patients with BrS are often adolescents who are highly active, and conventional ICDs are associated with a high rate of complications (inappropriate therapy, lead failure) of 8.9% per year.[287] Although S-ICDs may have a slightly higher rate of inappropriate therapy than conventional ICDs, the use of S-ICDs is expected in the future because of its low lead-related complications.

4.4.4 | *Congenital long QT syndrome*

Congenital long QT syndrome (LQTS) is characterized by prolonged QT interval and polymorphic VT known as torsade de pointes (TdP), causing syncope and sudden death.[288-290] This syndrome consists of 2 types: the Jervell and Lange-Nielsen syndrome (with autosomal recessive inheritance and hearing loss), and the Romano-Ward syndrome (with autosomal dominant inheritance and no hearing loss). Molecular genetic studies have shown that many inherited arrhythmias are caused by mutations in genes encoding the ion channels that form the action potential of the myocardium, as well as associated cell membrane proteins. Mutations in the causative gene are identified in more than half of the cases diagnosed clinically as congenital LQTS.[291] For the major genotypes of Romano-Ward syndrome type 1 (LQT1), type 2 (LQT2), and type 3 (LQT3), the relationship between the genotype and clinical findings (phenotype) has

TABLE 22 Recommendations and evidence levels for ICD for Brugada syndrome

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients Patients with type 1 Brugada ECG pattern and aborted SCD or documented VT/VF	I	B	A	IVa
ICD should be considered for patients Patients with type 1 Brugada ECG pattern and arrhythmic syncope or nocturnal agonal respiration	IIa	C	B	IVa
ICD should be considered for patients with type 1 Brugada ECG pattern and unexplained syncope, and with inducible VF with ≤2 extrastimuli	IIa	C	C1	IVa
ICD may be considered for patients with spontaneous type 1 Brugada ECG pattern and considerable clinical or ECG findings (age, sex, family history, SCN5A mutation, QRS fragmentation, J-wave, etc), and with inducible VF with ≤2 extrastimuli	IIb	C	C1	V
ICD is not recommended for patients with life expectancy ≤12 months	III	C	C2	VI
ICD is not recommended for patients without consent to or cooperation with ICD therapy because of a psychiatric disorder or other reasons	III	C	C2	VI

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; SCD, sudden cardiac death; VF, ventricular fibrillation; VT, ventricular tachycardia.

been examined in detail. Clinical symptoms and specific treatments according to genotype and genotype-specific therapy have already been described.[288-290]

Schwartz's risk score [292] has long been used for the clinical diagnosis of congenital LQTS (Tables 23,24)[292,293]. In the 2012 revision, a new item (QTc ≥480 ms at 4 min during the recovery period of the exercise stress test) was recognized as an additional 1 point. Patients with a total score ≥3.5 are diagnosed with congenital LQTS.[294] The clinical diagnosis of congenital LQTS described in the consensus statement by the Heart Rhythm Society (HRS), European Heart Rhythm Association (EHRA), and Asia Pacific HRS (APHRS) published in 2013 includes that risk score of ≥3.5, but also states that patients are diagnosed with congenital LQTS if they have either an apparent pathological mutation in the gene associated with congenital LQTS, or QTc ≥500 ms[277] The diagnostic criteria are shown in Table 25. Cases of unexplained syncope without mutations in the gene can be diagnosed as congenital LQTS, if the patient has a QTc of 480-499 ms

If untreated, more than half of patients with congenital LQTS will develop cardiac events by age 40 years, and <5% will experience sudden death or cardiac arrest as the first symptom. The treatment of congenital LQTS generally involves lifestyle guidance and pharmacotherapy; however, non-pharmacotherapy is selected if such treatment has been fully implemented but failed to control the life-threatening arrhythmia.[295]

In terms of the ICD indications for congenital LQTS (Table 26), LQT3 is reported to have a lower incidence of life-long cardiac events, but a higher incidence of fatal cardiac events, than LQT1 and LQT2.[296] This was considered in the previous revision of the guideline. The current guideline follows the previous version, and it was decided that the ICD indication should be based on a combination of 3 items: (1) TdP or a history of syncope, (2) family history of sudden death, and (3) effectiveness of beta-blockers. However, ICD therapy is only a symptomatic treatment, and complications during and after implantation, as well as frequent inappropriate therapy after implantation,

TABLE 23 Congenital long QT syndrome risk score and diagnostic criteria

	Points
ECG findings	
A. Prolonged QT interval (QTc)[a]	
≥480 ms	3
460-479 ms	2
450-459 ms (in males)	1
B. QTc at the 4th minute of recovery from an exercise stress test	
≥480 ms	1
C. TdP[b]	2
D. T-wave alternans	1
E. Notched T-wave in 3 leads	1
F. Low heart rate for age[c]	0.5
Clinical history	
A. Syncope[b]	
With stress	2
Without stress	1
B. Congenital deafness	0.5
Family history[d]	
A. Family members with definite LQTS[e]	1
B. Unexplained sudden cardiac death before age 30 years	0.5

Score: ≤1 point, low probability of LQTS; 1.5-3 points, intermediate probability of LQTS; ≥3.5 points, high probability of LQTS.
(From Schwartz et al, 2011.[292] with permission.)
[a]In the absence of medications or disorders known to affect these ECG features, and QTc calculated using Bazett's formula, where QTc = /√RR.
[b]Mutually exclusive.
[c]Resting heart rate below the 2nd percentile for age (Table 24).
[d]The same family member cannot be counted in both A and B.
[e]Family members with LQTS risk score ≥ 3.5.

may cause mental disorders. The indications should be determined by properly assessing the risk and benefit, especially for young people.[297] Therefore, the class of recommendation is III for asymptomatic patients with congenital LQTS who have not been treated with beta-blockers. After ICD implantation, treatment should be programmed for VF therapy only, and the detection heart rate zone should be set higher than normal, at ≥220-240 beats/min, so as not to activate TdP, which often terminates spontaneously without syncope.

The efficacy of left cardiac sympathetic denervation (LCSD) for congenital LQTS has been reported in Europe for drug-resistant patients.[298-300] The 2013 HRS/EHRA/APHRS Consensus Statement pronounces that high-risk patients who are contraindicated for ICD or refuse implantation, or patients for whom beta-blockers are contraindicated or have difficulty with administration (because of non-responsiveness or intolerance) have a class I recommendation.[277] However, in Japan, this treatment is not covered by insurance and not frequently practiced. The recommendations for LCSD are shown in Table 27 (see also **Chapter III, "6.2.3 Non-pharmacotherapies other than catheter ablation or devices"**).

TABLE 24 Resting heart rate below the 2nd percentile between neonatal period and age 3 years

Age	Boys	Girls
0-1 months	129	136
1-3 months	126	126
3-6 months	112*	122*
6-12 months	106	106
1-3 years	97	95

*Because of small sample data, 95% confidence intervals are used.
(Data from Rijnbeek et al, 2001.[293])

TABLE 25 Diagnosis of congenital LQTS (HRS/EHRA/APHRS expert consensus statement)

1. LQTS is diagnosed:
   a. In the presence of an LQTS risk score ≥ 3.5 in the absence of a secondary cause for QT prolongation *and/or*
   b. In the presence of an unequivocally pathogenic mutation in one of the LQTS genes *or*
   c. In the presence of a QT interval corrected for heart rate using Bazett's formula (QTc) ≥500 ms in repeated 12-lead ECGs and in the absence of a secondary cause for QT prolongation.
2. LQTS can be diagnosed in the presence of a QTc between 480 and 499 ms in repeated 12-lead ECGs in a patient with unexplained syncope in the absence of a secondary cause for QT prolongation and in the absence of a pathogenic mutation.

(From Priori et al, 2013.[277] with permission.)

4.4.5 | *Catecholaminergic polymorphic VT (CPVT)*

CPVT is a disease that causes polymorphic VT and VF triggered by exercise and stress, and leads to sudden death.[301-304] Given that gene mutations in the ryanodine receptor (*RyR2*) and calsequestrin 2 (*CASQ2*) are detected in approximately 60% of cases, it is believed that this condition is caused by abnormalities in the calcium control mechanism in myocardial cells.[305-309] Organic heart disease is absent, and the prevalence is about 1 in 10,000 people. There is no sex difference, and symptoms commonly appear between the ages of 7 and 10 years. There have been reports of cases associated with supraventricular arrhythmias and conduction abnormalities. At rest, relative bradycardia is observed; however, with an exercise test or an adrenaline provocative test, PVCs gradually increase, progressing from polymorphic or typical bidirectional VT to rapid polymorphic VT (350-400/min) and occasionally transitioning to VF.

The mechanism of PVCs is considered to be a delayed afterdepolarization due to intracellular calcium overload. The following are suggested criteria for the diagnosis of CPVT,[277] of which (1) to (3) translate into a definitive diagnosis and (4) into a suspected diagnosis):

1. If an exercise test or an adrenaline provocative test induces bidirectional VT, polymorphic VT, or multifocal PVCs with no other known cause in patients with a normal ECG, and are younger than 40 years without structural heart disease.
2. If the proband or family members have a pathogenic mutation associated with CPVT.

TABLE 26 Recommendations and evidence levels for ICD for congenital long QT syndrome

		COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients with documented VF or previous cardiac arrest		I	B	A	IVa
1. TdP or syncope 2. Family history of SCD 3. Refractory to beta-blocker* therapy	ICD is should be considered if 2 or 3 conditions are satisfied	IIa	B	C1	IVa
	ICD may be considered if one or no condition is satisfied	IIb	B	C1	IVa
ICD is not recommended for patients Asymptomatic patients without use of beta-blockers		III	C	C2	IVb

*The efficacy of beta-blockers is evaluated according to both symptoms and QT prolongation during exercise. Beta-blocker therapy is automatically ineffective in patients with LQT3.

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; TdP, torsade de pointes; VF, ventricular fibrillation.

TABLE 27 Recommendations and evidence levels for left cardiac sympathetic denervation for congenital long QT syndrome

	COR	LOE	GOR (MINDS)	LOE (MINDS)
High-risk patients with a diagnosis of LQTS in whom: 1) ICD therapy is contraindicated or refused *and/or* 2) Beta-blockers are either not effective in preventing syncope/arrhythmias, not tolerated, or contraindicated	IIa	C	C1	V
Patients taking beta-blockers or with an ICD implant but are experiencing multiple shocks	IIb	C	C1	VI

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; LQTS, long QT syndrome.

TABLE 28 Recommendations and evidence levels for ICD in patients with catecholaminergic polymorphic ventricular tachycardia

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended in CPVT patients in whom cardiac arrest, recurrent syncope, or polymorphic or bidirectional VT occurs after appropriate pharmacological therapy and/or left cardiac sympathetic denervation (LCSD)	I	C	A	V
ICD monotherapy is not recommended for asymptomatic CPVT patients	III	C	D	V

Abbreviations: COR, class of recommendation; CPVT, catecholaminergic polymorphic VT; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; VT, ventricular tachycardia.

3. If an exercise test induces multifocal PVCs, bidirectional VT, or polymorphic VT in the family members of the proband, despite the absence of heart disease.
4. If an exercise test or an adrenaline provocative test induces bidirectional VT, polymorphic VT, or multifocal PVCs with no other known cause in patients with a normal ECG, who are 40 years or older and with neither structural heart disease nor coronary artery disease.

The 2013 HRS/EHRA/APHRS Consensus Statement made recommendations for the management and treatment of CPVT.[277] Similar strategies are presented in the 2015 ESC Guidelines (Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death),[310] and the 2017 ACC/AHA/HRS Guidelines (Guideline for the Evaluation and Management of Patients with Syncope).[60] Exercise restriction is essential in all cases and pharmacotherapy is used, mainly focused on beta-blockers and flecainide, but left stellate ganglionectomy and ICD implantation can also be performed depending on the patient's condition.[311-314] Recently, there have been reports on the effects of catheter ablation.[315,316]

As with other diseases, ICD treatment is recommended as secondary prevention; however, there are some precautions.[317] As CPVT often develops in young patients or early in life, it is necessary to consider several factors such as implantation method, device selection, lead fracture, system replacement with patient growth, and inappropriate therapy. For appropriate therapy, it is important to devise ways to minimize shock discharge. In CPVT, the pain and burden associated with shock discharge may induce sympathetic hyperactivity, causing further arrhythmias, more frequent discharge, and ultimately death.[317,318] For this reason, it is important that an ICD is introduced not alone but in combination with pharmacotherapy.[277,310] It is also necessary to program the device to avoid shock discharge for NSVT or slow VT without hemodynamic failure (set to a longer time until shock is discharged and to a higher VT detection rate). Shock therapy is effective for VF (or short-cycle polymorphic VT); however, it causes an increased risk of creating a proarrhythmic effect in case of bidirectional VT due to delayed after depolarization. CPVT is a rare disorder, and it must be noted that ICD implantation does not provide sufficient long-term outcomes. The role of ICDs for primary prevention is a topic for future discussion; however, owing to the above mentioned characteristics, treatment with ICD alone must be avoided. The recommendations are shown in Table 28.

4.4.6 | Other specific heart diseases (besides HOCM, ARVC, BrS, congenital LQTS, and CPVT)

This is a group of diseases without organic heart disease, and includes idiopathic VF (IVF; in a narrow sense) and its related disorders, such as early repolarization syndrome (ERS) and short QT syndrome (SQTS) excluding channelopathies such as Brugada syndrome (BrS), LQTS, and CPVT. ICD has a class I recommendation for

any of these diseases in patients who have had at least 1 episode of VF or cardiac resuscitation due to VF. Conversely, there is little evidence for implantation for primary prevention in asymptomatic cases with abnormal ECG only, and there are no clear indication criteria for ICD implantation.

a. | Idiopathic VF. IVF is a disease that causes VF in patients without an apparent organic heart disease and ECG abnormalities. BrS is broadly included in this category; however, the IVF described in this section refers to IVF in a narrow definition, which excludes BrS and other diseases associated with ECG abnormalities (Table 29). For IVF patients after cardiac arrest or VF resuscitation who are expected to survive for at least 1 year, ICD is indicated regardless of catheter ablation for triggering PVC and of pharmacotherapy such as quinidine[319]) (class of recommendation I, level of evidence B). However, the risk of recurrence of VF is considered relatively lower than in disease groups for which other causes have been identified.[320]

Meanwhile, there is no evidence for prophylactic ICD implantation in family members of IVF patients.

b. | Early repolarization syndrome. ERS is diagnosed when there is a J-wave or early repolarization (ER) of ≥0.1 mV in ≥2 leads on the lower wall (II, III, aVF) and/or the anterior wall (I, V4-V6) of a 12-lead ECG with a history of VF.[321] According to the 2013 EHRS/EHRA/APHRS Expert Consensus, ERS can be diagnosed in an sudden cardiac death victim with a negative autopsy and medical chart review with a previous ECG demonstrating typical J-point elevation.[277] J waves or early repolarization (ER) are observed in 5.8% of healthy subjects and are common in men; however, VF relapse is known to be more common in early repolarization syndrome (ERS) patients after VF resuscitation.[321-323] ICD implantation is indicated for ERS patients with a history of cardiac arrest or VF resuscitation (class of recommendation I, level of evidence B). There are no clear criteria or evidence for primary prevention, and it is not always possible to determine the ICD indication based on a history of syncope, a family history of sudden death, or induction of symptoms with electrophysiology methods, as in BrS. However, if the patient has a history of suspected arrhythmogenic syncope, seizures, or paroxysmal nocturnal dyspnea, and the patient's family members have an ER pattern with a familial history of sudden juvenile cardiac death, then ICD implantation can be considered, after obtaining consent, if the patient expresses a preference for the treatment (class of recommendation IIb). There is no ICD indication for asymptomatic ER patterns. The recommendations are shown in Table 30 and Figure 8.

c. | Short QT syndrome. The prevalence of QT shortening (QTc <340 ms) is reported to be approximately 5 per 10,000 young people under the age of 21 years, and there is a higher prevalence in males. The diagnosis of SQTS is based on QTc ≤330 ms or QTc <360 ms, with a genetic mutation, a family history of SQTS (SQTS

TABLE 29 Recommendations and evidence levels for ICD for idiopathic ventricular fibrillation

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients with documented VF or previous cardiac arrest	I	B	A	IVa

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; VF, ventricular fibrillation.

TABLE 30 Recommendations and evidence levels for ICD in patients with early repolarization (ER) ECG pattern

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients with documented VF or previous cardiac arrest	I	B	A	IVa
ICD may be considered for patients with arrhythmic syncope, seizure, or nocturnal agonal respiration, and with family history of juvenile unexplained sudden cardiac death	IIb	C	C1	VI
ICD may be considered for asymptomatic patients with high-risk ECG pattern*, and with family history of sudden cardiac death of juvenile unexplained sudden cardiac death	IIb	C	C1	IVa
ICD is not recommended for asymptomatic patients with ER ECG pattern	III	C	D	VI

*Extensive J-point elevation in inferior and/or lateral ECG leads, J-point elevation (≥0.2 mV), J-point elevation with horizontal/descending ST-segment, dynamic circadian and/or day-by-day variation in J-point elevation.

Abbreviations: COR, class of recommendation; ER, early repolarization; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; VF, ventricular fibrillation.

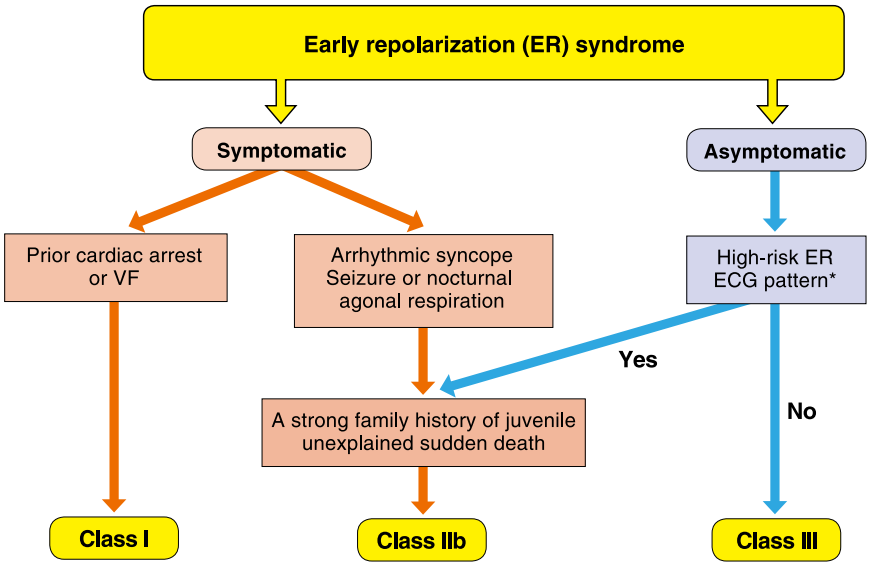


FIGURE 8 ICD indication for patients with early repolarization (ER) pattern on ECG. * High-risk ER electrocardiographic patterns: extensive J-point elevation at inferior and/or lateral ECG leads, J-p[oint elevation (≥0.2 mV), J-point elevation with horizontal/descending ST-segment, and dynamic circadian and/or day-by-day variations in J-point elevation. ER, early repolarization; VF, ventricular fibrillation

TABLE 31 Recommendations and evidence levels for ICD for short QT syndrome

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients with documented VF or previous cardiac arrest	I	B	A	IVa
ICD may be considered for patients with SQTS (QTc <320 ms) with family history of unexplained sudden cardiac death or arrhythmic syncope	IIb	C	C1	VI
ICD is not recommended for asymptomatic patients with SQTS	III	C	D	VI

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; SQTS, short QT syndrome.

in a 1st-degree relative or sudden death before age 40 years) or VT/VF.[277,324] VF frequently recurs in patients with SQTS after cardiac arrest or VF resuscitation, and ICD implantation is recommended if survival for >1 year is expected (class of recommendation I, level of evidence B).[325] There is no clear evidence for primary prevention, but ICD can be considered if SQTS patients (QTc <320 ms) with a family history of sudden cardiac death or a history of suspected arrhythmogenic syncope desire ICD implantation, after obtaining adequate informed consent (class of recommendation IIb). In addition, although asymptomatic SQTS patients with QT shortening of QTc <320 ms are not immediately indicated for ICD implantation, they require regular follow-up. The recommendations are shown in Table 31 and Figure 9.

4.5 | Subcutaneous ICD

The development of the modern ICD has contributed to expansion of its usage; however, the requirement for a transvenous approach to place the leads has raised a variety of problems, including complications associated with ICD lead insertion, lead injury, and bacteremia associated with device infection.[326] The S-ICD was developed to solve these problems. Similar to the transvenous ICD, the S-ICD consists of a generator and an ICD lead. ICD leads are often implanted subcutaneously near the sternum, and the generator is usually implanted between the serratus anterior muscle and the latissimus dorsi muscle at the level of the mid-axillary and posterior axillary lines.[327] The sensing vector is selected from 3 different vectors recorded between 2 electrodes attached to the lead of 14 cm apart, or between an electrode and the generator. Preoperative screening tests must be performed to avoid oversensing of T waves, and at least 1 of the 3 vectors must meet the criteria. When VT/VF is detected by a discrimination algorithm that recognizes the rate and QRS form, defibrillation is performed between the generator and the coil. The energy delivered is 80 J, approximately twice that of a transvenous ICD.

According to previous reports, the S-ICD is effective in preventing sudden death.[189,310,328-335] The EFFORTLESS (Evaluation of Factors Impacting the Clinical Outcome and Cost-effectiveness of the S-ICD) study examined complications and inappropriate ICD therapies in 985 S-ICD patients who had been followed for >1 year. The rates of complications associated with the S-ICD system and

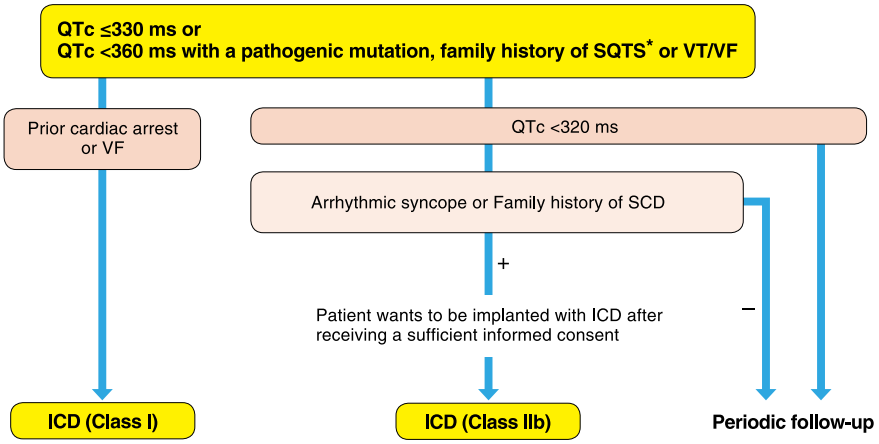


FIGURE 9 ICD indication for patients with short QT syndrome (SQTS). *: short-QT syndrome (SQTS) or sudden death under 40-year-old within the second-degree relatives. ICD, implantable cardioverter-defibrillator; SCD, sudden cardiac death; SQTS, short QT syndrome; VF, ventricular fibrillation

TABLE 32 Recommendations and evidence levels for subcutaneous ICD (S-ICD)

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients who meet the criteria for ICD implantation who have inadequate vascular access or a high risk for infection, and in whom pacing for bradycardia or VT termination or as part of CRT is neither needed nor anticipated	I	B	B	IVa
ICD should be considered for patients who meet the criteria for ICD implantation, if pacing for bradycardia or VT termination or as a part of CRT is neither needed nor anticipated	IIa	B	B	IVa
ICD may be considered for patients who meet the criteria for ICD implantation who have inadequate vascular access, young age, or a high risk for infection	IIb	C	C1	V

Abbreviations: COR, class of recommendation; CRT, cardiac resynchronization therapy; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; VT, ventricular tachycardia.

procedure were 4.1% at 30 days and 8.4% at 360 days.[335] The inappropriate ICD therapy rate was 8.1% at 1 year and 11.7% at 3.1 years; the appropriate ICD therapy rate was 5.8% at 1 year and 13.5% at 5 years; and the sinus rhythm recovery rate for spontaneous VT/VF was 97.4%. In addition to the dual-zone programming, a high-pass filter that suppresses T-wave oversensing reduced the inappropriate ICD therapy rate to 4.3% at 1 year.[336] The inappropriate ICD therapy rate of the S-ICD is considered to be equivalent to that reported in recent studies using the program recommended for intravenous ICD (2.3%–5% per year).[337-339] Lead injury and bacteremia, which are problems of intravenous ICD, were not reported in the EFFORTLESS study.

The S-ICD is considered suitable for patients without venous access, young patients, immunocompromized patients, and patients who underwent removal of transvenous devices (Table 32). Conversely, it is not suitable for bradyarrhythmia patients who need pacing, patients who need CRT, and patients with VT that can be terminated with antitachycardia pacing. However, there are several case reports[340-344] on the successful combination of the S-ICD and a pacemaker or leadless pacemaker, such as after the elimination of infection, when venous access is difficult, or when a pacemaker was previously implanted. But, regarding this issue, further studies are expected in the future.

Although S-ICDs may have an important role in primary prevention, no studies have shown long-term results, and a RCT[345] is ongoing.

5 | Cardiac resynchronization therapy

5.1 | CRT

Introduction

Heart failure (HF) is often complicated by intraventricular conduction disturbance, and dyssynchrony in atrioventricular, intraventricular, and interventricular conductions. CRT resolves dyssynchrony, prevents worsening of HF, or improves cardiac function, subjective symptoms, and prognosis.

According to previous clinical studies,[346-351] CRT is effective for moderate to severe HF, even after sufficient optimized

pharmacotherapy, with reduced LVEF and a QRS width ≥120-150 ms The effect differs depending on the conduction disturbance (bundle block type). Although diagnostic imaging such as echocardiography is expected to be useful in evaluating dyssynchrony, its utility has not been proven in large-scale studies. CRT is effective not only for patients with NYHA class III or IV, but also for those with class II HF if they meet the indication criteria. It is also useful for patients with AF if a high percentage of biventricular pacing can be achieved. The placement of the left ventricular lead depends on the anatomical characteristic of the coronary veins; thus, surgical lead placement is sometimes performed. If CRT is not effective, various factors are considered, including appropriate programming, improvement of percentage of biventricular pacing, pacing site change, or multipoint (multisite) pacing.

5.1.1 | CRT indication based on NYHA class

a. | Indication for NYHA class III–IV. In the 1990s, CRT was started for the treatment of HF with dyssynchrony of left ventricular contraction.[346,347] Since 2001, RCTs on CRT have been performed mainly in patients with severe HF with NYHA class III–IV, resistant to pharmacotherapy, with LVEF ≤35% and sinus rhythm QRS width ≥120 ms[216,348-355] The results showed that CRT improved QOL, including exercise tolerance, reduced the left ventricular diameter (improved left ventricular remodeling), and increased the LVEF. In addition, the COMPANION study showed a significant reduction in total mortality or hospitalization for HF,[216] and CARE-HF (Cardiac Resynchronization in Heart Failure) showed a significant reduction in total mortality.[355] A meta-analysis also showed that CRT reduced the total mortality by 26%.[356] However, the introduction of CRT should be considered before HF becomes severe because CRT has been reported to be less effective in patients with NYHA class IV.[357]

b. | Indication for NYHA class I–II. The REVERSE (Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction) study in patients with mild HF showed that CRT improved LVEF and reduced the risk of hospitalization for HF in patients with HF of NYHA class I or II, LVEF ≤40%, and QRS width ≥120 ms[358] In the MADIT-CRT study, ICD with CRT (CRT-D) significantly reduced the total mortality or hospitalization for HF compared with ICD for patients with HF of NYHA class I or II, LVEF ≤30%, and QRS width ≥130 ms (hazard ratio (HR) 0.59, 95% confidence interval (CI) 0.47-0.74, $P < .001$).[359] The RAFT (Resynchronization for Ambulatory Heart Failure Trial) study included patients with NYHA class II or III who had a slightly more severe condition than those included in MADIT-CRT; however, the other registration criteria were almost the same (LVEF ≤30%, QRS width ≥120 ms). The total mortality or event-free rate of HF was significantly better with CRT-D (HR 0.75, 95% CI 0.64-0.87, $P < .001$), with an improvement in overall mortality (HR 0.75, 95% CI 0.62-0.91, $P = .003$).[360]

A subgroup analysis of both studies showed that CRT was highly effective in patients with NYHA class II and QRS width ≥150 ms (especially left bundle block). Therefore, CRT is considered useful in patients with HF symptoms of NYHA class II or higher and HF with left ventricular dysfunction (LVEF ≤30%) and QRS width ≥150 ms

c. | CRT effect according to QRS waveform and QRS width. Even with CRT, it has been found that about 30%–40% of patients become non-responders in whom CRT no longer exerts a sufficient effect. A meta-analysis of the QRS waveform showed that CRT is useful only in patients with CLBBB waveform.[361] Concerning CRT efficacy in patients with right branch block, a subanalysis of the MIRACLE (Multicenter In Sync Randomized Clinical Evaluation) study[349] showed improvement in cardiac function and QOL, especially in cases of left anterior or posterior hemiblock.[362] However, an integrated analysis of MIRACLE[349] and CONTAK-CD (VENTAK® CHF/CONTAK® CD/EASYTRAK® Biventricular Pacing Study)[353] concluded that the effect of CRT was not sufficient in cases of right branch block;[363] thus, care should be taken when indicating this treatment.

In contrast, many clinical studies target patients with QRS width ≥120 ms; however, in COMPANION[216] and CARE-HF,[355] the mortality rate was significantly reduced in patients whose QRS width was ≥148 or ≥160 ms, respectively. From the perspective of mortality, the effect is more remarkable in patients with a wide QRS (≥150 ms). A meta-analysis[364] and the DESIRE (Daivobet®/Dovobet® Experience Study In Regions of Europe) study[365] reported that CRT improved the QOL and LVEF in patients with HF in whom dyssynchrony was detected with echocardiography studies, despite a relatively narrow QRS width. Conversely, the effectiveness of CRT was not confirmed in the RethinQ (Resynchronization Therapy in Narrow QRS) study, which investigated patients with HF who had dyssynchrony on echocardiography with NYHA class III, LVEF ≤35%, and QRS width <130 ms[366] Although the efficacy of CRT for patients with a relatively narrow QRS is still a matter of controversy, the EchoCRT (Echocardiography Guided Cardiac Resynchronization Therapy) study,[367] published in 2013, compared the clinical outcomes of patients with HF of NYHA class III or IV, dyssynchrony on echocardiography, and a QRS width <130 ms who were randomly divided into CRT-on and CRT-off groups. There was no significant difference between the 2 groups in total mortality or the incidence hospitalization for HF (HR 1.2, 95% CI 0.92-1.57, $P = .15$).

On the basis of these results, it can be concluded that CRT has little effect in patients with a relatively narrow QRS width (QRS <130 ms).[317,368] However, most of the previous RCTs and meta-analyses demonstrating the effectiveness of CRT for CLBBB used registration criteria including QRS width ≥120 ms Studies since 2013 have shown that drug treatment for HF is less effective in CLBBB patients than in non-CLBBB patients,[369] and that septal flash, which is an echocardiographic index predicting the effectiveness of CRT, was recognized in >60% of female CLBBB patients with a small body surface area, even in patients with 120 ≤ QRS < 130 ms[370] Furthermore, a subanalysis of EchoCRT, which had demonstrated negative results for CRT indication for QRS widths <130 ms, conversely suggested

the usefulness of CRT in patients with a small left ventricular end-diastolic volume.[371]

In view of the new findings in recent years and the characteristics of Japanese patients, who tend to be smaller than their Western counterparts, CRT can be considered useful for CLBBB patients with 120 ≤ QRS < 130 ms After summarizing all the results, we concluded that the lower limit of the QRS width should be set at 120 ms in the CRT indication criteria in this guideline. It should be noted, however, that clinical evidence has been established for patients with QRS width ≥130 ms As shown in Table 33, there are differences among guidelines in terms of the indication level of CRT based on QRS width in CLBBB patients, and there is currently no fixed consensus on this matter.[317,368,372-374] The recommendations are shown in Table 34.

d. | Optimization of pharmacotherapy. Drug therapy such as beta-blockers may improve cardiac function and generate reverse remodeling of the left ventricle in patients with HF. Therefore, the indications for treatment should be considered after sufficient pharmacotherapy. CRT, in particular, is not indicated within 3 months after revascularization or within 3 months after the introduction of new pharmacotherapy for HF, except for special reasons. Meanwhile, the dose of beta-blockers can be increased after CRT induction in some patients;[375] thus, it may be indicated in situations in which maximization of the dose cannot be achieved.

5.1.2 | CRT for patients with heart failure and with indication of bradycardia pacing

It has been reported that right ventricular pacing increases the incidence of AF and HF when pacemakers are indicated for patients with reduced cardiac function or bradycardia.[376,377] The BLOCK HF (Biventricular vs. Right Ventricular Pacing in Heart Failure Patients with Atrioventricular Block) study[378] compared the effects of CRT and right ventricular pacing in patients with indications for bradycardia pacing with atrioventricular block, NYHA class I, II, or III HF, and LVEF ≤50%. Over a mean observation period of 37 months, CRT significantly reduced the worsening of total mortality, acute HF, and left ventricular remodeling (HR 0.74, 95% CI 0.60-0.90, $P < .001$). Furthermore, a recent meta-analysis showed that biventricular pacing is clinically more useful than right ventricular pacing in patients who require bradycardia ventricular pacing and have LVEF >35%.[379] On the basis of these results, CRT should be considered for patients with reduced cardiac function and who newly require ventricular pacing.

Heart failure may be exacerbated in patients who depend on right ventricular pacing by pacemaker or ICD. The HOBIPACE (Homburg Biventricular Pacing Evaluation)[380] and RD-CHF[381] studies compared the effects of right ventricular pacing and biventricular pacing in patients with impaired cardiac function after device implantation, and demonstrated the usefulness of switching (upgrading) to CRT. Several subsequent retrospective or prospective studies, although small in scale, have reported that upgrading to CRT improves HF when patients with HF present with prolonged right ventricular apical pacing.[382,383] The recommendations are shown in Table 35.

5.1.3 | CRT for AF

Most clinical trials of CRT are performed in patients with sinus rhythm, and there is no consensus on the effects of CRT on AF patients. However, patients with chronic HF often have AF, and it is found in approximately one-quarter of patients with CRT.[384,385] In a subanalysis of the MADIT-CRT study, patients with left branch block and a history of supraventricular tachyarrhythmia, LVEF <30% excluding NYHA class III–IV, and QRS width ≥130 ms were classified into an ICD group and CRT-D group and compared for HF or mortality rate. The results indicated that events were significantly inhibited in the CRT-D group.[386] However, a RAFT subanalysis compared death or hospitalization for HF in patients with permanent AF and NYHA class II– III, LVEF ≤30%, and QRS width ≥120 ms, who were randomly assigned to ICD and CRT-D groups. There was no significant difference between the 2 groups in the incidence of events, and the usefulness of CRT in patients with permanent AF and HF was not proven.[387] In addition, a subanalysis of the COMPANION study did not indicate the usefulness of CRT in a comparison of the onset of the above events with a drug treatment group of patients with a history of AF/atrial flutter according to NYHA class III–IV.[388]

The reasons why CRT is less effective in AF patients include inability to restore atrioventricular synchrony and a decrease in the percentage of biventricular pacing due to increased atrioventricular conduction (AF tachycardia). A high percentage of

TABLE 33 Recommendations for CRT in patients with clbbb in other guidelines

	QRS (ms)					
	120-129		130-149		≥150	
Guideline	NYHA III–IV	NYHA II	NYHA III–IV	NYHA II	NYHA III–IV	NYHA II
ESC 2016[368]	III	III	I	I	I	I
ESC/EHRA 2013[317]	I	I	I	I	I	I
ACCF/AHA 2013[373]	IIa	IIa	IIa	IIa	I	I
CCS 2017[374]	III	III	I	I	I	I

Abbreviation: NYHA, New York Heart Association class.

TABLE 34 Recommendations and evidence levels for CRT

	COR	LOE	GOR (MINDS)	LOE (MINDS)
NYHA class III–IV				
CRT is recommended for patients who meet all of the following criteria: 1. Receiving optimal medical therapy 2. LVEF ≤35% 3. LBBB with QRS duration ≥120 ms 4. Sinus rhythm	I	A	A	I
CRT should be considered for patients who meet all of the following criteria: 1. Receiving optimal medical therapy 2. LVEF ≤35% 3. Non-LBBB with QRS duration ≥150 ms 4. Sinus rhythm	IIa	B	B	II
CRT may be considered for patients who meet all of the following criteria: 1. Receiving optimal medical therapy 2. LVEF ≤35% 3. Non-LBBB with QRS duration 120-149 ms 4. Sinus rhythm	IIb	B	C1	III
NYHA class II				
CRT is recommended for patients who meet all of the following criteria: 1. Receiving optimal medical therapy 2. LVEF ≤30% 3. LBBB with QRS duration ≥150 ms 4. Sinus rhythm	I	B	B	II
CRT should be considered for patients who meet all of the following criteria: 1. Receiving optimal medical therapy 2. LVEF ≤30% 3. Non-LBBB with QRS duration ≥150 ms 4. Sinus rhythm	IIa	B	B	II
CRT is reasonable should be considered for patients who meet all of the following criteria: 1. Receiving optimal medical therapy 2. LVEF ≤30% 3. LBBB with QRS duration 120-149 ms 4. Sinus rhythm	IIa	B	B	II
CRT may be considered for patients who meet all of the following criteria: 1. Receiving optimal medical therapy 2. LVEF ≤30% 3. Non-LBBB with QRS duration 120-149 ms 4. Sinus rhythm	IIb	B	C1	III
NYHA class I–IV				
CRT is not recommended for patients who meet either of the following criteria: 1. Limited physical activity due to chronic disease 2. Predicted life expectancy ≤ 12 months	III	C	C2	VI

Abbreviations: COR, class of recommendation; CRT, cardiac resynchronization therapy; GOR, grade of recommendation; LBBB, left bundle branch block; LOE, level of evidence; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.
[Correction added on 29 June, after first online publication: '2. Predicted life expectancy ≤ 1 12 months' under 'NYHA class I–IV' has been amended to '2. Predicted life expectancy ≤ 12 months'.]

biventricular pacing during CRT, irrespective of the presence of AF, has been shown to reduce total mortality and hospital admission for HF,[389,390] and the 2015 American HRS/EHRA/APHRS/Latin American Society of Electrophysiology and Cardiac Stimulation (SOLAECE) Expert Consensus Statement recommends a percentage of biventricular pacing of ≥98%.[337] Therefore, it is important to suppress atrioventricular conduction when a high percentage of biventricular pacing cannot be assured because of AF tachycardia, and if pharmacotherapy is not sufficiently effective, atrioventricular node ablation or ablation for AF should be considered.[391]

According to CERTIFY (Cardiac Resynchronization Therapy in Atrial Fibrillation Patients Multinational Registry), an international prospective study on CRT patients, AF patients who underwent atrioventricular node ablation had better prognosis than AF patients treated with pharmacotherapy only, and had a survival outcome similar to that of sinus rhythm patients.[392] The recommendations are shown in Table 36.

TABLE 35 Recommendations and evidence levels for CRT in patients with reduced LV systolic function and indication for ventricular pacing, or who have a high percentage of RV pacing after implantation of a pacemaker or an ICD

	COR	LOE	GOR (MINDS)	LOE (MINDS)
NYHA class III–IV				
CRT should be considered for patients who meet all of the following criteria: 1. Receiving optimal medical therapy 2. LVEF ≤50% 3. Indicated for pacing or ICD 4. Expected to require a high percentage of ventricular pacing	IIa	B	B	II
CRT should be considered for patients who meet all of the following criteria: 1. Receiving optimal medical therapy 2. LVEF ≤35% 3. Developing HF and having a high percentage of RV pacing after implantation of a pacemaker or an ICD	IIa	B	C1	IVa
NYHA class II				
CRT should be considered for patients who meet all of the following criteria: 1. Receiving optimal medical therapy 2. LVEF ≤50% 3. Indicated for pacing or ICD 4. Expected to require a high percentage of ventricular pacing	IIa	B	B	II
CRT should be considered for patients who meet all of the following criteria: 1. Receiving optimal medical therapy 2. LVEF ≤35% 3. Developing HF and having a high percentage of RV pacing after implantation of a pacemaker or an ICD	IIa	B	C1	IVa
NYHA class I				
CRT may be considered for patients who meet all of the following criteria: 1. Receiving optimal medical therapy 2. LVEF ≤ 50% 3. Indicated for pacing or ICD 4. Expected to require a high percentage of ventricular pacing	IIb	B	B	II

Abbreviations: COR, class of recommendation; CRT, cardiac resynchronization therapy; GOR, grade of recommendation; HF, heart failure; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; RV, right ventricular.
[Correction added on 29 June, after first online publication: '2. LVEF < 50%' under 'NYHA class I' has been amended to '2. LVEF ≤ 50%'.]

TABLE 36 Recommendations and evidence levels for CRT in patients with AF

NYHA class III–IV	COR	LOE	GOR (MINDS)	LOE (MINDS)
CRT should be considered for patients who meet all of the following criteria: 1. Receiving optimal medical therapy 2. LVEF ≤35% 3. LBBB with QRS duration ≥120 ms or non-LBBB with QRS duration ≥150 ms 4. Expected to achieve a high percentage of biventricular pacing during AF	IIa	B	B	II
It should be considered for AF patients to receive a strategy to ensure the highest achievable percentage of biventricular pacing, preferably near 100%	IIa	B	B	IVa
CRT may be considered for patients with reduced LV systolic function in whom AV node catheter ablation is required to control heart rate	IIb	B	B	II

Abbreviations: AF, atrial fibrillation; AV, atrioventricular; COR, class of recommendation; CRT, cardiac resynchronization therapy; GOR, grade of recommendation; LBBB, left bundle branch block; LOE, level of evidence; LVEF, left ventricular ejection fraction.
[Correction added on 29 June, after first online publication: '3. LBBB with QRS duration ≥150 ms or …' under 'NYHA class III–IV' has been amended to '3. LBBB with QRS duration ≥120 ms or …'.]

5.1.4 | Summary of CRT indications

Table 37 lists the classes of recommendation and associated conditions for CRT indication.

5.2 | CRT-D

A meta-analysis of RCTs on CRT was published in 2006, and showed that CRT significantly suppressed death from HF but did not prevent sudden cardiac death.[393] However, a subsequently published long-term follow-up of CARE-HF (comparing the effect of CRT with pharmacotherapy) showed that CRT significantly reduced HF deaths by 45% and sudden deaths by 46%. This suggests that CRT not equipped with ICD may also have a protective effect against sudden death.[394]

CRT-D has the function of terminating life-threatening arrhythmias with electrotherapy and may further reduce the risk of sudden death in patients with CRT.[197,198,200,205] In COMPANION, a prospective study of HF patients with QRS width ≥120 ms and NYHA class III–IV, the sudden cardiac death rate (per 100 persons per year) was 5.9 and 2.2 in the CRT and CRT-D groups, respectively.[216] Furthermore, in a prospective enrollment and observational study at 4 European institutions, CRT-D reduced sudden cardiac death by 96% ($P < .002$) compared with CRT.[395]

Thus, CRT-D may be more effective than CRT from the perspective of preventing sudden cardiac death; however, it must be noted that no significant difference in total mortality has been observed between the 2 devices in any clinical trial.[216,395] A Danish study that prospectively evaluated the efficacy of ICDs in patients with non-ischemic HF did not find a significant difference in total mortality between groups.[213] Therefore, cost-effectiveness should be duly taken into account when considering the indications for expensive CRT-D. According to European guidelines, CRT-D is indicated if good physical function can be expected for ≥1 year.[368] It is necessary to select the type of CRT after considering the necessity of ICD function, the patient's status, and the patient's condition (age, sex, severity of HF, life expectancy, ischemia, renal function, comorbidities, frailty, etc) for cases indicated for CRT.

5.3 | CRT/CRT-D using epicardial electrodes

The transvenous approach is the standard method for left ventricular lead placement in adult patients undergoing CRT. However, there have been cases of unsuccessful left ventricular lead placement with the transvenous approach because of coronary sinus anatomy, phrenic nerve stimulation, high pacing thresholds, and lead instability within the coronary sinus.[396,397] In the early 2000s, unsuccessful placements occurred in about 10% of cases;[396,397] however, the recent advent of new devices, such as cardiac vein access devices (various guiding sheaths, guidewires) and left ventricular leads (over the wire, quadrupoles), has reduced the unsuccessful rate of left ventricular lead placement to around 2%–3%.[398]

However, this method has not completely eliminated unsuccessful placement, and an epicardial approach has been considered for placement of the left ventricular lead. The epicardial method is also useful in CRT for children.[399] Several reports have concluded that the transvenous and epicardial approaches have similar effects of improving cardiac function with CRT.[400-403]

Placement of epicardial electrodes requires a surgical procedure, including the standard left thoracotomy, thoracotomy with a small incision as a minimally invasive method,[404] and thoracoscopic methods.[405,406] There are no major issues in the technical safety of placement of the epicardial electrodes,[404-406] and it has been reported that there are no problems with the performance and durability of epicardial leads.[405] However, it is necessary to consider the risk of general anesthesia. It is assumed that the effect of epicardial CRT on cardiac function is the same as that of transvenous CRT. The advantage of epicardial electrode placement is that electrodes can be placed at optimal sites regardless of the location of the coronary veins, and the myocardial properties of the pacing site and the fixation of the electrodes can be visually confirmed.[407] If a patient is receiving CRT while undergoing other cardiac surgery, epicardial electrode placement may be considered after ascertaining the location of the coronary veins.

TABLE 37 Summary of recommendations for CRT

NYHA class	Optimal medical therapy	LVEF (%)	QRS morphology	QRS duration (ms)	Rhythm	COR
III–IV	o	≤35	LBBB	≥120	SR	I
	o	≤35	Non-LBBB	≥150	SR	IIa
	o	≤35	Non-LBBB	120-149	SR	IIb
II	o	≤30	LBBB	≥150	SR	I
	o	≤30	Non-LBBB	≥150	SR	IIa
	o	≤30	LBBB	120-149	SR	IIa
	o	≤30	Non-LBBB	120-149	SR	IIb
III–IV	o	≤35	LBBB	≥120	AF	IIa*
	o	≤35	Non-LBBB	≥150	AF	IIa*
I–IV	Patients who have limited physical activity due to chronic disease, or with life expectancy ≤12 months					III

*Expected to achieve high percentage of biventricular pacing.

Abbreviations: AF, atrial fibrillation; COR, class of recommendation; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SR, sinus rhythm.

[Correction added on 22 June, after first online publication: 'QRS morphology' column has been amended with correct information.]

6 | Transcutaneous lead extraction

Lead extraction is considered an important treatment for infections and other complications of implantable cardiac electrical devices. Procedures include percutaneous lead extraction using devices such as snares and sheaths, as well as surgical lead extraction through thoracotomy and open-heart surgery.[408,409] In the USA and Europe, percutaneous lead removal devices have been used since the 1990s. However, in Japan, devices have been approved for insurance coverage at different times: the excimer laser sheath (Philips) in 2010, lead locking device (Philips) in 2011, mechanical sheath snare (Cook Medical) in 2015, and the Rotation Dilator Sheath Set (Cook Medical) in 2018. The medical fees for percutaneous lead extraction procedures were newly established in 2012. Japan has a time lag of >10 years compared with Europe and the USA. However, these devices have gradually become widely used, and the number of facilities and patients are increasing.

The indications for lead extraction are broadly classified as infectious or non-infectious (Tables 38,39).[50,51,410,411] With infectious indications, it is generally recommended to remove the entire device system. With non-infectious indications, the recommendation varies depending on the pathology. Indications should not be determined solely based on the pathology; rather, it is necessary to consider factors such as the patient's age, body size, comorbidities, number of years with the lead in place, number of leads, type of lead, and preference, as well as the operator's experience. When determining the indication, it is necessary to compare the risk of extraction with the risk of no extraction. If the risk of no extraction is high, it is possible to perform the operation in any situation; thus, the class of recommendation III (grade C2, D) is not set.

Percutaneous lead extraction procedures include simple traction, whereby the lead is removed by simply pulling it out; insertion of a lead locking device into the lead (stylet lumen) followed by traction; and use of a special sheath to detach adhesions between the lead and blood vessels and the heart. The types of sheaths include mechanical sheaths (stainless steel, polypropylene, polytetrafluoroethylene) with a simple telescope structure, laser sheaths that can emit an excimer laser from the tip, and sheaths that rotate like a drill at the tip. These methods are used when extracting the lead from the implantation site. When extracting the entire lead or a part of a broken lead from the femoral vein, internal jugular vein, or locations other than the device implantation site, a snare that grips the lead is used.

It is desirable to use these various medical devices for lead extraction based on their characteristics and features, and the medical economic aspects (price of single-use medical devices and excimer laser generators, as well as procedure fees). However, in Japan, because cutting-edge and high-cost laser sheath removal has been introduced ahead of other procedures, it is favour to use. When the introduction of medical equipment for lead extraction is completed and has reached the levels of practice in the USA and Europe, it will be necessary to reconsider the selection of extraction methods.

In addition to hemorrhagic complications such as cardiac tamponade, hemothorax, and wound bleeding, serious complications can occur during lead extraction, including cardiac injury, valve injury, arrhythmias (such as atrioventricular block, VT, and VF), and embolism (thrombus, air embolism, infectious cardiac vegetation, and lead fragments). Emergency surgery may be required, especially when hemorrhagic complications occur; thus, a cardiovascular surgeon's support is needed. The clinical results (success rate,

TABLE 38 Recommendations and evidence levels for patients with infection of CIED system

	COR	LOE	GOR (MINDS)	LOE (MINDS)
Complete device and lead removal is recommended for all patients with valvular endocarditis without definite involvement of the lead and/or device	I	B	B	III
Complete device and lead removal is recommended for all patients with definite CIED system infection. Complete device and lead removal for all patients with valvular endocarditis without definite involvement of the lead and/or device	I	B	B	III
Complete device and lead removal is recommended for patients with persistent or recurrent bacteremia or fungemia, despite appropriate antibiotic therapy and no other identifiable source for relapse or continued infection	I	B	B	III

In the JCS guideline on infective endocarditis,[410] part of the recommendation level is inconsistent with that in this guideline, because the recommendations for surgical removal and cardiac vegetation are described in the JCS guideline on infective endocarditis.

Abbreviations: CIED, cardiac implantable electronic device; COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence.

TABLE 39 Recommendations and evidence levels for patients without infection of CIED system

		COR	LOE	GOR (MINDS)	LOE (MINDS)
A. Chronic pain	Device and/or lead removal should be considered for patients with severe chronic pain at the device or lead insertion site, or believed to be secondary to the device, which causes significant patient discomfort, is not manageable by medical or surgical techniques, and for which there is no acceptable alternative.	IIa	C	C1	VI
B. Thrombosis/ vascular issues	Lead removal is recommended for patients with clinically significant thromboembolic events attributable to thrombus on a lead or a lead fragment that cannot be treated by other means	I	C	C1	VI
	Lead removal is recommended for patients with SVC stenosis or occlusion that prevents implantation of a necessary lead.	I	C	C1	VI
	Lead removal is recommended as part of a comprehensive plan for maintaining patency for patients with SVC stenosis or occlusion with limiting symptoms	I	C	C1	VI
	Lead removal is recommended for patients with planned stent deployment in a vein already containing a transvenous lead, to avoid entrapment of the lead	I	C	C1	VI
	Lead removal should be considered for patients with ipsilateral venous occlusion preventing access to the venous circulation for required placement of an additional lead	IIa	C	C1	V
C. Other	Lead removal is recommended for patients with life-threatening arrhythmias secondary to retained leads	I	C	C1	VI
	Lead removal should be considered for patients with a CIED location that interferes with the treatment of a malignancy	IIa	C	C1	VI
	Lead removal should be considered for patients if CIED implantation would require >4 leads on one side or >5 leads through the SVC	IIa	C	C1	V
	Lead removal should be considered for patients with an abandoned lead that interferes with the operation of a CIED system	IIa	C	C1	VI
	Lead removal should be considered for patients to facilitate access to MRI*	IIa	C	C1	VI
	Lead removal may be considered for patients with leads that due to their design or their failure pose a potential future threat to the patient if left in place	IIb	C	C1	V
	Lead removal may be considered in the setting of normally functioning non-recalled pacing or defibrillation leads for selected patients after a shared decision-making process	IIb	C	C1	VI

*Recommendation level to facilitate access to MRI has been demoted to class IIb indication in the Heart Rhythm Society expert consensus in 2017. This decision was based on recently established methods[411] and safety[50,51] to obtain MRI imaging with MRI non-conditional devices. However, in this guideline, we still recommend class IIa because general consensus has not been obtained in Japan.

Abbreviations: CIED, cardiac implantable electronic device; COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence; SVC, superior vena cava.

complications, etc.) in the USA and Europe have been reported in the LExICON (Lead Extraction in the Contemporary Setting)[412] and ELECTRa (European Lead Extraction Controlled Registry)[413] studies, respectively.

The physician and institutional requirements for performing lead extraction procedures are set forth in the Japanese Heart Rhythm Society Statement. The Guidelines for Prevention and Treatment of Infective Endocarditis (2017 revision)[410] also include descriptions of the same pathological conditions as in this guideline with respect to lead extraction, although some classes of recommendation differ between the guidelines, because the Guidelines for Prevention and Treatment of Infective Endocarditis also consider surgical removal procedures and cardiac vegetation.

7 | CIEDs in children and patients with congenital heart disease

7.1 | Pacemakers in children and patients with congenital heart disease

The indications for pediatric pacemakers are (1) symptomatic sinus bradycardia, (2) bradycardia–tachycardia syndrome, and (3) advanced or complete AV block. The pediatric pacemaker indications for these arrhythmias are similar to those for adults; however, there are problems specific to children and patients with congenital heart disease: (1) in children, the criteria for bradycardia vary with age; (2) it is necessary to set the heart rate and AV interval according to each

individual in patients with congenital heart disease;[415,416] (3) transvenous endocardial lead implantation is sometimes difficult in small infants and patients with congenital heart disease for whom access to the heart from the vein is anatomically difficult, so it is necessary to consider transthoracic epicardial leads; and (4) most of the levels of evidence are C because RCTs have not been performed for children and patients with congenital heart disease.

In general, symptomatic bradycardia (heart rate ≤40 beats/min or cardiac arrest for ≥3 s) is an indication for pacemaker implantation.[118,130,417] Reports indicate that sinus dysfunction as a complication of sustained or atrial reentrant atrial tachycardia in congenital heart disease has a high mortality rate,[418,419] and long-term atrial pacing and atrial antitachycardia pacing have been reported to be effective in preventing and terminating atrial reentrant tachycardia.[420,421] Catheter ablation[422] and surgery[423] should be considered in cases in which circulatory and arrhythmic improvements can be expected.

Although it is difficult to determine the pacemaker indications for asymptomatic complete congenital AV block, indications should be considered in reference to the mean heart rate, cardiac arrest time, complex cardiac malformations, QT time, exercise tolerance, and other factors.[424-426] Although some studies have found that implanting a pacemaker in asymptomatic patients with congenital complete AV block is effective in improving long-term survival and preventing syncope,[427,428] there have also been reports of autoimmune myocardial damage after pacemaker implantation and heart failure due to pacemaker-induced cardiac dyssynchrony;[429-432] therefore, follow-up evaluation of cardiac function is important.

Complete AV block after surgery for congenital heart disease is known to have a poor prognosis,[433] and cases of advanced AV block that are unlikely to recover or cases of complete AV block are assigned to class I recommendation.[434] Transient perioperative AV block has been reported to progress to complete AV block several years or decades later, and may increase the risk of sudden death.[435-437] Moreover, if progressive PR prolongation occurs with a bifascicular block, it can progress to advanced or complete AV block,[438] and patients with intermittent AV block and a history of unexplained syncope are considered to have class IIa recommendation.

It has been reported that right ventricular pacing affects left ventricular function in adults;[439] however, in children with congenital complete AV block, the pacing lead position is related to the subsequent pump function, contraction efficiency, and left ventricular synchrony, and reports have shown that positioning the pacing lead at the left ventricular apex or the left ventricular medial wall has a superior effect.[440] It has also been reported that the incidence of non-ischemic cardiomyopathy after the implantation of a pacemaker for congenital complete AV block depends on the pacing lead location, and left ventricular pacing does not cause non-ischemic cardiomyopathy.[432] On the basis of these findings, the left ventricular apex is considered the first choice when implanting an epicardial lead in a patient with AV block, and the right ventricular free wall should be avoided as much as possible.[441,442] The differences between transvenous endocardial leads and transthoracic epicardial leads are shown in Table 40.[442,444-456]

The recommendations for pacemaker implantation for pediatric and congenital heart disease according to the 2012 ACC Foundation (ACCF)/AHA/HRS Guidelines,[116] 2013 ESC Guidelines,[457] 2013 European Heart Rhythm Association (EHRA)/Association for

TABLE 40 Differences between transvenous endocardial leads and transthoracic epicardial leads

	Transvenous endocardial lead	Transthoracic epicardial lead
Applicable age	Depending on the institution >10-20 kg in Western countries[442] From newborn infants in several reports[445]	No limitation
Condition	Generally contraindicated in patients with intracardiac shunts[446] Feasible vascular access	No limitation
Venous obstruction	Possibility of venous obstruction or thromboemboli[447] Limitation of the number of implantable leads	None
Pacing site	Localized	Selectable
Implantation technique	Less invasive	More invasive
Lead durability (cumulative freedom from lead failure)	Better (adults 10 years: 96.6-99.9%[448], pediatric cardiology population 5 years: 84-89%[449,450])	Less (5 years: 34-95%[449-455])
Cause of lead failure	Insulation breaks, dislodgement[442]	Lead fracture, exit block[447]
MRI-conditional devices (As of November, 2017)	Available	Unavailable
Possibility of cardiac strangulation	None	Possible[456]

(Adapted from Miyazaki, 2014[444].)

European Paediatric and Congenital Cardiology (AEPC) Consensus Statement,[442] and 2014 American Pediatric and Congenital Electrophysiology Society (PACES)/HRS Expert Consensus Statement[458] are shown in Table 41.[114,116,118,130,416-418,421,424-430,433-436,438,442,446,459-464]

7.2 | ICDs in children and patients with congenital heart disease

ICDs are rarely indicated in children and patients with congenital heart disease, and most cases of ICD implantation are performed

TABLE 41 Recommendations and evidence levels for pacemaker implantation in children and patients with congenital heart disease

	COR	LOE	GOR (MINDS)	LOE (MINDS)
Permanent pacemaker implantation is recommended for patients with advanced 2nd- or 3rd-degree AVB associated with symptomatic bradycardia, ventricular dysfunction, or low cardiac output	I	C	A	VI
Permanent pacemaker implantation is recommended for patients with sinus node dysfunction with correlation of symptoms during age-inappropriate bradycardia including bradycardia–tachycardia syndrome (definition of bradycardia varies with the patient's age and expected heart rate). (Sinus node dysfunction due to secondary to antiarrhythmic drugs is included)	I	C	A	V
Permanent pacemaker implantation is recommended for patients with congenital 3rd-degree AVB with a wide QRS escape rhythm, complex ventricular ectopy, ventricular dysfunction, or prolongation of QTc	I	B	A	V
Permanent pacemaker implantation is recommended for patients with congenital 3rd-degree AVB in infants with a ventricular rate < 55 beats/min or with congenital heart disease and a ventricular rate < 70 beats/min	I	C	A	V
Permanent pacemaker implantation is recommended for patients with postoperative advanced 2nd- or 3rd-degree AVB that is not expected to resolve	I	C	A	V
Permanent pacemaker implantation should be considered for patients with congenital 3rd-degree AVB beyond the first year of life with an average heart rate ≤50 beats/min, abrupt pauses in ventricular rate that are 2- or 3-fold the basic cycle length, or associated with symptoms due to chronotropic incompetence	IIa	C	B	IVb
Permanent pacemaker implantation should be considered for patients with sinus bradycardia with complex congenital heart disease with a resting heart rate ≤40 beats/min or pauses in ventricular rate ≥3 s	IIa	C	B	VI
Permanent pacemaker implantation should be considered for patients with congenital heart disease and impaired hemodynamics due to sinus bradycardia or loss of AV synchrony	IIa	C	B	V
Permanent pacemaker implantation should be considered for patients with unexplained syncope in patients with prior congenital heart surgery complicated by transient AVB with residual fascicular block	IIa	B	B	IVb
Permanent pacemaker implantation may be considered for patients with transient postoperative 3rd-degree AVB that reverts to sinus rhythm with residual bifascicular block	IIb	C	C2	V
Permanent pacemaker implantation may be considered for patients with congenital 3rd-degree AVB in asymptomatic patients with an acceptable rate for the age, a narrow QRS complex, and normal ventricular function	IIb	B	C2	IVb
Permanent pacemaker implantation is not recommended for patients with transient postoperative AVB with return of normal AV conduction in otherwise asymptomatic patients	III	B	C2	V
Permanent pacemaker implantation is not recommended for patients with bifascicular block with or without 1st-degree AVB after surgery for congenital heart disease in the absence of prior transient complete AVB	III	C	C2	VI
Permanent pacemaker implantation is not recommended for patients with asymptomatic Wenckebach-type 2nd-degree AVB	III	C	C2	VI
Permanent pacemaker implantation is not recommended for patients with asymptomatic sinus bradycardia with the longest RR interval <3 s and a minimum heart rate ≥40 beats/min	III	C	C2	VI
Permanent pacemaker implantation is not recommended for patients with endocardial leads in patients with intracardiac shunts (risk assessment regarding hemodynamic circumstances, concomitant anticoagulation, shunt closure prior to endocardial lead placement, or alternative approaches for lead access should be individualized)	III	B	D	IVb

Abbreviations: AV, atrioventricular; AVB, atrioventricular block; COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence.

for the secondary prevention of sudden death.[465,466] This is because there are a few lethal arrhythmias associated with structural heart diseases such as ischemic heart disease, and there is limited venous access for implanting shock leads. Cardiomyopathy, channelopathies, congenital heart disease, and coronary artery anomaly are the main causes of sudden cardiac death in childhood, and arrhythmic deaths due to underlying diseases are common among these cardiac deaths.[260,467,468] Therefore, the number of cases of implantation of an ICD in a child who survives sudden cardiac death is expected to increase in the future.[467]

Various innovative methods for implanting shock leads have been reported for ICD implantation in small children and patients with congenital heart disease who have anatomically limited venous access for lead implantation.[469-471] S-ICDs, which became available in Japan in February 2016, are useful for patients who have limited venous access; however, as the S-ICD cannot perform bradycardia pacing, it is not suitable for conditions associated with bradycardia. It is also not suitable for small children and is indicated for children weighing at least 25-30 kg; however, there have been reports of S-ICD implantation in children weighing ≤25 kg.[472,473]

In children and patients with congenital heart disease, ICD implantation for the prevention of sudden death secondary to irreversible causes has class I recommendation.[474-478] The indications for ICD implantation for the primary prevention of sudden death in children with cardiomyopathy and channelopathy should follow the guidelines for each disease group.

Risk stratification of sudden death is difficult in congenital heart disease due to complex cardiovascular abnormalities and various condition before and after surgical corrections. Because of the difficulty in conducting RCTs, there is still much controversy over ICD indications for the primary prevention of sudden cardiac death.[116] Previous studies of sudden death after surgical correction of tetralogy of Fallot have identified left ventricular systolic or diastolic dysfunction, NSVT, QRS duration ≥180 ms, extensive right ventricular scarring, and sustained ventricular arrhythmias inducible in electrophysiological study as risk factors for ventricular arrhythmia and sudden death.[479-485] However, in Japan, the incidence of sudden death with tetralogy of Fallot is lower than in Europe and the USA.[486,487] In this guideline, cases with ≥3 of these risk factors are assigned class of recommendation of IIa (Table 42).[116,446,474-485,488-497]

TABLE 42 Recommendations and evidence levels for ICD in children and patients with congenital heart disease

	COR	LOE	GOR (MINDS)	LOE (MINDS)
ICD is recommended for patients with survivors of cardiac arrest due to VF or hemodynamically unstable VT with irreversible cause	I	B	A	IVa
ICD is recommended for patients with symptomatic sustained VT in patients with congenital heart disease (catheter ablation or surgical repair may offer a possible alternative in carefully selected patients)	I	B	A	IVa
ICD should be considered for patients with recurrent syncope of undetermined origin in patients with congenital heart disease, and the presence of either ventricular dysfunction with systemic ventricular ejection fraction ≤35% or inducible ventricular arrhythmias in electrophysiological study	IIa	B	B	IVa
ICD should be considered for patients with repaired tetralogy of Fallot and >3 risk factors for sudden cardiac death (left ventricular systolic or diastolic dysfunction, NSVT, QRS duration ≥180 ms, extensive right ventricular scarring, or inducible sustained ventricular arrhythmias in electrophysiological study)	IIa	B	B	IVb
ICD should be considered for patients with congenital heart disease, and ventricular dysfunction with systemic ventricular ejection fraction ≤35%, NSVT, and NYHA class II or III symptoms	IIa	C	C1	IVb
ICD may be considered for patients after surgical revascularization for an anomalous origin of the coronary artery with a history of VF[497]	IIb	C	C1	V
ICD is not recommended for patients with a predicted life expectancy ≤12 months	III	C	C2	VI
ICD is not recommended for patients who do not give consent or cannot cooperate with treatment because of significant psychiatric illness or other causes	III	C	C2	VI
ICD is not recommended for patients with VT or VF due to an obvious acute cause (eg, acute ischemia, electrolyte imbalance, or drugs) that is determined to be preventable by treating the cause	III	C	C2	VI
ICD is not recommended for patients with frequent VT or VF that is uncontrollable with antiarrhythmic medications or catheter ablation	III	C	C2	VI
ICD is not recommended for NYHA class IV patients with drug-refractory congestive heart failure who are not candidates for cardiac transplantation, CRT, or insertion of a LVAD	III	C	C2	VI
ICD is not recommended for patients with endocardial leads in patients with intracardiac shunts (risk assessment with respect to hemodynamic circumstances, concomitant anticoagulation, shunt closure before endocardial lead placement, or alternative approaches for lead access should be individualized)	III	B	D	IVb

Abbreviations: COR, class of recommendation; CRT, cardiac resynchronization therapy; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence, LVAD, left ventricular assist device; NSVT, nonsustained ventricular tachycardia; NYHA, New York Heart Association; VF, ventricular fibrillation; VT, ventricular tachycardia.

The ICD implantation guidelines for children and patients with congenital heart disease are described according to the 2012 ACCF/AHA/HRS Guidelines,[116] 2013 EHRA/AEPC Consensus Statement,[442] and 2014 PACES/HRS Expert Consensus Statement[458] (Table 42).

7.3 | CRT/CRT-D in children and patients with congenital heart disease

The indications for CRT in children without congenital heart disease are similar to those for CRT in adults. In a multicenter study in the field of pediatric cardiology, including congenital heart disease, non-ischemic cardiomyopathy in children was reported as a risk factor for CRT non-response.[498] However, pediatric non-ischemic cardiomyopathy rarely presents with left bundle branch block, which is presumed to be a possible cause of CRT non-response.[499]

CRT for patients with congenital heart disease significantly differs from that for adults, because of the diverse ventricular morphology found in this condition. The systemic ventricle is broadly divided into the left ventricle, right ventricle, and single ventricle (single ventricle physiology).[498,500-506] In addition, subpulmonary ventricular dyssynchrony must also be considered.[507-511] A pattern of intraventricular dyssynchrony is observed in the systemic right ventricle or single ventricle physiology, which differs from that of the systemic left ventricle.[506] Moreover, interventricular dyssynchrony in hemodynamics specific to congenital heart disease cannot be ignored.[505] As in primary prevention with an ICD, it is difficult to determine the effect with RCTs because the condition is associated with a wide variety of cardiovascular abnormalities in the heart structure. Therefore, the indications must be decided with consideration of the anatomy and ventricular dyssynchrony patterns found in individual patients.

As there are very few reports on ICDs (CRT-D) with biventricular pacing for children and patients with congenital heart disease, this guideline does not include a description.

The CRT implantation guidelines for patients with congenital heart disease are described on the basis of the 2014 PACES/HRS Expert Consensus Statement[458] (Table 43).[116,349,355,432,440,441,498,500-516]

TABLE 43 Recommendations and evidence levels for CRT in children and patients with congenital heart disease

	COR	LOE	GOR (MINDS)	LOE (MINDS)
CRT is recommended for patients with a systemic left ventricle, NYHA class II–IV symptoms, systemic LVEF ≤35%, complete left bundle branch block with QRS duration ≥ 120 ms, and sinus rhythm	I	B	A	II
CRT should be considered for patients with a systemic right ventricle, NYHA class II–IV symptoms, systemic right ventricular ejection fraction ≤35%, right ventricular dilatation, and complete right bundle branch block with QRS duration ≥120 ms	IIa	C	B	IVb
CRT should be considered for patients with congenital heart disease, NYHA class I–IV symptoms, systemic ventricular ejection fraction ≤35%, and an intrinsically narrow QRS complex in those undergoing new or replacement device implantation with anticipated requirement for ventricular pacing ≥40% (single-site pacing from the systemic ventricular apex/mid-lateral wall can be considered an alternative)	IIa	C	C1	IVb
CRT should be considered for patients with a single ventricular physiology, NYHA class II–IV symptoms, systemic ventricular ejection fraction ≤35%, ventricular dilatation, and QRS duration ≥120 ms due to intraventricular conduction delay that produces a complete RBBB or LBBB morphology	IIa	C	B	IVb
CRT may be considered for patients with congenital heart disease, NYHA class I–IV symptoms, systemic ventricular ejection fraction ≥35%, and an intrinsically narrow QRS complex in those undergoing new or replacement device implantation with anticipated requirement for ventricular pacing ≥40% (single-site pacing from the systemic ventricular apex/mid-lateral wall can be considered an alternative)	IIb	C	C2	IVb
CRT may be considered for patients undergoing cardiac surgery with NYHA class I–IV symptoms, QRS duration ≥120 ms, complete bundle branch block morphology ipsilateral to the systemic ventricle, and progressive systolic ventricular dysfunction and/or dilatation (especially if epicardial access is required to implement CRT)	IIb	B	C1	IVb
CRT may be considered for patients with a systemic right ventricle undergoing cardiac surgery for tricuspid valve regurgitation with NYHA class I–IV symptoms, QRS duration ≥120 ms, and complete RBBB	IIb	B	C1	IVb
CRT may be considered for patients with congenital heart disease with severe subpulmonary right ventricular dilatation and dysfunction, NYHA class II–IV symptoms, and complete RBBB with QRS duration ≥150 ms	IIb	C	C2	V
CRT may be considered for patients with NYHA class IV symptoms and severe systemic ventricular dysfunction, in an attempt to delay or prevent cardiac transplantation or mechanical support	IIb	C	C1	VI
CRT is not recommended for patients whose comorbidities and/or frailty limit survival with good functional capacity to <1 year	III	C	C2	VI

Abbreviations: COR, class of recommendation; CRT, cardiac resynchronization therapy; GOR, grade of recommendation; LBBB, left bundle branch block; LOE, level of evidence; NYHA, New York Heart Association; RBBB, right bundle branch block.

8 | Implantable cardiac monitor (ICM)

The ICM was first covered by medical insurance in Japan in October 2009 for patients with unexplained syncope and in September 2016 for the detection of AF in patients diagnosed with cryptogenic stroke. This device is an electrocardiograph that is inserted under the chest wall skin and has a battery life of about 2-3 years. It is an extremely useful tool for identifying the causative disease because it can capture ECG findings at the onset of syncope and that of AF that causes cryptogenic stroke. The event is recorded by the patient or a third person when symptoms appear, and the ECG is saved for several minutes before the event. Further, when a preset heart rate abnormality (eg, bradycardia, cardiac arrest, tachycardia, or AF) occurs, the ECG is automatically saved, enabling remote monitoring.

In a previous study, an ICM was used in 506 patients in whom the cause of syncope could not be identified after various examinations, and an ECG at syncope with an ICM was obtained in 176 of the patients (35%).[517] Of these, cardiac arrest was recorded in 56% and tachycardia was recorded in 11%; however, arrhythmia was not observed in the remaining 33%. In other words, the ICM can diagnose around two-thirds of syncope cases that remain unexplained even after performing other examinations. In addition, the ICM is particularly useful for diagnosing the cause of recurrent syncope in patients with irregular or relatively rare episodes.[60] However, previous studies have shown that the association between presyncopal symptoms and arrhythmias is relatively weak. The use of an ICM, therefore, is not currently recommended in patients with pre-syncopal symptoms only.[63,518]

Noninvasive ambulatory ECG monitoring for a 30-day event-triggered recorder significantly improved the detection of atrial fibrillation in patients who had a recent cryptogenic stroke or transient ischemic attack (TIA) and were ≥55 years of age, as compared with those detected with the conventional Holter ECG (EMBRACE [30-Day Cardiac Event Monitor Belt for Recording Atrial Fibrillation After a Cerebral Ischemic Event] trial).[519] In addition, a study of patients aged ≥40 years with unexplained cerebral infarction or TIA occurring within 90 days showed that the AF detection rate was significantly higher over the long term in the ICM group than in the conventional standard ECG group, including Holter ECG (CRYSTAL AF [Cryotogenic Stroke and Underlying Atrial Fibrillation] study).[520] It has also been reported that the diagnosis rate with extracorporeal loop-type long-term ECGs for the causes of transient loss of consciousness, including syncope, is rather high.[521] Therefore, it is recommended that the extracorporeal procedure is performed at least once before ICM insertion.[60] The recommendations are shown in Table 44.

9 | Wearable cardioverter-defibrillator

Although the usefulness of ICD in the primary prevention of sudden cardiac death is widely recognized,[197,198] the management of acute cases, in which the usefulness of ICD has not been proven, presents a challenge. It has been suggested that many life-threatening arrhythmia events occur soon after acute ischemia or heart failure;[522] however, the application of ICD in the acute stage has not been shown to improve the life prognosis.[206,523] Therefore, the world's leading guidelines limit the use of ICDs for primary prevention of sudden death to post-subacute cases.[310,368,524]

The WCD is a medical device with contact-type ECG electrodes and a defibrillation pad inside a wearable vest, and defibrillation is

TABLE 44 Recommendations and evidence levels for ICM indications

	COR	LOE	GOR (MINDS)	LOE (MINDS)
1. Early use of an ICM is recommended in patients with recurrent, infrequent, unexplained syncope but without high-risk factors* and without non-cardiac causes such as reflex syncope or orthostatic hypotension 2. Use of an ICM is recommended in patients with high-risk factors* but without an identified cause or a therapy for syncope after several evaluations 3. Use of an ICM is recommended for the detection of silent AF in patients with an unknown cause of cryptogenic stroke even after the use of Holter monitoring or external loop recorders	I	B	B	II
Use of an ICM should be considered to determine the indication of cardiac pacing therapy in patients with suspected reflex syncope combined with frequent recurrence and/or injury	IIa	C	C1	IVb

*High-risk factors suggesting a cardiogenic cause are listed in Table 17.

Abbreviations: AF, atrial fibrillation; COR, class of recommendation; GOR, grade of recommendation; ICM, implantable cardiac monitor; LOE, level of evidence.

automatically triggered when a life-threatening arrhythmia is detected by a wired controller. Although it is a relatively simple system that performs all procedures from the body surface, it has been shown to have diagnostic sensitivity and specificity comparable to those of ICDs.[193,195,211,525-527] WCDs became covered by insurance in Japan in January 2014, and physicians are steadily accumulating clinical experience.[193,195,528,529]

Because this device is non-invasive, the decision on its application or discontinuation can be easily and quickly made; therefore, it plays the role of a bridge therapy until the necessity of ICD therapy can be determined, regardless of the stability or cause of the underlying disease (ischemic or non-ischemic). The recommendations are shown in Table 45.

As there is a high risk of life-threatening arrhythmias soon after acute ischemia and acute heart failure,[522] a WCD is used to prevent sudden death until the indication for primary prevention with an ICD is confirmed.[211,525,527,530] In WEARIT-II (Prospective Registry of Patients Using the Wearable Defibrillator), the appropriate therapy rate during the observation period was higher than that reported in the MADIT-RIT (MADIT-Reduce Inappropriate Therapy) trial.[531] The percentage of cases judged to be indicated for an ICD after the observation period is 55%–68%.[211,525,527,531] Thus, it can be expected to appropriately prevent sudden death and may also prevent excessive ICD use. The use of WCDs has been reported to reduce the incidence of sudden death by 5%–15% also in patients with coronary angioplasty or coronary artery bypass graft surgery, and is especially effective in patients with left ventricular dysfunction.[210,532] VEST (Vest Prevention of Early Sudden Death) was an investigator-initiated and the largest RCT, which enrolled 2,302 patients with acute myocardial infarction and LVEF ≤ 35%. It did not show a significant reduction in the primary endpoint (arrhythmic death) owing to the limited wearing time of the WCD group; however, the on-treatment analysis demonstrated an improvement in the total mortality rate in the wearing group (0.26/100 patients per month) versus the non-wearing group (1.91/100 patients per month).[533]

TABLE 45 Recommendations and evidence levels for WCD indications

	COR	LOE	GOR (MINDS)	LOE (MINDS)
WCD should be considered for patients within 40 days after the onset of acute myocardial infarction with LVEF ≤35% and heart failure symptoms of NYHA class II or III	IIa	B	B	III
WCD should be considered for patients with LVEF ≤35% and within 90 days after coronary artery bypass or percutaneous coronary intervention, and with NYHA class II or III heart failure symptoms	IIa	B	B	III
WCD should be considered for patients with LVEF ≤35% and within 90 days after the acute onset of heart failure due to a non-ischemic etiology	IIa	B	B	III
WCD should be considered for patients with irreversible severe heart failure satisfying a heart transplant standby condition	IIa	C	C1	IVa
WCD should be considered for patients in whom ICD is recommended but surgery cannot be performed immediately owing to other physical conditions	IIa	C	C1	IVa
WCD should be considered for patients in whom ICD is temporarily removed for any reason, such as infection	IIa	C	C1	IVa
WCD may be considered for patients in whom ICD is recommended for secondary prevention of cardiac sudden death but priority is given to the determination of the effect of clinical follow-up and preventive treatment	IIb	C	C1	IVb
WCD may be considered for hospitalized patients who have a moderate or higher risk of life-threatening arrhythmia but cannot receive adequate arrhythmia monitoring	IIb	C	C1	IVb

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; WCD, wearable cardioverter-defibrillator.

Reports on the use of WCDs for non-ischemic cardiomyopathy are limited; however, sudden death during the early phase after the onset of post-myocarditis cardiomyopathy, takotsubo cardiomyopathy, postpartum cardiomyopathy, and idiopathic dilated cardiomyopathy has been described. As 25%–42% of patients recover left ventricular function within 6 months, WCDs may be useful during the limited period when the risk of sudden death is temporarily high.[534-539] Patients awaiting a heart transplant are also at a high risk of sudden death and may be eligible for a WCD.[538-542]

A WCD is also effective in achieving both safe management and reduced hospital stay for patients who undergo device removal because of infection or in cases in which treatment of other diseases needs to be prioritized.[193,529,542] In Europe and the USA, WCDs are usually used only outside of hospitals.[211,525,527,531] However, a study in Japan showed that appropriate shock therapy from a WCD was effective in terminating life-threatening ventricular tachyarrhythmias in hospitalized patients with a moderate risk of sudden death. A WCD may be useful in any environment where arrhythmia cannot be fully monitored.[195] In Japan, WCDs are generally used for a short period (3 months); however, it is necessary to investigate the long-term use of WCDs for low-risk patients and patients who require long-term recovery of cardiac function.[530]

III | CATHETER ABLATION

1 | Overview

1.1 | History and changes in catheter ablation

Catheter ablation is a treatment whereby energy is applied from outside the body to the target myocardial tissue via a catheter, to ablate and destroy tissue. Its clinical application began in 1982 with the creation of a block using direct current (DC) at the atrioventricular junction. In 1983, a successful case of accessory pathway ablation was reported.[543-546] Thereafter, in 1987, radiofrequency (RF) catheter ablation was performed, targeted to the atrioventricular junction, and the origins of supraventricular tachycardia (SVT) and ventricular tachycardia (VT).[547-549]

In Japan, DC catheter ablation was introduced in 1983, and in 1990 the Japanese Association for Cardiac Pacing and Electrophysiology (currently the Japanese Heart Rhythm Society) established the Catheter Ablation Committee,[550] which continues its activities to this day. The use of RF catheter ablation began to spread rapidly in Japan in 1994 when it became covered by insurance as a percutaneous myocardial ablation procedure, and the initial success rate for many arrhythmias exceeded 90%.

Advances in arrhythmia research and the development of catheter equipment and peripheral medical devices have played an important role in the development of catheter ablation. Ablation catheters developed in the 1990s include steerable catheters with adjustable tip curves and large-tip catheters capable of forming large ablation lesions. In 2009, an irrigation catheter was introduced in Japan, which made it possible to supply stable power independently of the surrounding blood flow, enabling creation of deep myocardial lesions while preventing thrombus formation. In 2012, a function to check the contact status between the catheter tip and myocardium was developed, resulting in the performance of safe and effective ablation procedures.

A 3D mapping system was developed in the late 1990s as a peripheral device, which enabled treatment while visualizing the catheter in a 3D image fusing electrical phenomena and structural information of the heart (from computed tomography [CT], ultrasound, MRI, and radiographic scans).

In 1998, abnormal excitation originating from the PV was reported to trigger atrial fibrillation (AF),[551] which led to studies on catheter ablation for AF.[551,552] The PVI procedure was reported in 2000. Various ablation methods have been devised to date, and the treatment results have improved. An important point in catheter ablation of AF is reliable PVI, and a balloon technique specifically for that purpose has been developed. In Japan, cryoballoon therapy became available in 2014, and hot-balloon therapy started in 2016. Endoscopic laser irradiation of the PV orifice (laser irradiation endoscopic ablation system) was introduced in 2018.

Recently, there have been several reports on catheter ablation for idiopathic and hereditary ventricular fibrillation (VF)/polymorphic VT.[315,553,554] A technique for treating arrhythmias of epicardial origin by inserting the ablation catheter into the pericardial space via percutaneous puncture has also been applied clinically.[555]

More than 70,000 ablation procedures were performed in Japan in 2016, and there are now >600 ablation facilities.[6] Although the number of arrhythmia patients who can benefit from catheter ablation is increasing, it is important to prevent serious complications such as cardiac tamponade, cerebral infarction, and damage to organs adjacent to the heart. It is necessary to develop appropriate guidelines for performing safe and effective catheter ablation, and to provide the treatment teams with the necessary knowledge and skills to execute these procedures.

1.2 | Required knowledge, equipment, doctors, medical staff, and facility requirements for ablation

Diagnosing arrhythmia and determining the treatment site for catheter ablation are based on electrophysiological knowledge. Accurate use of the catheter is reliant on understanding the anatomy of the heart and the characteristics of the ablation method used, as well as on performing the procedure after setting the appropriate energy. Catheter ablation is an invasive treatment and has the risk of serious complications, albeit rare; therefore, it requires knowledge and skills to be able to respond appropriately in an emergency. Recently, more complex arrhythmias are often being treated using multiple medical devices. It is necessary to share knowledge and experience not only with doctors but also with medical staff teams.

1.2.1 | *Required knowledge and technology for ablation*

The knowledge and techniques required for ablation are summarized in Tables 46 and 47.

Knowledge of ablation indications and contraindications is essential. It is necessary to determine the indication for each patient in consideration of the risks and benefits after determining the expected success rate and risk of complications. The treatment site for ablation is determined on the basis of an accurate electrophysiological diagnosis. Following the induction of tachycardia, interpretation of intracardiac electrograms during tachycardia, identification of tachycardia mechanisms such as entrainment, and evaluation of 3D mapping are all required to determine the treatment site.

It is also necessary to understand how to use antiarrhythmic drugs before and after surgery, to understand their pharmacology, and to consider the types of drugs and the required doses.

Further, it is necessary to prepare for the procedure by referring to preoperative images and ascertaining the anatomy of each heart chamber and related blood vessels, in order to manipulate the catheter accurately and safely.

RF energy is the main source of ablation energy; however, cryoablation and laser have also been used in recent years. Each type of energy has its own characteristics, and the different methods must be used according to need.

AF ablation is now performed under sedation in about 90% of facilities.[556] Knowledge and skills related to sedatives and airway management are required to perform sedation safely, and it is desirable that practitioners attend training and educational seminars held by academic societies.

1.2.2 | *Required equipment for ablation*

The facilities required for ablation are shown in Table 48.

a. | *Angiography equipment*. Catheter ablation is performed in an angiography imaging room. Plumbing is required to supply oxygen and for suction, and an exhaust system is needed to handle excess nitrous oxide gas required for cryoablation. Radioactive protection (radioprotective glasses, curtains, shield operation box) is necessary to protect the health of the staff during ablation with long procedure times.

b. | *Diagnostic catheters*. Diagnostic catheters differ in shape, number of electrodes, and other features, depending on the application. There are also dedicated catheters for 3D mapping, and the available catheters differ depending on the system used.

c. | *Ablation catheters*. RF ablation catheters may be irrigated or non-irrigated. The length of the tip electrode in non-irrigated catheters is 4, 8, or 10 mm. Increasing the electrode length means

TABLE 46 Required knowledge for catheter ablation

Electrophysiology
Current indications and contraindications of EP study and catheter ablation
Electrophysiological characteristics of target arrhythmias
Interpretation of intracardiac recording
Maneuver to identify the arrhythmia mechanism, such as entrainment
How to use a 3D mapping system
Antiarrhythmic drugs
Catheter ablation
How to prevent specific complications
Anatomical characteristics of the target ablation area
Technical consideration of each ablation energy
How to use sedative agents
Prevention of radiation damage

Abbreviations: 3D, 3-dimensional; CA, catheter ablation; EPS, electrophysiological study.

TABLE 47 Required technical skills for catheter ablation

EP catheter insertion by the transvenous, transarterial, or epicardial approach
Careful manipulation of the EP catheter and knowledge of the optimal location to record intracardiac electrograms at each area
Knowledge of the initiation and termination of arrhythmias by program stimulation
Optimal selection of the 3D mapping system
Angiography of each site (coronary artery, pulmonary vein, coronary vein, sinus of Valsalva)
Complications and their management
Cardioversion and defibrillation
Antiarrhythmic drugs
Sedation and anesthetic agents
Pericardiocentesis
Transseptal approach
Energy source of each ablation
Intracardiac echocardiography

Abbreviation: 3D, 3-dimensional; EP, electrophysiology.

TABLE 48 Required equipment for EP testing

Fluoroscope
Electrode and ablation catheters
Generators of ablation energy
EP recording system
Stimulator
3D mapping system
Defibrillator and first-aid kit
Infusion pump
Analyzers of activated clotting time (ACT)
Monitors (SpO_2, esophageal temperature)
Drugs (antiarrhythmic drugs, first-aid drugs, sedative agents, analgesics)

Abbreviations: 3D, 3-dimensional; EP, electrophysiology.

that RF energy power can be applied at high output because of the cooling effect of blood flow; however, this records a wider range of potentials, making it difficult to evaluate minute potentials. A temperature control system is used in non-irrigated catheters, in which the output is automatically adjusted according to the tip temperature. The risk of steam pop (ie, rupture of tissue with steam) is considered to be lower than in irrigated catheter ablation; however, thrombus formation around the electrode in areas with poor blood flow can sometimes impede output, resulting in failure to create the necessary cautery lesion. There are reports suggesting that the incidence of thrombus formation is higher with non-irrigated catheters than with irrigated catheters.[557]

Irrigated catheters can be actively cooled by perfusing saline from the tip electrode, and can generate a stable output without depending on the blood flow around the electrode. However, this method has the danger of causing steam pops because the output increases in all situations.[558] Moreover, if the total volume of perfused saline is excessive, it creates concerns about heart failure in patients with low cardiac function.

Recently developed catheters are equipped with sensors that measure the contact pressure of the tip electrode on the tissue, and appropriate cauterization is possible with a contact pressure of ≥10 g. As the contact pressure fluctuates because of respiration and heart rate, the device uses an integrated value of time and force and an index that takes output into account in these variables. These adaptations are expected to be useful for the ablation effect and for preventing complications.

The cryoablation catheter absorbs heat from the surrounding tissue when liquefied nitrous oxide evaporates at the tip of the catheter, thereby cooling the tissue. Cryoablation catheter is currently used for atrioventricular nodal reentrant tachycardia (AVNRT) or as an additional treatment after cryoballoon therapy for AF.

d. | *Balloon catheters*. Balloon catheters with regulatory approval at present include the cryoballoon, hot balloon, and laser balloon for PVI. Each balloon has different characteristics, and it is necessary to indicate treatment based on knowledge of the differences of each type.

e. | *3D mapping systems*. The 3D mapping system plays a major role not only in the diagnosis of tachycardia circuits and mechanisms, but also in accurate understanding of the anatomy through integration with intracardiac echocardiography and cardiac CT. To evaluate the effectiveness of cauterization, an automatic mapping system has been devised, which can display a color image if appropriate contact is obtained and can automatically obtain hundreds of data within a few minutes.

f. | *Other equipment*. The potential recorder and stimulator are essential equipment. Blood pressure and SpO_2 monitors, as well as an esophageal temperature monitor, may also be important in preventing complications.

1.2.3 | *Required staff for ablation*

At present, ablation is performed not solely by a doctor, but also by a team of clinical engineers, laboratory technicians, clinical radiologists, and nurses. Each team member is required to have the necessary knowledge and skills; however, above all, it is important for all staff to be responsible for one patient. It is desirable that all staff observe changes in the patient's status, such as vital signs, in addition to monitoring the onset and duration of tachycardia.

a. | *Operator's experience*. The experience needed by an operator to perform ablation, as recommended by the EHRA, American College of Physicians, ACC, and AHA, is shown in Table 49.[559-561] The standards for obtaining certification as an arrhythmia specialist in the USA are set by the American Board of Internal Medicine. Those standards were considered in the creation of this guideline, and recommendations have been made as shown in Table 49. As clinical cardiac electrophysiology studies have recently been performed less frequently as stand-alone study, those were counted together with ablation.

1.2.4 | *Facility standards*

It is preferable for facilities implementing ablation to satisfy the conditions stipulated in Table 50.

1.3 | Informed consent

Informed consent corresponds to the provisions of Chapter 1, Article 1-4, Paragraph 2 of the Medical Care Act: "In the delivery of medical

TABLE 49 Minimum recommended procedure numbers and competence level for heart rhythm specialists during training for invasive techniques

	Training period, months	EPS*, n	Ablation, n	LA/AF, n
EHRA[4]	24	200	150	10
ACP/ACC/AHA[5]	12	100	50-75	NA
ABIM[6]	24	NA	160	50
This guideline	24	150	100	50

*Includes the number of ablation procedures.

Abbreviations: ACP/AHCC/AHA, American College of Physicians/American College of Cardiology/American Heart Association; AF, atrial fibrillation; EHRA, European Heart Rhythm Association; ABIM, American Board of Internal Medicine; EPS, electrophysiological study; LA, left atrium; NA, not applicable.

TABLE 50 Facility criteria

1. Department of Cardiology or Department of Pediatric Cardiology providing medical service under health-care insurance
2. At least one board-certificated electrophysiologist on a full-time basis
3. Department of Cardiac Surgery or collaboration with another facility performing cardiac surgery
4. A registered clinical engineer on a full-time basis

care, a physician, dentist, pharmacist, nurse, or other medical care professional shall give appropriate explanations and endeavor to foster understanding in the recipients of medical care." This means that the doctor may not unilaterally decide on the medical treatment (medication, procedures, tests, etc), but rather shall only provide medical care after explaining the following information to the patient and their family, for obtaining consent: (1) specific and easy-to-understand information on the disease name, pathology, and purpose and content of treatment; (2) details of medical treatment and associated risks; (3) expected results; (4) adverse reactions; (5) possible alternative medical treatments and details thereof; (6) expected results if the treatment in question is not implemented; (7) assurance that the patient will not be disadvantaged in any way if the testing or treatment is refused; (8) information that the patient has the right and opportunity to obtain a second opinion; and (9) information that consent can be withdrawn at any time. Medical treatment has to be patient-centric.

The targets of informed consent collection are the healthcare professionals involved in testing and treatment, and the patients and their families. This requires "explanation and understanding" and "consent" from the patient side. If the patient is unable to express his or her intentions or is a minor, a suitable representative, such as a family member or legal representative, may act on the patient's behalf. Ultimately, the signatures of all attendees (including those on the medical side) shall be obtained.

Catheter ablation is an invasive procedure and can cause various complications. It is important to provide sufficient information to patients and their families for this treatment. The typical complications include (1) thromboembolism; (2) cardiac tamponade; (3) vascular injury or coronary artery injury; (4) bleeding, hematoma, or arteriovenous fistula; (5) infection; (6) allergy; (7) radiation exposure; (8) bradycardia; (9) transient drop in blood pressure due to vasovagal reflex; (10) new arrhythmia; (11) damage to the teeth and mouth, or esophageal injury; and (12) others (including pneumonia, lung injury, pneumothorax, liver and/or kidney impairment, phrenic nerve paralysis, PV stenosis, esophageal disorders such as left atrioesophageal fistula, gastric peristalsis disorder, damage or dropping off of the embedded lead, and failure of the artificial valve or artificial patch).

There is no fixed form for obtaining informed consent; however, it is preferable to create a form at each facility, referencing the "Study on the Actual Conditions of Informed Consent Burden on Medical Professionals (IC Study)"[562] by the Social Insurance Union of Societies Related to Internal Medicine (Table 51).

TABLE 51 Necessary content of an informed consent form

1.	Patient's name, ID number
2.	Date of explanation
3.	Diagnosis
4.	Current condition of disease
5.	Purpose of ablation therapy
6.	Method of ablation therapy (eg, preparation for therapy, anesthesia and sedation, catheter insertion point, therapy method, therapy point, procedure time, hemostatic treatment, treatment after therapy, rest time)
7.	Benefit/therapeutic effect of ablation therapy
8.	Adverse effects/complications/aftereffects of ablation therapy and their management
9.	Progress without ablation therapy
10.	Alternative therapy
11.	Cost of ablation therapy
12.	Agreement for withdrawal
13.	Date of agreement
14.	Signature (patient or representative)
15.	Signature of attending or explaining physician, and hospital attendees

1.4 | Management, sedation, and pain relief during the procedure

Sedation and analgesia are performed to eliminate the patient's pain during catheter ablation and to perform the procedure safely and appropriately by maintaining a restful state. Stable sedation and analgesia increase both the patient's satisfaction and the success rate of the procedure, and are key points for preventing complications such as cardiac tamponade and air embolism.[563,564]

1.4.1 | Levels and methods of sedation to general anesthesia

Sedation and general anesthesia are classified into 4 stages, according to response to stimulation: (1) minimal sedation (anxiolysis), (2) moderate sedation (conscious sedation), (3) deep sedation, and (4) general anesthesia.[565] The responses are on a continuum, with no clear boundaries between the different stages. The deeper the sedation, the less pain the patient experiences, but the greater the risk of respiratory and circulatory suppression and airway obstruction. Therefore, a suitable depth of sedation must be selected based on the extent of pain during the procedure, duration of the procedure, and condition and wishes of the patient.

Reports indicate that PVI in AF ablation has a better success rate under general anesthesia than under conscious sedation.[563,564] Refer to the "Guidelines for the use of anesthetics and anesthetic-related drugs"[566] for the methods of use of each drug.

a. | Minimal sedation (anxiolysis). Minimal sedation is defined as a state in which cognitive and cooperative functions are suppressed but the patient can respond to verbal commands, and respiratory and cardiovascular functions are maintained.[565] Drugs such as diazepam and pentazocine are used.[575]

b. | Moderate sedation (conscious sedation). Moderate sedation is defined as a state in which consciousness is suppressed but the patient can respond purposefully to verbal instructions and light tactile stimuli. Respiratory and circulatory functions are maintained,

and host defense responses are not suppressed.[565] Drugs such as dexmedetomidine are used in combination with analgesics such as fentanyl and pentazocine, as appropriate.[566]

c. | Deep sedation. Deep sedation is defined as a state in which the patient is not easily roused but will ultimately respond to repeated pain stimuli. Circulatory function is maintained, but it is likely that the body's defense response and spontaneous respiration will be insufficient, and it will be necessary to maintain the airway.[565] Propofol and midazolam are used (not covered by insurance). Analgesics such as fentanyl are used as appropriate. Respiratory assistance, including airway and mask positive-pressure breathing, is required.[567]

d. | General anesthesia. Under general anesthesia, patients are not roused by pain stimuli, there is insufficient spontaneous respiration, airway management is often required, and circulatory function may be impaired.[565] Drugs such as propofol and fentanyl are used.[566] It is useful to secure the airway with a supraglottic device such as i-gel.[561]

1.4.2 | System for providing sedation

a. | Staff and hospital system. The physician performing the sedation must have education and training in the pharmacology of the drug being used for sedation. The physician must understand and be able to correctly use the appropriate doses, dosing intervals, and the respective antagonists, as well as understand the interactions between opioids and sedatives/anesthetics.[565] When performing deep sedation, one person other than the operator shall be assigned and dedicated to monitoring the patient. It is desirable to achieve consensus within the facility, including the anesthesiology department and medical safety department, with respect to the responsibilities and system for sedation, the aptitude of the physician performing the sedation, and the hospital protocol in the event of an emergency.

b. | Vital sign monitoring and recording. A pulse oximeter is attached to continuously monitor blood oxygenation. However, as it takes time for oxygen saturation to decrease because of apnea or hypoventilation, continuous monitoring of exhaled carbon dioxide with a capnometer is more useful for monitoring respiration. Blood pressure is measured at least every 5 min, and arterial pressure is continuously monitored as needed. The depth of sedation should be regularly evaluated using the Observer's Assessment of Alertness/Sedation scale,[568] which is an evaluation based on responses to voice prompts and physical stimuli. Bispectral index (BIS) monitors are useful for assessing the level of sedation. A BIS monitor specializes in analyzing the forehead EEG waveform and displays the sedation depth as a value from 0 to 100. The awake state is graded as 100. The lower the value, the deeper the sedation.[569]

The observed vital signs are recorded on a chart at appropriate intervals.

1.5 | X-ray exposure

X-ray exposure during catheter ablation has been significantly reduced owing to advances in mapping. Furthermore, knowledge of the effects of exposure and use of protective equipment enable low-exposure procedures. Exposure has always been a major problem for physicians; however, since 2013, when high rates of head and neck tumors in interventional cardiologists and radiologists were reported, there has been much interest in reducing radiation exposure.[570]

1.5.1 | Effect of exposure

Exposure has deterministic and stochastic effects (Figure 10).[571] For the deterministic effects, the severity of damage increases with the dose above a certain threshold, including skin and eye lens damage. Stochastic effects include carcinogenesis and chromosomal abnormalities, which have no threshold but have increasing incidence with increasing dose.[572] It is important to share knowledge about X-ray exposure among staff in the catheter laboratory.

1.5.2 | Exposure dose

The patient's exposure source is the X-ray tube, whereas the physician's exposure source is scattered radiation from the patient's body. Table 52 summarizes[573] the units of exposure dose and the measurement method, and Table 53 summarizes the factors affecting exposure.

1.5.3 | Perioperative precautions

Generally, a low pulse rate is used during ablation because fluoroscopy is mainly used. Therefore, there is little imaging, unlike with endovascular treatment in which catheter electrodes are used, which are easier to recognize than guidewires. Furthermore, less fluoroscopy is needed for catheter use and position confirmation with a 3D mapping system. However, fluoroscopy is often used with a fixed irradiation angle, and the same site is often irradiated continuously. Care must be taken because long-term irradiation in the left anterior oblique position may cause intensive exposure of the right subscapular region and the right arm.[573] Efforts should be made to remove

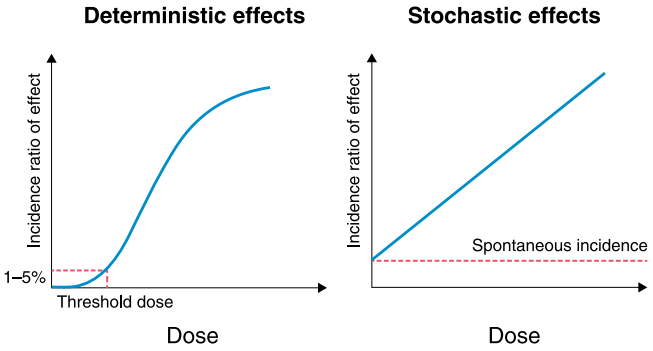


FIGURE 10 Deterministic and stochastic radiation risks. (From Japanese Circulation Society Joint Working Group, 2011[571] with permission.)

TABLE 52 Units and methods of measurement of radiation exposure

Terminology	Unit	Measurement
Equivalent dose	mSv	Allows estimation of the risk in tissue. Equivalent dose (H_T) is calculated by multiplying the absorbed dose to the tissue (D_T) with the radiation weighting factor (w_R). The w_R for X-ray is 1
Effective dose	Sv	Used to compare the stochastic risk of non-uniform exposure to radiation. It is calculated by multiplying the equivalent dose by a tissue weighting factor (Wt)
Dose area product or air kerma area product	Gy*cm^2	Measured or calculated by the X-ray system and yields the effective dose
Personal dose equivalent	mSv	Measured by the personal occupational dosimeter

The unit of medical radiation dose is Gy, the unit of the absorbed dose, whereas Sv is used for radioprotection doses. Gy = Sv can be considered for X-rays and γ-rays. (From Heidbuchel et al, 2014[573] with permission.)

TABLE 53 Factors affecting radiation exposure and effects thereof

Factor	Effect on radiation exposure
Pulse rate, frame rate	A lower pulse/frame rate decreases the radiation dose. As some fluoroscopic systems automatically increase the pulse width, knowledge of the settings and characteristics of the system is important
Body habitus of the patient	A 10-cm increment in thickness increases the incident dose 4-fold (both for the patient and the operator)
Distance between the image intensifier and the patient	A 10-cm distance increases the incident radiation by 15%
Distance between the X-ray tube and the patient	A 10-cm distance decreases the incident radiation by 13%
Collimation	Dose in a certain irradiated area remains the same, but a reduced area is desirable
Angle	The spinal cord and other cardiac tissues fall in between the heart in the left anterior oblique (LAO) projection, resulting in an increased dose
Device and lead	If the device is in the center of the field, the radiation dose increases
Arm in the field	If the arm is in the center, the radiation dose significantly increases, given the shorter distance. If it is not in the center, the distance to the arm still becomes short, thus increasing the radiation dose

(From Japanese Circulation Society, 2011[571] with permission.)

the upper arm from the irradiation field as much as possible, such as by using low-rate pulsed fluoroscopy and keeping the upper arm away from the trunk.

1.5.4 | Advances in 3D mapping systems

The frequently used CARTO® system (Biosense Webster) and EnSite NavX™ system (Abbott) display the strength and orientation of the contact together with the exact catheter position. Furthermore, displaying the images on a fluoroscopic image or cine taken in advance makes it is possible to manipulate the catheter in an environment similar to ordinary fluoroscopy (CARTO Univu™ module, Biosense Webster).[574] The MediGuide™ system (Abbott) can reproduce the captured fluoroscopic images at any time in line with the patient's heart rate, and a dedicated catheter can be displayed on the image, enabling catheter treatment with minimal fluoroscopy.[575]

1.5.5 | Awareness and efforts to reduce radiation exposure

Dosimeters are worn on the outside and inside of protective clothing. The outer part is attached to the head and neck to measure the exposure dose to the eye lens and head. The inside part is worn inside the protective clothing on the abdomen or chest. Protective clothing has lead equivalents of 0.25, 0.35, and 0.5 mm. The higher the lead equivalent, the higher the protective ability; however, there is no significant difference in shielding ability between the commonly used 0.25 and 0.35 mm.

Protective clothing has an expiration date. The clothing should be stored on hangers without being folded, and should not be sat on, to prevent adding excess stress on the material. It is also necessary to use fluoroscopy to regularly check if the covering sheet has been torn.

Table 54 summarizes the types of X-ray protective equipment.

1.6 | Complications and measures

Complications of catheter ablation include not only mechanical damage to nearby tissues, such as blood vessels, myocardium, esophageal tissues, and nerves, but also damage caused by radiation exposure and drugs. The former is described here.

1.6.1 | Outline

A survey in Japan in the early days of catheter ablation[576] revealed that pericardial effusion accounted for 79% of serious complications, followed by high-grade atrioventricular block at 15%. Although the incidence of complications varies according to the treated arrhythmia, there was a tendency for complications to increase at institutions treating a small number of cases.

Table 55 shows[577] the rates of complications and the treatment results for cases treated between 2008 and 2010, as tabulated by the Catheter Ablation Committee of the Japanese Heart Rhythm Society. Catheter ablation has a relatively high complication rate for some arrhythmias, and the complications remain the same in paroxysmal supraventricular tachycardia and atrial flutter (AFL), for which techniques are already established. Irreversible atrioventricular block requires the implantation of a permanent pacemaker, which is a complication of catheter ablation that particularly needs attention. It can occur during cauterization of some accessory pathways, although most cases occur during ablation of AVNRT.

Recently, asymptomatic cerebral embolism associated with left heart ablation has been attracting attention. It is known to occur at a high rate in AF ablation (Table 56);[578] however, it has been reported that new micro-cerebral infarction also occurs postoperatively in more than half of patients treated with left ventricular endocardial ablation for VT and premature ventricular contraction (PVC).[579] Therefore, awareness of this outcome is essential.

TABLE 54 X-ray protective devices

Shield type	Comment
Lead apron	Protects the body
Leaded glasses	Protects the face, especially the eyes
Thyroid collar	Protects the thyroid
Head protector	Light non-lead type protector (RadCap®) made of bismuth antimonide
Table-suspended drape	Protects the lower body of the operator. In the case of a left-sided device implant, it needs to be repositioned on the left side of the table
Lead flap above the table	Protects the operator's abdomen. It needs to overlap with the ceiling-suspended shield
Ceiling-suspended leaded plastic shield	Protects the operator's upper body
Radioprotection cabin	Protect the operator's whole body

TABLE 55 Number of sessions, complication rates, and acute success rates of ablation

	No. of sessions	Repeat sessions (%)	Complications (%)	Success (%)
Preexcitation (WPW, symptomatic)	614	67 (10.9)	8 (1.3)	94.6
Preexcitation (WPW, asymptomatic)	27	6 (22.2)	1 (3.7)	74.1
Preexcitation (others)	14	4 (28.6)	0 (0)	85.7
Concealed WPW	401	50 (12.5)	6 (1.5)	96.3
AVNRT	1412	130 (9.2)	24 (1.7)	98.4
SANRT	25	0 (0)	0 (0)	100
IST	7	2 (28.6)	0 (0)	100
PAC	26	6 (23.1)	1 (3.8)	88.5
AFL	1966	227 (11.5)	26 (1.3)	97.9
AT	538	97 (18)	12 (2.2)	77.3
Surgical scar-related AT/AFL	150	28 (18.7)	2 (1.3)	88
CA-related AT/AFL	67	45 (67.2)	3 (4.5)	86.6
AVJ	87	8 (9.2)	1 (1.1)	89.7
AF	2260	492 (21.8)	41 (1.8)	NA
PVC	309	46 (14.9)	3 (1.0)	78.6
nsVT	280	28 (10)	1 (0.3)	81.1
sVT	362	69 (19.1)	12 (3.3)	84
Total	8545	1305 (15.3)	141 (1.7)	NA

Abbreviations: AF, atrial fibrillation; AFL, atrial flutter; AT, atrial tachycardia; AVJ, atrioventricular junction; AVNRT, atrioventricular nodal reentrant tachycardia; CA, catheter ablation; IST, inappropriate sinus tachycardia; NA, not applicable; nsVT, non-sustained ventricular tachycardia; PAC, premature atrial contraction; PVC, premature ventricular contraction; SART, sinoatrial reentrant tachycardia; sVT, sustained ventricular tachycardia; WPW, Wolff-Parkinson-White syndrome.

(From Murakawa et al, 2012[577] with permission.)

[Correction added on 29 June, after first online publication: '96.6' and '8.5' under 'Success (%)' have been amended to '96.3' and '88.5' respectively.]

TABLE 56 Incidence and prevention of selected complications of AF ablation

Complications	Incidence (%)	Selected prevention techniques
Air embolism	<1	Sheath management
Asymptomatic cerebral emboli	2-15	Anticoagulation, catheter and sheath management, TEE
Atrioesophageal fistula	0.02-0.11	Reduce power, force, and RF time on the posterior wall; monitor esophageal temperature; use proton pump inhibitors; avoid energy delivery over the esophagus
Cardiac tamponade	0.2-5	Cather manipulation; transseptal technique; reduce power, force, and RF time
Coronary artery stenosis	<0.1	Avoid high-power energy delivery near coronary arteries
Death	<0.1-0.4	Meticulous performance of the procedure, attentive postprocedural care
Gastric hypomotility	0-17	Reduce power, force, and RF time on the posterior wall
Mitral valve entrapment	<0.1	Avoid circular catheter placement near or across the mitral valve; clockwise torque on the catheter
Pericarditis	0-50	None proven
Permanent phrenic nerve paralysis	0-0.4	Monitoring the diaphragm during phrenic pacing, CMAP monitoring, phrenic pacing to identify location and adjust lesion location
Pulmonary vein stenosis	<1	Avoid energy delivery within PVs
Radiation injury	<0.1	Minimize fluoroscopy exposure, especially in obese and repeat ablation patients; use x-ray protective equipment
Stiff left atrial syndrome	<1.5	Limit the extent of left atrial ablation
Stroke and TIA	0-2	Pre-, post-, and intraprocedural anticoagulation; catheter and sheath management; TEE
Vascular complications	0.2-1.5	Vascular access techniques, ultrasound-guided access, anticoagulation management

Abbreviations: AF, atrial fibrillation; CMAP, compound motor action potential; PV, pulmonary vein; RF, radiofrequency; TEE, transesophageal electrocardiogram; TIA, transient ischemic attack. (From Calkins et al, 2017;[578] Reprinted from Heart Rhythm, 14, Calkins et al., 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation, e275–e444, 2017, with permission from Elsevier.)

1.6.2 | AF catheter ablation

The cauterization target in catheter ablation for AF tends to cover a wide range of myocardial regions, and the types and incidence of complications differ from those of other arrhythmias.

The rate of complications varies across reports, because of the effect of the technique, timing, and device specifications. PV stenosis, which was relatively common in the beginning of AF ablation, was rarely reported with RF ablation catheters; however, caution is required because it has shown a tendency to increase again with the widespread use of balloon ablation.

In the USA, a total of 93,801 ablation procedures[580] had complication rates of 5.33% in 2000, and 7.48% in 2010. Therefore, the rate has not decreased. The rate of bleeding requiring postoperative blood transfusion increased from 0.30% to 1.03%. The overall rate of in-hospital mortality was 0.42%. It has been suggested that the complication rate tends to correlate with the age of the patients. Table 56 shows[578] the complication rates and preventive approaches to complications, as compiled for the consensus report on AF ablation.

a. | Tamponade. An international joint study by Michowitz et al found that tamponade occurred in 0.9% of approximately 35,000 AF ablation procedures.[581] The complication rate inversely correlated with the number of cases treated at the medical facility and was higher among women. According to a nationwide survey in Japan, complications occurred in 4.8% of 8,319 patients, and pericardial effusion requiring invasive treatment occurred in 1.0%.[582] The incidence of pericardial effusion was high when a 3D mapping system was not used. However, unlike overseas observations, no association was found with sex differences or the number of cases treated at the medical facility.

b. | Left atrioesophageal fistula. Although the incidence of left atrioesophageal fistula is as low as 0.02%–0.11%, the mortality rate is as high as 70%–80%.[578,580,583] Multiple factors have been suggested as the onset mechanism, including esophageal burn injury due to cauterization (heating or cryoablation) in the vicinity of the esophagus, as well as ischemia, gastric acid reflux, and infection due to esophageal small artery occlusion.[580]

This condition usually occurs about 2-4 weeks postoperatively, rather than immediately after surgery, and often presents with symptoms such as fever, chest pain, impaired consciousness, and shock.[580] It is important to explain to patients that they need to contact their doctor if they develop discomfort or pain on swallowing, or abdominal distension (vagal esophageal disorder) after surgery. Chest CT to identify thoracic air leaks outside the esophagus is useful for early diagnosis; however, because endoscopy may exacerbate fistulas and cause air embolism due to increased esophageal pressure, it is essential to use carbon dioxide gas.[580,583,584] Depending on the degree of injury, esophageal stents and conservative measures may be possible for cases in which a pericardial esophageal fistula does not extend as far as the left atrium. Nevertheless, surgical repair before the patient's general condition worsens is fundamental.[580]

Ablation methods that differ from ordinary RFCA, such as various balloon ablation methods, have recently been introduced. Although knowledge of complications specific to these new methods is still accumulating, it is vital to consider the puncture procedures,

manipulation of the sheath and catheter, ablation site, and nearby tissues that may be affected by the procedure, to avoid complications.

2 | Electrophysiological study

Introduction

Early cardiac electrophysiology studies (EPS) introduced into clinical practice in the 1970s were aimed at recording the bundle of His potential, and evaluating sinus node function and atrioventricular conduction; however, in the 1980s, these studies evolved into testing methods for a range of purposes, from analysis of the tachycardia mechanism to ablation therapy. In 1990, a 3D mapping system was developed in which a 3D image of the heart integrating arrhythmia information was depicted on a computer display, which enabled searching for the ablation target site while analyzing the arrhythmia mechanism. In the 2000s, fluoroscopy equipment and remote-control systems were developed to assist in catheter manipulation, and the current arrhythmia catheterization laboratory has changed considerably that it could not exist without these high technologies.

2.1 | Electrophysiological study during catheter ablation

The purpose of the EPS is to induce tachycardia, elucidate the tachycardia mechanism, identify the tachycardia circuit or tachycardia origin site, identify the ablation site, and determine the effect after ablation. The mechanism of tachycardia is broadly divided into (1) reentry, (2) abnormal automaticity, and (3) triggered activity.

If the mechanism of tachycardia is reentry, a provocation method using extrastimulation and burst stimulation with a short cycle length (programmed stimulation method) is used. Tachycardia is usually difficult to induce by programmed stimulation in abnormal automaticity; thus, an induction method using continuous intravenous isoproterenol is used. A provocation method using frequent stimuli with a relatively long cycle is used for triggered activity.

Elucidation of the tachycardia mechanism and identification of the tachycardia circuit include methods using conventional electrophysiological techniques and mapping using a 3D mapping system. Current 3D mapping systems have made it possible to identify rapid and high-resolution tachycardia circuits, which has contributed to the elucidation of tachycardia mechanisms. These systems are becoming increasingly used because of their contribution to reducing radiation exposure. With either method, the optimal ablation site is the earliest excitation site in tachycardia owing to abnormal automaticity or local (micro) reentry, and the essential conduction pathway within the reentrant circuit in macroreentrant tachycardia. The effect of ablation is confirmed by the fact that tachycardia is not induced by drug loading, such as isoproterenol, or a programmed stimulus for the former mechanisms, and non-inducibility and disruption of essential conduction pathways for the latter mechanism.

EPS for ablation of accessory pathway syndrome are implemented for the evaluation of the conduction properties of accessory pathways, for diagnosis of the site, for differential diagnosis of multiple accessory pathways or atriofascicular fibers (Mahaim fibers), and for provocation of atrioventricular reentrant tachycardia (AVRT).

In AVNRT, the EPS is implemented to diagnose typical (slow/fast) and atypical (fast/slow, slow/slow) forms, to make a differential diagnosis between fast/slow AVNRT and the permanent form of junctional reentrant tachycardia with a slow accessory pathway, and to differentiate adenosine triphosphate (ATP)-sensitive atrial tachycardia.

With atrial tachycardia, the EPS can distinguish ectopic atrial tachycardia, local reentrant atrial tachycardia, and macroreentrant atrial tachycardia based on the tachycardia induction method and responsiveness to ATP.

In AFL, the EPS is used to diagnose common AFL rotating around the tricuspid annulus by recording the right atrial potential with a multipolar catheter electrode, and entrainment mapping is performed from the isthmus between the tricuspid annulus and the inferior vena cava, to confirm that the isthmus is an essential conduction pathway. In isthmus-independent AFL, the reentrant circuit is identified with 3D mapping and the optimal ablation site is examined.

In AF, the EPS aims to induce the triggers that contribute to the onset and maintenance of AF and to identify their origin, to confirm PVI (bidirectional block) after ablation, to evaluate AF inducibility, and to assess whether there are other atrial tachyarrhythmias such as AFL or atrial tachycardia.

It is important to select the appropriate induction method and mapping method for VT, depending on the tachycardia mechanism and disease type, including idiopathic outflow tract VT, verapamil-sensitive VT, and macroreentrant VT with arrhythmogenic substrate as the structural heart disease. The optimal ablation site is identified through activation mapping, pace mapping, entrainment mapping, arrhythmia substrate mapping, etc.

2.2 | 3D mapping systems

2.2.1 | CARTO®

The CARTO® system (Biosense Webster) acquires electrophysiologic information while simultaneously acquiring anatomical information using a magnetic sensor in the catheter, to render a 3D image of the heart chamber, and displays the excitation pattern within the heart chamber and potential information at various sites. The catheter can be manipulated without fluoroscopy, thereby reducing radiation exposure. The mapping system also contributes to improving the effectiveness and safety of ablation by measuring and displaying the contact force at the tip of the catheter (contact force) in real time.

The 4 main functions of the CARTO® system are described below.

a. | Diagnosis of excitation pattern. The reentrant circuit and the earliest excitation site are displayed to provide useful information

for determining the ablation site. The automatic mapping function, called the CONFIDENCE™ Module, enables acquisition of a large amount of information in a short time using a multipolar catheter. Previously, the conduction time compared with the reference was displayed as excitation propagation in the order of red-orange-yellow-green-blue-indigo-violet (isochronous map). However, at present, the Ripple Mapping function can be used to display the excitation and potential peaks of each site with bar heights and timing. This function can continuously display the excitation sites on an equipotential map independent of the reference, which is expected to enable analysis of more complex circuits.

b. | Depiction of the arrhythmia substrate. The pathological myocardium has low-voltage amplitude on bipolar or unipolar recordings (low-voltage area [LVA]). Thus, pathological sites such as areas of fibrosis and surgical scars can be visualized on the basis of this principle. In addition, abnormal potentials such as fractionated electrograms are recorded at conduction delay sites. These "arrhythmogenic substrates" are the essential site of reentrant circuits, and ablation methods based on these substrates are now commonly used, especially in VT ablation in which mapping during tachycardia is difficult. In bipolar potential recordings, the normal amplitude in the atrium is generally >0.5 mV, that in scar sites is <0.1 mV, and that in the ventricles is >1.5 and <0.5 mV, respectively. However, the amplitude is affected by factors such as electrode spacing, direction of excitation, and tissue characteristics.

c. | Display of anatomical information. The real-time anatomical information obtained by the CARTO® system can be integrated with pre-installed CT images and real-time echo images of intracardiac echograms (CARTOSOUND®). CARTOSOUND® is useful for recognizing important structures, such as the aortic valve and papillary muscle, during VT ablation. It greatly contributes to the understanding of the complex anatomy in congenital heart disease.

d. | Display of ablation information. Ablation information includes the ablation site, setting power output, and catheter tip contact force. These are integrated and displayed as a tag, and whether or not sufficient ablation was performed at a stable catheter location is displayed with color density. The ablation index, which is calculated using the combination of time, contact force, and RF power, is used for ablation of cardiac tissue. As the ablation index positively correlates with the size of the ablation lesion in particular, it is expected to enable safe and effective ablation.

2.2.2 | NavX™

a. | Basic principles. With the NavX™ system (Abbott), 3 pairs of electrodes are attached along the X, Y, and Z axes of the body surface. Thereafter, a small current is generated from the electrodes to create an impedance field around the heart. It measures the voltage attenuation of the catheter electrode in the heart chamber, determines the spatial position, and displays the catheter on the screen. With an electrode catheter, navigation is possible irrespective of the type and manufacturer of the catheter. In addition, the coordinates of each electrode are recorded by moving the electrode catheter in the heart cavity, and a 3D image of the heart is constructed.

Recently, a field frame that generates a magnetic field under a table and a Sensor Enabled™ catheter with a dedicated position sensor have been used to enable the creation of high-precision 3D models combining the conventional impedance field and magnetic field accuracy.

b. | Clinical application. Use of the impedance field allows simultaneous display of multiple electrode catheters in real time, which is useful for reducing radiation exposure.

The AutoMap Module for morphological matching of ECG waveforms can be used to acquire potential information. Furthermore, using the TurboMap function to reproduce the recorded data 10 times faster and recreating the AutoMap with the changed settings for each parameter have enabled rapid mapping of secondary arrhythmias that are common in conditions such as ventricular arrhythmia.

The SparkleMap function visualizes 2 sets of data related to the tachycardia circuit, namely excitation propagation and local voltage amplitude, on a single map, which is useful for the analysis of arrhythmia diagnosis.

In addition, clinical studies have demonstrated that measurement of the contact pressure between the tip of the catheter electrode and the tissue is a factor affecting the effectiveness of the procedure.[585,586] The TactiCath™ Quartz ablation catheter using optical interferometry, which led to the creation of recommended guidelines, was introduced into the EnSite™ system. As a result, the measured contact pressure at the tip of the catheter can be displayed in real time in the EnSite system (Figure 11). The contact pressure can be updated in the AutoMap settings. A TactiCath Contact Force ablation catheter with the aforementioned Sensor Enabled™ function will be introduced sometime in the future.

Furthermore, it is possible to use AutoMark Module, which automatically displays the amount of ablation represented by the size and color of marking spheres according to the user-defined requirements. This function allows the operator to freely select the conditions to reference and is expected to improve the consistency of the procedure and the stability of the catheter.

2.2.3 | RHYTHMIA™

a. | Basic principles. RHYTHMIA™ (Boston Scientific) is a system that can automatically capture only those beats that meet certain recording conditions, enabling accurate and rapid acquisition of a multiple-point map.[587]

A dedicated IntellaMap Orion™ mapping catheter with a magnetic sensor is used for mapping. The electrodes of this catheter have a very small surface area of 0.4 mm^2, which can clearly display

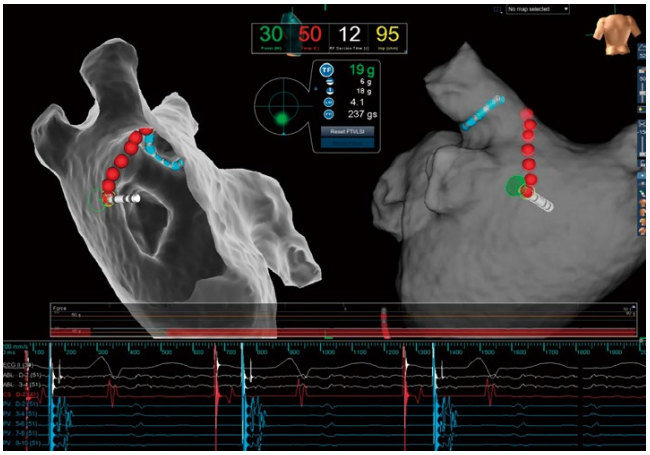


FIGURE 11 Pulmonary vein isolation using the TactiCath™ Quartz ablation catheter. The location of the catheter and the contact force measurement value are visualized. During PVI, the site of the catheter in contact with the tissue, the contact area, and the contact pressure are presented in a bullseye map format (Center)

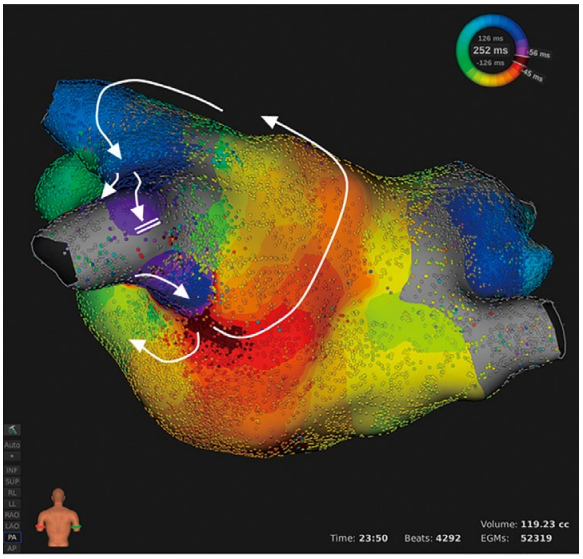


FIGURE 12 RHYTHMIA™ mapping clearly demonstrating the atrial reentrant tachycardia related to 2 left atrial–pulmonary vein gaps. A total of 52,319 points can be acquired in 10 min, and clear gap-to-gap reentrant data are depicted

and acquire potentials that were previously difficult to analyze, such as abnormal potentials in LVAs. The position identification method uses hybrid technology that combines magnetism-based technology and electric resistance-based technology.

In continuous mapping mode, each beat can be evaluated for a maximum of 7 recording conditions and 4 trigger channels predetermined by the user before mapping, and points and geometry can be automatically acquired simultaneously.[587] The dedicated IntellaMap Orion™ mapping catheter has a total of 64 electrodes, with 8 poles on 8 splines. The surface area can be reduced by using a printed electrode attached only to the outside of the spline, to obtain local potential information.

b. | Clinical application. Automation of local potential interpretation, the large number of points, and the characteristics of the electrodes on the IntellaMap Orion mapping catheter allow for accurate depiction of scars, incision lines, and sites of delayed conduction even in atrial tachycardia caused by complex circuits.[588] Figure 12 shows a mapping image of a reentrant case with rotation in 2 places in the gap between the left atrium and the PV after a PVI procedure.

A 12-lead waveform recognition function is provided for ventricular arrhythmias, which enables automatic and accurate recognition.[589]

2.3 | Navigation systems

2.3.1 | Niobe™

a. | Basic principles. The Niobe™ system (stereotaxis) can guide the tip of a special catheter containing magnets by tilting and rotating around a strong magnetic field from magnets installed on both sides of the catheter examination table. The catheter is very flexible; the angle is controlled in 1-degree increments; the drive is controlled in 1-mm units with directional control using magnetism; and the advance and retreat motions are controlled by the catheter drive.[590] As catheter manipulation can be performed in the control room, the operator is completely protected from radiation exposure and the patient's exposure is reduced.[591] It is used as CARTO RMT™, together with the CARTO system and can be manipulated under 3D constructed cardiac imaging.[592] A method used in combination with the EnSite system has also recently been developed.[593]

b. | Clinical application. Compared with catheters with normal manual operation, it is necessary to provide instructions, separating the direction setting and advance/retreat motions within the space, which requires a certain degree of skill. As the catheters are very flexible, the risk of cardiac perforation is extremely low and good contact can be obtained. Results comparable to those of manual operation have been reported for AVNRT,[590] atrial tachycardia, AF,[592] and VT.[594] Results superior to those of manual operations by physicians have been obtained in ablation for adult congenital heart disease using a transaortic retrograde approach to the systemic atrium after atrial switch operation and catheter manipulation for difficult-to-reach sites in the left atrium and both ventricles.[595-597]

2.3.2 | MediGuide™

MediGuide™ (Abbott) displays real-time catheters, sheaths, and guidewires with dedicated miniature sensors on fluoroscopy images prerecorded under heart rate synchronization, which enables the creation of a normal operating environment as if using fluoroscopy.[598] A reference magnetic sensor is attached to the patient's chest, and an ECG signal is inputted for synchronizing with the cardiac cycle. Image shift due to body motion, respiration, and heartbeat is corrected. The transmitter attached to the X-ray detector forms an electromagnetic field and indicates the position of a

dedicated catheter and other devices with the reference as standard. The fluoroscopic video captures the image in an arbitrary direction for ≈3 s, and it is played back in a loop adjusted with heart rate. The position accuracy is reported to be within 1 mm.[599]

a. | Catheter ablation. When used in combination with the EnSite Velocity™ system, the accuracy of the catheter and electrode position information is increased, and more accurate maps are created. It is also possible to display the tip and shaft of the electrode catheter in fluoroscopy, and to display the ablation site with a tag (Figure 13), enabling the use of these devices without changing the normal flow of the procedures. It has been reported that it significantly reduces fluoroscopy time during ablation for conditions such as AF,[575,600] and AFL.[601] Preserving the aortic and coronary angiograms will be useful for PVCs originating from the aortic cusps and for epicardial-approach ablation.

b. | CRT device implantation. Cardiac resynchronization therapy (CRT) is known to have high radiation exposure during operation owing to the frequent use of the LAO position, the inability to use a shield to maintain a clean area, and the close proximity of the X-ray tube to the operator. Using the MediGuide system, a CRT device can be implanted with the dedicated guiding sheath, subselection catheter, and 0.014-inch guidewire displayed on an image. A comparative study using MediGuide and normal fluoroscopy showed that radiation exposure was reduced by 81.8% and the procedure time was also decreased.[602]

c. | Limitations. There are only a limited number of devices equipped with dedicated magnetic sensors. Therefore, not all catheters and sheaths can be visualized. Further development is expected in the future.

3 | Supraventricular tachycardias

3.1 | WPW syndrome and other ventricular preexcitation syndromes

3.1.1 | Catheter ablation indication

In 1930, Wolff, Parkinson, and White reported a paroxysmal tachycardia that developed in a healthy young person, together with the specific ECG findings observed during sinus rhythm, and this condition was named WPW syndrome.[603] Table 57 shows the recommendations for catheter ablation for WPW syndrome. Since that time, it has been suggested that there is an accessory pathway (Kent fiber) connecting the atrium and ventricle other than the atrioventricular node. It is often referred to as preexcitation syndrome, and this syndrome causes various tachycardia attacks because of the presence of a reentrant circuit not involved in healthy individuals. WPW syndrome was classified by Rosenbaum et al as type A with a high R wave in the V1 lead and an accessory pathway in the posterior wall of the left ventricle, and as type B with an rS pattern in the V1 lead and an accessory pathway in the right ventricle.[604] Furthermore, the QS pattern in the V1 lead suggests the presence of a septal accessory pathway. In Japan, this type is classified as type C.[605] Arruda et al have reported that the location of the accessory pathway can be estimated by examining in detail the polarity of the delta wave in a 12-lead ECG.[606]

Although the disease generally has a good prognosis, caution is needed because of the risk of the development of life-threatening ventricular arrhythmia when AF occurs in patients with preexcitation syndrome. RF catheter ablation for WPW syndrome has been performed for more than 20 years,[607] with an extremely high success rate of 93%–95% and a low risk of serious complications of 2%–3%.[608,609] The recurrence rate is reported to be 8%, with some cases requiring repeat ablation procedures. Catheter ablation is a radical therapy, unlike pharmacological therapy. Successful catheter ablation eliminates the need for regular outpatient visits and medications, and is an excellent treatment both in terms of medical economics and patients' QOL. Therefore, it is now considered the first-line therapy for patients with symptomatic preexcitation syndrome. In addition, the Mahaim fibers, which connect the atrium and fascicular fibers, have anterograde decremental conduction properties without retrograde conduction. Antidromic atrioventricular reciprocating tachycardia (AVRT) may occur; therefore, catheter ablation is effective for its treatment, as in WPW syndrome.[610]

Catheter ablation is recommended regardless of antegrade or retrograde AVRT in patients with preexcitation syndrome, who often show recurrent palpitations. There is a risk of sudden death if AF develops with dizziness or syncope; thus, catheter ablation is also recommended in these cases.

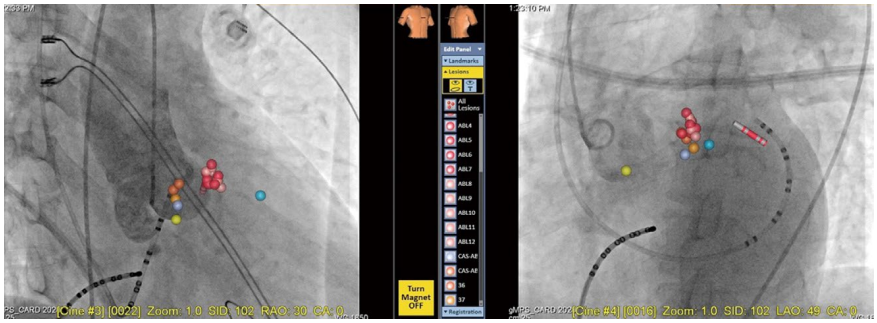


FIGURE 13 MediGuide™ system. The real-time position of the ablation catheter is displayed, and sites of interest can be tagged on the looped cineangiogram

TABLE 57 Recommendations and evidence levels for catheter ablation in patients with preexcitation syndrome

	COR	LOE	GOR (MINDS)	LOE (MINDS)
Catheter ablation of the accessory pathway is recommended in patients with symptomatic supraventricular tachycardia associated with the accessory pathway	I	B	A	III
Catheter ablation of the accessory pathway is recommended in patients with severe symptom associated with preexcited tachycardiac AF/AT	I	B	A	III
Catheter ablation of the accessory pathway should be considered in asymptomatic patients if the presence of preexcitation precludes specific employment that places the patient or others at risk	IIa	B	B	III
Catheter ablation of the accessory pathway should be considered in asymptomatic patients with a high risk for arrhythmic events	IIa	B	B	III
Catheter ablation of the accessory pathway may be considered for asymptomatic patients with preexcitation syndrome when indicated by patient preference	IIb	C	C1	VI

Abbreviations: AF, atrial fibrillation; AT, atrial tachycardia; COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence.

Catheter ablation may be considered for cases in which the first tachyarrhythmia attack might cause a serious accident involving the life of the affected individual and others even in the absence of symptoms, such as in professional drivers or competitive athletes.[611] For more information on working after ablation, see **Chapter VI, Returning to/attending school or work after non-pharmacotherapy**.

Although overt WPW syndrome may be detected in school medical examinations, cases of a relatively narrow QRS width may include fascicular ventricular accessory pathways.[612] Tachycardia attacks do not occur in these cases, and no intervention such as antiarrhythmic drugs or ablation is required. Intravenous adenosine triphosphate (not approved by insurance) and atrial stimulation from multiple sites can differentiate this condition from WPW syndrome (atrioventricular accessory pathway).[613]

In general, patients with asymptomatic WPW syndrome have a good prognosis, and the rate of sudden cardiac death is 0.05%–0.2% per year.[612] Rather than the symptom of palpitations, a shortened antegrade effective refractory period is considered to be a risk factor for the development of VF. Patients with WPW syndrome and a history of cardiac arrest often have an antegrade effective refractory period of <220 ms[613] In the USA, even if a patient is asymptomatic, if the anterograde refractory period of the accessory pathway is <240 ms in the EPS, the patient is classified as high risk,[609] and catheter ablation is considered. Invasive tests to measure the effective refractory period of accessory pathways are not routinely performed in Japan. If the shortest RR interval is <250 ms during AF with preexcitation, the patient is classified as high risk regardless of the presence or absence of symptoms,[614,615] and catheter ablation is considered. Conversely, the risk of VF is low in intermittent WPW syndrome in which the delta wave intermittently disappears,[616] and this is an important finding for risk stratification.

In a registry study of 2,169 patients, VF developed in 15 of 1,001 (1.5%) patients who had not undergone catheter ablation over a follow-up period of 22 months, and 13 (87%) patients were asymptomatic until VF episodes occurred.[609]

Considering these risks and the possibility of AF development, catheter ablation is considered if patients prefer to receive the therapy. However, because there is a risk of the unavoidable complications associated with the ablation procedure, it is important that informed consent is obtained from the patients after providing them with an explanation about the benefits and risks of the treatment.

3.1.2 | *Catheter ablation procedures*

Ablation procedures for WPW syndrome have different approaches depending on the location of the accessory pathway. With right accessory pathways, the supravalvular approach from the right atrium is chosen. However, when the accessory pathway is in the free wall, stable catheter manipulation can be achieved by using a (steerable) long sheath. For left accessory pathways, either a transseptal approach using the Brockenbrough method or a retrograde transaortic approach is used. Some patients have multiple or broad connecting accessory pathways; thus, detailed mapping before ablation is important. Although catheter ablation can be performed with only an electro-guided approach by using a multipolar electrode catheter, also using a 3D mapping system enables safer and more accurate identification of the successful ablation site.

In overt WPW syndrome, the earliest ventricular activation site is identified during sinus rhythm or atrial stimulation; however, in concealed WPW syndrome, the earliest atrial activation

site is identified during ventricular pacing in order to determine the optimal ablation site. When the bipolar electrograms from the tip of the ablation catheter shows fusion of the atrial and ventricular electrograms, elimination of the accessory pathway can be achieved by RF energy delivery at that site with a high success rate. In overt WPW syndrome, elimination of the accessory pathway can be achieved at the ablation site where the unipolar recording from the distal ablation catheter electrode shows a PQS pattern.

If ventricular preexcitation is prominent via the accessory pathway existing at the anterior septum or the mid-septum, it may not be possible to record the His bundle electrogram clearly. In such cases, the His electrogram can be identified by single atrial extrastimulation, which produces the refractory period of the accessory pathway. RF energy is applied from a low power using a 4-mm tip ablation catheter to prevent atrioventricular block. The posteroseptal accessory pathway is often close to the coronary sinus ostium. Elimination of the accessory pathway may be difficult because of the presence of accessory pathways at the epicardium. It is useful to determine the anatomy of the coronary sinus ostium and to confirm the presence of a coronary diverticulum using coronary venography to determine the optimal ablation site.

3.1.3 | *Catheter ablation complications*

Except for the common complications associated with all ablation procedures, a notable complication in WPW syndrome is complete atrioventricular block caused by RF current delivery to the accessory pathway from the anteroseptum to the mid-septum. The incidence is reported to be 2%–10%.[617,618] The recurrence rate of accessory pathways at the same site is 11%–25%, which is higher than that of other complications.[618,619] The efficacy and safety of ablation of accessory pathways in the septal area have improved in recent years;[620] however, informed consent, especially with respect to the complications, is particularly important when the location of the accessory pathway is suggested to be in the septal area in patients with overt WPW syndrome.

3.2 | Atrioventricular nodal reentrant tachycardia

3.2.1 | *Ablation indication*

Table 58 shows the ablation recommendations for AVNRT.

AVNRT is a tachycardia with a fast pathway that enters the atrioventricular junction (compact atrioventricular node) from the anterior (upper) side and a slow pathway from the posterior (lower) side. It is classified as either typical (slow/fast type) or atypical. Atypical AVNRT was previously classified into fast/slow and slow/slow types,[621] although leftward inferior extension slow/fast, left atrial slow/fast,[622] and superior fast/slow[623] types have also been reported. However, some reports suggest that they should be treated collectively as atypical AVNRT.[624] Randomized controlled trials (RCTs) have also reported that ablation for AVNRT is more useful than pharmacotherapy.[625]

3.2.2 | *Ablation procedure*

a. | Ablation for typical AVNRT. The target of ablation in AVNRT is the slow pathway. There are 2 methods: targeting a specific potential recording area (electrogram-based approach) and anatomically targeting a specific area (anatomical approach). With the former method, ablation is performed at the area known as the Jackman potential[626] recording area in the posteroseptum to mid-septum region of the tricuspid annulus or the area known as the Haïssaguerre potential[627] recording area in the septum, as well as in areas where the atrial potential is smaller than the ventricular potential (≤0.2). The anatomical approach is a method in which RF energy application is attempted from the coronary sinus ostium of the posteroseptum (Figure 14A, P1, P2 areas). If ineffective, the ablation site is gradually moved to a higher position (Figure 14A, M1, M2 areas). In practice, the electrogram-based approach and the anatomical approach are often used in combination. If attempts are unsuccessful, radiofrequency energy application within the coronary sinus (Figure 14B, CS apical edge) may be effective.

The risk of atrioventricular block generally increases as the ablation site moves in an anterior-superior direction. Care should be

TABLE 58 Recommendations and evidence levels for catheter ablation of AVNRT

	COR	LOE	GOR (MINDS)	LOE (MINDS)
Catheter ablation of the slow pathway is recommended in symptomatic patients with AVNRT	I	B	A	II
Catheter ablation of the slow pathway should be considered when AVNRT is noninducible, but a dual AVN physiology is observed in an EPS and an ECG of a supraventricular tachycardia is documented	IIa	C	C1	V
Catheter ablation of the slow pathway should be considered when AVNRT is contingently induced in an electrophysiological study or during catheter ablation therapy for another tachycardia	IIa	C	C1	V

Abbreviations: AVN, atrioventricular nodal; AVNRT, atrioventricular nodal reentrant tachycardia; COR, class of recommendation; EPS, electrophysiological study;GOR, grade of recommendation; LOE, level of evidence.

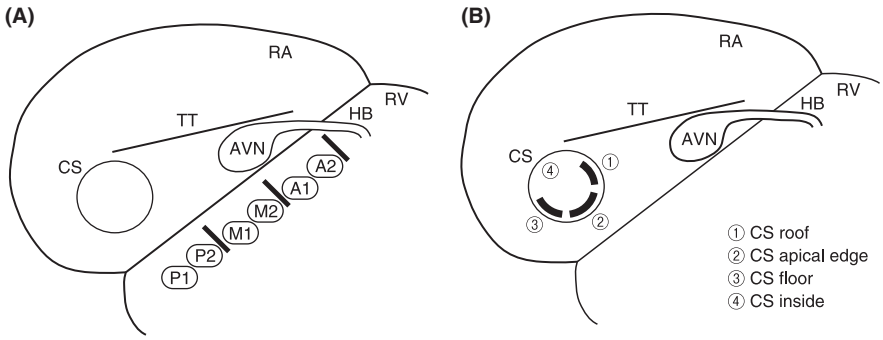


FIGURE 14 Slow pathway ablation using the anatomical approach. AVN, atrioventricular node; CS, coronary sinus; HB, His bundle; RA, right atrium; RV, right ventricle; TT, tendon of Todaro

taken even with RF energy application on the posteroseptum region because there are rare cases in which the fast conduction pathway deviates posteriorly.

b. | Method of RF energy application. It is important to fix the electrodes and maintain good contact with the tissue to ensure that the slow conduction pathway is definitely ablated, and atrioventricular block is avoided. It should be confirmed that the electrodes are in contact with the atrial septum on the LAO view. Selecting a long sheath can be useful in some cases. Normally, a non-irrigated catheter is used. In this case, the output settings are a maximum electrode–tissue interface temperature of 50-55°C and maximum power of 30-35 W. If atrioventricular junction rhythm does not appear within 20-30 s of starting the application, the application should be stopped, and the ablation site should be changed.

In ablation of slow pathways, the appearance of atrioventricular junction rhythm during RF energy application is an indicator of effective ablation. If atrioventricular conduction can be confirmed at a 1:1 ratio during atrioventricular junction rhythm, the application is continued.[628] The appearance of atrioventricular block should be carefully monitored, and the application should be stopped as soon as the block appears. Attention should be paid to prolonged PR interval and the appearance of atrioventricular block during sinus rhythm. If the atrioventricular conduction is originally poor, atrial pacing is performed at a rate higher than the heart rate of the junction rhythm, and RF energy is applied while confirming that there is no prolongation of the PR interval. It has been reported that rapid junction rhythm with a heart rate of ≥100 beats/min is a risk factor for atrioventricular block.[629] The endpoint of ablation should be non-inducibility of AVNRT with programmed stimulation or burst stimulation after isoproterenol loading. However, up to 1-2 atrial echo waves are allowed.

3.2.3 | Outcomes

a. | Success rate. The success rate of AVNRT ablation was high, at 97%, in the North American Society of Pacing and Electrophysiology (NASPE) survey[630] reported in 1995, and high rates of 96.1%–97.3% were maintained in subsequent reports.[631,632] The long-term results are excellent, with a recurrence rate ≤1% in 5 years in patients successfully treated during the acute phase.[633]

TABLE 59 Short-term success, recurrence, and risk of atrioventricular block (AVB) after catheter ablation for AVNRT

Approach	n	Short-term success	Recurrence	AVB
Posterior	620	98%	3.7%	0.8%
Mid-septal	189	98%	0.6%	2.6%
Anterior	177	89%	9.6%	8.0%

Abbreviations: AVB, atrioventricular block; AVNRT, atrioventricular nodal reentrant tachycardia. (From Naccarelli et al, 1995[634] with permission.)

b. | Complications. According to the NASPE survey,[630] atrioventricular block occurred in 0.1% of cases. According to another survey on the results of slow pathway ablation during the 5-year interval of 1997-2002,[633] the incidence of high-grade atrioventricular block requiring pacemaker implantation was 0.4% among 8,230 patients with AVNRT. The incidence of atrioventricular block is closely related to the site of RF energy application, with a higher incidence in the mid- and anteroseptum than in the posteroseptum (Table 59).[634] Conversely, the amount and duration of RF energy application tend to be insufficient in these regions, which is likely to increase the recurrence rate. If the ECG during sinus rhythm shows a marked first-degree atrioventricular block, there is increased incidence of atrioventricular block after slow pathway ablation.[635] Marked first-degree atrioventricular block may lack anterograde conduction through the fast pathway; thus, complete loss of slow pathway conduction indicates atrioventricular block. Ablation of the retrograde fast pathway may be attempted. However, the patient's consent must be obtained with respect to the associated risk, and sufficient care is needed to avoid atrioventricular block. Long-term postoperative follow-up is necessary for the occurrence of atrioventricular block.

c. | Recurrence rate. According to the survey described above,[633] 1.3% of cases required a repeat ablation procedure, and a meta-analysis reported a repeat procedure rate of 3.2%.[632]

d. | Cryoablation. Cryoablation is now available in Japan for AVNRT. Cryoablation is reported to reduce the occurrence of atrioventricular block, and it may be useful in young patients. However, a multicenter study by Deisenhofer et al[636] and a meta-analysis by Henninen et al[637] reported that the efficacy and safety of

cryoablation are almost the same as those of RF ablation, whereas, conversely, the recurrence rate in the chronic phase is higher with cryoablation. As the procedures of cryoablation differ from those of RF ablation, care is needed during the former.[636,637]

3.3 | Typical AFL (involving the tricuspid annulus-inferior vena cava isthmus)

3.3.1 | Ablation indication

Table 60 shows the recommendations for catheter ablation of AFL.

AFL has a macroreentrant mechanism that rotates around the right atrial tricuspid annulus in a counterclockwise direction and is characterized by a negative sawtooth wave on the ECG inferior leads. When turning clockwise, it is called a reverse typical AFL, and flutter waves induced by the inferior leads become positive.[638]

In both cases, the tricuspid annulus forms an anterior anatomic barrier, with the superior vena cava, inferior vena cava, and Eustachian ridge forming the posterior anatomic barriers. The presence of the crista terminalis[639] and the sinus venosa area[640] as a posterior functional barrier allows tachycardia to persist. In the tachycardia circuit, the anatomical isthmus (cavotricuspid isthmus [CTI]) between the tricuspid annulus and the inferior vena cava is an essential conduction pathway, and can be radically cured by linear cauterization of the same area. The ablation procedure for AFL is relatively simple, and its safety and therapeutic effect are superior to those of pharmacotherapy.[641-643] Therefore, treatment is naturally indicated if the disease is symptomatic because it may exacerbate heart failure if complicated by reduced cardiac function;[644] however, treatment should also be actively considered even for asymptomatic cases and may also be considered for asymptomatic recurrent cases.[632,641,645]

AFL may develop during treatment with group I antiarrhythmic drugs for AF. Most of the AFLs that occur during the use of class I drugs are counterclockwise normal AFLs due to the specific therapeutic effect of these drugs in the CTI.[646] Therefore, improvement in the pathology can be expected with linear ablation of the CTI and continued use of antiarrhythmic drugs;[611,647,648] however, relapse of AF during follow-up is not uncommon.[647] Ablation should be considered for symptomatic AF.

Linear ablation of the CTI should be added if AFL is induced during ablation for AF, if AFL is detected before ablation, or if it is determined that AFL is likely to appear after AF ablation.[578,649,650] It has been reported that when both AF and AFL are clinically present, triggers (non-PV foci) from sources other than the PV are likely to provoke AF.[651]

3.3.2 | Ablation procedure

The risk of thromboembolism increases even in persistent AFL, and is about one-third the risk of AF.[652] Anticoagulant therapy should be

TABLE 60 Recommendations and evidence levels for catheter ablation of typical AFL

	COR	LOE	GOR (MINDS)	LOE (MINDS)
Catheter ablation is recommended for patients with typical AFL that is either symptomatic or refractory to pharmacological rate/rhythm control	I	B	B	I
Catheter ablation is recommended for patients with typical AFL that is either symptomatic or refractory to pharmacological rate/rhythm control	I	B	B	II
Catheter ablation of AFL should be considered for patients with typical AFL that occurs as a result of antiarrhythmic therapy for AF	IIa	B	B	III
Catheter ablation should be considered for patients with asymptomatic typical AFL, structural heart disease, and reduced cardiac function	IIa	C	B	IVa
Catheter ablation of typical AFL should be considered for patients with typical AFL that is induced inadvertently at the time of catheter ablation for tachycardia other than AF	IIa	C	C1	VI
Catheter ablation should be considered for patients with typical AFL that requires pharmacological rate/rhythm control therapy	IIa	C	C1	VI
Catheter ablation may be considered for patients with asymptomatic recurrent typical AFL	IIb	C	C1	V

Abbreviations: AF, atrial fibrillation; AFL, atrial flutter; COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence.

administered in the perioperative period in accordance with AF anticoagulant therapy for AFL with a $CHADS_2$ score ≥2 or persistent AFL (refer to Guidelines for pharmacotherapy of atrial fibrillation [JCS 2013][3]) for detailed information).

Typical AFL is diagnosed by analyzing the excitation sequence using a multielectrode catheter placed in the tricuspid annulus. Furthermore, the postpacing interval (PPI) period immediately after entrainment pacing from the CTI should match the flutter cycle; thus, it should be confirmed that this area is included in the tachycardia circuit. However, in approximately 20% of cases, the PPI after CTI pacing may be longer than the flutter cycle by ≥30 ms, sometimes by almost 100 ms, which hinders diagnosis. This has been attributed to local pacing latencies or conduction delays proximal to the pacing.[654] In this case, the pacing cycle length should be moved closer to the flutter cycle length, or the pacing site should be moved slightly within the CTI and the examination should be performed again.

Non-irrigated or irrigated catheters are used for ablation. Ablation is started from the tricuspid annulus where a large ventricular potential is observed, and application of RF energy is repeated at sites moving a few millimeters away at a time to perform a linear ablation as far as the inferior vena cava. When the catheter reaches the inferior vena cava, the advancement of the catheter tip into the inferior vena cava is recognized with fluoroscopy and the atrial potential disappears; thus, RF energy delivery should be stopped. A bidirectional conduction block in the CTI is determined by a change in the excitation sequence of a multielectrode catheter placed in the tricuspid annulus during pacing from the coronary sinus or the lower right atrial wall. However, a change in the sequence of excitation often indicates that a conduction gap remains despite the block appearing to be complete (pseudo-CTI block).[655] If the presence of a gap is revealed by analysis of the potential along the ablation line after linear ablation[655,656] or differential pacing,[657] it is important to achieve a complete bidirectional block with additional applications of RF energy.

AFL ablation is a well-established effective and safe procedure; however, it can be difficult to create blocks with complex anatomical features such as the presence of pouch-like recess or concave CTI.[658] These cases also pose a risk of complications such as right coronary artery injury, spasm, and cardiac tamponade. In such cases, it is better to consider a new target in the septal isthmus with a flatter structure, rather than insisting on completing the transection at the same site.[659] However, as the ablation line includes the coronary sinus and the surrounding tissue, care is needed to avoid creating an atrioventricular block.

3.4 | Atrial tachycardia

3.4.1 | Catheter ablation indication

Table 61 shows the recommendations for catheter ablation of focal atrial tachycardia.

Atrial tachycardia includes conditions with a focal excitation due to abnormal automaticity (ectopic automaticity, triggered activity) or microreentry (hereinafter, focal atrial tachycardia) and conditions caused by macroreentry. The classification of the latter is ambiguous when differentiating from non-isthmus-dependent atypical AFL. Focal atrial tachycardia can originate from the sinus node area (sinus node reentrant tachycardia); the atrioventricular node area; the vicinity of the bundle of His;[660-663] and the annulus, crista terminalis, PV, superior vena cava, coronary sinus ostium, atrial septum, and atrial appendage.[664-667] Of these, the types originating from the atrial appendage or PV are more likely to involve ventricular dysfunction.[668]

TABLE 61 Recommendations and evidence levels for catheter ablation of focal atrial tachycardia

	COR	LOE	GOR (MINDS)	LOE (MINDS)
For patients with symptomatic recurrent focal atrial tachycardia, catheter ablation is recommended	I	C	B	IVa
For patients with recurrent focal atrial tachycardia, especially if incessant, catheter ablation is recommended	I	C	B	IVa
For patients with focal atrial tachycardia and tachycardiomyopathy, catheter ablation is recommended	I	C	B	IVb
For patients with focal atrial tachycardia and depressed LV function due to structural heart disease, catheter ablation should be considered	IIa	C	C1	V
For patients with symptomatic focal atrial tachycardia who do not prefer antiarrhythmic medication, catheter ablation should be considered	IIa	C	C1	VI

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence; LV, left ventricular.

Medi et al[668] reported that 8 of 30 (27%) people with tachycardia-induced cardiomyopathy had an atrial appendage origin, and 8 of 19 (42%) people with atrial tachycardia originating from the atrial appendage had tachycardia-induced cardiomyopathy. Moreover, 8 of 44 (18%) people with atrial tachycardia originating from the PV had tachycardia-induced cardiomyopathy. Ablation should be considered if atrial tachycardia is present in patients with structural heart disease with impaired cardiac function, regardless of the presence or absence of symptoms.[669]

According to the German Ablation Registry, a prospective multicenter database, 431 of 12,566 (3.4%) patients underwent ablation therapy in 2007-10 for focal atrial tachycardia.[670] The acute-phase success rate was 84%, and the symptoms disappeared or improved after 12 months in 81% of cases. The cumulative incidence of serious adverse events in cardiovascular and cerebral vessels was 3.7%.[671]

3.4.2 | *Ablation procedures*

The origin of focal atrial tachycardia can be predicted if a P-wave can be confirmed on a 12-lead ECG (Figure 15).[671] Atrial septal puncture is necessary if there is a possibility of approaching the left atrium. In addition, intracardiac mapping can be performed efficiently by predicting the origin, and it also assists in the prevention of complications and clarification of countermeasures in advance.

The optimal site of ablation for tachycardia with focal excitation, such as focal atrial tachycardia, is usually determined by activation and pace mapping. Activation mapping is a method of identifying the earliest activation site and the activation pattern from the potential of an electrode catheter or ablation catheter placed in the heart chamber during tachycardia or during premature atrial contractions that are the same type as the tachycardia. Pace mapping is a method for comparing the 12-lead ECG findings with clinical atrial tachycardia by applying a stimulus from the mapping catheter during sinus rhythm that matches the tachycardia or extrasystole cycle/coupling cycle. However, when the T-wave overlaps with the P-wave, it is often difficult to observe the P-wave and accurate pace mapping becomes impossible.

Ablation can be performed more accurately by recording and displaying the earliest activation site, the position of the implemented pace mapping, and the potential findings of each site on 3D mapping.

Finding a unipolar electrogram recording during activation mapping for focal atrial tachycardia is also useful for determining the optimal ablation site. A QS pattern in the unipolar lead with a steep descending leg is an important finding for determining the optimal ablation site, as well as the preceding degree of the local atrial potential.

For atrial tachycardias originating from the atrioventricular node area or near the bundle of His, an ablation method targeting the remote site (entrance site of the tachycardia circuit) from the atrioventricular junction has been reported,[663] other than the conventional ablation method targeting the earliest activation site (exit site).

After identifying the earliest activation site during tachycardia, rapid atrial pacing at a rate 5 beats/min faster than the tachycardia rate is delivered from multiple sites of the atrium during tachycardia to define the direction of the proximity of the reentrant circuit. After the identification of manifest entrainment and orthodromic capture of the earliest activation site, RF energy is delivered, starting at a site 2 cm away from the earliest activation site in the direction of the pacing site. The RF energy application site is then gradually advanced toward the earliest activation site until the tachycardia terminates.

Conversely, there have also been reports[672] of multiple entrances, for which successful application of RF energy was achieved only at the non-coronary sinus of Valsalva, which has an equally early excitation as the earliest activation site on the anterior septum of the right atrium. Thus, in focal atrial tachycardia originating in the atrioventricular node area and close to the bundle of His, the tachycardia may be cured by RF energy application from the non-coronary sinus of Valsalva.[662,673] When applying RF energy from the aortic sinuses of Valsalva for atrial tachycardia, it should be ensured that the bundle of His potential is not recorded to avoid atrioventricular block. RF energy application should be terminated if the tachycardia does not stop within 10-20 s after starting the application.

3.4.3 | *Special atrial tachycardias*

Inappropriate sinus tachycardia is a tachyarrhythmia that commonly occurs in young women.[674,675] Ablation has been reported as a treatment, but its effectiveness has not been established. Ablation therapy for tachycardia originating in the sinus node

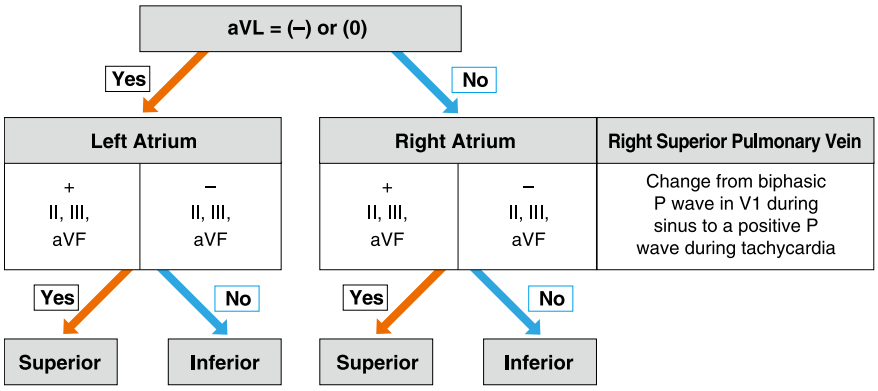


FIGURE 15 Proposed algorithm for predicting atrial tachycardia origin on the basis of the P-wave configuration from 12-lead ECG recordings (From Tang et al, 1995[671] with permission.)

or atrioventricular junction area may lead to complications of sinus dysfunction and atrioventricular conduction disturbance. When performing ablation in the superior vena cava region, care is needed with respect to phrenic nerve damage as a complication.[676]

3.5 | Atrioventricular nodal ablation

3.5.1 | *Catheter ablation indication*

Table 62 shows the recommendations for atrioventricular (AV) nodal ablation.

This method is often effective if catheter ablation for supraventricular tachycardia is unsuccessful or cannot be performed for any reason, and/or if pharmacotherapy is either ineffective for heart rate control or is difficult to use, in patients with severe symptoms due to tachycardia, severe decline in cardiac function, or reduced QOL.[677-682] As this method requires pacemaker implantation, its usefulness must be examined for each case to determine the indication. Determining whether catheter ablation will be successful or unsuccessful for supraventricular tachycardia itself should be left to the discretion of facilities with experience in treating a large number of patients.

This method is often effective in patients undergoing CRT when adequate ventricular pacing cannot be achieved owing to supraventricular tachyarrhythmia.[683,684]

3.5.2 | *Ablation procedures*

The most common procedure involves direct ablation of the AV junction.[685] A pacing catheter is placed in the right ventricle to prepare for AV block. Immediately after creating the AV block, a permanent pacemaker is implanted. The ablation catheter is inserted through the femoral vein and is placed at the site where the His bundle electrogram is recorded. The ablation catheter is gradually pulled back while applying tension in a clockwise direction and fixed at a site where a large atrial potential, small His bundle potential, and small ventricular potential are obtained. Application of RF energy creates junctional rhythm immediately after the application, but often becomes an AV block in approximately 10 s. If it is difficult to create an AV block with the right-sided approach, ablation at the site where the His bundle potential is recorded in the left ventricle may be effective.

There is also a treatment (modification of the AV node) involving ablation of the slow pathway of the AV node to reduce AV conductivity; however, heart rate control is insufficient with this method and the indications are limited.[686]

3.5.3 | *Precautions for treatment*

This treatment has a known risk of sudden death, which may be caused by prolonged QT due to rapid improvement of tachycardia and increased inhomogeneity of ventricular repolarization (QT interval dispersion).[687] To prevent sudden death, the pacing rate of the pacemaker is set slightly higher (80-90 beats/min) after ablation, and thereafter gradually reduced to the normal rate.[688] Care is needed when setting the rate response mode immediately after implantation, as it may cause ventricular arrhythmia.[689] It is essential to be aware that this therapy results in asynchronous ventricular contraction due to right ventricular pacing. The effectiveness of AV nodal ablation and CRT for permanent AF associated with chronic heart failure has been reported.[677,683] In making decisions on whether to use right ventricular pacing, CRT, or a pacemaker with defibrillation function for a pacemaker after creating an AV block, the situation of each case, including the LVEF, should be considered.[457,690]

TABLE 62 Recommendations and evidence levels for atrioventricular (AV) nodal ablation

	COR	LOE	GOR (MINDS)	LOE (MINDS)
In patients with supraventricular tachyarrhythmia who have serious symptoms or severe ventricular dysfunction due to tachycardia, in whom pharmacotherapy is ineffective or cannot be continued because of adverse drug reactions and for whom conventional catheter ablation for supraventricular arrhythmia was not successful or cannot be performed, AV nodal ablation with subsequent pacing is recommended	I	B	B	I
In patients with supraventricular tachyarrhythmia and substantial deterioration of QOL in whom pharmacotherapy is ineffective or difficult to perform and for whom conventional catheter ablation for supraventricular arrhythmia was not successful or cannot be performed, AV nodal ablation with subsequent pacing should be considered	IIa	B	B	I
In CRT recipients for whom adequate ventricular pacing is not achievable with optimal pharmacotherapy because of supraventricular tachyarrhythmia, AV nodal ablation should be considered	IIa	B	B	I
In patients for whom AV conduction should be maintained considering the risk and benefit, or patients for whom prior rate control medications were not attempted, AV nodal ablation is not recommended	III	C	C2	VI

Abbreviations: COR, class of recommendation; CRT, cardiac resynchronization therapy; GOR, grade of recommendation; LOE, level of evidence; QOL, quality of life.

4 | Atrial fibrillation

4.1 | Classification, mechanism, and indications for treatment

4.1.1 | *Classification and natural history of AF*

a. | Classification of AF. AF is classified into 5 types based on factors such as clinical stage, duration, and presence or absence of spontaneous termination:[578,691]

1. First-diagnosed AF
   Defined as AF that is first confirmed on ECG, irrespective of the duration or whether it is truly the first episode. The AF is then classified as paroxysmal, persistent, or long-standing persistent (described below) based on the clinical course after diagnosis.
2. Paroxysmal AF
   Defined as AF that returns to sinus rhythm within 7 days of occurrence. Many cases of AF spontaneously terminate within 48 hours, but can last up to 7 days. If the patient is defibrillated within 7 days after the occurrence, it is also classified as paroxysmal AF.
3. Persistent AF
   Defined as AF that persists for >7 days after occurrence. It includes cases of defibrillation after 7 days with drug or DC defibrillation.
4. Long-standing persistent AF
   Defined as AF persisting for >1 year.
5. Permanent AF
   AF is accepted as permanent by both the patient and the physician. When considering the return and maintenance of sinus rhythm, it is not classified as "permanent" but as "persistent" or "long-standing persistent."

b. | Natural history of AF. AF is a progressive disease, with almost all cases starting as paroxysmal, which then progresses to persistent and long-standing persistent types. Although some reports claim that the progression is relatively slow (22% of cases progress from paroxysmal to persistent in 3 years),[692] other reports indicate that the condition progresses rapidly (15% of cases progress from paroxysmal to persistent within 1 year).[693] Age, hypertension, a history of stroke, obstructive pulmonary disease, and heart failure have been reported as factors that accelerate progression.[692,693]

4.1.2 | *AF mechanism (onset mechanism) and theoretical grounds for ablation*

a. | Cytological mechanism of AF onset. Many factors are intricately involved in the mechanism of AF generation at the micro level. These include myocardial fibrosis through the activation of fibroblast tissue, replacement of myocardial tissue with connective tissue, infiltration of adipocytes and inflammatory cells, myocardial cell hypertrophy and necrosis, and amyloid deposition.[694-697] These myocardial anatomical and electrical changes (ie, remodeling) can result in localized conduction disturbances, causing reentry and triggering AF.[698,699]

b. | AF initiation mechanism. In 1997, Jaïs et al reported the presence of focal AF caused by localized high-frequency excitation.[700] This is a relatively rare type; however, in relatively young patients with no underlying disease, AF is generated by irregular and rapid bursts of excitation from the same site and can be cured by local ablation treatment. In 1998, Haïssaguerre et al from the same Bordeaux group reported that 94% of extrasystoles triggering AF were of PV origin, and that ablation targeting extrasystoles eliminated AF in 62% of cases.[551]

Since then, it has been revealed that the extrasystoles that trigger AF occur mainly from venous vessels such as the superior vena cava, coronary sinus, Marshall vein (ligament), and inferior vena cava in addition to the PV. The atrial muscle extends from several millimeters to several centimeters in these blood vessels (myocardial sleeve),[701] and it is considered that these areas are prone to ectopic excitation because the sleeve contains sinus node cells and cells similar to Purkinje fibers,[702] and because of the occurrence of abnormal automaticity or trigger activity.[703] It has also been reported that in some cases of AF, the triggers occur in atrial myocardium unrelated to these venous systems.

c. | AF establishment mechanism. The mechanism by which a trigger that emerges from the PV, as described above, causes AF has been explained by intra-atrial reentrant theories. Of these, the widely accepted are the multiple wavelets reentry theory,[704] and the single meandering reentry theory.[705] The former is the theory of random reentry, based on the hypothesis that multiple reentrant circuits exist in the atrium at the same time, which repeatedly fuse and divide in a complex manner, and the direction and size of the excitation waves change randomly and rotate. The latter explains the mechanism of fibrillation as AF persisting when a single spiral wave causes meandering.

d. | Theoretical rationale for AF ablation. Necessary and appropriate catheter ablation according to the type of AF is required for both the initiation mechanism and the establishment mechanism described above. Electrical isolation of the PVs (and other triggering sites) acting as the AF initiation mechanism from the left atrium is the basis and rationale for ablation therapy in all types of AF.[578,691,706,707] Outside the PV entrance (PV antrum), both the PV and its surrounding tissue are electrically isolated from the left atrium (extended PVI method).

Triggers play a major role in paroxysmal AF, and it has been reported that 80%–90% of cases can be cured with extended PVI.[706,707] Extended PVI has also been reported to provide sufficient therapeutic effect in mild persistent AF with remodeling progression.[708]

However, PVI alone as a treatment for the trigger is often inadequate for persistent and long-standing persistent AF, because the maintenance mechanism of AF has a greater involvement than

the trigger alone. Strategies for eliminating the AF maintenance mechanism have been developed and include intra-atrial linear ablation,[709,710] complex fractionated atrial electrogram (CFAE) ablation,[711] ganglionated plexus (GP) ablation,[712] driver ablation,[713,714] and LVA ablation.[715]

Linear ablation is a technique that maintains sinus rhythm by extending the reentrant cycle, disrupting random reentrant circuits in the atrium with linear ablation of the roof of the left atrium, mitral valve isthmus, and the bottom of the left atrial posterior wall. It is believed that the complex potential known as CFAE in the atrium reflects conduction delay, the pivot point of reentrant circuits, and local driver excitation; thus, ablation of these areas can be expected to terminate AF. GPs present on the left atrial epicardium are intimately involved in the initiation and maintenance of AF, and many reports have indicated the efficacy of a technique for identifying and ablating ganglion sites from the endocardium (GP ablation). The most recent methods have included several systems for identifying and ablating the driver in the atrium as the mechanism for the establishment of AF, and a verification of these techniques is expected.

As described above, many approaches have been devised and implemented as strategies to capture the fibrillation matrix (AF maintenance mechanism) dispersed within the atrium; however, there are major limitations in the use of these techniques for the treatment of highly advanced AF (long-standing persistent AF). Even if treatments are performed multiple times using a combination of several techniques, a realistic outcome is final suppression of recurrence in approximately 60% of cases.[716-718]

4.1.3 | *AF ablation therapy indications*

a. | Rhythm control therapy for symptomatic AF. Figure 16 is a flowchart of rhythm control treatment for symptomatic AF based on the type of AF.

b. | AF catheter ablation indications with various pathologies (Table 63)

i. | Catheter ablation therapy as first-line therapy. Three RCTs[719-721] have examined the advantages and disadvantages of choosing catheter ablation as the first-line therapy without first using antiarrhythmic drugs for symptomatic paroxysmal and persistent AF, and a meta-analysis of these RCTs has also been reported[722] (98.7% were paroxysmal AF). The results demonstrated that the rate of AF elimination was significantly higher in the ablation group, whereas the complication rate was the same. These findings suggest that using catheter ablation as the first-line therapy for symptomatic paroxysmal AF cases is a valid option (Table 63).

Conversely, there is insufficient evidence for catheter ablation as a first-line therapy for persistent and long-standing persistent AF. However, considering that antiarrhythmic drugs are less effective for these cases than for paroxysmal AF, it is appropriate to use catheter ablation as a first-line therapy, especially in symptomatic recurrent cases.

ii. | AF with heart failure (left ventricular dysfunction). There is a close association between AF and heart failure. Heart failure triggers AF through increased left ventricular filling pressure, left atrial enlargement, and fibrosis, whereas AF tends to cause a decline in cardiac function owing to loss of atrial contraction and the effect of tachycardia and pulse arrhythmias. The presence of AF has been reported to lead to worse prognosis in patients with heart failure, and maintaining sinus rhythm is particularly significant in heart failure.[723] It has been shown that maintaining sinus rhythm with pharmacotherapy does not improve the prognosis of heart failure patients with AF, even compared with rate control.[724]

Five RCTs comparing the efficacy rates between pharmacotherapy (rate control therapy) and catheter ablation in heart failure patients with reduced cardiac function have been reported to date,[725-729] and a meta-analysis of these RCTs has also been published.[730] A total of 224 patients were randomized, 83% of whom had persistent AF. In the catheter ablation group, the LVEF increased by an average of 8.5% compared with the rate control group, and improvements in QOL and maximum oxygen consumption were also observed. There was no significant difference in the incidence of complications between the 2 groups.[730] The AATAC (Ablation vs. Amiodarone for Treatment of Persistent Atrial Fibrillation in Patients with Congestive Heart Failure and an Implanted ICD/CRT-D) trial compared the effect of catheter ablation and rhythm control with amiodarone in patients with AF-associated heart failure, and showed that the sinus rhythm maintenance rate after ablation was significantly higher than after amiodarone therapy (70% vs. 34%), resulting in significant

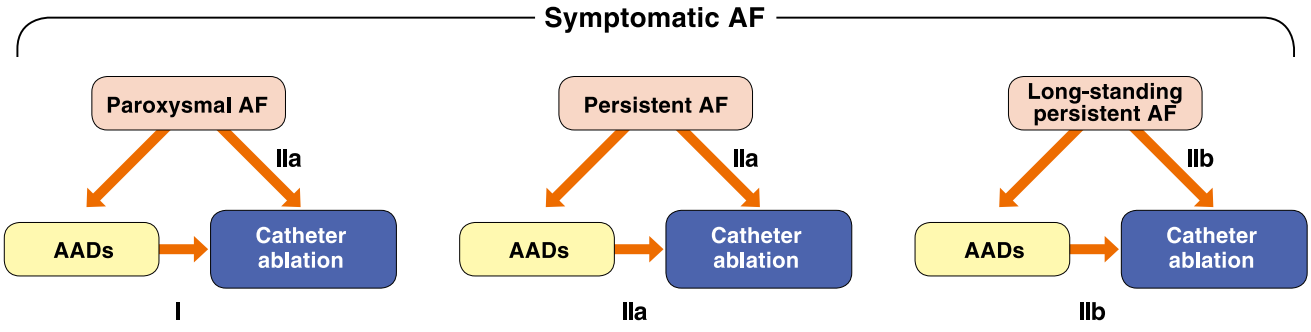


FIGURE 16 Indications for catheter ablation of symptomatic atrial fibrillation (AF). AAD, antiarrhythmic drug

TABLE 63 Recommendations and evidence levels for catheter ablation of AF

	COR	LOE	GOR (MINDS)	LOE (MINDS)
For patients with symptomatic paroxysmal AF refractory or intolerant to AADs and without severe left atrial enlargement or severe left ventricular dysfunction, catheter ablation is recommended	I	A	A	I
For patients with symptomatic recurrent paroxysmal AF before the initiation of AADs, catheter ablation should be considered as the first-line therapy	IIa	B	B	I
For selected patients with heart failure, it should be considered to use similar indications for AF ablation as in patients without heart failure	IIa	B	B	I
For patients with tachycardia–bradycardia syndrome, it should be considered to offer AF ablation	IIa	B	B	III
For patients with symptomatic persistent AF, catheter ablation should be considered	IIa	B	B	II
For patients with symptomatic long-standing persistent AF, catheter ablation may be considered	IIb	B	B	II
For patients with asymptomatic recurrent paroxysmal AF, catheter ablation may be considered	IIb	C	C1	III
For patients with asymptomatic persistent AF, catheter ablation may be considered	IIb	C	C1	III
For patients with suspected left atrial thrombus, catheter ablation should not be performed	III	A	D	V
For patients who are contraindicated to anticoagulation therapy, catheter ablation is not recommended	III	A	D	V

Abbreviations: AAD, antiarrhythmic drug; AF, atrial fibrillation; COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence.

improvements in QOL and mortality rates.[731] In addition, the CASTLE-AF (Catheter Ablation for Atrial Fibrillation with Heart Failure) trial compared the prognostic effect between catheter ablation and pharmacotherapy (rate or rhythm control) in patients with AF-associated heart failure, and showed that despite a relatively high recurrence rate in the catheter ablation group, the number of all-cause and cardiac deaths was approximately half of that in the pharmacotherapy group, and there was a significant improvement in prognosis.[391]

On the basis of these results, this guideline determines that catheter ablation therapy in AF patients with heart failure is an option that can be expected to improve prognosis, and recommends applying the same indication level with or without heart failure.

iii. | Paroxysmal AF with bradycardia–tachycardia syndrome. The efficacy of AF catheter ablation instead of permanent pacemaker implantation in patients with symptomatic bradycardia during AF arrest (bradycardia–tachycardia syndrome: sick sinus syndrome type III) has been reported for > 15 years. Although it is an established therapy, the only reports to date have been retrospective.[732] It has been reported that unsuccessful AF catheter ablation and the progression of sinus node dysfunction over time result in 8% of patients ultimately requiring permanent pacemaker implantation;[733] thus, careful follow-up is required after ablation surgery.

iv. | AF in the elderly. Many AF patients are elderly. Although there have been many studies on the efficacy and safety of catheter ablation treatment in the elderly, the majority are retrospective studies of relatively few patients.[734-737] Although most reports indicate that catheter ablation therapy for the elderly is adequately effective and safe, there are also reports indicating that the long-term recurrence rate and the risk of complications are high.[738]

In cases of paroxysmal AF, for which ablation is highly effective, it is considered appropriate to consider the treatment indication in elderly patients (≥75 years) in a similar manner to that for young people, providing that the elderly patients are maintaining activities of daily living. However, the suitability of catheter ablation for persistent and long-standing persistent AF in the elderly population is judged to be lower than that in the young population. At present, ablation therapy has limited therapeutic effect for persistent and long-standing persistent AF, and multiple treatments are often required. It is relatively frequently recommended to choose a means of coping with AF using conservative pharmacotherapy (rate control), especially for asymptomatic persistent AF in the elderly. It is important to fully explain the risks and benefits of ablation to each patient and to choose a treatment strategy that reflects the patient's wishes.

v. | Catheter ablation therapy for asymptomatic AF. AF is not a life-threatening disease. Thus, the main principle of catheter ablation therapy has been to improve the patient's QOL by maintaining sinus rhythm (improving palpitations, shortness of breath, fatigue, and exercise tolerance). In other words, the indications for AF catheter ablation in the conventional guidelines have been limited to symptomatic AF.[691]

However, it has recently been reported that ablation can improve the prognosis of AF patients with or without symptoms,[739] and that the prognosis of asymptomatic AF patients is worse than that of symptomatic AF patients.[740] This guideline has introduced a new ablation indication for asymptomatic AF, suggesting that catheter ablation may be indicated providing that it can improve the future prognosis of the patient, even if there are no subjective symptoms at the stage of diagnosis of AF and especially if QOL is not reduced.

At present, catheter ablation for asymptomatic paroxysmal AF tends to be performed widely and aggressively, and the validity

of the indication can be considered close to that for symptomatic paroxysmal AF. However, the validity of the indication is somewhat lower for asymptomatic persistent AF than for asymptomatic paroxysmal AF or symptomatic persistent AF, given the uncertainty of the effect of ablation therapy. It is necessary to carefully consider the indications for each patient with respect to age (ablation indications for the elderly).

Four studies have been published on the therapeutic effect and safety of catheter ablation for asymptomatic AF.[741-744] Some studies report that the effect of ablation treatment is the same as for asymptomatic AF and symptomatic AF,[741] whereas other studies report that the effect is worse for asymptomatic AF.[738] However, catheter ablation has also been reported to improve exercise tolerance, B-type natriuretic peptide levels, and QOL.[743,744] To date, there have been no published RCTs that examined the risks and benefits of catheter ablation for asymptomatic AF.

vi. | Conditions for which simple application of ablation therapy should be avoided. Thus far, the indications for AF catheter ablation in various disease states have been described. However, there are some conditions for which simple application of catheter ablation should be avoided.

1. First-episode AF

Approximately half (50/106) of the patients with first episode of paroxysmal AF showed no recurrence during 5 years of follow-up.[745] In other words, in patients with first episode of paroxysmal AF, the indications for catheter ablation should be considered after confirming the recurrence of AF.

2. Reversible cause of AF

Some of the factors that can cause AF are reversible.[746,747] The main reversible factors are shown in Table 64. If these factors can be resolved with treatment and lifestyle improvements, AF may disappear. Moreover, the effect of catheter ablation is known to be lower in patients with reversible factors than in those without these factors.[746,747] On the basis of the above findings, the principle for treating AF patients with reversible factors is to consider other solutions first and thereafter to consider the indication of catheter ablation for residual AF after correction.

vii. | Importance of comprehensive judgment for AF catheter ablation indication. As mentioned earlier, the indication of catheter ablation for AF involves a complex set of factors in individual patients. Three factors in particular must be considered for all patients: age, presence and degree of symptoms, and extent of AF progression (Figure 17).

TABLE 64 Reversible risk factors of AF

Hyperthyroidism
Obesity
Sleep apnea syndrome
Hypertension
Diabetes
Hyperlipidemia
Excessive alcohol intake
Smoking

In general, the indications are higher for younger patients than for their elderly counterparts, and for symptomatic AF than for asymptomatic AF. Ablation provides a higher cure rate in mildly advanced paroxysmal AF; therefore, treatment of this condition is more suitable than for persistent and long-standing persistent AF, for which treatment is less effective for suppressing recurrence. Rather than considering these 3 factors individually, it is essential to make a comprehensive judgment for each patient when considering indications for ablation treatment.

4.2 | Ablation procedures

4.2.1 | Pulmonary vein isolation

a. | Radiofrequency ablation. Most AF triggers originate in the pulmonary vein (PV).[551] A reentry in the PV–left atrial junction and in the PV also plays an important role in sustaining AF.[748] Therefore, PVI is a fundamental technique for ablation and performed first in all types of AF. Furthermore, if the AF is found to originate in the superior vena cava or non-PV areas, ablation for those triggers is added. The AF-free rate for paroxysmal AF with PVI is as high as 62%–84%.[749-752]

The purpose of PVI is to block conduction between the PV and the left atrium. The techniques include a method of individual PVI with EP-guided segmental RF applications,[749] and an anatomical isolation technique that enlarges the ipsilateral upper and lower PVs[750] (Figure 18). Box isolation,[753] which isolates not only the PV but also the posterior wall of the left atrium, has been developed (Figure 18). Isolating the posterior wall of the left atrium enables surrounding of the posterior wall trigger, CFAE, and LVAs, thereby blocking reentry.[752,753] Increasing the area of isolation has been shown to improve the success rate, particularly in persistent AF.[752-761] Recently,

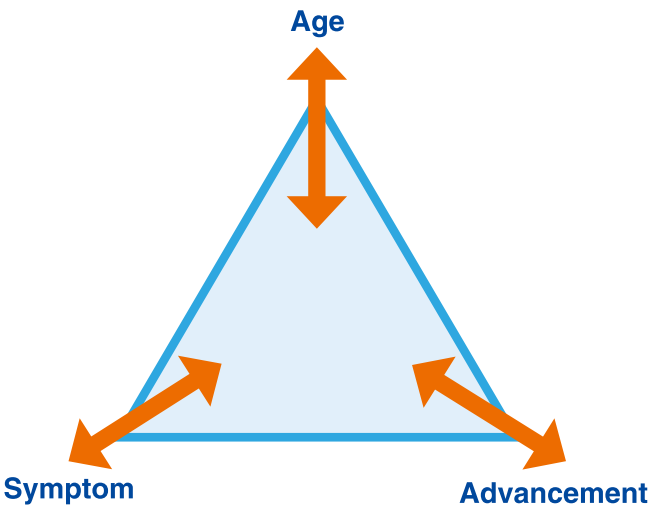


FIGURE 17 Importance of general judgments for the indication of AF catheter ablation. It is essential to consider 3 factors (age, degree of symptom, and advancement), not individually but in total

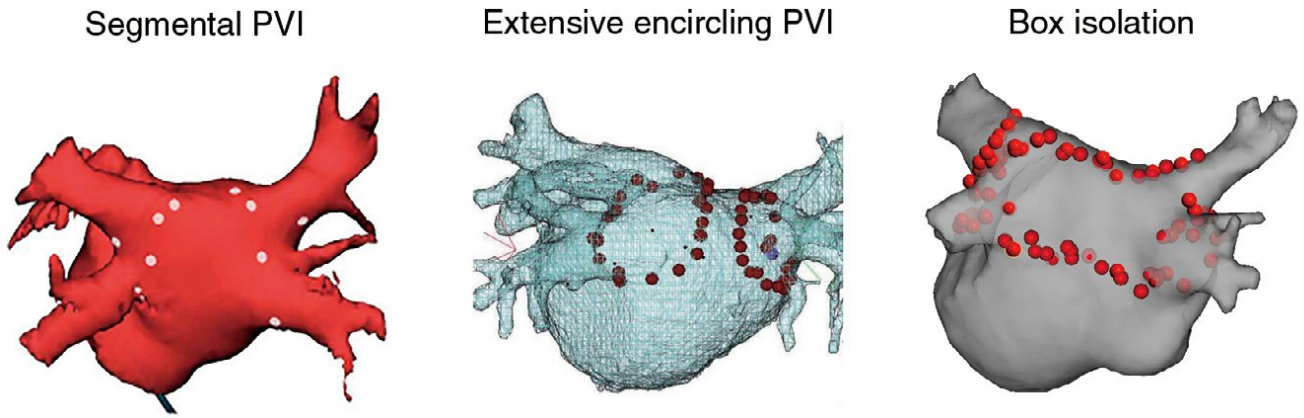


FIGURE 18 Techniques of pulmonary vein isolation (PVI)

anatomical approaches to PVI under 3D imaging have become more commonplace owing to the development and widespread use of 3D mapping systems such as the CARTO® and EnSite NavX™ systems.

Factors that affect the size and depth of the ablation lesion using RF include output, impedance, temperature, energy application time, and contact force (the force at which the catheter tip contacts the myocardium).[762,763] If the output is high and the contact is good, a larger ablation lesion is formed and the ablation is effective; however, the high contact temperature at the tip of the electrode can cause carbonization and thrombus formation. Therefore, an irrigation catheter that can be perfused with saline from the electrode tip was developed, making it possible to cool the endocardial surface, prevent carbonization and impedance increase, and provide high output. As a result, deeper transmural ablation lesions can be formed, and thrombus formation can be prevented. Irrigation catheters are commonly used at present.

Contact force is one of the factors that determines the size of the ablation lesion.[764-767] An effective ablation lesion is not formed without sufficient contact force; however, excessive contact force can cause cardiac perforation, as well as esophageal or phrenic nerve injury. It has become apparent that the ablation focus capacity could be controlled by controlling the contact force, in the same way the output and energy application time are controlled, and there are currently 2 types of contact force catheters available (ThermoCool Smart-Touch™ [Biosense Webster] and TactiCath™ [Abbott]).[558,768-772] These catheters can measure the strength and direction of the contact force. The areas with high contact force are the posterior wall of the bilateral PVs and the left atrial roof,[770] whereas the areas with low contact force are the anterior wall of the left superior PV and the right carina.[585,586,773,774] Sites with low contact force are associated with PV reconnection.[774] The use of contact force catheters has been reported to reduce impedance increase, cardiac perforation, steam pop, and thrombus formation while simultaneously creating more effective ablation lesions.[558,585,586,770,775-777]

A study comparing a group using the ThermoCool SmartTouch catheter with a group using a conventional catheter without the contact force sensing function showed that the use of the SmartTouch catheter resulted in lower rates of reconnection owing to conduction gap and adenosine, reduced fluoroscopy time, and lower rates of AF recurrence.[772,776,778-781] Conversely, a recent RCT in patients with paroxysmal AF who underwent ablation using a SmartTouch catheter were compared with a group whose ablation contact force information was disclosed to the operator and a group whose information was not disclosed. The PV reconnection in the acute phase was lower in the group whose information was disclosed (22% vs. 32%); however, there was no difference in long-term outcomes, fluoroscopy time, or complications.[782] At present, there is no evidence from RCTs that contact force monitoring can increase the success rate of AF ablation or can reduce complications.

b. | PVI using balloons. This guideline describes PVI techniques using the 3 currently available balloons. The following balloon therapy devices have been developed to isolate PVs and Table 65 shows the characteristics of the 3 types.

The following are common complications associated with PVI using balloons.

1. | Phrenic nerve injury. This event was seen in 1.5% of cases in a postmarketing surveillance of cryoballoons in Japan.[783] As a means of prevention, it is recommended to conduct the treatment with electromyogram monitoring of the diaphragm during freezing of the right PV.[784,785] It has been reported that nerve injury can be detected earlier and at a milder stage by keeping the electrical output of the phrenic nerve stimulation as low as possible.[786]

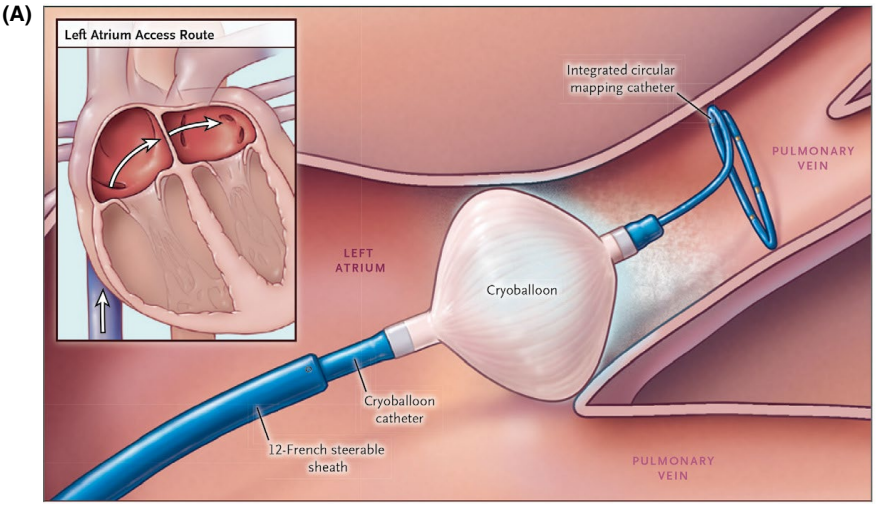
2. | PV stenosis. It has been reported that PV stenosis occurred in 4.1% of cases treated with cryoballoon and in 5.2% of cases treated with RF hot balloons.[787,788] This event can be prevented by observing the anatomy of the left atrium–PV and carefully performing ablation in the area proximal to the PV and in the vestibular area. Reports have demonstrated that it is effective to keep the minimum temperature of the balloon at −60°C or lower in cryoballoon therapy.[787,789,791]

TABLE 65 Characteristics of balloon devices available in Japan for PVI

	Cryoballoon	RF hot balloon	Laser balloon
Company	Medtronic	Toray	CardioFocus
Balloon size (diameter)	Fixed (28 or 23 mm)	Variable (max. 33 mm)	Variable
Shaft size (Fr)	10.5	12	12
One-shot device	Yes	Yes	No
Use of guidewire for balloon placement	Yes	Yes	No
Recording of PV electrogram during ablation	Possible	Not possible	Not possible
Facility to emit gas	Necessary	Not necessary	Not necessary

Abbreviation: RF, radiofrequency.

FIGURE 19 Cryoballoon ablation. (A) Schematic representation of pulmonary vein isolation procedure with the use of a cryoballoon catheter. (From Kuck et al, 2016[808] with permission.) (B) Fluoroscopic view during pulmonary vein occlusion with a cryoballoon, with the contrast medium retained in the distal portion of the left superior pulmonary vein



3. | Esophageal-related complications (left atrioesophageal fistula, paralysis of periesophageal vagal nerve). Overseas reports on cryoballoon therapy are few; however, in Japan, no complications related to this therapy have been reported in approximately 19,000 cases of clinical use (left atrioesophageal fistula). Although the recommended temperature varies depending on the report, many recommended that the temperature in the esophagus should be kept at or below 15°C.[791-794] Injection of cold water is recommended if there is an increase in esophageal temperature during RF hot-balloon therapy (>39°C).

i. | Cryoballoon ablation. This is a new ablation method that was introduced in Japan in July 2014 (Figure 19, Arctic Front Advance [Medtronic]). Devices that can be used in Japan as a cryoablation system deliver pressurized liquid nitrous oxide from the tank in the console to the tip of the cryoballoon via the catheter lumen tube, and the ultra-low temperature of the balloon caused by heat of vaporization (Joule-Thomson effect)[795] induces a freezing injury to the myocardial tissue in contact with the balloon. The upper hemisphere of the balloon becomes cryogenic, and the myocardial tissue at the site of balloon placement undergoes frozen necrosis.[796]

The balloon diameters are 23 or 28 mm, and are selected according to the size of the PV. Before inserting the balloon into the FlexCath sheath, efforts should be made to remove any air adhering to the folded balloon in a vessel filled with heparinized saline to eliminate the risk of air embolism (the balloon tip should be moved around or the balloon surface should be gently massaged).[797-800] It has been reported that expanding the balloon in a container filled with heparinized saline before inserting the balloon into the sheath and removing the air adhering to the folded balloon can help reduce the incidence of air embolisms.[801]

Studies have shown that the better the status of PV occlusion by the balloon, the lower the minimum attainable temperature, the greater the success rate of PVI, and the better the long-term results of isolation.[802,803] Recent reports have shown that one freezing ablation is considered sufficient,[804,805] and a single freezing time of 180 s is recommended.[806,807]

Postmarketing surveillance conducted in Japan showed that the success rate in the acute phase of PVI was > 99%, and that the sinus rhythm maintenance effect in the 6-month follow-up after the 3-month blanking period was good at approximately 88%.[783]

A large-scale RCT comparing the conventional irrigated RF system and the cryoballoon system found that the procedure time and the indwelling time of the ablation catheter in the left atrium were significantly shorter in the cryoballoon group; however, there was no significant difference in the AF recurrence suppression effect and safety between the 2 groups.[808]

The advantages and disadvantages of the cryoballoon system compared with the irrigated high-frequency system are detailed below.

Advantages

1. A single freeze can create a full-circumferential lesion, and the procedure time is shorter than that with the RF ablation point-by-point method.[809-811]
2. Operation with the balloon inflated has a low risk of cardiac perforation.[783,807]
3. The risk of left atrioesophageal fistula development is lower than with the RF point-by-point method.[810-812]
4. Ablation is associated with fewer symptoms, such as chest pain, than with the use of RF energy.[636,642,813]

Disadvantages

1. This method is essentially only applicable to PVI.
2. The PVI site cannot be arbitrarily selected. (Isolation can only be performed at the site where the balloon occludes the PV.)
3. Nitrous oxide exhaust equipment is required after the procedure.
4. The incidence of phrenic nerve injury is higher than with RF ablation.[808,809]

ii. | Radiofrequency hot-balloon ablation

1. | Basic principles. The RF hot-balloon system consists of a SATAKE Hot-Balloon catheter (Toray Industries Inc) and a SATAKE Hot-Balloon generator, which is the RF generator. The diluted contrast agent in the balloon is heated by RF energy application and by stirring the liquid in the balloon to maintain a uniform balloon surface temperature. Furthermore, the contact surface of the PV entrance with the balloon is heated by heat conduction. The output is automatically adjusted (up to 150 W) to ensure that the core temperature of the balloon (up to 70°C, or up to 73°C only in the upper left PV) reaches the set temperature. The depth of the ablation lesion depends on the balloon surface temperature and the ablation time.

A feature of the RF hot balloon is that the balloon size (max. diameter 33 mm) can be changed by adjusting the amount injected (max. 20 mL) into the balloon. Adopting a flexible compliance balloon means that it can be crimped into various PV shapes (Figure 20). In addition, the distance from the tip of the catheter to the proximal part of the balloon is short, resulting in superior catheter operability in the left atrium. Adequate sedation and analgesia are required during surgery owing to pain associated with the current.

2. | Efficacy and safety. Radiofrequency hot balloons have been developed in Japan. At present, they are used for AF treatment only in Japan, and the evidence for treatment is limited. The efficacy and safety of RF hot balloons for paroxysmal AF have been verified in an RCT conducted in Japan.[788] In the same study, one PV entrance and antrum could be repeatedly energized up to 3 times, and 98% of the PVs could be electrically isolated by energizing the balloon alone. One year after ablation, the sinus rhythm maintenance rate was 59%, indicating that the

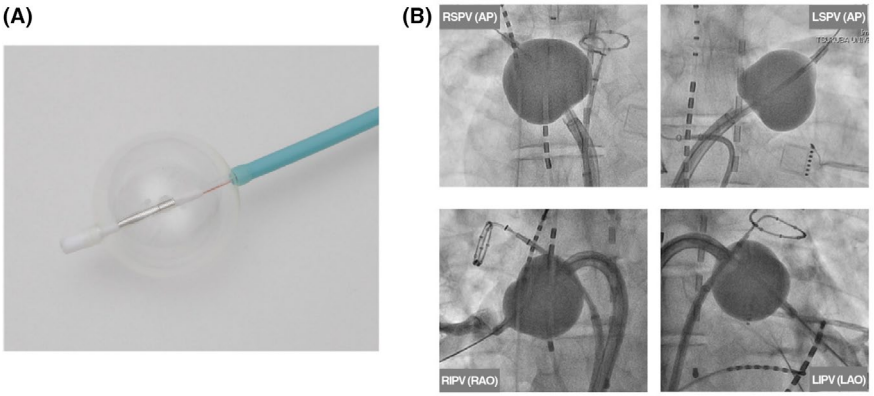


FIGURE 20 Radiofrequency hot-balloon ablation. (A) Appearance of the SATAKE Hot-Balloon. (B) Selective pulmonary vein angiograms using a hot balloon catheter. AP, anteroposterior; LAO, left anterior oblique; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RAO, right anterior oblique; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein

sinus rhythm maintenance effect was superior to that of antiarrhythmic drugs (4.7%).

However, phrenic nerve palsy was reported in 3.7% and severe PV stenosis (>70%) in 5.2% of cases as a result of energizing the PV inlet with a small volume of injection medium into the balloon. Although the effectiveness of RF hot balloons for paroxysmal AF was confirmed, safety concerns were also raised. It is recommended to inject at least 10 mL of diluted contrast medium into the balloon for treatment, to avoid phrenic nerve paralysis and postoperative PV stenosis. A method of energizing the PV antrum by sufficiently expanding the balloon has been attempted;[813] however, the optimal duration of energy application for each PV has not been established. In the future, it will be necessary to verify the efficacy and safety of treatment targeting the PV antrum.

When performing PVI using a RF hot balloon, it is recommended to use cold water if an increase in esophageal temperature (>39°C) is observed, to avoid damaging the esophageal mucosa after energizing the left atrial posterior wall.[815] When the esophagus is excluded by the dilated balloon, the injected chilled water is prevented from passing through the excluded esophagus behind the balloon; thus, it may not be possible to rapidly reduce the esophageal temperature. Excessive infusion of chilled water may cause cold water to flow back into the trachea, which can cause aspiration pneumonia. Therefore, if the esophageal temperature is not promptly reduced with injection of cold water, it is vital to avoid excess increase in the esophageal temperature by immediately stopping the energy application or temporarily interrupting the balloon crimping to the posterior wall of the left atrium.

iii. | Visually guided laser balloon ablation

1. | Basic principles. The visually guided laser balloon ablation system (Heart-Light® [CardioFocus]) is a device that irradiates an infrared laser (wavelength 980 nm) to ablate the entrance of the PV circumferentially and to isolate the PV. The balloon at the tip of the catheter is expanded; blood is excluded by the balloon, maintaining close contact with the PV entrance, and ablation is performed while visualizing the procedure with the endoscope inserted into the balloon (Figure 21). The balloon at the tip of the catheter is highly compliant, adaptable to a wide range of dissections of various PV structures, and can deliver titrated energy based on anatomical considerations. The size of the balloon can be controlled by changing the volume of dilatation fluid to match the size of the target PV. The operator adjusts the ablation area by rotating the dial on the catheter with the balloon fixed in place.

As the infrared laser used for ablation is not visible, the ablation area is indicated by green and red guide lights. The PV perimeter is continuously laser ablated circumferentially while overlapping to ensure there are no gaps (moving approximately 30° each time, about 12 times in total). Before and after ablation, the PV potential is mapped using a conventional mapping catheter to confirm whether the PV is isolated. Heavy water is used as an expansion fluid to change the size of the balloon. Heavy water minimizes the absorption of infrared laser in the balloon and suppresses the temperature increase due to reflux of the fluid.

2. | Clinical outcomes. In a trial conducted by the US Food and Drug Administration, visually guided laser balloon ablation was shown to be non-inferior to RF ablation. The success rate of single PVI was 87.8% in the visually guided laser balloon ablation group and 83.3% in the RF ablation group (97.7% and 99.1%, respectively, in the acute phase). Visually guided laser balloon ablation has been reported to have significantly less PV reconnection during the procedure than RF ablation (2.71% vs. 5.72%), and no esophageal fistula or PV stenosis was reported.[816]

Schmidt et al,[817] in their study on the therapeutic outcome of laser balloon ablation, reported that PVI was possible in 134 of 137 (98%) veins ablated using only endoscopic visualization of the PV for guidance without referencing electrical signals. In addition, during the mean observation period of 266 days, 27 of 35 (77%) patients had no recurrence of AF in the absence of antiarrhythmic medication. Bordignon et al achieved higher success rates with higher energy levels (8.5-12 W), with an 89% success rate in the acute period and an 83% success rate in the long term (median follow-up period: 311 days), but reported a long-term success rate of 60% with lower energy levels (5.5-8.5 W).[818] Šedivá et al[819] reported that 692 of 698

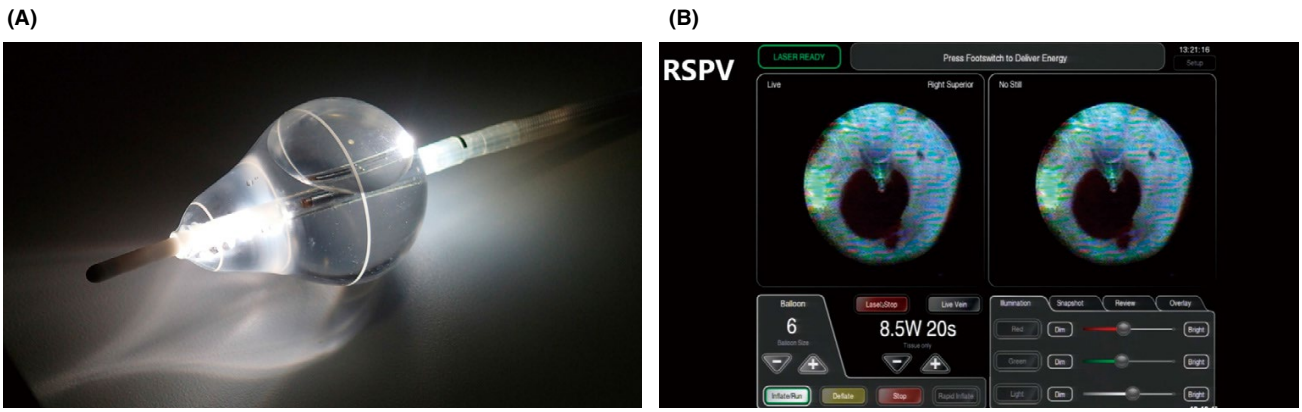


FIGURE 21 Visually guided laser balloon ablation system. (A) Inflated shape of the Heart-Light® laser balloon. (B) Endoscopic view of the antrum of the right superior pulmonary vein (RSPV) during laser energy application (green light)

(99.1%) PVs could be isolated as a result of ablation in 194 patients with paroxysmal and persistent AF using visually guided laser balloon ablation. No relapse occurred in 75% of patients with persistent AF after 1 year. For paroxysmal AF, the proportion of patients with no relapse was 82.3% after 1 year, 75.9% after 2 years, 75.9% after 3 years, and 75% after 4 years, indicating that the long-term outcomes were also favorable. The authors also reported complications including phrenic nerve injury in 2.06%, cardiac tamponade (pericardial effusion) in 0.51%, and cerebral infarction or TIA in 0.514% of patients.

The visually guided laser balloon ablation system is a new technology,[820] and it has been covered by insurance in Japan since July 2018. In the future, more cases will be accumulated, and the efficacy of this treatment will be examined.

4.2.2 | *Ablation techniques other than PVI*

a. | Linear ablation, CFAE ablation, and ablation of non-PV triggers

i. | Intra-atrial linear ablation. Intra-atrial linear ablation is a method for modifying the fibrillation matrix, and it was developed as an additional ablation for patients for whom PVI was not sufficiently effective. The sites most often targeted for ablation are the lines connecting both superior PVs with the roof of the left atrium (roof line),[710] and with the mitral valve isthmus (mitral isthmus line).[821] To isolate the left atrial posterior wall, a line along the posterior wall of the left atrium that connects with both inferior PVs (bottom line) may be added together with the roof line.[822,823]

The roof line is created on the premise that both superior PVs are isolated, and the roof of the left atrium between the superior PVs or slightly toward the posterior wall is ablated. Completion of the block line is confirmed by a continuous double potential along the ablation line under pacing (mostly left atrial appendage pacing) from the roof at the anterior wall, and through the excitation of the posterior wall of the left atrium from the bottom to the top.[710]

The bottom line is often created in combination with the roof line to isolate the left atrial posterior wall, with linear ablation performed between the inferior PVs. In addition to ablation of the anterior walls of both PVs, box isolation has also been reported, whereby the roof and the bottom line are created to simultaneously isolate the PVs and the left atrial posterior wall.[753] The endpoints are disappearance of the potential in the left atrial posterior wall, confirmation of the potential dissociated from areas other than the left atrial posterior wall, and loss of atrial capture based on pacing from the left atrial posterior wall.

The mitral isthmus line is the linear ablation site between the left inferior PV and the mitral annulus, and it is often difficult to form a complete block because of poor catheter contact or the heat radiation effect due to the presence of the coronary sinus. Ablation from the coronary sinus is required in 20%–25% of cases. It has been reported that using a steerable sheath[824,825] and creating a transseptal puncture site[826] have improved catheter contact and the successful block creation rates. The block is confirmed using the differential pacing method.

Linear ablation is an effective method for atrial tachycardia after PVI and atrial focus in the left atrial posterior wall not originating from the PVs. However, new atrial tachycardia often occurs owing to incomplete lines or resumption of conduction.[827,828] When performing linear ablation, it is recommended to aim for a complete block. The effect of linear ablation on improving the outcome of persistent AF has not been established and remains controversial.[708]

ii. | CFAE ablation. In this method, RF energy application is performed during AF, targeting an abnormal atrial potential called CFAE.[711] CFAE is a low-voltage electrogram (≤0.15 mV), and is a split potential consisting of ≥ 2 deflections or a potential that shows continuous baseline deflection, defined as an atrial potential with a very short cycle (<120 ms).[711] It is considered to reflect conduction delay, the pivot point of a reentrant circuit, and localized driver excitation. The most reported sites are the PV, atrial septum, left atrial roof, left atrial septum annulus, and the coronary sinus ostium. Although this method was originally developed as a single treatment, it is usually recommended to be used in combination with extended PVI. The endpoint is disappearance of CFAE or termination of AF, and the outcome is reported to be favorable when AF is terminated.[829] If CFAE disappears and the patient transitions to AFL or atrial tachycardia, a return to sinus rhythm can be expected through mapping and ablation of the tachycardia. However, problems associated with CFAE ablation include the need for extensive ablation, difficulty in eliminating all CFAEs in the atrium, and failure to terminate AF in some cases. Moreover, meta-analyses and RCTs have reported that there is no difference in the outcome of PVI and CFAE, even when CFAE is added to PVI.[708,830]

Meanwhile, a stepwise approach combining PVI, CFAE ablation, and linear ablation reported that > 80% of AFs terminated or transitioned to atrial tachycardia.[831,832] The sinus rhythm maintenance rate after the first ablation was low in the 5-year long-term outcome report,[718,833] and the method has not become general practice. In addition, RCT results have reported that this stepwise approach does not improve treatment outcomes.[830,834]

iii. | Ablation of non-PV triggers. It has been reported that AF triggers (non-PV triggers) originating from sources other than the PV are found in approximately 10%–20% of cases.[835-838] Patients with non-PV triggers have poor ablation outcomes;[838,839] however, ablation of non-PV triggers has better outcomes than when ablation is impossible.[836,840,841] Therefore, ablation is recommended if a non-PV trigger is detected, irrespective of whether the condition is paroxysmal or persistent AF. To perform ablation for non-PV triggers, cardioversion is performed as needed after placement of multiple catheters, and the presence of non-PV triggers and their origins are mapped under sinus rhythm. If the trigger does not appear, it is advisable to gradually increase isoproterenol while closely monitoring blood pressure and pulse, and to induce AF with a high dose (up to around 20-30 μg/min).[842] The most common sites for non-PV triggers include the superior vena cava, posterior wall of the left atrium, crista terminalis, coronary sinus (inferior mitral annulus), and Marshall ligament (remaining left superior vena cava).[842] If the origin

is the superior vena cava, the remaining left superior vena cava, or the posterior wall of the left atrium, these areas can be isolated, but other sites require detailed mapping and local ablation. However, mapping of non-PV triggers is often difficult and frequently unsuccessful,[836,840,843] because the triggers rarely occur or rapidly transition to AF and require frequent defibrillation.[843] Empirical ablation of the above mentioned sites and concomitant use of antiarrhythmic drugs are considered for unsuccessful cases. Although there is no reliable way to predict the presence of non-PV triggers, factors including persistent AF, young age, female sex, left atrial enlargement, and low atrial potential have been linked to the presence of non-PV triggers.[839,844]

b. | Ablation of GPs, drivers, and LVAs

i. | GP ablation

1. | Theoretical background. The role of the autonomic nervous system in the onset of AF has been previously studied, and it has been reported that vagal nerve excitation is involved, especially at night and at rest. GP ablation for AF was designed to suppress autonomic nervous activity at the onset of AF.[845,846]

Animal studies and clinical cases have demonstrated that excitation of the intrinsic cardiac GP directly causes focal triggers of the PV and superior vena cava.[847,848] A conceivable mechanism is that the GP contains cholinergic neurons and adrenergic neurons, and excitation of these neurons simultaneously shortens the duration of action potentials and increases/extends calcium transients, resulting in early afterdepolarization and firing activity. Patterson et al experimentally demonstrated that shortening the duration of action potentials and increasing/extending calcium transients associated with this autonomic nervous activity resulted in focal firing from the PVs.[847] Vaitkevicius et al anatomically observed that autonomic nerve fibers extend from the intrinsic GP into the PV.[848]

GPs are present in the epicardial adipose layer, and the following 5 types are found in the left atrium (Figure 22): (1) superior left GP (antrum superior to the left superior PV), (2) anterior right GP (from the antrum anterosuperior to the right PV to the septum), (3) Marshall tract GP (ridged area between the left PV and the left atrial appendage), (4) inferior left GP (posterior lower wall inferior to the left inferior PV), and (5) inferior right GP (posterior lower wall inferior to the right inferior PV).

2. | GP ablation methods. To identify the GP site, a high-frequency stimulus with a cycle of 50 ms is applied from an ablation catheter at 20 V for 5 s with a pulse width of 10 ms Areas where the stimulus causes a vagal response, such as sinus bradycardia, sinus arrest, and atrioventricular block, are identified as GP sites. The order of ablation is important in GP ablation. Autonomic nervous system stimulation of the sinus node is conducted from the superior left GP, inferior left GP, and Marshall tract GP via the anterior right GP and inferior right GP. Therefore, ablation must start from the left GP and the anterior right GP must be ablated last.

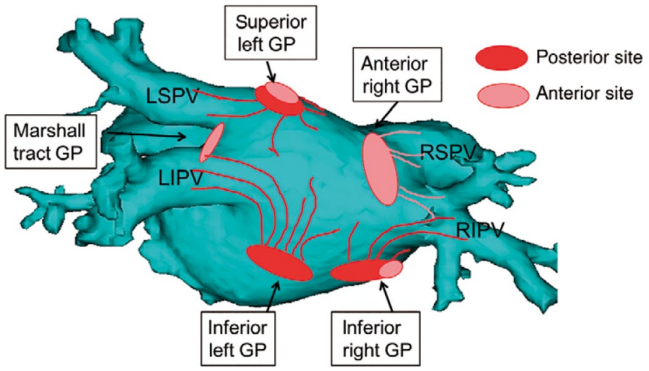


FIGURE 22 Localization of the ganglioplexus (GP) outside the atrium. LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein

As the GPs are contained in the epicardial adipose layer, high output application is required when using RF energy from the endocardium. Ablation at 30-35 W for 50-60 s with a contact force guide catheter is advisable. After ablation, RF stimulation similar to that before energy application is performed, and disappearance of the vagal nerve response is the endpoint.

3. | Problems associated with GP ablation. Re-innervation in the chronic phase has been reported in surgical GP ablation, and permanent GP suppression is an issue. The long-term results of a multicenter study on surgical GP ablation have shown no clear usefulness and have also demonstrated many complications.[849]

ii. | Driver ablation. Jalife et al[850,851] were able to visually analyze the excitation pattern during AF using optical mapping techniques, and have proven the existence of a rotor in an animal model. They have also proposed a hypothesis (mother rotor theory) that a reentry with a very short excitation cycle of several millimeters in diameter exists in the atrium, and that the reentrant mechanism drives the atrium, thereby maintaining AF.

Thereafter, attempts have been made to visualize the excitatory kinetics in clinical AF, to try to understand the process intuitively. The following systems have been put into practical use, although evidence has not been established for any of the systems.

- FIRM (focal impulse and rotor modulation)[852-854] (not yet approved in Japan).
- Cardioinsight[714,855] (not yet approved in Japan).
- ExTRa Mapping.[856]

FIRM is a system that inserts a 64-pole basket catheter into both atria and visualizes the rotor using a proprietary algorithm.[852,853] However, its efficacy was not recognized in a multicenter trial on persistent AF.[854]

Cardioinsight is a system that projects the excitation pattern created using a vest that records ECG data from the body surface and displays it onto a cardiac CT image.[714,855] No multicenter trial has yet reported its efficacy.

ExTRa Mapping is an online real-time arrhythmia imaging system created in Japan.[856] It has been reported that the system has achieved phase mapping close to optical mapping by adding information on membrane potential changes, acquired through in silico analysis, to the transit time of the excitation wavefront based on bipolar leads recorded with a spiral 20-pole 2.5-cm-diameter catheter and spatiotemporal signal complementation using artificial intelligence.

iii. | Ablation of LVAs. The involvement of LVAs recorded during sinus rhythm has attracted attention as a finding that reflects the substrate in persistent AF. Ablation of LVAs has recently been reported to be useful owing to the ease of identifying LVA sites (bipolar potential wave height <0.5 mV).[857]

LVAs are distributed on the septum, anterior wall, and posterior wall, and often have complex potential waveforms such as double potentials and fractionated electrograms.

Rolf et al[715] reported that only 10% of patients with paroxysmal AF have LVAs, whereas 35% of patients with persistent AF have LVAs. Furthermore, ablation of these LVAs with an individual approach is reported to have a non-recurrence rate of 75%–80% in patients with persistent AF. Similarly, in Japan, Yamaguchi et al reported a 20%–30% AF suppression rate with PVI alone, but a 70%–80% suppression rate with PVI plus LVA ablation in patients with persistent AF.[858]

An advantage of ablating LVAs is that no special catheter or software is required. Conversely, the problems with this method are as follows: the local atrial potential changes with the heart rhythm;[859] the ablation method is determined by the localization of the LVA; and, for sites without anatomical barriers, such as the anterior wall of the left atrium, there is no alternative but to ablate the margins or the entire LVA. Furthermore, a report suggested that the usefulness of LVA ablation cannot be confirmed,[860] and no evidence has been established.

c. | Chemical ablation of the marshall vein

i. | Significance and indication. An additional technique for AF ablation is injection of ethanol into the Marshall vein (not covered by insurance; Figure 23).[861,862] The implementation of this method as part of AF ablation has the following significant effects.

1. Suppression of extrastimuli that trigger AF originating from the Marshal vein.[863-865]
2. Suppression of parasympathetic nerve-dependent AF by a localized parasympathetic plexus crushing effect of atrial tissue.[866,867]
3. Ablation to the mitral valve isthmus (suppressing effect on macroreentrant atrial tachycardia rotating around the mitral valve annulus).[868,869]

Arrhythmias requiring this treatment include (1) atrial tachycardia dependent on the mitral isthmus (between the left inferior PV and the mitral annulus) that cannot be treated with ablation from the endocardial side or from within the coronary sinus and (2) atrial arrhythmia originating from the Marshall vein that cannot be treated

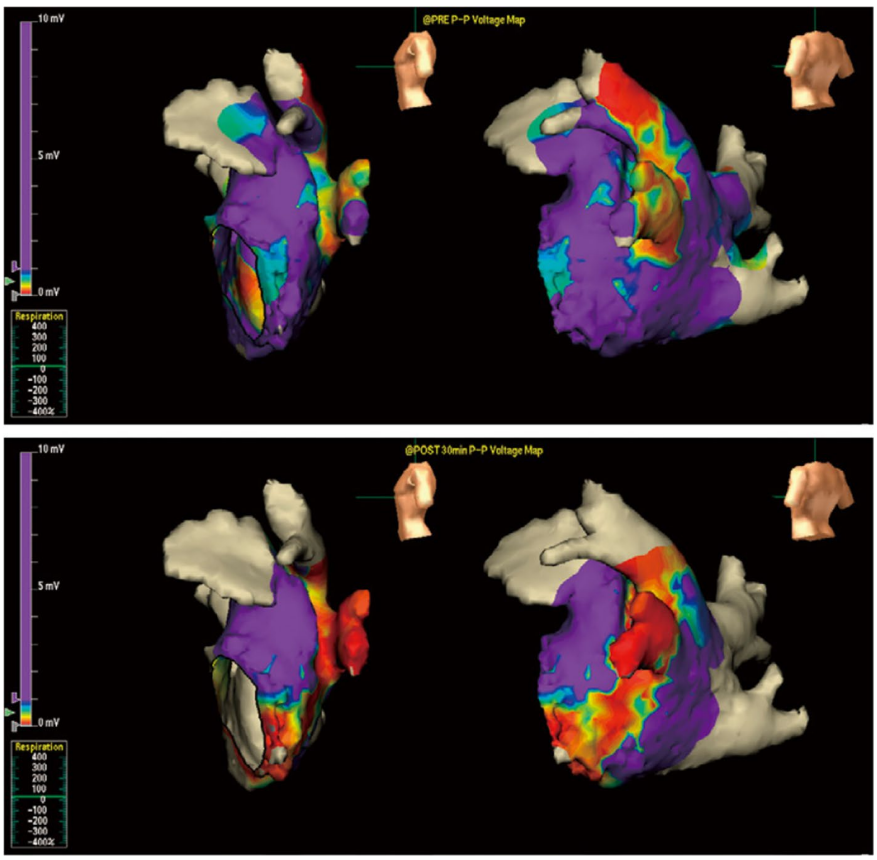


FIGURE 23 Voltage map of the left atrium before and after ethanol injection into the vein of Marshall. After ethanol injection (Lower panel), a low-voltage zone (<0.5 mV) is observable at the mitral isthmus area

with ablation from the endocardial side or from within the coronary sinus.

ii. | *Method.* A balloon catheter available for angioplasty, with a diameter of 1.5-2.0 mm, is inserted over the wire to the distal end of the Marshall vein via a long guide sheath inserted into the coronary sinus. The balloon is inflated, and anhydrous ethanol is slowly (over 60-90 s) injected several times.[861,862,867,868]

iii. | *Complications.* Marshall vein penetration can often achieve hemostasis by inflating a balloon proximal to the site of penetration, and rarely causes cardiac tamponade. Coronary sinus and Marshall vein dissection can occur during coronary sinus and Marshall venography, as well as during procedures within the same vessels. Another problem with this method is that the injury range due to alcohol injection is sometimes larger than expected.

4.2.3 | Atrial tachycardia after AF ablation

a. | *Overview.* With the widespread use of catheter ablation treatment for AF, the onset of atrial tachycardia after ablation has attracted attention as a major problem.[870] When atrial tachycardia develops, the heart rate tends to be higher than at the time of initial AF, and many patients complain that the subjective symptoms worsen after ablation. Certain associations between the catheter ablation procedures for AF and the onset of postoperative atrial tachycardia have also been indicated.

b. | *Prevalence.* As shown in Table 66,[807,871-878] postoperative atrial tachycardia more frequently occurs with the following 3 situations than when the target conduction block is completed.

1. Incomplete ablation in PVI (the area around the PV is ablated but the vein is not electrically isolated).
2. Linear ablation that does not result in the creation of a conduction block.
3. CFAE ablation.

TABLE 66 Incidence of atrial tachycardia (AT) after various procedures of AF catheter ablation

	Creation of conduction block at lesion	Incidence of AT (%)
Segmental PVI[871,872]	Yes	1-2.9
Circumferential PV ablation (CPVA)[873]	No	24
Circumferential PVI (CPVI)[874]	Yes	19
Cryoballoon PVI[809]	Yes	0.8
CPVA plus linear ablation[875,876]	No	31
CPVI plus linear ablation[877]	Yes	11
PVI plus CFAE[877]	No (CFAE)	29
PVI plus linear ablation plus CFAE (stepwise)[878]	No (CFAE)	40

Abbreviations: CFAE, complex fractionated atrial electrogram; PVI, pulmonary vein isolation.

Insufficient ablation that does not result in completion of a conduction block (the conduction block is incomplete or reconduction occurs) is believed to be related to creating a new substrate for the formation of the reentrant circuit (described later).

c. | *Onset mechanisms of atrial tachycardia.* Atrial tachycardia that occurs after AF catheter ablation can be broadly classified into 2 types according to the mechanism: (1) focal atrial tachycardia and (2) macroreentrant atrial tachycardia.

Focal atrial tachycardia is diagnosed when 3D mapping shows that the excitation spreads from the local area to the surrounding area in a circular manner. The occurrence mechanism is often local reentry due to microreentry; however, very occasionally, tachycardia has been reported to be caused by a non-reentrant mechanism (abnormal automaticity or firing).[879] The most common type of microreentry is a circuit that rotates through the conduction gap of a previously ablated or isolated PV.[875]

Atrial tachycardia due to macroreentry often results from reentry around the intra-atrial anatomical structures or reentry of the iatrogenic site created during AF catheter ablation. Iatrogenic reentrant circuits may result from incomplete PVI ablation, linear ablation without creating a conduction block, or CFAE ablation.

Analysis of the causes of macroreentrant atrial tachycardia that actually occurred after AF ablation showed that there are 3 common types: (1) mitral valve circuit, (2) PV circuit, and (3) tricuspid valve circuit.[875,880] In addition, atrial tachycardia that occurs through two or more gaps in the PVs that have resumed conduction is often found to be iatrogenic.[881]

d. | *Treatment strategies.* Atrial tachycardia after AF ablation often develops relatively early after the procedure. It is not uncommon for the condition to occur only during the blanking period (3 months after ablation). Therefore, the initial treatment is generally conservative. First, the patient's progress is monitored with ventricular rate control to relieve symptoms caused by tachycardia. If atrial tachycardia does not disappear, antiarrhythmic drug treatment or cardioversion is considered. Re-ablation is considered for atrial tachycardia that occurs beyond the blanking period or recurrent atrial tachycardia.

In ablation for atrial tachycardia, the tachycardia circuit is analyzed in detail using a 3D mapping system (see section **"3.4 Atrial tachycardia"** in this chapter). For reentrant atrial tachycardia due to incomplete ablation, a complete block is created by additional ablation of the PV reconnection site or the incomplete block line. For the most frequent reentrant atrial tachycardia around the mitral valve, it is essential to create a complete conduction block in the mitral isthmus; however, this procedure is known to be highly technically difficult. It has been reported that using a steerable sheath as the guiding sheath for the ablation catheter improves

the rate of successful creation of complete conduction blocks in the mitral isthmus.[824]

4.3 | Perioperative anticoagulation therapy for AF ablation

Thromboembolism is one of the most serious complications in AF ablation. Appropriate preoperative, intraoperative, and postoperative anticoagulant therapy is extremely important to reduce the risk. This guideline recommends perioperative anticoagulation for ablation, including direct-acting oral anticoagulants (DOACs) in addition to conventional warfarin, as shown in Table 67.[578,882-894]

4.3.1 | Preoperative management

First, it is necessary to check for left atrial thrombi. The gold standard for diagnosis is transesophageal echocardiography (TEE) observation, which considers (1) the type of AF (paroxysmal or persistent), (2) the duration of AF, (3) the history of cerebral infarction, and (4) the $CHADS_2$ score. TEE is performed before ablation. The complication rate of left atrial thrombus is ≤0.3% in patients with a CHA_2DS_2-VASc score of 0, whereas it is ≥5% in patients with a score ≥2. Preoperative TEE is strongly recommended in high-risk patients with long-standing persistent AF, enlarged left atrial diameter, and high $CHADS_2$ score.

In addition, a filled image of the left atrial appendage on contrast CT can be helpful, although caution is needed for contrast CT scans taken >1 month before the date of ablation. Observation by intravascular echocardiography is also useful.

Preoperative anticoagulant therapy should follow the guidelines for AF defibrillation and should be used for at least 3 weeks in cases of persistent AF and in high-risk patients ($CHADS_2$ score ≥2).[578,882]

Although there is no definitive consensus for paroxysmal AF and low-risk cases ($CHADS_2$ score 0-1), many institutions use warfarin or DOAC for >1-3 weeks.

With respect to withdrawal and continuation of anticoagulants before ablation, warfarin is conventionally temporarily discontinued, with heparinization before ablation. However, cerebral embolism has been frequently observed when resuming warfarin postoperatively. Therefore, ablation has been attempted while continuing warfarin, and Wazni et al reported a significant reduction in both hemorrhagic and ischemic complications in the warfarin continuation group compared with the group that temporarily stopped warfarin preoperatively and was bridged to high- or low-dose heparin.[883]

DOACs became available in Japan in 2011, and 4 types are currently in use: dabigatran, rivaroxaban, apixaban, and edoxaban. DOACs have a short half-life of around 5-17 hours and a short time to peak. Thus, they are frequently used as anticoagulant drugs instead of warfarin.

TABLE 67 Recommendations and evidence levels for anticoagulation strategies before, during, and after AF ablation

	COR	LOE	GOR (MINDS)	LOE (MINDS)
For patients with persistent AF or those with paroxysmal AF and a high risk for embolism (CHADS2 score ≥2), systemic anticoagulation with warfarin or a DOAC should be considered for at least 3 weeks before AF ablation	IIa	C	C1	VI
For patients who have been therapeutically anticoagulated with warfarin or dabigatran, performance of the ablation procedure without interruption of warfarin or dabigatran is recommended	I	A	A	I
For patients who have been therapeutically anticoagulated with rivaroxaban or apixaban, performance of the ablation procedure without interruption of rivaroxaban or apixaban should be considered	IIa	B	B	II
For patients who have been therapeutically anticoagulated with edoxaban, performance of the ablation procedure without interruption of edoxaban should be considered	IIa	B	B	III
For patients who have been therapeutically anticoagulated with a DOAC before AF ablation, it should be considered to interrupt one or two doses of the DOAC before AF ablation with re-initiation after ablation	IIa	B	B	II
Heparin is recommended to be administered immediately after femoral venous puncture or transseptal puncture during AF ablation procedures and adjusted to achieve and maintain an ACT ≥300 s	I	B	B	III
Systemic anticoagulation with warfarin or a DOAC should be considered for at least 3 months after AF ablation, regardless of the presence or absence of AF recurrence	IIa	C	C1	VI
For patients with a high risk for embolism (CHADS2 score ≥2), continuation of systemic anticoagulation with warfarin or a DOAC should be considered after 3 months of AF ablation, considering AF recurrence during the follow-up period	IIa	C	C1	VI

Abbreviations: ACT, activated clotting time; AF, atrial fibrillation; COR, class of recommendation; DOAC, direct oral anticoagulant; GOR, grade of recommendation; LOE, level of evidence.

[Correction added on 29 June, after first online publication: In the first description, '... at least 3 months before AF ablation' has been amended to '... at least 3 weeks before AF ablation'.]

Several RCTs have compared perioperative continuous administration of warfarin and continuous administration of DOAC for ablation. The RE-CIRCUIT (Randomized Evaluation of Dabigatran Etexilate Compared to Warfarin in Pulmonary Vein Ablation – Assessment of an Uninterrupted Periprocedural Anticoagulation Strategy) trial[884] showed no significant difference in ischemic complications between the dabigatran continuation group and the warfarin continuation group. However, in terms of safety, significantly more major bleeding events, such as cardiac tamponade and inguinal hematoma, were observed in the warfarin continuation group. In the VENTURE-AF trial,[885] which compared rivaroxaban continuation with warfarin continuation, there was no significant difference in efficacy or safety between the 2 groups; thus, ablation with rivaroxaban continuation is now also acceptable. Similar results were obtained in AXAFA-AFNET 5 (Anticoagulation Using the Direct Factor Xa Inhibitor Apixaban during AF Catheter Ablation),[886-888] which examined continuation of apixaban, and the detection rates of asymptomatic microinfarcts using brain MRI were similar.

Various studies have also been conducted on AF ablation with perioperative DOAC withdrawal.[889-891] In Japan, an RCT (ABRIDGE-J [Ablation Preoperative Dabigatran in Use Envisioning in Japan][889]) was conducted to compare short-term discontinuation of dabigatran with continuation of warfarin. Although there was no significant difference in ischemic complications between the 2 groups, there were significantly more bleeding events such as cardiac tamponade and inguinal hematoma in the warfarin continuation group, as seen in RE-CIRCUIT. Furthermore, an RCT in Japan that compared continuation and withdrawal of 4 DOACs reported that there was no significant difference in embolism or bleeding complications in any of the DOACs.[890]

On the basis of these findings, the use of DOACs as a perioperative anticoagulant for AF ablation is recommended over warfarin, regardless of whether the drugs are stopped or continued, except for cases in which DOACs are contraindicated, such as in the presence of severe renal impairment or after artificial valve replacement. Furthermore, it is important to carefully consider the risk of thromboembolism and bleeding and to select the appropriate anticoagulant drug according to the clinical profile. Idarucizumab, which specifically reverses the effect of dabigatran, is currently available, and other DOAC (factor Xa inhibitor) neutralizers are being developed.

4.3.2 | *Intraoperative management*

Heparin administration during ablation is essential. A study using intracardiac echocardiography reported that maintaining the activated clotting time (ACT) at ≥300 seconds could reduce left atrial thrombus formation.[892] Wazni et al also reported that bleeding complications do not increase if the ACT value is kept high, providing it is ≤400 seconds.[893]

Heparin administration during ablation is started immediately after groin puncture or immediately after atrial septum puncture, and the ACT is maintained at 300-350 seconds. Continuous perfusion with heparinized saline from the sheath inserted into the left atrium and avoiding long-term placement of the sheath or guidewire in the left atrium also help prevent thrombus formation.

4.3.3 | *Postoperative management*

After ablation, if it is confirmed that there are no bleeding complications, anticoagulants are administered from the evening of the ablation or the following morning. When restarting administration from the following morning, intravenous heparin administration may be continued in the interim (heparin bridging). However, as increased bleeding complications have been reported,[891] this method is not currently recommended except in high-risk patients.

It is recommended that postoperative anticoagulant therapy be continued for at least 3 months,[578,882] because the 3 months after AF ablation is considered the blanking period, when AF attacks are known to occur. The cause of attacks during the blanking period is believed to be resumption of conduction at the ablation site and non-PV foci, as well as inflammation associated with the ablation and the effect on the autonomic nervous system.

Late recurrence after ablation is not uncommon in patients with persistent AF. Considering possible recurrence, it is advisable to continue anticoagulant therapy for longer than 3 months after ablation in patients with a high risk for thromboembolism.

However, anticoagulants can be discontinued after 3 months in patients with paroxysmal AF, a $CHADS_2$ score of 0 and no enlargement of the left atrium. Although it is difficult to judge with a $CHADS_2$ score of 1, the decision to stop or continue administration should be based on the overall condition of the patient (including whether the AF is paroxysmal or persistent), embolism risk and bleeding risk, left atrium diameter, B-type natriuretic peptide value, D-dimer value, and the patient's wishes. AF recurrence is evaluated using ECG, Holter ECG, and a portable ECG. However, caution is required because asymptomatic AF can also occur. In paroxysmal AF, in addition to 12-lead ECG at each postoperative outpatient visit, when a decision has been made to discontinue antiarrhythmic drugs or anticoagulants at 3 months postoperatively when the blanking period ends, evaluation with Holter ECG at the end of outpatient follow-up (12 months after ablation) is recommended. In persistent AF, antiarrhythmic drugs and anticoagulants are often used continuously. Therefore, in addition to the aforementioned evaluations, Holter ECG every 6 months is recommended.

5 | Atrial tachycardias after heart surgery and tachycardia in congenital heart disease

5.1 | Atrial tachycardias after heart surgery

Various arrhythmic substrates form after heart surgery, including foreign bodies in the heart such as artificial valves and artificial pericardium, sutures and other scar tissue, and pericarditis due to pericardiotomy, resulting in various atrial tachycardias. The mechanisms are diverse, including incision line reentrant tachycardia,

macroreentry around the tricuspid or mitral annulus, reentry due to delayed conduction in scar tissue, triggered activity due to surgical invasion or hemodynamic load, and enhanced automaticity.[895] Recent advances in 3D mapping systems have made it easier to visualize and understand circuits in individual patients.[896] Myocardium protected by scar tissue is difficult to ablate and contributes to cases refractory to ablation treatment.

5.1.1 | Types of atrial tachycardia

a. | Right atrium free wall macroreentrant atrial tachycardia. The crista terminalis of the right atrial free wall can become an arrhythmic substrate; however, after heart surgery, right atrial incision lines and cannulation scars in the extracorporeal circulation complicate the arrhythmogenic substrate.[896,897]

i. | Reentrant circuit. Many circuits rotate around the right atrial incision line. Delayed conduction normally occurs in the isthmus created between the lower edge of the atrial incision line and the site of the inferior vena cava cannulation, but delayed conduction may also occur in the isthmus between the upper edge of the incision line and the superior vena cava cannulation.[897] The direction of rotation can be either clockwise or counterclockwise. When it is clockwise, a macroreentry and a double-loop reentry that make the tricuspid annulus counterclockwise may form. A counterclockwise rotation of the right atrial free wall forms a double-loop reentry with a macroreentry that rotates around the tricuspid annulus clockwise.[898]

ii. | Ablation site. Linear ablation of either the atrial incision line to the inferior vena cava, atrial incision line to the superior vena cava, or atrial incision line to the tricuspid annulus can close the macroreentrant circuit. Inferior vena cava cannulation scars exist between the lower edge of the atrial incision line and the inferior vena cava, and the procedure to block conduction at this site is relatively straightforward and is often selected. The distance between the upper edge of the atrial incision line and the superior vena cava is relatively long, and there may be no cannulation scar site near the superior vena cava. Ablation procedures between the upper edge of the atrial incision line and the superior vena cava require caution owing to the proximity to the sinus node. Using the catheter for linear ablation between the atrial incision line and the tricuspid annulus is very difficult, but has the advantage that any tachycardia can be treated with ablation to the common circuit of a double-loop reentry. When ablation is performed between the atrial incision line and the inferior vena cava or between the atrial incision line and the superior vena cava, the reentrant circuit of the tricuspid annulus causing normal AFL remains. Therefore, additional linear ablation is needed between the inferior vena cava and the tricuspid annulus.

b. | Macroreentrant atrial tachycardia after mitral valve surgery. This condition can occur from both the right and left atria. Surgical procedures to reach the mitral valve include right atrial free wall incision plus atrial septal incision, right-side left atrial incision, and bi-atrial incision (superior transseptal approach). Atrial tachycardia can occur with any of these procedures.

i. | Reentrant circuit. The left atrial macroreentrant circuit rotates around the mitral valve annulus, right PV, and left PV, each of which may cause reentry alone or double-loop reentry. Longitudinal incision on the right side of the left atrium causes scarring anterior to the right PV (atrial septum), forming a site of delayed conduction, and can cause macroreentrant atrial tachycardia around the right PV. When conducting the scar from top to bottom, a double-loop reentry may occur counterclockwise around the mitral annulus. Conversely, when conducting from bottom to top, a double-loop reentry may occur clockwise around the mitral annulus. When delayed conduction is observed in damaged myocardium in the left atrial posterior wall, macroreentry in the mitral annulus or left PV alone, double-loop reentry in the left and right PVs, or double-loop reentry in the mitral annulus and the left PV can occur.

ii. | Ablation site. The lower PV to the mitral annulus is the isthmus in right PV macroreentry, and is targeted for ablation. Delayed conduction occurs when the site is close to the incision scar on the right side of the left atrium. The isthmus between the left and right PVs and the incision scars on the right side of the left atrium anterior to the right PV (atrial septum side) may also be ablation targets. In left PV macroreentry, the isthmus is between the lower part of the left PV and the mitral annulus and between the left and right PVs, and is the target site for ablation. In macroreentry around the mitral annulus, the isthmus between the PV and the mitral annulus is ablated. In patients with severe mitral valve lesions requiring mitral valve surgery, the left atrial myocardium is often extensively injured, and it is necessary to determine the ablation site with detailed mapping.[821]

c. | Macroreentrant atrial tachycardia after the maze procedure. This tachycardia[899] may originate in the right or left atrium, and the mechanism includes macroreentry associated with incision line breaks in the maze procedure or failure of linear ablation near the annulus, reentry due to conduction delay in scars caused by surgical invasion, and common AFL. It is necessary to perform detailed mapping according to the specific case characteristics and to analyze the mechanism.

d. | Macroreentrant atrial tachycardia after the Fontan procedure. After a long time from the implementation of the classic Fontan procedure of atriopulmonary connection (APC), myocardial injury with marked right atrial enlargement progresses to form an arrhythmogenic substrate. When the atrial septal defect is repaired and an atrial septum is created with an artificial pericardium, these surgical scars provide a location for a reentrant circuit. For general information on the Fontan procedure, pathology, and other arrhythmias, see section **"5.2.1.e Fontan surgery"** in this chapter.

i. | Reentrant circuit. Although most atrial tachycardias occur in the right atrium, it is difficult to assume a unique reentrant circuit

after the Fontan procedure because the arrhythmic substrates are dispersed throughout the enlarged right atrium. Detailed mapping is required for each case.

ii. | *Ablation site.* There are few macroreentry areas around the incision line, and many macroreentrant atrial tachycardias are caused by delayed conduction due to scar tissue. Therefore, LVAs related to delayed conduction are targeted as ablation sites. Multiple atrial tachycardias often appear, and atrial tachycardia attacks may result in deterioration of hemodynamics, making detailed mapping during tachycardia difficult. Therefore, LVAs identified with 3D mapping may require extensive ablation. Atrial tachycardia after Fontan surgery is refractory, and the recurrence rate after ablation treatment is high.

e. | *Macroreentrant atrial tachycardia after the atrial switch procedure.* Long sutures are created in the atrium during both the Mustard and Senning procedures, and various supraventricular tachycardias develop in the long term. A frequently occurring tachycardia is a macroreentry that rotates around the atrioventricular annulus, which is equivalent to common AFL in a normal heart; however, treatment is difficult after an atrial switch procedure owing to the presence of the artificial septum created by surgery in the isthmus between the inferior vena cava and the atrioventricular annulus.[900]

i. | *Reentrant circuit.* A reentrant circuit rotating around the atrioventricular annulus between the pulmonary atria and the body of the ventricle is the most commonly occurring macroreentrant atrial tachycardia. Atrial tachycardia associated with surgical scars also occurs, but tachycardia on both the atrial side of the systemic vein and the atrial side of the PV is also seen. Therefore, it is necessary to map according to each tachycardia.

ii. | *Ablation site.* The reentrant circuit around the atrioventricular annulus between the PV and the ventricle body is the isthmus between the inferior vena cava and the atrioventricular annulus, as in common AFL, and this area is the target of ablation.[901,902] The ablation procedure is not simple because there is a septum unique to the atrial switch procedure between the inferior vena cava and the atrioventricular annulus. The approach from the inferior vena cava can allow ablation only from the intra-atrial septum to the inferior vena cava, and additional ablation from the atrioventricular annulus to the septum is required to completely block isthmus conduction. To approach this site, it is necessary to puncture the septum using the Brockenbrough technique or to use a transaortic retrograde approach, both of which are very difficult procedures.[903] A magnetic catheter navigation system (Niobe™ [Stereotaxis]) is useful for complicated catheter procedures using the transaortic retrograde approach.[904]

5.1.2 | Catheter ablation indication

Refer to section **"3.4 Atrial tachycardia"** in this chapter.

5.2 | Tachycardias in adult congenital heart disease

Patients with congenital heart disease are now surviving long term, and the proportion of adult patients over the age of 20 years is increasing. By around the year 2000, the ratio of outpatients with congenital heart disease under the age of 20 years to those aged 20 years or older was 1:1, and adult patients now outnumber pediatric patients. Thus, the need for adult congenital heart disease departments has been proposed.[905]

Problems associated with adult congenital heart disease include heart failure, arrhythmia, and cyanosis. Among them, arrhythmia particularly requires attention and management. Both pediatric cardiologists and general cardiologists should be aware of this information.[906]

Substrates causing arrhythmias associated with adult congenital heart disease include scars due to endocardial repair and myocardial lesions due to impaired cardiac function and cyanosis, and the complexity of these substrates varies depending on the underlying heart disease (Figure 24).[907] For example, when atrial switching is performed in adult patients for transposition of the great arteries, atrial tachycardia or AFL may occur because of atrial scarring from endocardial repair. Furthermore, because the anatomical right ventricle becomes the systemic ventricle (functionally the left ventricle), cardiac function declines, which can cause life-threatening ventricular arrhythmias. It is also known that Ebstein's disease is often associated with WPW syndrome.[908]

Depending on the underlying heart disease or endocardial repair, treatment of tachyarrhythmia alone is not sufficient, and care is needed with respect to the appearance of bradyarrhythmia.

5.2.1 | Catheter ablation indication

Catheter ablation is recommended for symptomatic tachycardia associated with adult congenital heart disease, as shown in Table 68. It is recommended that all treatments be conducted at a facility with operators experienced in ablation for congenital heart disease.

The prevalence of tachyarrhythmias gradually increases in adulthood in patients with congenital heart disease, and catheter ablation is an effective treatment.[907,909] However, the outcomes are poor when compared with those in patients without structural heart disease. The reasons for these poor outcomes include the need to understand cardiac malformations and complex anatomy due to surgery, difficulty in reaching the ablation target during catheter manipulation, surgical scars, and artificial pericardium in the heart acting as a barrier.[910-914] Multiple atrial arrhythmias are seen after the Fontan procedure because the entire right atrium may become an arrhythmogenic substrate, and this becomes even more complicated after an atrial switch procedure.[422,915,916] It is recommended that ablation for refractory cases is performed at a facility with abundant experience.

a. | *Atrial septal defect.* Although atrial septal defect is the most common adult congenital heart disease, it tends to occur with atrial

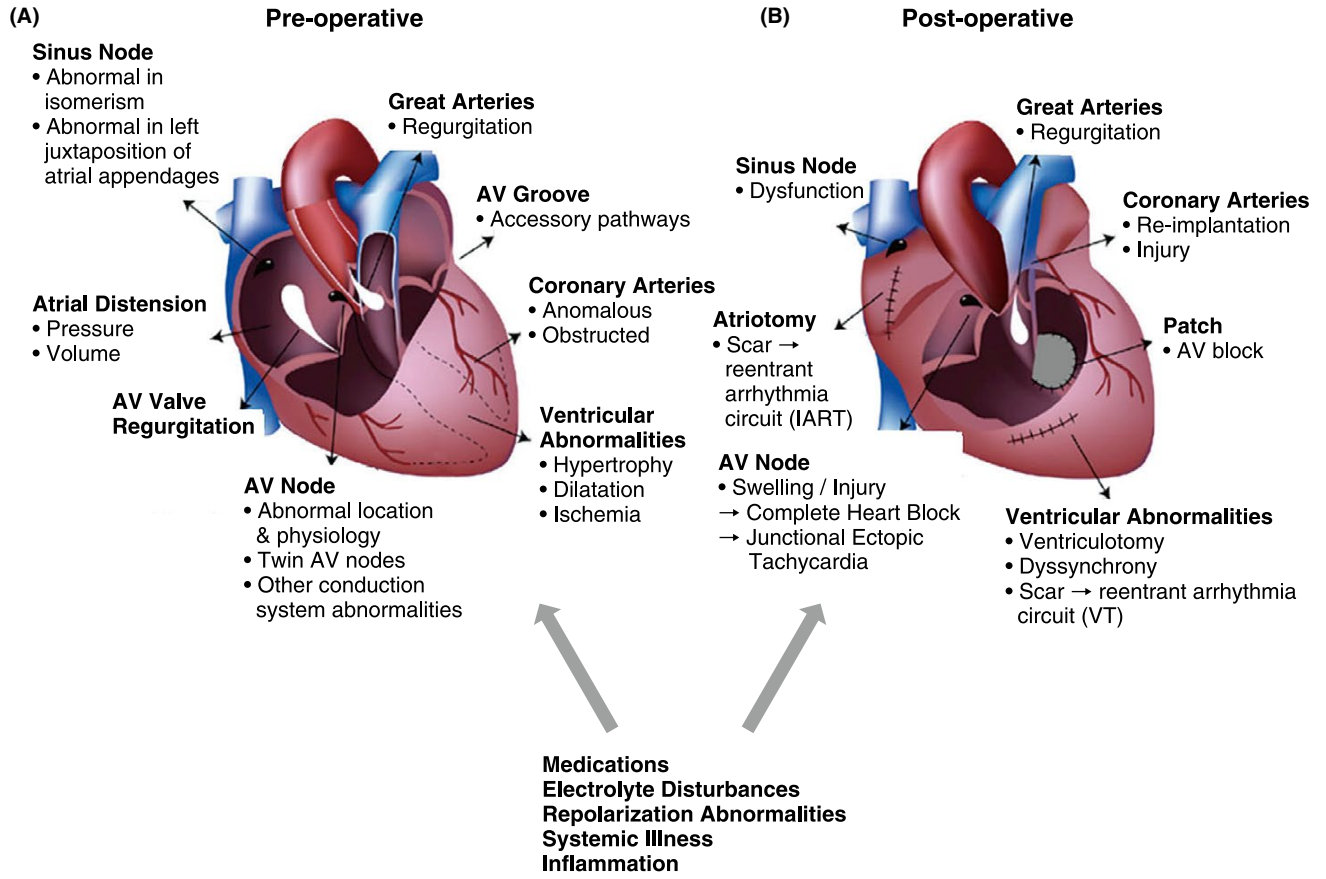


FIGURE 24 Schematic of factors leading to arrhythmias in (A) pre- and (B) postoperative congenital heart disease. AV, atrioventricular; IART, intra-atrial reentrant tachycardia; VT, ventricular tachycardia (From Escudero et al, 2013[906] with permission.)

TABLE 68 Recommendations and evidence levels for catheter ablation of tachyarrhythmias in adults with congenital heart disease

	COR	LOE	GOR (MINDS)	LOE (MINDS)
Catheter ablation is recommended for drug-refractory and/or drug-intolerant symptomatic supraventricular tachycardia in adults with congenital heart disease	I	C	C1	V
Catheter ablation should be considered for drug-refractory and/or drug-intolerant symptomatic ventricular tachycardia in adults with congenital heart disease	IIa	C	C1	V

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence.

tachycardia, common AFL, and AF, and there are many opportunities for ablation treatment.[917]

For preoperative cases, when surgery is not planned, the indications for ablation therapy are based on the guidelines for atrial tachycardia, AFL, and AF. When surgery is planned, it is necessary to determine whether catheter ablation should be performed preoperatively or whether arrhythmia treatment should be performed during surgery. Surgery outperforms ablation treatment in persistent and permanent AF. As ablation treatment has good results for paroxysmal AF, catheter treatment is also a promising option. However, it is difficult to repeat ablation for recurrent AF after atrial septal defect closure. Therefore, surgical treatment should be considered. Percutaneous atrial septum closure with a device has recently been widely performed instead of endocardial repair. However, in these cases, the transatrial septal approach becomes difficult once closure is performed; thus, ablation needs to be completed before the surgery.

Reentrant atrial tachycardia resulting from an arrhythmic substrate due to surgical invasion is more likely to occur after intracardiac repair[918] (for details, see section **"5.1 Atrial tachycardia after heart surgery"** in this chapter). Attempts have been made to prevent this iatrogenic tachycardia by intraoperatively extending the lower edge of the right atrial incision line to the inferior vena cava, including the conduit scar, thereby cutting off the circuit of the right atrial free wall.[919]

b. | *Ventricular septal defect.* Ventricular septal defect is the second most common adult congenital heart disease after atrial septal defect; however, the occurrence of tachyarrhythmias that need to be ablated is rather uncommon.

c. | *Teratology of Fallot.* Many patients who reach adulthood have already undergone intracardiac repair. The right atrial incision line, ventricular incision line, artificial pericardial patch with formation of right ventricular outflow tract, conduit scarring to the superior and inferior vena cava, and other areas become arrhythmic substrates, causing supraventricular and ventricular tachyarrhythmias.[485,920-922]

The approach and treatment for supraventricular arrhythmias are similar to those for atrial septal defect. Pharmacotherapy and ICD implantation are the basic treatments for ventricular arrhythmias (VT and VF), but catheter ablation can be performed when the ICD is frequently activated in patients refractory to pharmacotherapy. VT is often caused by surgical scars (such as patches) when forming the right ventricular outflow tract, but may also be associated with right and left ventricular dysfunction, and can be generated from areas unrelated to surgical scars. Linear ablation between the pulmonary artery and the scar or between the tricuspid annulus and the scar has been reported for macroreentrant VT around the surgical scars of the right ventricular outflow tract. However, it is extremely difficult to create a transmural ablation line in tissue adjacent to the scar, in addition to the presence of right ventricular hypertrophy due to the underlying heart disease. In many cases, the reentrant circuit is present not only in the free wall of the right ventricle but also in the ventricular septum and the lower part of the tricuspid annulus because the pulmonary artery and the surgical scar are continuous. Thus, it is necessary to take a case-specific approach.[923-925]

d. | *Ebstein's disease.* Part of the tricuspid valve (mainly the septal and posterior cusps) deviates into the right ventricle, typically reaching the septum (septomarginal trabecula). Part of the right ventricle forms the right atrial cavity (atrialized right ventricle) and may also become thinner. A connection between muscles with electrical conduction characteristics tends to occur between the atrialized right ventricle and the right atrium, and WPW syndrome develops. In these cases, the accessory pathway is often composed of multiple accessory pathways, a broad accessory pathway, and a slow conduction pathway, and wide QRS atrioventricular reentrant tachycardia with an anterograde accessory pathway and wide QRS tachycardia during AF (known as pseudo-VT) are not uncommon. This kind of tachycardia can cause hemodynamic disruption, and catheter ablation is recommended. Accessory pathway mapping during ablation is performed while considering the possibility of multiple and a wide range of accessory pathways. In addition, the delta waves are small for accessory pathways with slow conduction velocity; thus, it is necessary to devise mapping outside sinus rhythm, such as atrial pacing near the tricuspid annulus. In addition, an accessory pathway with conduction characteristics of Mahaim fibers may also occur.

Ebstein's anomaly is frequently associated with tricuspid regurgitation and atrial septal defect. Care is needed to prevent paradoxical embolism in the perioperative period of ablation because right-to-left shunts may occur under right heart overload.

e. | *Fontan procedure.* This is a palliative operation performed to improve cyanosis in congenital heart diseases such as tricuspid valve atresia and univentricular heart. The surgical procedures include APC and total cavopulmonary connection (TCPC). The latter includes techniques using an extracardiac conduit (extracardiac TCPC) and an intracardiac conduit (lateral tunnel TCPC). The Fontan procedure skips the ventricle, causing venous blood to directly circulate to the pulmonary artery, which generally results in increases in systemic venous pressure. In APC, the right atrial pressure also increases accordingly, leading to significant right atrial enlargement and formation of an arrhythmogenic substrate.[926] When repairing atrial septal defects and creating an intra-atrial septum using an artificial pericardium, it is necessary to consider the arrhythmic substrate associated with this surgical scar. Atrial arrhythmias are usually variable and refractory. Approximately half of the patients develop conditions such as macroreentrant atrial tachycardia, atrial tachycardia caused by a focal mechanism, AFL, and AF, and the prevalence increases in the follow-up period.[926] In asplenia syndrome, 2 (twin) atrioventricular nodes are present in the atrioventricular annulus, and AVRT rotating around the nodes may be initiated.[927,928] The incidence of supraventricular tachycardia decreases in the order of APC, intracardiac conduit TCPC, and extracardiac conduit TCPC. However, access to the heart cavity via a venous route becomes rather difficult after TCPC; thus, either transaortic retrograde access or a transfenestration route created during surgery is usually attempted. Conduit punctures can be performed with a classic Brockenbrough needle; however, this procedure is not easy to implement.

After the Fontan procedure, patients may have significant hypotension or shock, even in cases of supraventricular tachycardia. Therefore, it is important to be aware of hemodynamic deterioration when tachycardia is induced during catheter ablation. This tendency is exacerbated when venous pressure is reduced with dehydration. Sufficient fluid replacement is required before ablation. The outcome of catheter ablation is generally poor, and a high incidence of recurrence and new arrhythmias occur despite effective treatment in the acute phase. Concurrent pharmacotherapy such as amiodarone is needed, and post-APC patients require surgical treatment for arrhythmic substrates, including right atrial plication, when performing TCPC conversion.[423,929,930]

f. | *Atrial switch procedure.* For information on postoperative atrial tachycardia, refer to section **"5.1.1.e Macroreentrant atrial tachycardia after the atrial switch procedure"** in this chapter.

If the anatomical right ventricle is the systemic ventricle, as in conditions for which the atrial switch procedure was performed for transposition of the great arteries, cardiac enlargement progresses owing to factors including tricuspid regurgitation and left

heart failure, with an increased incidence of VT, VF, and AF complications. In general, catheter ablation for these arrhythmias is difficult, and pharmacotherapy with amiodarone and/or implantation of ICD or ICD with biventricular pacing function (CRT-D) are implemented for VT, whereas pharmacotherapy is the first choice for AF.

6 | Ventricular arrhythmias

6.1 | Sustained VT

6.1.1 | Catheter ablation indications

Table 69 shows the recommendations for catheter ablation for sustained monomorphic VT.

The indication of catheter ablation for sustained VT should be determined with careful consideration of the risks and benefits based on the patient's general condition and the level of experience of the physician. Ablation for idiopathic VT without structural heart disease has almost stable treatment outcomes, as well as a relatively high acute success rate and low recurrence rate during long-term follow-up, especially for VT originating from the right ventricular outflow tract[931-940] and verapamil-sensitive reentrant fascicular VT involving Purkinje tissue.[941-951]

ICD implantation is the mainstay of treatment for preventing sudden death in sustained VT associated with structural heart disease such as prior myocardial infarction and cardiomyopathy.[84,197,198,951] However, it has also been reported that frequent VT attacks and DC shocks caused by an ICD worsen the patient's QOL and increase the mortality.[952-957] In VT or VF with hemodynamic compromise, the patient is more likely to experience syncope even if the ICD is activated, and it may conversely cause fear and discomfort if DC shocks are delivered while the patient is conscious. In addition, it has been shown that DC shock itself worsens cardiac function.[955,957] Concomitant use of antiarrhythmic drugs reduces the number of ICD activations; however, this treatment has problems such as not being curative and having associated adverse effects.[958-960] In these situations, catheter ablation can be an effective treatment to suppress VT attacks.[961,962] Ablation for sustained VT due to structural heart disease has conventionally been difficult, and arrhythmias frequently recurred. However, treatment outcomes have significantly improved owing to advances in technologies, such as 3D mapping systems[963-974] and irrigated-tip ablation catheters,[962,975-977] as well as the combined use of modalities such as cardiac MRI.[978-984]

Several RCTs on ablation treatment after ICD implantation for sustained VT associated with prior myocardial infarction have been performed.[183,186,985] In SMASH-VT (Substrate Mapping and Ablation in Sinus Rhythm to Halt VT)[186] and VTACH (VT Ablation in Coronary Heart Disease),[183] the ablation group had significantly fewer ICD interventions than the non-ablation group. However, in the CALYPSO (Catheter Ablation for VT in Patients with an ICD) pilot study,[985] which compared antiarrhythmic drug treatment with ablation treatment, no superiority of ablation treatment to antiarrhythmic drug treatment was observed. VANISH (VT Ablation vs. Escalated Antiarrhythmic Drug Therapy in Ischemic

TABLE 69 Recommendations and evidence levels for catheter ablation of sustained monomorphic VT

	COR	LOE	GOR (MINDS)	LOE (MINDS)
In patients with symptomatic idiopathic sustained VT for whom AADs are ineffective, not tolerated, or not the patient's preference, catheter ablation is recommended	I	B	B	III
In patients with asymptomatic or mild symptomatic idiopathic sustained VT for whom AADs are ineffective, not tolerated, or not the patient's preference, catheter ablation should be considered	IIa	B	B	IVb
In patients with structural heart disease and incessant monomorphic VT or VT storm, for whom AADs are ineffective or not tolerated, catheter ablation is recommended	I	C	C1	IVb
In patients with IHD and symptomatic sustained monomorphic VT for whom AADs are ineffective or not tolerated, catheter ablation is recommended	I	B	A	II
In patients with IHD, sustained monomorphic VT, and an ICD who experience frequent ICD therapies, catheter ablation is recommended	I	B	A	II
In patients with IHD and sustained monomorphic VT who undergo ICD implantation, perioperative catheter ablation should be considered to reduce the risk of recurrent VT or ICD therapies	IIa	B	B	II
In patients with IHD who experience recurrent monomorphic VT despite chronic amiodarone therapy, catheter ablation is recommended in preference to escalating AAD therapy	I	B	A	II
In patients with non-ischemic cardiomyopathy and sustained monomorphic VT for whom AADs are ineffective or not tolerated, catheter ablation should be considered	IIa	B	B	IVa
In patients with bundle branch reentrant VT, catheter ablation is recommended for reducing the risk of recurrent VT	I	C	A	V

Abbreviations: AAD, antiarrhythmic drug; COR, class of recommendation; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; IHD, ischemic heart disease; LOE, level of evidence; VT, ventricular tachycardia.

Heart Disease),[986] which compared ablation and escalation of antiarrhythmic medication in patients with post-myocardial infarction VT, found significantly fewer ICD shocks in the ablation therapy group. However, in the subgroups of patients who did not take amiodarone at baseline before randomization, there was no difference between escalation of antiarrhythmic drug therapy and catheter ablation.

In studies that included ischemic and non-ischemic heart disease as the underlying heart diseases, the VT-free survival was lower in non-ischemic heart disease than in ischemic heart disease, and tachycardia inducibility after ablation was a prognostic predictor.[987,988]

Catheter ablation can also be an effective preventive tool for drug-refractory frequent ICD shocks (electrical storms) in ischemic or non-ischemic heart disease.[188,989] The recurrence rate of electrical storm is low, at least if clinical VT is suppressed, which also affects cardiac mortality.

6.1.2 | *Ablation procedures*

The recent technological advances in catheter ablation have significantly improved the outcomes for sustained VT. To achieve reliable ablation, it is important to identify the appropriate ablation site with precise mapping and electrophysiological techniques. The treatment is relatively difficult, especially for VT with underlying structural heart disease. Thus, it is preferable that the treatment is performed in a facility with abundant experience or by an experienced physician.

a. | *Mapping systems.* The 3D mapping system constructs a 3D image of the myocardial surface (endocardium or epicardium), and displays the arrhythmia substrate, arrhythmia origin, reentrant circuit, and position of the ablation catheter. It is especially useful for ablation of VT with structural heart disease. The position of the tip of the ablation catheter is determined from the magnetic field and the impedance ratio.[963-967,973,974] The method of reconstructing the heart anatomy using intracardiac echocardiography is also useful.[968] Every system has good reproducibility of the electrode tip position and is useful for reducing X-ray exposure.

b. | *Methods for determining the ablation site.* Idiopathic VT often has a typical QRS waveform, and it can be classified into several subtypes depending on its mechanism, QRS waveform, and the anatomical structures that cause the arrhythmia. The most common origin of idiopathic VT is the right ventricular outflow tract.[931-940] Other origins of tachycardia (or sites of successful ablation) include the tricuspid annulus,[990] para-Hisian region,[941,991,992] pulmonary artery,[993-995] left ventricular outflow tract,[996-998] mitral valve annulus,[999,1000] sinus of Valsalva,[1001-1004] left and right peripheral Purkinje networks,[941-950,1005] coronary veins,[1006-1008] papillary muscles,[951,1009-1014] summit,[1015-1019] and crux.[1020,1021]

Conversely, the causes of sustained VT associated with underlying heart disease are diverse, including myocardial infarction,[1022-1027] arrhythmogenic right ventricular cardiomyopathy,[1028-1032] hypertrophic cardiomyopathy,[1033] dilated cardiomyopathy,[1034,1035] post-cardiac surgery scar,[1036,1037] sarcoidosis,[1038-1040] and myocarditis.[1041-1043] Moreover, the ECG waveforms during VT are varied.

The methods for determining the ablation site for sustained VT include propagation mapping, entrainment mapping, pace mapping, and substrate mapping. Usually, the ablation site is determined using a combination of these methods.

i. | *Propagation mapping.* In this method, after VT induction, an intracardiac electrogram is recorded and the propagation during VT is analyzed. This mapping can only be performed in patients with monomorphic VT with a stable QRS waveform and stable hemodynamics during tachycardia. If the mechanism of VT is ectopic automaticity or microreentry, the earliest activation site in the ventricle is the optimal ablation site. If the earliest excitation site is healthy myocardium in idiopathic VT, the unipolar lead recording exhibits a QS pattern and a presystolic potential may sometimes be seen before the ventricular potential.

The mechanism of sustained VT with structural heart disease, especially VT with scar tissue on the endocardial side, is often macroreentry, and propagation mapping is important. As the macroreentrant circuit is continuous, this mapping does not involve the concept of the earliest activation site.[1022,1044] Figure 25 is a schematic diagram of a reentrant circuit in VT with scar tissue (scar-related VT).[1045] There is an excitation exit at the boundary between the scar and the healthy myocardium, and the diastolic potential is often recorded during tachycardia within the LVA close to the exit.[1022-1027] However, the diastolic potential may be a bystander unrelated to the tachycardia circuit. In addition, even if the potential is on the circuit, it is difficult to interrupt the circuit with catheter ablation unless the site is in a narrow isthmus between non-excitable regions. Therefore, the optimal ablation site in reentrant VT should be determined using propagation mapping and other methods, including entrainment mapping, as discussed below.

ii. | *Entrainment mapping.* This is a method that can identify the reentrant circuit, distinguish the potential on the circuit from the

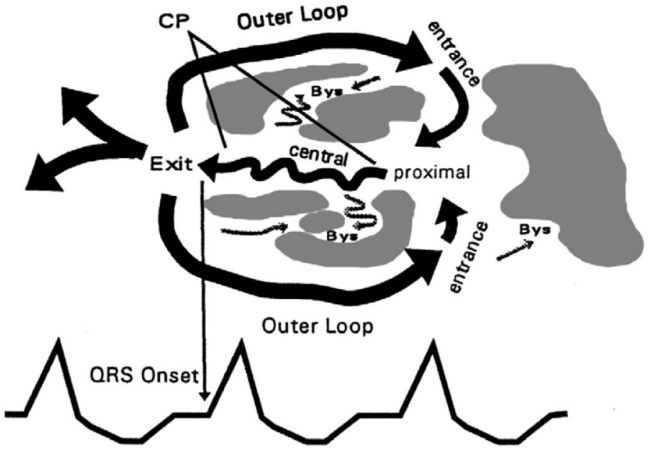


FIGURE 25 Schematic illustration of scar-related macroreentrant VT. Bys, bystander; CP, common pathway. (From Stevenson et al, 1997[1045] with permission.)

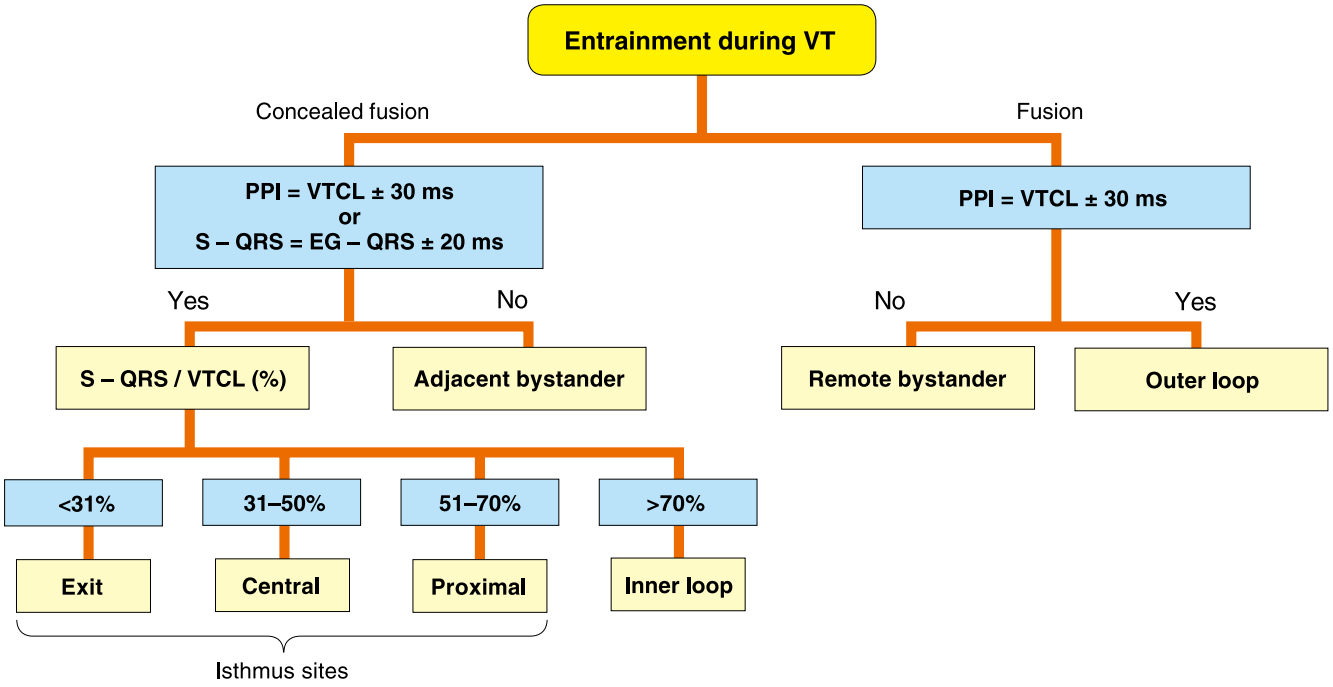


FIGURE 26 Flowchart of the entrainment mapping scheme. EG, electrogram; PPI, postpacing interval; S, stimulus; VT, ventricular tachycardia; VTCL, ventricular tachycardia cycle length. (From Stevenson et al, 1997[1045] with permission.)

bystander potential, and evaluate whether the site is a slow conduction pathway at the isthmus between non-excitable regions.[1046-1053] A flowchart is shown in Figure 26. Burst stimulation is performed using a cycle 10-30 ms shorter than the cycle during VT (entrainment), to observe the QRS waveform during stimulation and the return cycle immediately after stimulation. To satisfy the conditions that the potential recording site is on the circuit and in the isthmus with slow conduction, the QRS waveform during entrainment must match the VT (concealed fusion) and the return cycle should match the tachycardia cycle. Alternatively, the difference must be <30 ms and the stimulus–QRS interval during entrainment must match the preceding potential–QRS interval during tachycardia, or the difference must be <20 ms Furthermore, it is important that the stimulus–QRS interval is ≤70% of the tachycardia cycle for the site to be the center of the common isthmus between the scars that are the optimal sites for ablation.[1052] Even if the criteria for concealed fusion and return cycle are satisfied, if the stimulus–QRS interval is >70% of the tachycardia cycle, the site is likely to be on an inner loop that is not a common pathway, which will have a poor tachycardia suppression effect[1045] (Figures 25,26).

iii. | *Pace mapping.* This is a method in which pacing is performed from the ablation catheter during sinus rhythm at almost the same cycle length as the VT, and the QRS waveform and VT waveform are compared. It is useful mainly for VT with a focal trigger, in which the pace map waveform is almost identical to the VT at the optimal ablation site. This method is particularly useful because most idiopathic VTs originating from the outflow tract exhibit a focal trigger, and VT is often not induced during catheter ablation. Pace mapping is also useful in predicting the exit to healthy myocardium in macroreentry associated with scar tissue; however, in this case, the QRS waveforms often do not completely match.[1055-1057] When the ablation catheter is in the slow conduction region of the isthmus, the pace map waveform may coincide with the tachycardia with a pacing delay ≥40 ms[187,1054,1057] Furthermore, when pacing upstream of the tachycardia circuit isthmus, the stimulus–QRS interval gradually increases with the same QRS waveform; however, thereafter, the pacing QRS waveform suddenly changes from a certain site. This is because the main stimulus excitation propagates in the entrance direction instead of the exit direction. A new pace mapping method for estimating the tachycardia circuit isthmus based on these sudden changes in the pace map waveform has also been reported.[1058,1059] It should be kept in mind that the pace mapping waveform is also affected by the stimulation cycle and output.

iv. | *Substrate mapping.* Substrate mapping is a method for identifying arrhythmic substrates during sinus rhythm in VT associated with structural heart disease.[187,964,1030,1053,1060-1065] It can be a means of determining the ablation site, particularly when monomorphic VT cannot be induced or when hemodynamics are unstable during VT. It is useful for VT with scar tissue in the ventricle and has evolved with the advent of the 3D mapping system.

Intracardiac potential is recorded during sinus rhythm or during tachycardia. Areas where the QRS potential peak is ≥1.5 mV are defined as healthy myocardium, and areas where the potential peak is <0.5 mV or the ventricle is not captured even with high-output pacing are defined as scarred.[187,964] Given that the tachycardia circuit is believed to exist in LVAs between the 2 aforementioned

levels, detailed potential recording of the same area and the aforementioned pace mapping are performed to estimate the arrhythmia substrate and the site of the tachycardia circuit. Furthermore, by finely adjusting the voltage threshold (usually setting the low voltage upper limit to 0.4-0.8 mV), the tachycardia circuit isthmus may be depicted as a "relatively high-voltage area in the LVA," which is a useful technique (voltage threshold adjustment method).[1053,1065]

During sinus rhythm, late potentials or isolated late potentials may be recorded behind the QRS waves.[187,1030-1065] These potentials are considered to indicate the slow conduction properties of degenerated myocardium remaining between the scars, and it has been shown that eliminating all these isolated late potentials leads to suppression of tachycardia recurrence.[1030,1032,1066,1067] However, not all recorded late potentials are related to the target VT circuit. Moreover, a new concept has been proposed, called local abnormal ventricular activity (LAVA), which incorporates not only late potentials observed in LVAs but also late potentials in healthy areas and abnormal potentials within the QRS wave phase.[1068] Various methods, such as scar homogenization,[1069] core isolation,[1070] and dechanneling,[1071] have been reported as ablation methods for similar arrhythmic substrates (Figure 27). Scar homogenization is a method of ablating all LVAs, and it has been shown that tachycardia recurrence is low in the group treated on both the endocardium and epicardium.[1069] However, areas unrelated to the initiation and maintenance of tachycardia may also be ablated. Dechanneling is a method of blocking all isthmuses in LVAs at their entrance,[1071] which can limit unnecessary ablation in scar homogenization. Core isolation is a method of isolating LVAs, including the estimated VT circuit isthmus, from the surrounding areas,[1070] and the late potential recorded from the isthmus between the scars disappears or is electrically dissociated after ablation.

Although this method is a highly elegant electrophysiological technique, it is often difficult to use with a substrate with little scarring that exhibits patchy fibrosis, such as non-ischemic cardiomyopathy. LAVA is a local ventricular abnormal potential that includes not only the late potentials observed in LVAs but also late potentials in healthy areas and abnormal potentials contained within the QRS waves.[1068] The prognosis of arrhythmia recurrence has been demonstrated to improve in the group with complete ablation of LAVAs; however, as potentials within the QRS wave in healthy potential areas are also LAVAs, the definition of complete ablation remains questionable. A new method of analyzing frequency has been reported as a technique for discriminating characteristics other than visual potential characteristics, such as intracardiac voltage and late potentials in abnormal areas.[1072,1073]

v. | VT with a specific reentrant circuit. VTs with specific ablation sites include bundle branch reentry and interfascicular reentry tachycardias,[941,942,1074-1077] and verapamil-sensitive idiopathic left fascicular VT.[941-950]

Bundle branch reentry and interfascicular reentry tachycardias are more likely to occur in patients with low cardiac function and intraventricular conduction disturbance, and the tachycardia cycle is usually short. Diagnosis is important because it can be suppressed by ablation of the right bundle (RB) or the left bundle. With a clearly recorded His bundle electrocardiogram (H), a definitive diagnosis can be made according to changes in the H–H, RB–RB, and V–V intervals during tachycardia, comparing the H–V intervals during tachycardia and sinus rhythm, and entrainment pacing from the apical septum of the right ventricle. Bundle branch reentry and interfascicular reentry tachycardias are classified into 3 types depending on the bundle branch used in the circuit and its direction (Figure 28).[942,1077] The

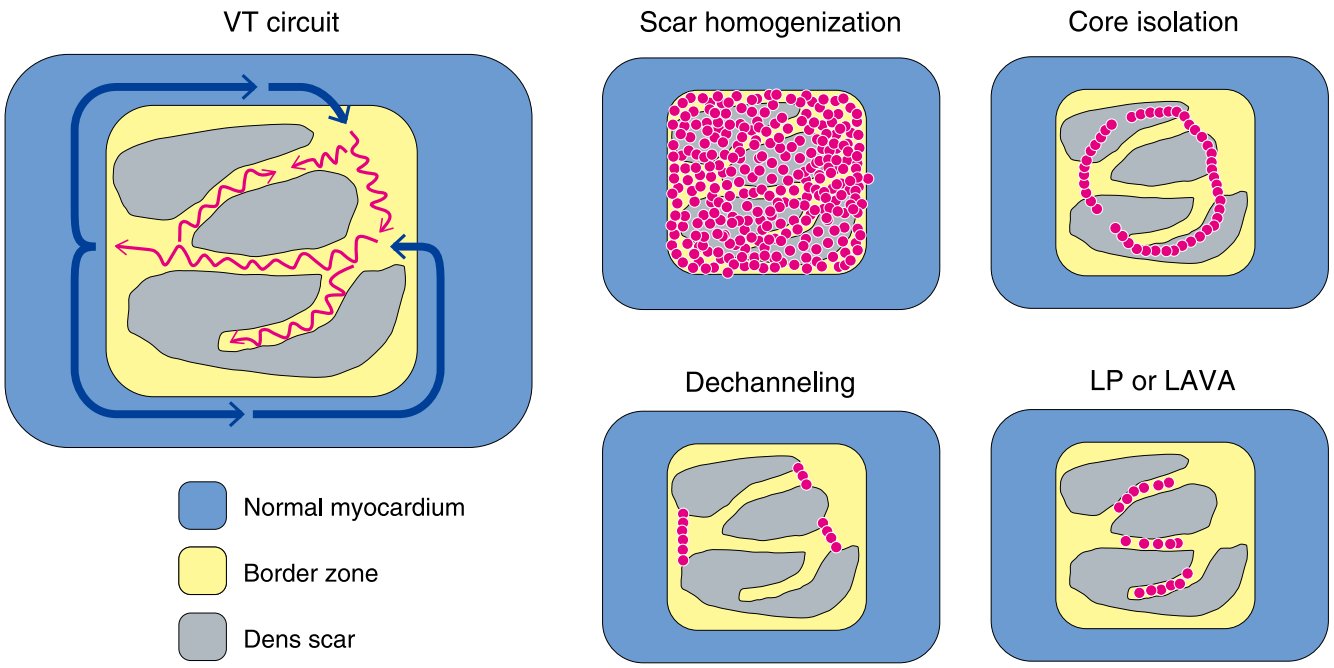


FIGURE 27 Ablation methods with substrate mapping. LAVA, local abnormal ventricular activity; LP, late potential; VT, ventricular tachycardia

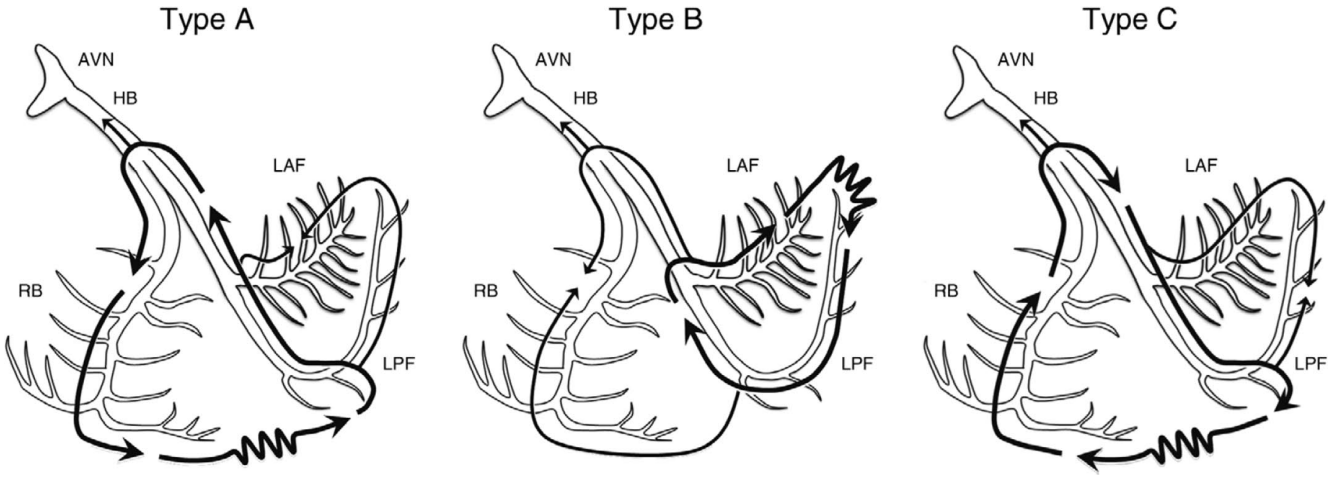


FIGURE 28 Schematic illustrations of reentrant circuits for bundle branch reentry and interfascicular reentry tachycardias. AVN, atrioventricular node; HB, His bundle; LAF, left anterior fascicle; LPF, left posterior fascicle; RB, right bundle. (From Nogami et al, 2011[942] with permission.)

right or left bundle is the ablation site, a complete bundle branch block appears after the procedure, and an atrioventricular block may appear in some cases.

Verapamil-sensitive idiopathic left fascicular VT has several subtypes depending on waveform and the site of successful ablation.[942,948-950]In all cases, it is important to look for abnormal Purkinje potentials with decremental conduction recorded as diastolic potentials during tachycardia. No evidence exists that normal bundle branches are part of the circuit. Therefore, there is no need to create a bundle branch block or a fascicular hemiblock.[942,946,947]

c. | Radiofrequency energy application. The ablation catheter electrode tip is passively heated by Joule heating generated by RF energy. If the temperature exceeds 70°C, blood protein components and blood cells around the electrodes coagulate, which may result in not only an insufficient ablation effect but also complications such as thrombosis.[1078] The use of an irrigation system that perfuses saline from the tip electrode prevents overheating of the tip electrode and allows sufficient energy to flow.

Non-irrigated catheters can be used for ablation in the right ventricle. Normally, the RF energy delivery is performed at an output of 30-50 W and a set temperature ≤60°C; however, in many cases, sufficient output cannot be obtained because of temperature increase. When using an irrigated-tip ablation catheter, the temperature is set to ≤42°C, and ablation is started from an output of about 20 W and thereafter adjusted to a maximum of around 40 W. Irrigated-tip ablation catheters are often used for scar-related VT, VT with an epicardial origin, and especially VT originating from areas with thick myocardium such as the tricuspid annulus. In areas where conduction disturbance is a concern (close to the atrioventricular node, bundle of His, bundle branch), energy application is started from a sufficiently low output setting (≤15 W).

An irrigated catheter is usually used for VT originating in the left ventricle from the viewpoint of thrombosis prevention; however, when using a non-irrigated catheter, the maximum temperature should be set lower than that in the right ventricle (≈55°C).

For confirming sufficient lesion formation, the ST-segment on the unipolar electrogram being more elevated than before ablation, even without excessive catheter pressure, or reduction of the local voltage and increase of the pacing threshold can be used as indicators.

Although there is no reliable method to prevent the steam pop phenomenon when using irrigation systems, according to previous reports, in 80% of energy delivery that generated steam pop, the impedance decreased by >18 ohms, which was the only difference with non-pop energy delivery.[1079] If a sudden impedance change ≥15-20 ohms occurs, the energy delivery should be stopped or the output should be reduced to prevent steam pop during energy application.[1078,1079] In irrigation systems, physiological saline is released into the heart chamber through the electrode perfusion hole; thus, it is necessary to monitor urine output and manage the water balance with intravenous administration of diuretics as needed.

d. | Special ablation techniques. If the VT substrate is on the epicardial side and the endocardial approach is unsuccessful, epicardial ablation via pericardial puncture may be necessary.[1080-1083] The use of an irrigation system is essential in epicardial ablation; however, as the physiological saline is retained in the epicardial space, hemodynamic indicators such as blood pressure must be monitored, and pericardial effusion must be drained as needed. Pericardial puncture can be difficult in some cases of pericardial adhesion, such as in a patient with a history of heart surgery. In these cases, after making a small surgical incision, the catheter sheath can be inserted in the epicardial space.[1081]

It is highly likely that the tachycardia origin is in the myocardium if endocardial and epicardial approaches are unsuccessful, or if treatment of tachycardia originating in the ventricular septum is unsuccessful with both the right and left approaches. Arrhythmia surgery

must be considered in such cases (see **Chapter V**). Moreover, several special ablation techniques are available, including bipolar RF ablation (not covered by Japan's National Health Insurance),[1084,1085] simultaneous unipolar RF ablation,[1086] chemical (ethanol) ablation (not covered by Japan's National Health Insurance),[1087-1090] and needle ablation (unapproved).[1091]

6.2 | Polymorphic VT and VF

6.2.1 | *Catheter ablation indications*

Table 70 shows the recommendations for catheter ablation for polymorphic VT/VF.

PVCs originating in the right ventricular outflow tract or distal Purkinje fibers can trigger idiopathic polymorphic VT and VF.[1092-1094] Recurrence of polymorphic VT and VF can be suppressed by targeting the PVC with catheter ablation,[319,553,1095-1097] and the long-term outcome is good.[319]

Many reports have shown that similar ablation of distal Purkinje fibers is also effective for polymorphic VT or VF in acute or remote myocardial infarction and ischemic cardiomyopathy.[1098-1104] The basic treatment for recurrent polymorphic VT/VF complicated by these conditions includes class III antiarrhythmic drugs, beta-blockers, deep sedation, heart failure management, electrolyte correction, and elimination of myocardial ischemia; however, if polymorphic VT/VF cannot be suppressed with these treatments, catheter ablation plays a significant role as a bailout therapy.

Endocardial ablation for PVC that triggers VF,[1105,1106] and epicardial ablation for abnormal potential areas of the free wall of the right ventricular outflow tract,[554,1107-1109] have been reported for Brugada syndrome with frequent ICD shocks. Many cases have already been reported, particularly for the latter procedure, and the long-term prognosis is good. Catheter ablation in other diseases (such as early repolarization syndrome, myocarditis, amyloidosis, valvular disease, non-ischemic cardiomyopathy, long QT syndrome, and catecholamine-induced polymorphic VT) has been reported in only a small number of patients,[1110-1114] and its effects and long-term prognosis are still unknown.

6.2.2 | *Catheter ablation procedures*

To map the PVCs that trigger polymorphic VT/VF, it is desirable that the target PVC be present during ablation. Deciding when to ablate is important because recurrent, non-sustained polymorphic VTs are easier to map when they occur spontaneously.[1106] If the target PVC does not exist at the time of ablation, pace mapping is performed. For this reason, it is extremely important to record in advance the PVC that triggers polymorphic VT/VF with a 12-lead ECG.

Idiopathic polymorphic VTs/VFs are often PVCs originating from the right ventricular outflow tract,[553,1093,1095,1096] and short-coupled variant of torsade de pointes (TdP) originating from distal Purkinje fibers.[319,553,1092,1094,1097]

Catheter ablation for polymorphic VT/VF originating from the right ventricular outflow tract is similar to ablation for normal idiopathic PVC or VT originating from the right ventricular outflow tract. It is important that mapping be performed not only in the right ventricular outflow tract but also in the pulmonary artery. The short-coupled variant of TdP is a polymorphic VT that begins with a PVC with a very short coupling interval,[1113,1114] and its origin is the Purkinje tissue in the left or right ventricle. The mechanism of the PVC itself is believed to be the triggered activity from Purkinje fibers because it is transiently suppressed by verapamil and induced by burst stimulation of the atrium or ventricle. Catheter ablation of recurrent polymorphic VT/VF in ischemic heart disease targets the distal Purkinje potential of the left bundle branch preceding the triggering PVC.[1094,1098-1103] It should be noted that Purkinje fiber-related monomorphic VT may occur after ablation of a triggering PVC.[1103]

6.2.3 | *Non-pharmacotherapies other than catheter ablation or devices*

Table 71 shows the recommendations for thoracic sympathetic denervation for VT/VF.

TABLE 70 Recommendations and evidence levels for catheter ablation of polymorphic VT/VF

	COR	LOE	GOR (MINDS)	LOE (MINDS)
In patients with idiopathic VF focally triggered by PVC from the RVOT or Purkinje system for whom AADs are ineffective or not tolerated, catheter ablation is recommended	I	B	B	V
In patients with IHD and recurrent VF or polymorphic VT focally triggered by PVC from the Purkinje system for whom AADs and myocardial ischemic therapies are ineffective or not tolerated, catheter ablation should be considered	IIa	B	B	V
In patients with Brugada syndrome who experience recurrent VF and for whom AADs and ischemic therapies are ineffective or not tolerated, catheter ablation may be considered	IIb	C	C1	V
In patients with structural and/or electrical heart disease (myocarditis, amyloidosis, valvular heart disease, non-ischemic cardiomyopathies, long QT syndrome, early repolarization syndrome, catecholaminergic polymorphic VT) who experience recurrent VF focally triggered by PVC from the RVOT or Purkinje system and for whom AADs are ineffective or not tolerated, catheter ablation may be considered	IIb	C	C1	V

Abbreviations: AAD, antiarrhythmic drug; COR, class of recommendation; GOR, grade of recommendation; IHD, ischemic heart disease; LOE, level of evidence; PVC, premature ventricular contraction; RVOT, right ventricular outflow tract; VF, ventricular fibrillation; VT, ventricular tachycardia.

TABLE 71 Recommendations and evidence levels for surgical autonomic modulation for VT/VF

	COR	LOE	GOR (MINDS)	LOE (MINDS)
In patients with long QT syndrome and recurrent appropriate ICD shocks despite maximum tolerated doses of a beta-blocker and/or additional AADs, left cardiac sympathetic denervation is recommended (not covered by Japan's National Health Insurance)	IIa	C	C1	IVa
In patients with catecholaminergic polymorphic VT and recurrent sustained VT or syncope, while receiving adequate or maximally tolerated beta-blocker with/without additional AADs, left cardiac sympathetic denervation is recommended (not covered by Japan's National Health Insurance)	IIa	C	C1	IVa
In patients with VT/VF storm in whom a beta-blocker, other AADs, and catheter ablation are ineffective, not tolerated, or not possible, cardiac sympathetic denervation (cardiac sympathectomy or thoracic epidural anesthesia) should be considered (not covered by Japan's National Health Insurance)	IIa	C	C1	IVa

Abbreviations: AAD, antiarrhythmic drug; COR, class of recommendation; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; VF, ventricular fibrillation; VT, ventricular tachycardia.

Thoracic sympathetic denervation[297,1115-1122] has been used as an additional treatment for severe ventricular arrhythmias for which beta-blockers and antiarrhythmic drugs are ineffective or unusable. Thoracic sympathetic denervation includes stellate ganglion block,[1115] thoracic sympathetic ganglionectomy,[297-300,1116-1118,1120-1122] and thoracic epidural anesthesia.[1117,1119] Thoracic sympathetic ganglionectomy includes conventional surgery and video-assisted thoracoscopic surgery (VATS) [1116-1119] the use of which has recently become more widespread. The lower half of the stellate ganglion and the thoracic sympathetic ganglion from T2 to T4 are resected. In the largest study on long QT syndrome, investigating 147 patients, a >80% event reduction was observed after surgical left sympathetic ganglionectomy.[297] In a registered study of 226 catecholaminergic polymorphic VT (CPVT) patients, 18 (8%) had undergone left sympathetic ganglionectomy and the treatment was effective in >70% of them.[1122]

The effectiveness of thoracic sympathetic denervation for VT and VF refractory to treatment, in the presence of underlying heart disease, has also been reported.[1117-1119] Thoracic sympathetic denervation with VATS in VT or VF storm patients with underlying heart disease was demonstrated to result in fewer arrhythmic recurrences and deaths in the bilateral sympathetic denervation group than in the left sympathetic denervation only group.[1118] In addition, thoracic epidural anesthesia was performed in patients with VT storm with underlying heart disease, and VT was completely suppressed in approximately half of the patients.[1119]

Thoracic sympathetic denervation for refractory VT and VF has been reported to be effective in all procedures; however, in Japan, it is not covered by national health insurance and the practice is not yet widely adopted.

6.3 | PVC and NSVT

6.3.1 | Catheter ablation indication

Table 72 shows the recommendations for catheter ablation of PVCs and nonsustained VTs (NSVTs).

When a PVC triggers polymorphic VT or VF,[1092,1093] catheter ablation of the PVC can prevent the occurrence of polymorphic VT or VF.[552,1105,1123,1124] Frequent PVCs can cause cardiac dysfunction, and ablation can improve cardiac dysfunction and the associated symptoms.[1125-1128] CRT plays an important role in the treatment of heart failure; however, the effect of CRT is reduced when the biventricular pacing rate decreases because of frequent PVCs/NSVTs. Therefore, ablation of the PVCs/NSVTs improves cardiac function by increasing the biventricular pacing rate.[1129]

In patients with frequent PVCs originating from the outflow tract, PVCs may lead to cardiac dysfunction in the future;[1130] thus, ablation should be considered. An RCT demonstrated that ablation therapy was more effective than antiarrhythmic medication in patients with frequent PVCs originating from the right ventricular outflow tract.[1131] PVCs/NSVTs often originate from the right ventricular outflow tract; however, they can also originate from other sites, such as the pulmonary artery, aortic sinuses of Valsalva, coronary vein, left ventricular outflow tract, left ventricular epicardial site, ventricular annulus, and papillary muscles.[931,990,991,993,999,1001,1009,1015,1022,1132,1133] Therefore, attempting to diagnose and assess PVCs and NSVTs from the waveforms of the surface 12-lead ECG before the ablation procedure, performing detailed mapping and assessment of the intracardiac electrograms obtained during the ablation procedure, and obtaining a precise assessment of the anatomical relationships between the arrhythmia origin and coronary arteries and heart valves are crucial for avoiding futile RF energy applications and the ensuing complications, and for successfully eliminating the PVCs/NSVTs. The indication for ablation should be considered, taking into account possible complications at each ablation site.

It remains to be determined whether idiopathic PVCs or NSVTs cause heart failure (PVC-induced cardiomyopathy) or, conversely, if arrhythmia appears as a symptom of heart failure.[1125,1126] Cardiac function is known to decrease in patients with frequent PVCs (approximately ≥10 000 beats/day, or approximately ≥10% of the total number of heart beats).[1127,1128,1130,1134-1136] Other risk factors for PVC-induced cardiomyopathy include the duration of symptoms due

TABLE 72 Recommendations and evidence levels for catheter ablation of PVC/NSVT

	COR	LOE	GOR (MINDS)	LOE (MINDS)
In patients with PVCs that trigger idiopathic polymorphic VT or idiopathic VF and for whom AADs are ineffective or not tolerated, catheter ablation is recommended	I	B	B	V
In patients with frequent PVCs/NSVTs (≥10% of the total number of beats) who have serious symptoms or severe ventricular dysfunction due to tachycardia and for whom AADs are ineffective, not tolerated, or not the patient's preference, catheter ablation is recommended	I	B	A	I
In patients with symptomatic idiopathic PVCs originating from the right/left ventricular outflow tract and for whom AADs are ineffective, not tolerated, or not the patient's preference, catheter ablation should be considered	IIa	B	C1	III
In non-responders to CRT with frequent PVCs/NSVTs limiting optimal biventricular pacing for whom AADs are ineffective or not tolerated, catheter ablation should be considered	IIa	B	B	IVa
In patients with frequent ICD discharges due to NSVTs and for whom AADs are ineffective or not tolerated, catheter ablation is recommended	I	B	A	IVa
In patients with symptomatic idiopathic PVCs originating from sites other than the ventricular outflow tract and for whom AADs are ineffective, not tolerated, or not the patient's preference, catheter ablation may be considered	IIb	B	C1	IVb
In patients with asymptomatic idiopathic NSVTs originating from the right/left ventricular outflow tract and for AADs are not desired, catheter ablation may be considered	IIb	C	C1	VI
In patients with structural heart disease and frequent PVCs for whom AADs are not desired, catheter ablation should be considered	IIa	B	B	IVb

Abbreviations: AAD, antiarrhythmic drug; COR, class of recommendation; CRT, cardiac resynchronization therapy; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; NSVT, nonsustained ventricular tachycardia; PVC, premature ventricular contraction; VF, ventricular fibrillation; VT, ventricular tachycardia.

to PVCs, such as a longer duration of palpitations, or, conversely, asymptomatic PVCs,[1135-1137] PVCs with a wide QRS width,[1138,1139] PVCs originating from the epicardium,[1137] a large number of interpolated PVCs,[1140] a wide variation in the coupling interval,[1141] and a short coupling interval of PVCs followed by early atrial contraction.[1142]

It has been also reported that ablation can improve cardiac function in patients with frequent PVCs with structural heart disease.[1143-1145]

6.3.2 | Catheter ablation procedures

a. | Mapping methods. Estimating the origin of PVCs/NSVTs from the waveforms of a surface 12-lead ECG before ablation is important for improving the success rate and reducing the operation time.[931,990,999,1001,1146-1152] Activation mapping is started from the right ventricle in cases in which a right ventricular origin is suspected from the ECG waveform, or when it is difficult to determine whether the origin is the right ventricle or the left ventricle. Usually, mapping is started after an electrode catheter is placed at the high right atrium, right ventricular apex, and/or in the His bundle region. Electrode catheters with extracardiac electrodes placed in sites such as the inferior vena cava are useful as indifferent electrodes during unipolar recordings.

If PVCs or NSVTs occur frequently, a mapping catheter should be placed at the site of origin anticipated from the 12-lead ECG waveform to identify the site of the earliest activation. Local ventricular activation that precedes the onset of the QRS complex by 20-40 ms is often recorded at the earliest activation site (successful ablation site), and the unipolar recording shows a steep QS pattern. Ablation is often unsuccessful when unipolar recordings show rS patterns. A presystolic potential preceding the QRS complex is often recorded at the ablation site in PVCs/NSVTs originating from the aortic sinus of Valsalva.[1001,1003,1153]

Pace mapping is also useful to determine the ablation site. Pace mapping relies on the principle that pace stimulation of the origin of PVCs or NSVTs will result in a surface QRS complex that exactly matches the target PVC morphology on all 12 surface ECG leads. When the same pace mapping waveform as the PVC/NSVT QRS waveform is obtained (perfect or excellent pace map), the success rate of ablation at the site is high. Pace mapping is particularly useful when activation mapping is not possible because of suppression of clinical PVCs/NSVTs. If clinical PVCs/NSVTs do not spontaneously occur during the procedure, rapid pacing and programmed extrastimuli from the atria or ventricles might be useful to induce them. Intravenous isoproterenol drip infusion (1-3 μg/min) is used in cases in which PVCs/NSVTs are frequently observed during exercise or during the day, and phenylephrine, which enhances vagal tone, is used in cases in which PVCs/NSVTs frequently occur during the night or at rest (ventricular pacing should be performed when it causes severe bradycardia; this is not performed in patients presenting with high blood pressure, as it may cause a transient increase in blood pressure). Alternatively, anticholinesterase drugs, such as edrophonium and neostigmine, may also be useful in inducing PVCs/NSVTs. In cases in which PVCs/NSVTs are induced or increased by programmed electrical stimulation or drug administration, a similar procedure is performed after ablation to confirm that ablated PVCs/NSVTs do not appear.

b. | *Radiofrequency energy application.* Right ventricular outflow tract ablation may be performed using a non-irrigated ablation catheter, and the maximum power of 35-50 W at a maximum electrode–tissue interface temperature of ≤60°C. The duration of the application of RF energy is 60-120 seconds. When ablation is effective, PVCs/NSVTs often disappear within 10 seconds. If the effect is insufficient, the RF energy application should be stopped early. When RF ablation is performed at the aortic sinus of Valsalva with a non-irrigated ablation catheter, the maximum power should be 30-35 W, the temperature should be set to a maximum of 55°C, and the duration of 1 application should be <60 seconds, to avoid damage to the coronary arteries and the aortic valve. To prevent damage to the coronary arteries, the ablation site must be at least 8 mm from the coronary artery ostium,[1003] and it is necessary to confirm the ostium by imaging the left and right coronary arteries before ablation. When using an irrigated catheter, ablation is started from a power of about 20 W to a maximum of 40 W (for ablation at the aortic sinus of Valsalva, up to approximately 35 W), and the temperature should be set to a maximum of 42°C. The application power and duration vary greatly depending on the individual patient and the contact and stability of the ablation catheter. Therefore, it is necessary to judge the degree of myocardial damage caused by ablation based on the decrease in impedance during RF energy application, the decrease in the amplitude of local electrograms, and the increase in pacing threshold after ablation, and perform adjustments accordingly.

The usefulness of catheter ablation with the transthoracic epicardial approach has been reported even for PVCs or NSVTs originating from the epicardial region.[1017] There have been reports of some successful cases of ablation with a coronary venous or epicardial approach (pericardial puncture or small surgical incision) and bipolar RF ablation (not covered by health insurance) for cases of unsuccessful ablation from the endocardial side.[1016,1154,1155]

7 | Catheter ablation for children

The treatment results and safety of catheter ablation for children has improved with advances in technology. However, a fatal case was reported in 2002, and the complication rate was reported to be as high as 3.0%.[1156] Typical complications include complete atrioventricular block, ventricular perforation, pericardial effusion, and embolism.[1156] The risk associated with catheter ablation in children depends on their body size. Body weight <15 kg and age <4 or 5 years have been used as cutoff criteria for high-risk standards for catheter ablation. A 2016 consensus report from the PACES/HRS proposed the 15 kg weight criterion, given that weight has a greater effect on risk.[1157] This guideline also considers the recommendations for catheter ablation separately for children weighing ≥15 kg and children weighing <15 kg, in accordance with the aforementioned recommendation.

It should be noted that tachycardia in children has different characteristics from those of adults. The intrinsic conduction time of the conduction system is short, and tachycardia via the atrioventricular node exhibits a higher heart rate in children than in adults. The type and frequency of tachycardia varies with age, and the condition may spontaneously resolve in some cases.[1156,1158,1159]

7.1 | Catheter ablation procedures

7.1.1 | Anesthesia and sedation

Catheter ablation in children often requires general anesthesia and/or deep sedation, and is often performed by an anesthesiologist with the patient under endotracheal intubation and general anesthesia. Situations in which general anesthesia is particularly recommended are shown in Table 73.

Propofol anesthesia is usually recommended for catheter ablation in patients with preexcitation syndrome because the inhaled anesthetics desflurane and sevoflurane are reported to suppress conduction of the accessory pathway.[1160] There are no restrictions on anesthetics for catheter ablation for other conditions; however, if arrhythmogenicity is suppressed by anesthesia, it is necessary to make adjustments, such as changing the anesthetic or using a shallow plane of anesthesia that will allow spontaneous respiration. Use of intravenous anesthetics requires an ECG, respiratory monitor, and blood pressure, oxygen saturation, and exhaled CO_2 monitors. Furthermore, monitoring the depth of anesthesia using the bispectral index (BIS) or other system is also recommended. For detailed information on how to use each drug, refer to the Guidelines for the use of anesthetics and anesthetic-related drugs, issued by the Japanese Society of Anesthesiologists.[566]

7.1.2 | Medical devices used for catheter ablation

Because the diameter of children's blood vessels is small, the size and number of catheters are limited. The minimum diameter of an electrode catheter in Japan is 2F, and quadripolar steerable catheters

TABLE 73 Cases and conditions for which general anesthesia is recommended during catheter ablation in children

Age ≤12 years
Complex congenital heart disease
Heart failure
Pulmonary hypertension
Hemodynamic instability
Respiratory comorbidities
Significant systemic comorbidities
Prediction of a prolonged procedure
A procedure near the coronary orifices or AV conduction system
Percutaneous epicardial approach
Patient or parent choice

(From Philip Saul et al, 2016[1157].)

are also available. There is also a system that can introduce three 2F electrode catheters from one 5F sheath at once. The minimum diameter of currently available ablation catheters is 5F (Ablaze, Japan Lifeline Co., Ltd.), and the length of the tip electrode is 4 mm. In general, for infants (weighing ≤10 kg), catheters are introduced from both sides of the groin; however, the maximum diameter on one side should be ≤7F. For a child weighing 15-30 kg, it is possible to introduce 2 catheters from the left and right groin, but the size of the selected catheter should be as small as possible. In children weighing ≥30 kg, the number and size of catheters are almost similar to those in adults.

Cryoablation (Freezor®, Medtronic) is recommended for AVNRT in children. The greatest advantage of cryoablation is the lower risk of atrioventricular block than with catheter ablation using RF energy.[1161] It can also monitor the PR intervals and evaluate the success of slow pathway ablation by atrial stimulation because junctional rhythm does not appear during cryoablation. Cryoadhesion, which means stabilization of the ablation catheter by adhesion to the target tissue by cooling down the catheter, is another advantage of this technique. Reduction of coronary artery damage,[1162] and a reduced risk of thrombosis, because it does not damage the intima,[1163] are also reported. Conversely, the manipulation of this catheter is limited, and the procedure time tends to become long.[1164] The success rate of cryoablation has been reported to be 91%–100% (with a recurrence rate of 1.7%–22.4%), which is comparable to the success rate of RF ablation. From the safety perspective, there has been only 1 report of first-degree atrioventricular block with cryoablation.[1165] Although some reports recommend cryoablation in infants,[1166] it is not very suitable for infants because of the size (7F) and stiffness of the catheter.[442]

Selecting a 3D mapping system for children is based on the body size of the children and the size of the patch for the 3D mapping system. The EnSite™ Velocity™ system (Abbott) has a small body surface patch and is able to recognize the aforementioned 5F ablation catheter, which is also useful for small children.

7.1.3 | Radiation exposure

It has been reported that children may be 2-3-fold more sensitive to radiation than adults.[1167] In addition, on average, children have a longer life expectancy and are more likely to have long-term radiation-induced health effects.[1167] There are no reports on the risk of cancer from catheter ablation in children. Nevertheless, efforts must be made to reduce exposure as much as possible. Exposure can be reduced by using a 3D mapping system, intracardiac echocardiography, and a system that superimposes radiographs taken in advance on 3D mapping (CartoUnivu™ module, Biosense Webster) (see section "**1.5 X-ray exposure**" in this chapter).

7.2 | Catheter ablation for children weighing <15 kg

The complications of RF ablation occur more often and more severely in children weighing <15 kg than in those weighing ≥15 kg.[615,1156,1168-1172] Pharmacotherapy is the first-line treatment for children weighing <15 kg. Ablation therapy may be considered for infants with life-threatening arrhythmias and drug resistance; however, this procedure should be performed by a well-experienced pediatric electrophysiologist.

7.3 | Catheter ablation indication for children without structural heart disease

7.3.1 | Atrioventricular reciprocating tachycardia

The most common tachycardia in children is AVRT caused by accessory pathways.[1173] Although the incidence of AVRT is high during the neonatal period, tachycardia disappears by the age of 1 year in 90% of cases, and it has been reported that the tachycardia relapses in approximately 30% of patients by the age of 7-8 years.[1158] It has also been reported that antegrade and retrograde conduction in accessory pathways disappears by 1 year of age in about 40% of cases.[1172] The indication of catheter ablation for AVRT in early infancy must be determined by taking into account that the properties of the accessory pathways may change, and that recurrence may not occur.

The problems with asymptomatic preexcitation syndrome without AVRT are cardiac arrest and sudden death due to rapid ventricular response in association with AF,[1175] and a decrease in cardiac function due to ventricular dyssynchrony;[1176] however, this condition is rare in children. No study has evaluated the risk factors for cardiac arrest and sudden death in preexcitation syndrome by using electrophysiology studies under general anesthesia in children; thus, the criteria for the risk of sudden death are the same standards as those used for adults (shortest RR interval during AF and rapid atrial pacing <250 ms, or the presence of multiple conduction pathways) (refer to section "**3.1.1 Catheter ablation indication**" in this chapter).

7.3.2 | Atrioventricular nodal reentrant tachycardia

The second most common tachycardia in children is AVNRT.[1156] Its incidence in children increases with age,[1177] and the average age of children with this condition is about 10 years higher than that of children with AVRT. This is believed to be due to physiological changes in atrioventricular node function.[1178,1179]

7.3.3 | Atrial tachycardia

Atrial tachycardia in children aged ≤ 3 years without congenital heart disease is often controlled with antiarrhythmic drugs; however, resistance to drug treatment increases after age 3 years.[1180,1181] More than 70% of cases in children aged <3 years that can be treated with drugs resolve spontaneously. However, among patients aged >3 years, <50% achieve sinus rhythm with pharmacotherapy and spontaneous remission has been reported in <25% of cases.[1180,1181] Catheter ablation is a reasonable option if the patient is >3 years old and tachycardia can be treated by this method.

The recommendations for catheter ablation for AVRT, AVNRT, and atrial tachycardia are shown in Table 74,[615,1168,1180-1188] and the

TABLE 74 Recommendations and evidence levels for catheter ablation of AVRT, AVNRT, and AT in children without structural heart disease

	COR	LOE	GOR (MINDS)	LOE (MINDS)
For pediatric patients with documented recurrent or persistent SVT, when medical therapy is either not effective or is associated with intolerable adverse effects, catheter ablation is recommended (medical therapy should be used prior to ablation in patients with body weight <15 kg)	I	C	B	IVa
For pediatric patients with body weight ≥15 kg and documented recurrent or persistent SVT associated with ventricular dysfunction, catheter ablation is recommended	I	C	B	IVa
For pediatric patients with body weight ≥15 kg and documented recurrent or persistent SVT, when the patient's family does not desire prophylactic AADs, catheter ablation is recommended	I	C	B	IVa
For pediatric patients with body weight ≥15 kg and recurrent acute hemodynamic compromise (hypotension or syncope) due to SVT, catheter ablation is recommended	I	C	B	IVa
For pediatric patients with body weight ≥15 kg and recurrent palpitation, when AVRT is inducible or an AV accessory pathway is observed in an EPS, catheter ablation of the accessory pathway should be considered	IIa	C	C1	IVa
For pediatric patients with body weight ≥15 kg and documented SVT, when SVT is noninducible, but a dual AV nodal physiology is observed in an EPS, catheter ablation of the AV nodal slow pathway should be considered	IIa	C	C1	IVa
For pediatric patients with body weight <15 kg and recurrent acute hemodynamic compromise (hypotension or syncope) due to SVT, catheter ablation may be considered	IIb	C	C2	IVa
For pediatric patients with body weight <15 kg and atrial tachyarrhythmias refractory to all medications and substrate-targeted catheter ablation, AV nodal ablation with subsequent pacing may be considered	IIb	C	C2	IVb

Abbreviations: AAD, antiarrhythmic drug; AT, atrial tachycardia; AV, atrioventricular; AVRT, atrioventricular reciprocating tachycardia; COR, class of recommendation; EPS, electrophysiological study; GOR, grade of recommendation; LOE, level of evidence; SVT, supraventricular tachycardia.

TABLE 75 Recommendations and evidence levels for catheter ablation for preexcitation syndrome in children without a history of AVRT

	COR	LOE	GOR (MINDS)	LOE (MINDS)
In pediatric patients with preexcitation syndrome following resuscitated cardiac arrest, catheter ablation of the accessory pathway is recommended	I	C	B	IVb
In pediatric patients with preexcitation syndrome and syncope when there are predictors of a high risk for cardiac arrest, catheter ablation of the accessory pathway is recommended (see Chapter III, section 3.1.1 Catheter ablation indication)	I	C	B	IVb
In pediatric patients with preexcitation syndrome, body weight ≥15 kg, and ventricular dysfunction presumed to be due to dyssynchrony; or in pediatric patients with preexcitation syndrome, body weight <15 kg, and ventricular dysfunction presumed to be due to dyssynchrony when medical therapy is either not effective or associated with intolerable adverse effects, catheter ablation of the accessory pathway should be considered	IIa	C	C1	IVb
In pediatric patients with preexcitation syndrome and body weight ≥15 kg, when the patient and the patient's family request for ablation, catheter ablation of the accessory pathway may be considered to reduce the risk of arrhythmic events	IIb	C	C2	IVb
In pediatric patients with preexcitation syndrome, catheter ablation of the fasciculoventricular accessory pathway is not recommended	III	C	D	IVb

Abbreviations: AVRT, atrioventricular reciprocating tachycardia; COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence.

recommendations for preexcitation syndrome without a history of AVRT are shown in Table 75.[613,1176,1189-1198]

7.3.4 | Ventricular arrhythmia

Ventricular arrhythmias in children have different characteristics from those in adults. VT in children often does not disrupt hemodynamics and has a low risk of sudden death,[1199,1200] and spontaneous regression has been reported in 17%–90% of the cases.[1159,1201-1203] Frequent PVCs can impair cardiac function in children, as in adults; however, PVCs account for 10%–24% of the total number of heartbeats, which may lead to the development of decreased cardiac function in adults[1204] compared with ≥30%–50% in children.[1201,1205] If PVCs are present in ≥0% of the total number of heartbeats, even in children, careful follow-up should be performed with attention to cardiac function, while considering catheter ablation.

The outcomes of catheter ablation in children are good for VT and PVC originating from the outflow tract, and for idiopathic left

posterior fascicular VT.[1206] However, idiopathic left anterior fascicular VT is more difficult to treat and there is increased risk of complications.[1197] There are no large-scale studies of the complications and prognosis of catheter ablation for ventricular arrhythmias in children. There are reports of catheter ablation for VT disrupting hemodynamics in infants in which the patients were rescued;[1170,1207,1208] however, catheter ablation in infants with conditions controllable with drugs should generally be delayed until the child weighs ≥15 kg (Table 76).[1092,1157,1159,1200,1201,1203,1209-1211]

7.3.5 | Other arrhythmias

Other rare arrhythmias in children include AFL, AF, and junctional ectopic tachycardia. However, as few reports on catheter ablation include many pediatric cases, the descriptions of recommendations have been omitted. These tachycardias in children are characterized by the AFL/junctional ectopic tachycardia seen in the early neonatal period, which often subsides as the child grows.[1212,1213] AFL and AF seen in school children and adolescents may sometimes be induced by AVRT or AVNRT.[1214]

7.4 | Catheter ablation for children with congenital heart disease

7.4.1 | General remarks

Tachyarrhythmia complicated by congenital heart disease increases the risk of lower cardiac output and heart failure, and has a large clinical impact. It is also important to understand that each congenital heart disease has a characteristic tachyarrhythmia.

Catheter ablation for congenital heart disease has a lower success rate and a higher recurrence rate than that for the normal heart.[1215] However, a 2014 consensus report on the treatment of arrhythmias in adult congenital heart disease indicated that pharmacotherapy is problematic in terms of adverse reactions and efficacy, and recommended early application of catheter ablation.[458] Particularly when an arrhythmogenic substrate is present before intracardiac repair, treatment is difficult if tachycardia appears during the perioperative period, and catheter access may be difficult postoperatively. Therefore, aggressive catheter ablation is preferred, regardless of body weight, for tachycardia with accessory pathways other than cases attributable to reversible causes (transitory neonatal period, within 3 months after surgery, stimulation during catheter manipulation, electrolyte abnormality).

Refer to the separate section in this chapter for information on delayed-onset tachycardia after surgery for congenital heart disease (**5.1 Atrial tachycardia after heart surgery**).

7.4.2 | Secondary pathways associated with Ebstein's disease

Refer to section **"5.2.1.d. Ebstein's disease"** disease in this chapter.

7.4.3 | Supraventricular tachycardia in atrioventricular discordance

A condition in which the right atrium and the left ventricle are continuous, and the left atrium and the right ventricle are continuous, as typified by a congenitally corrected transposition of the great arteries, is called an atrioventricular discordance. Cases complicated by preexcitation syndrome and AVNRT have also

TABLE 76 Recommendations and evidence levels for catheter ablation of ventricular arrhythmias in children

	COR	LOE	GOR (MINDS)	LOE (MINDS)
In pediatric patients with body weight ≥15 kg and recurrent or persistent sustained VT with ventricular dysfunction for whom medical therapy is either not effective or is associated with intolerable adverse effects, catheter ablation is recommended as an alternative to antiarrhythmic medications	I	C	B	IVb
In pediatric patients with body weight ≥15 kg and symptomatic frequent PVCs, catheter ablation of PVCs should be considered	IIa	C	C1	IVb
In pediatric patients with body weight ≥15 kg and accelerated idioventricular rhythm with symptoms and ventricular dysfunction, catheter ablation may be considered	IIb	C	C2	IVb
In pediatric patients with recurrent or frequent polymorphic VT, catheter ablation of the PVCs that trigger polymorphic VT or arrhythmogenic substrate may be considered	IIb	B	C1	IVb
In pediatric patients with body weight <15 kg and ventricular arrhythmias that are either controlled medically or hemodynamically well tolerated without ventricular dysfunction, catheter ablation is not recommended	III	C	D	IVb
In pediatric patients with body weight <15 kg and accelerated idioventricular rhythm, catheter ablation is not recommended	III	C	D	IVb
In pediatric patients with asymptomatic ventricular arrhythmias that are not suspected of causing or leading to ventricular dysfunction, catheter ablation is not recommended	III	C	D	IVb
In pediatric patients with ventricular arrhythmias due to transient reversible causes, such as acute myocarditis or drug toxicity, catheter ablation is not recommended	III	C	D	IVb

Abbreviations: COR, class of recommendation, GOR, grade of recommendation; LOE, level of evidence; PVC, premature ventricular contraction; VT, ventricular tachycardia.

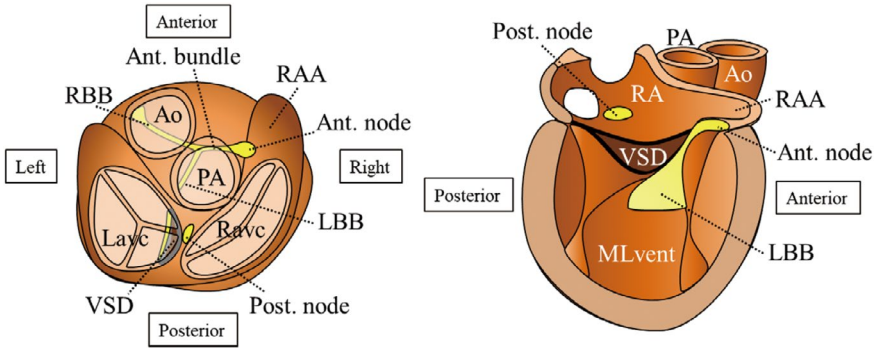


FIGURE 29 Conduction system in atrioventricular discordance. Ant., anterior; Ao, aorta; Lavc, left atrioventricular canal; LBB, left bundle branch; MLvent, morphological left ventricle; PA, pulmonary artery; Post., posterior; RA, right atrium; Ravc, right atrioventricular canal; RAA, right atrial appendage; RBB, right bundle branch; VSD, ventricular septal defect. (Modified from Anderson et al, 1973[1217] with permission.)

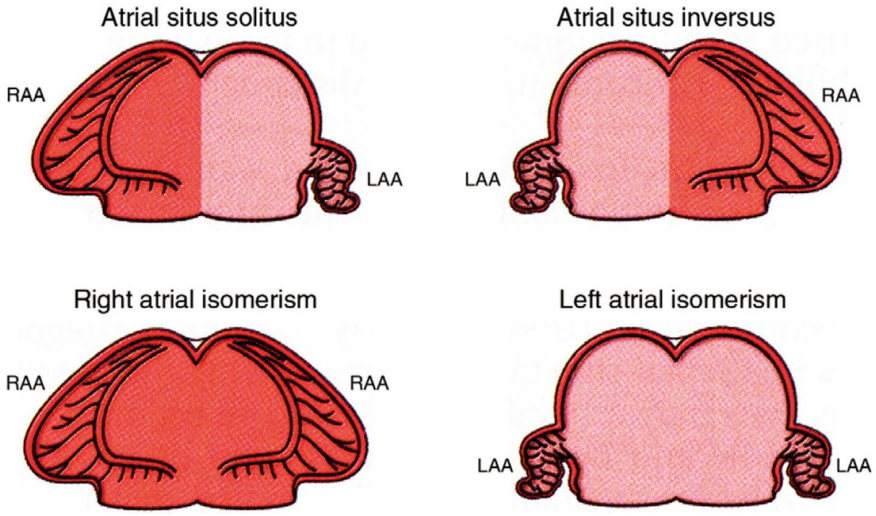


FIGURE 30 Atrial situs solitus: morphological right atrium on the right and morphological left atrium on the left. Atrial situs inversus: morphological left atrium on the right and morphological right atrium on the left. Right atrial isomerism: bilateral morphological right atria. Left atrial isomerism: bilateral morphological left atria. LAA, left atrial appendage; RAA, right atrial appendage. (From Anderson, 2010[1220] with permission.)

been reported. Points to note during catheter ablation include the location and alignment of the atrioventricular node. Depending on the alignment of the atrial and ventricular septum, through the development process, only the anterior or only the posterior atrioventricular node may be remaining, or both the anterior and posterior atrioventricular nodes may remain (twin atrioventricular nodes).[1216,1217] The posterior atrioventricular node should be located in the Koch triangle, whereas the anterior atrioventricular node is located at the point where the mitral valve annulus comes into contact with the pulmonary artery, and the lower conduction pathway extends to the ventricular septum anterior to the pulmonary artery (Figure 29).[1217] If both the anterior and posterior atrioventricular nodes remain, tachycardia that circulates between the 2 atrioventricular nodes can be initiated (twin atrioventricular node reentrant tachycardia).[1218]

Ablation therapy for preexcitation syndrome is performed in the usual manner. As AVNRT is located in an unusual site, the site of ablation should be carefully determined, and care is needed to avoid atrioventricular block. Furthermore, the coronary sinus and cardiac veins are positioned differently from a normal heart;[1219] therefore, the positions should be confirmed when placing the electrode catheter.

7.4.4 | Supraventricular tachycardia in heterotaxy syndrome

Heterotaxy syndrome is a concept that describes the left–right differentiation disorder of organs. In this disorder, atrial, thoracic, or abdominal organs present with isomerism (symmetric structure) (Figure 30).[1220] Disorders of the conduction system also frequently occur. Because the sinus nodes and atrioventricular nodes are right-sided organs, the 2 sinus nodes and 2 atrioventricular nodes are often in right atrial isomerism. Hypoplastic and/or aplastic sinus nodes are in left atrial isomerism, often resulting in atrioventricular conduction disturbance.[1221] When there are 2 atrioventricular nodes, twin atrioventricular node reentrant tachycardia may arise,[1218] in which the tachycardia rotates around the 2 atrioventricular nodes. The crista terminalis, which serves as an electrical barrier during intra-atrial reentrant tachycardia, is a right-sided structure. Therefore, it is present in both atria in right atrial isomerism and is often absent in left atrial isomerism.[1220] Therefore, the incidence of atrial reentrant tachycardia is high for right atrial isomerism and low for left atrial isomerism.[1222,1223] As the incidence of arrhythmias before and after surgery is high, the presence of arrhythmia should be closely monitored, and catheter access routes should be carefully examined.

Table 77 shows the recommendations for catheter ablation for tachyarrhythmias in congenital heart disease.[928,1215,1218,1224-1227]

TABLE 77 Recommendations and evidence levels for catheter ablation of tachyarrhythmias in children with congenital heart disease

	COR	LOE	GOR (MINDS)	LOE (MINDS)
In pediatric patients with CHD, body weight ≥15 kg, and recurrent or persistent SVT, when medical therapy is either not effective or associated with intolerable adverse effects, catheter ablation is recommended as an alternative to AADs	I	C	B	IVb
In pediatric patients with CHD, body weight ≥15 kg, and recurrent symptomatic AT occurring >3 months after surgery, when medical therapy is either not effective or associated with intolerable adverse effects, catheter ablation is recommended as an alternative to AADs	I	C	B	IVb
In pediatric patients with CHD, body weight ≥15 kg, symptomatic preexcitation syndrome, and high-risk factors, as commonly encountered in Ebstein's disease, catheter ablation of the accessory pathway is recommended	I	C	B	IVb
In pediatric patients with CHD, body weight ≥15 kg, and sustained monomorphic VT causing symptoms or hypotension, when medical therapy is either not effective or associated with intolerable adverse effects, catheter ablation should be considered as an alternative to AADs	IIa	C	B	IVb
In pediatric patients with moderate or complex CHD, body weight ≥15 kg, and recurrent or persistent AVNRT when medical therapy is either not effective or associated with intolerable adverse effects, catheter ablation of AVNRT should be considered	IIa	C	B	IVb
In pediatric patients with CHD and substrates that have a reasonable likelihood of contributing to tachyarrhythmias in the postoperative period, when impending congenital heart surgery will result in restriction of vascular or chamber access following surgery, presurgical catheter ablation of arrhythmic substrates should be considered	IIa	C	B	IVb
In pediatric patients with CHD, body weight ≥15 kg, and frequent monofocal PVCs thought to be contributing to deteriorating ventricular function, and in pediatric patients with CHD, body weight <15 kg, and frequent monomorphic PVCs thought to be contributing to deteriorating ventricular function when medical therapy is either not effective or associated with intolerable adverse effects, catheter ablation of PVC should be considered	IIa	C	C1	VI
In pediatric patients with CHD, body weight <15 kg, and SVT with acute hemodynamic compromise, catheter ablation of SVT may be considered	IIb	C	C2	IVb
In pediatric patients with CHD and atrial tachyarrhythmias refractory to all medications and substrate-targeted catheter ablation, AV nodal ablation with subsequent pacing may be considered	IIb	C	C2	VI
In pediatric patients with CHD and atrial tachyarrhythmias or junctional ectopic tachycardia that can be managed medically in the early postoperative period (<3 months postoperatively), catheter ablation is not recommended	III	C	D	IVb
In pediatric patients with CHD and ventricular arrhythmias who are deemed to be at an increased risk for sudden cardiac death and in whom an ICD is otherwise indicated, prophylactic catheter ablation is not recommended	III	C	C2	VI

Abbreviations: AAD, antiarrhythmic drug; AT, atrial tachycardia; AV, atrioventricular; AVNRT, atrioventricular nodal reentrant tachycardia; CHD, congenital heart disease; COR, class of recommendation; GOR, grade of recommendation; LOE, level of evidence; PVC, premature ventricular contraction; SVT, supraventricular tachycardia; VT, ventricular tachycardia.
[Correction added on 29 June, after first online publication: In the eighth description, 'In pediatric patients with CHD, body weight ≥15 kg, ...' has been amended to 'In pediatric patients with CHD, body weight <15 kg, ...'.]

IV | LEFT ATRIAL APPENDAGE CLOSURE DEVICE

The left atrial appendage closure (LAAC) device was developed as a non-pharmacotherapy option for preventing cardiogenic thromboembolism in patients with non-valvular atrial fibrillation (NVAF) who are unable to tolerate long-term anticoagulation therapy. More than 90% of thrombi formed in the atria originate in the left atrial appendage (LAA) in NVAF patients.[1228] Therefore, LAA surgical resection, suturing closure, or LAAC or resection using an automatic suturing device is performed during heart surgery (see **Chapter V, 1.3.2 LAAC or resection**). Recently, a LAAC system using a percutaneously inserted catheter has been developed as an alternative therapy for oral anticoagulant therapy. In Europe and the USA, a number of LAAC devices are already in clinical use, including WATCHMAN™ (Boston Scientific, approved by the Pharmaceutical and Medical Devices Act in February 2019; Figure 31);[1229] AMULET™ (Abbott, unapproved in Japan); and LARIAT™ (SentreHEART, unapproved in Japan), which ligates the LAA from the epicardial side via epicardial puncture. Two randomized controlled trial (RCTs), PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients with AF)[1230] and PREVAIL (Watchman LAAC Device in Patients with Atrial Fibrillation versus Long-term Warfarin Therapy)[1231] have been conducted to investigate the non-inferiority of the WATHCMAN™ device to long-term warfarin administration in patients with a cerebral infarction risk ($CHADS_2$ score ≥1).

In a combined analysis of the 2 trials (target patients: 1,114, follow-up: 4,343 person-years), there was no significant difference in the primary efficacy endpoints (stroke, systemic

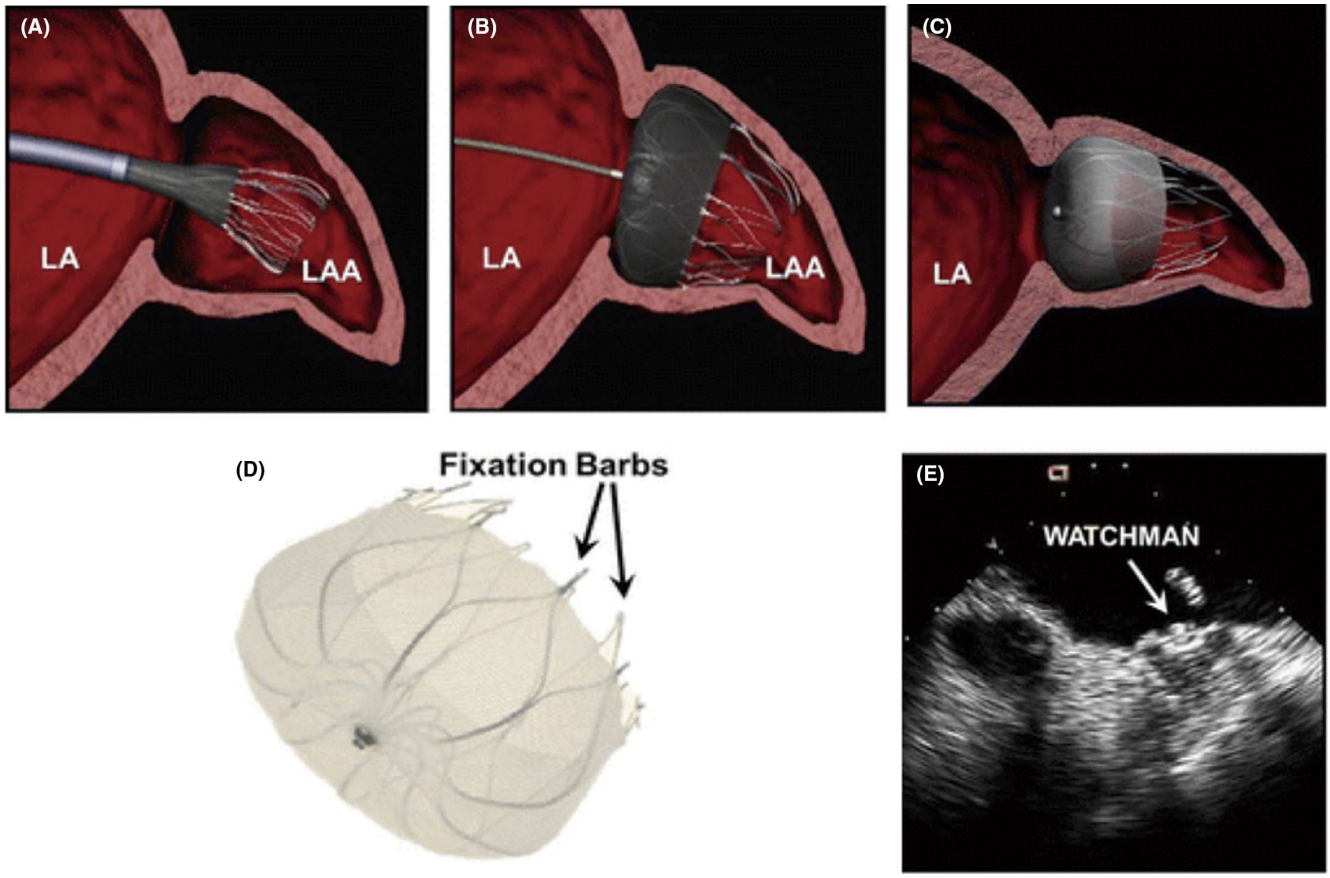


FIGURE 31 WATCHMAN™ device. Schema of implantation: delivery (A), deployment (B), and release (C). (D) Close-up view of the WATCHMAN device. (E) Transesophageal echocardiographic image of an occluded LAA following deployment of a WATCHMAN™ device. LA, left atrium, LAA, left atrial appendage. (From De Backer et al, 2014[1229] with permission.)

embolism, cardiovascular death/death with unknown cause) for the WATCHMAN device group and the long-term oral warfarin group nor in the primary safety endpoints (serious bleeding and procedure-related complications).[1232] Although there was no significant difference in the incidence of cerebral infarction events between the 2 groups, the incidence of hemorrhagic stroke (hazard ratio (HR) 0.2, 95% confidence interval (CI) 0.07-0.56, $P = .0022$), stroke with disabling/fatal stroke (HR 0.45, 95% CI 0.21-0.94, $P = .034$), and cardiovascular death/death with unknown cause (HR 0.59, 95% CI 0.37-0.94, $P = .027$) was significantly lower in the WATCHMAN group. The results indicated that the LAAC device could be an alternative to anticoagulant therapy for NVAF patients at high risk for bleeding events. In PROTECT AF, the high number of perioperative complications (cardiac tamponade, cerebral infarction, device embolism) was problematic; however, after procedural improvements, a high procedure success rate was reported in post-marketing registration studies conducted in Europe and the USA (>95%; definition of procedural success: ≤5 mm leakage around the device), with a reduced incidence of perioperative complications (<2%).[1233,1234] In the SALUTE study,[1235] implemented in Japan to verify the efficacy and safety of WATCHMAN in Japanese NVAF patients at a risk for cerebral infarction (CHA_2DS_2-VASc score ≥2), the procedural success rate and safety were similar to those in studies in Europe and the USA, and efficacy up to 6 months after procedure was demonstrated.

The LAAC device is a potential alternative to long-term warfarin treatment for NVAF. However, no RCTs have been performed to verify the efficacy and safety of the LAAC device versus direct-acting oral anticoagulants (DOACs), which are as effective as, but safer than, warfarin. In the 2 previous RCTs on the WATCHMAN device, combination therapy of warfarin and aspirin was immediately used after device implantation. Therefore, the safety of the LAAC device has not been established for patients who are unable to tolerate anticoagulation therapy immediately after procedure.

When selecting a LAAC device, it is important to accurately evaluate the LAA morphology using transesophageal echocardiography (TEE) and contrast-enhanced computed tomography. Inappropriate selection of a LAAC device can result in postoperative device embolization and >5 mm peri-device leakage.

V | ARRHYTHMIA SURGERY

1 | Atrial fibrillation

Table 78 shows the recommendations for surgical procedures for AF.

The maze procedure,[1236-1238] developed by Cox et al in 1987, has become the gold standard for AF surgery. However, modifying and simplifying the atrial incision lines, and substituting cryoablation and radiofrequency to make incision lines, have been used as alternatives to simplify the procedure and to make it less invasive.[1239-1246] The maze procedure restores AF to sinus rhythm in 70%–90% of cases when performed in appropriate patients.[1247-1252] Clinical data have been accumulated, and even after the publication of the 2012 guidelines, consensus statements and guidelines of various overseas academic societies were updated based on the new data.[7,578,691,1253-1255]

1.1 | Surgery for AF with structural heart disease

The maze procedure became widely used in Japan in the 1990s as a concomitant procedure for heart surgery for structural heart disease,[1239,1250] and its use has since spread overseas with advancements in devices.[1256] Surgery for the underlying disease is broadly classified into mitral valve surgery, which requires left atrial incision, and aortic valve replacement and coronary artery bypass, which do not require left atrial incision. Regardless of the difference in invasiveness, the operative mortality rate is not increased by concomitant AF surgery.[1257-1261] A meta-analysis of 10 RCTs and 14 non-RCTs[1255] and an analysis of the Society of Thoracic Surgeons (STS) database[1262] indicated that AF surgery can improve the postoperative 30-day mortality. A meta-analysis found no significant difference in the incidence of cerebral infarction or other major complications during the perioperative period; however, the frequency of implantation of a new pacemaker after surgery increased with the application of the maze procedure.[1255] Another meta-analysis did not find a significant difference in postoperative renal function impairment, although the incidence was increased according to an analysis of the STS database.[1262]

The effect of improving life prognosis in the long-term postoperative period was not significantly different up to 1 year after surgery in an RCT; however, a meta-analysis of 28 articles, including non-RCTs with extended follow-up, showed that AF surgery significantly improved the long-term prognosis.[1255]

A meta-analysis of 11 articles including RCTs and non-RCTs (RCT analysis up to 1 year after surgery) did not show any significant effect in preventing postoperative late-stage cerebral infarction.[1255] Conversely, 2 studies from Japan[1263,1264] (up to 10 and 8 years of follow-up) showed significant prevention of cerebral infarction in the late stage, and a meta-analysis of 5 non-RCTs, including those 2 articles,[1255] found similar results. Another meta-analysis[1260] showed that the longer the postoperative observation period, the higher the odds ratio of preventing cerebral infarction. It has been shown that quality of life (QOL) in the long-term postoperative period is improved in the sinus rhythm maintenance group after the maze procedure.[1255,1265,1266]

The basic mechanisms of eliminating AF in the maze procedure are electrical isolation of the pulmonary veins with high-frequency repetitive activation and preventing reentry with multiple atrial incision lines; however, AF has been terminated in some patients with pulmonary vein isolation (PVI) alone,[1267] and indications for simplified surgery depending on the case have been investigated. AF surgery is broadly classified into (1) bi-atrial incision surgery typified by maze III and IV;[1267-1269] (2) "left atrial maze" procedure, in which the maze incision lines are limited to the left atrium;[1270,1271] and (3) bilateral PVI only, based on the lesion set. When selecting these lesion sets, it is essential to consider the indications and effects of (1) combined surgery with a left atrial incision, (2) combined surgery with no left atrial incision, and (3) single AF procedure for isolated AF. It is also necessary to take into account factors such as whether the AF

TABLE 78 Recommendations and evidence levels for surgical procedures for AF

Procedure		COR	LOE	GOR (MINDS)	LOE (MINDS)
Concomitant surgical ablation of AF	For patients with AF who undergo LA open procedures, such as mitral valve surgeries, concomitant surgical ablation of AF is recommended	I	A	A	I
	For patients with AF who undergo non-LA open procedures, such as CABG or AVR, concomitant surgical ablation of AF is recommended	I	B	B	III
Stand-alone surgical ablation of AF	For patients with symptomatic AF and without structural heart disease, stand-alone surgical ablation of AF should be considered	IIa	B	B	I
	For patients with unsuccessful catheter ablation for AF, stand-alone surgical ablation of AF should be considered	IIa	B	B	III
	For patients with AF and LA thrombi, stand-alone surgical ablation of AF should be considered	IIa	C	C1	V
LA excision or occlusion	In conjunction with surgical ablation of AF, LA excision or occlusion should be considered	IIa	C	C1	IVa
	In conjunction with cardiac procedures for patients with AF, LA excision or occlusion but without surgical ablation of AF should be considered	IIa	C	C1	IVa

Abbreviations: AF, atrial fibrillation; AVR, aortic valve replacement, CABG, coronary artery bypass grafting, COR, class of recommendation; GOR, grade of recommendation; LA, left atrium; LOE, level of evidence.

is paroxysmal or persistent (or long-term persistent), and the extent of left atrial enlargement.

With respect to the lesion sets concomitant with cardiac surgery for structural heart disease, some reports have indicated that the bi-atrial procedure is more effective,[1272,1273] although PVI only without a block line on the left atrium is ineffective according to other reports.[1274] However, in 2015, a multicenter RCT reported no difference in the AF-free rate at 1 year postoperatively between the bi-atrial maze procedure and PVI in combined surgery with mitral valve surgery.[1275] However, the uniformity of the different facilities, including the appropriateness of the surgery, is unknown, and further studies are needed.

On the basis of the analysis of the Japan Adult Cardiovascular Surgery Database Organization[1276] and the US STS database,[1262] PVI is performed in almost half of patients who do not require atrial incisions, as a combined surgery without a left atrial incision such as aortic valve replacement or coronary artery bypass surgery. PVI alone may be effective because the left atrial load is relatively low in patients undergoing these procedures; however, in patients with marked left atrial enlargement, the effect of PVI alone on AF is diminished.[1254,1277]

1.2 | Surgery for isolated AF

AF surgery for isolated AF (not associated with structural heart disease) has shown better results than catheter ablation in a large number of studies, including meta-analyses and RCTs;[1278-1281] however, postoperative complications are more common with AF surgery than with catheter ablation.[1278-1282] In Japan, <100 cases of maze procedure are performed annually for isolated AF.[1283] AF surgery for isolated AF is usually performed in relatively young patients with a short history of AF, and is often performed as a minimally invasive heart surgery in the USA.[1254] The conventional maze procedure under cardiopulmonary bypass with a right thoracotomy or an endocardial approach using simplified maze procedures has been performed.[1284,1285] Given that PVI alone using catheter ablation has also been shown to be effective to a certain degree,[1278,1286,1287] the procedure was developed into minimally invasive surgery, such as small thoracotomy and thoracoscopic surgery.[1245,1288,1289] However, there have been reports on the possibility of leaving incomplete block lines,[1290] and low efficacy for persistent (or long-term persistent) AF,[1291] and device improvements and refinement of the lesion set are ongoing.[1292-1294] With respect to the safety of minimally invasive surgery for isolated AF, a review of 23 articles in 2013 showed that the operative morality rate was 0.4% and the complication rate was 3.2%,[1295] whereas the operative morality rate in the US STS database was 0.74%.[1254]

Despite the aforementioned problems of minimally invasive AF surgery, it has the advantage of allowing intraoperative electrophysiological studies to be performed because it is a beating heart surgical procedure. This means that additional treatment for residual conduction gaps and non-PVI foci based on the study results is also possible. Hybrid surgery, in which surgical epicardial ablation and percutaneous endocardial ablation are performed simultaneously (1-stage surgery) or within 6 months from each other (2-stage surgery), is a reasonable treatment strategy.[1296,1297] Although additional procedures can be performed immediately based on the results of intraoperative electrophysiological studies in 1-stage surgery,[1298] there is no evidence that the outcomes of 2-stage surgery are inferior. A variety of surgical procedures has been reported as hybrid surgery, combining various approaches (bilateral or unilateral transthoracic approach, subxiphoid approaches, etc), various lesion sets, and LAAC.[1299-1309] However, the effectiveness of these methods has yet to be objectively verified.

The maze procedure for patients with unsuccessful catheter ablation achieves return to sinus rhythm more frequently than does additional catheter ablation.[1278,1289,1310] In patients with AF complicated by left atrial thrombosis, surgical thrombectomy and appropriate postoperative anticoagulant therapy are performed if the patient has a history of, or is at a high risk for, thromboembolism because of poorly lytic thrombi. In addition, objective studies are needed to determine whether recurrence of left atrial thrombosis and thromboembolism can be prevented by restoring sinus rhythm with a simultaneous maze procedure.

In this guideline, the class of recommendation for AF surgery for isolated AF is IIa. Thoracoscopic and robot-assisted surgical treatments are expected to become more commonplace in the future; however, it is necessary to consider the effectiveness of this treatment for persistent AF and to compare it with that of catheter ablation.

1.3 | Additional surgical treatment for AF

1.3.1 | GP ablation

In recent years, ganglionated plexus (GP) ablation has been performed as part of AF surgery.[1311-1313] A meta-analysis found that the addition of GP ablation to the maze procedure or PVI resulted in better short- and mid-term outcomes than either surgery alone.[1314] Conversely, an RCT (AFACT [AF Ablation and Autonomic Modulation via Thoracoscopic Surgery]) at a single facility reported that GP ablation had no effect.[849] Therefore, reports from multicenter RCTs are awaited.

1.3.2 | LAAC or resection

The LAA is a common site of thrombus formation, and may be involved in up to 90% of cerebral infarction cases in non-rheumatic AF patients.[1228] Focal triggers from the LAA are also among the non-pulmonary vein foci.[1315-1318]

The LAA has long been targeted to prevent cerebral thromboembolism associated with AF after open-heart surgery, as well as AF surgery, and procedures include (1) surgical resection and suture closure, (2) suture closure from inside the left atrium, and (3) closure from outside the heart using devices such as an automatic suture device. On the basis of postoperative evaluation of residual blood flow

and stump length in the LAA, some reports suggested that these procedures do not completely prevent cerebral infarction;[1319,1320] however, a meta-analysis found that cerebral infarction was reduced in the early and chronic postoperative phases (≥50% in the chronic phase).[1321] LAAC with a clip-type device has been reported to have a small residual margin, and no cerebral infarction has been seen in the long-term results.[1322,1323] Recent large-scale retrospective studies have demonstrated the efficacy of simultaneous LAAC with cardiac surgery for preventing cerebral infarction and improving life prognosis in patients with AF.[1324,1325] However, the efficacy of stand-alone treatment and the necessity of continuing postoperative anticoagulant therapy have not been investigated in detail.

2 | Ventricular tachycardia

The recommendations for surgical ablation of ventricular tachycardia (VT) are shown in Table 79.

From the viewpoint of implementing a life-saving procedure, surgical ablation of VT is indicated for monomorphic sustained VT for which pharmacotherapy or catheter ablation is ineffective or in which frequent VT attacks are not suppressed, or when there is frequent activation of an implantable cardioverter-defibrillator (ICD) associated with the above condition, irrespective of whether or not the patient has underlying heart disease.[955,1326-1329] Preoperative and intraoperative endocardial and epicardial mapping for identifying the origin of the tachycardia and the site of the reentrant circuit is essential, and close collaboration between the physician and surgeon is required. The tachycardic origin of VT indicated for surgical treatment is generally located in the deep myocardium, below the epicardial adipose tissue, or near the coronary artery, which cannot be reached by catheter ablation. Myocardial dissection or cryoablation is performed to ensure full-thickness necrosis at these sites.[1330,1331]

Resection and cryoablation of left ventricular endocardium with white fibrosis are performed, together with left ventricular reconstruction and thrombectomy, in VT with heart failure or thromboembolism caused by ventricular aneurysm or left ventricular wall asynergy after myocardial infarction. Even in VT involving the blood drainage part of a left ventricular assist device, the boundary between the scar and the normal myocardium is considered an arrhythmic substrate, and cryoablation is performed on this area.[1332-1335] In VT associated with cardiac tumors, it has been reported that VT attacks are suppressed by surgical treatment, including tumor resection.[1336-1338]

VI | RETURNING TO/ATTENDING SCHOOL OR WORK AFTER NON-PHARMACOTHERAPY

1 | Cardiac implantable electronic devices

1.1 | Attending school after CIED implantation

Pediatric patients with a cardiac implantable electronic device (CIED) have underlying arrhythmias and heart disease, and the severity of heart failure determines their school attendance. In general, patients with New York Heart Association cardiac function class I can enroll in school, those with class II have restricted enrollment, and those with class III or higher experience difficulties in school. Physical education, exercise, and extracurricular lessons are managed using the School Activity Management tables (Tables 80-82).[1339] When permitting exercise, caution is needed for activities involving impact of devices with body parts, including the chest and abdomen (ball sports and contact sport), and activities in which lead overextension is a concern (tennis, swimming). There have been reports of incomplete or complete disconnection of transvenous leads due to body growth. Although there are reports showing that psychological factors such as anxiety and depression are more pertinent to the QOL of children wearing an ICD than the severity of the underlying heart disease, particularly

TABLE 79 Recommendations and evidence levels for surgical ablation of VT

	COR	LOE	GOR (MINDS)	LOE (MINDS)
In patients with recurrent sustained monomorphic VT or frequent ICD therapies for whom antiarrhythmic medications are ineffective or for whom catheter ablation is not successful, surgical ablation is recommended	I	C	B	V
For patients with sustained monomorphic VT after MI who have heart failure or thromboembolism associated with LV aneurysm or asynergy, surgical ablation should be considered	IIa	C	B	V
For patients with sustained monomorphic VT after MI, surgical ablation may be considered	IIb	C	C1	V
For patients with sustained monomorphic VT originating from the insertion site of LVAD, surgical ablation may be considered	IIb	C	B	IVb
For patients with sustained monomorphic VT associated with cardiac tumors, surgical ablation may be reasonable	IIb	C	C1	V

Abbreviations: COR, class of recommendation; GOR, grade of recommendation; ICD, implantable cardioverter-defibrillator; LOE, level of evidence; MI, myocardial infarction; VT, ventricular tachycardia.

TABLE 80 School activity management table

Categories of allowable intensity of exercise and daily activities:
"No management required" or "Management required," rated from A to E.
The categories A–E are defined as follows:
A: Requires treatment at home or in the hospital
B: Able to go to school but must avoid exercise
C: Able to do mild-intensity exercise for average students of the same age
D: Able to do moderate-intensity exercise for average students of the same age
E: Able to do vigorous-intensity exercise for average students of the same age
(a) Mild exercise
Physical activities that do not cause panting for breath in average students of the same age (eg, ball sports without footwork). Resistance (isometric) exercise is not defined as mild exercise
(b) Moderate exercise
Physical activities that may cause shortness of breath in average students of the same age, that may allow talking easily during exercise, and that have no close body contact. Moderate exercise includes resistance (isometric) exercise without full-strength effort
(c) Intense exercise
Physical activities that cause shortness of breath in average students of the same age. Intense exercise includes isometric exercise associated with teeth clenching, shouting, facial redness during and after movement, and rapid breathing

The instruction consists of a code for the allowable intensity of exercise and daily activities, as well as a guide for school sports club activity (allowed or prohibited), for example, "D-prohibited (moderate exercise is allowed but school sport club activity is prohibited)" and "E-allowed (intense exercise and school sport club activity are allowed)."
From Japan Society of School Health.[1344]

problems involving immaturity and psychology specific to adolescents,[1340] other reports suggest that ICD activation does not affect QOL.[1341] School teachers may have a poor understanding of underlying heart diseases and devices; thus, it is important to ensure cooperation among the child (home), teacher, school nurse, school doctor, and attending physician.[1342,1343]

If the cardiac function is normal in patients with a pacemaker, the School Activity Management Table (Table 80)[1339] suggests that the child can be managed with the E-allowed criterion (Table 80 Note). The presence of a pacemaker and complete atrioventricular block related to an atrioventricular septal defect are associated with subclinical heart failure, and children with these conditions require the D or E-prohibited management criterion (Table 80 Note). For patients with implants after surgery for congenital heart disease, exercise restrictions are based on individual circumstances. The management criteria are B or C for patients with heart failure, and D or E for patients without heart failure.

Many patients with ICD have long QT syndrome or catecholaminergic polymorphic VT, and often have normal cardiac function and are able to commute to school. In these patients, torsade de pointes and ventricular fibrillation may be induced by exercise and an increase in sympathetic tone, which pose a risk of ICD-induced dimmed vision and syncope. Therefore, these children should not be allowed to commute to school alone, and it is necessary to limit activities such as riding a bicycle to school and exercising. The management criteria are C or D. Swimming, in particular, is generally prohibited; however, swimming may be permitted, always under supervision, according to the C and D criteria.[1344,1345]

Many patients with cardiac resynchronization therapy have heart failure conditions such as dilated cardiomyopathy, and some patients may find it difficult to go up and down stairs. If the commute to school is beyond the cardiac function of the child, going to school by bus, train or private car is recommended. Exercise is generally difficult and therefore prohibited in severe cases, although certain exercises may be allowed depending on the degree of heart failure. In patients with arrhythmogenic right ventricular cardiomyopathy, it should be noted that movement exacerbates the lesion and worsens both arrhythmia and right heart failure.[1346,1347]

1.2 | Working and driving after CIED implantation

For patients with a CIED who are returning to work, it is necessary to provide employment guidance that considers 4 points in terms of health and safety management after the return to work. These are described below.

1.2.1 | Driving restrictions (particularly for patients with an ICD)

According to the Road Traffic Law in Japan, if a patient with an implanted pacemaker has improved syncope symptoms, driving is generally permitted and submission of a medical certificate to the Public Safety Commission is not required. In addition, companies often make their own decisions about occupational driving by patients with a pacemaker (eg, bus drivers, taxi drivers, drivers of transportation companies, etc), taking into account their physical/cardiac disability. Working as an aircraft pilot or a train driver is considered impossible because such patients would not meet the applicable standards of the Civil Aeronautics Act (Aviation Physical Examination Standards) and the Ministerial Ordinance on Motorized Vehicle Driver License (Ministry of Land, Infrastructure, Transport, and Tourism Ordinance). However, although persons with an ICD are generally prohibited from private driving, those with a medical certificate stating that driving need not be restricted may be allowed to drive by the Public Safety Commission. Commuting and driving on duty can be problematic. A joint statement has been issued by the relevant academic societies with respect to the driving restriction periods for these patients (Table 83).[1348] Patients with an ICD are prohibited from professional driving or from obtaining class 2 driver license.

TABLE 81 School activity management table (for elementary school children)

[Revised in 2011]

School Activity Management Table (for Elementary School Children)

Name M / F Birth date (years) School Grade Class Date

1. Diagnosis (findings)	2. Level of management	3. School sport club activity	4. Next visit	Name of institution:
	Management needed: A, B, C, D, E	Name of club ( )	___ years ____ months later	Name of physician: (seal)
	No management needed	Allowed (Note:)・Prohibited	or when symptoms develop	

[Level of management: A – Requires treatment at home or in hospital, B – Able to go to school but must avoid exercise, C – Able to do mild exercise, D – Able to do moderate exercise, E – Able to do intense exercise]

Sport activity / Intensity of exercise				Mild exercise (C, D, E – allowed)	Moderate exercise (D, E – allowed)	Intense exercise (E – allowed)
Type of sport	Basic exercise*	Warming-up exercise Exercise-play to improve athletic ability	Grade 1–2	Balance exercise-play (play consisting of different body postures such as lying down, sitting up/down, and standing up)	Exercise-play using apparatus (grabbing, releasing, rotating, rolling, or going through the apparatus)	Exercise-play to change location (crawling, running, jumping, and hopping)
		Warming-up exercise Exercise to improve athletic ability	Grade 3–4	Balance exercise (exercise consisting of different body postures such as lying down, sitting up/down, standing up, and hopping)	Exercise using apparatus (grabbing, holding, rotating, and releasing the apparatus, and exercise using a rope)	Strength competition (pushing or pulling a partner, or a strength contest), combination of basic movements
		Warming-up exercise Strength-training exercise	Grade 5–6	Exercise to improve flexibility (including stretching), light walking	Exercise to improve techniques (rhythmic exercise and exercise using ball, hoop, or clubs)	Full-body activities within a given time/course (short-rope jumping, long-rope jumping, long-distance running)
	Athletics	Running and jumping exercise-play	Grade 1–2	Walking in different ways, rubber rope jumping	Kemper play	Full-strength foot race, straight-course relay race, relay race with low obstacles
		Running and jumping exercise	Grade 3–4	Walking and light standing broad jump	Slow jogging, light jumping (standing long/high jump)	Full-strength foot race, round-course relay race, low hurdle race, long/high jump with short running start
		Athletics	Grade 5–6			Full-strength sprint, hurdle race, long jump with running start, high jump with running start
	Ball sports	Games, ball games, tag (for early grades), games using goals or nets, baseball-type games (for middle grades)	Grade 1–2	Target shooting with ball throwing, bouncing, and catching without changing of position	Target shooting with ball kicking and holding, ball kicking, tag, encampment games	Competition-style exercise
			Grade 3–4	Basic ball handling (passing, catching, kicking, dribbling, shooting, and batting)	Simple games (games with basic exercises with modified rules to fit the place and apparatus used)	
		Ball sports	Grade 5–6			
	Apparatus gymnastics	Exercise-play using apparatus	Grade 1–2	Exercise-play using climbing frames	Exercise-play using monkey bars and wall bars	Exercise-play using mat, horizontal bars, and vaulting horse
		Apparatus gymnastics using mats, vaulting horse, or horizontal bars	Grade 3–4 Grade 5–6	Basic exercises Mat exercise (basic movements such as forward roll, backward roll, handstand against wall, and bridging) Vaulting horse (basic movements such as jumping with legs apart) Horizontal bars (basic movements such as forward roll landing)	Basic techniques Mat exercise (e.g., forward/backward rolls, forward/backward rolls with legs apart, handstand against wall, and handstand with support) Vaulting horse (e.g., jumping with legs apart with short running start, jumping with legs folded, and forward roll on the horse) Horizontal bars (e.g., back hip circle with support, forward roll landing with a leg over the bar, front hip circle, and back hip circle)	Combination of gymnastic movements
	Swimming	Play with water	Grade 1–2	Play with water (splashing water on each other, playing "train" in swimming pool)	Floating and diving (e.g., prone float with hands against the wall, and paper-rock-scissors or staring game in water)	Relay race in the pool, bubbling, and bobbing
		Floating and swimming	Grade 3–4	Floating (e.g., prone float, back float, jellyfish float) Swimming movements (flutter kicks, frog kicks)	Floating (e.g., kicking and floating) Swimming (e.g., repeated bobbing)	Freestyle and breaststroke with supportive apparatus
		Swimming	Grade 5–6			Freestyle and breaststroke
	Dance	Rhythmic play	Grade 1–2	Pretend play (e.g., birds, bugs, dinosaurs, and animals)	Pretend play (e.g., airplane, fun-park rides)	Rhythmic play (e.g., bouncing, whirling, twisting, and skipping)
		Expression movement	Grade 3–4 Grade 5–6	Improvised expression movement	Light rhythmic dance, folk dance, or simple Japanese folk dance	Combination of variable movements (e.g., rock and samba dance) Japanese folk dance with strenuous movements
	Outdoor activities such as playing in the snow or on ice, skiing, skating, and waterfront activities			Playing in the snow or on ice	Walking with ski plates or skates and waterfront activities	Skiing and skating
Cultural activities				Cultural activities without prolonged tasks requiring physical strength	Most cultural activities not described in the right column	Playing instruments requiring physical exertion (e.g., trumpet, trombone, oboe, bassoon, horn), playing or conducting quick rhythmical music, playing in a marching band
School events and other activities				・Follow the above intensity of exercise during a sports festival, athletic meetings, ball sports competitions, and exercise tests. ・Students other than those in category "E" should consult with the school physician or attending physician in determining whether they can participate in other special school activities such as class trips, training camp, school trip, camp schools, and seaside schools. ・Consult with the school physician or attending physicians for the distance of running and swimming allowed (refer to the school curriculum guidelines).		

Remarks

Definitions
Mild exercise: Physical activities that do not cause panting for breath in average children of the same age.
Moderate exercise: Physical activities that may cause shortness of breath in average children of the same age, and that allow talking easily during exercise.
Intense exercise: Physical activities that cause shortness of breath in average children of the same age.

* Basic exercise: including resistance (isometric) exercise.

(Modified from Japan Society of School Health, 2013[1339])

TABLE 82 School activity management table (for junior and senior high school students)

[Revised in 2011]

School Activity Management Table (for Junior and Senior High School Students)

Name M / F Birth date (years) School Grade Class Date

1. Diagnosis (findings)	2. Level of management	3. School sport club activity	4. Next visit	Name of institution:
	Management needed: A, B, C, D, E	Name of club ( )	___ years ____ months later	Name of physician: (seal)
	No management needed	Allowed (Note:) • Prohibited	or when symptoms develop	

[Level of management: A – Requires treatment at home or in hospital, B – Able to go to school but must avoid exercise, C – Able to do mild exercise, D – Able to do moderate exercise, E – Able to do intense exercise]

Sport activity \ Intensity of exercise				Mild exercise (C, D, E – allowed)		Moderate exercise (D, E – allowed)		Intense exercise (E – allowed)	
Type of sport	Basic exercise*	Warming-up exercise Strength-training exercise		Light exercise or rhythmic movement to communicate with other students Basic movements (throwing, hitting, catching, kicking, jumping)		Exercise to improve flexibility, techniques, high-force movement, and endurance		Exercise with maximum endurance, speed, and muscle strength	
	Apparatus gymnastics	(mat, vaulting horse, horizontal bar, and balance beam)		Calisthenics, light mat exercise, balance exercise, light jumping		Practice of low-level technique, running start to perform holding, jumping and basic techniques (including rotation)		Performance, competition, combination of actions	
	Athletics	(racing, jumping, throwing)		Basic motion, standing broad jump, light throwing, light jumping (must avoid running)		Jogging, short run, and jumping		Long-distance running, sprint race, competition, time race	
	Swimming	(freestyle, breaststroke, backstroke, butterfly)		Easy movement in water (floating, prone floating, kicking and floating, etc.)		Slow swimming		Competition, swimming marathon, time race, start and turn	
	Ball sports	Goal games	Basketball	Slow exercise without running	Basic movements (e.g., passing, shooting, dribbling, feinting, lifting, trapping, throwing, kicking, and handling)	Training with footwork (with no close body contact)	Simple games using basic movements (adjust games according to the available time, space, and apparatus to practice collaborative playing, and offensive/defensive components)	Time race, applied practice, simplified game, game, competition	Competition
			Handball						
			Soccer						
			Rugby						
		Net games	Volleyball		Basic movements (e.g., passing, serving, receiving, tossing, feinting, stroking, and shooting)				
			Table tennis						
			Tennis						
			Badminton						
		Baseball-type games	Softball		Basic movements (e.g., pitching, catching, and batting)				
			Baseball						
		Golf			Basic movements (light swinging)		Practicing at a golf range		
	Martial arts	Judo, kendo, sumo wrestling		Greeting with bowing or squatting, basic movement (e.g., break fall in judo, practice swinging in kendo, handling in sumo wrestling)		Practicing simple techniques and forms with modest basic movements		Applied practice, competition	
	Dance	Original dance, folk dance, modern dance		Basic movement (e.g., hand gesture, steps, expressions)		Dancing with modest basic movements, etc.		Dance recitals, etc.	
	Outdoor activity	Play in the snow or on the ice, skiing, skating, camping, climbing, swimming marathon, waterfront activities		Playing on water, snow, or ice		Walking with ski plates or skates, slow skiing/skating, hiking on flatlands, playing in the water, etc.		Climbing, swimming marathon, diving, canoeing, boating, surfing, wind surfing, etc.	
Cultural activities				Cultural activities not requiring long-term physical tasks		Most cultural activities not described in the right column		Playing instruments requiring physical exertion (e.g., trumpet, trombone, oboe, bassoon, horn), playing or conducting quick rhythmical music, playing in a marching band	
School events and other activities				• Follow the above intensity of exercise during a sports festival, athletic meetings, ball sport competitions, and exercise tests. • Students other than those in category "E" should consult with the school physician or attending physicians in determining whether they can participate in other special school activities such as class trips, training camp, school trip, camp schools, and seaside schools.					

Remarks

Definitions
Mild exercise: Physical activities that do not cause panting for breath in average children of the same age.
Moderate exercise: Physical activities that may cause shortness of breath in average children of the same age, and that allow talking easily during exercise.
Intense exercise: Physical activities that cause shortness of breath in average children of the same age.

* Basic exercise: including resistance (isometric) exercise.

(Modified from The Japanese Society of School Health, 2013;[1339] *Circ J* 2014; **78:** 2521–2562. Epub 2014 Sep 22.)

TABLE 83 Driving restriction periods for patients with an ICD

ICD	Driving restriction period
New implantation (primary prevention)	7 days
New implantation (secondary prevention)	6 months
Post-appropriate therapy	3 months
Post-inappropriate therapy	No restriction if no loss of consciousness
Generator replacement	7 days
Lead replacement	7 days

Abbreviation: ICD, implantable cardioverter-defibrillator. (Modified from Watanabe et al, 2017.[1348])

1.2.2 | Problems caused by the work environment

Patients with a CIED encounter problems caused by the work environment, including physical and mental burden (eg, electromagnetic interference in the workplace and difficulties related to shift work), as well as occupational accidents caused by loss of consciousness due to ICD activation (when working in high places, handling dangerous materials, etc). An electromagnetic environmental survey of the workplace is required if there is a possibility of electromagnetic interference. In addition, patients must be instructed to avoid work that adds physical load to the CIED (especially transvenous leads), as much as possible.[1347]

1.2.3 | Workplace (employer) factors

Companies (employers) have an obligation to ensure worker safety (health) under the Industrial Safety and Health Law (Article 1) and the Labor Contracts Law (Article 5). The workplace should be arranged in line with the health status of the workers (including rearrangement of the workplace, if needed), in consultation with an industrial physician, and instructions should be provided for the required management to ensure overall safety.

1.2.4 | Psychosocial factors for patients

Workers with a CIED can experience anxiety about their own health and psychosocial problems related to their cardiac disability. These patients also need to regularly visit medical institutions after hospital discharge, which requires understanding from the workplace. The Handicapped Persons' Employment Promotion Act, which was designed to promote active social participation among persons with disabilities, has established a statutory employment rate of persons with disabilities for private companies and national/local governments with >45 employees (≥2.2% and ≥2.5%, respectively, from April 2018). Private companies that do not meet this target have payment penalties imposed.

The attending physician of a patient with a CIED who is working or is returning to work must share information with the industrial physician (health supervisor) at the company, and provide support for the patient with respect to balancing work and health (work support from the company or industrial physician and medical support from medical institutions).

2 | Catheter ablation

2.1 | Attending school after catheter ablation

Most pediatric patients have normal cardiac function without any structural heart disease after catheter ablation. With successful ablation treatment, there are generally no restrictions on school enrollment. However, determining whether patients with a structural heart disease (ie, dilated cardiomyopathy or hypertrophic cardiomyopathy) after surgery for congenital heart disease, or those who have undergone catheter ablation therapy for arrhythmia, can attend school depends on the degree of heart failure or the underlying disease. Some patients may have problems with cardiac function after a successful catheter ablation, and these patients may be able to attend school without problems. In patients with cyanotic heart diseases, catheter ablation is performed for tetralogy of Fallot, for complete transposition of the great arteries, and after the Fontan procedure. The ability to attend school depends on the severity of the underlying disorder or heart failure. Table 84 shows the school activity management guidance categories for such diseases.[1347]

Whether patients with cardiomyopathy that requires catheter ablation can attend school is determined by the severity of the underlying disease or heart failure. In many cases, it is possible to attend classes in school, with exercise restriction. Table 85 shows the school activity management guidance categories for the major cardiomyopathies.[1347]

2.2 | Working after catheter ablation

With respect to employment-related concerns after catheter ablation, recurrence cannot be ruled out in patients with life-threatening arrhythmia with low cardiac function or underlying heart disease; thus, it is desirable to handle each case based on the individual circumstances of the patient with an ICD. However, catheter ablation has a very high cure rate for many supraventricular tachyarrhythmias, including paroxysmal supraventricular tachycardia, as well as for premature ventricular contraction and VT without underlying heart disease, and the recurrence rate has been shown to be low. Therefore, after ablation in a patient with supraventricular arrhythmias or ventricular arrhythmia in whom cardiac function is maintained without underlying cardiac disease, there should be no impediment to employment other than in special occupations, provided there are no recurrent symptoms such as palpitations or syncope in subsequent follow-up, or any findings suggestive of recurrence based on various tests, including ECG. In addition, no special employment regulations are applied to patients who have undergone AF ablation surgery if there is no recurrence of AF during regular postoperative follow-up. However, in patients with certain types of occupations (those that could endanger human life, including that of others and self, or those involving special working environments), such as professional drivers of public transport vehicles, an arrhythmia attack may lead to serious (life-threatening) accidents. It is not always possible to judge whether a person is fit to work from a medical perspective alone,

TABLE 84 Conditions and management categories of exercise for patients with right-to-left shunt heart disease

Heart disease	Conditions	Management category
Tetralogy of Fallot	Asymptomatic; none or mild pulmonary valve regurgitation/tricuspid valve regurgitation; none to moderate right ventricular enlargement with intact right ventricular systolic function; normal or slightly increased right ventricular pressure; intact left ventricular systolic function; and no induction of tachyarrhythmia during exercise	E-allowed
	Asymptomatic but significant pulmonary valve regurgitation/tricuspid valve regurgitation/right ventricular enlargement; or significant right ventricular outflow tract stenosis with an increase in right ventricular pressure and a right/left systolic pressure ratio ≤ 50%; or tachyarrhythmia controlled with drug therapy or catheter ablation	D, E-prohibited, or E-allowed
	Symptomatic, mild to moderate decrease in exercise capacity, moderate or severe pulmonary valve regurgitation and right ventricular enlargement; moderate or severe right ventricular outflow tract stenosis with a right/left systolic pressure ratio ≥ 50% (≥70% if left ventricular dysfunction is present); or exercise-induced tachyarrhythmia not controllable with any treatment	C or D
Complete transposition of the great arteries	Asymptomatic, good exercise capacity, no residual abnormality with good right and left ventricular function, and no induction of tachycardia during exercise	E-allowed
	Asymptomatic, mild residual abnormality (eg, small ventricular septal defect, mild stenosis/regurgitation of new aortic/pulmonary valves, or mild arrhythmia such as isolated extrasystoles), and no abnormal ECG findings during exercise	E-prohibited or E-allowed
	Significant residual abnormality (right ventricular outflow tract stenosis ≥ 30 mmHg, significant regurgitation of new aortic valves), significant left/right ventricular hypertrophy, left/right ventricular dysfunction, or tachyarrhythmia	D or E-prohibited
	Moderate or severe right ventricular outflow tract/pulmonary artery stenosis with a right/left ventricular systolic pressure ratio of ≥ 50%, moderate or severe new aortic valve regurgitation, or induction of tachyarrhythmia or ST depression during exercise ECG	B, C or D
Functional single ventricle (after the Fontan procedure)	The patient should be assessed comprehensively for arrhythmia, ventricular function, valve function, oxygen saturation and exercise capacity, and should be allowed to participate in daily physical activities and physical education to a certain extent, under circumstances where the patient can take a rest whenever necessary	B, C, D or E-prohibited, in some cases E-allowed (adjust intensity individually)

From JCS guideline, 2013.[1347]

[Correction added on 29 June, after first online publication: 'C-prohibited or D-prohibited' and 'B, C or D-prohibited' under 'Management category' have been amended to 'C or D' and 'B, C or D' respectively.]

TABLE 85 Conditions and management categories of exercise for patients with cardiomyopathies

Heart disease	Conditions	Management category
Hypertrophic cardiomyopathy	Asymptomatic	D
	Those with chest pain, syncope or other symptoms, and those with obstructive cardiomyopathy	B or C
	High-risk children	A, B or C
Dilated cardiomyopathy	Asymptomatic	D
	Symptomatic	C
Arrhythmogenic right ventricular cardiomyopathy	Exercise is contraindicated	C

From JCS guideline, 2013.[1347]

even after catheter ablation for arrhythmias with a high cure rate. Therefore, cases should be handled on an individual basis, taking into account the opinion of industrial physicians and other authorities. In Japan, proper placement of drivers of public transport vehicles (such as pilots and train drivers) may be determined in accordance with laws and regulations. Therefore, it is essential to ask patients about their specific occupation before surgery.[1342,1347] Careful consideration should also be given to preventive ablation therapy for asymptomatic WPW syndrome on ECG, as it may affect subsequent employment in some cases.

REFERENCES

1. Tsutsui H, Isobe M, Ito H, Okumura K, Ono M, Kitakaze M, et al. Japanese Circulation Society and the Japanese Heart Failure Society Joint Working Group. JCS 2017/JHFS 2017 Guideline on diagnosis and treatment of acute and chronic heart failure: Digest version. Circ J. 2019;83:2084–184.
2. Japanese Circulation Society Joint Working Group. Guidelines for diagnosis and management of inherited arrhythmias (JCS 2017) [in Japanese]. http://www.j-circ.or.jp/guideline/pdf/JCS2017_aonuma_h.pdf (Accessed Nov. 2018)
3. Japanese Circulation Society Joint Working Group. Guidelines for pharmacotherapy of atrial fibrillation (JCS 2013) [in Japanese]. http://www.j-circ.or.jp/guideline/pdf/JCS2013_inoue_h.pdf (Accessed Nov. 2018).
4. Japan Resuscitation Council. JCR guidelines for resuscitation 2015 [in Japanese]. http://www.japanresuscitationcouncil.org/

wp-content/uploads/2016/04/0e5445d84c8c2a31aaa17db0a9c67b76.pdf (Accessed Nov. 2018)
5. Japan Arrhythmia Device Industry Association home page [in Japanese]. https://www.jadia.or.jp/ (Accessed Nov. 2018)
6. The Japanese Circulation Society. Japanese registry of all cardiac and vascular diseases (JROAD) survey report [in Japanese]. http://www.j-circ.or.jp/jittai_chosa/jittai_chosa2017web.pdf (Accessed Nov. 2018)
7. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, et al. AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. Circulation. 2014;2014(130):e199–e267.
8. Mind Treatment Guideline Selection Committee. Minds handbook for clinical practice guideline development, Fukui T, Yoshida M, Yamaguchi N, editors. Tokyo: Igaku-Shoin; 2007. [in Japanese].
9. Statement for clinical use of leadless intracardiac transcatheter pacing system (Micra®). Scientific Statement from Japanese Heart Rhythm Society (published on September 1, 2017) [in Japanese]. http://new.jhrs.or.jp/guideline/statement201709_01/ (Accessed Nov. 2018)
10. Deleted in proof.
11. Statement for implantation of subcutaneous intracardiac cardioverter defibrillator system. Scientific Statement from Japanese Heart Rhythm Society (published on January 22, 2016) [in Japanese]. http://new.jhrs.or.jp/guideline/s-icd20160122/ (Accessed Nov. 2018)
12. Statement for clinical use of wearable cardioverter defibrillator. Scientific Statement from Japanese Heart Rhythm Society (published on September 2, 2017) [in Japanese]. http://new.jhrs.or.jp/pdf/guideline/statement201709_02 (Accessed Nov. 2018)
13. Stokes KB, Kay GN. Artificial electric cardiac stimulation. In: Ellenbogen KA, Kay GN, Wilkoff BL. Clinical Cardiac Pacing. 1st edn. WB Saunders;1995:3–37.
14. Huang TY, Baba N. Cardiac pathology of transvenous pacemakers. Am Heart J. 1972;83:469–74.
15. Pauletti M, Pingitore R, Contini C. Superior vena cava stenosis at site of intersection of two pacing electrodes. Br Heart J. 1979;42:487–9.
16. Gould L, Reddy CV, Yacob U, Teich M, DeMartino A, DePalma D, et al. Perforation of the tricuspid valve by a transvenous pacemaker. JAMA. 1974;230:86–7.
17. Cairns KB, Kloster FE, Bristow JD, Lees MH, Griswold HE. Problems in the hemodynamic diagnosis of tricuspid insufficiency. Am Heart J. 1968;75:173–9.
18. Zager J, Berberich SN, Eslava R, Klieman C. Dynamic tricuspid valve insufficiency produced by a right ventricular thrombus from a pacemaker. Chest. 1978;74:455–6.
19. Padfield GJ, Steinberg C, Bennett MT, Chakrabarti S, Deyell MW, Bashir J, et al. Preventing cardiac implantable electronic device infections. Heart Rhythm. 2015;12:2344–56.
20. Polyzos KA, Konstantelias AA, Falagas ME. Risk factors for cardiac implantable electronic device infection: A systematic review and meta-analysis. Europace. 2015;17:767–77.
21. Greenspon AJ, Patel JD, Lau E, Ochoa JA, Frisch DR, Ho RT, et al. 16-year trends in the infection burden for pacemakers and implantable cardioverter-defibrillators in the United States 1993 to 2008. J Am Coll Cardiol. 2011;58:1001–6.
22. Howard JL, Hanssen AD. Principles of a clean operating room environment. J Arthroplasty. 2007;22:6–11.
23. Healthcare Engineering Association of Japan. Hospital facilities design guideline (air conditioning equipment edition) HEAS-02-2013 [in Japanese].
24. Korniewicz DM, Rabussay DP. Surgical glove failures in clinical practice settings. AORN J. 1997;66:660–73.
25. Makama JG, Okeme IM, Makama EJ, Ameh EA. Glove perforation rate in surgery: a randomized, controlled study to evaluate the efficacy of double gloving. Surg Infect (Larchmt). 2016;17:436–42.
26. Advisory Committee of Clinical Practice Guidelines for antimicrobial prophylaxis in surgery: Japanese Clinical Practice Guidelines for antimicrobial prophylaxis in surgery. J Jpn Soc Surg Infect. 2016;13:79–158. [in Japanese].
27. Baddour LM, Epstein AE, Erickson CC, Knight BP, Levison ME, Lockhart PB, et al. Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, Council on Cardiovascular Surgery and Anesthesia, Council on Cardiovascular Nursing, Council on Clinical Cardiology; and the Interdisciplinary Council on Quality of Care and Outcomes Research. Update on cardiovascular implantable electronic device infections and their management: A scientific statement from the American Heart Association. Circulation. 2010;121:458–77.
28. Ellenbogen KA, Hellkamp AS, Wilkoff BL, Camunãs JL, Love JC, Hadji TA, et al. Complications arising after implantation of DDD pacemakers: The MOST experience. Am J Cardiol. 2003;92:740–1.
29. Udo EO, Zuithoff NP, van Hemel NM, de Cock CC, Hendriks T, Doevendans PA, et al. Incidence and predictors of short- and long-term complications in pacemaker therapy: The FOLLOWPACE study. Heart Rhythm. 2012;9:728–35.
30. Ramza BM, Rosenthal L, Hui R, Nsah E, Savader S, Lawrence JH, et al. Safety and effectiveness of placement of pacemaker and defibrillator leads in the axillary vein guided by contrast venography. Am J Cardiol. 1997;80:892–6.
31. Jones DG, Stiles MK, Stewart JT, Armstrong GP. Ultrasound-guided venous access for permanent pacemaker leads. Pacing Clin Electrophysiol. 2006;29:852–7.
32. Magney JE, Staplin DH, Flynn DM, Hunter DW. A new approach to percutaneous subclavian venipuncture to avoid lead fracture or central venous catheter occlusion. Pacing Clin Electrophysiol. 1993;16:2133–42.
33. Tang M, Chen KP, Wang FZ, Hua W, Zhang S. Clinical study on 29 pacemaker and defibrillator lead fractures. Zhonghua Xin Xue Guan Bing Za Zhi. 2005;33:912–5. [in Chinese].
34. Antonelli D, Rosenfeld T, Freedberg NA, Palma E, Gross JN, Furman S. Insulation lead failure: is it a matter of insulation coating, venous approach, or both? Pacing Clin Electrophysiol. 1998;21:418–21.
35. Klug D, Balde M, Pavin D, Hidden-Lucet F, Clémenty J, Sadoul N, et al. PEOPLE Study Group. Risk factors related to infections of implanted pacemakers and cardioverter-defibrillators: Results of a large prospective study. Circulation. 2007;116:1349–55.
36. Rohacek M, Baddour LM. Cardiovascular implantable electronic device infections: Associated risk factors and prevention. Swiss Med Wkly. 2015;145:w14157.
37. Japanese Heart Rhythm Society. Cautions for daily life in patients with pacemaker or implantable cardioverter defibrillator (ICD) [in Japanese]. https://www.jadia.or.jp/images/poster/wide/2011.pdf (Accessed Nov. 2018)
38. Varma N, Epstein AE, Irimpen A, Schweikert R, Love C, TRUST Investigators. Efficacy and safety of automatic remote monitoring for implantable cardioverter-defibrillator follow-up: The Lumos-T Safely Reduces Routine Office Device Follow-up (TRUST) trial. Circulation. 2010;122:325–32.
39. Watanabe E, Kasai A, Fujii E, Yamashiro K, Brugada P. Reliability of implantable cardioverter defibrillator home monitoring in forecasting the need for regular office visits, and patient perspective: Japanese HOME-ICD study. Circ J. 2013;77:2704–11.
40. Guedon-Moreau L, Lacroix D, Sadoul N, Clémenty J, Kouakam C, Hermida JS, et al.; ECOST trial Investigators. A randomized study of remote follow-up of implantable cardioverter defibrillators: safety and efficacy report of the ECOST trial. Eur Heart J. 2013;34:605–14.

41. Parthiban N, Esterman A, Mahajan R, Twomey DJ, Pathak RK, Lau DH, et al. Remote monitoring of implantable cardioverter-defibrillators: a systematic review and meta-analysis of clinical outcomes. J Am Coll Cardiol. 2015;65:2591–600.
42. Landolina M, Perego GB, Lunati M, Curnis A, Guenzati G, Vicentini A, et al. Remote monitoring reduces healthcare use and improves quality of care in heart failure patients with implantable defibrillators: the evolution of management strategies of heart failure patients with implantable defibrillators (EVOLVO) study. Circulation. 2012;125:2985–92.
43. Crossley GH, Boyle A, Vitense H, Chang Y, Mead RH, CONNECT Investigators. The CONNECT (Clinical Evaluation of Remote Notification to Reduce Time to Clinical Decision) trial: The value of wireless remote monitoring with automatic clinician alerts. J Am Coll Cardiol. 2011;57:1181–9.
44. Saxon LA, Hayes DL, Gilliam FR, Heidenreich PA, Day J, Seth M, et al. Long-term outcome after ICD and CRT implantation and influence of remote device follow-up: The ALTITUDE survival study. Circulation. 2010;122:2359–67.
45. Hindricks G, Taborsky M, Glikson M, Heinrich U, Schumacher B, Katz A, et al. IN-TIME study group. Implant-based multiparameter telemonitoring of patients with heart failure (IN-TIME): a randomised controlled trial. Lancet. 2014;384:583–90.
46. Japan Arrhythmia Device Industry Association. Information disclosure site for MRI use in the patients with arrhythmia devices [in Japanese]. http://cieds-mri.com/jadia/public/ (Accessed Nov. 2018).
47. Slotwiner D, Varma N, Akar JG, Annas G, Beardsall M, GFogel RI, et al. HRS Expert Consensus Statement on remote interrogation and monitoring for cardiovascular implantable electronic devices. Heart Rhythm. 2015;12:e69–e100.
48. Hayes DL, Holmes DR, Gray JE. Effect of 1.5 tesla nuclear magnetic resonance imaging scanner on implanted permanent pacemakers. J Am Coll Cardiol. 1987;10:782–6.
49. Nazarian S, Roguin A, Zviman MM, Lardo AC, Dickfeld TL, Calkins H, et al. Clinical utility and safety of a protocol for noncardiac and cardiac magnetic resonance imaging of patients with permanent pacemakers and implantable-cardioverter defibrillators at 1.5 tesla. Circulation. 2006;114:1277–84.
50. Nazarian S, Hansford R, Rahsepar AA, Weltin V, McVeigh D, Gucuk Ipek E, et al. Safety of magnetic resonance imaging in patients with cardiac devices. N Engl J Med. 2017;377:2555–64.
51. Russo RJ, Costa HS, Silva PD, Anderson JL, Arshad A, Biederman RWW, et al. Assessing the risks associated with MRI in patients with a pacemaker or defibrillator. N Engl J Med. 2017;376:755–64.
52. Mandel WJ, Hayakawa H, Allen HN, Danzig R, Kermaier AI. Assessment of sinus node function in patients with the sick sinus syndrome. Circulation. 1972;46:761–9.
53. Jordan JL, Yamaguchi I, Mandel WJ. Studies on the mechanism of sinus node dysfunction in the sick sinus syndrome. Circulation. 1978;57:217–23.
54. Kasanuki H. Electrophysiological and clinical study of sick sinus syndrome using the overdrive suppression test. Jpn Circ J. 1980;44:505–17.
55. Yagi H, Suzuki H, Sugino K, et al. Clinical significance of overdrive suppression on sinus node automaticity and sino-atrial conduction, and influence of autonomic nervous system on overdrive suppression: Evaluation by sinus node electrograms. Jpn J Electrocardiol. 1996;16:360–8. [in Japanese].
56. Narula OS, Scherlag BJ, Javier RP, Hildner FJ, Samet P. Analysis of the A-V conduction defect in complete heart block utilizing His bundle electrograms. Circulation. 1970;41:437–48.
57. Endo M, Kasanuki H, Ohnishi S, et al. Clinical, electrophysiological and long-term follow-up studies in patients with His bundle block. Kokyu to Junkan. 1986;34:43–9. [in Japanese].
58. Nakazato Y, Nakata Y. Electrophysiological studies in advanced and complete atrioventricular block. Jpn J Cardiac Pacing Electrophysiol. 1987;3:355–63. [in Japanese].
59. Moya A, Garcia-Civera R, Croci F, Menozzi C, Brugada J, Ammirati F, et al. Bradycardia detection in Bundle Branch Block (B4) study: Diagnosis, management, and outcomes of patients with syncope and bundle branch block. Eur Heart J. 2011;32:1535–41.
60. Shen WK, Sheldon RS, Benditt DG, Cohen MI, Forman DE, Goldberger ZD, et al. 2017 ACC/AHA/HRS guideline for the evaluation and management of patients with syncope: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Circulation. 2017;136:e60–e122 (erratum in Circulation 2017; 136: e271–e272).
61. Krahn AD, Klein GJ, Yee R, Skanes AC. Randomized assessment of syncope trial: Conventional diagnostic testing versus a prolonged monitoring strategy. Circulation. 2001;104:46–51.
62. Fujimura O, Yee R, Klein GJ, Sharma AD, Boahene KA. The diagnostic sensitivity of electrophysiologic testing in patients with syncope caused by transient bradycardia. N Engl J Med. 1989;321:1703–7.
63. Moya A, Sutton R, Ammirati F, Blanc JJ, Brignole M, Dahm JB, et al. European Heart Rhythm Association, Heart Failure Association, Heart Rhythm Society. Guidelines for the diagnosis and management of syncope (version 2009): The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC). Eur Heart J. 2009;30:2631–71.
64. Englund A, Bergfeldt L, Rosenqvist M. Pharmacological stress testing of the His-Purkinje system in patients with bifascicular block. Pacing Clin Electrophysiol. 1998;21:1979–87.
65. Scheinman MM, Weiss AN, Shafton E, Benowitz N, Rowland M. Electrophysiologic effects of procaine amide in patients with intraventricular conduction delay. Circulation. 1974;49:522–9.
66. Hirao K, Otomo K, Wang X, Beckman KJ, McClelland JH, et al. Para-Hisian pacing: a new method for differentiating retrograde conduction over an accessory AV pathway from conduction over the AV node. Circulation. 1996;94:1027–35.
67. Takahashi A, Iesaka Y, Igawa M, Tokunaga T, Amemiya H, Fujiwara H, et al. Atrioventricular nodal physiology after slow pathway ablation. Pacing Clin Electrophysiol. 1994;17:2137–42.
68. Nogami A, Suguta M, Tomita T, Naito S, Taniguchi K, Aonuma K, et al. Novel form of atrial tachycardia originating at the atrioventricular annulus. Pacing Clin Electrophysiol. 1998;21:2691–4.
69. Kasanuki H, Ohnishi S, Tanaka E, Hirosawa K. Idiopathic sustained ventricular tachycardia responsive to verapamil: clinical electrocardiographic and electrophysiologic considerations. Jpn Circ J. 1986;50:109–18.
70. Onishi T, Kasanuki H, Shoda M, et al. Slow conduction in ventricular tachycardia. In: Sugimoto T, editor. Cardiac arrhythmia. Tokyo: Nankodo; 1992. p. 311–20. [in Japanese].
71. Tamashita T. Electrophysiologic study. In: Inoue H, Okumura K, editors. Electrophysiologic study, 2nd edn. Tokyo: Igaku-Shoin; 2002. p. 39–82. [in Japanese].
72. Chinushi M, Aizawa Y, Ohhira K, Abe A, Shibata A. Long-term results of radiofrequency catheter ablation in non-ischemic sustained ventricular tachycardia with underlying heart disease: Nonuniform arrhythmogenic substrate and mode of ablation. Jpn Heart J. 1996;37:183–94.
73. Suyama K, Kurita T, Shimizu W, Matsuo K, Taguchi A, Aihara N, et al. Radiofrequency catheter ablation of concealed atrioventricular accessory pathways using a “simultaneous pacing method”. Pacing Clin Electrophysiol. 1998;21:1693–9.
74. Satoh M, Aizawa Y, Funazaki T, Niwano S, Ebe K, Miyajima S, et al. Electrophysiologic evaluation of asymptomatic patients with

the Wolff-Parkinson-White pattern. Pacing Clin Electrophysiol. 1989;12:413–20.
75. Kasanuki H, Ohnishi S, Hirosawa K. Availability of electrophysiological approach to the selection and assessment of antiarrhythmic drugs for recurrent ventricular tachycardia. Jpn Circ J. 1983;47:105–23.
76. Kasanuki H, Onishi S, Hirosawa K. The usefulness of electrophysiological-pharmacologic studies in the long-term therapy of paroxysmal tachycardias. Jpn Circ J. 1985;49:351–61.
77. Ebe K, Aizawa Y, Shibata A. Clinical characteristics and EPS guided therapy in 142 cases of sustained ventricular tachycardia. Jpn Heart J. 1996;37:73–84.
78. Niwano S, Furushima H, Taneda K, Abe A, Ohira K, Aizawa Y. The usefulness of Holter monitoring in selecting pharmacologic therapy for patients with sustained monomorphic ventricular tachycardia: Studies in patients in whom no effective pharmacologic therapy could be determined by electrophysiologic study. Jpn Circ J. 1998;62:347–52.
79. Mason JW, Electrophysiologic Study versus Electrocardiographic Monitoring Investigators. A comparison of seven antiarrhythmic drugs in patients with ventricular tachyarrhythmias. N Engl J Med. 1993;329:452–8.
80. Niwano S, Yamaura M, Yoshizawa N, Moriguchi M, Kitano Y, Aizawa Y, et al. Electrophysiologic parameters to predict clinical recurrence of ventricular tachycardia in patients under electrophysiologic study-guided effective pharmacological therapy. Jpn Circ J. 1999;63:674–80.
81. Aiba T, Yamagata K, Shimizu W, Taguchi A, Satomi K, Noda T, et al. Electrophysiologic study-guided amiodarone for sustained ventricular tachyarrhythmias associated with structural heart diseases. Circ J. 2008;72:88–93.
82. Kasanuki H, Ohnishi S, Nirei T, Shoda M, Hosoda S. Evaluation of proarrhythmic effect of antiarrhythmic drugs on ventricular tachycardia associated with congestive heart failure. Jpn Circ J. 1992;56:69–76.
83. Chinushi M, Aizawa Y, Miyajima S, Funazaki T, Tamura M, Shibata A. Proarrhythmic effects of antiarrhythmic drugs assessed by electrophysiologic study in recurrent sustained ventricular tachycardia. Jpn Circ J. 1991;55:133–41.
84. Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. N Engl J Med. 1997;337:1576–83.
85. Iesaka Y, Nogami A, Aonuma K, Nitta J, Fujiwara H, Hiraoka M. Prognostic significance of sustained monomorphic ventricular tachycardia induced by programmed ventricular stimulation using up to triple extrastimuli in survivors of acute myocardial infarction. Am J Cardiol. 1990;65:1057–63.
86. Miyajima S, Aizawa Y, Suzuki K, Satoh M, Niwano S, Ebe K, et al. Sustained ventricular tachycardia responsive to verapamil in patients with hypertrophic cardiomyopathy: Clinical and electrophysiological assessment of drug efficacy. Jpn Heart J. 1989;30:241–9.
87. Iesaka Y, Hiroe M, Aonuma K, Nitta J, Nogami A, Tokunaga T, et al. Usefulness of electrophysiologic study and endomyocardial biopsy in differentiating arrhythmogenic right ventricular dysplasia from idiopathic right ventricular tachycardia. Heart Vessels Suppl. 1990;5:65–9.
88. Takahashi M, Kimura M, Kobayashi I, Aizawa Y, Shibata A. Clinical value of electrophysiologic study in patients with nonsustained ventricular tachycardia. Jpn Heart J. 1994;35:141–51.
89. Josephson ME. Electrophysiologic investigation. In Clinical cardiac electrophysiology, 2nd edn. Philadelphia: Lea & Febiger; 1993. p. 5–70.
90. Deleted in proof.
91. Tohei Y, Nakazawa K, Ozawa A, et al. Epidemiology of electrocardiogram with right bundle branch block and ST elevation. Jpn J Electrocardiol. 1995;15:223–6. [in Japanese].
92. Fujimori K, Hen Y, Hirata N, et al. Incidence of asymptomatic Brugada syndrome among middle to high aged subjects: An exhaustive investigation of local residents in Miyagi Prefecture. Jpn Circ J. 2001;65(Suppl):504.
93. Atarashi H, Ogawa S, Harumi K, Hayakawa H, Sugimoto T, Okada R, et al.; Idiopathic Ventricular Fibrillation Investigators. Characteristics of patients with right bundle branch block and ST-segment elevation in right precordial leads. Am J Cardiol. 1996;78:581–3.
94. Aizawa Y, Naitoh N, Washizuka T, Takahashi K, Uchiyama H, Shiba M, et al. Electrophysiological findings in idiopathic recurrent ventricular fibrillation: special reference to mode of induction, drug testing, and long-term outcomes. Pacing Clin Electrophysiol. 1996;19:929–39.
95. Brugada J, Brugada R, Antzelevitch C, Towbin J, Nademanee K, Brugada P. Long-term follow-up of individuals with the electrocardiographic pattern of right bundle branch block and ST-segment elevation in precordial leads V1 to V3. Circulation. 2002;105:73–8.
96. Brugada P, Brugada R, Brugada J. Should patients with an asymptomatic Brugada electrocardiogram undergo pharmacological and electrophysiological testing? Circulation. 2005;112:279–92.
97. Delise P, Allocca G, Marras E, Giustetto C, Gaita F, Sciarra L, et al. Risk stratification in individuals with the Brugada type 1 ECG pattern without previous cardiac arrest: Usefulness of a combined clinical and electrophysiologic approach. Eur Heart J. 2011;32:169–76.
98. Okamura H, Kamakura T, Morita H, Tokioka K, Nakajima I, Wada M, et al. Risk stratification in patients with Brugada syndrome without previous cardiac arrest: prognostic value of combined risk factors. Circ J. 2015;79:310–7.
99. Conte G, Sieira J, Ciconte G, de Asmundis C, Chierchia GB, Baltogiannis G, et al. Implantable cardioverter-defibrillator therapy in Brugada syndrome: A 20-year single-center experience. J Am Coll Cardiol. 2015;65:879–88.
100. Sieira J, Conte G, Ciconte G, de Asmundis C, Chierchia GB, Baltogiannis G, et al. Prognostic value of programmed electrical stimulation in Brugada syndrome: 20 years experience. Circ Arrhythm Electrophysiol. 2015;8:777–84.
101. Makimoto H, Kamakura S, Aihara N, Noda T, Nakajima I, Yokoyama T, et al. Clinical impact of the number of extrastimuli in programmed electrical stimulation in patients with Brugada type 1 electrocardiogram. Heart Rhythm. 2012;9:242–8.
102. Sroubek J, Probst V, Mazzanti A, Delise P, Hevia JC, Ohkubo K, et al. Programmed ventricular stimulation for risk stratification in the brugada syndrome: a pooled analysis. Circulation. 2016;133:622–30.
103. Takagi M, Sekiguchi Y, Yokoyama Y, Aihara N, Hiraoka M, Aonuma K, et al. The prognostic impact of single extra-stimulus on programmed ventricular stimulation in Brugada patients without previous cardiac arrest: Multi-centre study in Japan. Europace. 2018;20:1194–200.
104. Probst V, Veltmann C, Eckardt L, Meregalli PG, Gaita F, Tan HL, et al. Long-term prognosis of patients diagnosed with Brugada syndrome: results from the FINGER Brugada Syndrome Registry. Circulation. 2010;121:635–43.
105. Kamakura S, Ohe T, Nakazawa K, Aizawa Y, Shimizu A, Horie M, et al; Brugada Syndrome Investigators in Japan. Long-term prognosis of probands with Brugada pattern ST-elevation in leads V1–V3. Circ Arrhythm Electrophysiol. 2009;2:495–503.
106. Priori SG, Gasparini M, Napolitano C, Della Bella P, Ottonelli AG, Sassone B, et al. Risk stratification in Brugada syndrome: results

of the PRELUDE (Programmed ELectrical stimUlation preDictive valuE) registry. J Am Coll Cardiol. 2012;59:37–45.
107. Takagi M, Yokoyama Y, Aonuma K, Aihara N, Hiraoka M, Japan Idiopathic Ventricular Fibrillation Study (J-IVFS) Investigators. Clinical characteristics and risk stratification in symptomatic and asymptomatic patients with brugada syndrome: Multicenter study in Japan. J Cardiovasc Electrophysiol. 2007;18:1244–51.
108. Roguin A, Zviman MM, Meininger GR, Rodrigues ER, Dickfeld TM, Bluemke DA, et al. Modern pacemaker and implantable cardioverter/defibrillator systems can be magnetic resonance imaging safe: In vitro and in vivo assessment of safety and function at 1.5 T. Circulation. 2004;110:475–82.
109. Reddy VY, Knops RE, Sperzel J, Miller MA, Petru J, Simon J, et al. Permanent leadless cardiac pacing: results of the LEADLESS trial. Circulation. 2014;129:1466–71.
110. Kimura K, Kimura T, Ishihara M, Nakagawa Y, Nakao K, Miyauchi K, et al. Japanese Circulation Society Joint Working Group. JCS 2018 guideline on diagnosis and treatment of acute coronary syndrome. Circ J. 2019;83:1085–196 [in Japanese].
111. Tokano T, Nakata Y, Yasuda M, et al. Clinical electrophysiologic study of Wenckebach type atrio-ventricular block in His-Purkinje conduction system. Electrocardiology. 1996;16:1–14. [in Japanese].
112. Sumiyoshi M, Nakata Y, Yasuda M, Tokano T, Ohno Y, Ogura S, et al. Changes of conductivity in patients with second- or third-degree atrioventricular block after pacemaker implantation. Jpn Circ J. 1995;59:284–91.
113. Nakazato Y, Nakata Y, Tokano T, Yasuda M, Ohno Y, Hisaoka T, et al. Intra-His bundle block corresponds with interruption of the branching portion of the His bundle. Pacing Clin Electrophysiol. 1994;17:1124–33.
114. Glikson M, Dearani JA, Hyberger LK, Schaff HV, Hammill SC, Hayes DL. Indications, effectiveness, and long-term dependency in permanent pacing after cardiac surgery. Am J Cardiol. 1997;80:1309–13.
115. Langberg JJ, Chin MC, Rosenqvist M, Cockrell J, Dullet N, Van Hare G, et al. Catheter ablation of the atrioventricular junction with radiofrequency energy. Circulation. 1989;80:1527–35.
116. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA 3rd, Freedman RA, Gettes LS, et al. 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2013;61:e6–e75.
117. Strasberg B, Amat-Y-Leon F, Dhingra RC, Palileo E, Swiryn S, Bauernfeind R, et al. Natural history of chronic second-degree atrioventricular nodal block. Circulation. 1981;63:1043–9.
118. Ector H, Rolies L, De Geest H. Dynamic electrocardiography and ventricular pauses of 3 seconds and more: etiology and therapeutic implications. Pacing Clin Electrophysiol. 1983;6:548–51.
119. Fukatani M, Hashiba K. Long-term follow-up after cardiac pacing in bradyarrhythmias. Jpn Circ J. 1978;42:257–68.
120. Yanaga T, Otsuka K, Ichimaru Y, Hata Y, Okamoto K, Nakanishi H, et al. Usefulness of 24-hour recordings of electrocardiogram for the diagnosis and treatment of arrhythmias with special reference to the determination of indication of artificial cardiac pacing. Jpn Circ J. 1981;45:366–75.
121. Sumiyoshi M. Clinical, electrophysiologic and pathological study of intra-His atrio-ventricular block. Juntendo Med J. 1988;34:344–56. [in Japanese].
122. Tokano T, Nakata Y, Yasuda M, et al. Induction of atrio-ventricular block by transvenous administration of class Ia anti-arrhythmic agents on paroxysmal atrio-ventricular block. Shinzo. 1997;29:193–204. [in Japanese].
123. Nakata Y. Clinical and electrophysiologic study of brady arrhythmias. Electrocardiology. 1982;2(Suppl):111–5. [in Japanese].
124. Levine S, Miller H, Penton GB. Some clinical features of complete heart block. Circulation. 1956;13:801–24.
125. McAnulty JH, Rahimtoola SH, Murphy E, DeMots H, Ritzmann L, Kanarek PE, et al. Natural history of high-risk bundle-branch block: final report of a prospective study. N Engl J Med. 1982;307:137–43.
126. Scheinman MM, Peters RW, Suave MJ, Desai J, Abbott JA, Cogan J, et al. Value of the H-Q interval in patients with bundle branch block and the role of prophylactic permanent pacing. Am J Cardiol. 1982;50:1316–22.
127. Dhingra RC, Wyndham C, Bauernfeind R, Swiryn S, Deedwania PC, Smith T, et al. Significance of block distal to the His bundle induced by atrial pacing in patients with chronic bifascicular block. Circulation. 1979;60:1455–64.
128. Josephson ME. Clinical cardiac electrophysiology: Techniques and interpretations, 2nd edn. Philadelphia: Lea & Febiger; 1993. p. 145.
129. Shaw DB, Holman RR, Gowers JI. Survival in sinoatrial disorder (sick-sinus syndrome). BMJ. 1980;280:139–41.
130. Kay R, Estioko M, Wiener I. Primary sick sinus syndrome as an indication for chronic pacemaker therapy in young adults: incidence, clinical features, and long-term evaluation. Am Heart J. 1982;103:338–42.
131. Kusumoto FM, Goldschlager N. Cardiac pacing. N Engl J Med. 1996;334:89–97.
132. Dreifus LS, Michelson EL, Kaplinsky E. Bradyarrhythmias: Clinical significance and management. J Am Coll Cardiol. 1983;1:327–38.
133. Rasmussen K. Chronic sinus node disease: Natural course and indications for pacing. Eur Heart J. 1981;2:455–9.
134. Rubenstein JJ, Schulman CL, Yurchak PM, DeSanctis RW. Clinical spectrum of the sick sinus syndrome. Circulation. 1972;46:5–13.
135. Phibbs B, Friedman HS, Graboys TB, Lown B, Marriott HJ, Nelson WP, et al. Indications for pacing in the treatment of bradyarrhythmias: report of an independent study group. JAMA. 1984;252:1307–11.
136. Ishikawa T, Sumita S, Kimura K, Kikuchi M, Kosuge M, Endo T, et al. Sinus node recovery time assessment by the overdrive suppression test employing an intravenous injection of disopyramide phosphate. Europace. 2000;2:54–9.
137. Pitcher D, Papouchado M, James MA, Rees JR. Twenty-four hour ambulatory electrocardiography in patients with chronic atrial fibrillation. Br Med J (Clin Res Ed). 1986;292:594.
138. Pollak A, Falk RH. Pacemaker therapy in patients with atrial fibrillation. Am Heart J. 1993;125:824–30.
139. Sutton R, Brignole M, Menozzi C, Raviele A, Alboni P, Giani P, et al.; Vasovagal Syncope International Study (VASIS) Investigators. Dual-chamber pacing in the treatment of neurally mediated tilt-positive cardioinhibitory syncope: Pacemaker versus no therapy: a multicenter randomized study. Circulation. 2000;102:294–9.
140. Ammirati F, Colivicchi F, Santini M; Syncope Diagnosis and Treatment Study Investigators. Permanent cardiac pacing versus medical treatment for the prevention of recurrent vasovagal syncope: a multicenter, randomized, controlled trial. Circulation. 2001;104:52–7.
141. Connolly SJ, Sheldon R, Roberts RS, Gent M. The North American Vasovagal Pacemaker Study (VPS): a randomized trial of permanent cardiac pacing for the prevention of vasovagal syncope. J Am Coll Cardiol. 1999;33:16–20.
142. Connolly SJ, Sheldon R, Thorpe KE, Roberts RS, Ellenbogen KA, Wilkoff BL, et al.; VPS II Investigators. Pacemaker therapy for prevention of syncope in patients with recurrent severe vasovagal syncope: Second Vasovagal Pacemaker Study (VPS II): A randomized trial. JAMA. 2003;289:2224–9.

143. Raviele A, Giada F, Menozzi C, Speca G, Orazi S, Gasparini G, et al.; Vasovagal Syncope and Pacing Trial Investigators. A randomized, double-blind, placebo-controlled study of permanent cardiac pacing for the treatment of recurrent tilt-induced vasovagal syncope: The vasovagal syncope and pacing trial (SYNPACE). Eur Heart J. 2004;25:1741–8.
144. Sud S, Massel D, Klein GJ, Leong-Sit P, Yee R, Skanes AC, et al. The expectation effect and cardiac pacing for refractory vasovagal syncope. Am J Med. 2007;120:54–62.
145. Brignole M, Donateo P, Tomaino M, Massa R, Iori M, Beiras X, et al.; International Study on Syncope of Uncertain Etiology 3 (ISSUE-3) Investigators. Benefit of pacemaker therapy in patients with presumed neurally mediated syncope and documented asystole is greater when tilt test is negative: an analysis from the third International Study on Syncope of Uncertain Etiology (ISSUE-3). Circ Arrhythm Electrophysiol. 2014;7:10–6.
146. Brignole M, Moya A, de Lange FJ, Deharo JC, Elliott PM, Fanciulli A, et al. ESC Scientific Document Group. 2018 ESC guidelines for the diagnosis and management of syncope. Eur Heart J. 2018;39:1883–948.
147. Kerr SR, Pearce MS, Brayne C, Davis RJ, Kenny RA. Carotid sinus hypersensitivity in asymptomatic older persons: implications for diagnosis of syncope and falls. Arch Intern Med. 2006;166:515–20.
148. Brignole M, Menozzi C, Lolli G, Bottoni N, Gaggioli G. Long-term outcome of paced and nonpaced patients with severe carotid sinus syndrome. Am J Cardiol. 1992;69:1039–43.
149. Claesson JE, Kristensson BE, Edvardsson N, Wahrborg P. Less syncope and milder symptoms in patients treated with pacing for induced cardioinhibitory carotid sinus syndrome: a randomized study. Europace. 2007;9:932–6.
150. Fananapazir L, Epstein ND, Curiel RV, Panza JA, Tripodi D, McAreavey D. Long-term results of dual-chamber (DDD) pacing in obstructive hypertrophic cardiomyopathy: evidence for progressive symptomatic and hemodynamic improvement and reduction of left ventricular hypertrophy. Circulation. 1994;90:2731–42.
151. McDonald K, McWilliams E, O'Keeffe B, Maurer B. Functional assessment of patients treated with permanent dual chamber pacing as a primary treatment for hypertrophic cardiomyopathy. Eur Heart J. 1988;9:893–8.
152. Jeanrenaud X, Goy JJ, Kappenberger L. Effects of dual-chamber pacing in hypertrophic obstructive cardiomyopathy. Lancet. 1992;339:1318–23.
153. Maron BJ, Nishimura RA, McKenna WJ, Rakowski H, Josephson ME, Kieval RS; M-PATHY Study Investigators. Assessment of permanent dual-chamber pacing as a treatment for drug-refractory symptomatic patients with obstructive hypertrophic cardiomyopathy: A randomized, double-blind, crossover study (M-PATHY). Circulation. 1999;99:2927–33.
154. Kappenberger LJ, Linde C, Jeanrenaud X, Daubert C, McKenna W, Meisel E, et al.; Pacing in Cardiomyopathy (PIC) Study Group. Clinical progress after randomized on/off pacemaker treatment for hypertrophic obstructive cardiomyopathy. Europace. 1999;1:77–84.
155. Galve E, Sambola A, Saldana G, eQuispe I, Nieto E, Diaz A. Late benefits of dual-chamber pacing in obstructive hypertrophic cardiomyopathy: a 10-year follow-up study. Heart. 2010;96:352–6.
156. Haruki S, Minami Y, Kajimoto K, Yashiro B, Suzuki T, Kawana M, et al. Possible acute and chronic synergistic effect of dual chamber pacing and disopyramide in obstructive hypertrophic cardiomyopathy: a case report. Eur J Heart Fail. 2010;12:94–7.
157. Minami Y, Kajimoto K, Kawana M, Hagiwara N, Sherrid MV. Synergistic effect of dual chamber pacing and disopyramide in obstructive hypertrophic cardiomyopathy. Int J Cardiol. 2010;141:195–7.
158. Daubert C, Gadler F, Mabo P, Linde C. Pacing for hypertrophic obstructive cardiomyopathy: an update and future directions. Europace. 2018;20:908–20.
159. Soejima K, Edmonson J, Ellingson ML, Herberg B, Wiklund C, Zhao J. Safety evaluation of a leadless transcatheter pacemaker for magnetic resonance imaging use. Heart Rhythm. 2016;13:2056–63.
160. Omdahl P, Eggen MD, Bonner MD, Iaizzo PA, Wika K. Right ventricular anatomy can accommodate multiple Micra transcatheter pacemakers. Pacing Clin Electrophysiol. 2016;39:393–7.
161. Reynolds D, Duray GZ, Omar R, Oejima K, Neuzil P, Zhang S,, et al.; Micra Transcatheter Pacing Study Group. A leadless intracardiac transcatheter pacing system. N Engl J Med. 2016;374:533–41.
162. Duray GZ, Ritter P, El-Chami M, Narasimhan C, Omar R, Tolosana JM, et al.; Micra Transcatheter Pacing Study Group. Long-term performance of a transcatheter pacing system: 12-month results from the Micra Transcatheter Pacing Study. Heart Rhythm. 2017;14:702–9.
163. Soejima K, Asano T, Ishikawa T, Kusano K, Sato T, Okamura H, et al.; Micra Transcatheter Pacing Study Group. Performance of leadless pacemaker in Japanese patients vs. rest of the world: results from a global clinical trial. Circ J. 2017;81:1589–95.
164. Roberts PR, Clementy N, Al Samadi F, Garweg C, Martinez-Sande JL, Iacopino S, et al. A leadless pacemaker in the real-world setting: The Micra Transcatheter Pacing System Post-Approval Registry. Heart Rhythm. 2017;14:1375–9.
165. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA 3rd, Freedman RA, Gettes LS, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices): Developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. Circulation. 2008;117:e350–e408.
166. Tops LF, Schalij MJ, Bax JJ. The effects of right ventricular apical pacing on ventricular function and dyssynchrony implications for therapy. J Am Coll Cardiol. 2009;54:764–76.
167. Tse HF, Lau CP. Long-term effect of right ventricular pacing on myocardial perfusion and function. J Am Coll Cardiol. 1997;29:744–9.
168. Deshmukh P, Casavant DA, Romanyshyn M, Anderson K. Permanent, direct His-bundle pacing: a novel approach to cardiac pacing in patients with normal His-Purkinje activation. Circulation. 2000;101:869–77.
169. Occhetta E, Bortnik M, Magnani A, Francalacci G, Piccinino C, Plebani L, et al. Prevention of ventricular desynchronization by permanent para-Hisian pacing after atrioventricular node ablation in chronic atrial fibrillation: a crossover, blinded, randomized study versus apical right ventricular pacing. J Am Coll Cardiol. 2006;47:1938–45.
170. Zanon F, Svetlich C, Occhetta E, Catanzariti D, Cantu F, Padeletti L, et al. Safety and performance of a system specifically designed for selective site pacing. Pacing Clin Electrophysiol. 2011;34:339–47.
171. Sharma PS, Dandamudi G, Naperkowski A, Oren JW, Storm RH, Ellenbogen KA, et al. Permanent His-bundle pacing is feasible, safe, and superior to right ventricular pacing in routine clinical practice. Heart Rhythm. 2015;12:305–12.
172. Vijayaraman P, Naperkowski A, Ellenbogen KA, Dandamudi G. Electrophysiologic insights into site of atrioventricular block: Lessons from permanent His bundle pacing. JACC Clin Electrophysiol. 2015;1:571–81.
173. Kronborg MB, Mortensen PT, Poulsen SH, Gerdes JC, Jensen HK, Nielsen JC. His or para-His pacing preserves left ventricular

function in atrioventricular block: A double-blind, randomized, crossover study. Europace. 2014;16:1189–96.
174. Abdelrahman M, Subzposh FA, Beer D, Durr B, Naperkowski A, Sun H, et al. Clinical outcomes of His bundle pacing compared to right ventricular pacing. J Am Coll Cardiol. 2018;71:2319–30.
175. Zanon F, Ellenbogen KA, Dandamudi G, Sharma PS, Huang W, Lustgarten DL, et al. Permanent His-bundle pacing: a systematic literature review and meta-analysis. Europace. 2018;20:1819–26.
176. Kusumoto FM, Schoenfeld MH, Barrett C, Edgerton JR, Ellenbogen KA, Gold MR, et al. 2018 ACC/AHA/HRS guideline on the evaluation and management of patients with bradycardia and cardiac conduction delay: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2019;74:e51–e156.
177. Sharma PS, Dandamudi G, Herweg B, Wilson D, Singh R, Naperkowski A, et al. Permanent His-bundle pacing as an alternative to biventricular pacing for cardiac resynchronization therapy: a multicenter experience. Heart Rhythm. 2018;15:413–20.
178. Vijayaraman P, Dandamudi G. How to perform permanent His bundle pacing: tips and tricks. Pacing Clin Electrophysiol. 2016;39:1298–304.
179. Shimizu A, Nitta T, Kurita T, Imai K, Kobayashi Y, Soejima K, et al. Actual conditions of implantable defibrillation therapy over 5 years in Japan. J Arrhythm. 2012;28:263–72.
180. Kuck KH, Cappato R, Siebels J, Rüppel R. Randomized comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest: The Cardiac Arrest Study Hamburg (CASH). Circulation. 2000;102:748–54.
181. Connolly SJ, Gent M, Roberts RS, Dorian P, Roy D, Sheldon RS, et al. Canadian implantable defibrillator study (CIDS): a randomized trial of the implantable cardioverter defibrillator against amiodarone. Circulation. 2000;101:1297–302.
182. Noda T, Kurita T, Nitta T, Chiba Y, Furushima H, Matsumoto N, et al. Significant impact of electrical storm on mortality in patients with structural heart disease and an implantable cardiac defibrillator. Int J Cardiol. 2018;255:85–91.
183. Kuck KH, Schaumann A, Eckardt L, Willems S, Ventura R, Delacrétaz E, et al.; VTACH study group. Catheter ablation of stable ventricular tachycardia before defibrillator implantation in patients with coronary heart disease (VTACH): a multicentre randomised controlled trial. Lancet. 2010;375:31–40.
184. Connolly SJ, Hallstrom AP, Cappato R, Schron EB, Kuck KH, Zipes DP, et al. Meta-analysis of the implantable cardioverter defibrillator secondary prevention trials: AVID, CASH and CIDS studies. Antiarrhythmics vs Implantable Defibrillator study. Cardiac Arrest Study Hamburg. Canadian Implantable Defibrillator Study. Eur Heart J. 2000;21:2071–8.
185. Domanski MJ, Sakseena S, Epstein AE, Hallstrom AP, Brodsky MA, Lancaster S, et al.; AVID Investigators [Antiarrhythmics Versus Implantable Defibrillators]. Relative effectiveness of the implantable cardioverter-defibrillator and antiarrhythmic drugs in patients with varying degrees of left ventricular dysfunction who have survived malignant ventricular arrhythmias. J Am Coll Cardiol. 1999;34:1090–5.
186. Reddy VY, Reynolds MR, Neuzil P, Richardson AW, Taborsky M, Jongnarangsin K, et al. Prophylactic catheter ablation for the prevention of defibrillator therapy. N Engl J Med. 2007;357:2657–65.
187. Soejima K, Stevenson WG, Maisel WH, Sapp JL, Epstein LM. Electrically unexcitable scar mapping based on pacing threshold for identification of the reentry circuit isthmus: feasibility for guiding ventricular tachycardia ablation. Circulation. 2002;106:1678–83.
188. Carbucicchio C, Santamaria M, Trevisi N, Maccavelli G, Giraldi F, Fassini G, et al. Catheter ablation for the treatment of electrical storm in patients with implantable cardioverter-defibrillators: short- and long-term outcomes in a prospective single-center study. Circulation. 2008;117:462–9.
189. Al-Khatib SM, Stevenson WG, Ackerman MJ, Bryant WJ, Callans DJ, Curtis AB, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Circulation. 2018;138:e272–e391 (erratum in Circulation 2018; 138: e419–e420).
190. Volpi A, Cavalli A, Santoro L, Negri E. Incidence and prognosis of early primary ventricular fibrillation in acute myocardial infarction: results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI-2) database. Am J Cardiol. 1998;82:265–71.
191. Takagi Y, Takahashi J, Yasuda S, Miyata S, Tsunoda R, Ogata Y, et al.; Japanese Coronary Spasm Association. Prognostic stratification of patients with vasospastic angina: a comprehensive clinical risk score developed by the Japanese Coronary Spasm Association. J Am Coll Cardiol. 2013;62:1144–53.
192. Meisel SR, Mazur A, Chetboun I, Epshtein M, Canetti M, Gallimidi J, et al. Usefulness of implantable cardioverter-defibrillators in refractory variant angina pectoris complicated by ventricular fibrillation in patients with angiographically normal coronary arteries. Am J Cardiol. 2002;89:1114–6.
193. Sasaki S, Tomita H, Shibutani S, Izumiyama K, Higuma T, Itoh T, et al. Usefulness of the wearable cardioverter-defibrillator in patients at high risk for sudden cardiac death. Circ J. 2014;78:2987–9.
194. Desai AS, Fang JC, Maisel WH, Baughman KL. Implantable defibrillators for the prevention of mortality in patients with nonischemic cardiomyopathy: a meta-analysis of randomized controlled trials. JAMA. 2004;292:2874–9.
195. Sasaki S, Shoji Y, Ishida Y, Kinjo T, Tsushima Y, Seno M, et al. Potential roles of the wearable cardioverter-defibrillator in acute phase care of patients at high risk of sudden cardiac death: a single-center Japanese experience. J Cardiol. 2017;69:359–63.
196. Sacher F, Roberts-Thomson K, Maury P, Tedrow U, Nault I, Steven D, et al. Epicardial ventricular tachycardia ablation a multicenter safety study. J Am Coll Cardiol. 2010;55:2366–72.
197. Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H, et al.; Multicenter Automatic Defibrillator Implantation Trial Investigators. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. N Engl J Med. 1996;335:1933–40.
198. Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, et al.; Multicenter Automatic Defibrillator Implantation Trial II Investigators. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med. 2002;346:877–83.
199. Goldenberg I, Gillespie J, Moss AJ, Hall WJ, Klein H, McNitt S, et al. Executive Committee of the Multicenter Automatic Defibrillator Implantation Trial II. Long-term benefit of primary prevention with an implantable cardioverter-defibrillator: an extended 8-year follow-up study of the Multicenter Automatic Defibrillator Implantation Trial II. Circulation. 2010;122:1265–71.
200. Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, et al.; Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Investigators. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med. 2005;352:225–37.
201. Shiga T, Hagiwara N, Ogawa H, Takagi A, Nagashima M, Yamauchi T, et al.; Heart Institute of Japan Acute Myocardial Infarction-II (HIJAMI-II) Investigators. Sudden cardiac death and left ventricular ejection fraction during long-term follow-up after acute myocardial infarction in the primary percutaneous coronary intervention era: Results from the HIJAMI-II registry. Heart. 2009;95:216–20.
202. Tanno K, Miyoshi F, Watanabe N, Minoura Y, Kawamura M, Ryu S, et al. The Multicenter Automatic Defibrillator Implantation Trial.

Are the MADIT II criteria for ICD implantation appropriate for Japanese patients? Circ J. 2005;69:19–22.
203. Satake H, Fukuda K, Sakata Y, Miyata S, Nakano M, Kondo M, et al. CHART-2 Investigators. Current status of primary prevention of sudden cardiac death with implantable cardioverter defibrillator in patients with chronic heart failure: a report from the CHART-2 Study. Circ J. 2015;79:381–90.
204. Greenberg H, Case RB, Moss AJ, Brown MW, Carroll ER, Andrews ML, et al. Analysis of mortality events in the Multicenter Automatic Defibrillator Implantation Trial (MADIT-II). J Am Coll Cardiol. 2004;43:1459–65.
205. Buxton AE, Lee KL, DiCarlo L, Gold MR, Greer GS, Prystowsky EN, et al.; Multicenter Unsustained Tachycardia Trial Investigators. Electrophysiologic testing to identify patients with coronary artery disease who are at risk for sudden death. N Engl J Med. 2000;342:1937–45.
206. Hohnloser SH, Kuck KH, Dorian P, Roberts RS, Hampton JR, Hatala R, et al. Prophylactic use of an implantable cardioverter-defibrillator after acute myocardial infarction. N Engl J Med. 2004;351:2481–8.
207. Pouleur AC, Barkoudah E, Uno H, Skali H, Finn PV, Zelenkofske SL, et al; VALIANT Investigators. Pathogenesis of sudden unexpected death in a clinical trial of patients with myocardial infarction and left ventricular dysfunction, heart failure, or both. Circulation. 2010;122:597–602.
208. Scientific Statement from Japanese Heart Rhythm Society. Statement for clinical use of wearable cardiac defibrillator [in Japanese]. http://new.jhrs.or.jp/pdf/guideline/statement201505_01.pdf (Accessed Nov. 2018)
209. Opreanu M, Wan C, Singh V, Salehi N, Ahmad J, Szymkiewicz SJ, et al. Wearable cardioverter-defibrillator as a bridge to cardiac transplantation: a national database analysis. J Heart Lung Transplant. 2015;34:1305–9.
210. Zishiri ET, Williams S, Cronin EM, Blacksone EH, Ellis SG, Roselli EE, et al. Early risk of mortality after coronary artery revascularization in patients with left ventricular dysfunction and potential role of the wearable cardioverter defibrillator. Circ Arrhythm Electrophysiol. 2013;6:117–28.
211. Chung MK, Szymkiewicz SJ, Shao M, Zishiri E, Niebauer MJ, Lindsay BD, et al. Aggregate national experience with the wearable cardioverter-defibrillator: Event rates, compliance, and survival. J Am Coll Cardiol. 2010;56:194–203.
212. Kadish A, Dyer A, Daubert JP, Quigg R, Estes NAM, Anderson KP, et al.; Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) Investigators. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. N Engl J Med. 2004;350:2151–8.
213. Kober L, Thune JJ, Nielsen JC, Haarbo J, Videbæk L, Korup E, et al.; DANISH Investigators. Defibrillator implantation in patients with nonischemic systolic heart failure. N Engl J Med. 2016;375:1221–30.
214. Bansch D, Antz M, Boczor S, Volkmer M, Tebbenjohanns J, Seidl K, et al. Primary prevention of sudden cardiac death in idiopathic dilated cardiomyopathy: The Cardiomyopathy Trial (CAT). Circulation. 2002;105:1453–8.
215. Strickberger SA, Hummel JD, Bartlett TG, Frumin HI, Schuger CD, Beau SL, et al. Amiodarone versus implantable cardioverter-defibrillator: Randomized trial in patients with nonischemic dilated cardiomyopathy and asymptomatic nonsustained ventricular tachycardia: AMIOVIRT. J Am Coll Cardiol. 2003;41:1707–12.
216. Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T, et al.; Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) Investigators. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med. 2004;350:2140–50.
217. Golwala H, Bajaj NS, Arora G, Arora P. Implantable cardioverter-defibrillator for nonischemic cardiomyopathy: an updated meta-analysis. Circulation. 2017;135:201–3.
218. Barakat AF, Saad M, Elgendy AY, Mentias A, Abuzaid A, Mahmoud AN, et al. Primary prevention implantable cardioverter defibrillator in patients with non-ischaemic cardiomyopathy: a meta-analysis of randomised controlled trials. BMJ Open. 2017;7:e016352.
219. Kawashiro N, Kasanuki H, Ogawa H, Matsuda N, Hagiwara N, Heart Institute of Japan –Department of Cardiology (HIJC) Investigators. Clinical characteristics and outcome of hospitalized patients with congestive heart failure: Results of the HIJC-HF registry. Circ J. 2008;72:2015–20.
220. Shiba N, Shimokawa H. Chronic heart failure in Japan: implications of the CHART studies. Vasc Health Risk Manag. 2008;4:103–13.
221. Ruwald MH, Okumura K, Kimura T, Aonuma K, Shoda M, Kutyifa V, et al. Syncope in high-risk cardiomyopathy patients with implantable defibrillators: frequency, risk factors, mechanisms, and association with mortality: Results from the multicenter automatic defibrillator implantation trial-reduce inappropriate therapy (MADIT-RIT) study. Circulation. 2014;129:545–52.
222. Garcia-Moran E, Mont L, Cuesta A, Matas M, Brugada J. Low recurrence of syncope in patients with inducible sustained ventricular tachyarrhythmias treated with an implantable cardioverter-defibrillator. Eur Heart J. 2002;23:901–7.
223. Pezawas T, Stix G, Kastner J, Wolzt M, Mayer C, Moertl D, et al. Unexplained syncope in patients with structural heart disease and no documented ventricular arrhythmias: value of electrophysiologically guided implantable cardioverter defibrillator therapy. Europace. 2003;5:305–12.
224. Fonarow GC, Feliciano Z, Boyle NG, Knight L, Woo MA, Moriguchi JD, et al. Improved survival in patients with nonischemic advanced heart failure and syncope treated with an implantable cardioverter-defibrillator. Am J Cardiol. 2000;85:981–5.
225. Russo AM, Verdino R, Schorr C, Nicholas M, Dias D, Hsia H, et al. Occurrence of implantable defibrillator events in patients with syncope and nonischemic dilated cardiomyopathy. Am J Cardiol. 2001;88:1444–6.
226. Cecchi F, Olivotto I, Betocchi S, Rapezzi C, Conte MR, Sinagra G, et al. The Italian Registry for hypertrophic cardiomyopathy: a nationwide survey. Am Heart J. 2005;150:947–54.
227. Maron BJ, Olivotto I, Spirito P, Casey SA, Bellone P, Gohman TE, et al. Epidemiology of hypertrophic cardiomyopathy-related death: revisited in a large non-referral-based patient population. Circulation. 2000;102:858–64.
228. Elliott PM, Gimeno JR, Thaman R, Shah J, Ward D, Dickie S, et al. Historical trends in reported survival rates in patients with hypertrophic cardiomyopathy. Heart. 2006;92:785–91.
229. Maron BJ, Shirani J, Poliac LC, Mathenge R, Roberts WC, Mueller FO. Sudden death in young competitive athletes: clinical, demographic, and pathological profiles. JAMA. 1996;276:199–204.
230. Maron BJ, Spirito P, Shen WK, Haas TS, Formisano F, Link MS, et al. Implantable cardioverter-defibrillators and prevention of sudden cardiac death in hypertrophic cardiomyopathy. JAMA. 2007;298:405–12.
231. Cecchi F, Maron BJ, Epstein SE. Long-term outcome of patients with hypertrophic cardiomyopathy successfully resuscitated after cardiac arrest. J Am Coll Cardiol. 1989;13:1283–8.
232. Elliott PM, Sharma S, Varnava A, Poloniecki J, Rowland E, McKenna WJ. Survival after cardiac arrest or sustained ventricular tachycardia in patients with hypertrophic cardiomyopathy. J Am Coll Cardiol. 1999;33:1596–601.

233. Maron BJ, Haas TS, Shannon KM, Almquist A, Hodges JS. Long-term survival after cardiac arrest in hypertrophic cardiomyopathy. Heart Rhythm. 2009;6:993–7.
234. O'Mahony C, Lambiase PD, Quarta G, Cardona M, Calcagnino M, Tsovolas K, et al. The long-term survival and the risks and benefits of implantable cardioverter defibrillators in patients with hypertrophic cardiomyopathy. Heart. 2012;98:116–25.
235. Syska P, Przybylski A, Chojnowska L, Lewandowski M, Sterliński M, Maciag A, et al. Implantable cardioverter-defibrillator in patients with hypertrophic cardiomyopathy: efficacy and complications of the therapy in long-term follow-up. J Cardiovasc Electrophysiol. 2010;21:883–9.
236. Elliott PM, Anastasakis A, Borger MA, Borggrefe M, Cecchi F, Charron P, et al. 2014 ESC guidelines on diagnosis and management of hypertrophic cardiomyopathy: The Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J. 2014;35:2733–79.
237. Gersh BJ, Maron BJ, Bonow RO, Dearani JA, Fifer MA, Link MS, et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2011;58:e212–e260.
238. Maron BJ. Contemporary insights and strategies for risk stratification and prevention of sudden death in hypertrophic cardiomyopathy. Circulation. 2010;121:445–56.
239. Bos JM, Maron BJ, Ackerman MJ, Haas TS, Sorajja P, Nishimura RA, et al. Role of family history of sudden death in risk stratification and prevention of sudden death with implantable defibrillators in hypertrophic cardiomyopathy. Am J Cardiol. 2010;106:1481–6.
240. Spirito P, Autore C, Rapezzi C, Bernabò P, Badagliacca R, Maron MS, et al. Syncope and risk of sudden death in hypertrophic cardiomyopathy. Circulation. 2009;119:1703–10.
241. Elliott PM, Gimeno Blanes JR, Mahon NG, Polonecki JD, McKenna WJ. Relation between severity of left-ventricular hypertrophy and prognosis in patients with hypertrophic cardiomyopathy. Lancet. 2001;357:420–4.
242. Spirito P, Bellone P, Harris KM, Bernabo P, Bruzzi P, Maron BJ. Magnitude of left ventricular hypertrophy and risk of sudden death in hypertrophic cardiomyopathy. N Engl J Med. 2000;342:1778–85.
243. Elliott PM, Poloniecki J, Dickie S, Sharma S, Monserrat L, Varnava A, et al. Sudden death in hypertrophic cardiomyopathy: identification of high risk patients. J Am Coll Cardiol. 2000;36:2212–8.
244. Sadoul N, Prasad K, Elliott PM, Bannerjee S, Frenneaux MP, McKenna WJ. Prospective prognostic assessment of blood pressure response during exercise in patients with hypertrophic cardiomyopathy. Circulation. 1997;96:2987–91.
245. Olivotto I, Maron BJ, Montereggi A, Mazzuoli F, Dolara A, Cecchi F. Prognostic value of systemic blood pressure response during exercise in a community-based patient population with hypertrophic cardiomyopathy. J Am Coll Cardiol. 1999;33:2044–51.
246. Maki S, Ikeda H, Muro A, Yoshida N, Shibata A, Koga Y, et al. Predictors of sudden cardiac death in hypertrophic cardiomyopathy. Am J Cardiol. 1998;82:774–8.
247. Monserrat L, Elliott PM, Gimeno JR, Sharma S, Penas-Lado M, McKenna WJ. Non-sustained ventricular tachycardia in hypertrophic cardiomyopathy: an independent marker of sudden death risk in young patients. J Am Coll Cardiol. 2003;42:873–9.
248. O'Mahony C, Jichi F, Pavlou M, Monserrat L, Anastasakis A, Rapezzi C, et al.; Hypertrophic Cardiomyopathy Outcomes Investigators. A novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCM risk-SCD). Eur Heart J. 2014;35:2010–20.
249. Vriesendorp PA, Schinkel AF, Liebregts M, Theuns DAQMJ, van Cleemput J, Ten Cate FJ, et al. Validation of the 2014 European Society of Cardiology guidelines risk prediction model for the primary prevention of sudden cardiac death in hypertrophic cardiomyopathy. Circ Arrhythm Electrophysiol. 2015;8:829–35.
250. O'Mahony C, Jichi F, Ommen SR, Christiaans I, Arbustini E, Garcia-Pavia P, et al. International External Validation Study of the 2014 European Society of Cardiology Guidelines on Sudden Cardiac Death Prevention in Hypertrophic Cardiomyopathy (EVIDENCE-HCM). Circulation. 2018;137:1015–23.
251. European Society of Cardiology. HCM risk-SCD calculator. http://www.doc2do.com/hcm/webHCM.html (Accessed Nov. 2018)
252. Schinkel AF, Vriesendorp PA, Sijbrands EJ, Jordaens LJLM, ten Cate FJ, Michels M. Outcome and complications after implantable cardioverter defibrillator therapy in hypertrophic cardiomyopathy: systematic review and meta-analysis. Circ Heart Fail. 2012;5:552–9.
253. Kawarai H, Kajimoto K, Minami Y, Hagiwara N, Kasanuki H. Risk of sudden death in end-stage hypertrophic cardiomyopathy. J Card Fail. 2011;17:459–64.
254. Maron MS, Finley JJ, Bos JM, Hauser TH, Manning WJ, Haas TS, et al. Prevalence, clinical significance, and natural history of left ventricular apical aneurysms in hypertrophic cardiomyopathy. Circulation. 2008;118:1541–9.
255. Minami Y, Kajimoto K, Terajima Y, Yashiro B, Okayama D, Haruki S, et al. Clinical implications of midventricular obstruction in patients with hypertrophic cardiomyopathy. J Am Coll Cardiol. 2011;57:2346–55.
256. Behr ER, Elliott P, McKenna WJ. Role of invasive EP testing in the evaluation and management of hypertrophic cardiomyopathy. Card Electrophysiol Rev. 2002;6:482–6.
257. Jacoby D, McKenna WJ. Genetics of inherited cardiomyopathy. Eur Heart J. 2012;33:296–304.
258. Marcus FI, Fontaine GH, Guiraudon G, Frank R, Laurenceau JL, Malergue C, et al. Right ventricular dysplasia: a report of 24 adult cases. Circulation. 1982;65:384–98.
259. Basso C, Corrado D, Thiene G. Cardiovascular causes of sudden death in young individuals including athletes. Cardiol Rev. 1999;7:127–35.
260. Corrado D, Basso C, Thiene G. Sudden cardiac death in young people with apparently normal heart. Cardiovasc Res. 2001;50:399–408.
261. Tabib A, Loire R, Chalabreysse L, Meyronnet D, Miras A, Malicier D, et al. Circumstances of death and gross and microscopic observations in a series of 200 cases of sudden death associated with arrhythmogenic right ventricular cardiomyopathy and/or dysplasia. Circulation. 2003;108:3000–5.
262. Thiene G, Nava A, Corrado D, Rossi L, Pennelli N. Right ventricular cardiomyopathy and sudden death in young people. N Engl J Med. 1988;318:129–33.
263. Corrado D, Thiene G, Nava A, Rossi L, Pennelli N. Sudden death in young competitive athletes: clinicopathologic correlations in 22 cases. Am J Med. 1990;89:588–96.
264. Marcus FI, McKenna WJ, Sherrill D, Basso C, Bauce B, Bluemke DA, et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria. Circulation. 2010;121:1533–41.
265. Kikuchi N, Yumino D, Shiga T, Suzuki A, Hagiwara N. Long-term prognostic role of the diagnostic criteria for arrhythmogenic right ventricular cardiomyopathy/dysplasia. JACC Clin Electrophysiol. 2016;2:107–15.

266. Kimura Y, Noda T, Matsuyama TA, Otsuka Y, Kamakura T, Wada M, et al. Heart failure in patients with arrhythmogenic right ventricular cardiomyopathy: What are the risk factors? Int J Cardiol. 2017;241:288–94.
267. Corrado D, Wichter T, Link MS, Hauer RN, Marchlinski FE, Anastasakis A, et al. Treatment of arrhythmogenic right ventricular cardiomyopathy/dysplasia: an international task force consensus statement. Circulation. 2015;132:441–53.
268. Corrado D, Leoni L, Link MS, Della Bella P, Gaita F, Curnis A, et al. Implantable cardioverter-defibrillator therapy for prevention of sudden death in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia. Circulation. 2003;108:3084–91.
269. Link MS, Laidlaw D, Polonsky B, Zareba W, McNitt S, Gear K, et al. Ventricular arrhythmias in the North American multidisciplinary study of ARVC: predictors, characteristics, and treatment. J Am Coll Cardiol. 2014;64:119–25.
270. Lemola K, Brunckhorst C, Helfenstein U, Oechslin E, Jenni R, Duru F. Predictors of adverse outcome in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy: long term experience of a tertiary care centre. Heart. 2005;91:1167–72.
271. Hulot JS, Jouven X, Empana JP, Frank R, Fontaine G. Natural history and risk stratification of arrhythmogenic right ventricular dysplasia/cardiomyopathy. Circulation. 2004;110:1879–84.
272. Wichter T, Paul M, Wollmann C, Acil T, Gerdes P, Ashraf O, et al. Implantable cardioverter/defibrillator therapy in arrhythmogenic right ventricular cardiomyopathy: single-center experience of long-term follow-up and complications in 60 patients. Circulation. 2004;109:1503–8.
273. Pinamonti B, Dragos AM, Pyxaras SA, Merlo M, Pivetta A, Barbati G, et al. Prognostic predictors in arrhythmogenic right ventricular cardiomyopathy: results from a 10-year registry. Eur Heart J. 2011;32:1105–13.
274. Corrado D, Calkins H, Link MS, Leoni L, Favale S, Bevilacqua M, et al. Prophylactic implantable defibrillator in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia and no prior ventricular fibrillation or sustained ventricular tachycardia. Circulation. 2010;122:1144–52.
275. Bhonsale A, James CA, Tichnell C, Murray B, Gagarin D, Philips B, et al. Incidence and predictors of implantable cardioverter-defibrillator therapy in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy undergoing implantable cardioverter-defibrillator implantation for primary prevention. J Am Coll Cardiol. 2011;58:1485–96.
276. Brugada P, Brugada J. Right bundle branch block, persistent ST segment elevation and sudden cardiac death: a distinct clinical and electrocardiographic syndrome. A multicenter report. J Am Coll Cardiol. 1992;20:1391–6.
277. Priori SG, Wilde AA, Horie M, Cho Y, Behr ER, Berul C, et al. HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes: document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013. Heart Rhythm. 2013;10:1932–63.
278. Antzelevitch C, Yan GX, Ackerman MJ, Borggrefe M, Corrado D, Guo J, et al. J-Wave syndromes expert consensus conference report: emerging concepts and gaps in knowledge. J Arrhythm. 2016;32:315–39.
279. Brugada J, Brugada R, Brugada P. Pharmacological and device approach to therapy of inherited cardiac diseases associated with cardiac arrhythmias and sudden death. J Electrocardiol. 2000;33(Suppl):41–7.
280. Nademanee K, Veerakul G, Mower M, Likittanasombat K, Krittayapong R, Bhuripanyo K, et al. Defibrillator versus beta-blockers for unexplained death in Thailand (DEBUT): a randomized clinical trial. Circulation. 2003;107:2221–6.
281. Take Y, Morita H, Toh N, Nishii N, Nagase S, Nakamura K, et al. Identification of high-risk syncope related to ventricular fibrillation in patients with Brugada syndrome. Heart Rhythm. 2012;9:752–9.
282. Raju H, Papadakis M, Govindan M, Bastiaenen R, Chandra N, O'Sullivan A, et al. Low prevalence of risk markers in cases of sudden death due to Brugada syndrome relevance to risk stratification in Brugada syndrome. J Am Coll Cardiol. 2011;57:2340–5.
283. Casado-Arroyo R, Berne P, Rao JY, Rodriguez-Mañero M, Levinstein M, Conte G, et al. Long-term trends in newly diagnosed Brugada syndrome: Implications for risk stratification. J Am Coll Cardiol. 2016;68:614–23.
284. Yokokawa M, Okamura H, Noda T, Satomi K, Suyama K, Kurita T, et al. Neurally mediated syncope as a cause of syncope in patients with Brugada electrocardiogram. J Cardiovasc Electrophysiol. 2010;21:186–92.
285. Letsas KP, Efremidis M, Gavrielatos G, Filippatos GS, Sideris A, Kardaras F. Neurally mediated susceptibility in individuals with Brugada-type ECG pattern. Pacing Clin Electrophysiol. 2008;31:418–21.
286. Yamagata K, Horie M, Aiba T, Ogawa S, Aizawa Y, Ohe T, et al. Genotype-phenotype correlation of *SCN5A* mutation for the clinical and electrocardiographic characteristics of probands with Brugada syndrome: a Japanese multicenter registry. Circulation. 2017;135:2255–70.
287. Sacher F, Probst V, Iesaka Y, Jacon P, Laborderie J, Mizon-Gérard F, et al. Outcome after implantation of a cardioverter-defibrillator in patients with Brugada syndrome: a multicenter study. Circulation. 2006;114:2317–24.
288. Shimizu W, Horie M. Phenotypic manifestations of mutations in genes encoding subunits of cardiac potassium channels. Circ Res. 2011;109:97–109.
289. Shimizu W. Update of diagnosis and management of inherited cardiac arrhythmias. Circ J. 2013;77:2867–72.
290. Hayashi M, Shimizu W, Albert CM. The spectrum of epidemiology underlying sudden cardiac death. Circ Res. 2015;116:1887–906.
291. Tester DJ, Will ML, Haglund CM, Ackerman MJ. Effect of clinical phenotype on yield of long QT syndrome genetic testing. J Am Coll Cardiol. 2006;47:764–8.
292. Schwartz PJ, Crotti L. QTc behavior during exercise and genetic testing for the long-QT syndrome. Circulation. 2011;124:2181–4.
293. Rijnbeek PR, Witsenburg M, Schrama E, Hess J, Kors JA. New normal limits for the paediatric electrocardiogram. Eur Heart J. 2001;22:702–11.
294. Schwartz PJ, Crotti L, Insolia R. Long-QT syndrome: From genetics to management. Circ Arrhythm Electrophysiol. 2012;5:868–77.
295. Jons C, Moss AJ, Goldenberg I, Liu J, McNitt S, Zareba W, et al. Risk of fatal arrhythmic events in long QT syndrome patients after syncope. J Am Coll Cardiol. 2010;55:783–8.
296. Zareba W, Moss AJ, Schwartz PJ, Vincent GM, Robinson JL, Priori SG, et al.; International Long-QT Syndrome Registry Research Group. Influence of the genotype on the clinical course of the long-QT syndrome. N Engl J Med. 1998;339:960–5.
297. Schwartz PJ, Spazzolini C, Priori SG, Crotti L, Vicentini A, Landolina M, et al. Who are the long-QT syndrome patients who receive an implantable cardioverter-defibrillator and what happens to them? Data from the European Long-QT Syndrome Implantable Cardioverter-Defibrillator (LQTS ICD) Registry. Circulation. 2010;122:1272–82.
298. Schwartz PJ, Priori SG, Cerrone M, Spazzolini C, Odero A, Napolitano C, et al. Left cardiac sympathetic denervation in the management of high-risk patients affected by the long-QT syndrome. Circulation. 2004;109:1826–33.

299. Hwang SW, Thomas JG, Whitehead WE, Curry DJ, Dauser RC, Kim ES, et al. Left thoracopic sympathectomy for refractory long QT syndrome in children. J Neurosurg Pediatr. 2011;8:455–9.
300. Odero A, Bozzani A, De Ferrari GM, Schwartz PJ. Left cardiac sympathetic denervation for the prevention of life-threatening arrhythmias: the surgical supraclavicular approach to cervicothoracic sympathectomy. Heart Rhythm. 2010;7:1161–5.
301. Leenhardt A, Lucet V, Denjoy I, Grau F, Ngoc DD, Coumel P. Catecholaminergic polymorphic ventricular tachycardia in children: a 7-year follow-up of 21 patients. Circulation. 1995;91:1512–9.
302. Eisenberg SJ, Scheinman MM, Dullet NK, Finkbeiner WE, Griffin JC, Eldar M, et al. Sudden cardiac death and polymorphous ventricular tachycardia in patients with normal QT intervals and normal systolic cardiac function. Am J Cardiol. 1995;75:687–92.
303. Hayashi M, Denjoy I, Extramiana F, Maltret A, Buisson NR, Lupoglazoff JM, et al. Incidence and risk factors of arrhythmic events in catecholaminergic polymorphic ventricular tachycardia. Circulation. 2009;119:2426–34.
304. Sumitomo N, Harada K, Nagashima M, Yasuda T, Nakamura Y, Arigaki Y, et al. Catecholaminergic polymorphic ventricular tachycardia: electrocardiographic characteristics and optimal therapeutic strategies to prevent sudden death. Heart. 2003;89:66–70.
305. Priori SG, Napolitano C, Memmi M, Colombi B, Drago F, Gasparini M, et al. Clinical and molecular characterization of patients with catecholaminergic polymorphic ventricular tachycardia. Circulation. 2002;106:69–74.
306. Laitinen PJ, Brown KM, Piippo K, Swan H, Devaney JM, Brahmbhatt B, et al. Mutations of the cardiac ryanodine receptor (RyR2) gene in familial polymorphic ventricular tachycardia. Circulation. 2001;103:485–90.
307. Priori SG, Napolitano C, Tiso N, Memmi M, Vignati G, Bloise V, et al. Mutations in the cardiac ryanodine receptor gene (*hRyR2*) underlie catecholaminergic polymorphic ventricular tachycardia. Circulation. 2001;103:196–200.
308. Aizawa Y, Ueda K, Komura S, Washizuka T, Chinushi M, Inagaki N, et al. A novel mutation in FKBP12.6 binding region of the human cardiac ryanodine receptor gene (R2401H) in a Japanese patient with catecholaminergic polymorphic ventricular tachycardia. Int J Cardiol. 2005;99:343–5.
309. Lahat H, Eldar M, Levy-Nissenbaum E, Bahan T, Friedman E, Khoury A, et al. Autosomal recessive catecholamine- or exercise-induced polymorphic ventricular tachycardia: clinical features and assignment of the disease gene to chromosome 1p13–21. Circulation. 2001;103:2822–7.
310. Priori SG, Blomstrom-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, et al. 2015 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). Eur Heart J. 2015;36:2793–867.
311. van der Werf C, Zwinderman AH, Wilde AA. Therapeutic approach for patients with catecholaminergic polymorphic ventricular tachycardia: state of the art and future developments. Europace. 2012;14:175–83.
312. van der Werf C, Nederend I, Hofman N, van Geloven N, Ebink C, Frohn-Mulder IME, et al. Familial evaluation in catecholaminergic polymorphic ventricular tachycardia: disease penetrance and expression in cardiac ryanodine receptor mutationcarrying relatives. Circ Arrhythm Electrophysiol. 2012;5:748–56.
313. Watanabe H, Chopra N, Laver D, Hwang HS, Davies SS, Roach DE, et al. Flecainide prevents catecholaminergic polymorphic ventricular tachycardia in mice and humans. Nat Med. 2009;15:380–3.
314. Wilde AA, Bhuiyan ZA, Crotti L, Facchini M, De Ferrari GM, Paul T, et al. Left cardiac sympathetic denervation for catecholaminergic polymorphic ventricular tachycardia. N Engl J Med. 2008;358:2024–9.
315. Kaneshiro T, Naruse Y, Nogami A, Tada H, Yoshida K, Sekiguchi Y, et al. Successful catheter ablation of bidirectional ventricular premature contractions triggering ventricular fibrillation in catecholaminergic polymorphic ventricular tachycardia with *RyR2* mutation. Circ Arrhythm Electrophysiol. 2012;5:e14–e17.
316. Shirai Y, Goya M, Ohno S, Horie M, Doi S, Isobe M, et al. Elimination of ventricular arrhythmia in catecholaminergic polymorphic ventricular tachycardia by targeting "catecholamine-sensitive area": a dominant-subordinate relationship between origin sites of bidirectional ventricular premature contractions. Pacing Clin Electrophysiol. 2017;40:600–4.
317. Russo AM, Stainback RF, Bailey SR, Epstein AE, Heidenreich PA, Jessup M, et al. ACCF/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR 2013 appropriate use criteria for implantable cardioverter-defibrillators and cardiac resynchronization therapy: a report of the American College of Cardiology Foundation appropriate use criteria task force, Heart Rhythm Society, American Heart Association, American Society of Echocardiography, Heart Failure Society of America, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. J Am Coll Cardiol. 2013;61:1318–68.
318. Roses-Noguer F, Jarman JW, Clague JR, Till J. Outcomes of defibrillator therapy in catecholaminergic polymorphic ventricular tachycardia. Heart Rhythm. 2014;11:58–66.
319. Knecht S, Sacher F, Wright M, Hocini M, Nogami A, Arentz T, et al. Long-term follow-up of idiopathic ventricular fibrillation ablation: a multicenter study. J Am Coll Cardiol. 2009;54:522–8.
320. Conte G, Caputo ML, Regoli F, Marcon S, Klersy C, Adjibodou B, et al. True idiopathic ventricular fibrillation in out-of-hospital cardiac arrest survivors in the Swiss Canton Ticino: Prevalence, clinical features, and long-term follow-up. Europace. 2017;19:259–66.
321. Haissaguerre M, Sacher F, Nogami A, Komiya N, Bernard A, Probst V, et al. Characteristics of recurrent ventricular fibrillation associated with inferolateral early repolarization role of drug therapy. J Am Coll Cardiol. 2009;53:612–9.
322. Siebermair J, Sinner MF, Beckmann BM, Laubender RP, Martens E, Sattler S, et al. Early repolarization pattern is the strongest predictor of arrhythmia recurrence in patients with idiopathic ventricular fibrillation: results from a single centre long-term follow-up over 20 years. Europace. 2016;18:718–25.
323. Cheng YJ, Lin XX, Ji CC, Chen XM, Liu LJ, Tang K, et al. Role of early repolarization pattern in increasing risk of death. J Am Heart Assoc. 2016;5:e003375.
324. Mazzanti A, Kanthan A, Monteforte N, Memmi M, Bloise R, Novelli V, et al. Novel insight into the natural history of short QT syndrome. J Am Coll Cardiol. 2014;63:1300–8.
325. Villafane J, Atallah J, Gollob MH, Maury P, Wolpert C, Gebauer R, et al. Long-term follow-up of a pediatric cohort with short QT syndrome. J Am Coll Cardiol. 2013;61:1183–91.
326. Haines DE, Wang Y, Curtis J. Implantable cardioverter-defibrillator registry risk score models for acute procedural complications or death after implantable cardioverter-defibrillator implantation. Circulation. 2011;123:2069–76.
327. Winter J, Siekiera M, Shin DI, Meyer C, Kropil P, Clahsen H, et al. Intermuscular technique for implantation of the subcutaneous implantable cardioverter defibrillator: long-term performance and complications. Europace. 2017;19:2036–41.
328. Weiss R, Knight BP, Gold MR, Leon AR, Herre JM, Hood M, et al. Safety and efficacy of a totally subcutaneous implantable-cardioverter defibrillator. Circulation. 2013;128:944–53.

329. Bardy GH, Smith WM, Hood MA, Crozier IG, Melton IC, Jordaens L, et al. An entirely subcutaneous implantable cardioverter-defibrillator. N Engl J Med. 2010;363:36–44.
330. Jarman JW, Lascelles K, Wong T, Markides V, Clague JR, Till J. Clinical experience of entirely subcutaneous implantable cardioverter-defibrillators in children and adults: cause for caution. Eur Heart J. 2012;33:1351–9.
331. Olde Nordkamp LR, Dabiri Abkenari L, Boersma LV, Maass AH, de Groot JR, van Oostrom AJHHM, et al. The entirely subcutaneous implantable cardioverter-defibrillator: initial clinical experience in a large Dutch cohort. J Am Coll Cardiol. 2012;60:1933–9.
332. Aydin A, Hartel F, Schluter M, Butter C, Kobe J, Seifert M, et al. Shock efficacy of subcutaneous implantable cardioverter-defibrillator for prevention of sudden cardiac death: initial multicenter experience. Circ Arrhythm Electrophysiol. 2012;5:913–9.
333. Jarman JW, Todd DM. United Kingdom national experience of entirely subcutaneous implantable cardioverter-defibrillator technology: important lessons to learn. Europace. 2013;15:1158–65.
334. Kobe J, Reinke F, Meyer C, Shin DI, Martens E, Kaab S, et al. Implantation and follow-up of totally subcutaneous versus conventional implantable cardioverter-defibrillators: a multicenter case-control study. Heart Rhythm. 2013;10:29–36.
335. Boersma L, Barr C, Knops R, Theuns D, Eckardt L, Neuzil P, et al.; EFFORTLESS Investigator Group. Implant and midterm outcomes of the subcutaneous implantable cardioverter-defibrillator registry: The EFFORTLESS Study. J Am Coll Cardiol. 2017;70:830–41.
336. Theuns DAMJ, Brouwer TF, Jones PW, Allavatam V, Donnelley S, Auricchio A, et al. Prospective blinded evaluation of a novel sensing methodology designed to reduce inappropriate shocks by the subcutaneous implantable cardioverter-defibrillator. Heart Rhythm. 2018;15:1515–22.
337. Wilkoff BL, Fauchier L, Stiles MK, Morillo CA, Al-Khatib SM, Almendral J, et al. 2015 HRS/EHRA/APHRS/SOLAECE expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. Heart Rhythm. 2016;13:e50–e86.
338. Moss AJ, Schuger C, Beck CA, Brown MW, Cannom DS, Daubert JP, et al.; MADIT-RIT Trial Investigators. Reduction in inappropriate therapy and mortality through ICD programming. N Engl J Med. 2012;367:2275–83.
339. Gasparini M, Proclemer A, Klersy C, Kloppe A, Lunati M, Ferrer JB, et al. Effect of long-detection interval vs standard-detection interval for implantable cardioverter-defibrillators on antitachycardia pacing and shock delivery: the ADVANCE III randomized clinical trial. JAMA. 2013;309:1903–11.
340. Porterfield C, DiMarco JP, Mason PK. Effectiveness of implantation of a subcutaneous implantable cardioverter-defibrillator in a patient with complete heart block and a pacemaker. Am J Cardiol. 2015;115:276–8.
341. Gemein C, Haj M, Schmitt J. Combining a subcutaneous ICD and a pacemaker with abdominal device location and bipolar epicardial left ventricular lead: First-in-man approach. Europace. 2016;18:1279.
342. Mondesert B, Dubuc M, Khairy P, Guerra PG, Gosselin G, Thibault B. Combination of a leadless pacemaker and subcutaneous defibrillator: first in-human report. HeartRhythm Case Rep. 2015;1:469–71.
343. Tjong FV, Brouwer TF, Smeding L, Kooiman KM, de Groot JR, Ligon D, et al. Combined leadless pacemaker and subcutaneous implantable defibrillator therapy: feasibility, safety, and performance. Europace. 2016;18:1740–7.
344. Huang J, Patton KK, Prutkin JM. Concomitant use of the subcutaneous implantable cardioverter defibrillator and a permanent pacemaker. Pacing Clin Electrophysiol. 2016;39:1240–5.
345. Olde Nordkamp LR, Knops RE, Bardy GH, Blaauw Y, Boersma LVA, Bos JS, et al. Rationale and design of the PRAETORIAN trial: A Prospective, RAndomizEd comparison of subcuTaneOus and tRansvenous ImplANtable cardioverter-defibrillator therapy. Am Heart J. 2012;163(753–760):e2.
346. Cazeau S, Ritter P, Bakdach S, Lazarus A, Limousin M, Henao L, et al. Four chamber pacing in dilated cardiomyopathy. Pacing Clin Electrophysiol. 1994;17:1974–9.
347. Bakker PF, Meijburg HW, de Vries JW, Mower MM, Thomas AC, Hull ML, et al. Biventricular pacing in end-stage heart failure improves functional capacity and left ventricular function. J Interv Card Electrophysiol. 2000;4:395–404.
348. Cazeau S, Leclercq C, Lavergne T, Walker S, Varma C, Linde C, et al.; Multisite Stimulation in Cardiomyopathies (MUSTIC) Study Investigators. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. N Engl J Med. 2001;344:873–80.
349. Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, et al. MIRACLE Study Group [Multicenter InSync Randomized Clinical Evaluation]. Cardiac resynchronization in chronic heart failure. N Engl J Med. 2002;346:1845–53.
350. Leclercq C, Walker S, Linde C, Clementy J, Marshall AJ, Ritter P, et al. Comparative effects of permanent biventricular and right-univentricular pacing in heart failure patients with chronic atrial fibrillation. Eur Heart J. 2002;23:1780–7.
351. Auricchio A, Stellbrink C, Sack S, Block M, Vogt J, Bakker P, et al.; Pacing Therapies in Congestive Heart Failure (PATH-CHF) Study Group. Long-term clinical effect of hemodynamically optimized cardiac resynchronization therapy in patients with heart failure and ventricular conduction delay. J Am Coll Cardiol. 2002;39:2026–33.
352. Young JB, Abraham WT, Smith AL, Leon AR, Lieberman R, Wilkoff B, et al. Multicenter InSync ICD Randomized Clinical Evaluation (MIRACLE ICD) Trial Investigators. Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: The MIRACLE ICD Trial. JAMA. 2003;289:2685–94.
353. Higgins SL, Hummel JD, Niazi IK, Giudici MC, Worley SJ, Saxon LA, et al. Cardiac resynchronization therapy for the treatment of heart failure in patients with intraventricular conduction delay and malignant ventricular tachyarrhythmias. J Am Coll Cardiol. 2003;42:1454–9.
354. Abraham WT, Young JB, Leon AR, Adler S, Bank AJ, Hall SA, et al.; Multicenter InSync ICD II Study Group. Effects of cardiac resynchronization on disease progression in patients with left ventricular systolic dysfunction: an indication for an implantable cardioverter-defibrillator, and mildly symptomatic chronic heart failure. Circulation. 2004;110:2864–8.
355. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, et al.; Cardiac Resynchronization-Heart Failure (CARE-HF) Study Investigators. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med. 2005;352:1539–49.
356. Salukhe TV, Dimopoulos K, Francis D. Cardiac resynchronization may reduce all-cause mortality: meta-analysis of preliminary COMPANION data with CONTAK-CD, InSync ICD, MIRACLE and MUSTIC. Int J Cardiol. 2004;93:101–3.
357. Lindenfeld J, Feldman AM, Saxon L, Boehmer J, Carson P, Ghali JK, et al. Effects of cardiac resynchronization therapy with or without a defibrillator on survival and hospitalizations in patients with New York Heart Association class IV heart failure. Circulation. 2007;115:204–12.
358. Linde C, Abraham WT, Gold MR, St John Sutton M, Ghio S, Daubert C, et al. Randomized trial of cardiac resynchronization in mildly symptomatic heart failure patients and in asymptomatic

patients with left ventricular dysfunction and previous heart failure symptoms. J Am Coll Cardiol. 2008;52:1834–43.
359. Moss AJ, Hall WJ, Cannom DS, Klein H, Brown MW, Daubert JP, et al.; MADIT-CRT Trial Investigators. Cardiac-resynchronization therapy for the prevention of heart-failure events. N Engl J Med. 2009;361:1329–38.
360. Tang AS, Wells GA, Talajic M, Arnold MO, Sheldon R, Connolly S, et al.; Resynchronization-Defibrillation for Ambulatory Heart Failure Trial Investigators. Cardiac-resynchronization therapy for mild-to-moderate heart failure. N Engl J Med. 2010;363:2385–95.
361. Sipahi I, Chou JC, Hyden M, Rowland DY, Simon DI, Fang JC, et al. Effect of QRS morphology on clinical event reduction with cardiac resynchronization therapy: meta-analysis of randomized controlled trials. Am Heart J. 2012;163(260–267):e3.
362. Aranda JM, Conti JB, Johnson JW, Petersen-Stejskal S, Curtis AB. Cardiac resynchronization therapy in patients with heart failure and conduction abnormalities other than left bundle-branch block: analysis of the Multicenter InSync Randomized Clinical Evaluation (MIRACLE). Clin Cardiol. 2004;27:678–82.
363. Egoavil CA, Ho RT, Greenspon AJ, Pavri BB. Cardiac resynchronization therapy in patients with right bundle branch block: analysis of pooled data from the MIRACLE and Contak CD trials. Heart Rhythm. 2005;2:611–5.
364. Jeevanantham V, Zareba W, Navaneethan S, Fitzgerald D, Yu CM, Achilli A, et al. Metaanalysis on effects of cardiac resynchronization therapy in heart failure patients with narrow QRS complex. Cardiol J. 2008;15:230–6.
365. Cazeau SJ, Daubert JC, Tavazzi L, Frohlig G, Paul V. Responders to cardiac resynchronization therapy with narrow or intermediate QRS complexes identified by simple echocardiographic indices of dyssynchrony: The DESIRE study. Eur J Heart Fail. 2008;10:273–80.
366. Beshai JF, Grimm RA, Nagueh SF, Baker JH 2nd, Beau SL, Greenberg SM, et al.; RethinQ Study Investigators. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. N Engl J Med. 2007;357:2461–71.
367. Ruschitzka F, Abraham WT, Singh JP, Bax JJ, Borer JS, Brugada J, et al.; EchoCRT Study Group. Cardiac-resynchronization therapy in heart failure with a narrow QRS complex. N Engl J Med. 2013;369:1395–405.
368. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al.; ESC Scientific Document Group. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016;37:2129–200 (erratum in Eur Heart J 2018; 39: 860).
369. Sze E, Samad Z, Dunning A, Campbell KB, Loring Z, Atwater BD, et al. Impaired recovery of left ventricular function in patients with cardiomyopathy and left bundle branch block. J Am Coll Cardiol. 2018;71:306–17 (erratum in J Am Coll Cardiol 2018; 71: 1296).
370. De Pooter J, Kamoen V, El Haddad M, Stroobandt R, De Buyzere M, Jordaens L, et al. Gender differences in electro-mechanical characteristics of left bundle branch block: Potential implications for selection and response of cardiac resynchronization therapy. Int J Cardiol. 2018;257:84–91.
371. Varma N, Sogaard P, Bax JJ, Abraham WT, Borer JS, Dickstein K, et al. Interaction of left ventricular size and sex on outcome of cardiac resynchronization therapy among patients with a narrow QRS duration in the EchoCRT Trial. J Am Heart Assoc. 2018;7:e009592 (erratum in J Am Heart Assoc 2018; 7: e004259).
372. Normand C, Linde C, Singh J, Dickstein K. Indications for cardiac resynchronization therapy: A comparison of the major international guidelines. JACC Heart Fail. 2018;6:308–16.
373. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al. ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol. 2013;2013(62):e147–e239.
374. Ezekowitz JA, O'Meara E, McDonald MA, Abrams H, Chan M, Ducharme A, et al. 2017 comprehensive update of the Canadian Cardiovascular Society guidelines for the management of heart failure. Can J Cardiol. 2017;33:1342–433.
375. Mullens W, Kepa J, De Vusser P, Vercammem J, Rivero-Ayerza M, Wagner P, et al. Importance of adjunctive heart failure optimization immediately after implantation to improve long-term outcomes with cardiac resynchronization therapy. Am J Cardiol. 2011;108:409–15.
376. Wilkoff BL, Cook JR, Epstein AE, Greene HL, Hallstrom AP, Hsia H, et al.; Dual Chamber and VVI Implantable Defibrillator Trial Investigators. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. JAMA. 2002;288:3115–23.
377. Sweeney MO, Hellkamp AS, Ellenbogen KA, Greenspon AJ, Freedman RA, Lee KL, et al.; MOde Selection Trial Investigators. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. Circulation. 2003;107:2932–7.
378. Curtis AB, Worley SJ, Adamson PB, Chung ES, Niazi I, Sherfesee L, et al. Biventricular versus Right Ventricular Pacing in Heart Failure Patients with Atrioventricular Block (BLOCK HF) Trial Investigators. Biventricular pacing for atrioventricular block and systolic dysfunction. N Engl J Med. 2013;368:1585–93.
379. Slotwiner DJ, Raitt MH, Del-Carpio Munoz F, Mulpuru SK, Nasser N, Peterson PN. Impact of physiologic pacing versus right ventricular pacing among patients with left ventricular ejection fraction greater than 35%: a systematic review for the 2018 ACC/AHA/HRS guideline on the evaluation and management of patients with bradycardia and cardiac conduction delay. J Am Coll Cardiol. 2019;74:988–1008.
380. Kindermann M, Hennen B, Jung J, Giesel J, Bohm M, Frohlig G. Biventricular versus conventional right ventricular stimulation for patients with standard pacing indication and left ventricular dysfunction: The Homburg Biventricular Pacing Evaluation (HOBIPACE). J Am Coll Cardiol. 2006;47:1927–37.
381. Leclercq C, Cazeau S, Lellouche D, Fossati F, Anselme F, Davy JM, et al. Upgrading from single chamber right ventricular to biventricular pacing in permanently paced patients with worsening heart failure: The RD-CHF Study. Pacing Clin Electrophysiol. 2007;30(Suppl):S23–S30.
382. Paparella G, Sciarra L, Capulzini L, Francesconi A, De Asmundis C, Sarkozy A, et al. Long-term effects of upgrading to biventricular pacing: differences with cardiac resynchronization therapy as primary indication. Pacing Clin Electrophysiol. 2010;33:841–9.
383. van Geldorp IE, Vernooy K, Delhaas T, Prins MH, Crijns HJ, Prinzen FW, et al. Beneficial effects of biventricular pacing in chronically right ventricular paced patients with mild cardiomyopathy. Europace. 2010;12:223–9.
384. Maisel WH, Stevenson LW. Atrial fibrillation in heart failure: epidemiology, pathophysiology, and rationale for therapy. Am J Cardiol. 2003;91(Suppl):2–8.
385. Tolosana JM, Hernandez Madrid A, Brugada J, Sitges M, Garcia Bolao I, Fernandez Lozano I, et al. Comparison of benefits and mortality in cardiac resynchronization therapy in patients with atrial fibrillation versus patients in sinus rhythm (Results of the Spanish Atrial Fibrillation and Resynchronization [SPARE] Study). Am J Cardiol. 2008;102:444–9.

386. Ruwald AC, Pietrasik G, Goldenberg I, Kutyifa V, Daubert JP, Ruwald MH, et al. The effect of intermittent atrial tachyarrhythmia on heart failure or death in cardiac resynchronization therapy with defibrillator versus implantable cardioverter-defibrillator patients: A MADIT-CRT substudy (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy). J Am Coll Cardiol. 2014;63:1190–7.
387. Healey JS, Hohnloser SH, Exner DV, Birnie DH, Parkash R, Connolly SJ, et al. Cardiac resynchronization therapy in patients with permanent atrial fibrillation: results from the Resynchronization for Ambulatory Heart Failure Trial (RAFT). Circ Heart Fail. 2012;5:566–70.
388. Kalscheur MM, Saxon LA, Lee BK, Steinberg JS, Mei C, Buhr KA, et al. Outcomes of cardiac resynchronization therapy in patients with intermittent atrial fibrillation or atrial flutter in the COMPANION trial. Heart Rhythm. 2017;14:858–65.
389. Koplan BA, Kaplan AJ, Weiner S, Jones PW, Seth M, Christman SA. Heart failure decompensation and all-cause mortality in relation to percent biventricular pacing in patients with heart failure: is a goal of 100% biventricular pacing necessary? J Am Coll Cardiol. 2009;53:355–60.
390. Hayes DL, Boehmer JP, Day JD, Gilliam FR 3rd, Heidenreich PA, Seth M, et al. Cardiac resynchronization therapy and the relationship of percent biventricular pacing to symptoms and survival. Heart Rhythm. 2011;8:1469–75.
391. Marrouche NF, Brachmann J, Andresen D, Siebels J, Boersma L, Jordaens L, et al.; CASTLE-AF Investigators. Catheter ablation for atrial fibrillation with heart failure. N Engl J Med. 2018;378:417–27.
392. Gasparini M, Leclercq C, Lunati M, Landolina M, Auricchio A, Santini M, et al. Cardiac resynchronization therapy in patients with atrial fibrillation: the CERTIFY study (Cardiac Resynchronization Therapy in Atrial Fibrillation Patients Multinational Registry). JACC Heart Fail. 2013;1:500–7.
393. Rivero-Ayerza M, Theuns DA, Garcia-Garcia HM, Boersma E, Simoons M, Jordaens LJ. Effects of cardiac resynchronization therapy on overall mortality and mode of death: a meta-analysis of randomized controlled trials. Eur Heart J. 2006;27:2682–8.
394. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, et al. Longer-term effects of cardiac resynchronization therapy on mortality in heart failure [the CArdiac REsynchronization-Heart Failure (CARE-HF) trial extension phase]. Eur Heart J. 2006;27:1928–32.
395. Auricchio A, Metra M, Gasparini M, Lamp B, Klersy C, Curnis A, et al.; Multicenter Longitudinal Observational Study (MILOS) Group. Long-term survival of patients with heart failure and ventricular conduction delay treated with cardiac resynchronization therapy. Am J Cardiol. 2007;99:232–8.
396. Salukhe TV, Francis DP, Sutton R. Comparison of medical therapy, pacing and defibrillation in heart failure (COMPANION) trial terminated early: combined biventricular pacemaker-defibrillators reduce all-cause mortality and hospitalization. Int J Cardiol. 2003;87:119–20.
397. Alonso C, Leclercq C, d'Allonnes FR, Pavin D, Victor F, Mabo P, et al. Six year experience of transvenous left ventricular lead implantation for permanent biventricular pacing in patients with advanced heart failure: technical aspects. Heart. 2001;8:405–10.
398. Crossley GH, Biffi M, Johnson B, Lin A, Hussin A, Cuffio A, et al. Performance of a novel left ventricular lead with short bipolar spacing for cardiac resynchronization therapy: primary results of the Attain Performa quadripolar left ventricular lead study. Heart Rhythm. 2015;12:751–8.
399. Sasaki T, Nemoto S, Tokumaru T, Morimoto T. Improvement of cardiac geometry and function after cardiac resynchronization therapy for relapsed deterioration of pediatric dilated cardiomyopathy due to a noncompacted left ventricle and cardiac dyssynchrony. Pediatr Cardiol. 2012;33:158–61.
400. van Dijk VF, Fanggiday J, Balt JC, Wijffels MCEF, Daeter EJ, Kelder JC, et al. Effects of epicardial versus transvenous left ventricular lead placement on left ventricular function and cardiac perfusion in cardiac resynchronization therapy: a randomized clinical trial. J Cardiovasc Electrophysiol. 2017;28:917–23.
401. Chen L, Fu H, Pretorius VG, Yang D, Wiste HJ, Yuan H, et al. clinical outcomes of cardiac resynchronization with epicardial left ventricular lead. Pacing Clin Electrophysiol. 2015;38:1201–9.
402. Rickard J, Johnston DR, Price J, Tedford R, Baranowski B, Bassiouny M, et al. Reverse ventricular remodeling and long-term survival in patients undergoing cardiac resynchronization with surgically versus percutaneously placed left ventricular pacing leads. Heart Rhythm. 2015;12:517–23.
403. Garikipati NV, Mittal S, Chaudhry F, Musat DL, Sichrovsky T, Preminger M, et al. Comparison of endovascular versus epicardial lead placement for resynchronization therapy. Am J Cardiol. 2014;113:840–4.
404. Navia JL, Atik FA, Grimm RA, Garcia M, Vega PR, Myhre U, et al. Minimally invasive left ventricular epicardial lead placement: surgical techniques for heart failure resynchronization therapy. Ann Thorac Surg. 2005;79:1536–44.
405. Fernandez AL, Garcia-Bengochea JB, Ledo R, Vega M, Amago A, Alverez J, et al. Minimally invasive surgical implantation of left ventricular epicardial leads for ventricular resynchronization using video-assisted thoracoscopy. Rev Esp Cardiol. 2004;57:313–9 [in English, Spanish].
406. Nesher N, Ganiel A, Paz Y, Kramer A, Mohr R, Ben-Gal Y, et al. Thoracoscopic epicardial lead implantation as an alternative to failed endovascular insertion for cardiac pacing and resynchronization therapy. Innovations (Phila). 2014;9:427–31.
407. Dekker AL, Phelps B, Dijkman B, van der Nagel T, van der Veen FH, Geskes GG, et al. Epicardial left ventricular lead placement for cardiac resynchronization therapy: optimal pace site selection with pressure-volume loops. J Thorac Cardiovasc Surg. 2004;127:1641–7.
408. Wilkoff BL, Love CJ, Byrd CL, Bongiorni MG, Carrillo RG, Crossley GH, et al.; Heart Rhythm Society. Transvenous lead extraction: Heart Rhythm Society expert consensus on facilities, training, indications, and patient management: this document was endorsed by the American Heart Association (AHA). Heart Rhythm. 2009;6:1085–104.
409. Kusumoto FM, Schoenfeld MH, Wilkoff BL, Berul C, Birgersdotter-Green UM, Carrillo R, et al. 2017 HRS expert consensus statement on cardiovascular implantable electronic device lead management and extraction. Heart Rhythm. 2017;14:e503–e551.
410. Nakatani S, Ohara T, Ashihara K, Izumi C, Iwanaga S, Eishi K, et al. Japanese Circulation Society Joint Working Group. JCS 2017 guideline on prevention and treatment of infective endocarditis. Circ J. 2019;83:1767–809 [in Japanese].
411. Levine GN, Gomes AS, Arai AE, Bluemke DA, Flamm SD, Kanal E, et al, American Heart Association Committee on Diagnostic and Interventional Cardiac Catheterization; American Heart Association Council on Clinical Cardiology; American Heart Association Council on Cardiovascular Radiology and Intervention. Safety of magnetic resonance imaging in patients with cardiovascular devices: An American Heart Association Scientific Statement from the Committee on Diagnostic and Interventional Cardiac Catheterization, Council on Clinical Cardiology, and the Council on Cardiovascular Radiology and Intervention: Endorsed by the American College of Cardiology Foundation, the North American Society for Cardiac Imaging, and the Society for Cardiovascular Magnetic Resonance. Circulation. 2007;116:2878–91.

412. Wazni O, Epstein LM, Carrillo RG, Love C, Adler SW, Riggio DW, et al. Lead extraction in the contemporary setting: The LExICon study: An observational retrospective study of consecutive laser lead extractions. J Am Coll Cardiol. 2010;55:579–86.
413. Bongiorni MG, Kennergren C, Butter C, Deharo JC, Kutarski A, Rinaldi CA, et al.; ELECTRa Investigators. The European Lead Extraction ConTRolled (ELECTRa) study: A European Heart Rhythm Association (EHRA) Registry of Transvenous Lead Extraction Outcomes. Eur Heart J. 2017;38:2995–3005.
414. 2019 Japanese Heart Rhythm Society statement on cardiac implantable electronic device lead extraction [in Japanese]. http://new.jhrs.or.jp/guideline/statement201908/ (Accessed Nov. 2018)
415. Walsh EP, Cecchin F. Arrhythmias in adult patients with congenital heart disease. Circulation. 2007;115:534–45.
416. Cohen MI, Rhodes LA, Wernovsky G, Gaynor JW, Spray TL, Rychik J. Atrial pacing: an alternative treatment for protein-losing enteropathy after the Fontan operation. J Thorac Cardiovasc Surg. 2001;121:582–3.
417. Beder SD, Gillette PC, Garson A Jr, Porter CB, McNamara DG. Symptomatic sick sinus syndrome in children and adolescents as the only manifestation of cardiac abnormality or associated with unoperated congenital heart disease. Am J Cardiol. 1983;51:1133–6.
418. Garson A, Bink-Boelkens M, Hesslein PS, Hordof AJ, Keane JF, Neches WH, et al. Atrial flutter in the young: a collaborative study of 380 cases. J Am Coll Cardiol. 1985;6:871–8.
419. Gelatt M, Hamilton RM, McCrindle BW, Connelly M, Davis A, Harris L, et al. Arrhythmia and mortality after the Mustard procedure: a 30-year single-center experience. J Am Coll Cardiol. 1997;29:194–201.
420. Stephenson EA, Casavant D, Tuzi J, Alexander ME, Law I, Serwer G, et al. Efficacy of atrial antitachycardia pacing using the Medtronic AT500 pacemaker in patients with congenital heart disease. Am J Cardiol. 2003;92:871–6.
421. Silka MJ, Manwill JR, Kron J, McAnulty JH. Bradycardia-mediated tachyarrhythmias in congenital heart disease and responses to chronic pacing at physiologic rates. Am J Cardiol. 1990;65:488–93.
422. Triedman JK, Alexander ME, Love BA, Collins KK, Berul CI, Bevilacqua LM, et al. Influence of patient factors and ablative technologies on outcomes of radiofrequency ablation of intra-atrial reentrant tachycardia in patients with congenital heart disease. J Am Coll Cardiol. 2002;39:1827–35.
423. Mavroudis C, Backer CL, Deal BJ, Johnsrude C, Strasburger J. Total cavopulmonary conversion and maze procedure for patients with failure of the Fontan operation. J Thorac Cardiovasc Surg. 2001;122:863–71.
424. Pinsky WW, Gillette PC, Garson A Jr, McNamara DG. Diagnosis, management, and long-term results of patients with congenital complete atrioventricular block. Pediatrics. 1982;69:728–33.
425. Jaeggi ET, Hamilton RM, Silverman ED, Zamora SA, Hornberger LK. Outcome of children with fetal, neonatal or childhood diagnosis of isolated congenital atrioventricular block: a single institution's experience of 30 years. J Am Coll Cardiol. 2002;39:130–7.
426. Kurita T, Ohe T, Marui N, Aihara H, Kamakura S, Matsuhisa M, et al. Bradycardia-induced abnormal QT prolongation in patients with complete atrioventricular block with torsades de pointes. Am J Cardiol. 1992;69:628–33.
427. Sholler GF, Walsh EP. Congenital complete heart block in patients without anatomic cardiac defects. Am Heart J. 1989;118:1193–8.
428. Michaelsson M, Jonzon A, Riesenfeld T. Isolated congenital complete atrioventricular block in adult life: a prospective study. Circulation. 1995;92:442–9.
429. Moak JP, Barron KS, Hougen TJ, Wiles HB, Sreeram BN, Cohen MH, et al. Congenital heart block: development of late-onset cardiomyopathy, a previously underappreciated sequela. J Am Coll Cardiol. 2001;37:238–42.
430. Villain E, Coastedoat-Chalumeau N, Marijon E, et al. Presentation and prognosis of complete atrioventricular block in childhood, according to maternal antibody status. J Am Coll Cardiol. 2006;48:1682–7.
431. Kim JJ, Friedman RA, Eidem BW, Boudjemline Y, Piette JC, Bonnet D. Ventricular function and long-term pacing in children with congenital complete atrioventricular block. J Cardiovasc Electrophysiol. 2007;18:373–7.
432. Tsujii N, Miyazaki A, Sakaguchi H, Kagisaki K, Yamamoto T, Matsuoka M, et al. High incidence of dilated cardiomyopathy after right ventricular inlet pacing in patients with congenital complete atrioventricular block. Circ J. 2016;80:1251–8.
433. Lillehei CW, Sellers BRC, Eliot RS. Chronic postsurgical complete heart block: with particular reference to prognosis, management, and a new P-wave pacemaker. J Thorac Cardiovasc Surg. 1963;46:436–56.
434. Weindling SN, Saul JP, Gamble WJ, Mayer JE, Wessel D, Walsh EP. Duration of complete atrioventricular block after congenital heart disease surgery. Am J Cardiol. 1998;82:525–7.
435. Banks MA, Jenson J, Kugler JD. Late development of atrioventricular block after congenital heart surgery in down syndrome. Am J Cardiol. 2001;88:86–9.
436. Gross GJ, Chiu CC, Hamilton RM, Kirsh JA, Stephenson EA. Natural history of postoperative heart block in congenital heart disease: implications for pacing intervention. Heart Rhythm. 2006;3:601–4.
437. Hokanson JS, Moller JH. Significance of early transient complete heart block as a predictor of sudden death late after operative correction of tetralogy of Fallot. Am J Cardiol. 2001;87:1271–7.
438. Villain E, Ouarda F, Beyler C, Sidi D, Abid F. Predictive factors for late complete atrio-ventricular block after surgical treatment for congenital cardiopathy. Arch Mal Coeur Vaiss. 2003;96:495–8. [in French].
439. Manolis AS. The deleterious consequences of right ventricular apical pacing: time to seek alternate site pacing. Pacing Clin Electrophysiol. 2006;29:298–315.
440. Janoušek J, van Geldorp IE, Krupičkova S, Rosenthal E, Nugent K, Tomaske M, et al. Working Group for Cardiac Dysrhythmias and Electrophysiology of the Association for European Pediatric Cardiology. Permanent cardiac pacing in children: Choosing the optimal pacing site: A multicenter study. Circulation. 2013;127:613–23.
441. van Geldorp IE, Vanagt WY, Prinzen FW, Delhaas T. Chronic ventricular pacing in children: toward prevention of pacing-induced heart disease. Heart Fail Rev. 2011;16:305–14.
442. Brugada J, Blom N, Sarquella-Brugada G, Blomstrom-Lundqvist C, Deanfield J, Janousek J, et al. Pharmacological and nonpharmacological therapy for arrhythmias in the pediatric population: EHRA and AEPC-Arrhythmia Working Group joint consensus statement. Europace. 2013;15:1337–82.
443. Deleted in proof.
444. Miyazaki A. Atrioventricular block: Diagnosis and treatment based on pathophysiology of pediatric diseases. Jpn J Pediatr Med. 2014;46:391–5. [in Japanese].
445. Konta L, Chubb MH, Bostock J, Rogers J, Rosenthal E. Twenty-seven years experience with transvenous pacemaker implantation in children weighing <10 kg. Circ Arrhythm Electrophysiol. 2016;9:e003422.
446. Khairy P, Landzberg MJ, Gatzoulis MA, Mercier LA, Fernandes SM, Côté JM, et al.; Epicardial Versus ENdocardial pacing and Thromboembolic events Investigators. Transvenous pacing leads and systemic thromboemboli in patients with intracardiac shunts: a multicenter study. Circulation. 2006;113:2391–7.

447. Bar-Cohen Y, Berul CI, Alexander ME, Fortescue EB, Walsh EP, Triedman JK, et al. Age, size, and lead factors alone do not predict venous obstruction in children and young adults with transvenous lead systems. J Cardiovasc Electrophysiol. 2006;17:754–9.
448. Furman S, Benedek ZM. Survival of implantable pacemaker leads: the Implantable Lead Registry. Pacing Clin Electrophysiol. 1990;13:1910–4.
449. Sachweh JS, Vazquez-Jimenez JF, Schondube FA, Daebritz SH, Dorge H, Muhler EG, et al. Twenty years experience with pediatric pacing: Epicardial and transvenous stimulation. Eur J Cardiothorac Surg. 2000;17:455–61.
450. Fortescue EB, Berul CI, Cecchin F, Walsh EP, Triedman JK, Alexander ME. Patient, procedural, and hardware factors associated with pacemaker lead failures in pediatrics and congenital heart disease. Heart Rhythm. 2004;1:150–9.
451. Cohen MI, Bush DM, Vetter VL, Tanel RE, Wieand TS, Gaynor JW, et al. Permanent epicardial pacing in pediatric patients: seventeen years of experience and 1200 outpatient visits. Circulation. 2001;103:2585–90.
452. Kwak JG, Kim SJ, Song JY, Choi EY, Lee SY, Shim WS, et al. Permanent epicardial pacing in pediatric patients: 12-year experience at a single center. Ann Thorac Surg. 2012;93:634–9.
453. Murayama H, Maeda M, Sakurai H, Usui A, Ueda Y. Predictors affecting durability of epicardial pacemaker leads in pediatric patients. J Thorac Cardiovasc Surg. 2008;135:361–6.
454. Paech C, Kostelka M, Dahnert I, Flosdorff P, Riede FT, Gebauer RA. Performance of steroid eluting bipolar epicardial leads in pediatric and congenital heart disease patients: 15 years of single center experience. J Cardiothorac Surg. 2014;9:84.
455. Kubus P, Materna O, Gebauer RA, Matejka T, Gebauer R, Tláskal T, et al. Permanent epicardial pacing in children: long-term results and factors modifying outcome. Europace. 2012;14:509–14.
456. Carreras EM, Duncan WJ, Djurdjev O, Campbell AIM. Cardiac strangulation following epicardial pacemaker implantation: a rare pediatric complication. J Thorac Cardiovasc Surg. 2015;149:522–7.
457. Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA, et al. 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy: The Task Force on Cardiac Pacing and Resynchronization Therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). Eur Heart J. 2013;34:2281–329.
458. Khairy P, Van Hare GF, Balaji S, Berul CI, Cecchin F, Cohen MI, et al. PACES/HRS expert consensus statement on the recognition and management of arrhythmias in adult congenital heart disease: Developed in partnership between the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Endorsed by the governing bodies of PACES, HRS, the American College of Cardiology (ACC), the American Heart Association (AHA), the European Heart Rhythm Association (EHRA), the Canadian Heart Rhythm Society (CHRS), and the International Society for Adult Congenital Heart Disease (ISACHD). Heart Rhythm. 2014;11:e102–e165.
459. Kelly AM, Porter CJ, McGoon MD, Espinosa RE, Osborn MJ, Hayes DL. Breath-holding spells associated with significant bradycardia: Successful treatment with permanent pacemaker implantation. Pediatrics. 2001;108:698–702.
460. Pfammatter JP, Paul T, Lehmann C, Kallfelz HC. Efficacy and proarrhythmia of oral sotalol in pediatric patients. J Am Coll Cardiol. 1995;26:1002–7.
461. Rhodes LA, Walsh EP, Gamble WJ, Triedman JK, Saul JP. Benefits and potential risks of atrial antitachycardia pacing after repair of congenital heart disease. Pacing Clin Electrophysiol. 1995;18:1005–16.
462. Koplan BA, Stevenson WG, Epstein LM, Aranki SF, Maisel WH. Development and validation of a simple risk score to predict the need for permanent pacing after cardiac valve surgery. J Am Coll Cardiol. 2003;41:795–801.
463. Dewey RC, Capeless MA, Levy AM. Use of ambulatory electrocardiographic monitoring to identify high-risk patients with congenital complete heart block. N Engl J Med. 1987;316:835–9.
464. Krongrad E. Prognosis for patients with congenital heart disease and postoperative intraventricular conduction defects. Circulation. 1978;57:867–70.
465. Suzuki T, Sumitomo N, Yoshimoto J, Miyazaki A, Hinokiyama K, Ushinohama H, et al. Current trends in use of implantable cardioverter defibrillators and cardiac resynchronization therapy with a pacemaker or defibrillator in Japanese pediatric patients: Results from a nationwide questionnaire survey. Circ J. 2014;78:1710–6.
466. Kozak LJ, Owings MF, Hall MJ. National Hospital Discharge Survey: 2002 annual summary with detailed diagnosis and procedure data. Vital Health Stat 13. 2005;158:1–199.
467. Mitani Y, Ohta K, Ichida F, Nii M, Arakaki Y, Ushinohama H, et al. Circumstances and outcomes of out-of-hospital cardiac arrest in elementary and middle school students in the era of public-access defibrillation. Circ J. 2014;78:701–7.
468. Pilmer CM, Kirsh JA, Hildebrandt D, Krahn AD, Gow RM. Sudden cardiac death in children and adolescents between 1 and 19 years of age. Heart Rhythm. 2014;11:239–45.
469. Gasparini M, Mantica M, Galimberti P, Coltorti F, Ceriotti C, Priori SG. Inferior vena cava loop of the implantable cardioverter defibrillator endocardial lead: a possible solution of the growth problem in pediatric implantation. Pacing Clin Electrophysiol. 2000;23:2108–12.
470. Kantoch MJ, Rebeyka IM, Houlden LA, Dyck JD. Direct intracardiac placement of an automatic implantable cardioverter defibrillator coil lead in a small child. Europace. 2007;9:669–71.
471. Stephenson EA, Batra AS, Knilans TK, Gow RM, Gradaus R, Balaji S, et al. A multicenter experience with novel implantable cardioverter defibrillator configurations in the pediatric and congenital heart disease population. J Cardiovasc Electrophysiol. 2006;17:41–6.
472. Bordachar P, Marquie C, Pospiech T, Pasquié JL, Jalal Z, Haissaguerre M, et al. Subcutaneous implantable cardioverter defibrillators in children, young adults and patients with congenital heart disease. Int J Cardiol. 2016;203:251–8.
473. Burke MC, Gold MR, Knight BP, Barr CS, Theuns DAMJ, Boersma LVA, et al. Safety and efficacy of the totally subcutaneous implantable defibrillator: 2-year results from a pooled analysis of the IDE study and EFFORTLESS registry. J Am Coll Cardiol. 2015;65:1605–15.
474. Silka MJ, Kron J, Dunnigan A, Dick M 2nd. Sudden cardiac death and the use of implantable cardioverter-defibrillators in pediatric patients: the Pediatric Electrophysiology Society. Circulation. 1993;87:800–7.
475. Hamilton RM, Dorian P, Gow RM, Williams WG. Five-year experience with implantable defibrillators in children. Am J Cardiol. 1996;77:524–6.
476. Alexander ME, Cecchin F, Walsh EP, Triedman JK, Bevilacqua LM, Berul CI. Implications of implantable cardioverter defibrillator therapy in congenital heart disease and pediatrics. J Cardiovasc Electrophysiol. 2004;15:72–6.
477. Choi GR, Porter CB, Ackerman MJ. Sudden cardiac death and channelopathies: a review of implantable defibrillator therapy. Pediatr Clin North Am. 2004;51:1289–303.
478. Koyak Z, de Groot JR, Van Gelder IC, Bouma BJ, van Dessel PF, Budts W, et al. Implantable cardioverter defibrillator therapy in adults with congenital heart disease: Who is at risk of shocks? Circ Arrhythm Electrophysiol. 2012;5:101–10.

479. Khairy P, Harris L, Landzberg MJ, Viswanathan S, Barlow A, Gatzoulis MA, et al. Implantable cardioverter-defibrillators in tetralogy of Fallot. Circulation. 2008;117:363–70.
480. Khairy P, Landzberg MJ, Gatzoulis MA, Gatzoulis MA, Lucron H, Lambert J, et al. Value of programmed ventricular stimulation after tetralogy of Fallot repair: a multicenter study. Circulation. 2004;109:1994–2000.
481. Gatzoulis MA, Till JA, Somerville J, Redington AN. Mechanoelectrical interaction in tetralogy of Fallot: QRS prolongation relates to right ventricular size and predicts malignant ventricular arrhythmias and sudden death. Circulation. 1995;92:231–7.
482. Gatzoulis MA, Balaji S, Webber SA, Sui SC, Hokanson JS, Poile C, et al. Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot: a multicentre study. Lancet. 2000;356:975–81.
483. Babu-Narayan SV, Kilner PJ, Li W, Moon JC, Goktekin O, Davlouros PA, et al. Ventricular fibrosis suggested by cardiovascular magnetic resonance in adults with repaired tetralogy of Fallot and its relationship to adverse markers of clinical outcome. Circulation. 2006;113:405–13.
484. Valente AM, Gauvreau K, Assenza GE, Babu-Narayan SV, Schreier J, Gatzoulis MA, et al. Contemporary predictors of death and sustained ventricular tachycardia in patients with repaired tetralogy of Fallot enrolled in the INDICATOR cohort. Heart. 2014;100:247–53.
485. Khairy P, Aboulhosn J, Gurvitz MZ, Opotowsky AR, Mongeon FP, Kay J, et al. Alliance for Adult Research in Congenital Cardiology (AARCC). Arrhythmia burden in adults with surgically repaired tetralogy of Fallot: a multi-institutional study. Circulation. 2010;122:868–75.
486. Nakazawa M, Shinohara T, Sasaki A, Echigo S, Kado H, Niwa K, et al. Study Group for Arrhythmias Long-Term After Surgery for Congenital Heart Disease: ALTAS-CHD study. Arrhythmias late after repair of tetralogy of Fallot: A Japanese multicenter study. Circ J. 2004;68:126–30.
487. Nollert G, Fischlein T, Bouterwek S, Böhmer C, Klinner W, Reichart B. Long-term survival in patients with repair of tetralogy of Fallot: 36-year follow-up of 490 survivors of the first year after surgical repair. J Am Coll Cardiol. 1997;30:1374–83.
488. Karamlou T, Silber I, Lao R, McCrindle BW, Harris L, Downer E, et al. Outcomes after late reoperation in patients with repaired tetralogy of Fallot: the impact of arrhythmia and arrhythmia surgery. Ann Thorac Surg. 2006;81:1786–93.
489. Khairy P, Harris L, Landzberg MJ, Fernandes SM, Barlow A, Mercier LA, et al. Sudden death and defibrillators in transposition of the great arteries with intra-atrial baffles: a multicenter study. Circ Arrhythm Electrophysiol. 2008;1:250–7.
490. Mushlin AI, Hall WJ, Zwanziger J, Gajary E, Andrews M, Marron R, et al. The cost-effectiveness of automatic implantable cardiac defibrillators: results from MADIT [Multicenter Automatic Defibrillator Implantation Trial]. Circulation. 1998;97:2129–35.
491. Kammeraad JA, van Deurzen CH, Sreeram N, Bink-Boelkens MTH, Ottenkamp J, Helbing WA, et al. Predictors of sudden cardiac death after Mustard or Senning repair for transposition of the great arteries. J Am Coll Cardiol. 2004;44:1095–102.
492. Triedman JK. Should patients with congenital heart disease and a systemic ventricular ejection fraction less than 30% undergo prophylactic implantation of an ICD? Implantable cardioverter defibrillator implantation guidelines based solely on left ventricular ejection fraction do not apply to adults with congenital heart disease. Circ Arrhythm Electrophysiol. 2008;1:307–16.
493. Graham TP, Bernard YD, Mellen BG, Celermajer D, Baumgartner H, Cetta F, et al. Long-term outcome in congenitally corrected transposition of the great arteries: a multi-institutional study. J Am Coll Cardiol. 2000;36:255–61.
494. Cheezum MK, Liberthson RR, Shah NR, Villines TC, O'Gara PT, Landzberg MJ, et al. Anomalous aortic origin of a coronary artery from the inappropriate sinus of Valsalva. J Am Coll Cardiol. 2017;69:1592–608.
495. Brothers JA, McBride MG, Seliem MA, Marino BS, Tomlinson RS, Pampaloni MH, et al. Evaluation of myocardial ischemia after surgical repair of anomalous aortic origin of a coronary artery in a series of pediatric patients. J Am Coll Cardiol. 2007;50:2078–82.
496. Afari ME, Rehman MU, Atalay MK, Broderick RJ. Multimodal imaging after sudden cardiac arrest in an 18-year-old athlete. Tex Heart Inst J. 2015;42:548–51.
497. Nagashima K, Hiro T, Fukamachi D, Okumura Y, Watanabe I, Hirayama A, et al. Anomalous origin of coronary arteries coursing between the great vessels presenting with a cardiovascular event (J-CONOMALY Registry). Eur Heart J Cardiovasc Imaging. 2020;21:222–30.
498. Janousek J, Gebauer RA, Abdul-Khaliq H, Turner M, Kornyei L, Grollmuss O, et al. Working Group for Cardiac Dysrhythmias and Electrophysiology of the Association for European Paediatric Cardiology. Cardiac resynchronisation therapy in paediatric and congenital heart disease: Differential effects in various anatomical and functional substrates. Heart. 2009;95:1165–71.
499. Chen CA, Hsiao CH, Wang JK, Lin MT, Wu ET, Chiu SN, et al. Implication of QRS prolongation and its relation to mechanical dyssynchrony in idiopathic dilated cardiomyopathy in childhood. Am J Cardiol. 2009;103:103–9.
500. Dubin AM, Janousek J, Rhee E, Strieper MJ, Cecchin F, Law IH, et al. Resynchronization therapy in pediatric and congenital heart disease patients: an international multicenter study. J Am Coll Cardiol. 2005;46:2277–83.
501. Khairy P, Fournier A, Thibault B, Dubuc M, Thérien J, Vobecky SJ. Cardiac resynchronization therapy in congenital heart disease. Int J Cardiol. 2006;109:160–8.
502. Cecchin F, Frangini PA, Brown DW, Fynn-Thompson F, Alexander ME, Triedman JK, et al. Cardiac resynchronization therapy (and multisite pacing) in pediatrics and congenital heart disease: Five years experience in a single institution. J Cardiovasc Electrophysiol. 2009;20:58–65.
503. Jauvert G, Rousseau-Paziaud J, Villain E, Iserin L, Hidden-Lucet F, Ladoucer M, et al. Effects of cardiac resynchronization therapy on echocardiographic indices, functional capacity, and clinical outcomes of patients with a systemic right ventricle. Europace. 2009;11:184–90.
504. Janousek J, Tomek V, Chaloupecky VA, Reich O, Gebauer RA, Kautzner J, et al. Cardiac resynchronization therapy: a novel adjunct to the treatment and prevention of systemic right ventricular failure. J Am Coll Cardiol. 2004;44:1927–31.
505. Miyazaki A, Sakaguchi H, Noritake K, Hayama Y, Negishi J, Kagisaki K, et al. Interventricular dyssynchrony in a patient with a biventricular physiology and a systemic right ventricle. Heart Vessels. 2017;32:234–9.
506. Miyazaki A, Sakaguchi H, Kagisaki K, Kagisaki K, Tsujii N, Matsuoka M, et al. Optimal pacing sites for cardiac resynchronization therapy for patients with a systemic right ventricle with or without a rudimentary left ventricle. Europace. 2016;18:100–12.
507. Thambo JB, De Guillebon M, Xhaet O, Dos Santos P, Roubertie F, Labrousse L, et al. Biventricular pacing in patients with tetralogy of Fallot: Non-invasive epicardial mapping and clinical impact. Int J Cardiol. 2013;163:170–4.
508. Dubin AM, Feinstein JA, Reddy VM, Hanley FL, Van Hare GF, Rosenthal DN. Electrical resynchronization: a novel therapy for the failing right ventricle. Circulation. 2003;107:2287–9.

509. Kubuš P, Materna O, Tax P, Tomek V, Janoušek J. Successful permanent resynchronization for failing right ventricle after repair of tetralogy of Fallot. Circulation. 2014;130:e186–e190.
510. Janoušek J, Kovanda J, Ložek M, Tomek V, Vojtovič P, Gebauer R, et al. Pulmonary right ventricular resynchronization in congenital heart disease: acute improvement in right ventricular mechanics and contraction efficiency. Circ Cardiovasc Imaging. 2017;10:e006424.
511. Vojtovic P, Kucera F, Kubuš P, Gebauer R, Matejka T, Tláskal T, et al. Acute right ventricular resynchronization improves haemodynamics in children after surgical repair of tetralogy of Fallot. Europace. 2018;20:323–8.
512. van Geldorp IE, Bordachar P, Lumens J, de Guillebon M, Whinnett ZI, Prinzen FW, et al. Acute hemodynamic benefits of biventricular and single-site systemic ventricular pacing in patients with a systemic right ventricle. Heart Rhythm. 2013;10:676–82.
513. Thambo JB, Bordachar P, Garrigue S, Lafitte S, Sanders P, Reuter S, et al. Detrimental ventricular remodeling in patients with congenital complete heart block and chronic right ventricular apical pacing. Circulation. 2004;110:3766–72.
514. Gebauer RA, Tomek V, Kubus P, Razek V, Matejka T, Salameh A, et al. Differential effects of the site of permanent epicardial pacing on left ventricular synchrony and function in the young: Implications for lead placement. Europace. 2009;11:1654–9.
515. Tomaske M, Breithardt OA, Balmer C, Bauersfeld U. Successful cardiac resynchronization with single-site left ventricular pacing in children. Int J Cardiol. 2009;136:136–43.
516. Janousek J, Vojtovic P, Hucin B, Tláskal T, Gebauer RA, Gebauer R, et al. Resynchronization pacing is a useful adjunct to the management of acute heart failure after surgery for congenital heart defects. Am J Cardiol. 2001;88:145–52.
517. Edvardsson N, Frykman V, van Mechelen R, Mitro P, Mohii-Oskarsson A, Pasquié JL, et al.; PICTURE Study Investigators. Use of an implantable loop recorder to increase the diagnostic yield in unexplained syncope: results from the PICTURE registry. Europace. 2011;13:262–9.
518. Brignole M, Vardas P, Hoffman E, Vardas P, Hoffman E, Huikuri H, et al.; Task Force members. Indications for the use of diagnostic implantable and external ECG loop recorders. Europace. 2009;11:671–87.
519. Gladstone DJ, Spring M, Dorian P, Panzov V, Thorpe KE, Hall J, et al. EMBRACE Investigators and Coordinators. Atrial fibrillation in patients with cryptogenic stroke. N Engl J Med. 2014;370:2467–77.
520. Sanna T, Diener HC, Passman RS, Di Lazzaro V, Bernstein RA, Morillo CA, et al.; CRYSTAL AF Investigators. Cryptogenic stroke and underlying atrial fibrillation. N Engl J Med. 2014;370:2478–86.
521. Kohno R, Abe H, Benditt DG. Ambulatory electrocardiogram monitoring devices for evaluating transient loss of consciousness or other related symptoms. J Arrhythm. 2017;33:583–9.
522. Solomon SD, Zelenkofske S, McMurray JJ, Finn PV, Velazquez E, Ertl G, et al.; Valsartan in Acute Myocardial Infarction Trial (VALIANT) Investigators. Sudden death in patients with myocardial infarction and left ventricular dysfunction, heart failure, or both. N Engl J Med. 2005;352:2581–8.
523. Steinbeck G, Andresen D, Seidl K, Brachmann J, Hoffmann E, Wojciechowski D, et al.; IRIS Investigators. Defibrillator implantation early after myocardial infarction. N Engl J Med. 2009;361:1427–36.
524. JCS Joint Working Group. Guidelines for non-pharmacotherapy of cardiac arrhythmias (JCS 2011). Circ J. 2013;77:249–74.
525. Epstein AE, Abraham WT, Bianco NR, Kern KB, Mirro M, Rao SV, et al. Wearable cardioverter-defibrillator use in patients perceived to be at high risk early post-myocardial infarction. J Am Coll Cardiol. 2013;62:2000–7.
526. Wasnig NK, Gunther M, Quick S, Pfluecke C, Rottsttadt F, Szymkiewicz SJ, et al. Experience with the wearable cardioverter-defibrillator in patients at high risk for sudden cardiac death. Circulation. 2016;134:635–43.
527. Piccini JP, Allen LA, Kudenchuk PJ, Page RL, Patel MR, Turakhia MO, et al. American Heart Association Electrocardiography and Arrhythmias Committee of the Council on Clinical Cardiology and Council on Cardiovascular and Stroke Nursing. Wearable cardioverter-defibrillator therapy for the prevention of sudden cardiac death: A Science Advisory from the American Heart Association. Circulation. 2016;133:1715–27.
528. Kishihara J, Niwano S, Nakamura H, Igarashi T, Ishizue N, Fujiishi T, et al. An appropriate shock of the wearable cardioverter-defibrillator in an outpatient setting. J Arrhythm. 2016;32:67–9.
529. Niwano S. WCD for prevention of sudden cardiac death after infected ICD removal. In: APHRS2017 Meeting.
530. Niwano S, Sekiguchi Y, Ishii Y, Iwasaki Y, Kato R, Okamura H, et al. Clinical usefulness of wearable cardioverter defibrillator (WCD) and current understanding of its clinical indication in Japan. Circ J. 2018;82:1481–6.
531. Kutyifa V, Moss AJ, Klein H, Biton Y, McNitt S, MacKecknie B, et al. Use of the wearable cardioverter defibrillator in high-risk cardiac patients: data from the Prospective Registry of Patients Using the Wearable Cardioverter Defibrillator (WEARIT-II Registry). Circulation. 2015;132:1613–9.
532. Bigger JT, Whang W, Rottman JN, Kleiger RE, Gottlieb CD, Namerow PB, et al. Mechanisms of death in the CABG Patch trial: a randomized trial of implantable cardiac defibrillator prophylaxis in patients at high risk of death after coronary artery bypass graft surgery. Circulation. 1999;99:1416–21.
533. Olgin JE, Pletcher MJ, Vittinghoff E, Wranicz J, Malik R, Morin DP, et al. Wearable cardioverter-defibrillator after myocardial infarction. N Engl J Med. 2018;379:1205–15.
534. McNamara DM, Starling RC, Cooper LT, Boehmer JP, Mather PJ, Janosko KM, et al. Clinical and demographic predictors of outcomes in recent onset dilated cardiomyopathy: results of the IMAC (Intervention in Myocarditis and Acute Cardiomyopathy)-2 study. J Am Coll Cardiol. 2011;58:1112–8.
535. Teeter WA, Thibodeau JT, Rao K, Brickner ME, Toto KH, Nelson LL, et al. The natural history of new-onset heart failure with a severely depressed left ventricular ejection fraction: implications for timing of implantable cardioverterdefibrillator implantation. Am Heart J. 2012;164:358–64.
536. Duncker D, Haghikia A, Konig T, Hohmann S, Gutleben KJ, Westenfeld R, et al. Risk for ventricular fibrillation in peripartum cardiomyopathy with severely reduced left ventricular function: value of the wearable cardioverter/defibrillator. Eur J Heart Fail. 2014;16:1331–6.
537. Tsuchihashi K, Ueshima K, Uchida T, Oh-mura N, Kimura K, Owa M, et al.; Angina Pectoris-Myocardial Infarction Investigations in Japan. Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. J Am Coll Cardiol. 2001;38:11–8.
538. Sharkey SW, Windenburg DC, Lesser JR, Maron MS, Hauser RG, Lesser JN, et al. Natural history and expansive clinical profile of stress (tako-tsubo) cardiomyopathy. J Am Coll Cardiol. 2010;55:333–41.
539. Gronda E, Bourge RC, Costanzo MR, Deng M, Mancini D, Martinelli L, et al. Heart rhythm considerations in heart transplant candidates and considerations for ventricular assist devices: International Society for Heart and Lung Transplantation guidelines for the care of cardiac transplant candidates 2006. J Heart Lung Transplant. 2006;25:1043–56.
540. Da Rosa MR, Sapp JL, Howlett JG, Falkenham A, Legare JF. Implantable cardioverter-defibrillator implantation as a bridge to cardiac transplantation. J Heart Lung Transplant. 2007;26:1336–9.

541. Schmidinger H. The implantable cardioverter defibrillator as a "bridge to transplant": a viable clinical strategy? Am J Cardiol. 1999;83(Suppl):151D–157D.
542. Klein HU, Meltendorf U, Reek S, Smid J, Kuss S, Cygankiewicz I, et al. Bridging a temporary high risk of sudden arrhythmic death: experience with the wearable cardioverter defibrillator (WCD). Pacing Clin Electrophysiol. 2010;33:353–67.
543. Scheinman MM, Morady F, Hess DS, Gonzalez R. Catheter-induced ablation of the atrioventricular junction to control refractory supraventricular arrhythmias. JAMA. 1982;248:851–5.
544. Gallagher JJ, Svenson RH, Kasell JH, German LD, Bardy GH, Broughton A, et al. Catheter technique for closed-chest ablation of the atrioventricular conduction system. N Engl J Med. 1982;306:194–200.
545. Jackman WM, Friday KJ, Scherlag BJ, Dehning MM, Schechter E, Reynolds DW, et al. Direct endocardial recording from an accessory atrioventricular pathway: localization of the site of block, effect of antiarrhythmic drugs, and attempt at nonsurgical ablation. Circulation. 1983;68:906–16.
546. Weber H, Schmitz L. Catheter technique for closed-chest ablation of an accessory atrioventricular pathway. N Engl J Med. 1983;308:653–4.
547. Lavergne T, Guize L, Le Heuzey JY, Carcone P, Geslin J, Cousin MT. Closed-chest atrioventricular junction ablation by high-frequency energy transcatheter desiccation. Lancet. 1986;328:858–9.
548. Davis MJ, Murdock C. Radiofrequency catheter ablation of refractory ventricular tachycardia. Pacing Clin Electrophysiol. 1988;11:725–9.
549. Borggrefe M, Budde T, Podczeck A, Breithardt G. High frequency alternating current ablation of an accessory pathway in humans. J Am Coll Cardiol. 1987;10:576–82.
550. Japanese Heart Rhythm Society Catheter Ablation Committee. JHRS 1990 guidelines for catheter ablation. Jpn J Cardiac Pacing Electrophysiology. 1990;6:381. [in Japanese].
551. Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med. 1998;339:659–66.
552. Pappone C, Rosanio S, Oreto G, Tocchi M, Gugliotta F, Vicedomini G, et al. Circumferential radiofrequency ablation of pulmonary vein ostia: a new anatomic approach for curing atrial fibrillation. Circulation. 2000;102:2619–28.
553. Haissaguerre M, Shoda M, Jais P, Nogami A, Shah DC, Kautzner J, et al. Mapping and ablation of idiopathic ventricular fibrillation. Circulation. 2002;106:962–7.
554. Nademanee K, Veerakul G, Chandanamattha P, Chaothawee L, Ariyachaipanich A, Jirasirirojanakorn K, et al. Prevention of ventricular fibrillation episodes in Brugada syndrome by catheter ablation over the anterior right ventricular outflow tract epicardium. Circulation. 2011;123:1270–9.
555. Sosa E, Scanavacca M, D'Avila A, Piccioni J, Sanchez O, Velarde JL, et al. Endocardial and epicardial ablation guided by nonsurgical transthoracic epicardial mapping to treat recurrent ventricular tachycardia. J Cardiovasc Electrophysiol. 1998;9:229–39.
556. Inoue K, Murakawa Y, Nogami A, Shoda M, Naito S, Kumagai K, et al.; Japanese Heart Rhythm Society Members. Current status of catheter ablation of atrial fibrillation in Japan: Summary of the 4th survey of the Japanese Catheter Ablation Registry of Atrial Fibrillation (J-CARAF). J Cardiol. 2016;68:83–8.
557. Yokoyama K, Nakagawa H, Wittkampf FH, Pitha JV, Lazzara R, Jackman WM. Comparison of electrode cooling between internal and open irrigation in radiofrequency ablation lesion depth and incidence of thrombus and steam pop. Circulation. 2006;113:11–9.
558. Yokoyama K, Nakagawa H, Shah DC, Lambert H, Leo G, Aeby N, et al. Novel contact force sensor incorporated in irrigated radiofrequency ablation catheter predicts lesion size and incidence of steam pop and thrombus. Circ Arrhythm Electrophysiol. 2008;1:354–62.
559. Merino JL, Arribas F, Botto GL, Huikuri H, Kraemer LI, Linde C, et al. 2005–2007 Accreditation Committee of the European Heart Rhythm Association: Core curriculum for the heart rhythm specialist. Europace. 2009;11(Suppl):iii1–iii26.
560. Tracy CM, Akhtar M, DiMarco JP, Packer DL, Weitz HH, Creager MA, et al. American College of Cardiology/American Heart Association 2006 update of the clinical competence statement on invasive electrophysiology studies, catheter ablation, and cardioversion: a report of the American College of Cardiology/American Heart Association/American College of Physicians Task Force on Clinical Competence and Training: Developed in collaboration with the Heart Rhythm Society. Circulation. 2006;114:1654–68.
561. American Board of Internal Medicine. Clinical cardiac electrophysiology policies. http://www.abim.org/certification/policies/internal-medicine-subspecialty-policies/clinical-cardiac-electrophysiology.aspx (Accessed Nov. 2018)
562. Social Insurance Union of Societies Related to Internal Medicine. A report about the actual load of medical staff for the informed consent (IC study) (Report No. 1) [in Japanese]. http://www.naihoren.jp/modules/activity/index.php?content_id=12 (Accessed Nov. 2018)
563. Chikata A, Kato T, Yaegashi T, Sakagami S, Kato C, Saeki T, et al. General anesthesia improves contact force and reduces gap formation in pulmonary vein isolation: a comparison with conscious sedation. Heart Vessels. 2017;32:997–1005.
564. Di Biase L, Conti S, Mohanty P, Bai R, Sanchez J, Walton D, et al. General anesthesia reduces the prevalence of pulmonary vein reconnection during repeat ablation when compared with conscious sedation: results from a randomized study. Heart Rhythm. 2011;8:368–72.
565. American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology. 2002;96:1004–17.
566. Japanese Society of Anesthesiologists. Guideline for usage of anesthetics and associated drugs (version 3) [in Japanese]. http://www.anesth.or.jp/guide/guideline-iyakuhin-index.html (Accessed Nov. 2018).
567. Murakami T, Yamaji H, Numa K, Kawamura H, Murakami M, Higashiya S, et al. Adaptive-servo ventilation combined with deep sedation is an effective strategy during pulmonary vein isolation. Europace. 2013;15:951–6.
568. Bagchi D, Mandal MC, Das S, Basu SR, Sarkar S, Das J. Bispectral index score and observer's assessment of awareness/sedation score may manifest divergence during onset of sedation: Study with midazolam and propofol. Indian J Anaesth. 2013;57:351–7.
569. Schultz A, Siedenberg M, Grouven U, Kneif T, Schultz B. Comparison of Narcotrend Index, Bispectral Index, spectral and entropy parameters during induction of propofol-remifentanil anaesthesia. J Clin Monit Comput. 2008;22:103–11.
570. Roguin A, Goldstein J, Bar O, Goldstein JA. Brain and neck tumors among physicians performing interventional procedures. Am J Cardiol. 2013;111:1368–72.
571. Japanese Circulation Society Joint Working Group. Guideline for radiation safety in interventional cardiology (JCS 2011) [in Japanese]. http://www.j-circ.or.jp/guideline/pdf/JCS2011_nagai_rad_h.pdf (Accessed Nov. 2018)
572. Stewart FA, Akleyev AV, Hauer-Jensen M, Hendry JH, Kleiman NJ, Macvittie TJ, et al. authors on behalf of ICRP. ICRP publication 118: ICRP statement on tissue reactions and early and late effects of radiation in normal tissues and organs: Threshold doses

for tissue reactions in a radiation protection context. Ann ICRP. 2012;41:1–322.
573. Heidbuchel H, Wittkampf FH, Vano E, Ernst S, Schilling R, Picano E, et al. Practical ways to reduce radiation dose for patients and staff during device implantations and electrophysiological procedures. Europace. 2014;16:946–64.
574. Christoph M, Wunderlich C, Moebius S, Forkmann M, Sitzy J, Salmas J, et al. Fluoroscopy integrated 3D mapping significantly reduces radiation exposure during ablation for a wide spectrum of cardiac arrhythmias. Europace. 2015;17:928–37.
575. Sommer P, Rolf S, Piorkowski C, Gaspar T, Huo Y, Piedra C, et al. Nonfluoroscopic catheter visualization in atrial fibrillation ablation: Experience from 375 consecutive procedures. Circ Arrhythm Electrophysiol. 2014;7:869–74.
576. Kasanuki H, Sugimoto T, Hiejima K, et al. Report of catheter ablation of arrhythmias in Japan since 1994. Jpn J Cardiac Pacing Electrophysiol. 1999;15:353–8. [in Japanese].
577. Murakawa Y, Nogami A, Hirao K, Shoda M, Aonuma K, Ikeguchi S, et al. A brief report on the nationwide survey of catheter ablation in Japan/the Japanese Catheter Ablation Registry (JCAR). J Arrhythm. 2012;28:122–6.
578. Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. Heart Rhythm. 2017;14:e275–e444.
579. Whitman IR, Gladstone RA, Badhwar N, Hsia HH, Lee BK, Josephson SA, et al. Brain emboli after left ventricular endocardial ablation. Circulation. 2017;135:867–77.
580. Deshmukh A, Patel NJ, Pant S, Shah N, Chothani A, Mehta K, et al. In-hospital complications associated with catheter ablation of atrial fibrillation in the United States between 2000 and 2010: Analysis of 93 801 procedures. Circulation. 2013;128:2104–12.
581. Michowitz Y, Rahkovich M, Oral H, Zado ES, Tilz R, John S, et al. Effects of sex on the incidence of cardiac tamponade after catheter ablation of atrial fibrillation: results from a worldwide survey in 34 943 atrial fibrillation ablation procedures. Circ Arrhythm Electrophysiol. 2014;7:274–80.
582. Murakawa Y, Yamane T, Goya M, Inoue K, Naito S, Kumagai K, et al.; Japanese Heart Rhythm Society Members. Incidence and predictors of pericardial effusion as an early complication of catheter ablation for atrial fibrillation: The Japanese Catheter Ablation Registry of Atrial Fibrillation (J-CARAF). J Arrhythm. 2017;33:430–3.
583. Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J, et al. Prevalence and causes of fatal outcome in catheter ablation of atrial fibrillation. J Am Coll Cardiol. 2009;53:1798–803.
584. Khan MY, Siddiqui WJ, Iyer PS, Dirweesh A, Karabulut N. Left atrial to esophageal fistula: a case report and literature review. Am J Case Rep. 2016;17:814–8.
585. Reddy VY, Shah D, Kautzner J, Schmidt B, Saoudi N, Herrera C, et al. The relationship between contact force and clinical outcome during radiofrequency catheter ablation of atrial fibrillation in the TOCCATA study. Heart Rhythm. 2012;9:1789–95.
586. Neuzil P, Reddy VY, Kautzner J, Petru J, Wichterle D, Shah D, et al. Electrical reconnection after pulmonary vein isolation is contingent on contact force during initial treatment: results from the EFFICAS I study. Circ Arrhythm Electrophysiol. 2013;6:327–33.
587. Nakagawa H, Ikeda A, Sharma T, Lazzara R, Jackman WM. Rapid high resolution electroanatomical mapping: evaluation of a new system in a canine atrial linear lesion model. Circ Arrhythm Electrophysiol. 2012;5:417–24.
588. Luther V, Sikkel M, Bennett N, Guerrero F, Leong K, Qureshi N, et al. Visualizing localized reentry with ultra-high density mapping in iatrogenic atrial tachycardia: beware pseudo-reentry. Circ Arrhythm Electrophysiol. 2017;10.
589. Kosiuk J, Portugal G, Hilbert S, John S, Oliveira M, Hindricks G, et al. In vivo validation of a novel algorithm for automatic premature ventricular contractions recognition. J Cardiovasc Electrophysiol. 2017;28:828–33.
590. Ernst S, Ouyang F, Linder C, Hertting K, Stahl F, Chun J, et al. Initial experience with remote catheter ablation using a novel magnetic navigation system: magnetic remote catheter ablation. Circulation. 2004;109:1472–5.
591. Kim AM, Turakhia M, Lu J, Badhwar N, Lee BK, Lee RJ, et al. Impact of remote magnetic catheter navigation on ablation fluoroscopy and procedure time. Pacing Clin Electrophysiol. 2008;31:1399–404.
592. Schmidt B, Tilz RR, Neven K, ulian Chun KR, Fürnkranz A, Ouyang F. Remote robotic navigation and electroanatomical mapping for ablation of atrial fibrillation: Considerations for navigation and impact on procedural outcome. Circ Arrhythm Electrophysiol. 2009;2:120–8.
593. Lin C, Pehrson S, Jacobsen PK, Chen X. Initial experience of a novel mapping system combined with remote magnetic navigation in the catheter ablation of atrial fibrillation. J Cardiovasc Electrophysiol. 2017;28:1387–92.
594. Thornton AS, Jordaens LJ. Remote magnetic navigation for mapping and ablating right ventricular outflow tract tachycardia. Heart Rhythm. 2006;3:691–6.
595. Dinov B, Schonbauer R, Wojdyla-Hordynska A, Braunschweig F, Richter S, Altmann D, et al. Long-term efficacy of single procedure remote magnetic catheter navigation for ablation of ischemic ventricular tachycardia: a retrospective study. J Cardiovasc Electrophysiol. 2012;23:499–505.
596. Arya A, Eitel C, Bollmann A, Wetzel U, Sommer P, Gaspar T, et al. Catheter ablation of scar-related ventricular tachycardia in patients with electrical storm using remote magnetic catheter navigation. Pacing Clin Electrophysiol. 2010;33:1312–8.
597. Ueda A, Suman-Horduna I, Mantziari L, Gujic M, Marchese P, Ho SY, et al. Contemporary outcomes of supraventricular tachycardia ablation in congenital heart disease: a single-center experience in 116 patients. Circ Arrhythm Electrophysiol. 2013;6:606–13.
598. Gaspar T, Kircher S, Arya A, Sommer P, Rolf S, Hindricks G, et al. Enhancement of intracardiac navigation by new GPS-guided location system (MediGuide Technologies). Europace. 2012;14(Suppl): ii24–ii25.
599. Bourier F, Reents T, Ammar-Busch S, Buiatti A, Grebmer C, Telishevska M, et al. Sensor-based electromagnetic navigation (MediguideR): How accurate is it? A phantom model study. J Cardiovasc Electrophysiol. 2015;26:1140–5.
600. Rolf S, John S, Gaspar T, Dinov B, Kircher S, Huo Y, et al. Catheter ablation of atrial fibrillation supported by novel nonfluoroscopic 4D navigation technology. Heart Rhythm. 2013;10:1293–300.
601. Sommer P, Wojdyla-Hordynska A, Rolf S, Gaspar T, Eitel C, Arya A, et al. Initial experience in ablation of typical atrial flutter using a novel three-dimensional catheter tracking system. Europace. 2013;15:578–81.
602. Thibault B, Mondesert B, Macle L, Dubuc M, Dyrda K, Talajic M, et al. Reducing radiation exposure during CRT implant procedures: Single-center experience with low-dose fluoroscopy settings and a sensor-based navigation system (MediGuide). J Cardiovasc Electrophysiol. 2016;27:1337–43.
603. Wolff L, Parkinson J, White PD. Bundle-branch block with short P-R interval in healthy young people prone to paroxysmal tachycardia. 1930. Ann Noninvasive Electrocardiol. 2006;11:340–53.
604. Rosenbaum F, Hecht H, Wilson F, Johnston FD. The potential variations of the thorax and the esophagus in anomalous atrioventricular excitation (Wolff-Parkinson-White syndrome). Am Heart J. 1945;29:281–326.

605. Ueda H, Nameki C, Saruta H, Kawamura H, Yoshida A, Tsuzuku A. Further studies on the W.P.W. syndrome (pre-excitation syndrome) with special reference to the intracardiac and esophageal lead. Jpn Circ J. 1957;21:361–75.
606. Arruda MS, McClelland JH, Wang X, Beckman KJ, Widman LE, Gonzalez MD, et al. Development and validation of an ECG algorithm for identifying accessory pathway ablation site in Wolff-Parkinson-White syndrome. J Cardiovasc Electrophysiol. 1998;9:2–12.
607. Jackman WM, Wang XZ, Friday KJ, Roman CA, Moulton KP, Beckman KJ, et al. Catheter ablation of accessory atrioventricular pathways (Wolff-Parkinson-White syndrome) by radiofrequency current. N Engl J Med. 1991;324:1605–11.
608. Calkins H, Yong P, Miller JM, Olshansky B, Carlson M, Saul JP, et al.; The Atakr Multicenter Investigators Group. Catheter ablation of accessory pathways, atrioventricular nodal reentrant tachycardia, and the atrioventricular junction: Final results of a prospective, multicenter clinical trial. Circulation. 1999;99:262–70.
609. Pappone C, Vicedomini G, Manguso F, Saviano M, Baldi M, Pappone A, et al. Wolff-Parkinson-White syndrome in the era of catheter ablation: insights from a registry study of 2169 patients. Circulation. 2014;130:811–9.
610. McClelland JH, Wang X, Beckman KJ, Hazlitt HA, Prior MI, Nakagawa H, et al. Radiofrequency catheter ablation of right atriofascicular (Mahaim) accessory pathways guided by accessory pathway activation potentials. Circulation. 1994;89:2655–66.
611. Page RL, Joglar JA, Caldwell MA, Calkins H, Conti JB, Deal BJ, et al. 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm. 2016;13:e136–e221.
612. Obeyesekere MN, Leong-Sit P, Massel D, Manlucu J, Modi S, Krahn AD, et al. Risk of arrhythmia and sudden death in patients with asymptomatic preexcitation: a meta-analysis. Circulation. 2012;125:2308–15.
613. Cohen MI, Triedman JK, Cannon BC, Davis AM, Drago F, Janousek J, et al. PACES/HRS expert consensus statement on the management of the asymptomatic young patient with a Wolff-Parkinson-White (WPW, ventricular preexcitation) electrocardiographic pattern: Developed in partnership between the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Endorsed by the governing bodies of PACES, HRS, the American College of Cardiology Foundation (ACCF), the American Heart Association (AHA), the American Academy of Pediatrics (AAP), and the Canadian Heart Rhythm Society (CHRS). Heart Rhythm. 2012;9:1006–24.
614. Klein GJ, Bashore TM, Sellers TD, Pritchett EL, Smith WM, Gallagher JJ. Ventricular fibrillation in the Wolff-Parkinson-White syndrome. N Engl J Med. 1979;301:1080–5.
615. Kugler JD, Danford DA, Houston K, Felix G. Radiofrequency catheter ablation for paroxysmal supraventricular tachycardia in children and adolescents without structural heart disease. Pediatric EP Society, Radiofrequency Catheter Ablation Registry. Am J Cardiol. 1997;80:1438–43.
616. Wackel P, Irving C, Webber S, Beerman L, Arora G. Risk stratification in Wolff-Parkinson-White syndrome: the correlation between noninvasive and invasive testing in pediatric patients. Pacing Clin Electrophysiol. 2012;35:1451–7.
617. Brugada J, Puigfel M, Mont L, Figueiredo M, Matas M, Navarro-Lopez F. Radiofrequency ablation of anteroseptal, para-Hisian, and mid-septal accessory pathways using a simplified femoral approach. Pacing Clin Electrophysiol. 1998;21:735–41.
618. Tai CT, Chen SA, Chiang CE, Lee SH, Chang MS. Electrocardiographic and electrophysiologic characteristics of anteroseptal, midseptal, and para-Hisian accessory pathways: implication for radiofrequency catheter ablation. Chest. 1996;109:730–40.
619. Lorga Filho A, Sosa E, Scanavacca M, d'Avila A, Kuniyoshi R, de Horta J, et al. Electrocardiographic identification of mid-septal accessory pathways in close proximity to the atrioventricular conduction system. Pacing Clin Electrophysiol. 1996;19:1984–7.
620. Haghjoo M, Kharazi A, Fazelifar AF, Alizadeh A, Emkanjoo Z, Sadr-Ameli MA. Electrocardiographic and electrophysiologic characteristics of anteroseptal, midseptal, and posteroseptal accessory pathways. Heart Rhythm. 2007;4:1411–9.
621. Heidbuchel H, Jackman WM. Characterization of subforms of AV nodal reentrant tachycardia. Europace. 2004;6:316–29.
622. Nakagawa H, Jackman WM. Catheter ablation of paroxysmal supraventricular tachycardia. Circulation. 2007;116:2465–78.
623. Kaneko Y, Naito S, Okishige K, Morishima I, Tobiume T, Nakajima T, et al. Atypical fast-slow atrioventricular nodal reentrant tachycardia incorporating a “superior” slow pathway: a distinct supraventricular tachyarrhythmia. Circulation. 2016;133:114–23.
624. Katritsis DG, Josephson ME. Classification of electrophysiological types of atrioventricular nodal re-entrant tachycardia: a reappraisal. Europace. 2013;15:1231–40.
625. Katritsis DG, Zografos T, Katritsis GD, Giazitzoglou E, Vachliotis V, Paxinos G, et al. Catheter ablation vs. antiarrhythmic drug therapy in patients with symptomatic atrioventricular nodal reentrant tachycardia: a randomized, controlled trial. Europace. 2017;19:602–6.
626. Jackman WM, Beckman KJ, McClelland JH, Wang X, Friday KJ, Roman CA, et al. Treatment of supraventricular tachycardia due to atrioventricular nodal reentry by radiofrequency catheter ablation of slow-pathway conduction. N Engl J Med. 1992;327:313–8.
627. Haissaguerre M, Gaita F, Fischer B, Commenges D, Montserrat P, d'Ivernois C, et al. Elimination of atrioventricular nodal reentrant tachycardia using discrete slow potentials to guide application of radiofrequency energy. Circulation. 1992;85:2162–75.
628. Jentzer JH, Goyal R, Williamson BD, Man KC, Niebauer M, Daoud E, et al. Analysis of junctional ectopy during radiofrequency ablation of the slow pathway in patients with atrioventricular nodal reentrant tachycardia. Circulation. 1994;90:2820–6.
629. Thakur RK, Klein GJ, Yee R, Stites HW. Junctional tachycardia: a useful marker during radiofrequency ablation for atrioventricular node reentrant tachycardia. J Am Coll Cardiol. 1993;22:1706–10.
630. Scheinman MM. NASPE survey on catheter ablation. Pacing Clin Electrophysiol. 1995;18:1474–8.
631. Scheinman MM, Huang S. The 1998 NASPE prospective catheter ablation registry. Pacing Clin Electrophysiol. 2000;23:1020–8.
632. Spector P, Reynolds MR, Calkins H, Sondhi M, Xu Y, Martin A, et al. Meta-analysis of ablation of atrial flutter and supraventricular tachycardia. Am J Cardiol. 2009;104:671–7.
633. Morady F. Catheter ablation of supraventricular arrhythmias: state of the art. Pacing Clin Electrophysiol. 2004;27:125–42.
634. Naccarelli GV, Shih HT, Jalal S. Catheter ablation for the treatment of paroxysmal supraventricular tachycardia. J Cardiovasc Electrophysiol. 1995;6:951–61.
635. Reithmann C, Remp T, Oversohl N, Steinbeck G. Ablation for atrioventricular nodal reentrant tachycardia with a prolonged PR interval during sinus rhythm: the risk of delayed higher-degree atrioventricular block. J Cardiovasc Electrophysiol. 2006;17:973–9.
636. Deisenhofer I, Zrenner B, Yin YH, Pitschner HF, Kuniss M, Grossmann G, et al. Cryoablation versus radiofrequency energy for the ablation of atrioventricular nodal reentrant tachycardia (the CYRANO Study): results from a large multicenter prospective randomized trial. Circulation. 2010;122:2239–45.
637. Hanninen M, Yeung-Lai-Wah N, Massel D, Gula LJ, Skanes AC, Yee R, et al. Cryoablation versus RF ablation for AVNRT: a

meta-analysis and systematic review. J Cardiovasc Electrophysiol. 2013;24:1354–60.
638. Saoudi N, Cosio F, Waldo A, Chen SA, Iesaka Y, Lesh M, et al. A classification of atrial flutter and regular atrial tachycardia according to electrophysiological mechanisms and anatomical bases: A Statement from a Joint Expert Group from The Working Group of Arrhythmias of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Eur Heart J. 2001;22:1162–82.
639. Arenal A, Almendral J, Alday JM, Villacastín J, Ormaetxe JM, Sande JL, et al. Rate-dependent conduction block of the crista terminalis in patients with typical atrial flutter: influence on evaluation of cavotricuspid isthmus conduction block. Circulation. 1999;99:2771–8.
640. Friedman PA, Luria D, Fenton AM, Munger TM, Jahangir A, Shen WK, et al. Global right atrial mapping of human atrial flutter: the presence of posteromedial (sinus venosa region) functional block and double potentials: A study in biplane fluoroscopy and intracardiac echocardiography. Circulation. 2000;101:1568–77.
641. Natale A, Newby KH, Pisano E, Leonelli F, Fanelli R, Potenza D, et al. Prospective randomized comparison of antiarrhythmic therapy versus first-line radiofrequency ablation in patients with atrial flutter. J Am Coll Cardiol. 2000;35:1898–904.
642. Bastani H, Drca N, Insulander P, Schwieler J, Braunschweig F, Kennebäck G, et al. Cryothermal vs. radiofrequency ablation as atrial flutter therapy: a randomized comparison. Europace. 2013;15:420–8.
643. Poty H, Saoudi N, Nair M, Anselme F, Letac B. Radiofrequency catheter ablation of atrial flutter: further insights into the various types of isthmus block: Application to ablation during sinus rhythm. Circulation. 1996;94:3204–13.
644. Pizzale S, Lemery R, Green MS, Gollob MH, Tang ASL, Birnie DH, et al. Frequency and predictors of tachycardia-induced cardiomyopathy in patients with persistent atrial flutter. Can J Cardiol. 2009;25:469–72.
645. Perez FJ, Schubert CM, Parvez B, Pathak V, Ellenbogen KA, Wood MA. Long-term outcomes after catheter ablation of cavo-tricuspid isthmus dependent atrial flutter: a meta-analysis. Circ Arrhythm Electrophysiol. 2009;2:393–401.
646. Morita N, Kobayashi Y, Iwasaki YK, Hayashi M, Atarashi H, Katoh T, et al. Pronounced effect of procainamide on clockwise right atrial isthmus conduction compared with counterclockwise conduction: possible mechanism of the greater incidence of common atrial flutter during antiarrhythmic therapy. J Cardiovasc Electrophysiol. 2002;13:212–22.
647. Huang DT, Monahan KM, Zimetbaum P, Papageorgiou P, Epstein LM, Josephson ME, et al. Hybrid pharmacologic and ablative therapy: a novel and effective approach for the management of atrial fibrillation. J Cardiovasc Electrophysiol. 1998;9:462–9.
648. Hirao K, Okishige K, Yamamoto N, Otomo K, Azegami K, Isobe M. Long-term efficacy of hybrid pharmacologic and ablation therapy in patients with pilsicainide-induced atrial flutter. Clin Cardiol. 2005;28:338–42.
649. Mohanty S, Mohanty P, Di Biase L, Bai R, Santangeli P, Casella M, et al. Results from a single-blind, randomized study comparing the impact of different ablation approaches on long-term procedure outcome in coexistent atrial fibrillation and flutter (APPROVAL). Circulation. 2013;127:1853–60.
650. Wazni O, Marrouche NF, Martin DO, Gillinov AM, Saliba W, Saad E, et al. Randomized study comparing combined pulmonary vein–left atrial junction disconnection and cavotricuspid isthmus ablation versus pulmonary vein–left atrial junction disconnection alone in patients presenting with typical atrial flutter and atrial fibrillation. Circulation. 2003;108:2479–83.
651. Moreira W, Timmermans C, Wellens HJ, Mizusawa Y, Philippens S, Perez D, et al. Can common-type atrial flutter be a sign of an arrhythmogenic substrate in paroxysmal atrial fibrillation? Clinical and ablative consequences in patients with coexistent paroxysmal atrial fibrillation/atrial flutter. Circulation. 2007;116:2786–92.
652. Lip GY, Kamath S. Thromboprophylaxis for atrial flutter. Eur Heart J. 2001;22:984–7.
653. Deleted in proof.
654. Vollmann D, Stevenson WG, Luthje L, Sohns C, John RM, Zabel M, et al. Misleading long post-pacing interval after entrainment of typical atrial flutter from the cavotricuspid isthmus. J Am Coll Cardiol. 2012;59:819–24.
655. Maruyama M, Kobayashi Y, Miyauchi Y, Iwasaki YK, Morita N, Miyamoto S, et al. Mapping-guided ablation of the cavotricuspid isthmus: a novel simplified approach to radiofrequency catheter ablation of isthmus-dependent atrial flutter. Heart Rhythm. 2006;3:665–73.
656. Tada H, Oral H, Sticherling C, Chough SP, Baker RL, Wasmer K, et al. Double potentials along the ablation line as a guide to radiofrequency ablation of typical atrial flutter. J Am Coll Cardiol. 2001;38:750–5.
657. Chen J, de Chillou C, Basiouny T, Sadoul N, Filho JD, Magnin-Poull I, et al. Cavotricuspid isthmus mapping to assess bidirectional block during common atrial flutter radiofrequency ablation. Circulation. 1999;100:2507–13.
658. Da Costa A, Romeyer-Bouchard C, Dauphinot V, Lipp D, Abdellaoui L, Messier M, et al. Cavotricuspid isthmus angiography predicts atrial flutter ablation efficacy in 281 patients randomized between 8 mm- and externally irrigated-tip catheter. Eur Heart J. 2006;27:1833–40.
659. Nakagawa H, Lazzara R, Khastgir T, Beckman KJ, McClelland JH, Imai S, et al. Role of the tricuspid annulus and the eustachian valve/ridge on atrial flutter: Relevance to catheter ablation of the septal isthmus and a new technique for rapid identification of ablation success. Circulation. 1996;94:407–24.
660. Goya M, Iesaka Y, Takahashi A, Mitsuhashi T, Yamane T, Soejima Y, et al. Radiofrequency catheter ablation for sinoatrial node reentrant tachycardia: electrophysiologic features of ablation sites. Jpn Circ J. 1999;63:177–83.
661. Iesaka Y, Takahashi A, Goya M, Soejima Y, Okamoto Y, Fujiwara H, et al. Adenosine-sensitive atrial reentrant tachycardia originating from the atrioventricular nodal transitional area. J Cardiovasc Electrophysiol. 1997;8:854–64.
662. Ouyang F, Ma J, Ho SY, Bänsch D, Schmidt B, Ernst S, et al. Focal atrial tachycardia originating from the non-coronary aortic sinus: electrophysiological characteristics and catheter ablation. J Am Coll Cardiol. 2006;48:122–31.
663. Yamabe H, Okumura K, Morihisa K, Koyamia J, Kanazawa H, Hoshiyama T, et al. Demonstration of anatomical reentrant tachycardia circuit in verapamil-sensitive atrial tachycardia originating from the vicinity of the atrioventricular node. Heart Rhythm. 2012;9:1475–83.
664. Chen SA, Tai CT, Chiang CE, Ding YA, Chang MS. Focal atrial tachycardia: Reanalysis of the clinical and electrophysiologic characteristics and prediction of successful radiofrequency ablation. J Cardiovasc Electrophysiol. 1998;9:355–65.
665. Chen SA, Chiang CE, Yang CJ, Cheng CC, Wu TJ, Wang SP, et al. Sustained atrial tachycardia in adult patients: electrophysiological characteristics, pharmacological response, possible mechanisms, and effects of radiofrequency ablation. Circulation. 1994;90:1262–78.
666. Kistler PM, Roberts-Thomson KC, Haqqani HM, Fynn SP, Singarayar S, Vohra JK, et al. P-wave morphology in focal atrial tachycardia: development of an algorithm to predict the anatomic site of origin. J Am Coll Cardiol. 2006;48:1010–7.
667. Suenari K, Lin YJ, Chang SL, Lo LW, Hu YF, Chen SA. Lead aVL P-wave polarity: insight from mapping and ablation of atrial

arrhythmia initiated from superior vena cava. Pacing Clin Electrophysiol. 2010;33:e100–e101.
668. Medi C, Kalman JM, Haqqani H, Vohra JK, Morton JB, Sparks PB, et al. Tachycardia-mediated cardiomyopathy secondary to focal atrial tachycardia: long-term outcome after catheter ablation. J Am Coll Cardiol. 2009;53:1791–7.
669. Liu XY, Jacobsen PK, Pehrson S, Chen X. Catheter ablation of focal atrial tachycardia using remote magnetic navigation. J Invasive Cardiol. 2018;30:126–32.
670. Busch S, Forkmann M, Kuck KH, Lewalter T, Ince H, Straube F, et al. Acute and long-term outcome of focal atrial tachycardia ablation in the real world: results of the German ablation registry. Clin Res Cardiol. 2018;107:430–6.
671. Tang CW, Scheinman MM, Van Hare GF, Epstein LM, Fitxpatrick AP, Lee RJ, et al. Use of P wave configuration during atrial tachycardia to predict site of origin. J Am Coll Cardiol. 1995;26:1315–24.
672. Ueyama T, Shimizu A, Yoshiga Y, Ono M, Fumimoto T, Yano M. Macroreentrant form of an adenosine 5'-triphosphate-sensitive atrial tachycardia arising from the vicinity of the atrioventricular node involving the tricuspid and mitral annuli as its reentrant circuit. HeartRhythm Case Rep. 2017;3:289–93.
673. Sasaki T, Hachiya H, Hirao K, Higuchi K, Hayashi T, Furukawa T, et al. Utility of distinctive local electrogram pattern and aortographic anatomical position in catheter manipulation at coronary cusps. J Cardiovasc Electrophysiol. 2011;22:521–9.
674. Man KC, Knight B, Tse HF, Pelosi F, Michaud GF, Flemming M, et al. Radiofrequency catheter ablation of inappropriate sinus tachycardia guided by activation mapping. J Am Coll Cardiol. 2000;35:451–7.
675. Rodriguez-Manero M, Kreidieh B, Al Rifai M, Ibarra-Cortez S, Schurmann P, Alvarez PA, et al. Ablation of inappropriate sinus tachycardia: a systematic review of the literature. JACC Clin Electrophysiol. 2017;3:253–65.
676. Schmidt B, Chun KR, Ouyang F, Metzner A, Antz M, Kuck KH. Three-dimensional reconstruction of the anatomic course of the right phrenic nerve in humans by pace mapping. Heart Rhythm. 2008;5:1120–6.
677. Chatterjee NA, Upadhyay GA, Ellenbogen KA, McAlister FA, Choudhry NK, Singh JP. Atrioventricular nodal ablation in atrial fibrillation: a meta-analysis and systematic review. Circ Arrhythm Electrophysiol. 2012;5:68–76.
678. Wood MA, Brown-Mahoney C, Kay GN, Ellenbogen KA. Clinical outcomes after ablation and pacing therapy for atrial fibrillation: a meta-analysis. Circulation. 2000;101:1138–44.
679. Kay GN, Ellenbogen KA, Giudici M, Redfield MM, Jenkins LS, Mianulli M, et al. The Ablate and Pace Trial: a prospective study of catheter ablation of the AV conduction system and permanent pacemaker implantation for treatment of atrial fibrillation. J Interv Card Electrophysiol. 1998;2:121–35.
680. Brignole M, Menozzi C, Gianfranchi L, Musso G, Mureddu R, Bottoni N, et al. Assessment of atrioventricular junction ablation and VVIR pacemaker versus pharmacological treatment in patients with heart failure and chronic atrial fibrillation: a randomized, controlled study. Circulation. 1998;98:953–60.
681. Lim KT, Davis MJ, Powell A, Arnolda L, Moulden K, Bulsara M, et al. Ablate and pace strategy for atrial fibrillation: long-term outcome of AIRCRAFT trial. Europace. 2007;9:498–505.
682. Weerasooriya R, Davis M, Powell A, Szili-Torok T, Shah C, Whalley D, et al. The Australian Intervention Randomized Control of Rate in Atrial Fibrillation Trial (AIRCRAFT). J Am Coll Cardiol. 2003;41:1697–702.
683. Ganesan AN, Brooks AG, Roberts-Thomson KC, Lau DH, Kalman JM, Sanders P. Role of AV nodal ablation in cardiac resynchronization in patients with coexistent atrial fibrillation and heart failure a systematic review. J Am Coll Cardiol. 2012;59:719–26.
684. Wilton SB, Leung AA, Ghali WA, Faris P, Exner DV. Outcomes of cardiac resynchronization therapy in patients with versus those without atrial fibrillation: a systematic review and meta-analysis. Heart Rhythm. 2011;8:1088–94.
685. Marshall HJ, Griffith MJ. Ablation of the atrioventricular junction: technique, acute and long-term results in 115 consecutive patients. Europace. 1999;1:26–9.
686. Lee SH, Chen SA, Tai CT, Chiang CE, Wen ZC, Cheng JJ, et al. Comparisons of quality of life and cardiac performance after complete atrioventricular junction ablation and atrioventricular junction modification in patients with medically refractory atrial fibrillation. J Am Coll Cardiol. 1998;31:637–44.
687. Conti JB, Mills RM, Woodard DA, Curtis AB. QT dispersion is a marker for life-threatening ventricular arrhythmias after atrioventricular nodal ablation using radiofrequency energy. Am J Cardiol. 1997;79:1412–4.
688. Wang RX, Lee HC, Hodge DO, Cha YM, Friedman PA, Rea RF, et al. Effect of pacing method on risk of sudden death after atrioventricular node ablation and pacemaker implantation in patients with atrial fibrillation. Heart Rhythm. 2013;10:696–701.
689. Duff HJ, Raj SR, Exner DV, Sheldon RS, Roach D, Mitchell LB, et al. Randomized controlled trial of fixed rate versus rate responsive pacing after radiofrequency atrioventricular junction ablation: quality of life, ventricular refractoriness, and paced QT dispersion. J Cardiovasc Electrophysiol. 2003;14:1163–70.
690. Chatterjee NA, Upadhyay GA, Ellenbogen KA, McAlister FA, Choudhry NK, Singh JP. Atrioventricular nodal ablation in atrial fibrillation: a meta-analysis of biventricular vs. right ventricular pacing mode. Eur J Heart Fail. 2012;14:661–7.
691. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Europace. 2016;18:1609–78.
692. Kopecky SL, Gersh BJ, McGoon MD, Hisnant JP, Holmes DR, Ilstrup DM, et al. The natural history of lone atrial fibrillation: a population-based study over three decades. N Engl J Med. 1987;317:669–74.
693. de Vos CB, Pisters R, Nieuwlaat R, Prins MH, Tieleman RG, Coelen RJ, et al. Progression from paroxysmal to persistent atrial fibrillation clinical correlates and prognosis. J Am Coll Cardiol. 2010;55:725–31.
694. Chimenti C, Russo MA, Carpi A, Frustaci A. Histological substrate of human atrial fibrillation. Biomed Pharmacother. 2010;64:177–83.
695. Frustaci A, Chimenti C, Bellocci F, Morgante E, Russo MA, Maseri A. Histological substrate of atrial biopsies in patients with lone atrial fibrillation. Circulation. 1997;96:1180–4.
696. Venteclef N, Guglielmi V, Balse E, Gaborit B, Cotillard A, Atassi F, et al. Human epicardial adipose tissue induces fibrosis of the atrial myocardium through the secretion of adipo-fibrokines. Eur Heart J. 2015;36:795–805.
697. Rocken C, Peters B, Juenemann G, Saeger W, Klein HU, Huth C, et al. Atrial amyloidosis: an arrhythmogenic substrate for persistent atrial fibrillation. Circulation. 2002;106:2091–7.
698. Schotten U, Ausma J, Stellbrink C, Sabatschus I, Vogel M, Frechen F, et al. Cellular mechanisms of depressed atrial contractility in patients with chronic atrial fibrillation. Circulation. 2001;103:691–8.
699. Allessie MA, de Groot NM, Houben RP, Schotten U, Boersma E, Smeets JL, et al. Electropathological substrate of long-standing persistent atrial fibrillation in patients with structural heart disease: longitudinal dissociation. Circ Arrhythm Electrophysiol. 2010;3:606–15.
700. Jais P, Haissaguerre M, Shah DC, Chouairi S, Gencel L, Hocini M, et al. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. Circulation. 1997;95:572–6.

701. Nathan H, Eliakim M. The junction between the left atrium and the pulmonary veins: an anatomic study of human hearts. Circulation. 1966;34:412–22.
702. Perez-Lugones A, McMahon JT, Ratliff NB, Saliba WI, Schweikert RA, Marrouche NF, et al. Evidence of specialized conduction cells in human pulmonary veins of patients with atrial fibrillation. J Cardiovasc Electrophysiol. 2003;14:803–9.
703. Chen YJ, Chen SA, Chang MS, Lin CI. Arrhythmogenic activity of cardiac muscle in pulmonary veins of the dog: implication for the genesis of atrial fibrillation. Cardiovasc Res. 2000;48:265–73.
704. Moe GK. On the multiple wavelet hypothesis of atrial fibrillation. Arch Int Pharmacodyn Ther. 1962;140:183–8.
705. Ikeda T, Yashima M, Uchida T, Hough D, Fishbein MC, Mandel WJ, et al. Attachment of meandering reentrant wave fronts to anatomic obstacles in the atrium: role of the obstacle size. Circ Res. 1997;81:753–64.
706. Kuck KH, Hoffmann BA, Ernst S, Wegscheider K, Treszl A, Metzner A, et al.; Gap-AF–AFNET 1 Investigators. Impact of complete versus incomplete circumferential lines around the pulmonary veins during catheter ablation of paroxysmal atrial fibrillation: results from the gap-atrial fibrillation-German atrial fibrillation competence network 1 trial. Circ Arrhythm Electrophysiol. 2016;9:e003337.
707. Mujović N, Marinković M, Lenarczyk R, Roland Tilz R, Tatjana S, Potpara TS. Catheter ablation of atrial fibrillation: an overview for clinicians. Adv Ther. 2017;34:1897–917.
708. Verma A, Jiang CY, Betts TR, Chen J, Deisenhofer I, Mantovan R, et al.; STAR AF II Investigators. Approaches to catheter ablation for persistent atrial fibrillation. N Engl J Med. 2015;372:1812–22.
709. Jais P, Hsu LF, Rotter M, Sanders P, Takahashi Y, Rostock T, et al. Mitral isthmus ablation for atrial fibrillation. J Cardiovasc Electrophysiol. 2005;16:1157–9.
710. Hocini M, Jais P, Sanders P, Takahashi Y, Rotter M, Rostock T, et al. Techniques, evaluation, and consequences of linear block at the left atrial roof in paroxysmal atrial fibrillation: a prospective randomized study. Circulation. 2005;112:3688–96.
711. Nademanee K, McKenzie J, Kosar E, Schwab M, Sunsaneewitayakul B, Vasavakul T, et al. A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologic substrate. J Am Coll Cardiol. 2004;43:2044–53.
712. Choi EK, Zhao Y, Everett TH 4th, Chen PS. Ganglionated plexi as neuromodulation targets for atrial fibrillation. J Cardiovasc Electrophysiol. 2017;28:1485–91.
713. Narayan SM, Baykaner T, Clopton P, Schricker A, Lalani GG, Krummen DE, et al. Ablation of rotor and focal sources reduces late recurrence of atrial fibrillation compared with trigger ablation alone: extended follow-up of the CONFIRM trial (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation). J Am Coll Cardiol. 2014;63:1761–8.
714. Haissaguerre M, Hocini M, Denis A, Shah AJ, Komatsu Y, Yamashita S, et al. Driver domains in persistent atrial fibrillation. Circulation. 2014;130:530–8.
715. Rolf S, Kircher S, Arya A, Eitel C, Sommer P, Richter S, et al. Tailored atrial substrate modification based on low-voltage areas in catheter ablation of atrial fibrillation. Circ Arrhythm Electrophysiol. 2014;7:825–33.
716. Brooks AG, Stiles MK, Laborderie J, Lau DH, Kuklik P, Shipp NJ, et al. Outcomes of long-standing persistent atrial fibrillation ablation: a systematic review. Heart Rhythm. 2010;7:835–46.
717. Calkins H, Reynolds MR, Spector P, Sondhi M, Xu Y, Martin A, et al. Treatment of atrial fibrillation with antiarrhythmic drugs or radiofrequency ablation: two systematic literature reviews and meta-analyses. Circ Arrhythm Electrophysiol. 2009;2:349–61.
718. Scherr D, Khairy P, Miyazaki S, Aurillac-Lavignolle V, Pascale P, Wilton SB, et al. Five-year outcome of catheter ablation of persistent atrial fibrillation using termination of atrial fibrillation as a procedural endpoint. Circ Arrhythm Electrophysiol. 2015;8:18–24.
719. Wazni OM, Marrouche NF, Martin DO, Verma A, Bhargava M, Saliba W, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. JAMA. 2005;293:2634–40.
720. Cosedis Nielsen J, Johannessen A, Raatikainen P, Hindricks G, Walfridsson H, Kongstad O, et al. Radiofrequency ablation as initial therapy in paroxysmal atrial fibrillation. N Engl J Med. 2012;367:1587–95.
721. Morillo CA, Verma A, Connolly SJ, Kuck KH, Nair GM, Champagne J, et al. RAAFT-2 Investigators. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of paroxysmal atrial fibrillation (RAAFT-2): a randomized trial. JAMA. 2014;311:692–700.
722. Hakalahti A, Biancari F, Nielsen JC, Raatikainen MJP. Radiofrequency ablation vs. antiarrhythmic drug therapy as first line treatment of symptomatic atrial fibrillation: systematic review and meta-analysis. Europace. 2015;17:370–8.
723. Mamas MA, Caldwell JC, Chacko S, Garratt CJ, Fath-Ordoubadi F, Neyses L. A meta-analysis of the prognostic significance of atrial fibrillation in chronic heart failure. Eur J Heart Fail. 2009;11:676–83.
724. Roy D, Talajic M, Nattel S, Wyse DG, Dorian P, Lee KL, et al.; Atrial Fibrillation and Congestive Heart Failure Investigators. Rhythm control versus rate control for atrial fibrillation and heart failure. N Engl J Med. 2008;358:2667–77.
725. Khan MN, Jais P, Cummings J, Di Biase L, Sanders P, Martin DO, et al.; PABA-CHF Investigators. Pulmonary-vein isolation for atrial fibrillation in patients with heart failure. N Engl J Med. 2008;359:1778–85.
726. MacDonald MR, Connelly DT, Hawkins NM, Steedman T, Payne J, Shaw M, et al. Radiofrequency ablation for persistent atrial fibrillation in patients with advanced heart failure and severe left ventricular systolic dysfunction: a randomised controlled trial. Heart. 2011;97:740–7.
727. Hunter RJ, Berriman TJ, Diab I, Kamdar R, Richmond L, Baker V, et al. A randomized controlled trial of catheter ablation versus medical treatment of atrial fibrillation in heart failure (the CAMTAF trial). Circ Arrhythm Electrophysiol. 2014;7:31–8.
728. Jones DG, Haldar SK, Hussain W, Sharma R, Francis DP, Rahman-Haley SL, et al. A randomized trial to assess catheter ablation versus rate control in the management of persistent atrial fibrillation in heart failure. J Am Coll Cardiol. 2013;61:1894–903.
729. Prabhu S, Taylor AJ, Costello BT, Kaye DM, McLellan AJA, Voskoboinik A, et al. Catheter ablation versus medical rate control in atrial fibrillation and systolic dysfunction: The CAMERA-MRI study. J Am Coll Cardiol. 2017;70:1949–61.
730. Al Halabi S, Qintar M, Hussein A, Chadi Alraies M, Jones DG, Wong T, et al. Catheter ablation for atrial fibrillation in heart failure patients: a meta-analysis of randomized controlled trials. JACC Clin Electrophysiol. 2015;1:200–9.
731. Di Biase L, Mohanty P, Mohanty S, Santangeli P, Trivedi C, Lakkireddy D, et al. Ablation versus amiodarone for treatment of persistent atrial fibrillation in patients with congestive heart failure and an implanted device: results from the AATAC multicenter randomized trial. Circulation. 2016;133:1637–44.
732. Hocini M, Sanders P, Deisenhofer I, Jaïs P, Hsu LF, Scavée C, et al. Reverse remodeling of sinus node function after catheter ablation of atrial fibrillation in patients with prolonged sinus pauses. Circulation. 2003;108:1172–5.
733. Inada K, Yamane T, Tokutake K, Yokoyama K, Mishima T, Hioki M, et al. The role of successful catheter ablation in patients with

paroxysmal atrial fibrillation and prolonged sinus pauses: outcome during a 5-year follow-up. Europace. 2014;16:208–13.
734. Kusumoto F, Prussak K, Wiesinger M, Pullen T, Lynady C. Radiofrequency catheter ablation of atrial fibrillation in older patients: outcomes and complications. J Interv Card Electrophysiol. 2009;25:31–5.
735. Bunch TJ, Weiss JP, Crandall BG, May HT, Bair TL, Osborn JS, et al. Long-term clinical efficacy and risk of catheter ablation for atrial fibrillation in octogenarians. Pacing Clin Electrophysiol. 2010;33:146–52.
736. Santangeli P, Di Biase L, Mohanty P, Burkhardt JD, Horton R, Bai R, et al. Catheter ablation of atrial fibrillation in octogenarians: safety and outcomes. J Cardiovasc Electrophysiol. 2012;23:687–93.
737. Nademanee K, Amnueypol M, Lee F, Drew CM, Suwannasri W, Schwab MC, et al. Benefits and risks of catheter ablation in elderly patients with atrial fibrillation. Heart Rhythm. 2015;12:44–51.
738. Bunch TJ, May HT, Bair TL, Jacobs V, Crandall BG, Cutler M, et al. The impact of age on 5-year outcomes after atrial fibrillation catheter ablation. J Cardiovasc Electrophysiol. 2016;27:141–6.
739. Friberg L, Tabrizi F, Englund A. Catheter ablation for atrial fibrillation is associated with lower incidence of stroke and death: data from Swedish health registries. Eur Heart J. 2016;37:2478–87.
740. Boriani G, Laroche C, Diemberger I, Fantecchi E, Popescu MI, Rasmussen LH, et al. Asymptomatic atrial fibrillation: Clinical correlates, management, and outcomes in the EORP-AF Pilot General Registry. Am J Med. 2015;128(509–518):e2.
741. Forleo GB, De Martino G, Mantica M, Carreras G, Parisi Q, Zingarini G, et al. Clinical impact of catheter ablation in patients with asymptomatic atrial fibrillation: the IRON-AF (Italian registry on NavX atrial fibrillation ablation procedures) study. Int J Cardiol. 2013;168:3968–70.
742. Wu L, Lu Y, Zheng L, Chen G, Ding L, Hou B, et al. Comparison of radiofrequency catheter ablation between asymptomatic and symptomatic persistent atrial fibrillation: a propensity score matched analysis. J Cardiovasc Electrophysiol. 2016;27:531–5.
743. Mohanty S, Santangeli P, Mohanty P, Di Biase L, Holcomb S, Trivedi C, et al. Catheter ablation of asymptomatic longstanding persistent atrial fibrillation: Impact on quality of life, exercise performance, arrhythmia perception, and arrhythmia-free survival. J Cardiovasc Electrophysiol. 2014;25:1057–64.
744. Yagishita A, Yamauchi Y, Sato H, Yamashita S, Hirao T, Miyamoto T, et al. Improvement in the quality of life and exercise performance in relation to the plasma B-type natriuretic peptide level after catheter ablation in patients with asymptomatic persistent atrial fibrillation. Circ J. 2017;81:444–9.
745. Pappone C, Radinovic A, Manguso F, Vicedomini G, Ciconte G, Sacchi S, et al. Atrial fibrillation progression and management: a 5-year prospective follow-up study. Heart Rhythm. 2008;5:1501–7.
746. Pathak RK, Middeldorp ME, Lau DH, Mehta AB, Mahajan R, Twomey D, et al. Aggressive risk factor reduction study for atrial fibrillation and implications for the outcome of ablation: the ARREST-AF cohort study. J Am Coll Cardiol. 2014;64:2222–31.
747. Mohanty S, Mohanty P, Di Biase L, Bai R, Pump A, Santangeli P, et al. Impact of metabolic syndrome on procedural outcomes in patients with atrial fibrillation undergoing catheter ablation. J Am Coll Cardiol. 2012;59:1295–301.
748. Kumagai K, Ogawa M, Noguchi H, Yasuda T, Nakashima H, Saku K. Electrophysiologic properties of pulmonary veins assessed using a multielectrode basket catheter. J Am Coll Cardiol. 2004;43:2281–9.
749. Yamane T, Date T, Kanzaki Y, Inada K, Matsuo S, Shibayama K, et al. Segmental pulmonary vein antrum isolation using the "large-size" lasso catheter in patients with atrial fibrillation. Circ J. 2007;71:753–60.
750. Ouyang F, Bansch D, Ernst S, Schaumann A, Hachiya H, Chen M, et al. Complete isolation of left atrium surrounding the pulmonary veins: new insights from the double-Lasso technique in paroxysmal atrial fibrillation. Circulation. 2004;110:2090–6.
751. Takahashi A, Iesaka Y, Takahashi Y, Takahashi R, Kobayashi K, Takagi K, et al. Electrical connections between pulmonary veins: implication for ostial ablation of pulmonary veins in patients with paroxysmal atrial fibrillation. Circulation. 2002;105:2998–3003.
752. Kumagai K. Catheter ablation of atrial fibrillation: state of the art. Circ J. 2011;75:2305–11.
753. Kumagai K, Muraoka S, Mitsutake C, Takashima H, Nakashima H. A new approach for complete isolation of the posterior left atrium including pulmonary veins for atrial fibrillation. J Cardiovasc Electrophysiol. 2007;18:1047–52.
754. Yamaguchi Y, Kumagai K, Nakashima H, Saku K. Long-term effects of box isolation on sympathovagal balance in atrial fibrillation. Circ J. 2010;74:1096–103.
755. Lim TW, Koay CH, See VA, McCall R, Chik W, Zecchin R, et al. Single-ring posterior left atrial (box) isolation results in a different mode of recurrence compared with wide antral pulmonary vein isolation on long-term follow-up: longer atrial fibrillation-free survival time but similar survival time free of any atrial arrhythmia. Circ Arrhythm Electrophysiol. 2012;5:968–77.
756. Nalliah C, Lim TW, Bhaskaran A, Kizana E, Kovoor P, Thomas L, et al. Posterior left atrial isolation for atrial fibrillation in left ventricular diastolic impairment is associated with better arrhythmia free survival. Int J Cardiol. 2015;184:674–9.
757. O'Neill L, Hensey M, Nolan W, Keane D. Clinical outcome when left atrial posterior wall box isolation is included as a catheter ablation strategy in patients with persistent atrial fibrillation. J Interv Card Electrophysiol. 2015;44:63–70.
758. Cutler MJ, Johnson J, Abozguia K, Rowan S, Lewis W, Constantini O, et al. Impact of voltage mapping to guide whether to perform ablation of the posterior wall in patients with persistent atrial fibrillation. J Cardiovasc Electrophysiol. 2016;27:13–21.
759. Roberts JD, Gerstenfeld EP. Concomitant isolation of the pulmonary veins and posterior wall using a box lesion set in a patient with persistent atrial fibrillation and variant pulmonary venous anatomy. Card Electrophysiol Clin. 2016;8:145–9.
760. Kim JS, Shin SY, Na JO, Choi CU, Kim SH, Kim JW, et al. Does isolation of the left atrial posterior wall improve clinical outcomes after radiofrequency catheter ablation for persistent atrial fibrillation? A prospective randomized clinical trial. Int J Cardiol. 2015;181:277–83.
761. He X, Zhou Y, Chen Y, Wu L, Huang Y, He J. Left atrial posterior wall isolation reduces the recurrence of atrial fibrillation: a meta-analysis. J Interv Card Electrophysiol. 2016;46:267–74.
762. Jais P, Haissaguerre M, Shah DC, Takahashi A, Hocini M, Lavergne T, et al. Successful irrigated-tip catheter ablation of atrial flutter resistant to conventional radiofrequency ablation. Circulation. 1998;98:835–8.
763. Haines DE. The biophysics and pathophysiology of lesion formation during radiofrequency catheter ablation. In: Jalife J, Zipes D, editors. Cardiac electrophysiology: From cell to bedside, 4th edn. WB Saunders; 2006. p. 1018–27.
764. Di Biase L, Natale A, Barrett C, Tan C, Elayi CS, Ching CK, et al. Relationship between catheter forces, lesion characteristics, "popping", and char formation: experience with robotic navigation system. J Cardiovasc Electrophysiol. 2009;20:436–40.
765. Haines DE. Determinants of lesion size during radiofrequency catheter ablation: The role of electrode-tissue contact pressure and duration of energy delivery. J Cardiovasc Electrophysiol. 1991;2:509–15.
766. Strickberger SA, Vorperian VR, Man KC, Williamson BD, Kalbfleisch SJ, Hasse C, et al. Relation between impedance and endocardial contact during radiofrequency catheter ablation. Am Heart J. 1994;128:226–9.

767. Avitall B, Mughal K, Hare J, Helms R, Krum D. The effects of electrode-tissue contact on radiofrequency lesion generation. Pacing Clin Electrophysiol. 1997;20:2899–910.
768. Kuck KH, Reddy VY, Schmidt B, Natale A, Neuzil P, Saoudi N, et al. A novel radiofrequency ablation catheter using contact force sensing: Toccata study. Heart Rhythm. 2012;9:18–23.
769. Ikeda A, Nakagawa H, Lambert H, Shah DC, Fonck E, Yulzari A, et al. Relationship between catheter contact force and radiofrequency lesion size and incidence of steam pop in the beating canine heart: electrogram amplitude, impedance, and electrode temperature are poor predictors of electrode-tissue contact force and lesion size. Circ Arrhythm Electrophysiol. 2014;7:1174–80.
770. Nakagawa H, Kautzner J, Natale A, Peichl P, Cihak R, Wichterle D, et al. Locations of high contact force during left atrial mapping in atrial fibrillation patients: electrogram amplitude and impedance are poor predictors of electrode-tissue contact force for ablation of atrial fibrillation. Circ Arrhythm Electrophysiol. 2013;6:746–53.
771. Nakagawa H, Ikeda A, Govari A, Papaioannou T, Constantine G, Bar-Tal M, et al. Prospective study to test the ability to create RF lesions at predicted depth and diameter using a new formula incorporating contact force, radiofrequency power and application time (force-power-time index) in the beating heart. Heart Rhythm. 2014;11(Suppl):S548.
772. Natale A, Reddy VY, Monir G, Wilber DJ, Lindsay BD, McElderry HT, et al. Paroxysmal AF catheter ablation with a contact force sensing catheter: results of the prospective, multicenter SMART-AF trial. J Am Coll Cardiol. 2014;64:647–56.
773. Kumar S, Morton JB, Lee J, Halloran K, Spence SJ, Gorelik A, et al. Prospective characterization of catheter-tissue contact force at different anatomic sites during antral pulmonary vein isolation. Circ Arrhythm Electrophysiol. 2012;5:1124–9.
774. Haldar S, Jarman JW, Panikker S, Jones DG, Salukhe T, Gupta D, et al. Contact force sensing technology identifies sites of inadequate contact and reduces acute pulmonary vein reconnection: a prospective case control study. Int J Cardiol. 2013;168:1160–6.
775. Perna F, Heist EK, Danik SB, Barrett CD, Ruskin JN, Mansour M. Assessment of catheter tip contact force resulting in cardiac perforation in swine atria using force sensing technology. Circ Arrhythm Electrophysiol. 2011;4:218–24.
776. Kimura M, Sasaki S, Owada S, Horiuchi D, Sasaki K, Itoh T, et al. Comparison of lesion formation between contact force-guided and non-guided circumferential pulmonary vein isolation: a prospective, randomized study. Heart Rhythm. 2014;11:984–91.
777. Sohns C, Karim R, Harrison J, Arujuna A, Linton N, Sennett R, et al. Quantitative magnetic resonance imaging analysis of the relationship between contact force and left atrial scar formation after catheter ablation of atrial fibrillation. J Cardiovasc Electrophysiol. 2014;25:138–45.
778. Andrade JG, Monir G, Pollak SJ, Khairy P, Dubuc M, Roy D, et al. Pulmonary vein isolation using "contact force" ablation: the effect on dormant conduction and long-term freedom from recurrent atrial fibrillation: a prospective study. Heart Rhythm. 2014;11:1919–24.
779. Martinek M, Lemes C, Sigmund E, Derndorfer M, Aichinger J, Winter S, et al. Clinical impact of an open-irrigated radiofrequency catheter with direct force measurement on atrial fibrillation ablation. Pacing Clin Electrophysiol. 2012;35:1312–8.
780. Marijon E, Fazaa S, Narayanan K, Guy-Moyat B, Bouzeman A, Providencia R, et al. Real-time contact force sensing for pulmonary vein isolation in the setting of paroxysmal atrial fibrillation: procedural and 1-year results. J Cardiovasc Electrophysiol. 2014;25:130–7.
781. Sigmund E, Puererfellner H, Derndorfer M, Kollias G, Winter S, Aichinger J, et al. Optimizing radiofrequency ablation of paroxysmal and persistent atrial fibrillation by direct catheter force measurement: a case-matched comparison in 198 patients. Pacing Clin Electrophysiol. 2015;38:201–8.
782. Ullah W, McLean A, Tayebjee MH, Gupta D, Ginks MR, Haywood GA, et al.; UK Multicentre Trials Group. Randomized trial comparing pulmonary vein isolation using the SmartTouch catheter with or without real-time contact force data. Heart Rhythm. 2016;13:1761–7.
783. Okumura K, Matsumoto K, Kobayashi Y, Nogami A, Hokanson RB, Kueffer F, et al. Safety and efficacy of cryoballoon ablation for paroxysmal atrial fibrillation in Japan: results from the Japanese prospective post-market surveillance study. Circ J. 2016;80:1744–9.
784. Franceschi F, Dubuc M, Guerra PG, Khairy P. Phrenic nerve monitoring with diaphragmatic electromyography during cryoballoon ablation for atrial fibrillation: the first human application. Heart Rhythm. 2011;8:1068–71.
785. Lakhani M, Saiful F, Parikh V, Goyal N, Bekheit S, Kowalski M. Recordings of diaphragmatic electromyograms during cryoballoon ablation for atrial fibrillation accurately predict phrenic nerve injury. Heart Rhythm. 2014;11:369–74.
786. Okishige K, Aoyagi H, Kawaguchi N, Katoh N, Yamashita M, Nakamura T, et al. Novel method for earlier detection of phrenic nerve injury during cryoballoon applications for electrical isolation of pulmonary veins in patients with atrial fibrillation. Heart Rhythm. 2016;13:1810–6.
787. Narui R, Tokuda M, Matsushima M, Isogai R, Tokutake K, Yokoyama K, et al. Incidence and factors associated with the occurrence of pulmonary vein narrowing after cryoballoon ablation. Circ Arrhythm Electrophysiol. 2017;10:e004588.
788. Sohara H, Ohe T, Okumura K, Naito S, Hirao K, Shoda M, et al. Hot balloon ablation of the pulmonary veins for paroxysmal AF: a multicenter randomized trial in Japan. J Am Coll Cardiol. 2016;68:2747–57.
789. Thomas D, Katus HA, Voss F. Asymptomatic pulmonary vein stenosis after cryoballoon catheter ablation of paroxysmal atrial fibrillation. J Electrocardiol. 2011;44:473–6.
790. Su W, Kowal R, Kowalski M, Metzner A, Svinarich JT, Wheelan K, et al. Best practice guide for cryoballoon ablation in atrial fibrillation: the compilation experience of more than 3000 procedures. Heart Rhythm. 2015;12:1658–66.
791. Kawasaki R, Gauri A, Elmouchi D, Duggal M, Bhan A. Atrioesophageal fistula complicating cryoballoon pulmonary vein isolation for paroxysmal atrial fibrillation. J Cardiovasc Electrophysiol. 2014;25:787–92.
792. Vilades Medel D, Marti-Almor J, Montiel Serrano J, Sionis A, Petracca RL. Atrioesophageal fistula secondary to pulmonary vein cryo-ablation. Eur Heart J Cardiovasc Imaging. 2014;15:116.
793. Giacomino BD, Worden N, Marchigiani R, Keech J, Giudici MC. Pericardial-esophageal fistula complicating cryoballoon ablation for refractory atrial fibrillation. HeartRhythm Case Rep. 2017;3:2–6.
794. John RM, Kapur S, Ellenbogen KA, Koneru JN. Atrioesophageal fistula formation with cryoballoon ablation is most commonly related to the left inferior pulmonary vein. Heart Rhythm. 2017;14:184–9.
795. Avitall B, Kalinski A. Cryotherapy of cardiac arrhythmia: from basic science to the bedside. Heart Rhythm. 2015;12:2195–203.
796. Handler M, Fischer G, Seger M, Kienast R, Hanser F, Baumgartner C. Simulation and evaluation of freeze-thaw cryoablation scenarios for the treatment of cardiac arrhythmias. Biomed Eng Online. 2015;14:12.
797. Deneke T, Jais P, Scaglione M, Schmitt R, Di Biase L, Christopoulos G, et al. Silent cerebral events/lesions related to atrial fibrillation ablation: a clinical review. J Cardiovasc Electrophysiol. 2015;26:455–63.

798. Gaita F, Leclercq JF, Schumacher B, Scaglione M, Toso E, Halimi F, et al. Incidence of silent cerebral thromboembolic lesions after atrial fibrillation ablation may change according to technology used: comparison of irrigated radiofrequency, multipolar nonirrigated catheter and cryoballoon. J Cardiovasc Electrophysiol. 2011;22:961–8.
799. von Bary C, Deneke T, Arentz T, Schade A, Lehrmann H, Eissnert C, et al. Silent cerebral events as a result of left atrial catheter ablation do not cause neuropsychological sequelae: a MRI-controlled multicenter study. J Interv Card Electrophysiol. 2015;43:217–26.
800. Okishige K, Nakamura T, Aoyagi H, Kawaguchi N, Yamashita M, Kurabayashi M, et al. Comparative study of hemorrhagic and ischemic complications among anticoagulants in patients undergoing cryoballoon ablation for atrial fibrillation. J Cardiol. 2017;69:11–5.
801. Tokuda M, Matsuo S, Kato M, Sato H, Oseto H, Okajima E, et al. Effect of air removal with extracorporeal balloon inflation on incidence of asymptomatic cerebral embolism during cryoballoon ablation of atrial fibrillation. Heart Rhythm. 2017;14:1291–6.
802. Chierchia GB, Namdar M, Sarkozy A, Sorgente A, de Asmundis C, Casado-Arroyo R, et al. Verification of pulmonary vein isolation during single transseptal cryoballoon ablation: a comparison between the classical circular mapping catheter and the inner lumen mapping catheter. Europace. 2012;14:1708–14.
803. Nadji G, Hermida JS, Kubala M, Quenum S, Mouquet V, Traullé S, et al. Dual balloon size strategy for cryoisolation of the pulmonary veins in patients with atrial fibrillation: comparison of 23 and 28mm diameter cryoballoons. Arch Cardiovasc Dis. 2011;104:70–6.
804. Tebbenjohanns J, Hofer C, Bergmann L, Dedroogh M, Gaudin D, von Werder A, et al. Shortening of freezing cycles provides equal outcome to standard ablation procedure using second-generation 28 mm cryoballoon after 15-month follow-up. Europace. 2016;18:206–10.
805. Miyazaki S, Hachiya H, Nakamura H, Taniguchi H, Takagi T, Hirao K, et al. Pulmonary vein isolation using a second-generation cryoballoon in patients with paroxysmal atrial fibrillation: one-year outcome using a single big-balloon 3-minute freeze technique. J Cardiovasc Electrophysiol. 2016;27:1375–80.
806. Ciconte G, Sieira-Moret J, Hacioglu E, Mugnai G, Di Giovanni G, Velagic V, et al. Single 3-minute versus double 4-minute freeze strategy for second-generation cryoballoon ablation: a single-center experience. J Cardiovasc Electrophysiol. 2016;27:796–803.
807. Straube F, Dorwarth U, Hartl S, Bunz B, Wankerl M, Ebersberger U, et al. Outcome of paroxysmal atrial fibrillation ablation with the cryoballoon using two different application times: the 4- versus 3-min protocol. J Interv Card Electrophysiol. 2016;45:169–77.
808. Kuck KH, Brugada J, Furnkranz A, Metzner A, Ouyang F, Chun KR, et al.; FIRE AND ICE Investigators. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. N Engl J Med. 2016;374:2235–45.
809. Packer DL, Kowal RC, Wheelan KR, Irwin JM, Champagne J, Guerra PG, et al.; STOP AF Cryoablation Investigators. Cryoballoon ablation of pulmonary veins for paroxysmal atrial fibrillation: first results of the North American Arctic Front (STOP AF) pivotal trial. J Am Coll Cardiol. 2013;61:1713–23.
810. Schmidt M, Dorwarth U, Andresen D, Brachmann J, Kuck KH, Kuniss M, et al. Cryoballoon versus RF ablation in paroxysmal atrial fibrillation: results from the German Ablation Registry. J Cardiovasc Electrophysiol. 2014;25:1–7.
811. Aryana A, Singh SM, Kowalski M, Pujara DK, Cohen AI, Singh SK, et al. Acute and long-term outcomes of catheter ablation of atrial fibrillation using the second-generation cryoballoon versus open-irrigated radiofrequency: a multicenter experience. J Cardiovasc Electrophysiol. 2015;26:832–9.
812. Hunter RJ, Baker V, Finlay MC, Duncan ER, Lovell MJ, Tayebjee MH, et al. Point-by-point radiofrequency ablation versus the cryoballoon or a novel combined approach: a randomized trial comparing 3 methods of pulmonary vein isolation for paroxysmal atrial fibrillation (The Cryo versus RF trial). J Cardiovasc Electrophysiol. 2015;26:1307–14.
813. Lowe MD, Meara M, Mason J, Grace AA, Murgatroyd FD. Catheter cryoablation of supraventricular arrhythmias: a painless alternative to radiofrequency energy. Pacing Clin Electrophysiol. 2003;26:500–3.
814. Yamasaki H, Aonuma K, Shinoda Y, Komatsu Y, Masuda K, Hashimoto N,, et al. Initial result of antrum pulmonary vein isolation using the radiofrequency hot-balloon catheter with single shot technique. JACC Clin Electrophysiol. 2019;5:354–63.
815. Sohara H, Satake S, Takeda H, Yamaguchi Y, Nagasu N. Prevalence of esophageal ulceration after atrial fibrillation ablation with the hot balloon ablation catheter: what is the value of esophageal cooling? J Cardiovasc Electrophysiol. 2014;25:686–92.
816. Dukkipati SR, Cuoco F, Kutinsky I, Ariyana A, Bahnson TD, Lakkireddy D, et al.; HeartLight Study Investigators. Pulmonary vein isolation using the visually guided laser balloon: a prospective, multicenter, and randomized comparison to standard radiofrequency ablation. J Am Coll Cardiol. 2015;66:1350–60.
817. Schmidt B, Gunawardene M, Urban V, Kulikoglu M, Schulte-Hahn B, Nowak B, et al. Visually guided sequential pulmonary vein isolation: Insights into techniques and predictors of acute success. J Cardiovasc Electrophysiol. 2012;23:576–82.
818. Bordignon S, Chun KR, Gunawardene M, Urban V, Kulikoglu M, Miehm K, et al. Energy titration strategies with the endoscopic ablation system: lessons from the high-dose vs. low-dose laser ablation study. Europace. 2013;15:685–9.
819. Šediva L, Petrů J, Škoda J, Janotka M, Chovanec M, Reddy V, et al. Visually guided laser ablation: a single-centre long-term experience. Europace. 2014;16:1746–51.
820. Bordignon S, Chun KR, Gunawardene M, Schulte-Hahn B, Nowak B, Fuernkranz A, et al. Endoscopic ablation systems. Expert Rev Med Devices. 2013;10:177–83.
821. Jais P, Hocini M, Hsu LF, Sanders P, Scavee C, Weerasooriya R, et al. Technique and results of linear ablation at the mitral isthmus. Circulation. 2004;110:2996–3002.
822. Sanders P, Hocini M, Jais P, Sacher F, Hsu LF, Takahashi Y, et al. Complete isolation of the pulmonary veins and posterior left atrium in chronic atrial fibrillation: long-term clinical outcome. Eur Heart J. 2007;28:1862–71.
823. Tamborero D, Mont L, Berruezo A, Matiello M, Benito B, Sitges M, et al. Left atrial posterior wall isolation does not improve the outcome of circumferential pulmonary vein ablation for atrial fibrillation: a prospective randomized study. Circ Arrhythm Electrophysiol. 2009;2:35–40.
824. Matsuo S, Yamane T, Date T, Hioki M, Narui R, Ito K, et al. Completion of mitral isthmus ablation using a steerable sheath: prospective randomized comparison with a nonsteerable sheath. J Cardiovasc Electrophysiol. 2011;22:1331–8.
825. Wong KC, Qureshi N, Jones M, Rajappan K, Bashir Y, Betts TR. Mitral isthmus ablation using steerable sheath and high ablation power: a single center experience. J Cardiovasc Electrophysiol. 2012;23:1193–200.
826. Okubo K, Kuwahara T, Takigawa M, Tanaka Y, Nakajima J, Watari Y, et al. Impact of anteroinferior transseptal puncture on creation of a complete block at the mitral isthmus in patients with atrial fibrillation. J Interv Card Electrophysiol. 2017;48:317–25.
827. Sawhney N, Anousheh R, Chen W, Feld GK. Circumferential pulmonary vein ablation with additional linear ablation results in an increased incidence of left atrial flutter compared with segmental pulmonary vein isolation as an initial approach to ablation

of paroxysmal atrial fibrillation. Circ Arrhythm Electrophysiol. 2010;3:243–8.
828. Matsuo S, Wright M, Knecht S, Nault I, Lellouche N, Lim KT, et al. Peri-mitral atrial flutter in patients with atrial fibrillation ablation. Heart Rhythm. 2010;7:2–8.
829. O'Neill MD, Wright M, Knecht S, Jaïs P, Hocini M, Takahashi Y, et al. Long-term follow-up of persistent atrial fibrillation ablation using termination as a procedural endpoint. Eur Heart J. 2009;30:1105–12.
830. Providencia R, Lambiase PD, Srinivasan N, Ganesh Babu G, Bronis K, Ahsan S, et al. Is there still a role for complex fractionated atrial electrogram ablation in addition to pulmonary vein isolation in patients with paroxysmal and persistent atrial fibrillation? Meta-analysis of 1415 patients. Circ Arrhythm Electrophysiol. 2015;8:1017–29.
831. Haissaguerre M, Hocini M, Sanders P, Sacher F, Rotter M, Takahashi Y, et al. Catheter ablation of long-lasting persistent atrial fibrillation: clinical outcome and mechanisms of subsequent arrhythmias. J Cardiovasc Electrophysiol. 2005;16:1138–47.
832. Haissaguerre M, Hocini M, Sanders P, Takahashi Y, Rotter M, Sacher F, et al. Localized sources maintaining atrial fibrillation organized by prior ablation. Circulation. 2006;113:616–25.
833. Schreiber D, Rostock T, Frohlich M, Sultan A, Servatius H, Hoffmann BA, et al. Five-year follow-up after catheter ablation of persistent atrial fibrillation using the stepwise approach and prognostic factors for success. Circ Arrhythm Electrophysiol. 2015;8:308–17.
834. Fink T, Schluter M, Heeger CH, Lemes C, Maurer T, Reissmann B, et al. Stand-alone pulmonary vein isolation versus pulmonary vein isolation with additional substrate modification as index ablation procedures in patients with persistent and long-standing persistent atrial fibrillation: the Randomized Alster-Lost-AF Trial (Ablation at St. Georg Hospital for Long-Standing Persistent Atrial Fibrillation). Circ Arrhythm Electrophysiol. 2017;7:10.
835. Bhargava M, Di Biase L, Mohanty P, Prasas S, Martin DO, Williams-Andrews M, et al. Impact of type of atrial fibrillation and repeat catheter ablation on long-term freedom from atrial fibrillation: results from a multicenter study. Heart Rhythm. 2009;6:1403–12.
836. Hayashi K, An Y, Nagashima M, Hiroshima K, Ohe M, Makihara Y, et al. Importance of nonpulmonary vein foci in catheter ablation for paroxysmal atrial fibrillation. Heart Rhythm. 2015;12:1918–24.
837. Santangeli P, Zado ES, Hutchinson MD, Riley MP, Lin D, Frankel DS, et al. Prevalence and distribution of focal triggers in persistent and long-standing persistent atrial fibrillation. Heart Rhythm. 2016;13:374–82.
838. Hung Y, Lo LW, Lin YJ, Chang SL, Hu YF, Chung FP, et al. Characteristics and long-term catheter ablation outcome in long-standing persistent atrial fibrillation patients with non-pulmonary vein triggers. Int J Cardiol. 2017;241:205–11.
839. Chang HY, Lo LW, Lin YJ, Chang SL, Hu YF, Li CH, et al. Long-term outcome of catheter ablation in patients with atrial fibrillation originating from nonpulmonary vein ectopy. J Cardiovasc Electrophysiol. 2013;24:250–8.
840. Takigawa M, Takahashi A, Kuwahara T, Okubo K, Takahashi Y, Nakashima E, et al. Impact of non-pulmonary vein foci on the outcome of the second session of catheter ablation for paroxysmal atrial fibrillation. J Cardiovasc Electrophysiol. 2015;26:739–46.
841. Zhao Y, Di Biase L, Trivedi C, Mohanty S, Bai R, Mohanty P, et al. Importance of non-pulmonary vein triggers ablation to achieve long-term freedom from paroxysmal atrial fibrillation in patients with low ejection fraction. Heart Rhythm. 2016;13:141–9.
842. Santangeli P, Marchlinski FE. Techniques for the provocation, localization, and ablation of non-pulmonary vein triggers for atrial fibrillation. Heart Rhythm. 2017;14:1087–96.
843. Inoue K, Kurotobi T, Kimura R, Toyoshima Y, Itoh N, Masuda M, et al. Trigger-based mechanism of the persistence of atrial fibrillation and its impact on the efficacy of catheter ablation. Circ Arrhythm Electrophysiol. 2012;5:295–301.
844. Lee SH, Tai CT, Hsieh MH, Tsao HM, Lin YJ, Chang SL, et al. Predictors of non-pulmonary vein ectopic beats initiating paroxysmal atrial fibrillation: Implication for catheter ablation. J Am Coll Cardiol. 2005;46:1054–9.
845. Nakagawa H, Scherlag BJ, Patterson E, Ikeda A, Lockwood D, Jackman WM. Pathophysiologic basis of autonomic ganglionated plexus ablation in patients with atrial fibrillation. Heart Rhythm. 2009;6:S26–S34.
846. Yamashiro K, Sakamoto Y, Suzuki T, et al. Variety of the left atrial ganglionated plexi in the setting catheter ablation of atrial fibrillation. Heart Rhythm. 2010;7(Suppl):S324.
847. Patterson E, Po SS, Scherlag BJ, Lazzara R. Triggered firing in pulmonary veins initiated by in vitro autonomic nerve stimulation. Heart Rhythm. 2005;2:624–31.
848. Vaitkevicius R, Saburkina I, Rysevaite K, Vaitkeviciene I, Pauziene N, Zaliunas R, et al. Nerve supply of the human pulmonary veins: an anatomical study. Heart Rhythm. 2009;6:221–8.
849. Driessen AHG, Berger WR, Krul SPJ, van den Berg NWE, Neefs J, Piersma FR, et al. Ganglion plexus ablation in advanced atrial fibrillation: the AFACT study. J Am Coll Cardiol. 2016;68:1155–65.
850. Jalife J, Berenfeld O, Mansour M. Mother rotors and fibrillatory conduction: a mechanism of atrial fibrillation. Cardiovasc Res. 2002;54:204–16.
851. Pandit SV, Jalife J. Rotors and the dynamics of cardiac fibrillation. Circ Res. 2013;112:849–62.
852. Narayan SM, Krummen DE, Shivkumar K, Clopton P, Rappel WJ, Miller JM. Treatment of atrial fibrillation by the ablation of localized sources: CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) trial. J Am Coll Cardiol. 2012;60:628–36.
853. Narayan SM, Krummen DE, Clopton P, Shivkumar K, Miller JM. Direct or coincidental elimination of stable rotors or focal sources may explain successful atrial fibrillation ablation: on-treatment analysis of the CONFIRM trial (Conventional ablation for AF with or without focal impulse and rotor modulation). J Am Coll Cardiol. 2013;62:138–47.
854. Buch E, Share M, Tung R, Benharash P, Sharma P, Koneru J, et al. Long-term clinical outcomes of focal impulse and rotor modulation for treatment of atrial fibrillation: a multicenter experience. Heart Rhythm. 2016;13:636–41.
855. Lim HS, Hocini M, Dubois R, Denis A, Derval N, Zellerhoff S, et al. Complexity and distribution of drivers in relation to duration of persistent atrial fibrillation. J Am Coll Cardiol. 2017;69:1257–69.
856. Sakata K, Okuyama Y, Ozawa T, Haraguchi R, Nakazawa K, Tsuchiya T, et al. Not all rotors, effective ablation targets for nonparoxysmal atrial fibrillation, are included in areas suggested by conventional indirect indicators of atrial fibrillation drivers: ExTRa Mapping project. J Arrhythm. 2018;34:176–84.
857. Yagishita A, Gimbel JR, Oliveira DES, Manyam H, Sparano D, Cakulev I, et al. Long-term outcome of left atrial voltage-guided substrate ablation during atrial fibrillation: a novel adjunctive ablation strategy. J Cardiovasc Electrophysiol. 2017;28:147–55.
858. Yamaguchi T, Tsuchiya T, Nakahara S, Fukui A, Nagamoto Y, Murotani K, et al. Efficacy of left atrial voltage-based catheter ablation of persistent atrial fibrillation. J Cardiovasc Electrophysiol. 2016;27:1055–63.
859. Masuda M, Fujita M, Iida O, Okamoto S, Ishihara T, Nanto K, et al. Comparison of left atrial voltage between sinus rhythm and atrial fibrillation in association with electrogram waveform. Pacing Clin Electrophysiol. 2017;40:559–67.

860. Yang B, Jiang C, Lin Y, Yang G, Chu H, Cai H, et al. STABLE-SR Investigators. STABLE-SR (Electrophysiological Substrate Ablation in the Left Atrium During Sinus Rhythm) for the treatment of nonparoxysmal atrial fibrillation: A prospective, multicenter randomized clinical trial. Circ Arrhythm Electrophysiol. 2017;11:10.
861. Valderrabano M, Chen HR, Sidhu J, Rao L, Ling Y, Khoury DS, et al. Retrograde ethanol infusion in the vein of Marshall: Regional left atrial ablation, vagal denervation and feasibility in humans. Circ Arrhythm Electrophysiol. 2009;2:50–6.
862. Valderrabano M, Liu X, Sasaridis C, Sidhu J, Little S, Khoury DS. Ethanol infusion in the vein of Marshall: adjunctive effects during ablation of atrial fibrillation. Heart Rhythm. 2009;6:1552–8.
863. Hwang C, Wu TJ, Doshi RN, Peter CT, Chen PS. Vein of Marshall cannulation for the analysis of electrical activity in patients with focal atrial fibrillation. Circulation. 2000;101:1503–5.
864. Kurotobi T, Ito H, Inoue K, Iwakura K, Kawano S, Okamura A, et al. Marshall vein as arrhythmogenic source in patients with atrial fibrillation: correlation between its anatomy and electrophysiological findings. J Cardiovasc Electrophysiol. 2006;17:1062–7.
865. Keida T, Fujita M, Okishige K, Takami M. Elimination of non-pulmonary vein ectopy by ethanol infusion in the vein of Marshall. Heart Rhythm. 2013;10:1354–6.
866. Ulphani JS, Arora R, Cain JH, Villuendas R, Shen S, Gordon D, et al. The ligament of Marshall as a parasympathetic conduit. Am J Physiol Heart Circ Physiol. 2007;293:H1629–H1635.
867. Baez-Escudero JL, Keida T, Dave AS, Okishige K, Valderrabano M. Ethanol infusion in the vein of Marshall leads to parasympathetic denervation of the human left atrium: implications for atrial fibrillation. J Am Coll Cardiol. 2014;63:1892–901.
868. Baez-Escudero JL, Morales PF, Dave AS, Sasiridis CM, Kim YH, Okishige K, et al. Ethanol infusion in the vein of Marshall facilitates mitral isthmus ablation. Heart Rhythm. 2012;9:1207–15.
869. Yoshitani K, Kujira K, Okishige K. Simultaneous re-isolation of the left pulmonary veins and termination of peri-mitral flutter with only an ethanol infusion in the vein of Marshall: killing two birds with one stone. Europace. 2014;16:1180.
870. Saghy L, Tutuianu C, Szilagyi J. Atrial tachycardias following atrial fibrillation ablation. Curr Cardiol Rev. 2015;11:149–56.
871. Oral H, Knight BP, Tada H, Ozaydin M, Chugh A, Hassan S, et al. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. Circulation. 2002;105:1077–81.
872. Gerstenfeld EP, Callans DJ, Dixit S, Russo AM, Nayak H, Lin D, et al. Mechanisms of organized left atrial tachycardias occurring after pulmonary vein isolation. Circulation. 2004;110:1351–7.
873. Chugh A, Oral H, Lemola K, Hall B, Cheung P, Good E, et al. Prevalence, mechanisms, and clinical significance of macroreentrant atrial tachycardia during and following left atrial ablation for atrial fibrillation. Heart Rhythm. 2005;2:464–71.
874. Chang SL, Tsao HM, Lin YJ, Lo LW, Hu YF, Tuan TC, et al. Differentiating macroreentrant from focal atrial tachycardias occurred after circumferential pulmonary vein isolation. J Cardiovasc Electrophysiol. 2011;22:748–55.
875. Deisenhofer I, Estner H, Zrenner B, Schreieck J, Weyerbrock S, Hessling G, et al. Left atrial tachycardia after circumferential pulmonary vein ablation for atrial fibrillation: incidence, electrophysiological characteristics, and results of radiofrequency ablation. Europace. 2006;8:573–82.
876. Karch MR, Zrenner B, Deisenhofer I, Schreieck J, Ndrepepa G, Dong J, et al. Freedom from atrial tachyarrhythmias after catheter ablation of atrial fibrillation: a randomized comparison between 2 current ablation strategies. Circulation. 2005;111:2875–80.
877. Estner HL, Hessling G, Biegler R, Schreieck J, Fichtner S, Wu J, et al. Complex fractionated atrial electrogram or linear ablation in patients with persistent atrial fibrillation: a prospective randomized study. Pacing Clin Electrophysiol. 2011;34:939–48.
878. Rostock T, Drewitz I, Steven D, Hoffmann BA, Salukhe TV, Bock K, et al. Characterization, mapping, and catheter ablation of recurrent atrial tachycardias after stepwise ablation of long-lasting persistent atrial fibrillation. Circ Arrhythm Electrophysiol. 2010;3:160–9.
879. Gerstenfeld EP, Callans DJ, Sauer W, Jacobson J, Marchlinski FE. Reentrant and nonreentrant focal left atrial tachycardias occur after pulmonary vein isolation. Heart Rhythm. 2005;2:1195–202.
880. Chae S, Oral H, Good E, Dey S, Wimmer A, Crawford T, et al. Atrial tachycardia after circumferential pulmonary vein ablation of atrial fibrillation: mechanistic insights, results of catheter ablation, and risk factors for recurrence. J Am Coll Cardiol. 2007;50:1781–7.
881. Satomi K, Bansch D, Tilz R, Chun J, Ernst S, Antz M, et al. Left atrial and pulmonary vein macroreentrant tachycardia associated with double conduction gaps: a novel type of man-made tachycardia after circumferential pulmonary vein isolation. Heart Rhythm. 2008;5:43–51.
882. Japanese Circulation Society Joint Working Group. Guidelines for indications and procedural techniques of catheter ablation (JCS2012) [in Japanese]. http://www.j-circ.or.jp/guideline/pdf/JCS2012_okumura_h.pdf (Accessed Nov. 2018)
883. Wazni OM, Beheiry S, Fahmy T, Barrett C, Hao S, Patel D, et al. Atrial fibrillation ablation in patients with therapeutic international normalized ratio: comparison of strategies of anticoagulation management in the periprocedural period. Circulation. 2007;116:2531–4.
884. Calkins H, Gerstenfeld EP, Schilling R, Verma A, Willems S. RE-CIRCUIT Study Steering Committee. RE-CIRCUIT study: randomized evaluation of dabigatran etexilate compared to warfarin in pulmonary vein ablation: Assessment of an uninterrupted periprocedural anticoagulation strategy. Am J Cardiol. 2015;115:154–5.
885. Cappato R, Marchlinski FE, Hohnloser SH, Naccarelli GV, Xiang J, Wilber DJ, et al.; VENTURE-AF Investigators. Uninterrupted rivaroxaban vs. uninterrupted vitamin K antagonists for catheter ablation in non-valvular atrial fibrillation. Eur Heart J. 2015;36:1805–11.
886. Di Biase L, Lakkireddy D, Trivedi C, Deneke T, Martinek M, Mohanty S, et al. Feasibility and safety of uninterrupted periprocedural apixaban administration in patients undergoing radiofrequency catheter ablation for atrial fibrillation: Results from a multicenter study. Heart Rhythm. 2015;12:1162–8.
887. Kirchhof P, Haeusler KG, Blank B, De Bono J, Callans D, Elvan A, et al. Apixaban in patients at risk of stroke undergoing atrial fibrillation ablation. Eur Heart J. 2018;39:2942–55.
888. Reynolds MR, Allison JS, Natale A, Weisberg IL, Ellenbogen KA, Richards M, et al. A prospective randomized trial of apixaban dosing during atrial fibrillation ablation: The AEIOU Trial. JACC Clin Electrophysiol. 2018;4:580–8.
889. Nogami A, Harada T, Sekiguchi Y, Otani R, Yoshida Y, Yoshida K, et al. Safety and efficacy of minimally interrupted dabigatran vs uninterrupted warfarin therapy in adults undergoing atrial fibrillation catheter ablation: a randomized clinical trial. JAMA Netw Open. 2019;2:e191994.
890. Nakamura K, Naito S, Sasaki T, Take Y, Minami K, Kitagawa Y, et al. Uninterrupted vs. interrupted periprocedural direct oral anticoagulants for catheter ablation of atrial fibrillation: a prospective randomized single-centre study on post-ablation thrombo-embolic and haemorrhagic events. Europace. 2019;21:259–67.
891. Okumura K, Aonuma K, Kumagai K, Hirao K, Inoue K, Kimura M, et al. Efficacy and safety of rivaroxaban and warfarin in the perioperative period of catheter ablation for atrial fibrillation: outcome analysis from a prospective multicenter registry study in Japan. Circ J. 2016;80:2295–301.
892. Ren JF, Marchlinski FE, Callans DJ. Left atrial thrombus associated with ablation for atrial fibrillation: identification with intracardiac echocardiography. J Am Coll Cardiol. 2004;43:1861–7.

893. Wazni OM, Rossillo A, Marrouche NF, Saad EB, Martin DO, Bhargava M, et al. Embolic events and char formation during pulmonary vein isolation in patients with atrial fibrillation: impact of different anticoagulation regimens and importance of intracardiac echo imaging. J Cardiovasc Electrophysiol. 2005;16:576–81.
894. Schmidt M, Segerson NM, Marschang H, Akoum N, Rittger H, Clifford SM, et al. Atrial fibrillation ablation in patients with therapeutic international normalized ratios. Pacing Clin Electrophysiol. 2009;32:995–9.
895. Fiala M, Chovancik J, Neuwirth R, Nevralová R, Jiravský O, Sknouril L, et al. Atrial macroreentry tachycardia in patients without obvious structural heart disease or previous cardiac surgical or catheter intervention: characterization of arrhythmogenic substrates, reentry circuits, and results of catheter ablation. J Cardiovasc Electrophysiol. 2007;18:824–32.
896. Nakagawa H, Shah N, Matsudaira K, Overholt E, Chandrasekaran K, Beckman KJ, et al. Characterization of reentrant circuit in macroreentrant right atrial tachycardia after surgical repair of congenital heart disease: isolated channels between scars allow "focal" ablation. Circulation. 2001;103:699–709.
897. Ishii Y, Nitta T, Sakamoto S, Tanaka S, Asano G. Incisional atrial reentrant tachycardia: experimental study on the conduction property through the isthmus. J Thorac Cardiovasc Surg. 2003;126:254–62.
898. Huang JL, Tai CT, Lin YJ, Huang BH, Lee KT, Higa S, et al. Substrate mapping to detect abnormal atrial endocardium with slow conduction in patients with atypical right atrial flutter. J Am Coll Cardiol. 2006;48:492–8.
899. McElderry HT, McGiffin DC, Plumb VJ, Nanthakumar K, Epstein AE, Yamada T, et al. Proarrhythmic aspects of atrial fibrillation surgery: mechanisms of postoperative macroreentrant tachycardias. Circulation. 2008;117:155–62.
900. Flinn CJ, Wolff GS, Dick M 2nd, Campbell RM, Borkat G, Casta A, et al. Cardiac rhythm after the Mustard operation for complete transposition of the great arteries. N Engl J Med. 1984;310:1635–8.
901. Kanter RJ, Papagiannis J, Carboni MP, Ungerleider RM, Sanders WE, Wharton JM. Radiofrequency catheter ablation of supraventricular tachycardia substrates after Mustard and Senning operations for d-transposition of the great arteries. J Am Coll Cardiol. 2000;35:428–41.
902. Van Hare GF, Lesh MD, Ross BA, Perry JC, Dorostkar PC. Mapping and radiofrequency ablation of intraatrial reentrant tachycardia after the Senning or Mustard procedure for transposition of the great arteries. Am J Cardiol. 1996;77:985–91.
903. Perry JC, Boramanand NK, Ing FF. "Transseptal" technique through atrial baffles for 3-dimensional mapping and ablation of atrial tachycardia in patients with d-transposition of the great arteries. J Interv Card Electrophysiol. 2003;9:365–9.
904. Wu J, Pflaumer A, Deisenhofer I, Ucer E, Hess J, Zrenner B, et al. Mapping of intraatrial reentrant tachycardias by remote magnetic navigation in patients with d-transposition of the great arteries after Mustard or Senning procedure. J Cardiovasc Electrophysiol. 2008;19:1153–9.
905. Shiina Y, Toyoda T, Kawasoe Y, Tateno S, Shirai T, Wakisaka Y, et al. Prevalence of adult patients with congenital heart disease in Japan. Int J Cardiol. 2011;146:13–6.
906. Li W, Somerville J. Atrial flutter in grown-up congenital heart (GUCH) patients: Clinical characteristics of affected population. Int J Cardiol. 2000;75:129–37.
907. Escudero C, Khairy P, Sanatani S. Electrophysiologic considerations in congenital heart disease and their relationship to heart failure. Can J Cardiol. 2013;29:821–9.
908. Walsh EP. Arrhythmias in patients with congenital heart disease. Card Electrophysiol Rev. 2002;6:422–30.
909. Hernandez-Madrid A, Paul T, Abrams D, Aziz PF, Blom NA, Chen J, et al. Arrhythmias in congenital heart disease: A Position Paper of the European Heart Rhythm Association (EHRA), Association for European Paediatric and Congenital Cardiology (AEPC), and the European Society of Cardiology (ESC) Working Group on Grown-up Congenital heart disease, endorsed by HRS, PACES, APHRS, and SOLAECE. Europace. 2018;20:1719–53.
910. Triedman JK, Jenkins KJ, Colan SD, Saul JP, Walsh EP. Intra-atrial reentrant tachycardia after palliation of congenital heart disease: characterization of multiple macroreentrant circuits using fluoroscopically based three-dimensional endocardial mapping. J Cardiovasc Electrophysiol. 1997;8:259–70.
911. De Groot NM, Kuijper AF, Blom NA, Bootsma M, Schalij MJ. Three-dimensional distribution of bipolar atrial electrogram voltages in patients with congenital heart disease. Pacing Clin Electrophysiol. 2001;24:1334–42.
912. Delacretaz E, Ganz LI, Soejima K, Friedman PL, Walsh EP, Triedman JK, et al. Multi atrial maco-re-entry circuits in adults with repaired congenital heart disease: entrainment mapping combined with three-dimensional electroanatomic mapping. J Am Coll Cardiol. 2001;37:1665–76.
913. Triedman JK, Alexander ME, Berul CI, Bevilacqua LM, Walsh EP. Electroanatomic mapping of entrained and exit zones in patients with repaired congenital heart disease and intra-atrial reentrant tachycardia. Circulation. 2001;103:2060–5.
914. Nakagawa H, Jackman WM. Use of a three-dimensional, nonfluoroscopic mapping system for catheter ablation of typical atrial flutter. Pacing Clin Electrophysiol. 1998;21:1279–86.
915. Triedman JK, Bergau DM, Saul JP, Epstein MR, Walsh EP. Efficacy of radiofrequency ablation for control of intraatrial reentrant tachycardia in patients with congenital heart disease. J Am Coll Cardiol. 1997;30:1032–8.
916. Kalman JM, VanHare GF, Olgin JE, Saxon LA, Stark SI, Lesh MD. Ablation of 'incisional' reentrant atrial tachycardia complicating surgery for congenital heart disease: use of entrainment to define a critical isthmus of conduction. Circulation. 1996;93:502–12.
917. Kirsh JA, Walsh EP, Triedman JK. Prevalence of and risk factors for atrial fibrillation and intra-atrial reentrant tachycardia among patients with congenital heart disease. Am J Cardiol. 2002;90:338–40.
918. Triedman JK, Saul JP, Weindling SN, Walsh EP. Radiofrequency ablation of intra-atrial reentrant tachycardia after surgical palliation of congenital heart disease. Circulation. 1995;91:707–14.
919. Collins KK, Rhee EK, Delucca JM, Alexander ME, Bevilacqua LM, Berul CI, et al. Modification to the Fontan procedure for the prophylaxis of intra-atrial reentrant tachycardia: short-term results of a prospective randomized blinded trial. J Thorac Cardiovasc Surg. 2004;127:721–9.
920. Harrison DA, Siu SC, Hussain F, MacLoghlin CJ, Webb GD, Harris L. Sustained atrial arrhythmias in adults late after repair of tetralogy of Fallot. Am J Cardiol. 2001;87:584–8.
921. Bricker JT. Sudden death and tetralogy of Fallot: Risks, markers, and causes. Circulation. 1995;92:158–9.
922. Deanfield JE, Ho SY, Anderson RH, McKenna WJ, Allwork SP, Hallidie-Smith KA. Late sudden death after repair of tetralogy of Fallot: a clinicopathologic study. Circulation. 1983;67:626–31.
923. Rostock T, Willems S, Ventura R, Weiss C, Risius T, Meinertz T. Radiofrequency catheter ablation of a macroreentrant ventricular tachycardia late after surgical repair of tetralogy of Fallot using the electroanatomic mapping (CARTO). Pacing Clin Electrophysiol. 2004;27:801–4.
924. Gonska BD, Cao K, Raab J, Eigster G, Kreuzer H. Radiofrequency catheter ablation of right ventricular tachycardia late after repair of congenital heart defects. Circulation. 1996;94:1902–8.

925. Ressia L, Graffigna A, Salerno-Uriarte JA, Vigano M. The complex origin of ventricular tachycardia after the total correction of tetralogy of Fallot. G Ital Cardiol. 1993;23:905–10. [in Italian].
926. Fishberger SB, Wernovsky G, Gentles TL, Gauvreau K, Burnett J, Mayer JE Jr, et al. Factors that influence the development of atrial flutter after the Fontan operation. J Thorac Cardiovasc Surg. 1997;113:80–6.
927. Levine JC, Walsh EP, Saul JP. Radiofrequency ablation of accessory pathways associated with congenital heart disease including heterotaxy syndrome. Am J Cardiol. 1993;72:689–93.
928. Epstein MR, Saul JP, Weindling SN, Triedman JK, Walsh EP. Atrioventricular reciprocating tachycardia involving twin atrioventricular nodes in patients with complex congenital heart disease. J Cardiovasc Electrophysiol. 2001;12:671–9.
929. Kreutzer J, Keane JF, Lock JE, Walsh EP, Jonas RA, Castañeda AR, et al. Conversion of modified Fontan procedure to lateral atrial tunnel cavopulmonary anastomosis. J Thorac Cardiovasc Surg. 1996;111:1169–76.
930. Stamm C, Friehs I, Mayer JE Jr, Zurakowski D, Triedman JK, Moran AM, et al. Long-term results of the lateral tunnel Fontan operation. J Thorac Cardiovasc Surg. 2001;121:28–41.
931. Ito S, Tada H, Naito S, Kurosaki K, Ueda M, Hoshizaki H, et al. Development and validation of an ECG algorithm for identifying the optimal ablation site for idiopathic ventricular outflow tract tachycardia. J Cardiovasc Electrophysiol. 2003;14:1280–6.
932. Bunch TJ, Day JD. Right meets left: a common mechanism underlying right and left ventricular outflow tract tachycardias. J Cardiovasc Electrophysiol. 2006;17:1059–61.
933. Chinushi M, Aizawa Y, Takahashi K, Kitazawa H, Shibata A. Radiofrequency catheter ablation for idiopathic right ventricular tachycardia with special reference to morphological variation and long-term outcome. Heart. 1997;78:255–61.
934. Joshi S, Wilber DJ. Ablation of idiopathic right ventricular outflow tract tachycardia: current perspectives. J Cardiovasc Electrophysiol. 2005;16(Suppl 1):S52–S58.
935. Yoshida Y, Hirai M, Murakami Y, Kondo T, Inden Y, Akahoshi M, et al. Localization of precise origin of idiopathic ventricular tachycardia from the right ventricular outflow tract by a 12-lead ECG: a study of pace mapping using a multielectrode "basket" catheter. Pacing Clin Electrophysiol. 1999;22:1760–8.
936. Azegami K, Wilber DJ, Arruda M, Lin AC, Denman RA. Spatial resolution of pacemapping and activation mapping in patients with idiopathic right ventricular outflow tract tachycardia. J Cardiovasc Electrophysiol. 2005;16:823–9.
937. Ainsworth CD, Skanes AC, Klein GJ, Gula LJ, Yee R, Krahn AD, et al. Differentiating arrhythmogenic right ventricular cardiomyopathy from right ventricular outflow tract ventricular tachycardia using multilead QRS duration and axis. Heart Rhythm. 2006;3:416–23.
938. Kaseno K, Tada H, Ito S, Tadokoro K, Hashimoto T, Miyaji K, et al. Ablation of idiopathic ventricular tachycardia in two separate regions of the outflow tract: prevalence and electrocardiographic characteristics. Pacing Clin Electrophysiol. 2007;30(Suppl):S88–S93.
939. Miller JM, Pezeshkian NG, Yadav AV. Catheter mapping and ablation of right ventricular outflow tract ventricular tachycardia. J Cardiovasc Electrophysiol. 2006;17:800–2.
940. Proclemer A, Ciani R, Feruglio GA. Right ventricular tachycardia with left bundle branch block and inferior axis morphology: clinical and arrhythmological characteristics in 15 patients. Pacing Clin Electrophysiol. 1989;12:977–89.
941. Lopera G, Stevenson WG, Soejima K, Maisel WH, Koplan B, Sapp JL, et al. Identification and ablation of three types of ventricular tachycardia involving the His-Purkinje system in patients with heart disease. J Cardiovasc Electrophysiol. 2004;15:52–8.
942. Nogami A. Purkinje-related arrhythmias. Part I: Monomorphic ventricular tachycardias. Pacing Clin Electrophysiol. 2011;34:624–50.
943. Nakagawa H, Beckman KJ, McClelland JH, Wang X, Arruda M, Santoro I, et al. Radiofrequency catheter ablation of idiopathic left ventricular tachycardia guided by a Purkinje potential. Circulation. 1993;88:2607–17.
944. Ouyang F, Cappato R, Ernst S, Goya M, Volkmer M, Hebe J, et al. Electroanatomic substrate of idiopathic left ventricular tachycardia: Unidirectional block and macroreentry within the Purkinje network. Circulation. 2002;105:462–9.
945. Tsuchiya T, Okumura K, Honda T, Iwasa A, Yasue H, Tabuchi T. Significance of late diastolic potential preceding Purkinje potential in verapamil-sensitive idiopathic left ventricular tachycardia. Circulation. 1999;99:2408–13.
946. Nogami A, Naito S, Tada H, Taniguchi K, Okamoto Y, Nishimura S, et al. Demonstration of diastolic and presystolic Purkinje potentials as critical potentials in a macroreentry circuit of verapamil-sensitive idiopathic left ventricular tachycardia. J Am Coll Cardiol. 2000;36:811–23.
947. Morishima I, Nogami A, Tsuboi H, Sone T. Negative participation of the left posterior fascicle in the reentry circuit of verapamil-sensitive idiopathic left ventricular tachycardia. J Cardiovasc Electrophysiol. 2012;23:556–9.
948. Nogami A, Naito S, Tada H, Oshima S, Taniguchi K, Aonuma K, et al. Verapamil-sensitive left anterior fascicular ventricular tachycardia: results of radiofrequency ablation in six patients. J Cardiovasc Electrophysiol. 1998;9:1269–78.
949. Talib AK, Nogami A, Nishiuchi S, Kowase S, Kurosaki K, Matsui Y, et al. Verapamil-sensitive upper septal idiopathic left ventricular tachycardia: Prevalence, mechanism, and electrophysiological characteristics. JACC Clin Electrophysiol. 2015;1:369–80.
950. Komatsu Y, Nogami A, Kurosaki K, Morishima I, Masuda K, Ozawa T, et al. Fascicular ventricular tachycardia originating from papillary muscles: Purkinje network involvement in the reentrant circuit. Circ Arrhythm Electrophysiol. 2017;10:e004549.
951. Buxton AE, Lee KL, Fisher JD, e Josephson ME, Prystowsky EN, Hafley G,,; et al. A randomized study of the prevention of sudden death in patients with coronary artery disease. N Engl J Med. 1999;341:1882–90.
952. Irvine J, Dorian P, Baker B, O'Brien BJ, Roberts R, Gent M, et al. Quality of life in the Canadian Implantable Defibrillator Study (CIDS). Am Heart J. 2002;144:282–9.
953. Mark DB, Anstrom KJ, Sun JL, Clapp-Channing NE, Tsiatis AA, Davidson-Ray L, et al.; Sudden Cardiac Death in Heart Failure Trial Investigators. Quality of life with defibrillator therapy or amiodarone in heart failure. N Engl J Med. 2008;359:999–1008.
954. Moss AJ, Greenberg H, Case RB, Zareba W, Hall WJ, Brown MW, et al. Multicenter Automatic Defibrillator Implantation Trial-II (MADIT-II) Research Group. Long-term clinical course of patients after termination of ventricular tachyarrhythmia by an implanted defibrillator. Circulation. 2004;110:3760–5.
955. Poole JE, Johnson GW, Hellkamp AS, Anderson J, Callans DJ, Raitt MH, et al. Prognostic importance of defibrillator shocks in patients with heart failure. N Engl J Med. 2008;359:1009–17.
956. Schron EB, Exner DV, Yao Q, Jenkins LS, Steinberg JS, Cook JR, et al. Quality of life in the antiarrhythmics versus implantable defibrillators trial: impact of therapy and influence of adverse symptoms and defibrillator shocks. Circulation. 2002;105:589–94.
957. Daubert JP, Zareba W, Cannom DS, McNitt S, Rosero SZ, Wang P, et al. Inappropriate implantable cardioverter-defibrillator shocks in MADIT II: frequency, mechanisms, predictors, and survival impact. J Am Coll Cardiol. 2008;51:1357–65.
958. Bollmann A, Husser D, Cannom DS. Antiarrhythmic drugs in patients with implantable cardioverter-defibrillators. Am J Cardiovasc Drugs. 2005;5:371–8.

959. Connolly SJ, Dorian P, Roberts RS, Gent M, Bailin S, Fain ES, et al.; Optimal Pharmacological Therapy in Cardioverter Defibrillator Patients (OPTIC) Investigators. Comparison of beta-blockers, amiodarone plus beta-blockers, or sotalol for prevention of shocks from implantable cardioverter defibrillators: The OPTIC Study: a randomized trial. JAMA. 2006;295:165–71.
960. Pacifico A, Hohnloser SH, Williams JH, Tao B, Saksena S, Henry PD, et al.; d, l-Sotalol Implantable Cardioverter-Defibrillator Study Group. Prevention of implantable-defibrillator shocks by treatment with sotalol. N Engl J Med. 1999;340:1855–62.
961. Kuck KH, Tilz RR, Deneke T, Hoffmann BA, Ventura R, Hansen PS, et al. Impact of substrate modification by catheter ablation on implantable cardioverter-defibrillator interventions in patients with unstable ventricular arrhythmias and coronary artery disease: results from the multicenter randomized controlled SMS (substrate modification study). Circ Arrhythm Electrophysiol. 2017;10:e004422.
962. Marchlinski FE, Haffajee CI, Beshai JF, Dickfeld TML, Gonzalez MD, Hsai HH, et al. Long-term success of irrigated radiofrequency catheter ablation of sustained ventricular tachycardia: post-approval THERMOCOOL VT Trial. J Am Coll Cardiol. 2016;67:674–83.
963. Stevenson WG, Delacretaz E, Friedman PL, Ellison KE. Identification and ablation of macroreentrant ventricular tachycardia with the CARTO electroanatomical mapping system. Pacing Clin Electrophysiol. 1998;21:1448–56.
964. Marchlinski FE, Callans DJ, Gottlieb CD, Zado E. Linear ablation lesions for control of unmappable ventricular tachycardia in patients with ischemic and nonischemic cardiomyopathy. Circulation. 2000;101:1288–96.
965. Soejima K, Suzuki M, Maisel WH, Brunckhorst CB, Delacretaz E, Blier L, et al. Catheter ablation in patients with multiple and unstable ventricular tachycardias after myocardial infarction: short ablation lines guided by reentry circuit isthmuses and sinus rhythm mapping. Circulation. 2001;104:664–9.
966. Kautzner J, Cihak R, Peichl P, Vancura V, Bytesník J. Catheter ablation of ventricular tachycardia following myocardial infarction using three-dimensional electroanatomical mapping. Pacing Clin Electrophysiol. 2003;26:342–7.
967. Kottkamp H, Wetzel U, Schirdewahn P, Dorszewski A, Gerds-Li JH, Carbucicchio C, et al. Catheter ablation of ventricular tachycardia in remote myocardial infarction: substrate description guiding placement of individual linear lesions targeting noninducibility. J Cardiovasc Electrophysiol. 2003;14:675–81.
968. Khaykin Y, Skanes A, Whaley B, Hill C, Beardsall M, Seabrook C, et al. Real-time integration of 2D intracardiac echocardiography and 3D electroanatomical mapping to guide ventricular tachycardia ablation. Heart Rhythm. 2008;5:1396–402.
969. Schilling RJ, Peters NS, Davies DW. Simultaneous endocardial mapping in the human left ventricle using a noncontact catheter: comparison of contact and reconstructed electrograms during sinus rhythm. Circulation. 1998;98:887–98.
970. Gornick CC, Adler SW, Pederson B, Hauck J, Budd J, Schweitzer J. Validation of a new noncontact catheter system for electroanatomic mapping of left ventricular endocardium. Circulation. 1999;99:829–35.
971. Schilling RJ, Peters NS, Davies DW. Feasibility of a noncontact catheter for endocardial mapping of human ventricular tachycardia. Circulation. 1999;99:2543–52.
972. Klemm HU, Ventura R, Steven D, Johnsen C, Rostock T, Lutomsky B, et al. Catheter ablation of multiple ventricular tachycardias after myocardial infarction guided by combined contact and noncontact mapping. Circulation. 2007;115:2697–704.
973. Viswanathan K, Mantziari L, Butcher C, Hodkinson E, Lim E, Khan H, et al. Evaluation of a novel high-resolution mapping system for catheter ablation of ventricular arrhythmias. Heart Rhythm. 2017;14:176–83.
974. Takigawa M, Frontera A, Thompson N, Capellino S, Jais P, Sacher F. The electrical circuit of a hemodynamically unstable and recurrent ventricular tachycardia diagnosed in 35 s with the Rhythmia mapping system. J Arrhythm. 2017;33:505–7.
975. Reddy VY, Neuzil P, Taborsky M, Ruskin JN. Short-term results of substrate mapping and radiofrequency ablation of ischemic ventricular tachycardia using a saline-irrigated catheter. J Am Coll Cardiol. 2003;41:2228–36.
976. Stevenson WG, Wilber DJ, Natale A, Jackman WM, Marchlinski FE, Talbert T, et al.; Multicenter Thermocool VT Ablation Trial Investigators. Irrigated radiofrequency catheter ablation guided by electroanatomic mapping for recurrent ventricular tachycardia after myocardial infarction: The multicenter thermocool ventricular tachycardia ablation trial. Circulation. 2008;118:2773–82.
977. Tanner H, Hindricks G, Volkmer M, Furniss S, Kuhlkamp V, Lacroix D, et al. Catheter ablation of recurrent scar-related ventricular tachycardia using electroanatomical mapping and irrigated ablation technology: results of the prospective multicenter Euro-VT-study. J Cardiovasc Electrophysiol. 2010;21:47–53.
978. Tandri H, Saranathan M, Rodriguez ER, Martinez C, Bomma C, Nasir K, et al. Noninvasive detection of myocardial fibrosis in arrhythmogenic right ventricular cardiomyopathy using delayed-enhancement magnetic resonance imaging. J Am Coll Cardiol. 2005;45:98–103.
979. Roux JF, Dubuc M, Pressacco J, Roy D, Thibault B, Talajic M, et al. Concordance between an electroanatomic mapping system and cardiac MRI in arrhythmogenic right ventricular cardiomyopathy. Pacing Clin Electrophysiol. 2006;29:109–12.
980. Codreanu A, Odille F, Aliot E, Marie PY, Magnin-Poull I, Andronache M, et al. Electroanatomic characterization of post-infarct scars comparison with 3-dimensional myocardial scar reconstruction based on magnetic resonance imaging. J Am Coll Cardiol. 2008;52:839–42.
981. Andreu D, Ortiz-Perez JT, Boussy T, Fernández-Armenta J, de Caralt TM, Perea RJ, et al. Usefulness of contrast enhanced cardiac magnetic resonance in identifying the ventricular arrhythmia substrate and the approach needed for ablation. Eur Heart J. 2014;35:1316–26.
982. Acosta J, Fernandez-Armenta J, Penela D, Andreu D, Borras R, Vassanelli F, et al. Infarct transmurality as a criterion for first-line endo-epicardial substrate-guided ventricular tachycardia ablation in ischemic cardiomyopathy. Heart Rhythm. 2016;13:85–95.
983. Andreu D, Penela D, Acosta J, Fernández-Armenta J, Perea RJ, Soto-Iglesias D, et al. Cardiac magnetic resonance aided scar dechanneling: Influence on acute and long-term outcomes. Heart Rhythm. 2017;14:1121–8.
984. Siontis KC, Kim HM, Sharaf Dabbagh G, Latchamsetty R, Stojanovska J, Jongnarangsin K, et al. Association of preprocedural cardiac magnetic resonance imaging with outcomes of ventricular tachycardia ablation in patients with idiopathic dilated cardiomyopathy. Heart Rhythm. 2017;14:1487–93.
985. Al-Khatib SM, Daubert JP, Anstrom KJ, Daoud EG, Gonzalez M, Saba S, et al. Catheter ablation for ventricular tachycardia in patients with an implantable cardioverter defibrillator (CALYPSO) pilot trial. J Cardiovasc Electrophysiol. 2015;26:151–7.
986. Sapp JL, Wells GA, Parkash R, Stevenson WG, Blier L, Sarrazin JF, et al. Ventricular tachycardia ablation versus escalation of antiarrhythmic drugs. N Engl J Med. 2016;375:111–21.
987. Dinov B, Fiedler L, Schonbauer R, Bollmann A, Rolf S, Piorkowski C, et al. Outcomes in catheter ablation of ventricular tachycardia in dilated nonischemic cardiomyopathy compared with ischemic cardiomyopathy: results from the Prospective Heart Centre of Leipzig VT (HELP-VT) Study. Circulation. 2014;129:728–36.

988. Tung R, Vaseghi M, Frankel DS, Vergara P, Di Biase L, Nagashima K, et al. Freedom from recurrent ventricular tachycardia after catheter ablation is associated with improved survival in patients with structural heart disease: an International VT Ablation Center Collaborative Group study. Heart Rhythm. 2015;12:1997–2007.
989. Kozeluhova M, Peichl P, Cihak R, Wichterle D, Vancura V, Bytesnik J, et al. Catheter ablation of electrical storm in patients with structural heart disease. Europace. 2011;13:109–13.
990. Tada H, Tadokoro K, Ito S, Naito S, Hashimoto T, Kaseno K, et al. Idiopathic ventricular arrhythmias originating from the tricuspid annulus: Prevalence, electrocardiographic characteristics, and results of radiofrequency catheter ablation. Heart Rhythm. 2007;4:7–16.
991. Yamauchi Y, Aonuma K, Takahashi A, Sekiguchi Y, Hachiya H, Yokoyama Y, et al. Electrocardiographic characteristics of repetitive monomorphic right ventricular tachycardia originating near the His-bundle. J Cardiovasc Electrophysiol. 2005;16:1041–8.
992. Komatsu Y, Otomo K, Taniguchi H, Kakita K, Takayama K, Fujiwara H, et al. Catheter ablation of ventricular arrhythmias arising from the right ventricular septum close to the His bundle: features of the local electrogram at the optimal ablation site. J Cardiovasc Electrophysiol. 2011;22:878–85.
993. Tada H, Tadokoro K, Miyaji K, Ito S, Kurosaki K, Kaseno K, et al. Idiopathic ventricular arrhythmias arising from the pulmonary artery: prevalence, characteristics, and topography of the arrhythmia origin. Heart Rhythm. 2008;5:419–26.
994. Sekiguchi Y, Aonuma K, Takahashi A, Yamauchi Y, Hachiya H, Yokoyama Y, et al. Electrocardiographic and electrophysiologic characteristics of ventricular tachycardia originating within the pulmonary artery. J Am Coll Cardiol. 2005;45:887–95.
995. Timmermans C, Rodriguez LM, Crijns HJ, Moorman AF, Wellens HJ. Idiopathic left bundle-branch block-shaped ventricular tachycardia may originate above the pulmonary valve. Circulation. 2003;108:1960–7.
996. Hachiya H, Aonuma K, Yamauchi Y, Harada T, Igawa M, Nogami A, et al. Electrocardiographic characteristics of left ventricular outflow tract tachycardia. Pacing Clin Electrophysiol. 2000;23:1930–4.
997. Callans DJ, Menz V, Schwartzman D, Gottlieb CD, Marchlinski FE. Repetitive monomorphic tachycardia from the left ventricular outflow tract: electrocardiographic patterns consistent with a left ventricular site of origin. J Am Coll Cardiol. 1997;29:1023–7.
998. Miles WM. Idiopathic ventricular outflow tract tachycardia: where does it originate? J Cardiovasc Electrophysiol. 2001;12:536–7.
999. Tada H, Ito S, Naito S, Kurosaki K, Kubota S, Sugiyasu A, et al. Idiopathic ventricular arrhythmia arising from the mitral annulus: a distinct subgroup of idiopathic ventricular arrhythmias. J Am Coll Cardiol. 2005;45:877–86.
1000. Kumagai K, Yamauchi Y, Takahashi A, Yokoyama Y, Sekiguchi Y, Watanabe J, et al. Idiopathic left ventricular tachycardia originating from the mitral annulus. J Cardiovasc Electrophysiol. 2005;16:1029–36.
1001. Ouyang F, Fotuhi P, Ho SY, Hebe J, Volkmer M, Goya M, et al. Repetitive monomorphic ventricular tachycardia originating from the aortic sinus cusp: electrocardiographic characterization for guiding catheter ablation. J Am Coll Cardiol. 2002;39:500–8.
1002. Kanagaratnam L, Tomassoni G, Schweikert R, Pavia S, Bash D, Beheiry S, et al. Ventricular tachycardias arising from the aortic sinus of Valsalva: an underrecognized variant of left outflow tract ventricular tachycardia. J Am Coll Cardiol. 2001;37:1408–14.
1003. Hachiya H, Aonuma K, Yamauchi Y, Igawa M, Nogami A, Iesaka Y. How to diagnose, locate, and ablate coronary cusp ventricular tachycardia. J Cardiovasc Electrophysiol. 2002;13:551–6.
1004. Ito S, Tada H, Naito S, Kurosaki K, Ueda M, Shinbo G, et al. Simultaneous mapping in the left sinus of valsalva and coronary venous system predicts successful catheter ablation from the left sinus of valsalva. Pacing Clin Electrophysiol. 2005;28(Suppl 1):S150–S154.
1005. Talib AK, Nogami A, Morishima I, Oginosawa Y, Kurosaki K, Kowase S, et al. Non-reentrant fascicular tachycardia: clinical and electrophysiological characteristics of a distinct type of idiopathic ventricular tachycardia. Circ Arrhythm Electrophysiol. 2016;9:e004177.
1006. Hirasawa Y, Miyauchi Y, Iwasaki YK, Kobayashi Y. Successful radiofrequency catheter ablation of epicardial left ventricular outflow tract tachycardia from the anterior interventricular coronary vein. J Cardiovasc Electrophysiol. 2005;16:1378–80.
1007. Yamauchi Y, Aonuma K, Sekiguchi Y, Obayashi T, Kumagai K, Isobe M. Successful radiofrequency ablation of ventricular premature contractions within the coronary sinus. Pacing Clin Electrophysiol. 2005;28:1250–2.
1008. Obel OA, d'Avila A, Neuzil P, Saad EB, Ruskin JN, Reddy VY. Ablation of left ventricular epicardial outflow tract tachycardia from the distal great cardiac vein. J Am Coll Cardiol. 2006;48:1813–7.
1009. Yamada T, Doppalapudi H, McElderry HT, Okada T, Murakami Y, Inden Y, et al. Electrocardiographic and electrophysiological characteristics in idiopathic ventricular arrhythmias originating from the papillary muscles in the left ventricle: relevance for catheter ablation. Circ Arrhythm Electrophysiol. 2010;3:324–31.
1010. Doppalapudi H, Yamada T, McElderry HT, Plumb VJ, Epstein AE, Kay GN. Ventricular tachycardia originating from the posterior papillary muscle in the left ventricle: a distinct clinical syndrome. Circ Arrhythm Electrophysiol. 2008;1:23–9.
1011. Good E, Desjardins B, Jongnarangsin K, Oral H, Chugh A, Ebinger M, et al. Ventricular arrhythmias originating from a papillary muscle in patients without prior infarction: a comparison with fascicular arrhythmias. Heart Rhythm. 2008;5:1530–7.
1012. Yamada T, Doppalapudi H, McElderry HT, Okada T, Murakami Y, Inden Y, et al. Idiopathic ventricular arrhythmias originating from the papillary muscles in the left ventricle: prevalence, electrocardiographic and electrophysiological characteristics, and results of the radiofrequency catheter ablation. J Cardiovasc Electrophysiol. 2010;21:62–9.
1013. Yokokawa M, Good E, Desjardins B, Crawford T, Jongnarangsin K, Chugh A, et al. Predictors of successful catheter ablation of ventricular arrhythmias arising from the papillary muscles. Heart Rhythm. 2010;7:1654–9.
1014. Crawford T, Mueller G, Good E, Jongnarangsin K, Chugh A, Pelosi F Jr, et al. Ventricular arrhythmias originating from papillary muscles in the right ventricle. Heart Rhythm. 2010;7:725–30.
1015. Yamada T, McElderry HT, Doppalapudi H, Okada T, Murakami Y, Yoshida Y, et al. Idiopathic ventricular arrhythmias originating from the left ventricular summit: anatomic concepts relevant to ablation. Circ Arrhythm Electrophysiol. 2010;3:616–23.
1016. Yamada T, Maddox WR, McElderry HT, Doppalapudi H, Plumb VJ, Kay GN. Radiofrequency catheter ablation of idiopathic ventricular arrhythmias originating from intramural foci in the left ventricular outflow tract: efficacy of sequential versus simultaneous unipolar catheter ablation. Circ Arrhythm Electrophysiol. 2015;8:344–52.
1017. Santangeli P, Marchlinski FE, Zado ES, Benhayon D, Hutchinson MD, Lin D, et al. Percutaneous epicardial ablation of ventricular arrhythmias arising from the left ventricular summit: outcomes and electrocardiogram correlates of success. Circ Arrhythm Electrophysiol. 2015;8:337–43.
1018. Chen YH, Lin JF. Catheter ablation of idiopathic epicardial ventricular arrhythmias originating from the vicinity of the coronary sinus system. J Cardiovasc Electrophysiol. 2015;26:1160–7.
1019. Komatsu Y, Nogami A, Shinoda Y, Masuda K, Machino T, Kuroki K, et al. Idiopathic ventricular arrhythmias originating from the vicinity of the communicating vein of cardiac venous systems

at the left ventricular summit. Circ Arrhythm Electrophysiol. 2018;11:e005386.
1020. Doppalapudi H, Yamada T, Ramaswamy K, Ahn J, Kay GN. Idiopathic focal epicardial ventricular tachycardia originating from the crux of the heart. Heart Rhythm. 2009;6:44–50.
1021. Kawamura M, Gerstenfeld EP, Vedantham V, Rodrigues DM, Burkhardt JD, Kobayashi Y, et al. Idiopathic ventricular arrhythmia originating from the cardiac crux or inferior septum: epicardial idiopathic ventricular arrhythmia. Circ Arrhythm Electrophysiol. 2014;7:1152–8.
1022. Stevenson WG, Khan H, Sager P, Saxon LA, Middlekauff HR, Natterson PD, et al. Identification of reentry circuit sites during catheter mapping and radiofrequency ablation of ventricular tachycardia late after myocardial infarction. Circulation. 1993;88:1647–70.
1023. Bogun F, Kim HM, Han J, Tamarissa K, Tschopp D, Reich S, et al. Comparison of mapping criteria for hemodynamically tolerated, postinfarction ventricular tachycardia. Heart Rhythm. 2006;3:20–6.
1024. Miller JM, Harken AH, Hargrove WC, Josephson ME. Pattern of endocardial activation during sustained ventricular tachycardia. J Am Coll Cardiol. 1985;6:1280–7.
1025. Miller JM, Marchlinski FE, Buxton AE, Josephson ME. Relationship between the 12-lead electrocardiogram during ventricular tachycardia and endocardial site of origin in patients with coronary artery disease. Circulation. 1988;77:759–66.
1026. Bogun F, Bahu M, Knight BP, Weiss R, Paladino W, Harvey M, et al. Comparison of effective and ineffective target sites that demonstrate concealed entrainment in patients with coronary artery disease undergoing radiofrequency ablation of ventricular tachycardia. Circulation. 1997;95:183–90.
1027. El-Shalakany A, Hadjis T, Papageorgiou P, Monahan K, Epstein L, Josephson ME. Entrainment/mapping criteria for the prediction of termination of ventricular tachycardia by single radiofrequency lesion in patients with coronary artery disease. Circulation. 1999;99:2283–9.
1028. Miljoen H, State S, de Chillou C, Magnin-Poull I, Dotto P, Andronache M, et al. Electroanatomic mapping characteristics of ventricular tachycardia in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia. Europace. 2005;7:516–24.
1029. Reithmann C, Hahnefeld A, Remp T, Dorwarth U, Dugas M, Steinbeck G, et al. Electroanatomic mapping of endocardial right ventricular activation as a guide for catheter ablation in patients with arrhythmogenic right ventricular dysplasia. Pacing Clin Electrophysiol. 2003;26:1308–16.
1030. Nogami A, Sugiyasu A, Tada H, Kurosaki K, Sakamaki M, Kowase S, et al. Changes in the isolated delayed component as an endpoint of catheter ablation in arrhythmogenic right ventricular cardiomyopathy: predictor for long-term success. J Cardiovasc Electrophysiol. 2008;19:681–8.
1031. Berruezo A, Fernandez-Armenta J, Mont L, et al. Combined endocardial and epicardial catheter ablation in arrhythmogenic right ventricular dysplasia incorporating scar dechanneling technique. Circ Arrhythm Electrophysiol. 2012;5:111–21.
1032. Fernandez-Armenta J, Andreu D, Penela D, Penela D, Trucco E, Cipolletta L, et al. Sinus rhythm detection of conducting channels and ventricular tachycardia isthmus in arrhythmogenic right ventricular cardiomyopathy. Heart Rhythm. 2014;11:747–54.
1033. Igarashi M, Nogami A, Kurosaki K, Hanaki Y, Komatsu Y, Fukamizu S, et al. Radiofrequency catheter ablation of ventricular tachycardia in patients with hypertrophic cardiomyopathy and apical aneurysm. JACC Clin Electrophysiol. 2018;4:339–50.
1034. Hsia HH, Marchlinski FE. Characterization of the electroanatomic substrate for monomorphic ventricular tachycardia in patients with nonischemic cardiomyopathy. Pacing Clin Electrophysiol. 2002;25:1114–27.
1035. Muser D, Santangeli P, Castro SA, Pathak RK, Liang JJ, Hayashi T, et al. Long-term outcome after catheter ablation of ventricular tachycardia in patients with nonischemic dilated cardiomyopathy. Circ Arrhythm Electrophysiol. 2016;9:e004328.
1036. Eckart RE, Hruczkowski TW, Tedrow UB, Koplan BA, Epstein LM, Stevenson WG. Sustained ventricular tachycardia associated with corrective valve surgery. Circulation. 2007;116:2005–11.
1037. Kapel GF, Sacher F, Dekkers OM, Watanabe M, Blom NA, Thambo JB, et al. Arrhythmogenic anatomical isthmuses identified by electroanatomical mapping are the substrate for ventricular tachycardia in repaired tetralogy of Fallot. Eur Heart J. 2017;38:268–76.
1038. Koplan BA, Soejima K, Baughman K, Epstein LM, Stevenson WG. Refractory ventricular tachycardia secondary to cardiac sarcoid: electrophysiologic characteristics, mapping, and ablation. Heart Rhythm. 2006;3:924–9.
1039. Naruse Y, Sekiguchi Y, Nogami A, Okada H, Yamauchi Y, Machino T, et al. Systematic treatment approach to ventricular tachycardia in cardiac sarcoidosis. Circ Arrhythm Electrophysiol. 2014;7:407–13.
1040. Muser D, Santangeli P, Pathak RK, Castro SA, Liang JJ, Magnani S, et al. Long-term outcomes of catheter ablation of ventricular tachycardia in patients with cardiac sarcoidosis. Circ Arrhythm Electrophysiol. 2016;9:e004333.
1041. Zeppenfeld K, Blom NA, Bootsma M, Schalij MJ. Incessant ventricular tachycardia in fulminant lymphocytic myocarditis: evidence for origin in the Purkinje system and successful treatment with ablation. Heart Rhythm. 2007;4:88–91.
1042. Dello Russo A, Casella M, Pieroni M, Pelargonio G, Bartoletti S, Santangeli P, et al. Drug-refractory ventricular tachycardias after myocarditis: endocardial and epicardial radiofrequency catheter ablation. Circ Arrhythm Electrophysiol. 2012;5:492–8.
1043. Maccabelli G, Tsiachris D, Silberbauer J, Esposito A, Bisceglia C, Baratto F, et al. Imaging and epicardial substrate ablation of ventricular tachycardia in patients late after myocarditis. Europace. 2014;16:1363–72.
1044. el-Sherif N, Gough WB, Zeiler RH, Hariman R. Reentrant ventricular arrhythmias in the late myocardial infarction period. 12: Spontaneous versus induced reentry and intramural versus epicardial circuits. J Am Coll Cardiol. 1985;6:124–32.
1045. Stevenson WG, Friedman PL, Sager PT, Saxon LA, Kocovic D, Harada T, et al. Exploring postinfarction reentrant ventricular tachycardia with entrainment mapping. J Am Coll Cardiol. 1997;29:1180–9.
1046. Almendral JM, Gottlieb CD, Rosenthal ME, Stamato NJ, Buxton AE, Marchlinski FE, et al. Entrainment of ventricular tachycardia: explanation for surface electrocardiographic phenomena by analysis of electrograms recorded within the tachycardia circuit. Circulation. 1988;77:569–80.
1047. Callans DJ, Zardini M, Gottlieb CD, Josephson ME. The variable contribution of functional and anatomic barriers in human ventricular tachycardia: an analysis with resetting from two sites. J Am Coll Cardiol. 1996;27:1106–11.
1048. Kocovic DZ, Harada T, Friedman PL, Stevenson WG. Characteristics of electrograms recorded at reentry circuit sites and bystanders during ventricular tachycardia after myocardial infarction. J Am Coll Cardiol. 1999;34:381–8.
1049. Morady F, Frank R, Kou WH, Tonet JL, Nelson SD, Kounde S, et al. Identification and catheter ablation of a zone of slow conduction in the reentrant circuit of ventricular tachycardia in humans. J Am Coll Cardiol. 1988;11:775–82.
1050. Nitta T, Schuessler RB, Mitsuno M, Rokkas CK, Isobe F, Cronin CS, et al. Return cycle mapping after entrainment of ventricular tachycardia. Circulation. 1998;97:1164–75.

1051. Okumura K, Olshansky B, Henthorn RW, Epstein AE, Plumb VJ, Waldo AL. Demonstration of the presence of slow conduction during sustained ventricular tachycardia in man: use of transient entrainment of the tachycardia. Circulation. 1987;75:369–78.
1052. Rosenthal ME, Stamato NJ, Almendral JM, Gottlieb CD, Josephson ME. Resetting of ventricular tachycardia with electrocardiographic fusion: incidence and significance. Circulation. 1988;77:581–8.
1053. Hsia HH, Lin D, Sauer WH, Callans DJ, Marchlinski FE. Anatomic characterization of endocardial substrate for hemodynamically stable reentrant ventricular tachycardia: identification of endocardial conducting channels. Heart Rhythm. 2006;3:503–12.
1054. Brunckhorst CB, Delacretaz E, Soejima K, Maisel WH, Friedman PL, Stevenson WG. Identification of the ventricular tachycardia isthmus after infarction by pace mapping. Circulation. 2004;110:652–9.
1055. Bogun F, Bahu M, Knight BP, Weiss R, Goyal R, Daoud E, et al. Response to pacing at sites of isolated diastolic potentials during ventricular tachycardia in patients with previous myocardial infarction. J Am Coll Cardiol. 1997;30:505–13.
1056. Kadish AH, Schmaltz S, Morady F. A comparison of QRS complexes resulting from unipolar and bipolar pacing: implications for pace-mapping. Pacing Clin Electrophysiol. 1991;14:823–32.
1057. Oza S, Wilber DJ. Substrate-based endocardial ablation of postinfarction ventricular tachycardia. Heart Rhythm. 2006;3:607–9.
1058. de Chillou C, Groben L, Magnin-Poull I, Andronache M, MagdiAbbas M, Zhang N, et al. Localizing the critical isthmus of postinfarct ventricular tachycardia: the value of pace-mapping during sinus rhythm. Heart Rhythm. 2014;11:175–81.
1059. de Chillou C, Sellal JM, Magnin-Poull I. Pace mapping to localize the critical isthmus of ventricular tachycardia. Card Electrophysiol Clin. 2017;9:71–80.
1060. Arenal A, del Castillo S, Gonzalez-Torrecilla E, Atienza F, Ortiz M, Jimenez J, et al. Tachycardia-related channel in the scar tissue in patients with sustained monomorphic ventricular tachycardias: influence of the voltage scar definition. Circulation. 2004;110:2568–74.
1061. Zeppenfeld K, Kies P, Wijffels MC, Bootsma M, van Erven L, Schalij MJ. Identification of successful catheter ablation sites in patients with ventricular tachycardia based on electrogram characteristics during sinus rhythm. Heart Rhythm. 2005;2:940–50.
1062. Volkmer M, Ouyang F, Deger F, Ernst S, Goya M, Bansch D, et al. Substrate mapping vs. tachycardia mapping using CARTO in patients with coronary artery disease and ventricular tachycardia: Impact on outcome of catheter ablation. Europace. 2006;8:968–76.
1063. Cesario DA, Vaseghi M, Boyle NG, Fishbein MC, Valderrábano M, Narasimhan C, et al. Value of high-density endocardial and epicardial mapping for catheter ablation of hemodynamically unstable ventricular tachycardia. Heart Rhythm. 2006;3:1–10.
1064. Ciaccio EJ, Chow AW, Kaba RA, Davies DW, Segal OR, Peters NS. Detection of the diastolic pathway, circuit morphology, and inducibility of human postinfarction ventricular tachycardia from mapping in sinus rhythm. Heart Rhythm. 2008;5:981–91.
1065. Mountantonakis SE, Park RE, Frankel DS, Hutchinson MD, Dixit S, Cooper J, et al. Relationship between voltage map "channels" and the location of critical isthmus sites in patients with post-infarction cardiomyopathy and ventricular tachycardia. J Am Coll Cardiol. 2013;61:2088–95.
1066. Arenal A, Glez-Torrecilla E, Ortiz M, Villacastin J, Fdez-Portales J, Sousa E, et al. Ablation of electrograms with an isolated, delayed component as treatment of unmappable monomorphic ventricular tachycardias in patients with structural heart disease. J Am Coll Cardiol. 2003;41:81–92.
1067. Vergara P, Trevisi N, Ricco A, Petracca F, Baratto F, Cireddu M, et al. Late potentials abolition as an additional technique for reduction of arrhythmia recurrence in scar related ventricular tachycardia ablation. J Cardiovasc Electrophysiol. 2012;23:621–7.
1068. Jais P, Maury P, Khairy P, Sacher F, Nault I, Komatsu Y, et al. Elimination of local abnormal ventricular activities: A new end point for substrate modification in patients with scar-related ventricular tachycardia. Circulation. 2012;125:2184–96.
1069. Di Biase L, Santangeli P, Burkhardt DJ, Bai R, Mohanty P, Carbucicchio C, et al. Endo-epicardial homogenization of the scar versus limited substrate ablation for the treatment of electrical storms in patients with ischemic cardiomyopathy. J Am Coll Cardiol. 2012;60:132–41.
1070. Tzou WS, Frankel DS, Hegeman T, Supple GE, Garcia FC, Santangeli P, et al. Core isolation of critical arrhythmia elements for treatment of multiple scar-based ventricular tachycardias. Circ Arrhythm Electrophysiol. 2015;8:353–61.
1071. Berruezo A, Fernandez-Armenta J, Andreu D, Penela D, Herczku C, Evertz R, et al. Scar dechanneling: new method for scar-related left ventricular tachycardia substrate ablation. Circ Arrhythm Electrophysiol. 2015;8:326–36.
1072. Campos B, Jauregui ME, Marchlinski FE, Dixit S, Gerstenfeld EP. Use of a novel fragmentation map to identify the substrate for ventricular tachycardia in postinfarction cardiomyopathy. Heart Rhythm. 2015;12:95–103.
1073. Kuroki K, Nogami A, Igarashi M, Masuda K, Kowase S, Kurosaki K, et al. New substrate-guided method of predicting slow conducting isthmuses of ventricular tachycardia: preliminary analysis to the combined use of voltage limit adjustment and fast-fourier transform analysis. Circ Arrhythm Electrophysiol. 2018;11:e005705.
1074. Caceres J, Jazayeri M, McKinnie J, Avitall B, Denker ST, Tchou P, et al. Sustained bundle branch reentry as a mechanism of clinical tachycardia. Circulation. 1989;79:256–70.
1075. Blanck Z, Jazayeri M, Dhala A, Deshpande S, Sra J, Akhtar M. Bundle branch reentry: a mechanism of ventricular tachycardia in the absence of myocardial or valvular dysfunction. J Am Coll Cardiol. 1993;22:1718–22.
1076. Machino T, Tada H, Sekiguchi Y, Aonuma K. Three-dimensional visualization of the entire reentrant circuit of bundle branch reentrant tachycardia. Heart Rhythm. 2013;10:459–60.
1077. Tchou P, Mehdirad AA. Bundle branch reentry ventricular tachycardia. Pacing Clin Electrophysiol. 1995;18:1427–37.
1078. Nakagawa H, Yamanashi WS, Pitha JV, Arruda M, Wang X, Ohtomo K, et al. Comparison of in vivo tissue temperature profile and lesion geometry for radiofrequency ablation with a saline-irrigated electrode versus temperature control in a canine thigh muscle preparation. Circulation. 1995;91:2264–73.
1079. Seiler J, Roberts-Thomson KC, Raymond JM, Vest J, Delacretaz E, Stevenson WG. Steam pops during irrigated radiofrequency ablation: feasibility of impedance monitoring for prevention. Heart Rhythm. 2008;5:1411–6.
1080. Soejima K, Stevenson WG, Sapp JL, Selwyn AP, Couper G, Epstein LM. Endocardial and epicardial radiofrequency ablation of ventricular tachycardia associated with dilated cardiomyopathy: the importance of low-voltage scars. J Am Coll Cardiol. 2004;43:1834–42.
1081. Soejima K, Couper G, Cooper JM, Sapp JL, Epstein LM, Stevenson WG. Subxiphoid surgical approach for epicardial catheter-based mapping and ablation in patients with prior cardiac surgery or difficult pericardial access. Circulation. 2004;110:1197–201.
1082. d'Avila A, Houghtaling C, Gutierrez P, Vragovic O, Ruskin JN, Josephson ME, et al. Catheter ablation of ventricular epicardial tissue: a comparison of standard and cooled-tip radiofrequency energy. Circulation. 2004;109:2363–9.
1083. Baldinger SH, Kumar S, Barbhaiya CR, Mahida S, Epstein LM, Michaud GF, et al. Epicardial radiofrequency ablation failure during ablation procedures for ventricular arrhythmias: reasons

and implications for outcomes. Circ Arrhythm Electrophysiol. 2015;8:1422–32.
1084. Koruth JS, Dukkipati S, Miller MA, Neuzil P, d'Avila A, Reddy VY. Bipolar irrigated radiofrequency ablation: a therapeutic option for refractory intramural atrial and ventricular tachycardia circuits. Heart Rhythm. 2012;9:1932–41.
1085. Piers SR, Dyrda K, Tao Q, Zeppenfeld K. Bipolar ablation of ventricular tachycardia in a patient after atrial switch operation for dextrotransposition of the great arteries. Circ Arrhythm Electrophysiol. 2012;5:e38–e40.
1086. Iyer V, Gambhir A, Desai SP, Garan H, Whang W. Successful simultaneous unipolar radiofrequency ablation of septal ventricular tachycardia using 2 ablation catheters. Heart Rhythm. 2014;11:710–3.
1087. Tokuda M, Sobieszczyk P, Eisenhauer AC, Kojodjojo P, Inada K, Koplan BA, et al. Transcoronary ethanol ablation for recurrent ventricular tachycardia after failed catheter ablation: an update. Circ Arrhythm Electrophysiol. 2011;4:889–96.
1088. Gabus V, Jeanrenaud X, Eeckhout E, Pruvot E. Transcoronary ethanol for incessant epicardial ventricular tachycardia. Heart Rhythm. 2014;11:143–5.
1089. Baher A, Shah DJ, Valderrabano M. Coronary venous ethanol infusion for the treatment of refractory ventricular tachycardia. Heart Rhythm. 2012;9:1637–9.
1090. Kreidieh B, Rodriguez-Manero M, Schurmann P, Ibarra-Cortez SH, Dave AS, Valderrábano M. Retrograde coronary venous ethanol infusion for ablation of refractory ventricular tachycardia. Circ Arrhythm Electrophysiol. 2016;9(10):1161.
1091. Sapp JL, Beeckler C, Pike R, Parkash R, Gray CJ, Zeppenfeld K, et al. Initial human feasibility of infusion needle catheter ablation for refractory ventricular tachycardia. Circulation. 2013;128:2289–95.
1092. Haissaguerre M, Shah DC, Jais P, Shoda M, Kautzner J, Arentz T, et al. Role of Purkinje conducting system in triggering of idiopathic ventricular fibrillation. Lancet. 2002;359:677–8.
1093. Noda T, Shimizu W, Taguchi A, Aiba T, Satomi K, Suyama K, et al. Malignant entity of idiopathic ventricular fibrillation and polymorphic ventricular tachycardia initiated by premature extrasystoles originating from the right ventricular outflow tract. J Am Coll Cardiol. 2005;46:1288–94.
1094. Nogami A. Purkinje-related arrhythmias. Part II, Polymorphic ventricular tachycardia and ventricular fibrillation. Pacing Clin Electrophysiol. 2011;34:1034–49.
1095. Igarashi M, Tada H, Kurosaki K, Yamasaki H, Akiyama D, Sekiguchi Y, et al. Electrocardiographic determinants of the polymorphic QRS morphology in idiopathic right ventricular outflow tract tachycardia. J Cardiovasc Electrophysiol. 2012;23:521–6.
1096. Kurosaki K, Nogami A, Shirai Y, Kowase S. Positive QRS complex in lead I as a malignant sign in right ventricular outflow tract tachycardia: Comparison between polymorphic and monomorphic ventricular tachycardia. Circ J. 2013;77:968–74.
1097. Nogami A, Sugiyasu A, Kubota S, Kato K. Mapping and ablation of idiopathic ventricular fibrillation from the Purkinje system. Heart Rhythm. 2005;2:646–9.
1098. Bansch D, Oyang F, Antz M, Arentz T, Weber R, Val-Mejias JE, et al. Successful catheter ablation of electrical storm after myocardial infarction. Circulation. 2003;108:3011–6.
1099. Marrouche NF, Verma A, Wazni O, Schweikert R, Martin DO, Saliba W, et al. Mode of initiation and ablation of ventricular fibrillation storms in patients with ischemic cardiomyopathy. J Am Coll Cardiol. 2004;43:1715–20.
1100. Szumowski L, Sanders P, Walczak F, Hocini M, Jaïs P, Kepski R, et al. Mapping and ablation of polymorphic ventricular tachycardia after myocardial infarction. J Am Coll Cardiol. 2004;44:1700–6.
1101. Marchlinski F, Garcia F, Siadatan A, Sauer W, Beldner SW, Zado E, et al. Ventricular tachycardia/ventricular fibrillation ablation in the setting of ischemic heart disease. J Cardiovasc Electrophysiol. 2005;16(Suppl 1):S59–S70.
1102. Bode K, Hindricks G, Piorkowski C, Sommer P, Janousek J, Dagres N, et al. Ablation of polymorphic ventricular tachycardias in patients with structural heart disease. Pacing Clin Electrophysiol. 2008;31:1585–91.
1103. Masuda K, Nogami A, Kuroki K, Igarashi M, Sekiguchi Y, Komatsu Y, et al. Conversion to Purkinje-related monomorphic ventricular tachycardia after ablation of ventricular fibrillation in ischemic heart disease. Circ Arrhythm Electrophysiol. 2016;9:e004224.
1104. Komatsu Y, Hocini M, Nogami A, Maury P, Peichl P, Iwasaki YK,, et al. Catheter ablation of refractory ventricular fibrillation storm after myocardial infarction. Circulation. 2019;139:2315–25.
1105. Haissaguerre M, Extramiana F, Hocini M, Cauchemez B, Jaïs P, Cabrera JA, et al. Mapping and ablation of ventricular fibrillation associated with long-QT and Brugada syndromes. Circulation. 2003;108:925–8.
1106. Talib AK, Yui Y, Kaneshiro T, Sekiguchi Y, Nogami A, Aonuma K. Alternative approach for management of an electrical storm in Brugada syndrome: Importance of primary ablation within a narrow time window. J Arrhythm. 2016;32:220–2.
1107. Brugada J, Pappone C, Berruezo A, Vicedomini G, Manguso F, Ciconte G, et al. Brugada syndrome phenotype elimination by epicardial substrate ablation. Circ Arrhythm Electrophysiol. 2015;8:1373–81.
1108. Sunsaneewitayakul B, Yao Y, Thamaree S, Zhang S. Endocardial mapping and catheter ablation for ventricular fibrillation prevention in Brugada syndrome. J Cardiovasc Electrophysiol. 2012;23(Suppl 1):S10–S16.
1109. Zhang P, Tung R, Zhang Z, Sheng X, Liu Q, Jiang R, et al. Characterization of the epicardial substrate for catheter ablation of Brugada syndrome. Heart Rhythm. 2016;13:2151–8.
1110. Haissaguerre M, Derval N, Sacher F, Jesel L, Deisenhofer I, de Roy L, et al. Sudden cardiac arrest associated with early repolarization. N Engl J Med. 2008;358:2016–23.
1111. Mlcochova H, Saliba WI, Burkhardt DJ, Rodriguez RE, Cummings JE, Lakkireddy D, et al. Catheter ablation of ventricular fibrillation storm in patients with infiltrative amyloidosis of the heart. J Cardiovasc Electrophysiol. 2006;17:426–30.
1112. Sinha AM, Schmidt M, Marschang H, Gutleben K, Ritscher G, Brachmann J, et al. Role of left ventricular scar and Purkinje-like potentials during mapping and ablation of ventricular fibrillation in dilated cardiomyopathy. Pacing Clin Electrophysiol. 2009;32:286–90.
1113. Leenhardt A, Glaser E, Burguera M, Nürnberg M, Maison-Blanche P, Coumel P. Short-coupled variant of torsade de pointes: a new electrocardiographic entity in the spectrum of idiopathic ventricular tachyarrhythmias. Circulation. 1994;89:206–15.
1114. Kaneshiro T, Nogami A, Kato Y, Kuroki K, Komatsu Y, Tada H, et al. Effects of catheter ablation targeting the trigger beats in inherited catecholaminergic polymorphic ventricular tachycardia. JACC Clin Electrophysiol. 2017;3:1062–3.
1115. Nademanee K, Taylor R, Bailey WE, Rieders DE, Kosar EM. Treating electrical storm: Sympathetic blockade versus advanced cardiac life supportguided therapy. Circulation. 2000;102:742–7.
1116. Collura CA, Johnson JN, Moir C, Ackerman MJ. Left cardiac sympathetic denervation for the treatment of long QT syndrome and catecholaminergic polymorphic ventricular tachycardia using video-assisted thoracic surgery. Heart Rhythm. 2009;6:752–9.
1117. Bourke T, Vaseghi M, Michowitz Y, Sankhla V, Shah M, Swapna N, et al. Neuraxial modulation for refractory ventricular arrhythmias: value of thoracic epidural anesthesia and surgical left cardiac sympathetic denervation. Circulation. 2010;121:2255–62.

1118. Vaseghi M, Barwad P, Malavassi Corrales FJ, Tandri H, Mathuria N, Shah R, et al. Cardiac sympathetic denervation for refractory ventricular arrhythmias. J Am Coll Cardiol. 2017;69:3070–80.
1119. Do DH, Bradfield J, Ajijola OA, Vaseghi M, Le J, Rahman S, et al. Thoracic epidural anesthesia can be effective for the short-term management of ventricular tachycardia storm. J Am Heart Assoc. 2017;6:e007080.
1120. Schneider HE, Steinmetz M, Krause U, Kriebel T, Ruschewski W, Paul T. Left cardiac sympathetic denervation for the management of life-threatening ventricular tachyarrhythmias in young patients with catecholaminergic polymorphic ventricular tachycardia and long QT syndrome. Clin Res Cardiol. 2013;102:33–42.
1121. Hofferberth SC, Cecchin F, Loberman D, Fynn-Thompson F. Left thoracoscopic sympathectomy for cardiac denervation in patients with life-threatening ventricular arrhythmias. J Thorac Cardiovasc Surg. 2014;147:404–9.
1122. Roston TM, Vinocur JM, Maginot KR, Mohammed S, Salerno JC, Etheridge SP, et al. Catecholaminergic polymorphic ventricular tachycardia in children: analysis of therapeutic strategies and outcomes from an international multicenter registry. Circ Arrhythm Electrophysiol. 2015;8:633–42.
1123. Nogami A. Mapping and ablating ventricular premature contractions that trigger ventricular fibrillation: trigger elimination and substrate modification. J Cardiovasc Electrophysiol. 2015;26:110–5.
1124. Van Herendael H, Zado ES, Haqqani H, Tschabrunn CM, Callans DJ, Frankel DS, et al. Catheter ablation of ventricular fibrillation: importance of left ventricular outflow tract and papillary muscle triggers. Heart Rhythm. 2014;11:566–73.
1125. Laplante L, Benzaquen BS. A Review of the potential pathogenicity and management of frequent premature ventricular contractions. Pacing Clin Electrophysiol. 2016;39:723–30.
1126. Lee GK, Klarich KW, Grogan M, Cha YM. Premature ventricular contraction-induced cardiomyopathy: a treatable condition. Circ Arrhythm Electrophysiol. 2012;5:229–36.
1127. Takemoto M, Yoshimura H, Ohba Y, Matsumoto Y, Yamamoto U, Mohri M, et al. Radiofrequency catheter ablation of premature ventricular complexes from right ventricular outflow tract improves left ventricular dilation and clinical status in patients without structural heart disease. J Am Coll Cardiol. 2005;45:1259–65.
1128. Baman TS, Lange DC, Ilg KJ, Gupta SK, Alguire C, Armstrong W, et al. Relationship between burden of premature ventricular complexes and left ventricular function. Heart Rhythm. 2010;7:865–9.
1129. Lakkireddy D, Di Biase L, Ryschon K, Biria M, Swarup V, Reddy YM, et al. Radiofrequency ablation of premature ventricular ectopy improves the efficacy of cardiac resynchronization therapy in nonresponders. J Am Coll Cardiol. 2012;60:1531–9.
1130. Niwano S, Wakisaka Y, Niwano H, Fukaya H, Kurokawa S, Kiryu M, et al. Prognostic significance of frequent premature ventricular contractions originating from the ventricular outflow tract in patients with normal left ventricular function. Heart. 2009;95:1230–7.
1131. Ling Z, Liu Z, Su L, Zipunnikov V, Wu J, Du H, et al. Radiofrequency ablation versus antiarrhythmic medication for treatment of ventricular premature beats from the right ventricular outflow tract: Prospective randomized study. Circ Arrhythm Electrophysiol. 2014;7:237–43.
1132. Komatsu Y, Taniguchi H, Miyazaki S, Kusa S, Takayama K, Kakita K, et al. Two distinct electrocardiographic forms of idiopathic ventricular arrhythmia originating in the vicinity of the His bundle. Europace. 2012;14:1778–85.
1133. Santoro F, Biase DIL, Hranitzky P, Sanchez JE, Santangeli P, Perini AP,, et al. Ventricular tachycardia originating from the septal papillary muscle of the right ventricle: Electrocardiographic and electrophysiological characteristics. J Cardiovasc Electrophysiol. 2015;26:145–50.
1134. Pedersen CT, Kay GN, Kalman J, Borggrefe M, Della-Bella P, Dickfeld T, et al. EHRA/HRS/APHRS expert consensus on ventricular arrhythmias. J Arrhythm. 2014;30:327–49.
1135. Yokokawa M, Kim HM, Good E, Chugh A, Pelosi F Jr, Alguire C, et al. Relation of symptoms and symptom duration to premature ventricular complex-induced cardiomyopathy. Heart Rhythm. 2012;9:92–5.
1136. Hasdemir C, Ulucan C, Yavuzgil O, Yuksel A, Kartal Y, Simsek E, et al. Tachycardia-induced cardiomyopathy in patients with idiopathic ventricular arrhythmias: the incidence, clinical and electrophysiologic characteristics, and the predictors. J Cardiovasc Electrophysiol. 2011;22:663–8.
1137. Sadron Blaye-Felice M, Hamon D, Sacher F, Pascale P, Rollin A, Duparc A, et al. Premature ventricular contraction-induced cardiomyopathy: related clinical and electrophysiologic parameters. Heart Rhythm. 2016;13:103–10.
1138. Yokokawa M, Kim HM, Good E, Crawford T, Chugh A, Pelosi F Jr, et al. Impact of QRS duration of frequent premature ventricular complexes on the development of cardiomyopathy. Heart Rhythm. 2012;9:1460–4.
1139. Deyell MW, Park KM, Han Y, Frankel DS, Cooper JM, Hutchinson MD, et al. Predictors of recovery of left ventricular dysfunction after ablation of frequent ventricular premature depolarizations. Heart Rhythm. 2012;9:1465–72.
1140. Olgun H, Yokokawa M, Baman T, Kim HM, Armstrong W, Good E, et al. The role of interpolation in PVC-induced cardiomyopathy. Heart Rhythm. 2011;8:1046–9.
1141. Kawamura M, Badhwar N, Vedantham V, Tseng ZH, Lee BK, Lee RJ, et al. Coupling interval dispersion and body mass index are independent predictors of idiopathic premature ventricular complex-induced cardiomyopathy. J Cardiovasc Electrophysiol. 2014;25:756–62.
1142. Kuroki K, Tada H, Seo Y, Ishizu T, Igawa M, Yamasaki H, et al. Prediction and mechanism of frequent ventricular premature contractions related to haemodynamic deterioration. Eur J Heart Fail. 2012;14:1112–20.
1143. Penela D, Acosta J, Aguinaga L, Tercedor L, Ordoñez A, Fernández-Armenta J, et al. Ablation of frequent PVC in patients meeting criteria for primary prevention ICD implant: Safety of withholding the implant. Heart Rhythm. 2015;12:2434–42.
1144. El Kadri M, Yokokawa M, Labounty T, Mueller G, Crawford T, Good E, et al. Effect of ablation of frequent premature ventricular complexes on left ventricular function in patients with nonischemic cardiomyopathy. Heart Rhythm. 2015;12:706–13.
1145. Sarrazin JF, Labounty T, Kuhne M, Crawford T, Armstrong WF, Desjardins B, et al. Impact of radiofrequency ablation of frequent post-infarction premature ventricular complexes on left ventricular ejection fraction. Heart Rhythm. 2009;6:1543–9.
1146. Daniels DV, Lu YY, Morton JB, Santucci PA, Akar JG, Green A, et al. Idiopathic epicardial left ventricular tachycardia originating remote from the sinus of Valsalva: electrophysiological characteristics, catheter ablation, and identification from the 12-lead electrocardiogram. Circulation. 2006;113:1659–66.
1147. Hachiya H, Hirao K, Sasaki T, Higuchi K, Hayashi T, Tanaka Y, et al. Novel ECG predictor of difficult cases of outflow tract ventricular tachycardia: peak deflection index on an inferior lead. Circ J. 2010;74:256–61.
1148. Yoshida N, Inden Y, Uchikawa T, Kamiya H, Kitamura K, Shimano M, et al. Novel transitional zone index allows more accurate differentiation between idiopathic right ventricular outflow tract and aortic sinus cusp ventricular arrhythmias. Heart Rhythm. 2011;8:349–56.
1149. Betensky BP, Park RE, Marchlinski FE, Hutchinson MD, Garcia FC, Dixit S, et al. The V(2) transition ratio: a new electrocardiographic

criterion for distinguishing left from right ventricular outflow tract tachycardia origin. J Am Coll Cardiol. 2011;57:2255–62.
1150. Hachiya H, Hirao K, Nakamura H, Taniguchi H, Miyazaki S, Komatsu Y, et al. Electrocardiographic characteristics differentiating epicardial outflow tract-ventricular arrhythmias originating from the anterior interventricular vein and distal great cardiac vein. Circ J. 2015;79:2335–44.
1151. Yoshida N, Yamada T, McElderry HT, Inden Y, Shimano M, Murohara T, et al. A novel electrocardiographic criterion for differentiating a left from right ventricular outflow tract tachycardia origin: The V2S/V3R index. J Cardiovasc Electrophysiol. 2014;25:747–53.
1152. Kawamura M, Hsu JC, Vedantham V, Marcus GM, Hsia HH, Gerstenfeld EP, et al. Clinical and electrocardiographic characteristics of idiopathic ventricular arrhythmias with right bundle branch block and superior axis: comparison of apical crux area and posterior septal left ventricle. Heart Rhythm. 2015;12:1137–44.
1153. Hachiya H, Yamauchi Y, Iesaka Y, Yagishita A, Sasaki T, Higuchi K, et al. Discrete prepotential as an indicator of successful ablation in patients with coronary cusp ventricular arrhythmia. Circ Arrhythm Electrophysiol. 2013;6:898–904.
1154. Yamada T, Doppalapudi H, Maddox WR, McElderry HT, Plumb VJ, Kay GN. Prevalence and electrocardiographic and electrophysiological characteristics of idiopathic ventricular arrhythmias originating from intramural foci in the left ventricular outflow tract. Circ Arrhythm Electrophysiol. 2016;9:e004079.
1155. Teh AW, Reddy VY, Koruth JS, Miller MA, Choudry S, D'Avila A, et al. Bipolar radiofrequency catheter ablation for refractory ventricular outflow tract arrhythmias. J Cardiovasc Electrophysiol. 2014;25:1093–9.
1156. Kugler JD, Danford DA, Houston KA, Felix G, Pediatric Radiofrequency Ablation Registry of the Pediatric Radiofrequency Ablation Registry of the Pediatric Electrophysiology Society. Pediatric radiofrequency catheter ablation registry success, fluoroscopy time, and complication rate for supraventricular tachycardia: comparison of early and recent eras. J Cardiovasc Electrophysiol. 2002;13:336–41.
1157. Philip Saul J, Kanter RJ, Abrams D, Asirvatham S, Bar-Cohen Y, Blaufox AD, et al, Writing Commitee. PACES/HRS expert consensus statement on the use of catheter ablation in children and patients with congenital heart disease: Developed in partnership with the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Endorsed by the governing bodies of PACES, HRS, the American Academy of Pediatrics (AAP), the American Heart Association (AHA), and the Association for European Pediatric and Congenital Cardiology (AEPC). Heart Rhythm. 2016;13:e251–e289.
1158. Perry JC, Garson A. Supraventricular tachycardia due to Wolff-Parkinson-White syndrome in children: early disappearance and late recurrence. J Am Coll Cardiol. 1990;16:1215–20.
1159. Tsuji A, Nagashima M, Hasegawa S, Nagai N, Nishibata K, Goto M, et al. Long-term follow-up of idiopathic ventricular arrhythmias in otherwise normal children. Jpn Circ J. 1995;59:654–62.
1160. Hino H, Oda Y, Yoshida Y, Shimada M, Nishikawa K. Electrophysiological effects of desflurane in children with Wolff-Parkinson-White syndrome: a randomized crossover study. Acta Anaesthesiol Scand. 2018;62:159–66.
1161. Gaita F, Haissaguerre M, Giustetto C, Grossi S, Caruzzo E, Bianchi F, et al. Safety and efficacy of cryoablation of accessory pathways adjacent to the normal conduction system. J Cardiovasc Electrophysiol. 2003;14:825–9.
1162. Schneider HE, Kriebel T, Gravenhorst VD, Paul T. Incidence of coronary artery injury immediately after catheter ablation for supraventricular tachycardias in infants and children. Heart Rhythm. 2009;6:461–7.
1163. Schneider HE, Stahl M, Kriebel T, Schillinger W, Schill M, Jakobi J, et al. Double cryoenergy application (freeze-thaw-freeze) at growing myocardium: Lesion volume and effects on coronary arteries early after energy application: Implications for efficacy and safety in pediatric patients. J Cardiovasc Electrophysiol. 2013;24:701–7.
1164. Collins KK, Schaffer MS. Use of cryoablation for treatment of tachyarrhythmias in 2010: survey of current practices of pediatric electrophysiologists. Pacing Clin Electrophysiol. 2011;34:304–8.
1165. Avari JN, Jay KS, Rhee EK. Experience and results during transition from radiofrequency ablation to cryoablation for treatment of pediatric atrioventricular nodal reentrant tachycardia. Pacing Clin Electrophysiol. 2008;31:454–60.
1166. LaPage MJ, Reed JH, Collins KK, Law IH, Pilcher TA, Tanel RE, et al. Safety and results of cryoablation in patients <5 years old and/or <15 kilograms. Am J Cardiol. 2011;108:565–71.
1167. World Health Organization. Communicating radiation risks in paediatric imaging: Information to support healthcare discussions about benefit and risk. (WHO 2016) [in Japanese]. https://apps.who.int/iris/handle/10665/205033 (Accessed Nov. 2018)
1168. Aiyagari R, Saarel EV, Etheridge SP, Bradley DJ, Dick M 2nd, Fischbach PS. Radiofrequency ablation for supraventricular tachycardia in children < or =15 kg is safe and effective. Pediatr Cardiol. 2005;26:622–6.
1169. Chiu SN, Lu CW, Chang CW, Chang CC, Lin MT, Lin JL, et al. Radiofrequency catheter ablation of supraventricular tachycardia in infants and toddlers. Circ J. 2009;73:1717–21.
1170. Kantoch MJ, Gulamhusein SS, Sanatani S. Short- and long-term outcomes in children undergoing radiofrequency catheter ablation before their second birthday. Can J Cardiol. 2011;27:523.e3–523.e9 [in English, French].
1171. Turner CJ, Lau KC, Sholler GF. Outcomes of interventional electrophysiology in children under 2 years of age. Cardiol Young. 2012;22:499–506.
1172. An HS, Choi EY, Kwon BS, Kim GB, Bae EJ, Noh CI, et al. Radiofrequency catheter ablation for supraventricular tachycardia: a comparison study of children aged 0–4 and 5–9 years. Pacing Clin Electrophysiol. 2013;36:1488–94.
1173. Ko JK, Deal BJ, Strasburger JF, Benson DW Jr. Supraventricular tachycardia mechanisms and their age distribution in pediatric patients. Am J Cardiol. 1992;69:1028–32.
1174. Benson DW, Dunnigan A, Benditt DG. Follow-up evaluation of infant paroxysmal atrial tachycardia: Transesophageal study. Circulation. 1987;75:542–9.
1175. Montoya PT, Brugada P, Smeets J, Talajic M, Della Bella P, Lezaun R, et al. Ventricular fibrillation in the Wolff-Parkinson-White syndrome. Eur Heart J. 1991;12:144–50.
1176. Emmel M, Balaji S, Sreeram N. Ventricular preexcitation associated with dilated cardiomyopathy: a causal relationship? Cardiol Young. 2004;14:594–9.
1177. Anand RG, Rosenthal GL, Van Hare GF, Snyder CS. Is the mechanism of supraventricular tachycardia in pediatrics influenced by age, gender or ethnicity? Congenit Heart Dis. 2009;4:464–8.
1178. Blaufox AD, Rhodes JF, Fishberger SB. Age related changes in dual AV nodal physiology. Pacing Clin Electrophysiol. 2000;23:477–80.
1179. Tseng TW, Hu YF, Tsai CF, Tsao HM, Tai CT, Lin YJ, et al. Paradoxical aging changes of the atrioventricular nodal properties in patients with atrioventricular nodal re-entrant tachycardia. Circ J. 2011;75:1581–4.
1180. Kang KT, Etheridge SP, Kantoch MJ, Tisma-Dupanovic S, Bradley DJ, Balaji S, et al. Current management of focal atrial tachycardia in children: a multicenter experience. Circ Arrhythm Electrophysiol. 2014;7:664–70.
1181. Salerno JC, Kertesz NJ, Friedman RA, Fenrich AL Jr. Clinical course of atrial ectopic tachycardia is age-dependent: results and

treatment in children < 3 or > or =3 years of age. J Am Coll Cardiol. 2004;43:438–44.
1182. Van Hare GF, Carmelli D, Smith WM, Kugler J, Silka M, Friedman R, et al.; Pediatric Electrophysiology Society. Prospective assessment after pediatric cardiac ablation: design and implementation of the multicenter study. Pacing Clin Electrophysiol. 2002;25:332–41.
1183. Van Hare GF, Javitz H, Carmelli D, Saul JP, Tanel RE, Fischbach PS, et al.; Pediatric Electrophysiology Society. Prospective assessment after pediatric cardiac ablation: demographics, medical profiles, and initial outcomes. J Cardiovasc Electrophysiol. 2004;15:759–70.
1184. Van Hare GF, Colan SD, Javitz H, Knilans T, Schaffer M, Kugler J, et al.; Participating Members of the Pediatric Electrophysiology Society. Prospective assessment after pediatric cardiac ablation: fate of intracardiac structure and function, as assessed by serial echocardiography. Am Heart J. 2007;153(815–820):e6.
1185. Kugler JD, Danford DA, Deal BJ, Gillette PC, Perry JC, Silka M, et al.; The Pediatric Electrophysiology Society. Radiofrequency catheter ablation for tachyarrhythmias in children and adolescents. N Engl J Med. 1994;330:1481–7.
1186. Blaufox AD, Felix GL, Saul JP, Pediatric Catheter Ablation Registry. Radiofrequency catheter ablation in infants </=18 months old: When is it done and how do they fare? Short-term data from the pediatric ablation registry. Circulation. 2001;104:2803–8.
1187. Fishberger SB. Radiofrequency ablation of probable atrioventricular nodal reentrant tachycardia in children with documented supraventricular tachycardia without inducible tachycardia. Pacing Clin Electrophysiol. 2003;26:1679–83.
1188. Strieper MJ, Frias P, Goodwin N, Huber G, Costello L, Balfour G, et al. Radiofrequency modification for inducible and suspected pediatric atrioventricular nodal reentry tachycardia. J Interv Card Electrophysiol. 2005;13:139–43.
1189. Tomaske M, Janousek J, Razek V, Gebauer RA, Tomek V, Hindricks G, et al. Adverse effects of Wolff-Parkinson-White syndrome with right septal or posteroseptal accessory pathways on cardiac function. Europace. 2008;10:181–9.
1190. Park HE, Chang SA, Kim JH, Oh IY, Choi EK, Oh S. Left ventricular dyssynchrony in pre-excitation syndrome: effect of accessory pathway location and reversibility after ablation therapy. Heart Vessels. 2013;28:199–207.
1191. Abadir S, Fournier A, Dubuc M, Sarquella-Brugada G, Garceau P, Khairy P. Ventricular dyssynchrony and function improve following catheter ablation of nonseptal accessory pathways in children. Biomed Res Int. 2013;2013:158621.
1192. Dai CC, Guo BJ, Li WX, Xiao YY, Han L, Sun JP, et al. Dyssynchronous ventricular contraction in Wolff-Parkinson-White syndrome: a risk factor for the development of dilated cardiomyopathy. Eur J Pediatr. 2013;172:1491–500.
1193. Fukunaga H, Akimoto K, Furukawa T, Takahashi K, Kishiro M, Shimizu T, et al. Improvement in non-tachycardia-induced cardiac failure after radiofrequency catheter ablation in a child with a right-sided accessory pathway. Heart Vessels. 2013;28:802–7.
1194. Suzuki Y, Suzuki T, Imai Y, Inuzuka R, Suzuki T, Nakamura Y, et al. An infant with heart failure due to ventricular dyssynchrony and refractory tachycardia caused by a right anterolateral accessory pathway. Cardiology. 2012;123:108–12.
1195. Bromberg BI, Lindsay BD, Cain ME, Cox JL. Impact of clinical history and electrophysiologic characterization of accessory pathways on management strategies to reduce sudden death among children with Wolff-Parkinson-White syndrome. J Am Coll Cardiol. 1996;27:690–5.
1196. Gallagher JJ, Smith WM, Kasell JH, Benson DW Jr, Sterba R, Grant AO. Role of Mahaim fibers in cardiac arrhythmias in man. Circulation. 1981;64:176–89.
1197. Suzuki T, Nakamura Y, Yoshida S, Yoshida Y, Nakamura K, Sasaki T, et al. Radiofrequency catheter ablation of idiopathic left anterior fascicular ventricular tachycardia in children. Heart Rhythm. 2014;11:1948–56.
1198. Suzuki T, Nakamura Y, Yoshida S, Yoshida Y, Shintaku H. Differentiating fasciculoventricular pathway from Wolff-Parkinson-White syndrome by electrocardiography. Heart Rhythm. 2014;11:686–90.
1199. Crosson JE, Callans DJ, Bradley DJ, Dubin A, Epstein M, Etheridge S, et al. PACES/HRS expert consensus statement on the evaluation and management of ventricular arrhythmias in the child with a structurally normal heart. Heart Rhythm. 2014;11:e55–e78.
1200. Wang S, Zhu W, Hamilton RM, Kirsch JA, Stephenson EA, Gross GJ. Diagnosis-specific characteristics of ventricular tachycardia in children with structurally normal hearts. Heart Rhythm. 2010;7:1725–31.
1201. Spector ZZ, Seslar SP. Premature ventricular contraction-induced cardiomyopathy in children. Cardiol Young. 2016;26:711–7.
1202. Iwamoto M, Niimura I, Shibata T, Yasui K, Takigiku K, Nishizawa T, et al. Long-term course and clinical characteristics of ventricular tachycardia detected in children by school-based heart disease screening. Circ J. 2005;69:273–6.
1203. Pfammatter JP, Paul T, Working Group on Dysrhythmias and Electrophysiology of the Association for European Pediatric Cardiology. Idiopathic ventricular tachycardia in infancy and childhood: a multicenter study on clinical profile and outcome. J Am Coll Cardiol. 1999;33:2067–72.
1204. Gopinathannair R, Etheridge SP, Marchlinski FE, Spinale FG, Lakkireddy D, Olshanksy B. Arrhythmia-induced cardiomyopathies: mechanisms, recognition, and management. J Am Coll Cardiol. 2015;66:1714–28.
1205. Bertels RA, Harteveld LM, Filippini LH, Clur SA, Blom NA. Left ventricular dysfunction is associated with frequent premature ventricular complexes and asymptomatic ventricular tachycardia in children. Europace. 2017;19:617–21.
1206. Von Bergen NH, Bansal S, Gingerich J, Law IH. Nonfluoroscopic and radiation-limited ablation of ventricular arrhythmias in children and young adults: a case series. Pediatr Cardiol. 2011;32:743–7.
1207. Takeshita N, Kajiyama Y, Morishita Y, Ito T, Yamagishi M, Suzuki T. Successful radiofrequency catheter ablation for ventricular tachycardia of a 2.9 kg infant with Ebstein's anomaly. Europace. 2017;19:131.
1208. Thomas V, Lawrence D, Kogon B, Frias P. Epicardial ablation of ventricular tachycardia in a child on venoarterial extracorporeal membrane oxygenation. Pediatr Cardiol. 2010;31:901–4.
1209. Hasdemır C, Kartal Y, Sımsek E, Yavuzgıl O, Aydın M, Can LH. Time course of recovery of left ventricular systolic dysfunction in patients with premature ventricular contraction-induced cardiomyopathy. Pacing Clin Electrophysiol. 2013;36:612–7.
1210. Miszczak-Knecht M, Szumowski Ł, Posadowska M, Brzezińka-Paszke M, Pręgowska K, Walczak F, et al. Idiopathic ventricular arrhythmia in children and adolescents: early effectiveness of radiofrequency current ablation. Kardiol Pol. 2014;72:1148–55.
1211. Collins KK, Schaffer MS, Liberman L, Saarel E, Knecht M, Tanel RE, et al.; Pediatric and Congenital Electrophysiology Society. Fascicular and nonfascicular left ventricular tachycardias in the young: an international multicenter study. J Cardiovasc Electrophysiol. 2013;24:640–8.
1212. Texter KM, Kertesz NJ, Friedman RA, et al. Atrial flutter in infants. J Am Coll Cardiol. 2006;48:1040–6.
1213. Villain E, Vetter VL, Garcia JM, Cifarelli A, Garson A Jr. Evolving concepts in the management of congenital junctional ectopic tachycardia: a multicenter study. Circulation. 1990;81:1544–9.
1214. Furst ML, Saarel EV, Hussein AA, Wazni OM, Tchou P, Kanj M, et al. Medical and interventional outcomes in pediatric lone atrial fibrillation. JACC Clin Electrophysiol. 2018;4:638–48.

1215. Chetaille P, Walsh EP, Triedman JK. Outcomes of radiofrequency catheter ablation of atrioventricular reciprocating tachycardia in patients with congenital heart disease. Heart Rhythm. 2004;1:168–73.
1216. Kurosawa H. Development of the cardiac conduction system. In: Kurosawa H, editor. The conduction system for the cardiac surgery. Tokyo: Igaku-Shoin; 2013. p. 2–8. [in Japanese].
1217. Anderson RH, Arnold R, Wilkinson JL. The conducting system in congenitally corrected transposition. Lancet. 1973;301:1286–8.
1218. Wu MH, Wang JK, Lin JL, Lin MT, Chiu SN, Chen CA. Long-term outcome of twin atrioventricular node and supraventricular tachycardia in patients with right isomerism of the atrial appendage. Heart Rhythm. 2008;5:224–9.
1219. Uemura H, Ho SY, Anderson RH, Gerlis LM, Devine WA, Neches WH, et al. Surgical anatomy of the coronary circulation in hearts with discordant atrioventricular connections. Eur J Cardiothorac Surg. 1996;10:194–200.
1220. Anderson RH, et al. Terminology. In: Anderson RH, Baker EJ, Penny DJ, editor. Pediatric cardiology, 3rd edn. Churchill Livingstone; 2010.
1221. Uemura H, Ho SY, Devine WA, Kilpatrick LL, Anderson RH. Atrial appendages and venoatrial connections in hearts from patients with visceral heterotaxy. Ann Thorac Surg. 1995;60:561–9.
1222. Miyazaki A, Sakaguchi H, Ohuchi H, et al. The clinical course and incidence of supraventricular tachyarrhythmias after extra-cardiac conduit Fontan procedures in relation to an atrial situs. Circ J. 2011;75:413–20.
1223. Miyazaki A, Sakaguchi H, Ohuchi H, Yamada O, Kitano M, Yazaki S, et al. The incidence and characteristics of supraventricular tachycardia in left atrial isomerism: a high incidence of atrial fibrillation in young patients. Int J Cardiol. 2013;166:375–80.
1224. Shivapour JK, Sherwin ED, Alexander ME, Cechin F, Mah DY, Triedman JK, et al. Utility of preoperative electrophysiologic studies in patients with Ebstein's anomaly undergoing the Cone procedure. Heart Rhythm. 2014;11:182–6.
1225. Desai VC, Kelton CM, Czosek RJ, Heaton PC. Frequencies, costs, and complications of catheter ablation for tachyarrhythmias in children: 2000–2009. Pacing Clin Electrophysiol. 2013;36:1468–80.
1226. Kapel GF, Reichlin T, Wijnmaalen AP, Piers SR, Holman ER, Tedrow UB, et al. Re-entry using anatomically determined isthmuses: a curable ventricular tachycardia in repaired congenital heart disease. Circ Arrhythm Electrophysiol. 2015;8:102–9.
1227. Upadhyay S, Marie Valente A, Triedman JK, Walsh EP. Catheter ablation for atrioventricular nodal reentrant tachycardia in patients with congenital heart disease. Heart Rhythm. 2016;13:1228–37.
1228. Blackshear JL, Odell JA. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. Ann Thorac Surg. 1996;61:755–9.
1229. De Backer O, Arnous S, Ihlemann N, Vejlstrup N, Jorgensen E, Pehrson S, et al. Percutaneous left atrial appendage occlusion for stroke prevention in atrial fibrillation: An update. Open Heart. 2014;1:e000020.
1230. Reddy VY, Sievert H, Halperin J, Doshi SK, Buchbinder M, Neuzil P, et al.; PROTECT AF Steering Committee and Investigators. Percutaneous left atrial appendage closure vs warfarin for atrial fibrillation: a randomized clinical trial. JAMA. 2014;312:1988–98.
1231. Holmes DR, Kar S, Price MJ, Whisenant B, Sievert H, Doshi SK, et al. Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: The PREVAIL trial. J Am Coll Cardiol. 2014;64:1–12.
1232. Reddy VY, Doshi SK, Kar S, Gibson DN, Price MJ, Huber K, et al.; PREVAIL and PROTECT AF Investigators. 5-year outcomes after left atrial appendage closure: from the PREVAIL and PROTECT AF Trials. J Am Coll Cardiol. 2017;70:2964–75.
1233. Boersma LV, Schmidt B, Betts TR, Sievert H, Tamburino C, Teiger E, et al.; EWOLUTION investigators. Implant success and safety of left atrial appendage closure with the WATCHMAN device: Peri-procedural outcomes from the EWOLUTION registry. Eur Heart J. 2016;37:2465–74.
1234. Reddy VY, Gibson DN, Kar S, O'Neill W, Doshi SK, Horton RP, et al. Post-approval U.S. experience with left atrial appendage closure for stroke prevention in atrial fibrillation. J Am Coll Cardiol. 2017;69:253–61.
1235. Aonuma K, Yamasaki H, Nakamura M, Ootomo T, Takayama M, Ando K,, et al. Percutaneous WATCHMAN left atrial appendage closure for Japanese patients with nonvalvular atrial fibrillation at increased risk of thromboembolism: first results from the SALUTE trial. Circ J. 2018;82:2946–53.
1236. Cox JL, Schuessler RB, Boineau JP. The surgical treatment of atrial fibrillation. I: Summary of the current concepts of the mechanisms of atrial flutter and atrial fibrillation. J Thorac Cardiovasc Surg. 1991;101:402–5.
1237. Cox JL, Schuessler RB, D'Agostino HJ, et al. The surgical treatment of atrial fibrillation. III: Development of a definitive surgical procedure. J Thorac Cardiovasc Surg. 1991;101:569–83.
1238. Cox JL, Jaquiss RD, Schuessler RB Jr, Stone CM, Chang BC, Cain ME, et al. Modification of the maze procedure for atrial flutter and atrial fibrillation. II: Surgical technique of the maze III procedure. J Thorac Cardiovasc Surg. 1995;110:485–95.
1239. Kosakai Y, Kawaguchi AT, Isobe F, Sasako Y, Nakano K, Eishi K, et al. Modified maze procedure for patients with atrial fibrillation undergoing simultaneous open heart surgery. Circulation. 1995;92(Suppl):II359–II364.
1240. Sueda T, Nagata H, Orihashi K, Morita S, Okada K, Sueshiro M, et al. Efficacy of a simple left atrial procedure for chronic atrial fibrillation in mitral valve operations. Ann Thorac Surg. 1997;63:1070–5.
1241. Nitta T, Lee R, Schuessler RB, Boineau JP, Cox JL. Radial approach: A new concept in surgical treatment for atrial fibrillation. I: Concept, anatomic and physiologic bases and development of a procedure. Ann Thorac Surg. 1999;67:27–35.
1242. Isobe F, Kumano H, Ishikawa T, Sasaki Y, Kinugasa S, Nagamachi K, et al. A new procedure for chronic atrial fibrillation: Bilateral appendage-preserving maze procedure. Ann Thorac Surg. 2001;72:1473–8.
1243. Gaynor SL, Diodato MD, Prasad SM, Ishii Y, Schuessler RB, Bailey MS, et al. A prospective, single–center clinical trial of a modified Cox maze procedure with bipolar radiofrequency ablation. J Thorac Cardiovasc Surg. 2004;128:535–42.
1244. Abreu Filho CA, Lisboa LA, Dallan LA, Spina GS, Grinberg M, Scanavacca M, et al. Effectiveness of the maze procedure using cooled-tip radiofrequency ablation in patients with permanent atrial fibrillation and rheumatic mitral valve disease. Circulation. 2005;112:I20–I25.
1245. Wolf RK, Schneeberger EW, Osterday R, Miller D, Merrill W, Flege JB, et al. Video-assisted bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. J Thorac Cardiovasc Surg. 2005;130:797–802.
1246. Chevalier P, Leizorovicz A, Maureira P, Carteaux JP, Corbineau H, Caus T, et al. Left atrial radiofrequency ablation during mitral valve surgery: a prospective randomized multicentre study (SAFIR). Arch Cardiovasc Dis. 2009;102:769–75.
1247. Cox JL, Schuessler RB, Lappas DG, Boineau JP. An 8½-year clinical experience with surgery for atrial fibrillation. Ann Surg. 1996;224:267–75.
1248. Cox JL, Ad N, Palazzo T. Impact of the maze procedure on the stroke rate in patients with atrial fibrillation. J Thorac Cardiovasc Surg. 1999;118:833–40.
1249. Damiano RJ, Gaynor SL, Bailey M, Prasad S, Cox JL, Boineau JP, et al. The long-term outcome of patients with coronary disease and atrial fibrillation undergoing the Cox maze procedure. J Thorac Cardiovasc Surg. 2003;126:2016–21.

1250. Kosakai Y. Treatment of atrial fibrillation using the Maze procedure: the Japanese experience. Semin Thorac Cardiovasc Surg. 2000;12:44–52.
1251. Lall SC, Melby SJ, Voeller RK, Zierer A, Bailey MS, Guthrie TJ, et al. The effect of ablation technology on surgical outcomes after the Cox–maze procedure: a propensity analysis. J Thorac Cardiovasc Surg. 2007;133:389–96.
1252. Cherniavsky A, Kareva Y, Pak I, Rakhmonov S, Pokushalov E, Romanov A, et al. Assessment of results of surgical treatment for persistent atrial fibrillation during coronary artery bypass grafting using implantable loop recorders. Interact Cardiovasc Thorac Surg. 2014;18:727–31.
1253. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;130:e344–e426.
1254. Badhwar V, Rankin JS, Damiano RJ Jr, Gillinov AM, Bakaeen FG, Edgerton JR, et al. The Society of Thoracic Surgeons 2017 clinical practice guidelines for the surgical treatment of atrial fibrillation. Ann Thorac Surg. 2017;103:329–41.
1255. Ad N, Damiano RJ, Badhwar V, Calkins H, La Meir M, Nitta T, et al. Expert consensus guidelines: examining surgical ablation for atrial fibrillation. J Thorac Cardiovasc Surg. 2017;153(1330–1354):e1.
1256. Ad N, Suri RM, Gammie JS, Sheng S, O'Brien SM, Henry L. Surgical ablation of atrial fibrillation: trends and outcomes in North America. J Thorac Cardiovasc Surg. 2012;144:1051–60.
1257. Budera P, Straka Z, Osmančík P, Vaněk T, Jelínek Š, Hlavička J, et al. Comparison of cardiac surgery with left atrial surgical ablation vs. cardiac surgery without atrial ablation in patients with coronary and/or valvular heart disease plus atrial fibrillation: final results of the PRAGUE-12 randomized multicentre study. Eur Heart J. 2012;33:2644–52.
1258. McCarthy PM, Manjunath A, Kruse J, Andrei AC, LiZ MEC, et al. Should paroxysmal atrial fibrillation be treated during cardiac surgery? J Thorac Cardiovasc Surg. 2013;146:810–23.
1259. Attaran S, Saleh HZ, Shaw M, Ward A, Pullan M, Fabri BM. Does the outcome improve after radiofrequency ablation for atrial fibrillation in patients undergoing cardiac surgery? A propensity-matched comparison. Eur J Cardiothorac Surg. 2012;41:806–11.
1260. Cheng DC, Ad N, Martin J, Berglin EE, Chang BC, Doukas G, et al. Surgical ablation for atrial fibrillation in cardiac surgery: a meta-analysis and systematic review. Innovations (Phila). 2010;5:84–96.
1261. Ad N, Henry L, Hunt S, Holmes SD. Do we increase the operative risk by adding the Cox Maze III procedure to aortic valve replacement and coronary artery bypass surgery? J Thorac Cardiovasc Surg. 2012;143:936–44.
1262. Badhwar V, Rankin JS, Ad N, Grau-Sepulveda M, Damiano RJ, Gillinov AM, et al. Surgical ablation of atrial fibrillation in the United States: trends and propensity matched outcomes. Ann Thorac Surg. 2017;104:493–500.
1263. Nakajima H, Kobayashi J, Bando K, Yasumura Y, Nakatani S, Kimura K, et al. Consequence of atrial fibrillation and the risk of embolism after percutaneous mitral commissurotomy: the necessity of the maze procedure. Ann Thorac Surg. 2004;78:800–5.
1264. Bando K, Kobayashi J, Kosakai Y, Hirata M, Sasako Y, Nakatani S, et al. Impact of Cox maze procedure on outcome in patients with atrial fibrillation and mitral valve disease. J Thorac Cardiovasc Surg. 2002;124:575–83.
1265. Johansson B, Houltz B, Berglin E, Brandrup-Wognsen G, Karlsson T, Edvardsson N. Short-term sinus rhythm predicts long-term sinus rhythm and clinical improvement after intraoperative ablation of atrial fibrillation. Europace. 2008;10:610–7.
1266. Grubitzsch H, Dushe S, Beholz S, Dohmen PM, Konertz W. Surgical ablation of atrial fibrillation in patients with congestive heart failure. J Card Fail. 2007;13:509–16.
1267. Ishii Y, Sakamoto SI, Miyagi Y, Kawase Y, Otsuka T, Nitta T. Risk factors of recurrence of atrial fibrillation (AF) after AF surgery in patients with AF and mitral valve disease. Semin Thorac Cardiovasc Surg. 2018;30:271–8.
1268. Araki Y, Oshima H, Usui A, Ueda Y. Long-term results of the Maze procedure in patients with mechanical valve. Gen Thorac Cardiovasc Surg. 2012;60:326–33.
1269. Fujita T, Kobayashi J, Toda K, Nakajima H, Iba Y, Shimahara Y, et al. Long-term outcome of combined valve repair and maze procedure for nonrheumatic mitral regurgitation. J Thorac Cardiovasc Surg. 2010;140:1332–7.
1270. Sueda T, Uchida N, Takasaki T, Takahashi S, Kurosaki T, Katayama K, et al. Long-term results after the box pulmonary vein isolation procedure for chronic atrial fibrillation in mitral valve surgery. Ann Thorac Cardiovasc Surg. 2012;18:101–8.
1271. Takasaki T, Sueda T, Imai K, Orihashi K, Takahashi S, Kurosaki T, et al. Mid-term results of the box pulmonary vein isolation and the Cryo-Maze procedure for chronic atrial fibrillation associated with mitral valve disease. Gen Thorac Cardiovasc Surg. 2012;60:82–9.
1272. Barnett SD, Ad N. Surgical ablation as treatment for the elimination of atrial fibrillation: a meta-analysis. J Thorac Cardiovasc Surg. 2006;131:1029–35.
1273. Melo J, Santiago T, Aguiar C, Berglin E, Knaut M, Alfieri O, et al. Surgery for atrial fibrillation in patients with mitral valve disease: results at five years from the International Registry of Atrial Fibrillation Surgery. J Thorac Cardiovasc Surg. 2008;135:863–9.
1274. Gillinov AM, Bhavani S, Blackstone EH, Rajeswaran J, Svensson LG, Navia JL, et al. Surgery for permanent atrial fibrillation: impact of patient factors and lesion set. Ann Thorac Surg. 2006;82:502–14.
1275. Gillinov AM, Gelijns AC, Parides MK, DeRose JJ Jr, Moskowitz AJ, Voisine P, et al. Surgical ablation of atrial fibrillation during mitral-valve surgery. N Engl J Med. 2015;372:1399–409.
1276. Takai H, Miyata H, Motomura N, Sasaki K, Kunihara T, Takamoto S. Comparison of early outcomes of surgical ablation procedures for atrial fibrillation concomitant to non-mitral cardiac surgery: a Japan Adult Cardiovascular Surgery Database study. Gen Thorac Cardiovasc Surg. 2017;65:500–5.
1277. Kainuma S, Mitsuno M, Toda K, Funatsu T, Nakamura T, Miyagawa S, et al.; Osaka Cardiovascular Surgery Research (OSCAR) Group. Dilated left atrium as a predictor of late outcome after pulmonary vein isolation concomitant with aortic valve replacement and/or coronary artery bypass grafting. Eur J Cardiothorac Surg. 2015;48:765–77.
1278. Boersma LV, Castella M, van Boven W, Berruezo A, Yilmaz A, Nadal M, et al. Atrial fibrillation catheter ablation versus surgical ablation treatment (FAST): a 2-center randomized clinical trial. Circulation. 2012;125:23–30.
1279. Pokushalov E, Romanov A, Elesin D, Bogachev-Prokophiev A, Losik D, Bairamova S, et al. Catheter versus surgical ablation of atrial fibrillation after a failed initial pulmonary vein isolation procedure: a randomized controlled trial. J Cardiovasc Electrophysiol. 2013;24:1338–43.
1280. Phan K, Phan S, Thiagalingam A, Medi C, Yan TD. Thoracoscopic surgical ablation versus catheter ablation for atrial fibrillation. Eur J Cardiothorac Surg. 2016;49:1044–51.
1281. Kearney K, Stephenson R, Phan K, Chan WY, Huang MY, Yan TD. A systematic review of surgical ablation versus catheter ablation for atrial fibrillation. Ann Cardiothorac Surg. 2014;3:15–29.
1282. Wang J, Li Y, Shi J, Han J, Xu C, Ma C, et al. Minimally invasive surgical versus catheter ablation for the long-lasting persistent atrial fibrillation. PLoS One. 2011;6:e221–e222.

1283. Masuda M, Endo S, Natsugoe S, Shimizu H, Doki Y, Hirata Y, et al. Annual report by The Japanese Association for Thoracic Surgery. Gen Thorac Cardiovasc Surg. 2015;2018(66):581–615.
1284. Moten SC, Rodriguez E, Cook RC, Nifong LW, Chitwood WR Jr. New ablation techniques for atrial fibrillation and the minimally invasive Cryo-Maze procedure in patients with lone atrial fibrillation. Heart Lung Circ. 2007;16(Suppl):S88–S93.
1285. Ad N, Henry L, Friehling T, Wish M, Holmes SD. Minimally invasive stand-alone Cox-Maze procedure for patients with nonparoxysmal atrial fibrillation. Ann Thorac Surg. 2013;96:792–9.
1286. Wright M, Haissaguerre M, Knecht S, Matsuo S, O'Neill MD, Nault I, et al. State of the art: catheter ablation of atrial fibrillation. J Cardiovasc Electrophysiol. 2008;19:583–92.
1287. Maagh P, Butz T, Plehn G, Christoph A, Meissner A. Pulmonary vein isolation in 2012: Is it necessary to perform a time consuming electrophysical mapping or should we focus on rapid and safe therapies? A retrospective analysis of different ablation tools. Int J Med Sci. 2013;10:24–33.
1288. Pruitt JC, Lazzara RR, Dworkin GH, Badhwar V, Kuma C, Ebra G. Totally endoscopic ablation of lone atrial fibrillation: initial clinical experience. Ann Thorac Surg. 2006;81:1325–31.
1289. Pruitt JC, Lazzara RR, Ebra G. Minimally invasive surgical ablation of atrial fibrillation: the thoracoscopic box lesion approach. J Interv Card Electrophysiol. 2007;20:83–7.
1290. Melby SJ, Lee AM, Zierer A, Kaiser SP, Livhits MJ, Boineau JP, et al. Atrial fibrillation propagates through gaps in ablation lines: implications for ablative treatment of atrial fibrillation. Heart Rhythm. 2008;5:1296–301.
1291. Edgerton JR, McClelland JH, Duke D, Gerdisch MW, Steinberg BM, Bronleewe SH, et al. Minimally invasive surgical ablation of atrial fibrillation: six-month results. J Thorac Cardiovasc Surg. 2009;138:109–14.
1292. Edgerton JR, Jackman WM, Mack MJ. A new epicardial lesion set for minimal access left atrial Maze: the Dallas lesion set. Ann Thorac Surg. 2009;88:1655–7.
1293. Edgerton JR, Jackman WM, Mahoney C, Mack MJ. Totally thorascopic surgical ablation of persistent AF and long-standing persistent atrial fibrillation using the "Dallas" lesion set. Heart Rhythm. 2009;6(Suppl):S64–S70.
1294. Je HG, Shuman DJ, Ad N. A systematic review of minimally invasive surgical treatment for atrial fibrillation: a comparison of the Cox-Maze procedure, beating-heart epicardial ablation, and the hybrid procedure on safety and efficacy. Eur J Cardiothorac Surg. 2015;48:531–41.
1295. Krul SP, Driessen AH, Zwinderman AH, van Boven WJ, Wilde AAM, de Bakker JMT, et al. Navigating the mini-Maze: systematic review of the first results and progress of minimally-invasive surgery in the treatment of atrial fibrillation. Int J Cardiol. 2013;166:132–40.
1296. La Meir M, Gelsomino S, Luca F, Lorusso R, Gensini GF, Pison L, et al. Minimally invasive thoracoscopic hybrid treatment of lone atrial fibrillation: early results of monopolar versus bipolar radiofrequency source. Interact Cardiovasc Thorac Surg. 2012;14:445–50.
1297. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, et al. 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. J Interv Card Electrophysiol. 2012;33:171–257.
1298. La Meir M. Surgical options for treatment of atrial fibrillation. Ann Cardiothorac Surg. 2014;3:30–7.
1299. Pison L, Gelsomino S, Luca F, Parise O, Maessen JG, Crijns HJ, et al. Effectiveness and safety of simultaneous hybrid thoracoscopic and endocardial catheter ablation of lone atrial fibrillation. Ann Cardiothorac Surg. 2014;3:38–44.
1300. La Meir M, Gelsomino S, Luca F, et al. Minimally invasive surgical treatment of lone atrial fibrillation: early results of hybrid versus standard minimally invasive approach employing radiofrequency sources. Int J Cardiol. 2013;167:1469–75.
1301. Pison L, La Meir M, van Opstal J, Pison L, Parise O, Colella A, et al. Hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation. J Am Coll Cardiol. 2012;60:54–61.
1302. Mahapatra S, LaPar DJ, Kamath S, Payne J, Bilchick KC, Mangrum JM, et al. Initial experience of sequential surgical epicardial-catheter endocardial ablation for persistent and long-standing persistent atrial fibrillation with long-term follow-up. Ann Thorac Surg. 2011;91:1890–8.
1303. Kurfirst V, Mokráček A, Bulava A, Čanadyova J, Haniš J, Pešl L. Two-staged hybrid treatment of persistent atrial fibrillation: short-term single-centre results. Interact Cardiovasc Thorac Surg. 2014;18:451–6.
1304. Lee R, McCarthy PM, Passman RS, Kruse J, Malaisrie C, McGee EC, et al. Surgical treatment for isolated atrial fibrillation: minimally invasive vs. classic cut and sew Maze. Innovations (Phila). 2011;6:373–7.
1305. La Meir M, Gelsomino S, Lorusso R, Lucà F, Pison L, Parise O, et al. The hybrid approach for the surgical treatment of lone atrial fibrillation: one-year results employing a monopolar radiofrequency source. J Cardiothorac Surg. 2012;7:71.
1306. Bisleri G, Rosati F, Bontempi L, Curnis A, Muneretto C. Hybrid approach for the treatment of long-standing persistent atrial fibrillation: electrophysiological findings and clinical results. Eur J Cardiothorac Surg. 2013;44:919–23.
1307. Gehi AK, Mounsey JP, Pursell I, Landers M, Boyce K, Chung EH, et al. Hybrid epicardial-endocardial ablation using a pericardioscopic technique for the treatment of atrial fibrillation. Heart Rhythm. 2013;10:22–8.
1308. Geršak B, Zembala MO, Muller D, Folliguet T, Jan M, Kowalski O, et al. European experience of the convergent atrial fibrillation procedure: multicenter outcomes in consecutive patients. J Thorac Cardiovasc Surg. 2014;147:1411–6.
1309. Edgerton Z, Perini AP, Horton R, Trivedi C, Santangeli P, Bai R, et al. Hybrid procedure (endo/epicardial) versus standard manual ablation in patients undergoing ablation of longstanding persistent atrial fibrillation: results from a single center. J Cardiovasc Electrophysiol. 2016;27:524–30.
1310. Ad N, Henry L, Hunt S, Holmes SD. The outcome of the Cox Maze procedure in patients with previous percutaneous catheter ablation to treat atrial fibrillation. Ann Thorac Surg. 2011;91:1371–7.
1311. Onorati F, Curcio A, Santarpino G, Torella D, Mastroroberto P, Tucci L, et al. Routine ganglionic plexi ablation during Maze procedure improves hospital and early follow-up results of mitral surgery. J Thorac Cardiovasc Surg. 2008;136:408–18.
1312. Ware AL, Suri RM, Stulak JM, Sundt TH 3rd, Schaff HV. Left atrial ganglion ablation as an adjunct to atrial fibrillation surgery in valvular heart disease. Ann Thorac Surg. 2011;91:97–102.
1313. Sakamoto S, Fujii M, Watanabe Y, Hiromoto A, Ishii Y, Morota T, et al. Exploration of theoretical ganglionated plexi ablation technique in atrial fibrillation surgery. Ann Thorac Surg. 2014;98:1598–604.
1314. Zhou Q, Hou Y, Yang S. A meta-analysis of the comparative efficacy of ablation for atrial fibrillation with and without ablation of the ganglionated plexi. Pacing Clin Electrophysiol. 2011;34:1687–94.
1315. Di Biase L, Burkhardt JD, Mohanty P, Sanchez J, Horton R, Gallinghouse GJ, et al. Periprocedural stroke and management of major bleeding complications in patients undergoing catheter ablation of atrial fibrillation: the impact of periprocedural therapeutic international normalized ratio. Circulation. 2010;121:2550–6.
1316. Di Biase L, Burkhardt JD, Mohanty P, Sanchez J, Mohanty S, Horton R, et al. Left atrial appendage: an underrecognized trigger site of atrial fibrillation. Circulation. 2010;122:109–18.
1317. Lin WS, Tai CT, Hsieh MH, Tsai CF, Lin YK, Tsao HM, et al. Catheter ablation of paroxysmal atrial fibrillation initiated by non-pulmonary vein ectopy. Circulation. 2003;107:3176–83.

1318. Lakkireddy D, Reddy YM, Atkins D, Rajasingh J, Kanmanthareddy A, Olyaee M, et al. Effect of atrial fibrillation ablation on gastric motility: the atrial fibrillation gut study. Circ Arrhythm Electrophysiol. 2015;8:531–6.
1319. Kanderian AS, Gillinov AM, Pettersson GB, Blackstone E, Klein AL. Success of surgical left atrial appendage closure: assessment by transesophageal echocardiography. J Am Coll Cardiol. 2008;52:924–9.
1320. Lee R, Vassallo P, Kruse J, Malaisrie SC, Rigolin V, Andrei AC, et al. A randomized, prospective pilot comparison of 3 atrial appendage elimination techniques: internal ligation, stapled excision, and surgical excision. J Thorac Cardiovasc Surg. 2016;152:1075–80.
1321. Tsai YC, Phan K, Munkholm-Larsen S, Tian DH, La Meir M, Yan TD. Surgical left atrial appendage occlusion during cardiac surgery for patients with atrial fibrillation: a meta-analysis. Eur J Cardiothorac Surg. 2015;47:847–54.
1322. Ailawadi G, Gerdisch MW, Harvey RL, Hooker RL, Damiano RJ Jr, Salamon T, et al. Exclusion of the left atrial appendage with a novel device: early results of a multicenter trial. J Thorac Cardiovasc Surg. 2011;142:1002–1009.e1.
1323. Emmert MY, Puippe G, Baumuller S, Alkadhi H, Landmesser U, Plass A, et al. Safe, effective and durable epicardial left atrial appendage clip occlusion in patients with atrial fibrillation undergoing cardiac surgery: first long-term results from a prospective device trial. Eur J Cardiothorac Surg. 2014;45:126–31.
1324. Friedman DJ, Piccini JP, Wang T, Zheng J, Malaisrie SC, Holmes DR, et al. Association between left atrial appendage occlusion and readmission for thromboembolism among patients with atrial fibrillation undergoing concomitant cardiac surgery. JAMA. 2018;319:365–74.
1325. Yao X, Gersh BJ, Holmes DR, Melduni RM, Johnsrud DO, Sangaralingham LR, et al. Association of surgical left atrial appendage occlusion with subsequent stroke and mortality among patients undergoing cardiac surgery. JAMA. 2018;319:2116–26.
1326. Bhavani SS, Tchou P, Saliba W, Gillinov AM. Surgical options for refractory ventricular tachycardia. J Card Surg. 2007;22:533–4.
1327. Anter E, Hutchinson MD, Deo R, Haqqani HM, Callans DJ, Gerstenfeld EP, et al. Surgical ablation of refractory ventricular tachycardia in patients with nonischemic cardiomyopathy. Circ Arrhythm Electrophysiol. 2011;4:494–500.
1328. Choi EK, Nagashima K, Lin KY, Kumar S, Barbhaiya CR, Baldinger SH, et al. Surgical cryoablation for ventricular tachyarrhythmia arising from the left ventricular outflow tract region. Heart Rhythm. 2015;12:1128–36.
1329. Kumar S, Barbhaiya CR, Sobieszczyk P, Eisenhauer AC, Couper GS, Nagashima K, et al. Role of alternative interventional procedures when endo- and epicardial catheter ablation attempts for ventricular arrhythmias fail. Circ Arrhythm Electrophysiol. 2015;8:606–15.
1330. Sakamoto S, Nitta T, Murata H, Yoshio T, Ochi M, Shimizu K. Electroanatomical mapping-assisted surgical treatment of incessant ventricular tachycardia associated with an intramyocardial giant lipoma. J Interv Card Electrophysiol. 2012;33:109–12.
1331. Sakamoto S, Shibata M, Murata H, Nitta T. Intraoperative cardiac mapping in the treatment of an infant congenital fibroma. Ann Thorac Surg. 2015;99:1064–6.
1332. Dor V, Sabatier M, Montiglio F, Rossi P, Toso A, Di Donato M. Results of nonguided subtotal endocardiectomy associated with left ventricular reconstruction in patients with ischemic ventricular arrhythmias. J Thorac Cardiovasc Surg. 1994;107:1301–7.
1333. Sartipy U, Albage A, Straat E, Insulander P, Lindblom D. Surgery for ventricular tachycardia in patients undergoing left ventricular reconstruction by the Dor procedure. Ann Thorac Surg. 2006;81:65–71.
1334. Patel M, Rojas F, Shabari FR, Simpson L, Cohn W, Frazier OH, et al. Safety and feasibility of open chest epicardial mapping and ablation of ventricular tachycardia during the period of left ventricular assist device implantation. J Cardiovasc Electrophysiol. 2016;27:95–101.
1335. Mulloy DP, Bhamidipati CM, Stone ML, Ailawadi G, Bergin JD, Mahapatra S, et al. Cryoablation during left ventricular assist device implantation reduces postoperative ventricular tachyarrhythmias. J Thorac Cardiovasc Surg. 2013;145:1207–13.
1336. Takach TJ, Reul GJ, Ott DA, Cooley DA. Primary cardiac tumors in infants and children: Immediate and long-term operative results. Ann Thorac Surg. 1996;62:559–64.
1337. Miyake CY, Del Nido PJ, Alexander ME, Cecchin F, Berul CI, Triedman JK, et al. Cardiac tumors and associated arrhythmias in pediatric patients, with observations on surgical therapy for ventricular tachycardia. J Am Coll Cardiol. 2011;58:1903–9.
1338. Nathan M, Fabozzo A, Geva T, Walsh E, del Nida PJ. Successful surgical management of ventricular fibromas in children. J Thorac Cardiovasc Surg. 2014;148:2602–8.
1339. Japan Society of School Health home page [in Japanese]. http://www.hokenkai.or.jp/ (Accessed Nov. 2018)
1340. DeMaso DR, Lauretti A, Spieth L, van der Feen JR, Jay KS, Gauvreau K, et al. Psychosocial factors and quality of life in children and adolescents with implantable cardioverter-defibrillators. Am J Cardiol. 2004;93:582–7.
1341. Sears SF, Hazelton AG, St Amant J, Matchett M, Kovacs A, Vazquez LD, et al. Quality of life in pediatric patients with implantable cardioverter defibrillators. Am J Cardiol. 2011;107:1023–7.
1342. Japanese Circulation Society Joint Working Group. Guidelines for rehabilitation in society, attending school and working in patients treated with pacemaker, ICD and CRT (JCS 2008). Circ J. 2008;72(Suppl):1133–74 [in Japanese]. http://www.j-circ.or.jp/guideline/pdf/JCS2008_okunura_h.pdf (Accessed Nov. 2018).
1343. Guidelines for school life and exercise in pupils and students with congenital heart disease (JSPCCS 2012). Pediatr Cardiol Cardiac Surg. 2012;29:277–90 [in Japanese].
1344. Japanese Circulation Society and Japanese Society of Pediatric Cardiology and Cardiac Surgery Joint Working Group. Guidelines for heart disease screening in schools (JCS 2016/JSPCCS 2016) [in Japanese]. http://www.j-circ.or.jp/guideline/pdf/JCS2016_sumitomo_h.pdf (Accessed Nov. 2018)
1345. Kirchhof P, Fabritz L, Zwiener M, Witt H, Schäfers M, Zellerhoff S, et al. Age- and training-dependent development of arrhythmogenic right ventricular cardiomyopathy in heterozygous plakoglobin-deficient mice. Circulation. 2006;114:1799–806.
1346. James CA, Bhonsale A, Tichnell C, Murray B, Russell SD, Tandri H, et al. Exercise increases age-related penetrance and arrhythmic risk in arrhythmogenic right ventricular dysplasia/cardiomyopathy-associated desmosomal mutation carriers. J Am Coll Cardiol. 2013;62:1290–7.
1347. Japanese Circulation Society Joint Working Group. Guidelines for rehabilitation in society, attending school and working in patients treated with pacemaker, ICD and CRT (JCS 2013) [in Japanese]. http://www.j-circ.or.jp/guideline/pdf/JCS2008_okunura_h.pdf (Accessed Nov. 2018)
1348. Watanabe E, Abe H, Watanabe S, et al. Statement for driving of the patients with arrhythmias (version 3) [in Japanese]. http://new.jhrs.or.jp/pdf/guideline/statement201708_02.pdf (Accessed Nov. 2018)

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APPENDIX 2. DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST (COI)

Author	Employer / leadership position (private company)	Stock or stock options	Intellectual property / royalties	Speakers' bureau	Payment for manuscripts	Research grant	Scholarship (educational) grant	Endowed chair	Other rewards	Potential COI of the marital partner, first-degree family members, or those who share income and property	Declaration about the head of your affiliated organization/ department (if the participant is conducting joint research with the head of the organization / department)	
											Research grant	Scholarship (educational) grant
Chair: Takashi Kurita				TOA EIYO LTD., Bayer Yakuhin, Ltd., BIOTRONIK Japan, Inc, Bristol-Myers Squibb, Daiichi Sankyo, Boehringer Ingelheim Japan, Inc, Medtronic Japan Co., Ltd.								
Chair: Akihiko Nogami				Abbott Medical Japan Co., Ltd., St. Jude Medical Japan Co., Ltd., Bristol-Myers Squibb, Daiichi Sankyo, Boehringer Ingelheim Japan, Inc, Medtronic Japan Co., Ltd., Japan Lifeline Co.,Ltd.				Johnson & Johnson KK, DVx, Inc, Medtronic Japan Co., Ltd.				
Member: Haruhiko Abe				Daiichi Sankyo			Fides-one, Inc, Daiichi Sankyo, Japan Lifeline Co.,Ltd.	Abbott Medical Japan Co., Ltd., Boston Scientific Corporation, Medtronic Japan Co., Ltd.				Fides-one, Inc
Member: Kenji Ando				TERUMO CORPORATION, BIOTRONIK Japan, Inc, Boston Scientific Corporation, Medtronic Japan Co., Ltd., Japan Lifeline Co.,Ltd.								
Member: Katsuhiko Imai				Medtronic Japan Co., Ltd.								

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APPENDIX 2 (Continued)

Author	Employer / leadership position (private company)	Stock or stock options	Intellectual property / royalties	Speakers' bureau	Payment for manuscripts	Research grant	Scholarship (educational) grant	Endowed chair	Other rewards	Potential COI of the marital partner, first-degree family members, or those who share income and property	Declaration about the head of your affiliated organization/ department (if the participant is conducting joint research with the head of the organization / department)	
											Research grant	Scholarship (educational) grant
Member: Akihiko Usui							Edwards Lifesciences Corporation, St. Jude Medical Japan Co., Ltd., TERUMO CORPORATION, Nipro Corporation, Pfizer Japan Inc, iCorNet, Trestech.Co.,Ltd., SENKO MEDICAL INSTRUMENT Mfg. CO., LTD., Daiichi Sankyo, Mitsubishi Tanabe Pharma Corporation, Medtronic Japan Co., Ltd., Japan Lifeline Co.,Ltd.,					
Member: Kengo Kusano				Bayer Yakuhin, Ltd., Bristol-Myers Squibb, Daiichi Sankyo, Medtronic Japan Co., Ltd.		EPS Corporation, EP-CRSU Co., Ltd, Boston Scientific Corporation, Ono Pharmaceutical Co., Ltd., Medtronic Japan Co., Ltd.	Suzuken Memorial Foundation					
Member: Koichiro Kumagai				Century Medical,Inc, Bayer Yakuhin, Ltd. Daiichi Sankyo, Toray Industries, Inc, Boehringer Ingelheim Japan, Inc, Medtronic Japan Co., Ltd.								

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APPENDIX 2 (Continued)

Author	Employer / leadership position (private company)	Stock or stock options	Intellectual property / royalties	Speakers' bureau	Payment for manuscripts	Research grant	Scholarship (educational) grant	Endowed chair	Other rewards	Potential COI of the marital partner, first-degree family members, or those who share income and property	Declaration about the head of your affiliated organization/ department (if the participant is conducting joint research with the head of the organization / department)	
											Research grant	Scholarship (educational) grant
Member: Yoshinori Kobayashi	Fukuda Denshi Co., Ltd., Kowa Pharmaceutical Co., Ltd.,			Daiichi Sankyo, Boehringer Ingelheim Japan, Inc, Medtronic Japan Co., Ltd.			Boehringer Ingelheim Japan, Inc, St. Jude Medical Japan Co., Ltd., Daiichi Sankyo, Bayer Yakuhin, Ltd.					
Member: Wataru Shimizu				Bayer Yakuhin, Ltd., Pfizer Japan Inc, Bristol-Myers Squibb, Ono Pharmaceutical Co., Ltd., Daiichi Sankyo, Boehringer Ingelheim Japan, Inc			Astellas Pharma Inc, Eisai Co., Ltd., St. Jude Medical Japan Co., Ltd., Novartis Pharma KK, Bayer Yakuhin, Ltd. Pfizer Japan Inc, Bristol-Myers Squibb, Ono Pharmaceutical Co., Ltd., Otsuka Pharmaceutical Co., Ltd., Daiichi Sankyo, Mitsubishi Tanabe Pharma Corporation, Boehringer Ingelheim Japan, Inc					
Member: Morio Shoda				Medtronic Japan Co., Ltd., Boston Scientific Corporation, BIOTRONIK Japan, Inc				BIOTRONIK Japan, Inc, Medtronic Japan Co., Ltd., Boston Scientific Corporation, St. Jude Medical Japan Co., Ltd.				
Member: Naokata Sumitomo				Ono Pharmaceutical Co., Ltd.								

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APPENDIX 2 (Continued)

Author	Employer / leadership position (private company)	Stock or stock options	Intellectual property / royalties	Speakers' bureau	Payment for manuscripts	Research grant	Scholarship (educational) grant	Endowed chair	Other rewards	Potential COI of the marital partner, first-degree family members, or those who share income and property	Declaration about the head of your affiliated organization/ department (if the participant is conducting joint research with the head of the organization / department)	
											Research grant	Scholarship (educational) grant
Member: Atsushi Takahashi				Japan Lifeline Co.,Ltd.								
Member: Hiroshi Tada				Johnson & Johnson KK, BIOTRONIK Japan, Inc, Bristol-Myers Squibb, Kowa Pharmaceutical Co., Ltd., Daiichi Sankyo, Boehringer Ingelheim Japan, Inc, Medtronic Japan Co., Ltd.			MSD KK, Astellas Pharma Inc, Abbott Vascular Japan Co., Ltd., Sanofi KK, Central Medical Co., Ltd., D*sense Co., Ltd, DVx, Inc, Bayer Yakuhin, Ltd. Pfizer Japan Inc, Daiichi Sankyo, Boehringer Ingelheim Japan, Inc, Medtronic Japan Co., Ltd., Takeda Pharmaceutical Company Limited,					
Member: Shigeto Naito				Johnson & Johnson KK, Bristol-Myers Squibb, Boehringer Ingelheim Japan, Inc, Daiichi Sankyo								
Member: Yuji Nakazato				Abbott Medical Japan Co., Ltd., St. Jude Medical Japan Co., Ltd., BIOTRONIK Japan, Inc, Fukuda Denshi Co., Ltd., Boston Scientific Corporation, Daiichi Sankyo, Japan Lifeline Co.,Ltd.			Abbott Medical Japan Co., Ltd., St. Jude Medical Japan Co., Ltd., BIOTRONIK Japan, Inc, Boston Scientific Corporation, Medtronic Japan Co., Ltd., Japan Lifeline Co.,Ltd.					

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Author	Employer / leadership position (private company)	Stock or stock options	Intellectual property / royalties	Speakers' bureau	Payment for manuscripts	Research grant	Scholarship (educational) grant	Endowed chair	Other rewards	Potential COI of the marital partner, first-degree family members, or those who share income and property	Declaration about the head of your affiliated organization/ department (if the participant is conducting joint research with the head of the organization / department)	
											Research grant	Scholarship (educational) grant
Member: Takashi Nitta				Century Medical,Inc, Japan Lifeline Co.,Ltd., Ono Pharmaceutical Co., Ltd.								
Member: Nobuhisa Hagiwara				Boehringer Ingelheim Japan, Inc, Bristol-Myers Squibb, Bayer Yakuhin, Ltd.			Aegerion Pharmaceuticals Inc, Astellas Pharma Inc, Bayer Yakuhin, Ltd., Pfizer Japan Inc, Otsuka Pharmaceutical Co., Ltd., Daiichi Sankyo, Toray Industries, Inc, Boehringer Ingelheim Japan, Inc, Takeda Pharmaceutical Company Limited					
Member: Yuji Murakawa				Daiichi Sankyo, Bayer Yakuhin, Ltd., Bristol-Myers Squibb, Boehringer Ingelheim Japan, Inc	Boehringer Ingelheim Japan, Inc		Bayer Yakuhin, Ltd. Daiichi Sankyo, Boehringer Ingelheim Japan, Inc					
Member: Teiichi Yamane				Abbott Medical Japan Co., Ltd., St. Jude Medical Japan Co., Ltd., Bayer Yakuhin, Ltd., Bristol-Myers Squibb, Daiichi Sankyo, Boehringer Ingelheim Japan, Inc, Medtronic Japan Co., Ltd., Japan Lifeline Co.,Ltd.		Boehringer Ingelheim Japan, Inc, Bayer Yakuhin, Ltd.						

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Author	Employer / leadership position (private company)	Stock or stock options	Intellectual property / royalties	Speakers' bureau	Payment for manuscripts	Research grant	Scholarship (educational) grant	Endowed chair	Other rewards	Potential COI of the marital partner, first-degree family members, or those who share income and property	Declaration about the head of your affiliated organization/ department (if the participant is conducting joint research with the head of the organization / department)	
											Research grant	Scholarship (educational) grant
Collaborator: Takeshi Aiba				Ono Pharmaceutical Co., Ltd., Bristol-Myers Squibb			Boehringer Ingelheim Japan, Inc, Daiichi Sankyo	Medtronic Japan Co., Ltd.				
Collaborator: Koichi Inoue				Johnson & Johnson KK, Bayer Yakuhin, Ltd., Bristol-Myers Squibb, Daiichi Sankyo, Boehringer Ingelheim Japan, Inc, Medtronic Japan Co., Ltd.								
Collaborator: Yuki Iwasaki											Daiichi Sankyo, Boehringer Ingelheim Japan, Inc,	MSD KK, Astellas Pharma Inc, Abbott Vascular Japan Co., Ltd., Eisai Co., Ltd., St. Jude Medical Japan Co., Ltd., Ono Pharmaceutical Co., Ltd., Otsuka Pharmaceutical Co., Ltd., Daiichi Sankyo, Mitsubishi Tanabe Pharma Corporation, Boehringer Ingelheim Japan, Inc,

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Author	Employer / leadership position (private company)	Stock or stock options	Intellectual property / royalties	Speakers' bureau	Payment for manuscripts	Research grant	Scholarship (educational) grant	Endowed chair	Other rewards	Potential COI of the marital partner, first-degree family members, or those who share income and property	Declaration about the head of your affiliated organization/ department (if the participant is conducting joint research with the head of the organization / department)	
											Research grant	Scholarship (educational) grant
Collaborator: Yasuya Inden				Daiichi Sankyo, Medtronic Japan Co., Ltd., Bristol-Myers Squibb,		Boehringer Ingelheim Japan, Inc,						MSD KK, Astellas Pharma Inc, Pfizer Japan Inc, Daiichi Sankyo, Teijin Pharma Limited, Mitsubishi Tanabe Pharma Corporation, Takeda Pharmaceutical Company Limited
Collaborator: Masaomi Kimura				Abbott Medical Japan Co., Ltd., Johnson & Johnson KK, Bayer Yakuhin, Ltd., Boehringer Ingelheim Japan, Inc, Medtronic Japan Co., Ltd.,	Toray Industries, Inc,			Fukuda Denshi Co., Ltd., Medtronic Japan Co., Ltd.,				Abbott Medical Japan Co., Ltd., Johnson & Johnson KK, St. Jude Medical Japan Co., Ltd., BIOTRONIK Japan, Inc, Daiichi Sankyo,
Collaborator: Shingo Sasaki				BIOTRONIK Japan, Inc, Boston Scientific Corporation, Medtronic Japan Co., Ltd.			BIOTRONIK Japan, Inc	Fukuda Denshi Co., Ltd., Medtronic Japan Co., Ltd.				Abbott Vascular Japan Co., Ltd., Johnson & Johnson KK, Fukuda Denshi Co., Ltd., Medtronic Japan Co., Ltd.

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Author	Employer / leadership position (private company)	Stock or stock options	Intellectual property / royalties	Speakers' bureau	Payment for manuscripts	Research grant	Scholarship (educational) grant	Endowed chair	Other rewards	Potential COI of the marital partner, first-degree family members, or those who share income and property	Declaration about the head of your affiliated organization/ department (if the participant is conducting joint research with the head of the organization / department)	
											Research grant	Scholarship (educational) grant
Collaborator: Kazuhiro Satomi				Abbott Medical Japan Co., Ltd., Johnson & Johnson KK, St. Jude Medical Japan Co., Ltd., Bayer Yakuhin, Ltd., Bristol-Myers Squibb, Daiichi Sankyo, Boehringer Ingelheim Japan, Inc Medtronic Japan Co., Ltd., Japan Lifeline Co.,Ltd.				BIOTRONIK Japan, Inc				
Collaborator: Tsuyoshi Shiga				TOA EIYO LTD., Bayer Yakuhin, Ltd., Bristol-Myers Squibb, Daiichi Sankyo, Boehringer Ingelheim Japan, Inc,		Bayer Yakuhin, Ltd. Ono Pharmaceutical Co., Ltd., Daiichi Sankyo	Eisai Co., Ltd.,					
Collaborator: Yukio Sekiguchi	Fukuda Denshi Co., Ltd.,							Abbott Medical Japan Co., Ltd.				
Collaborator: Kyoko Soejima				Johnson & Johnson KK, St. Jude Medical Japan Co., Ltd., TOA EIYO LTD., Bayer Yakuhin, Ltd., BIOTRONIK Japan, Inc, Bristol-Myers Squibb, Boston Scientific Corporation, Daiichi Sankyo, Boehringer Ingelheim Japan, Inc, Medtronic Japan Co., Ltd.								
Collaborator: Masahiko Takagi				Abbott Medical Japan Co., Ltd., BIOTRONIK Japan, Inc, Pfizer Japan Inc, Bristol-Myers Squibb, Daiichi Sankyo, Japan Lifeline Co.,Ltd.			Abbott Medical Japan Co., Ltd., BIOTRONIK Japan, Inc, Boston Scientific Corporation,					

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											Research grant	Scholarship (educational) grant
Collaborator: Masaomi Chinushi							Daiichi Sankyo					
Collaborator: Nobuhiro Nishii				DVx, Inc, Abbott Medical Japan Co., Ltd., BIOTRONIK Japan, Inc, Boston Scientific Corporation, Medtronic Japan Co., Ltd.				Medtronic Japan Co., Ltd.,				
Collaborator: Takashi Noda				Medtronic Japan Co., Ltd., Boston Scientific Corporation,								
Collaborator: Takeshi Mitsuhashi				Abbott Medical Japan Co., Ltd., St. Jude Medical Japan Co., Ltd., BIOTRONIK Japan, Inc, Daiichi Sankyo, Medtronic Japan Co., Ltd.,								
Collaborator: Tomoshige Morimoto				Abbott Medical Japan Co., Ltd., St. Jude Medical Japan Co., Ltd., Medtronic Japan Co., Ltd., Japan Lifeline Co.,Ltd., Nihon Kohden Corp.								
Collaborator: Hiro Yamasaki				Century Medical,Inc,	Toray Industries, Inc, Century Medical,Inc							
Independent Assessment Committee: Tohru Ohe	Shionogi & Co., Ltd.,											

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Author	Employer / leadership position (private company)	Stock or stock options	Intellectual property / royalties	Speakers' bureau	Payment for manuscripts	Research grant	Scholarship (educational) grant	Endowed chair	Other rewards	Potential COI of the marital partner, first-degree family members, or those who share income and property	Declaration about the head of your affiliated organization/ department (if the participant is conducting joint research with the head of the organization / department)	
											Research grant	Scholarship (educational) grant
Independent Assessment Committee: Takeshi Kimura				Abbott Vascular Japan Co., Ltd., Sanofi KK, Bristol-Myers Squibb, Kowa Pharmaceutical Co., Ltd., Daiichi Sankyo, Boehringer Ingelheim Japan, Inc		EP-CRSU Co., Ltd, IQVIA Services Japan KK, Otsuka Pharmaceutical Co., Ltd., EPS Corporation	Astellas Pharma Inc, Boston Scientific Corporation, MID, Inc, Otsuka Pharmaceutical Co., Ltd., Sumitomo Dainippon Pharma Co., Ltd., Daiichi Sankyo, Mitsubishi Tanabe Pharma Corporation, Boehringer Ingelheim Japan, Inc, Takeda Pharmaceutical Company Limited					
Independent Assessment Committee: Hiroyuki Tsutsui				MSD KK, Astellas Pharma Inc, Novartis Pharma KK, Bayer Yakuhin, Ltd. Pfizer Japan Inc, Bristol-Myers Squibb, Otsuka Pharmaceutical Co., Ltd., Daiichi Sankyo, Mitsubishi Tanabe Pharma Corporation, Boehringer Ingelheim Japan, Inc, Takeda Pharmaceutical Company Limited,	Nipponrinshosha Co.,Ltd. Medical Review Co., Ltd.	IQVIA Services Japan KK, Actelion Pharmaceuticals Japan Ltd., Daiichi Sankyo, Mitsubishi Tanabe Pharma Corporation, Japan Tobacco Inc, Boehringer Ingelheim Japan, Inc,	MSD KK, Astellas Pharma Inc, Novartis Pharma KK, Daiichi Sankyo, Teijin Pharma Limited, Mitsubishi Tanabe Pharma Corporation, Takeda Pharmaceutical Company Limited					

Companies are listed only by name. The members and the collaborators other than the above have no relevant COIs.

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Collaborators: Kikuya Uno, Michio Ogano, Shunichiro Sakamoto, Tsugutoshi Suzuki, Hitoshi Hachiya, Masataka Mitsuno, Yasushi Miyauchi, Aya Miyazaki.

Independent Assessment Committee: Yoshifusa Aizawa, Kazuo Tanemoto, Hideo Mitamura.