

## Modern Treatment of Atrial Fibrillation

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Atrial fibrillation (AF) is the most common type of arrhythmia and has a large global burden. In general, treatment of AF is based on medication and consists of rate and rhythm control together with anticoagulation. However, surgical treatment may be required in patients with AF combined with organic valvular heart diseases or who experience recurrence despite medication. In addition, surgical treatment plays a role in the treatment of lone AF. This article reviews the various surgical treatment options for AF.

**Key words:** 1. Atrial fibrillation  
2. Catheter ablation  
3. Arrhythmia surgery

### INTRODUCTION

Atrial fibrillation (AF) is the most common type of arrhythmia. In 2010, its global burden, which is progressively increasing, was more than 45 million cases [1].

Although multiple theories about the etiology of AF have been previously proposed, the exact pathophysiological mechanism is unknown and is thought to be mostly multifactorial [2]. In addition, many experts have reported that in at least 10% of the cases, no underlying cause is ever found, a condition that is known as lone AF [3]. The most common surgical treatment for all types of AF is based on the well-known Cox-Maze procedure. Although this procedure is quite successful and has had good long-term results, it is not considered curative. Nevertheless, many cardiothoracic surgeons, employing a number of modifications with a common lesion set, use the Cox-Maze procedure. This paper reviews the current methods of surgical treatment for AF and offers some suggestions on how treatment methods can be further devel-

oped to facilitate better outcomes.

### DEFINITION AND DIAGNOSIS

AF is defined as an abnormal heart rhythm with the following characteristics on an electrocardiogram: (1) absolutely irregular RR intervals; (2) no distinct P waves, and (3) atrial cycle length (when visible) usually variable within 200 milliseconds (>300 beats per minute) [4]. AF is confirmed diagnostically if the above characteristics last sufficiently long enough for a 12-lead echocardiogram to be recorded or for at least 30 seconds on a rhythm strip.

### CLASSIFICATION

AF is classified based on presentation and duration. Many classifications have been adopted, but the most recent is that reported by the European Society of Cardiology (ESC) in 2010 as follows [4].

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1) Every patient who presents with AF for the first time is considered a patient with first diagnosed AF, irrespective of the duration of the arrhythmia or the presence and severity of AF-related symptoms.

2) Paroxysmal AF is self-terminating, usually within 48 hours. Although AF paroxysms may continue for up to 7 days, the 48-hour time point is clinically important-after this the likelihood of spontaneous conversion is low and anticoagulation must be considered.

3) Persistent AF is present when an AF episode either lasts longer than 7 days or requires termination by cardioversion, either with drugs or by direct current cardioversion.

4) Long-standing persistent AF has lasted for  $\geq 1$  year when it is decided to adopt a rhythm control strategy.

5) Permanent AF is said to exist when the presence of the arrhythmia is accepted by the patient (and physician). Hence, rhythm control interventions are, by definition, not pursued in patients with permanent AF. Should a rhythm control strategy be adopted, the arrhythmia is redesignated as 'long-standing persistent AF.'

In addition to the above classification, the guidelines published by the American College of Cardiology (ACC), American Heart Association (AHA), and ESC describe additional AF categories in terms of other characteristics as stated below [5].

1) Lone AF refers to AF in patients younger than 60 years of age without clinical or echocardiographic evidence of any sort of cardiopulmonary disease, including hypertension.

2) Nonvalvular AF refers to AF that occurs in the absence of rheumatic mitral valve disease, a prosthetic heart valve, or valve repair.

3) Secondary AF is a separate classification used in the context of acute myocardial infarctions, cardiac surgery, pericarditis, myocarditis, hyperthyroidism, or acute pulmonary disease. In these situations, AF is not the primary problem, and it is usually terminated with the concurrent treatment of the underlying disorder.

## MEDICAL MANAGEMENT

Medical management differs according to whether the therapeutic goal is rhythm control or rate control. Rhythm control

aims to restore and maintain sinus rhythm, whereas rate control allows AF to persist while attempting to control the ventricular rate response. The specific drugs used in the medical management of AF are listed in detail in the ACC/AHA/ESC guidelines [5]. In a review of these guidelines, the Atrial Fibrillation Follow-up Investigation of Rhythm Management, Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation Study, Atrial Fibrillation and Congestive Heart Failure trials found the mortality of the rhythm control strategy and rate control strategy to be approximately the same. Therefore, a rate control strategy without attempts at restoring or maintaining sinus rhythm can reasonably be used in some patients with AF, especially those who are elderly and asymptomatic. For such patients, rhythm control may become the main goal if rate control offers inadequate symptomatic relief.

## ROLE OF ANTICOAGULATION

Patients with AF have a risk for stroke approximately five times higher than those without AF, and AF is also known to cause an estimated 15% of all strokes [6,7]. Oral anticoagulation drugs may be used in combination with antiarrhythmic drugs to prevent stroke and other thromboembolic events. The vitamin K antagonist warfarin is by far the most commonly used oral anticoagulant mainly because warfarin can also be used universally for the management of implanted artificial valves in patients with AF who have received a valve replacement. However, warfarin is associated with a higher risk of bleeding and requires regular blood tests to monitor the international normalized ratio, which is usually controlled within a narrow target range. In patients not eligible for warfarin, antiplatelets such as aspirin alone or aspirin in combination with clopidogrel may be prescribed.

During recent years, new oral anticoagulants have been introduced as an alternative to prevent stroke in patients with lone or nonvalvular AF. The two main classes of new oral anticoagulants are direct factor IIa (thrombin) inhibitors and factor Xa inhibitors. In the Randomized Evaluation of Long-Term Anticoagulation Therapy study, the direct factor IIa (thrombin) inhibitor dabigatran etexilate was determined to prevent stroke at the same rate as warfarin, but with lower

rates of major bleeding [8]. Rivaroxaban [9], apixaban [10], edoxaban [11], and betrixaban [12] are examples of oral factor Xa inhibitors under development for the prevention of stroke.

### OTHER NON-SURGICAL TREATMENT MODALITIES REFRACTORY TO MEDICATION

Direct-current cardioversion is a procedure to electrically convert an arrhythmia to a normal sinus rhythm. Electrical cardioversion is most frequently used to treat AF with hemodynamic instability that persists despite medication. It also can be used to treat almost any type of arrhythmia, including atrial flutter and ventricular tachycardia.

Radiofrequency catheter ablation is a procedure performed percutaneously through one or both femoral veins as an option for symptomatic patients with AF refractory to antiarrhythmic drugs or where medication is contraindicated [13]. Although radiofrequency catheter ablation is known to be more effective than antiarrhythmic drugs [14], the rate of sinus rhythm restoration is low with a high rate of recurrence and reintervention [15].

While performing percutaneous transvenous catheter ablation, occlusion of the left atrial appendage (LAA) can be accomplished with devices such as the WATCHMAN [16], PLAATO [17], or the Amplatzer Cardiac Plug device [18]. However, these devices have been associated with procedural complications such as pericardial effusion, incomplete appendage closure, dislodgement of the device, thrombus formation on the device, and air embolism due to the catheter-based technique [19,20]. Despite the development of novel devices, internal occlusion of the LAA is very challenging due to its heterogeneous anatomy [21].

### SURGICAL MANAGEMENT

The Cox-Maze III procedure is the gold standard for the surgical treatment of AF. This procedure is usually performed concomitantly during open-heart surgery in AF patients with other valvular or coronary diseases through a median sternotomy. Another surgical approach is to perform a right thoracotomy for concomitant mitral valve surgery along with

the maze procedure [22].

The classical Cox-Maze III procedure, first introduced by Dr. James Cox in 1988, was performed in a cut-and-sew method using a biatrial lesion set [23]. This cut-and-sew procedure is rarely performed now since it requires extensive incisions over a prolonged period. This procedure was then modified using cryoablation to replace most of the cut-and-sew incisions of the lesion sets, resulting in the modified Cox-Maze III procedure [24]. Other than cryoablation, other various energy sources for the maze procedure have been reported, such as unipolar or bipolar radiofrequency, high intensity focused ultrasound, microwaves, and lasers. In 2002, the Cox-Maze IV procedure was developed to simplify the Cox-Maze III procedure by incorporating a combination of bipolar radiofrequency energy and cryoablation to further limit the incisions. The Cox-Maze IV lesion sets consist of bipolar radiofrequency ablation of the separate pulmonary artery box lesions and lines between both boxes superiorly and inferiorly, and cryoablation of only the tricuspid annular lesion and mitral isthmus lesion [25].

Cryoablation with argon or nitrous oxide is preferably used endocardially, while radiofrequency and high intensity focused ultrasound are used epicardially (radiofrequency can also be used endocardially) when performing the Cox-Maze III or IV procedure. Microwave energy can be applied either endocardially while performing other open-heart procedures or epicardially on the beating heart. However, transmural ablation cannot be guaranteed, and the results are variable with maintenance of sinus rhythm ranging from 42% to 81% one year after the procedure [26,27]. High intensity focused ultrasound is a relatively new and promising energy source that can feasibly create transmural lesions either endocardially or epicardially, but a recent study has reported a low success rate with a high complication rate [28].

Whichever energy source is used, the complete maze lesion set is not fully reproducible on the epicardial surface. To fully reproduce all maze lesions and further increase the success rate in minimally invasive approaches, a hybrid procedure of both surgical epicardial and percutaneous transvenous catheter ablation on the beating heart for lone AF has been introduced recently and can be performed simultaneously as a single-stage or two-stage procedure [29,30].

Surgical exclusion of the LAA is usually performed by internal obliteration when performing the maze procedure concomitantly with other open-heart surgery under cardiopulmonary bypass. The method of internal obliteration can be completed by simply oversewing the opening of the LAA or via a patch closure with a synthetic material. When performing minimally invasive surgical LAA exclusion on the beating heart, an external closure must be used. External closure is achieved by suturing, stapling, or ligating the base of the LAA.

## CONCLUSION

Since its introduction by Dr. James Cox in 1988, the Cox-Maze procedure has been regarded as the gold standard for the surgical treatment of AF. Subsequently, modifications of the Cox-Maze procedure have been developed by incorporating various energy sources to minimize the surgical incisions of the lesion sets and using minimally invasive approaches to avoid median sternotomy. Currently, the Cox-Maze IV procedure based on the classical Cox-Maze III lesion set is preferred, and minimally invasive procedures are reserved for lone AF. Although thoracoscopic epicardial ablation on the beating heart has the advantage of being minimally invasive without cardiopulmonary bypass, it has been shown to have difficulty in reproducing all lesion sets of the classical Cox-Maze III procedure [31].

To overcome this limitation and improve outcomes, a hybrid procedure of both surgical epicardial and percutaneous transvenous catheter ablation can be performed simultaneously as a single-stage or two-stage procedure [29,30]. If the minimally invasive approach is enhanced by further development of special ablation probes, a simpler and safer surgical maze procedure could be developed. Percutaneous catheter ablation also shows increasing success rates due to improved mapping and sensing techniques, although device closure in the LAA have led to various complications. Although surgical management of AF has usually only been performed concomitantly with open-heart surgery in patients with other valvular or coronary diseases, its applications have continued to expand for lone AF. Therefore, sole surgical ablation along with the further technical development of surgical excision of the LAA may emerge as the standard treatment for AF. The further de-

velopment of the maze operation, using a minimally invasive approach, will lead cardiac surgeons to promising future possibilities.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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