




ORIGINAL ARTICLE

Reassessment of practical usage and accumulation of real-world data of wearable cardioverter defibrillator (WCD) in Japan—Design paper for J-WCDR study

Shinichi Niwano MD¹  | Haruhiko Abe MD² | Masahiko Takagi MD³ | Yukio Sekiguchi MD⁴  | Yu-Ki Iwasaki MD⁵  | Ritsushi Kato MD⁶ | Yusuke Kondo MD⁷ | Takashi Kurita MD⁸ | Takashi Nitta MD⁵ | Akihiko Nogami MD⁹ | J-WCDR investigators

¹Department of Cardiovascular Medicine, Kitasato University School of Medicine, Sagami-hara, Japan

²Department of Heart Rhythm Management, University of Occupational and Environmental Health, Kitakyushu, Japan

³Department of Medicine II, Kansai Medical University, Osaka, Japan

⁴Division of Cardiology, Kasumigaura Medical Center, Tsuchiura, Japan

⁵Department of Cardiovascular Surgery, Nippon Medical School, Tokyo, Japan

⁶The Department of Cardiology, Saitama Medical University, International Medical Center, Saitama, Japan

⁷Department of Cardiovascular Medicine, Chiba University Graduate School of Medicine, Chiba, Japan

⁸Division of Cardiovascular Center, Kindai University, Osaka-Sayama, Japan

⁹Department of Cardiology, University of Tsukuba, Tsukuba, Japan

Correspondence

Shinichi Niwano, Department of Cardiovascular Medicine, Kitasato University School of Medicine, 1-15-1 Kitasato, Minami-ku, Sagami-hara 252-0374, Japan.

Email: shniwano@med.kitasato-u.ac.jp

Abstract

Although implantable cardioverter defibrillators (ICDs) are a powerful preventive therapy for cardiac sudden death, there are some populations in whom ICDs cannot be applied because of a lack of a definitive indication (grey-zone patients), such as in patients during the acute phase of cardiac injury with a susceptible risk for lethal arrhythmias. In such patients, wearable cardioverter defibrillators (WCDs) provide safer bridging period during the acute phase until the final decision-making for the ICD use and it may eliminate any inappropriate overuse of ICDs in the subacute phase. The JCS/JHRS practical guidelines provide the criteria for WCD use in Japan. Nevertheless, the evidence for that is totally limited in Japan and is dependent on the accumulation of actual real-world data from other countries in order to be able to discuss the appropriate criteria for WCD use. This study will be conducted retrospectively and/or prospectively, and is an observational and multicenter study among Japanese institutions (J-WCDR, Japan WCD Registry). This will provide evidence for WCD use in our own country and contribute to upcoming updates for the future guideline revisions.

KEYWORDS

defibrillation device, sudden cardiac death, ventricular arrhythmia, wearable cardioverter defibrillator

1 | INTRODUCTION

For the concept of prevention of sudden cardiac death, we have already obtained ultimate tools, that is, implantable defibrillation

devices, such as implantable cardioverter defibrillators (ICDs)¹⁻³ and/or cardiac resynchronization therapy devices with a defibrillation function (CRT-D).⁴ The efficacy of these devices has been evaluated in various clinical trials, and the clinical indications for these devices

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clearly have been described in the “practical guidelines” from various countries.⁵⁻⁷ However, these guidelines do not cover the so-called “grey-zone” patients, such as patients in the acute phase of myocardial injury including a myocardial infarction, myocarditis, acute heart failure, etc, because the usefulness of implantable devices has not been established or even denied.^{8,9} That is probably because of performing invasive ICD implantation procedures in hemodynamically unstable patients and/or an inadequate selection of patients with potential left ventricular dysfunction during the acute phase of the baseline disease.¹⁰⁻¹² To save such “grey-zone” patients, the wearable cardioverter defibrillator (WCD: LifeVest, Zoll Medical Corporation, USA) may provide a bridge during the gap period prior to receiving an ICD in the acute phase for the prevention of sudden cardiac death.¹²

2 | CONCEPT AND INDICATION FOR A WCD

The WCD is a unique defibrillation system, which can automatically detect life-threatening arrhythmias in patients at a risk of sudden cardiac death. The system includes a body fitting elastic vest, contact type body surface ECG electrodes, defibrillation pads with a self-releasing gel, and coded connected controller, which can automatically detect life-threatening arrhythmias and deliver defibrillation shock unless they are canceled. The entire system can be placed simply and noninvasively, but it achieves a high sensitivity and specificity for the therapy, which is almost comparable to the latest ICD model and/or CRT-D systems.¹³⁻¹⁶ The WCD also has a wireless connection with the “LifeVest Network System”, which provides high-quality patient monitoring similar to pacemaker/ICD remote monitoring. Because this system can be applied or removed immediately and noninvasively, it provides a feasible bridging option until an implantable device therapy can be provided in patients at risk for sudden cardiac death.

The indications for the use of a WCD were described in the JCS/JHRS practical guideline 2018 edition⁵ as follows:

1. Patients within 40 days after the onset of acute myocardial infarction with left ventricular ejection fraction $\leq 35\%$ and heart failure symptoms of NYHA class II or III (class IIa indication).
2. Patients with left ventricular ejection fraction $\leq 35\%$ and within 90 days after coronary artery bypass or percutaneous coronary intervention, and with NYHA class II or III heart failure symptoms (class IIa indication).
3. Patients with left ventricular ejection fraction $\leq 35\%$ and within 90 days after the acute onset of heart failure because of a nonischemic etiology (class IIa indication).
4. Patients with irreversible severe heart failure satisfying a heart transplant standby condition (class IIa indication).
5. Patients in whom ICD is recommended but surgery cannot be performed immediately owing to other physical conditions (class IIa indication).

6. Patients in whom ICD is temporarily removed for any reasons such as infection (class IIa indication).
7. 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 (class IIb indication).
8. Hospitalized patients who have a moderate or higher risk of life-threatening arrhythmia but cannot receive adequate arrhythmia monitoring (class IIb indication).

3 | POTENTIAL PROBLEMS OF WCD USE IN JAPAN

Since January 1, 2014, when the usage of the WCD systems was first approved in Japan, a serious deficit between the medical cost of the WCD system and insurance coverage occurred, which may have limited the WCD use. Fortunately, this problem was almost solved by April, 2020. However, over-use or off-label use will be of concern because WCDs can easily be attached and done so noninvasively. Because such inappropriate use has been concerning, the Japanese Heart Rhythm Society (JHRS) published a statement for WCD use in 2015 mentioning not only its indications but also the standards for the institution and prescribers because it is widely understood that similar society-led requirements for ICD use suppress the over-use of ICDs in Japan. On the other hand, there are other concerns that such complicated requirements may limit the use of WCDs in specific situations such as a lack of adequate WCD supporting team in individual institute.

The indications for the WCD use in the guidelines⁵ are strongly dependent on the evidence established in the United States and Germany. Although those criteria seem to be applicable to Japan, Japanese situation of clinical medicine is different from foreign countries, especially regarding β -blockers, ACE inhibitors, ARBs, and/or diuretics; therefore, Japan must provide its own evidence for WCD use in the Japanese population. Additionally, the insurance coverage is limited for the continuous use of WCDs to up to 3 months in Japan. This limit was set because the WCD usage period was <90 days in $>90\%$ of the patients in the United States data. This limit is also questionable when considering primary prevention of sudden death in cases with primary arrhythmias such as the Brugada and/or long-QT syndromes. It is clear that an accumulation of data in patients using WCDs from considerably large populations is necessary in order to discuss these points for future updates of the guidelines. The results of this study will surely contribute to the upcoming update of the guidelines in the future.

4 | DESIGN OF THE J-WCDR STUDY

Here, we designed a registry study for the J-WCDR (Japan WCD-Registry) study under the supervision of the JHRS.

4.1 | Purpose

By investigating the actual state of the WCD use in Japan and its clinical consequences, the adequacy of the WCD indication criteria and methods for performing the WCD use will be examined.

4.2 | Study population

Patients who will be prescribed a WCD in Japan, meet all of the following selection criteria, and do not meet any of exclusion criteria will be included. The study population includes cases in whom WCD use has been completed at the time of registration. The indication for the WCD use will comply with the latest JSC/JHRS guidelines.⁵ In patients enrolled for retrospective observations in whom the WCD was prescribed before the publication of the JSC/JHRS guidelines, the WCD was prescribed according to the JHRS statement.¹⁷ Selection criteria: any age, or gender, and patients with sufficient medical record information during the observation period will be included, and written informed consent should be obtained after a sufficient explanation in the prospective arm. In the retrospective arm, a sufficient explanation should be informed through opting out of the study. Exclusion criteria: patients in whom the prescribers determine that the WCD use will be inappropriate for any reason, such as an incompatible body size for the device, poor understanding of the WCD usage method, etc, will be excluded.

4.3 | Study design

Multicenter joint retrospective study using existing information and a prospective observational study without intervention.

4.4 | Outline of the study

In this study, information from the start of the WCD application will be registered in the database for the study subjects in whom consent was obtained. Since the maximum reimbursement period for a WCD is 3 months, the data at the end of the use (up to 3 months) will be registered in the database regardless of the period. From the information gathered in this study, whether the use of a WCD was appropriate will be examined by comparing the clinical background when the WCD was applied and the prognosis after that.

4.5 | Criteria for discontinuing the individual observation

(a) When a research subject requests to decline research participation or withdraws the consent, (b) if the entire study is discontinued, and (c) when it is appropriate for the researcher to stop the research because of other reasons.

4.6 | Scheduled period for research participation

The WCD usage period (up to 3 months).

4.7 | Observational items and schedule

Data registration: The items evaluated in the actual clinic during the observation period will be collected from the medical records.

At the start of the WCD use: The following information will be collected at the time of starting the WCD use.

1. *Basic items:* gender, age, starting date of the WCD use, WCD prescriber, purpose of the WCD use, reason for primary prevention or secondary prevention, prescribed institute, presence/absence of education on the WCD system, presence/absence of education on the WCD placement instructions, presence/absence of manufacturer assistance, prescribed medicine when the WCD was applied, presence/absence of renal dialysis, etc
2. *Patient background information:* height, weight, basic cardiac disease, presence/absence of coronary artery disease, findings from coronary angiography, history of revascularization before the implantation, presence/absence of atrial fibrillation/flutter, diseases other than heart disease, NYHA classification, left ventricular function, chest X-ray/electrocardiogram, presence/absence of nonsustained ventricular tachycardia (NSVT), history of treatment for VT/NSVT, blood chemistry test, etc

At the end of the observation: The following information will be collected after the follow-up of a maximum of 3 months. Patient information: The presence/absence of events (VT/VF occurrence, improper operation, death, hospitalization for heart failure, device-related complications, or a device-related reoperation), device treatment after the use of the WCD, additional examinations during or after the use of the WCD (NYHA classification, left ventricular function, signal averaged electrocardiogram, T-wave alternation [TWA], electrophysiological examination, and Holter electrocardiogram), additional treatments during the WCD use (internal loop recorder, catheter ablation, or revascularization), prescribed a medication at the end of the WCD use, the date when it was determined that follow-up was impossible, etc

4.8 | Evaluation and reporting of adverse events

This study will be a retrospective study using existing information and a prospective observational study without intervention, and is unlikely to cause new adverse events.

4.9 | Target number of cases

In principle, all cases with WCDs will be registered.

Prospective arm: All target cases will be enrolled. Since about 500 cases are expected to be accumulated annually, about 2,500 cases will be targeted during the enrollment period.

Retrospective arm: Out of approximately 1,000 cases in whom a WCD has already been used, we will target cases for which objective data can be collected from the medical records. Whether or not to use retrospective data will be judged after appropriately opting out, etc, to secure the opportunity to present the free will of the patients who do not allow the data to be used.

4.10 | Scheduled research period

The research period, registration period, and observation period are as follows. In addition, each will be reviewed every 5 years.

Research period: After October 1, 2020, following approval of the research at the facility-March 31, 2026.

Prospective arm: Registration period: October 1, 2020 to December 31, 2025. Observation period: October 1, 2020 to March 31, 2026.

Retrospective arm: Target period: January 1, 2015 to September 30, 2020.

4.11 | Study end point

Primary endpoint: Death, or implantable defibrillation device transfer rate.

Secondary endpoint: Occurrence of VT/VF, hospitalization for heart failure, or inappropriate operation.

In the case of survival, it will be discontinued after the use of the WCD.

In cases where follow-up is not possible, censorship will be discontinued on the last day when survival has been confirmed before the follow-up becomes impossible.

By considering the examination of the long-term prognosis of the patients with the WCD use, it may be considered desirable to follow-up the cases for a longer period regardless of the subsequent therapeutic strategy. However, this study employed a 3-month observational period aiming to investigate the medium-term prognosis and strategic results after the use of the WCD.

4.12 | Statistical matters

The information gathered in this study will be compared for differences in the clinical background between the primary and secondary assessments. The main studies will be a correlation between the presence or absence of a transition to an implantable defibrillation device and the clinical background, VT/VF events under observation, and background factors (especially left ventricular function, ventricular arrhythmia, which is considered to be strongly associated with the prognosis, and renal function) and the survival prognosis

by comparing what kind of patient background the WCD is likely to work with or whether it will be transferred to an implantable defibrillation device. Kaplan-Meier curves will be used for the prognosis, and a multivariate analysis will be used to determine the strength of the association. This will help examine the appropriate adaptation criteria for WCD use in Japanese. Cases of discontinuation/dropout or missing values shall be included as the data with limited observation period until the time of discontinuation.

4.13 | Ethical matters

All researchers involved in this research will conduct this research in accordance with the Declaration of Helsinki (2013, latest version) and "Ethical Guidelines for Medical Research for Humans" (revised February 28, 2017).

In the prospective arm of this study, in principle, a consent explanation document approved by the Ethics Review Committee will be given to the patient, a full explanation will be given in writing and verbally, and an informed consent from the study subject will be obtained in writing. In the retrospective arm, the opportunity to present the free will of the patient who does not allow the use of the data will be properly secured by opting out, etc. The details of the explanation and method of consent at each participating facility will follow the regulations of each facility.

When handling information related to the research implementation, a correspondence table with a number that is unrelated to the personal information of the research target person will be created, and it will be anonymized and due consideration to protecting the confidentiality of the research target person (connectable anonymization) will be given. Each investigator will use this number when sending information to the research institute or other related organizations and will make sure that the personal information of the research subject is not leaked outside the hospital. When publishing the results of the research, we will not include any information that can identify the research subject.

4.14 | Study registration

The study will be registered in the UMIN-CTR database.

Data Control and Analysis Committee: Yukio Sekiguchi, MD (Division of Cardiology, Kasumigaura Medical Center, Ibaraki, Japan) and Ritsushi Kato, MD (Department of Cardiology, Saitama Medical University International Medical Center, Saitama, Japan).

Monitoring Committee: Kenzo Hirao, MD (Division of Cardiovascular Medicine, AOI Universal Hospital, Kanagawa, Japan) and Yuji Nakazato, MD (Sakakibara Sapia Tower Clinic, Tokyo, Japan).

CONFLICT OF INTEREST

The authors have nothing to declare for a conflict of interest regarding this study. This study has been approved by the IRB of Kitasato University Hospital (B20-180, approved on August 19, 2020).

ORCID

Shinichi Niwano  <https://orcid.org/0000-0002-0702-0800>

Yukio Sekiguchi  <https://orcid.org/0000-0003-3649-4025>

Yu-Ki Iwasaki  <https://orcid.org/0000-0001-8783-1365>

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