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Original Article

Current status of cardiac resynchronization therapy with defibrillators and factors influencing its prognosis in Japan ☆

Akihiko Shimizu [a,*], Takeshi Mihashi [b], Hiroshi Furushima [c], Yukio Sekiguchi [d], Tetsuyuki Manaka [e], Nobuhiro Nishii [f], Takeshi Ueyama [g], Hisashi Yokoshiki [h], Norishige Morita [i], Takashi Nitta [j], Ken Okumura [k]

[a] Faculty of Health Sciences, Yamaguchi Graduate School of Medicine, 1-1-1 Minami-Kogushi, Ube, Yamaguchi 755-8505, Japan
[b] Cardiovascular Medicine, Jichi Medical University Saitama Medical Center, Japan
[c] Department of Cardiovascular Biology and Medicine, Niigata University Graduate School of Medical and Dental Sciences, Japan
[d] Cardiovascular Division, Faculty of Medicine, University of Tsukuba, Japan
[e] Department of Cardiology, Tokyo Women's Medical University, Japan
[f] Department of Cardiovascular Medicine, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Japan
[g] Division of Cardiology, Department of Medicine and Clinical Sciences, Yamaguchi Graduate School of Medicine, Japan
[h] Department of Cardiovascular Medicine, Hokkaido University Graduate School of Medicine, Japan
[i] Division of Cardiology, Department of Medicine, Tokai University Hachioji Hospital, Japan
[j] Cardiovascular Surgery, Nippon Medical School, Japan
[k] Department of Cardiology, Hirosaki University Graduate School of Medicine, Japan

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ABSTRACT

Purpose: The purpose of this study was to clarify the prognosis of cardiac resynchronization therapy with defibrillators (CRT-Ds) in Japan.
Methods: We selected 384 patients implanted with a CRT-D device from the observation database ($n=1482$) of the Japanese Cardiac Device Therapy Registry. We investigated the CRT criteria, including the presence of New York Heart Association (NYHA) class III/IV symptoms, left ventricular ejection fraction (LVEF) ≤35%, and QRS duration ≥120 ms. The patients were divided into 2 groups: the group fulfilling all of the 3 criteria (Group A, $n=229$) and the group not fulfilling the criteria (Group B, $n=155$). We compared mortality and appropriate shock rates between the 2 groups.
Results: There was no significant difference in mortality (17.9% vs. 13.5%) or appropriate shock rates (32.5% vs. 31.6%) during the observation period of 29.0 ± 15.7 months between the 2 groups. A logistic multivariate analysis showed that appropriate shocks (hazard ratio [HR]=1.85) and class III antiarrhythmic agents (HR=2.33) were independently associated with all-cause death, and that age ≥70 years (HR=0.55), male gender (HR=2.07), and presence of a single-chamber device (HR=1.78) were associated with appropriate shocks. The prognosis of Group A was better than that of the COMPANION trial.
Conclusions: Japanese patients with CRT-D devices had a better prognosis than did those in the COMPANION trial, but no significant differences were observed between patients fulfilling and those not fulfilling the above mentioned criteria.

1. Introduction

Cardiac resynchronization therapy (CRT) with an implantable cardioverter-defibrillator (ICD) or without an ICD (CRT-P) is recommended to reduce morbidity and mortality in patients who have New York Heart Association (NYHA) class III/IV heart failure, are symptomatic despite optimal medical therapy, and have a reduced left ventricular (LV) ejection fraction (LVEF) and electrical dyssynchrony [1–3]. The effects of CRT are reflected mainly by the degree and location of the dyssynchrony and by the successful insertion of lead into the optimal LV lead site [4,5]. No significant differences have been observed between the right ventricular apical and non-apical positions of the lead tip in a previous study [6].

In Japan, ICDs were approved by the Japanese Ministry of Health, Labor and Welfare (MHLW) in 1996. CRT-P and CRT with an ICD (CRT-D) were also approved in 2004 and 2006, respectively.

☆The Implantable Devices Registry and Assessment Committee of the Japanese Heart Rhythm Society.

* Corresponding author. Tel./fax: +81 836 22 2856.
E-mail address: ashimizu@yamaguchi-u.ac.jp (A. Shimizu).

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The Japan Cardiac Device Treatment Registry (JCDTR) was established by the Japan Heart Rhythm Society for investigating the actual conditions of implantable devices (ICD/CRT-D) [7]. New guidelines were set forth by the Japanese Circulation Society in 2007 [8] and were then updated in 2011 [9].

The number of CRT-D implantations has markedly increased since 2006 when they were approved by the MHLW. In particular, primary prevention using CRT-D devices has dramatically increased over the last 5 years in Japan according to the JCDTR enrollment database [10], but this database has shown no significant changes in the criteria involving the QRS duration, LVEF, and NYHA class in patients with a CRT-D device over these 5 years [11]. Thus, the increase in the number of CRT-D device implantations for primary prevention did not result from an increase in the number of patients with a relatively early phase of heart failure and electrophysiologic disturbance in Japan [11].

The prognosis and occurrence of appropriate shocks in the therapy for ventricular tachycardia/ventricular fibrillation are not clear in patients with implanted devices in Japan. Therefore, the purpose of this study was to clarify the prognosis in patients who were implanted with a CRT-D device in Japan.

2. Methods

2.1. Patient population

Between January 1, 2006 and December 31, 2010, 384 patients implanted with CRT-D devices were selected from 1482 patients from the JCDTR observation database (ICDs and CRT-Ds) from 16 facilities of the Devise Assessment Committee of the Japanese Heart Rhythm Society (JHRS) (Appendix). Data were collected by means of a retrospective multicenter study. Informed consent was waived for the analysis of preexisting clinical data.

The distribution of underlying heart disease in CRT-D patients was investigated in the primary prevention and secondary prevention groups. Underlying heart disease was classified into ischemic heart disease (IHD), dilated cardiomyopathy (DCM), secondary cardiomyopathy (2ndCM), hypertensive heart disease (HHD), valvular heart disease (VHD), congenital heart disease (CHD), hypertrophic cardiomyopathy (HCM), and miscellaneous (micell).

The prognoses of the survival rate and appropriate shocks were studied as the primary endpoints, and clinical variants associated with mortality and appropriate shock rate were then investigated. In this study, patients were divided into 2 groups according to the CRT-D criteria (NYHA class III/IV symptoms, LVEF≤35%, and QRS width ≥120 ms, as per the Japanese Circulation Society (JCS) 2011 Guidelines [9]): Group A comprised 229 patients who fulfilled all of the 3 criteria, and Group B comprised 155 patients who fulfilled 2 or fewer of the 3 criteria. Clinical characteristics, survival, and appropriate shock rate were compared between the 2 groups.

In this study, a single-chamber ICD was defined as an ICD with no lead placed in the atrium. An appropriate shock was defined as shock therapy or antitachycardia pacing for ventricular tachycardia and/or ventricular fibrillation.

2.2. Statistical analysis

The data are presented as the mean ± standard deviation (SD). The chi-square test and Student *t*-test for independent variables were used for comparisons between the groups. Kaplan–Meier curves with survival rates and appropriate shocks as the outcomes of interest were calculated. Further, the log-rank test statistic was used to determine the statistical significance of unadjusted differences in the time to the event. A univariate analysis (Mantel–Haenszel method) of the clinical variables in the JCDTR questionnaire followed by multivariate analyses (linear model method) of the clinical variables showing a significant difference in the univariate analysis were performed using the SPSS software (SPSS 16.0 Family for Windows, MapInfo, NY) for evaluating the association with mortality and appropriate shocks in the CRT-D patients. A value of $p < 0.05$ was considered statistically significant.

3. Results

3.1. Distribution of the underlying heart disease in the CRT-D patients

A higher number of patients was present in the primary prevention group ($n=247$; 64%) than in the secondary prevention group ($n=137$; 46%), as shown in Fig. 1. The percentage of IHD events was lower in the primary prevention group (19%) than in the secondary prevention group (31%). On the other hand, the percentage of CM events (DCM+2ndCM) was higher in the primary prevention group (66%) than in the secondary prevention group (54%). The percentage of IHD plus CM events in the primary prevention group (85%) was similar to that in the secondary prevention group (85%).

3.2. Clinical characteristics and medications

There were no significant differences in age, percentage of patients in the primary prevention group, and percentage of IHD events and single-chamber CRT-D devices between Groups A and

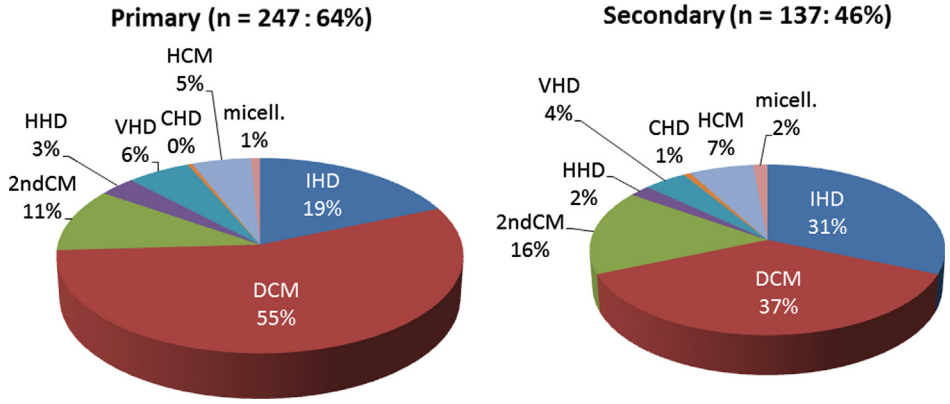

Fig. 1. Distribution of the underlying heart disease in the primary prevention and secondary prevention groups. Primary: primary prevention group; secondary: secondary prevention group; IHD: ischemic heart disease; DCM: dilated cardiomyopathy; 2ndCM: secondary cardiomyopathy; HHD: hypertensive heart disease; VHD: valvular heart disease; CHD: congenital heart disease; HCM: hypertrophic cardiomyopathy; micelle: miscellaneous.