

Mid-term feasibility and safety of downgrade procedure from defibrillator to pacemaker with cardiac resynchronization therapy

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ABSTRACT

Backgrounds: Some patients who undergo implantation of cardiac resynchronization therapy with defibrillator (CRT-D) survive long enough, thus requiring CRT-D battery replacement. Defibrillator therapy might become unnecessary in patients who have had significant clinical improvement and recovery of left ventricular ejection fraction (LVEF) after CRT-D implantation.

Methods: Forty-nine patients who needed replacement of a CRT-D battery were considered for exchange of CRT-D for cardiac resynchronization therapy with pacemaker (CRT-P) if they met the following criteria: LVEF >45%; the indication for an implantable cardioverter defibrillator was primary prevention at initial implantation and no appropriate implantable cardioverter defibrillator therapy was documented after initial implantation of the CRT-D.

Results: Seven patients (14.2%) were undergone a downgrade from CRT-D to CRT-P without any complications. No ventricular tachyarrhythmic events were observed during a mean follow-up of 39.7 ± 21.1 months and there was no significant change in LVEF between before and 1 year after device replacement ($53.5\% \pm 6.2\%$ vs. $56.4\% \pm 7.3\%$, $P = 0.197$).

Conclusions: This study confirmed mid-term feasibility and safety of downgrade from CRT-D to CRT-P alternative to conventional replacement with CRT-D.

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1. Introduction

Some patients with an implanted cardiac resynchronization therapy (CRT) device with defibrillator (CRT-D) are confirmed to have significant clinical improvement and recovery of left ventricular ejection fraction (LVEF) during follow-up and are therefore less likely to require implantable cardioverter-defibrillator (ICD) therapies [1]. In the Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT), patients who showed recovery of LVEF (>50%) after CRT were reported to have very low absolute and relative risks of ventricular tachycardia/fibrillation (VT/VF) [2]. These patients could be considered for downgrade from a CRT-D to a CRT with pacemaker (CRT-P) at the time of battery replacement. Although several observational studies [3–6] have indicated the possibility of such a downgrade procedure, there have been no relevant feasibility and safety studies.

In this study, we aimed to investigate the feasibility and safety of a downgrade from CRT-D to CRT-P in selected patients who achieved significant improvement of left ventricular function after CRT.

2. Materials and methods

2.1. Study population

This is a prospective, single-center, and non-randomized study involving 49 consecutive patients who underwent CRT-D generator replacement because of battery depletion from December 2012 to December 2017. Patients who needed device replacement because of device-related infection or lead malfunction/fracture were excluded.

2.2. Criteria for downgrade from CRT-D to CRT-P

Patients were deemed eligible for a downgrade from CRT-D to CRT-P if they met the following criteria: LVEF >45% on echocardiography at the time of battery depletion; initial ICD implantation for primary prevention; no VT/VF events since initial CRT-D implantation; and

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written informed consent obtained. The study protocol and use of the criteria to determine eligibility for the downgrade were approved by the ethics committee at our hospital. The study protocol also conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

2.3. Downgrade procedure

The atrial and LV leads in the CRT-D were connected to each atrial and LV port in the CRT-P without any arrangement. In patients with a CRT-D and a DF-1 lead, we used a diverged IS-1 lead to connect the IS-1 port in the CRT-P and capped the diverged superior vena cava and right ventricular coil. In patients with a CRT-D and a DF-4 lead, we implanted an additional IS-1 lead into the right ventricular apex and connected the IS-1 port in the CRT-P and capped the DF-4 lead. Patients who were ineligible for a downgrade underwent a conventional replacement procedure, i.e., generator exchange.

2.4. Device programming and follow-up

In patients who underwent a conventional replacement procedure, programming of the CRT-D, including ICD therapy, was the same as the original settings. The patients attended 6 monthly follow-up appointments for a device check. ICD therapies were assessed by two cardiologists. The numbers of ventricular arrhythmic events, hospitalizations for management of worsening heart failure (HF), and death from all causes were recorded.

2.5. Statistical methods

Continuous data are expressed as the mean and standard deviation. The Mann-Whitney *U* test was used to compare continuous baseline data between the two groups. Categorical variables are expressed as the number and percentage. Fisher's exact test was used to compare categorical baseline data between two groups. Continuous data were compared at follow-up using the Wilcoxon signed-rank test. The Kaplan-Meier method was used to analyze survival and freedom from hospitalization for HF and ICD therapy after replacement of the generator, and comparisons were made using the log-rank test. All statistical analyses were performed using SPSS for Windows (version 25.0, IBM Corp., Armonk, NY, USA).

3. Results

During the study period, replacement of the CRT-D generator was planned in 49 consecutive patients. Seven patients met the criteria outlined in Section 2.2 for a downgrade. Table 1 shows the clinical characteristics at the time of initial CRT-D implantation for patients who did and did not subsequently meet the criteria for a downgrade. The patients who met the criteria for a downgrade were more likely to have left bundle branch block (LBBB) than those who did not.

3.1. Downgrade procedure

One patient had undergone implantation of a CRT-D with a DF-4 lead. We implanted an additional IS-1 lead in this patient without any complications. There were no complications during replacement of the generator in any of the patients.

3.2. Follow-up

No ventricular arrhythmic events or hospitalizations for HF occurred in the patients who underwent the downgrade during a mean follow-up of 39.7 ± 21.1 months. However, 14 of the patients who did not undergo the downgrade experienced ventricular arrhythmias ($P = 0.029$) and 15 were admitted to the hospital because of worsening HF ($P = 0.020$;

Table 1

Demographic and clinical characteristics at the time of initial implantation of cardiac resynchronization therapy with a defibrillator device in patients who were and were not candidates for a downgrade.

Characteristic	Downgrade candidate (n = 7)	Downgrade not a candidate (n = 42)	P-value
Male sex	4 (57.1)	34 (81.0)	0.178
Age (years)	70 ± 12	65 ± 13	0.262
NYHA class			0.351
II	0 (0)	4 (9.5)	
III	7 (100.0)	32 (76.2)	
IV	0 (0)	6 (14.3)	
Ischemic cardiomyopathy	1 (14.2)	14 (33.3)	0.414
QRS duration (ms)	162.8 ± 40.6	151.1 ± 32.0	0.390
LVEF (%)	25.6 ± 10.0	26.6 ± 11.5	0.829
LVEDV (mL)	228.0 ± 111.8	248.5 ± 112.1	0.656
LVESV (mL)	175.7 ± 99.9	191.2 ± 111.8	0.732
LBBB	7 (100.0)	18 (42.9)	0.001
BNP (pg/mL)	513.2 ± 594.4	684.6 ± 1207.5	0.716
Medication at baseline			
ACE-I/ARB	6 (85.7)	40 (95.2)	0.377
MRA	5 (71.4)	38 (90.5)	0.199
Beta-blockers	6 (85.7)	38 (90.5)	0.554
Diuretics	6 (85.7)	29 (69.0)	0.656

The data are presented as the number (percentage) or the mean ± standard deviation. CRT, cardiac resynchronization therapy; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LBBB, left bundle branch block; BNP, brain natriuretic peptide; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; MRA, mineralocorticoid receptor antagonist.

Fig. 1). Patients who received the downgrade showed a lower tendency of all-cause mortality than patients who did not ($P = 0.054$). In the patients who underwent the downgrade, there was no change in LVEF between baseline and at 1 year after the replacement of the device ($53.5\% \pm 6.2\%$ vs. $56.4\% \pm 7.3\%$, $P = 0.197$).

4. Discussion

This study showed mid-term feasibility and safety of the downgrade from CRT-D to CRT-P. Patients who received the downgrade did not experience ventricular arrhythmias and had no HF hospitalization following the downgrade procedure in the 39.7 ± 21.1 -month average follow-up period. Although the validity of a downgrade from a CRT-D to a CRT-P has been discussed in previous observational studies [1–6], there has been no research on its actual feasibility. To our knowledge, our study is the first to report the actual downgrade procedure outcome from a CRT-D to a CRT-P.

Some patients with an implanted CRT-D and improved HF show no indication for ICD at the time of CRT-D battery depletion. However, determining which patients are eligible for a downgrade remains unclear. We selected 3 criteria to identify suitable candidates: 1) LVEF >45% on echocardiography at the time of device battery depletion; 2) initial ICD implantation for primary prevention; and 3) no VT/VF events since initial CRT-D implantation.

All patients with HF are at risk of ventricular arrhythmias, irrespective of their LVEF [7]. Implantation of an ICD for primary prevention has been shown to be cost-effective when the annual incidence of arrhythmic events is >3% [8]. A meta-analysis of recovery of LV function after implantation of a CRT device found that patients who achieved an LVEF >45% had an annual incidence of arrhythmic events under 3% [9], indicating that the use of an ICD for primary prevention may not be cost-effective in these patients. Therefore, we adopted an LVEF >45% at the time of battery depletion as one of the criteria for the downgrade.

Primary prevention as the indication for an ICD at the time of initial implantation of a CRT-D is also an important criterion for a subsequent downgrade, given that patients with a history of VT/VF are more likely to have recurrences of VT/VF after implantation of an ICD [10]. A study

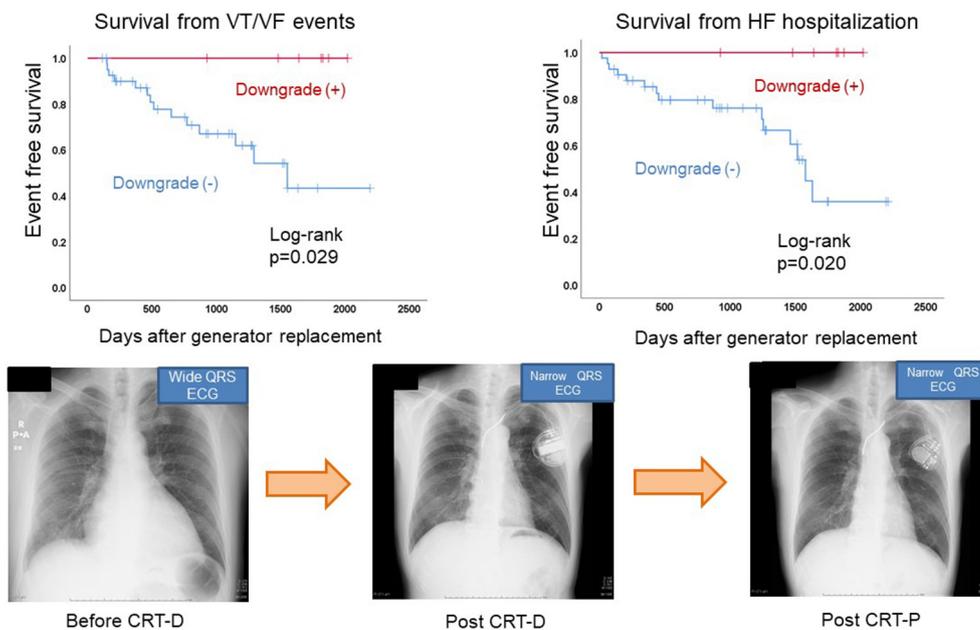


Fig. 1. Kaplan-Meier curves showing ventricular tachycardia/ventricular fibrillation events (upper left) and hospitalization for heart failure (upper right) in patients who did and did not receive a downgrade. Chest X-ray in a representative case from initial implantation of CRT-D to a downgrade to CRT-P is shown (lower figure). VT/VF = ventricular tachycardia/ventricular fibrillation, HF = heart failure, CRT-D = cardiac resynchronization therapy with defibrillator, CRT-P = cardiac resynchronization therapy with pacemaker.

that included patients in whom an ICD was implanted for both primary and secondary preventions could not demonstrate the validity of a downgrade despite marked improvement of LVEF after implantation of a CRT-D because patients with a history of VT/VF experienced recurrences post-implantation [11,12]. However, another study in which an ICD was only implanted for primary prevention recommended a downgrade in patients who showed a marked improvement in LVEF after CRT-D implantation [5].

Absence of newly developed ventricular tachyarrhythmias after initial CRT-D implantation is another important consideration with regard to a downgrade. Epicardial pacing by the LV lead has been reported to have proarrhythmic effects as a result of transmural dispersion of repolarization augmentation [13]. Emergence of new VT/VF indicates the presence of ongoing progressive underlying heart disease. An ICD is considered desirable in patients who experience new VT/VF after CRT-D implantation.

Patients who met the criteria for a downgrade experienced no ventricular arrhythmias or HF hospitalizations during the 39.7 ± 21.1 months average follow-up period. In contrast, several patients who did not meet the criteria experienced ventricular arrhythmias or HF hospitalization. There are some benefits associated with downgrade. Patients who underwent a downgrade might be satisfied with the smaller pocket size, and they have decreased likelihood of undergoing unnecessary ICD therapy. Furthermore, a downgrade reduces the health economic burden associated with HF, because a CRT-P is less costly than a CRT-D [14,15]. Although an extended follow-up period is needed, validity of the criteria for a downgrade in mid-term follow-up was confirmed in this study.

In our study, patients who met the criteria for a downgrade were more likely to have LBBB than those who did not. LBBB is known to be a strong predictor of a favorable response to CRT [16]. This study supports the use of CRT in LBBB patients. Complete resolution of LBBB-induced cardiomyopathy by CRT has recently been reported [17]. Patients who are expected to respond well to CRT might be prepared for a subsequent downgrade at the time of the initial CRT-D implantation.

Cardiac magnetic resonance imaging (MRI) has recently been reported to be a better predictor of VT/VF than LVEF [18]. However, in our study, some patients did not undergo implantation of an MRI-

conditional device. Assessment of suitability for a downgrade using MRI would be an important area of future research.

4.1. Study limitations

Our present findings are limited by our single-center study design and small study population. However, patients who undergo implantation of a CRT-D usually have severe HF and serious comorbidities [19], so can also succumb to non-cardiac conditions. Therefore, the number of patients who survive long enough to require generator replacement is small. One patient needed an IS-1 lead implant because this patient was implanted with a DF-4 ICD lead. Although we implanted the IS-1 lead without any complications, it can be difficult to implant additional leads in patients who show venous stenosis or occlusion. To undergo a smooth downgrade procedure, we hope that device manufacturers will release a suitable adaptor which can allow the DF-4 lead to connect into an IS-1 port, or a new CRT-P, in which a DF-4 ICD lead can connect to. Usage of DF-1 ICD leads instead of DF-4 leads in patients who are expected to respond well to CRT is another consideration [20].

5. Conclusions

In patients who underwent initial implantation of a CRT-D for primary prevention, in whom there was no documented VT/VF after the initial CRT-D implantation and in whom LVEF improved to $>45\%$, a downgrade from CRT-D to CRT-P at the time of generator replacement was feasible. The patients who received a downgrade did not experience ventricular arrhythmias or HF hospitalization following the downgrade at the mid-term period. Large-scale multicenter studies with longer follow-up are needed to confirm our results.

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Declaration of interest

None.

Author contributions

Michio Ogano: Contributed to conception of study, performed device implantation, collected data, analyzed all data, and wrote the first draft of the paper.

Yu-ki Iwasaki: Assisted with interpretation of data, provided critical analysis and supervised writing/composition of the manuscript, and corrected the text and figures in the paper.

Ippeï Tsuboi: Assisted with interpretation of preliminary data.

Hidekazu Kawanaka: Assisted with device implantation, followed up patients, and collected the data.

Masaharu Tajiri: Assisted with device implantation, followed up patients, and collected the data.

Jun Tanabe: Assisted with device implantation, followed up patients, and collected the data.

Hisato Takagi: Assisted with device implantation and followed up patients.

Wataru Shimizu: Supervised this study and critically reviewed the manuscript.

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