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Original Article

Current status of cardiac resynchronization therapy device optimization in Japan

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ABSTRACT

Background: Cardiac resynchronization therapy (CRT) is known to be effective for patients with heart failure. However, despite data suggesting that routine atrioventricular (AV) and interventricular (VV) delay optimization may play significant roles in CRT, there is no standard on how and when the CRT device should be optimized. The aim of this study was to characterize the current practice of CRT optimization in Japan.

Methods: A survey was conducted to collect information on the procedural aspects of AV and VV delay optimization. The key survey items concerned what method is used for optimization, when optimization is performed, and what factors limit repetitive optimization.

Results: Fifty-two physicians participated in the survey. Echocardiography was the chosen method for assessing AV and VV delays by 79.6% and 65.3% of physicians, respectively, and routine optimization was performed by 28.3%. The majority optimized the settings only once at pre-hospital discharge or on an "as-needed" basis. The factors limiting repeated optimization were the lack of available time (71.2%), qualified staff (53.8%), and reliable methods (55.8%).

Conclusions: Repetitive CRT optimization is infrequently performed in Japan. Lack of time, human resource, and reliable methods were the major factors affecting the number of routine CRT optimization.

1. Introduction

It is widely accepted that treatment with cardiac resynchronization therapy (CRT) is effective for patients with advanced heart failure, and this is supported by a series of randomized, controlled clinical trials [1–6]. The underlying mechanism of this therapy is to improve the contractile movement of the heart by adjusting the interventricular (VV) and intraventricular delays. This is done by correcting electrical and mechanical dyssynchrony through an optimally timed stimulation of the right ventricle (RV) and the left ventricle (LV). The clinical benefits conferred by CRT include improvements in the quality of life, New York Heart Association functional classification, and cardiac structure and function, as well as reduction in morbidity and mortality [1–8]. Although this therapy has been proven effective in numerous clinical trials, reports show that up to one-third of patients (the so-called nonresponders) do not receive the full clinical benefit of CRT [9,10]. The causes for this nonresponsiveness of patients are still unclear; however, inadequate patient selection, suboptimal lead position, and device programming may influence the outcome. Reports show relatively equal responder rates between a Japanese cohort [11] and patients from other countries [12]. This raised the question of how daily CRT management is being practiced in Japan.

Heart failure is a complex disease and the status of each patient is highly heterogeneous; therefore, nominal manufacturer-delivered device settings may not be optimal for all patients who receive CRT implantation. A growing body of evidence suggests hemodynamic and clinical status benefits associated with optimization of atrioventricular (AV) and VV delays [13–16]. However, alteration of the atrial and ventricular morphologies over time because of reverse remodeling may also influence these parameters, which may have been optimal at the time of implantation [17,18]. The optimization methods preferred by Japanese physicians and the duration between repeated optimizations are unknown, and there is no general consensus among physicians about the need for routine optimization. The goal of this study was to collect information on the current status of CRT device optimization in Japan.

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2. Methods

A questionnaire survey was conducted to collect information on the practice of CRT optimization of physicians who implant CRT devices in Japan. The collected data were focused on the method used to optimize AV and VV delays, the time required for the optimization, and the frequency of repetitive optimization during follow-up visits. The English translation of the questionnaire is shown in Table 1. Physicians who use device functions such as QuickOpt (St. Jude Medical, Minneapolis, MN, USA) [19], which monitor intracardiac electrograms, to optimize CRT parameters were instructed to mark "Other" and specify this on the answer sheets. The participating physicians were selected from centers that perform frequent CRT device implantations, nominally more than 10 procedures per year. Additional care was taken to minimize regional variance by selecting centers from each geographical area in Japan. Owing to the foreseen difficulty, centers in northeastern Japan were excluded because that region was severely affected by the March 11, 2011, earthquake. Descriptive statistics were performed for categorical variables. Statistical significance was not analyzed owing to the nature of this study.

3. Results

The questionnaires were retrieved from all 52 physicians from 47 centers in Japan, who were initially selected for participation between May 11 and July 25, 2011. Because the number of annual CRT implantation procedures was part of the center selection criteria, there was a trend of including centers in the metropolitan area; nevertheless, the overall distribution of the centers was well balanced throughout all geographical regions of Japan. No centers from northeastern Japan and the Shikoku Island area were enrolled for administrative reasons. As there are approximately 350 accredited CRT implanting centers in Japan, the survey covered $>10\%$ of the applicable sites. These centers implanted 910 of 2864 CRT devices in the year 2010, which accounted for 31.8% of all CRT implantations performed in the country.

3.1. Methods used to optimize AV and VV delays

The frequency distribution of the methods used to optimize AV and VV delays are shown in Fig. 1. Data from 49 (94.2%) physicians

Table 1
Survey questionnaire.

Please answer the following questions on the basis of your experiences with CRT optimization					
Questions	Answers				
Which method is being used the most to optimize A-V delay?	□Echocardiography (Please select one of the following options.) □ Iterative method □ Ritter's method □ Simplified (Meluzin) mitral inflow method □ Mitral inflow VTI □ Diastolic mitral regurgitation (Ishikawa) method □ Other (Specify:) □Invasive LV dP/dt_{max} □Impedance cardiography (ICG) □Electrocardiogram □Other (Specify:) □Do not optimize				
Which method is being used the most to optimize V-V delay?	□ Echocardiography (Please select one of the following options) □ LV dP/dt_{max} □ LV outflow tract VTI □ Tissue Doppler imaging □ Other (Specify:) □ Invasive LV dP/dt_{max} □ Other (Specify:) □ Do not optimize				
How long does it usually take you to complete optimization?	Both A-V and V-V: hour(s) and minutes A-V only: hour(s) and minutes V-V only: hour(s) and minutes				
How often do you optimize A-V and/or V-V delays after implantation?	□ Every month □ Every 2 months □ Every 3 months □ Every 6 months □ Other (Specify:)				
What percentage of your patients are optimized during each follow-up visit?	Visit	A-V and V-V	A-V only	V-V only	Not optimized
	Implantation	%	%	%	%
	Pre-hospital discharge	%	%	%	%
	3 months after implantation	%	%	%	%
	6 months after implantation	%	%	%	%
	12 months after implantation	%	%	%	%
Select the factor(s) limiting the performance of optimization, if any. (Multiple answers allowed.)	□ Time constraint □ Lack of qualified staff □ Highly reliable method not being established □ Other (Specify:)				

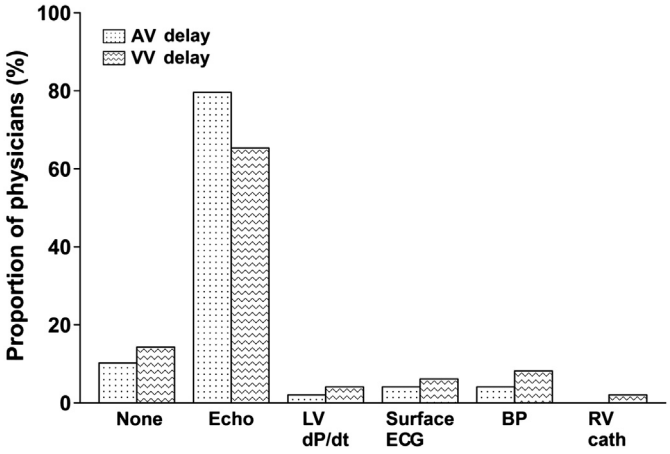

Fig. 1. Proportion of methods used to assess AV and VV delays. Echo, echocardiography; LV dP/dt_{max}, maximum rate of left ventricular pressure increase; BP, blood pressure; and RV cath, right ventricular catheterization.

Table 2
Time required for optimization.

	Optimized delays (no. of valid responses)		
	AV only ($n=30$)	VV only ($n=28$)	AV and VV ($n=39$)
Mean ± SD (min)	18 ± 9	20 ± 12	32 ± 15
Range (min)	5–40	5–60	10–60

SD, standard deviation.

were analyzed. Three survey responses were excluded because the physicians did not provide an answer or multiple selections were chosen, which was not allowed.

Most of the responding physicians (79.6%) used echocardiography as the method of choice for optimizing AV delay. The less frequently used methods were surface electrocardiogram (ECG) (4.1%), blood pressure (BP) monitoring (4.1%), and invasive LV dP/dt_{max} measurement (2.0%). The remaining 10.2% responded that they did not perform AV optimization. A similar trend was also observed for VV delay optimization, with a slightly higher variance in methods among physicians. Echocardiography was used by 65.3% of physicians, ECG by 6.1%, BP by 8.2%, LV dP/dt_{max} by 4.1%, and RV catheterization by 2.0%. The VV delay was not optimized by 14.3% of physicians, which was a slightly higher portion compared with the AV delay.

Thirty-five of 39 (89.7%) physicians who used echocardiography to optimize AV delay employed pulsed Doppler of LV diastolic filling to determine the optimal device parameters. Measurement of the LV outflow tract velocity–time integral (VTI) was the preferred method for selecting the optimal VV parameters by 24 of 32 (75.0%) physicians who used echocardiography for VV optimization.

None of the physicians chose device-monitored intracardiac electrograms, such as QuickOpt, as their most frequently used method for CRT optimization.

3.2. Time required for optimization

The time necessary to optimize AV and/or VV delays is shown in Table 2. To optimize either the AV or the VV delay, the responding physicians spent an average of 20 min, whereas more than 30 min was required to optimize both delays. If the data were limited to echocardiographic evaluation only, the time necessary to optimize AV, VV, and AV and VV delays were 17 ± 9, 17 ± 9, and 29 ± 14 min, respectively.

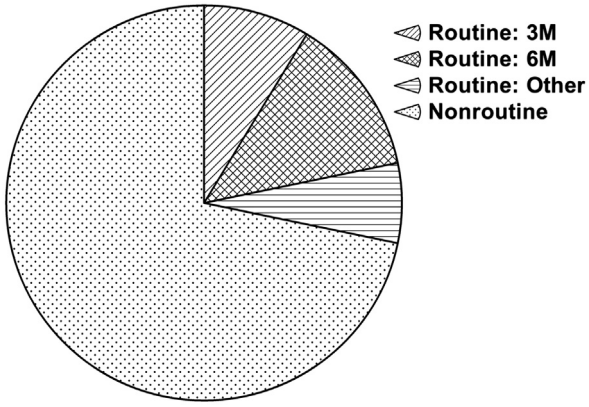

Fig. 2. Proportion of physicians who perform routine device optimization.

3.3. Frequency of optimization after implantation

The proportion of physicians who perform optimization regularly is shown in Fig. 2. Most of them (71.7%) optimized the device settings only once at pre-hospital discharge or on an "as-needed" basis, such as when symptoms worsened and/or when patients did not respond to CRT therapy. These cases are referred to as "nonroutine" optimization in the figure. Only a few of the physicians performed optimization at regularly scheduled intervals. The percentage of physicians who optimized the devices every 3 and 6 months was 8.7% and 13.0%, respectively, and 6.5% specified other time intervals.

The proportion of patients who undergo device optimization at each follow-up visit is shown in Fig. 3. More than half of the physicians optimized the device in all (100%) of their patients at pre-hospital discharge. In contrast, most of the physicians did not perform optimization in any of their patients during implantation and at the follow-up visits.

3.4. Obstacles to device optimization

The physicians were questioned about what may be limiting them from performing CRT optimization. They were allowed to report multiple reasons, and the most commonly reported factor was time constraint (71.2%). The other major factors were the lack of qualified staff (53.8%) and unreliable optimization methods (55.8%).

4. Discussion

This report describes the daily practices with regard to AV and VV delay optimization by physicians managing CRT patients in Japan. Most of the physicians responded that they only optimize AV and VV delays once at pre-hospital discharge and very few physicians regularly optimized AV and/or VV delay settings thereafter. A low rate of routine CRT device optimization has also been reported in physician surveys obtained from other countries [20]. The effectiveness of repetitive optimization is currently unclear, and it is presently unknown whether the device parameters optimized at pre-hospital discharge would remain optimal in the long term. The lack of time and human resources were the major obstacles preventing frequent optimization. The fact that there have been no established, reliable standardized methods for optimizing CRT may be another factor influencing the frequency of optimization. The physicians' perception toward optimization with unreliable methods may reflect upon their

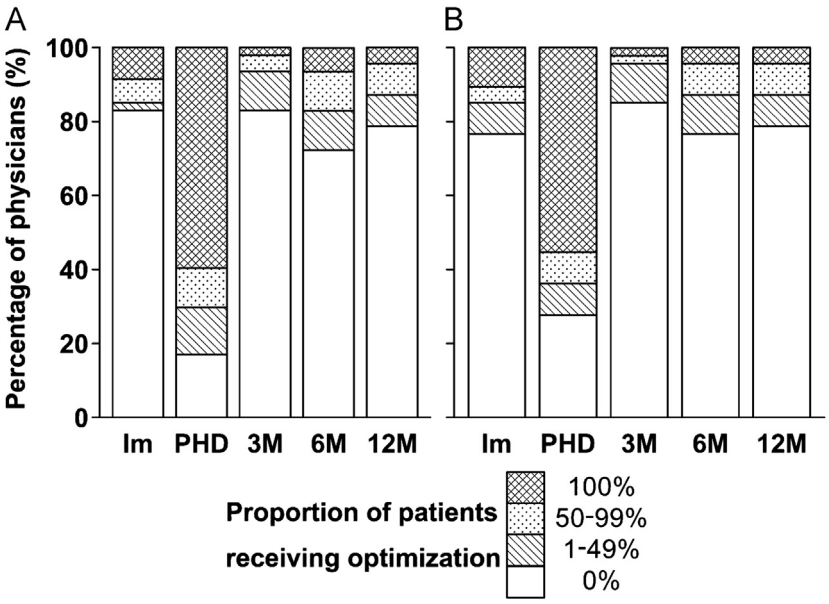

Fig. 3. Percentage of physicians optimizing certain proportion of patients for (A) AV and (B) VV delays at implantation (Im); pre-hospital discharge (PHD); and 3, 6, and 12 months.

judgment about the necessity of optimizing CRT devices, thus further reducing the rate of repetitive optimization. The correlation between a standardized optimization method and CRT responsiveness is yet to be elucidated.

Although echocardiographic evaluation can be time consuming and costly, this method is being used most frequently by Japanese physicians when performing device optimization, similar to previous reports from other countries [20]. To reduce the increasing burden of CRT device follow-up and to allow timely optimization of these devices, optimization algorithms such as QuickOpt [19] and SmartDelay (Boston Scientific, Natick, MA, USA) [21,22] have been developed. These features monitor the heart conditions of patients to calculate the most optimal AV and/or VV delays and assist the physicians in reprogramming the devices during follow-ups. Although none of the physicians chose either of those device algorithms as their most frequently used method for optimizing AV and/or VV delays, 2 of them stated that they do incorporate device-suggested values as a reference. One limitation of these algorithms is that they are not automated and still require compliance with routine in-office reprogramming. Another newly developed algorithm, SonR (Sorin CRM SAS, Clamart, France) [23–25], performs weekly automated optimization of the AV delay, but the patients need to visit the clinic in order to have the VV delay optimized. The requirement for multiple clinic visits and for the manual optimization of the CRT configuration by methods such as echocardiography and device functionalities may be burdensome to both patients and physicians. A fully automated and self-reprogramming CRT optimization algorithm may reduce the burden of optimization by minimizing the need for routine office visits and may prove beneficial by allowing continuous adjustment of device settings according to the most recent clinical status of the patient. The efficacy of repetitive CRT optimization is yet to be elucidated, as intermittent reprogramming of the device during each follow-up visit may not reflect the continuous change of biological status in patients. However, landmark trials such as MIRACLE [2], COMPANION [5], and CARE-HF [6] required the AV and VV delays to be optimized at pre-hospital discharge and during each follow-up visits. A new algorithm that continuously monitors cardiac conduction and automatically reprograms AV and VV delays is being evaluated [26]. With this new technology, it may be possible to constantly update the CRT parameters to reflect the most recent cardiac condition. As the effectiveness of AV and VV delay optimization is still under discussion, the next goal would be to clarify the correlation between the patient outcome and the optimal CRT in the long term.

4.1. Limitations

Owing to the design of this surveillance study, the information collected from each physician is subjective in nature, and the number of physicians who participated in the survey was relatively small. On planning this study, special care was taken to broadly collect data, including most geographical areas of Japan, in order to obtain generalized results. As it is difficult to standardize the definition of “responders” between centers, it is beyond the scope of this study to correlate AV and VV delay optimization with patient responsiveness to CRT therapy. This study was designed to elucidate the trend for the overall use of certain methods for CRT optimization. It is noteworthy that the method used during pre-hospital discharge may differ from that used at each follow-up. To further clarify the use of each method in correlation with patient outcomes, a study with a much larger cohort is needed.

5. Conclusions

A considerable proportion of Japanese physicians managing CRT device recipients do not routinely optimize AV and/or VV delay settings primarily owing to a lack of time and qualified staff. Although echocardiography is commonly employed to optimize AV and VV delays, the time and clinical resource burden associated with this technique may prevent its routine use during CRT device follow-ups.

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Conflict of interest

KD is an employee of Medtronic Japan Co., Ltd. TN and YS received speaking fees; HY received honoraria and speaking fees;

and KA received research grants, honoraria, and speaking fees from Medtronic Japan Co., Ltd.

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