Potential efficacy of multipoint pacing in the reduction of mitral regurgitation volume: a case report

Masato Wada¹, Hidekazu Kondo^{1*} ^(D), Tomoko Fukuda¹, Hiroki Sato², Hirochika Yamasaki¹, Keisuke Yonezu¹, Tetsuya Uemura¹, Naoko Ogawa¹, Shotaro Saito¹, Takashi Shuto³, Tomoyuki Wada³, Kunio Yufu¹, Seiki Nobe², Shinji Miyamoto³ and Naohiko Takahashi¹

¹Department of Cardiology and Clinical Examination, Faculty of Medicine, Oita University, Yufu, Japan; ²Department of Internal Medicine, Kunisaki City Hospital, Kunisaki, Japan; and ³Department of Cardiovascular Surgery, Faculty of Medicine, Oita University, Yufu, Japan

Abstract

A 70-year-old woman who had cardiac sarcoidosis and severe tethering mitral regurgitation (MR) and had been implanted with a biventricular pacemaker experienced recurrent hospitalisation due to decompensated heart failure (HF). Application of MultiPoint[™] pacing reduced the MR volume and maintained the symptoms under control; however, the predicted longevity of the device significantly decreased because of the very high threshold of the added pacing site. Transcatheter mitral valve repair (TMVR) using MitraClip[®] was performed to further diminish the severe MR, thereby enabling the switch from highly consumptive multipoint pacing (MPP) to energy-saving single-point pacing. MPP could further reduce MR compared to the conventional single-point pacing, and this could be a bridging therapy to TMVR in some patients implanted with a biventricular pacemaker. This is the first case to report that switching from conventional single-point pacing to MPP decreased the MR, to some extent, resulting in the improvement of HF symptoms.

Keywords Multipoint pacing; Transcatheter mitral valve repair; Mitral regurgitation; Heart failure

Received: 13 January 2022; Revised: 25 February 2022; Accepted: 4 April 2022

*Correspondence to: Hidekazu Kondo, Department of Cardiology and Clinical Examination, Faculty of Medicine, Oita University, 1-1 Idaigaoka, Hasama, Yufu, Oita 879-5593, Japan. Email: hkondo@oita-u.ac.jp

Introduction

Functional mitral regurgitation (FMR) is often observed in patients with heart failure (HF) together with reduced left ventricular ejection fraction (HFrEF). FMR is massively related to unfavourable outcomes, and the degree of FMR is associated with morbidity and mortality in patients with HFrEF.¹ The management of patients with HFrEF and FMR by surgical mitral valve repair is difficult to try, because it lacks satisfactory evidence.² Cardiac resynchronisation therapy (CRT) could be a promising option for FMR and HF.^{3,4} However, the treatment efficacy of conventional CRT for FMR may also be limited because of the inadequate rate of responders. Transcatheter mitral valve repair (TMVR) using MitraClip® is now widely accepted as a procedural alternative to surgical mitral valve repair in patients with severe FMR and high operative risk.⁵ Recently, several studies have demonstrated that multipoint left ventricular (LV) pacing from a quadripolar LV lead [MultiPoint[™] Pacing (MPP), Abbott, Sylmar, CA, USA]

further improves LV dyssynchrony^{6,7} and enhances mid-term and long-term LV reverse remodelling compared with single-point pacing.^{8–10} However, the additional potential value of MPP compared with that of single-point pacing in reducing FMR remains unclear. We present a case wherein the switch from single-point pacing to MPP succeeded in reducing FMR and improving the symptoms to some extent. TMVR was finally required to diminish the residual moderate-to-severe mitral regurgitation (MR) and enabled a change from the MPP with a high threshold of an additional pacing site to conventional single-point pacing.

Case report

A 70-year-old woman with cardiac sarcoidosis (Sarcoidosis Diagnostic Score with biopsy; 6) had recurrent hospitalisations (four times within a 3-month period) due to decompensated

© 2022 The Authors. ESC Heart Failure published by John Wiley & Sons Ltd on behalf of European Society of Cardiology.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes. HF at a previous hospital. She had been diagnosed with cardiac sarcoidosis 2 years previously and was treated with implantation of a defibrillator in addition to CRT (CRT-D) and oral steroid therapy (prednisolone; 10 mg/day). She had progressive dysphoea on exertion [New York Heart Association (NYHA) class III–IV] despite receiving optimal medical therapy (beta-blocker, sodium glucose co-transporter 2 inhibitor, angiotensin receptor-neprilysin inhibitor, and aldosterone antagonist at maximally tolerated doses) for HF. A transthoracic echocardiogram showed severe LV systolic dysfunction with a reduced ejection fraction (EF) of 28% (Figure 1A) and severe MR (Figure 1B) under conventional single-point pacing (effective regurgitant orifice area; 0.37 cm², regurgitation volume; 53 mL, regurgitation rate; 60%). Chest radiography showed severe cardiomegaly and pulmonary congestion (pacing site; LV2, Figure 1C). Every time she was admitted for congestive HF, treatment with intravenous diuretics was administered to compensate her condition for a few days. Because low output syndrome was concomitant with her pathological condition, her blood pressure was too low to administer oral diuretics (70-80/40-50 mmHg) or other medications, and her renal function gradually deteriorated. Her B-type natriuretic peptide (BNP) levels had elevated to 1712 pg/mL. Because TMVR using MitraClip® had been just started in our hospital, her transfer to our hospital was scheduled. Before she was transferred to our hospital to consider the indication for TMVR, MPP (Figure 2A) was delivered in a palliative manner to avoid continuous catecholamine infusion. Despite the QRS narrowing being marginal (Figure 2B), echocardiographic evaluation showed reduction in MR volume (*Figure 3A*), effective regurgitant orifice area; 0.18 cm², regurgitation volume; 27 mL, regurgitation rate; 39%, without any increase in EF and decrease in left ventricular end diastolic volume, leading to remarkable improvement in her symptoms (NYHA class II) in a few days. HF was compensated (pacing site; LV2 and LV4, *Figure 3B*), and her BNP level declined to 496 pg/mL. However, estimated battery longevity had shortened from 5.3 to 2.6 years due to high pacing threshold (5.0 V/0.4 ms) of the additional pacing site (LV4) in LV lead; therefore, we offered her the option of TMVR to reduce residual MR so that we could revert it to single-point pacing in the near future.

Five weeks after MPP delivery, TMVR was successfully performed using MitraClip[®]. Residual moderate MR diminished to a trivial level, and her ability to exercise further improved. Two weeks after TMVR, the switch from MPP to single-point pacing was performed to save the CRT-D battery because we believed that single-point pacing is sufficient to regulate MR at this time. As expected, the MR was not exacerbated after the configuration change, and the patient did not have any recurrent hospitalisation for HF during the 6-month follow-up.

Discussion

To the best of our knowledge, this is the first report to clearly demonstrate that switching from conventional single-point pacing to MPP decreased the MR to some extent, resulting

Figure 1 (A) Severe left ventricular systolic dysfunction (echocardiographic long-axis views at diastole and systole). (B) Severe mitral regurgitation on the four-chamber and long-axis views. (C) Chest radiography taken on admission (red arrow indicates the pacing site; LV2).

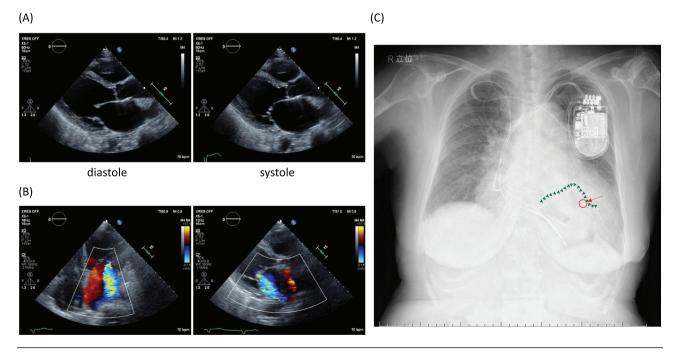


Figure 2 (A) Pacing configuration of cardiac resynchronisation therapy before and after the delivery of multipoint pacing. (B) Findings of 12-lead electrocardiograms (ECG) taken before and after the delivery of multipoint pacing.

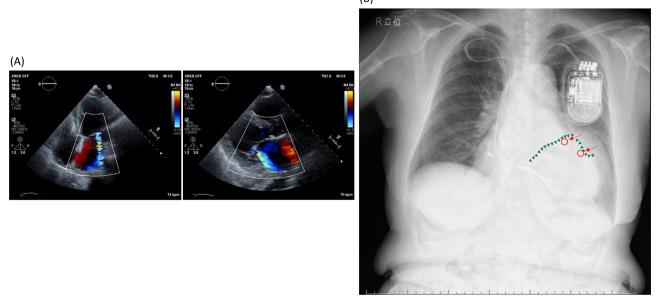
(A)

[CRT (MPP-off)] DDDR70-130, Sensed AV delay; 100 msec, Paced AV delay; 150msec, pacing site LV2, RV-LV2 delay: 0msec

[CRT (MPP-on)]

DDDR70-130, Sensed AV delay; 100 msec, Paced AV delay; 150msec, pacing site LV2 and LV4, LV2-LV4-RV delay: 5msec-5msec

Figure 3 (A) Reduction of mitral regurgitation volume observed on the four-chamber and long-axis views. (B) Chest radiography taken 5 days after the delivery of multipoint pacing (red arrows indicate the pacing site; LV2 and LV4).



in the improvement of HF symptoms. MPP was speculated to capture a larger LV myocardial mass, resulting in a quicker wavefront propagation throughout the ventricles, compared with the situation in conventional single-point pacing.¹¹ Considering this speculation, MPP could capture the papillary

muscle quicker than conventional biventricular pacing, which improved mitral valve closure and reduced the MR.

There are two major problems when MPP is applied to patients implanted with CRT: high pacing threshold and phrenic nerve stimulation of the second pacing site. In the present



case, wherein the patient was treated with steroids, the high pacing threshold of the second pacing site in the LV lead guided us to perform additional TMVR because future frequent replacement of the CRT-D generator may cause device-related infection. However, if patients do not have the aforementioned problems, then TMVR is not necessary. MPP could be useful in patients implanted with CRT devices and experiencing severe MR.

Multipoint pacing programmed with a wide LV electrode anatomical separation (\geq 30 mm) and shortest LV-LV and LV-right ventricle timing delays would be recommended to increase the response rate in two clinical trials.^{12,13} In the present case, the distance between LV2 and LV4 was 25 mm (LV1 could not be used because of capture loss), which is shorter than the recommended distance. However, cardiac size is dependent on body size. The fact that she

weighed 37 kg and her body mass index was 18.1 kg/m² might indicate that 25 mm was distant enough to perform effective MPP. Whether MPP is applied from the beginning of CRT implantation or to convert non-responders into responders remains controversial. This treatment option could be a bridging therapy to TMVR in some patients implanted with a biventricular pacemaker. Further studies are required to identify patients who can benefit greatly from CRT-MPP therapy.

Conflict of interest

None declared.

References

- Rossi A, Dini FL, Faggiano P, Agricola E, Cicoira M, Frattini S, Simioniuc A, Gullace M, Ghio S, Enriquez-Sarano M, Temporelli PL. Independent prognostic value of functional mitral regurgitation in patients with heart failure. A quantitative analysis of 1256 patients with ischaemic and non-ischaemic dilated cardiomyopathy. *Heart.* 2011; 97: 1675–1680.
- 2. Coats AJS, Anker SD, Baumbach A, Alfieri O, von Bardeleben RS, Bauersachs J, Bax JJ, Boveda S, Čelutkiene J, Cleland JG, Dagres N, Deneke T, Farmakis D, Filippatos G, Hausleiter J, Hindricks G, Jankowska EA, Lainscak M, Leclercq C, Lund LH, McDonagh T, Mehra MR, Metra M, Mewton N, Mueller C, Mullens W, Muneretto C, Obadia JF, Ponikowski P, Praz F, Rudolph V, Ruschitzka F, Vahanian A, Windecker S, Zamorano JL, Edvardsen T, Heidbuchel H, Seferovic PM, Prendergast B. The management of secondary mitral regurgitation in patients with heart failure: a joint position statement from the heart failure association (HFA), European Association of Cardiovascular Imaging (EACVI), European heart rhythm association (EHRA), and European Association of Percutaneous Cardiovascular Interventions (EAPCI) of the ESC. Eur Heart J. 2021: 42: 1254-1269.
- van Bommel RJ, Marsan NA, Delgado V, Borleffs CJ, van Rijnsoever EP, Schalij MJ, Bax JJ. Cardiac resynchronization therapy as a therapeutic option in patients with moderate-severe functional mitral regurgitation and high operative risk. *Circulation*. 2011; 124: 912–919.

- Akamine K, Kondo H, Yonezu K, Hirota K, Tawara K, Kodama N, Abe I, Fukuda T, Yufu K, Takahashi N. Suppression of acute heart failure rehospitalization by biventricular pacing in wide QRS and mid-range ejection fraction. *ESC Heart Fail.* 2021; 8: 4705–4709.
- Testa L, Popolo Rubbio A, Casenghi M, Pero G, Latib A, Bedogni F. Transcatheter mitral valve replacement in the transcatheter aortic valve replacement era. J Am Heart Assoc. 2019; 8: e013352.
- Rinaldi CA, Leclercq C, Kranig W, Kacet S, Betts T, Bordachar P, Gutleben KJ, Shetty A, Donal E, Keel A, Ryu K, Farazi TG, Simon M, Naqvi TZ. Improvement in acute contractility and hemodynamics with multipoint pacing via a left ventricular quadripolar pacing lead. J Interv Card Electrophysiol. 2014; 40: 75–80.
- Osca J, Alonso P, Cano O, Andrés A, Miro V, Tello MJ, Olagüe J, Martínez L, Salvador A. The use of multisite left ventricular pacing via quadripolar lead improves acute haemodynamics and mechanical dyssynchrony assessed by radial strain speckle tracking: Initial results. *Europace*. 2016; 18: 560–567.
- Pappone C, Ćalović Ž, Vicedomini G, Cuko A, McSpadden LC, Ryu K, Jordan CD, Romano E, Baldi M, Saviano M, Pappone A, Vitale R, Catalano C, Ciaccio C, Giannelli L, Ionescu B, Petretta A, Fragakis N, Fundaliotis A, Tavazzi L, Santinelli V. Improving cardiac resynchronization therapy response with multipoint left ventricular pacing: twelve-month follow-up study. *Heart Rhythm.* 2015; **12**: 1250–1258.
- 9. Forleo GB, Santini L, Giammaria M, Potenza D, Curnis A, Calabrese V,

Ricciardi D, D'agostino C, Notarstefano P, Ribatti V, Morani G, Mantica M, Di Biase L, Bertaglia E, Calò L, Zanon F. Multipoint pacing via a quadripolar left-ventricular lead: preliminary results from the Italian registry on multipoint left-ventricular pacing in cardiac resynchronization therapy (IRON-MPP). *Europace*. 2017; **19**: 1170–1177.

- Varma N, Baker J 2nd, Tomassoni G, Love CJ, Martin D, Sheppard R, Niazi I, Cranke G, Lee K, Corbisiero R. Left ventricular enlargement, cardiac resynchronization therapy efficacy, and impact of multipoint pacing. *Circ Arrhythm Electrophysiol.* 2020; 13: e008680.
- Menardi E, Ballari GP, Goletto C, Rossetti G, Vado A. Characterization of ventricular activation pattern and acute hemodynamics during multipoint left ventricular pacing. *Heart Rhythm*. 2015; **12**: 1762–1769.
- Niazi I, Baker J 2nd, Corbisiero R, Love C, Martin D, Sheppard R, Worley SJ, Varma N, Lee K, Tomassoni G, MPP Investigators. Safety and efficacy of multipoint pacing in cardiac resynchronization therapy: the multipoint pacing trial. JACC Clin Electrophysiol. 2017; 3: 1510–1518.
- Leclercq C, Burri H, Curnis A, Delnoy PP, Rinaldi CA, Sperzel J, Lee K, Calò L, Vicentini A, Concha JF, Thibault B. Cardiac resynchronization therapy non-responder to responder conversion rate in the more response to cardiac resynchronization therapy with multipoint pacing (MORE-CRT MPP) study: results from phase I. Eur Heart J. 2019; 40: 2979–2987.