


Suppression of acute heart failure rehospitalization by biventricular pacing in wide QRS and mid-range ejection fraction

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Abstract

We present a 66-year-old male patient with heart failure, mid-range ejection fraction and QRS widening suffering from recurrent hospitalization due to acute heart failure. We measured intra-cardiac pressure by cardiac catheterization to clearly demonstrate the augmentation of afterload by a vasoconstricting drug induced increase of left ventricular end-diastolic blood pressure and pulmonary capillary wedge pressure with pulmonary arterial V-wave augmentation (indicator of worsening of mitral regurgitation). Because the patient was considered as refractory to optimal medication, cardiac resynchronization therapy (CRT) was performed. After CRT implantation, these factors were improved, and the patient has not experienced recurrent hospitalization for >2 years.

Keywords Cardiac resynchronization therapy; HFmrEF; Acute heart failure; Mitral regurgitation; Dyssynchrony

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Introduction

Current guidelines offer clear boundaries for cardiac resynchronization therapy (CRT).¹ However, because of the lack of evidence on this topic, CRT is still not an indication for the treatment of patients with heart failure (HF) and mid-range ejection fraction (HFmrEF, EF: 40–49%) and QRS widening (>150 ms). In this population, exercise or emotional stress can frequently induce increased afterload and subsequently exacerbate EF and mitral regurgitation (MR), resulting in acute HF. A reduction in afterload induced by angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers, and sympathetic nerve suppression by beta-blockers are recommended for prevention. For patients with recurrent hospitalization despite the exhaustive titration of these drugs, CRT may be the appropriate therapy.

Case Report

A 66-year-old man with complete left bundle branch block and mid-range left ventricular EF at rest had he had recurrent hospitalization (three times within a 6 month period) due to clinical scenario 1 acute HF. Treatment with a nitrovasodilator immediately compensated his HF. He had been diagnosed with symptomatic sick sinus syndrome 2 years prior and was treated with the implantation of a dual-chamber pacemaker. After a thorough review of the examination results, he was diagnosed with dilated cardiomyopathy. The right ventricular pacing burden was marginal (<0.1%) owing to his normal atrioventricular conduction and the use of an algorithm of Intrinsic rhythm support (IRSplus) and Ventricular pacing suppression (VpS) of Biotronik pacemaker. The patient had progressive dyspnoea on exertion [New York Heart Association (NYHA) Class III]

even though he had received an implant of a rate-responsive pacemaker and optimal medical therapy (beta-blocker with a vasodilator activity, angiotensin receptor blocker and aldosterone antagonist at maximally tolerated doses) for the treatment of hypertension and heart failure. His home blood pressure at rest was 110/70 mmHg on average. Electrocardiogram showed an atrial pacing rhythm (60 ppm) with a complete left bundle branch block (QRS duration: 185 ms; *Figure 1A*). A transthoracic echocardiogram showed moderate left ventricular systolic dysfunction with a mid-range EF of 42%, trivial to mild MR, with a structurally normal valve at rest. Remarkable left ventricular (LV) dyssynchrony was observed between the septal and postero-lateral walls on speckle-tracking echocardiography (*Figure 1B*). However, the exercise stress echocardiogram demonstrated a decrease in LVEF with exercise to 33%, with an increase in systolic blood pressure (from 110 to 190 mmHg) and MR from mild to severe as the QRS width slightly increased (from 185 ms to 195 ms; *Figure 1C*). In addition, LV dyssynchrony was further worsened (*Figure 1D*) compared with the findings of resting echocardiography (*Figure 1B*). Interestingly, a phenylephrine-induced increase of afterload enhanced the elevation of left ventricular end-diastolic pressure (LVEDP), pulmonary capillary wedge pressure (PCWP), pulmonary arterial V-wave augmentation and MR, which was confirmed via intra-cardiac pressure measurement and echocardiography (*Figure 2A,B*) and QRS widening appeared.

Taking into consideration the patient's debilitating symptoms, we offered him the option of a biventricular pacemaker. His paced electrocardiogram is demonstrated in *Figure 3A* (QRS duration: 155 ms). A follow-up evaluation using the same methods as used previously demonstrated that LV dyssynchrony at rest was attenuated by biventricular pacing (*Figure 3B*) and stress echocardiography did not show exacerbation of dyssynchrony (*Figure 3C*); further, biventricular pacing reduced phenylephrine-induced MR and elevation of LVEDP, PCWP and pulmonary arterial V-wave augmentation (*Figure 4A,B*).

During the 2 year follow-up period, the patient reported a dramatic improvement in his exercise capacity, with NYHA Class I symptoms. We also noted an improvement in resting EF to 55%. The patient has not had any recurrent hospitalization due to HF.

Discussion

The latest findings suggest that patients with HFmrEF appear to benefit from therapies that have been demonstrated to improve outcomes in patients with HF with reduced EF (HFrEF). However, it remains unclear whether patients with HFmrEF represent a transitional phenotype between HFrEF and HF with preserved EF or a distinct pathophysiological

Figure 1 (A) 12-lead electrocardiogram (ECG) before cardiac resynchronization therapy (CRT). (B) Radial (2-D) strain with speckle-tracking echocardiography in the short-axis view at the papillary muscle. The colour coding of the strain curves refers to the respective left ventricular segments. (C) Exercise stress-induced QRS widening and (D) exacerbation of LV dyssynchrony during stress echocardiography.

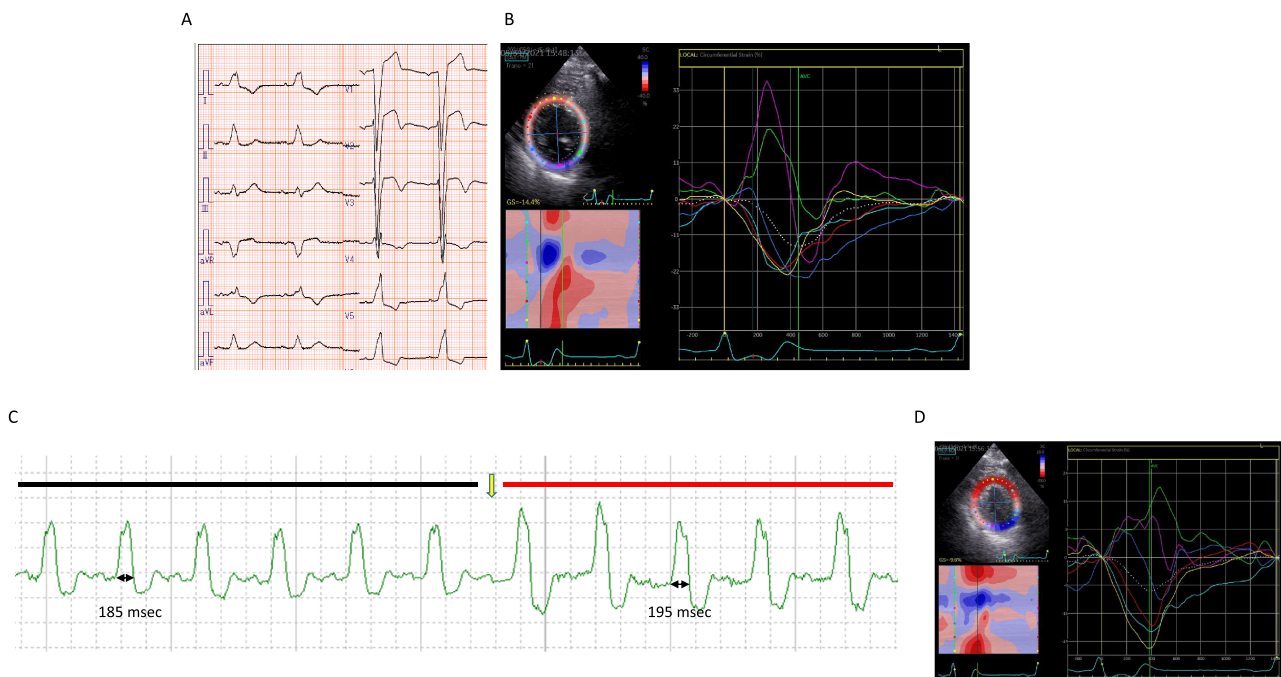


Figure 2 Waveform recording of the intra-left ventricular pressure and the pulmonary capillary wedge pressure (PCWP) and simultaneous echocardiography before CRT implantation. (A) PCWP, left ventricular end-diastolic pressure (LVEDP) and pulmonary arterial V-wave augmentation were massively augmented by phenylephrine infusion. (B) Trivial mitral regurgitation (MR) progressed to severe MR with phenylephrine infusion.

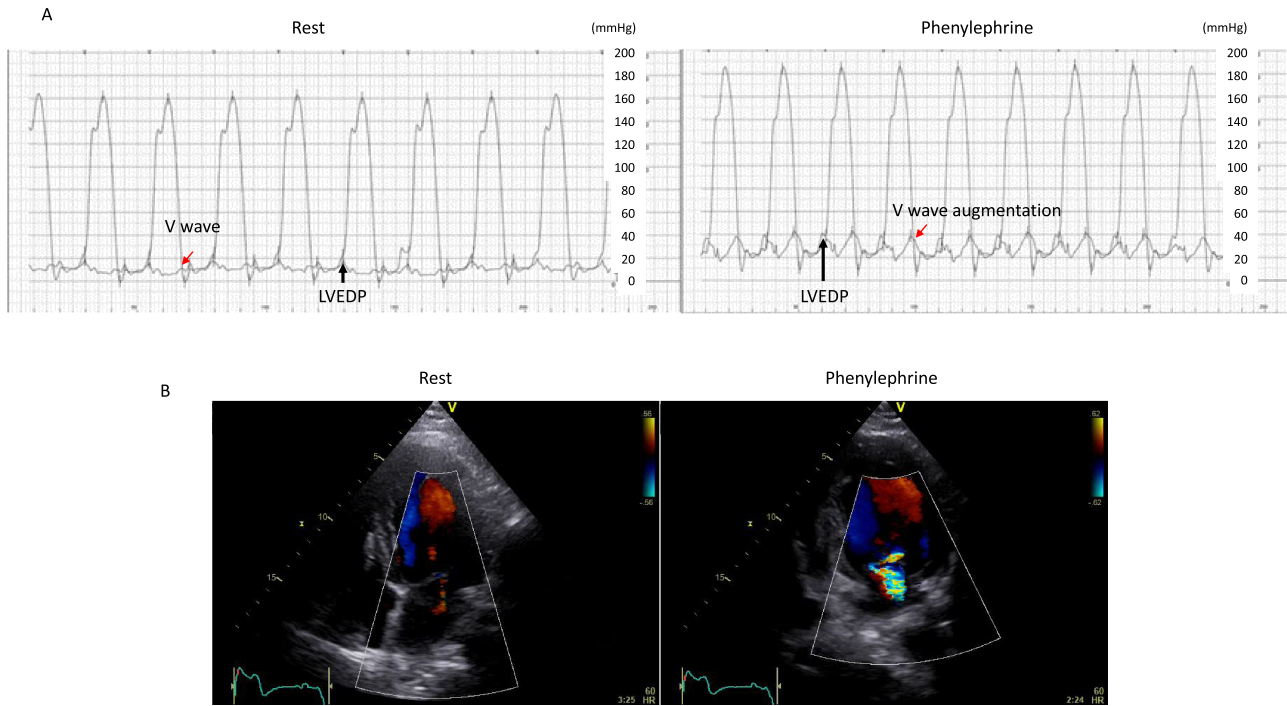
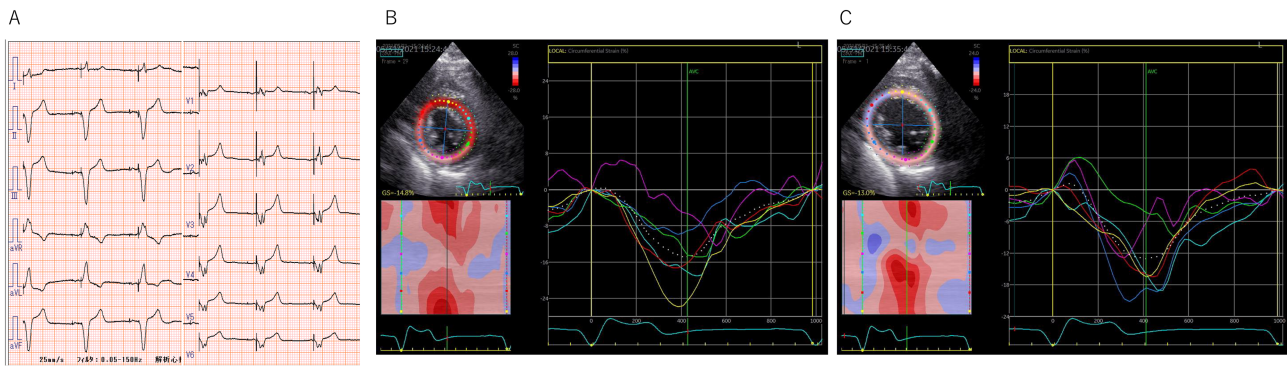


Figure 3 (A) 12-lead ECG before cardiac resynchronization therapy (CRT). (B) Attenuation of dyssynchrony with CRT, and (C) no remarkable worsening of dyssynchrony during stress echocardiography in radial (2-D) strain on speckle-tracking echocardiography.

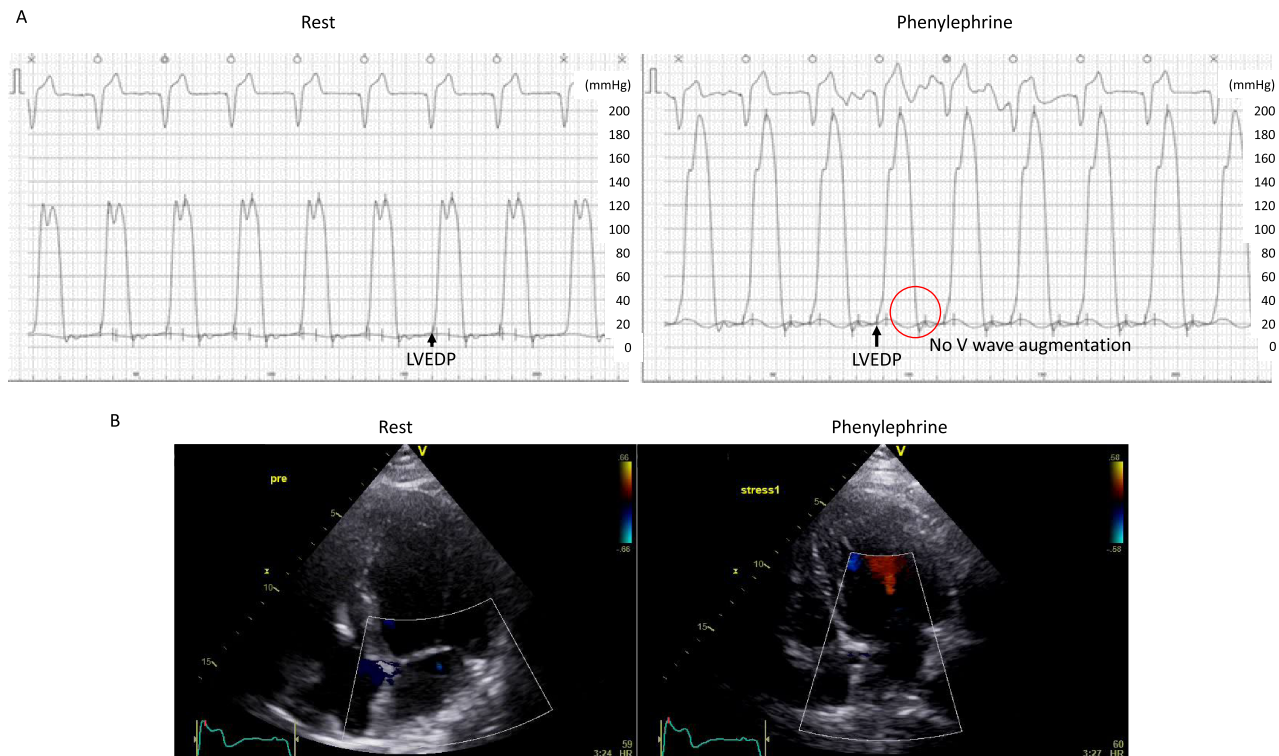


entity.² The implant of a CRT device in a patient with HFmrEF and wide QRS (>150 ms) signifies an off-guideline use of this therapy. However, none of the guidelines from major societies clearly state whether EF should be evaluated only at rest. We should consider that mild to moderate exercise in daily life could worsen LV dyssynchrony and systolic function in a specific population. In our patient, the official implantation guideline (2018 Japanese Circulation Society/Japanese Heart Rhythm Society Guideline on Non-Pharmacotherapy of

Cardiac Arrhythmias) criteria were met if we used exercise stress echocardiography (EF: 33%, QRS duration: 195 ms) instead of resting echocardiography.

To our knowledge, this is the first case report to clearly demonstrate that afterload augmentation-induced exacerbation of cardiac dyssynchrony elevates the LVEDP, PCWP, and pulmonary arterial V-wave augmentation by using intra-cardiac pressure measurement via cardiac catheterization. We also confirmed the effects of CRT on these factors

Figure 4 Waveform recording of the intra-left ventricular pressure and the PCWP and simultaneous echocardiography after CRT implantation. (A) Phenylephrine-induced augmentation of PCWP, LVEDP and pulmonary arterial V-wave were obviously attenuated. (B) MR worsening was not observed even after infusion of phenylephrine.



using the same method. In this case, the patient displayed NYHA Class III symptoms, which improved considerably after CRT implantation.

Findings from a previous study showed that patients with HFmrEF and a wide QRS duration benefited from CRT.³ Although this study did not include the assessment of EF with exercise, given the findings in our case, it would be important for future studies on CRT in patients with HFmrEF to evaluate EF with exercise to determine whether this is a consistent outcome. The MR that occurred with stress echocardiography was likely functional because of the dilation of the mitral annulus and left ventricular cavity resulting from afterload

augmentation-induced exacerbation of dyssynchrony. Although CRT cannot prevent stress-induced vasoconstriction, it can reduce MR by improving dyssynchrony.⁴

To clarify and identify patients with drug-refractory HFmrEF and wide QRS interval who can benefit from CRT therapy, further studies are required.

Conflict of interest

None declared.

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