Can we correct dyssynchrony by pacing the right side? The case for right ventricular–synchronized cardiac resynchronization therapy

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Introduction

In heart failure (HF) with reduced ejection fraction associated with left bundle branch block (LBBB) the benefits of cardiac resynchronization therapy (CRT) with coronary sinus lead and optimized device settings are universally recognized.[1] His bundle pacing and left bundle branch pacing are emerging alternatives when left ventricular (LV) placement in a coronary vein fails.[2,3] Although there is some evidence showing electromechanical delay reduction by CRT in patients with right bundle branch block (RBBB) associated with incomplete left fascicular delays (left anterior hemiblock or left posterior hemiblock) and QRS > 150 ms, the efficacy of CRT in patients with RBBB alone needs to be further elucidated, especially in the setting of conduction system pacing (CSP).[4]

Case report

A 63-year-old man (weight 105 kg, height 187 cm, and body surface area 2.34 m^2) was admitted to the emergency room for progressive dyspnea at minimal effort and lower limb edema over the past few months. A diagnosis of congestive HF was made, chest radiography showing lung congestion and C/T = 0.6; brain natriuretic peptide was 1054 pg/dL. An electrocardiogram (ECG) showed sinus rhythm, complete RBBB, QRS duration = 160 ms. Transthoracic echocardiography revealed severe biventricular dilation and systolic dysfunction, with LV ejection fraction (LVEF) of 28% and moderate-to-severe functional mitral valve regurgitation. LV end-systolic volume was 143 mL. Right ventricular (RV) fractional area change was 32%, tricuspid annulus plane systolic excursion was 1.5 cm, and RV S′ wave at tissue doppler imaging was 10 cm/s. HF medical therapy was started, and coronary angiography showed no signs of atherosclerotic coronary artery disease. Cardiac magnetic resonance imaging was also performed, consistent with a diagnosis of dilated cardiomyopathy without scarred LV segments.

Up-titration of medical therapy was achieved in the following 3 months, without any improvement in exercise tolerance, the patient remaining in NYHA class III. Echocardiography was repeated at 6 months, showing persistent severe biventricular dysfunction (Figure 1A and 1B, Supplemental Figure 1). The patient was then considered eligible for CRT.

KEY TEACHING POINTS

- In heart failure with reduced ejection fraction patients with wide QRS and complete isolated right bundle branch block (RBBB) stimulating the left ventricle (LV) by a coronary vein is not advisable owing to the absence of intraventricular LV conduction delay amenable to correction.
- Conduction system pacing has the premises to achieve resynchronization by correcting both atrioventricular and interventricular conduction delay.
- In RBBB patients who have preserved atrioventricular conduction, resynchronization therapy enabled by septal stimulation with fusion with the intrinsic conduction to the LV is a feasible alternative when conduction system pacing fails to correct the RBBB or causes too much energy drain.
- Aside from our single patient experience, randomized controlled studies in RBBB patients are warranted to prove that correction of ventricular activation can enable reverse cardiac remodeling.

KEYWORDS Heart failure; RBBB; CRT; Conduction system pacing; Pacing with fusion
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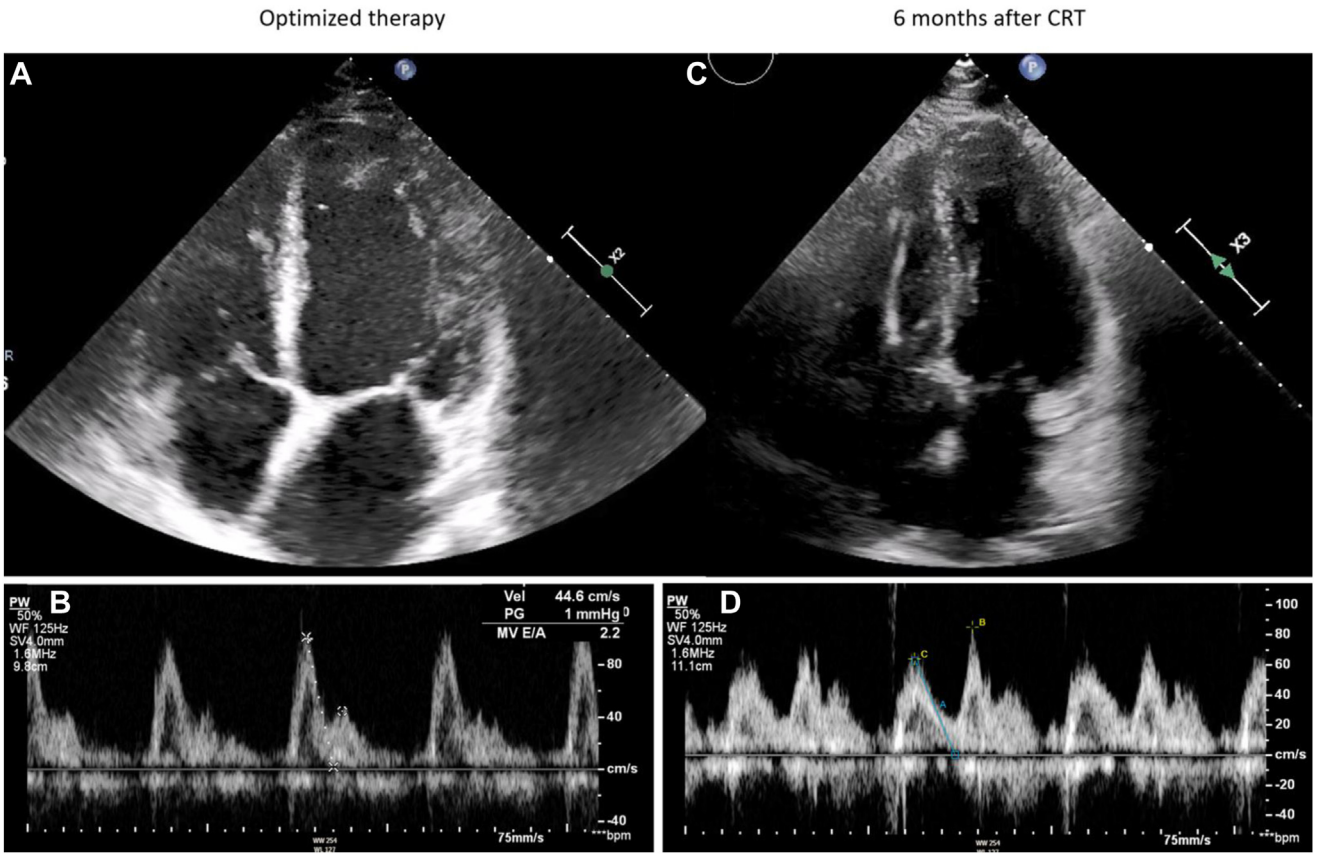

Figure 1 **A, C:** End-systolic 4-chamber view before (**A**) and 6 months after implantation (**C**) showing reduction of biventricular volumes. **B, D:** Left ventricular filling pattern before (**B**) and 6 months after implantation (**D**) showing diastolic dysfunction reversal and significant diastolic time increase.

A CRT device with defibrillator (Intica 7 HF-T; Biotronik SE & Co KG, Germany) was implanted. A bipolar single-coil implantable cardioverter-defibrillator lead with a floating atrial dipole (Plexa proMRI S 65; Biotronik SE & Co KG) was implanted in the right ventricle, and an LV lead was positioned in the lateral vein. However, because the electromechanical delay of this site was suboptimal (Q-LV = 100 ms, RV-LV = 60 ms), we decided to test CSP. A first attempt for His bundle pacing was made, but threshold values were too energy demanding (6 V @ 0.4 ms). We then tested right bundle area pacing using a stylet-driven pacing lead (Solia S60; Biotronik SE & Co KG). Once the distal His signal was found, the lead was advanced 1 cm below this recording site and screwed into the septum; the atrioventricular (AV) delay was programmed to obtain fusion between the intrinsic conduction and septal pacing only, resulting in nearly complete correction of the RBBB without any evidence of capture of the conduction system (Figure 2). Pacing and sensing parameters were optimal (0.4 V @ 0.5 ms, R wave 10 mV), enabling a low battery drain. Based on this, we opted for RV-synchronized CRT; that is, fusion of the intrinsic conduction along the His-Purkinje and RV stimulation synchronized to correct RBBB by ECG-based optimization of the AV delay: the patient was paced in VDD mode with a sensed AV delay (SAV) = 90 ms (Figure 2). It has to be noted that both the paced ECG (Figure 2B), echocardiography (Supplemental Figure 1), and chest radiograph (Supplemental Figures 2 and 3) hint at a right posterior-basal septal pacing site.

Thereafter, the patient reported an improvement of HF symptoms to NYHA class I during follow-up. At 6 months post CRT implantation, we observed marked improvement of echocardiographic parameters (Figure 1C and 1D, and Supplemental Figure 1): LV end-systolic volume was 75.6 mL (48% reduction when compared to baseline, Figure 1A and 1C) while LVEF improved to 47% (42% improvement from baseline). RV fractional area change was 38% (vs 32%), tricuspid annulus plane systolic excursion was 2.15 cm (vs 1.5 cm), and RV S′ wave at tissue doppler imaging was 14 cm/s (vs 10 cm/s), diastolic dysfunction improving from restrictive pattern to normal LV filling (Figure 1B and 1D). A paced QRS duration = 115 ms with persistent correction of the RBBB was observed at the ECG by stimulation of the right prospect of the interventricular septum (Figure 3A).

Discussion

CRT is a well-established treatment for HF with reduced ejection fraction and a broad QRS. Though current recommendations include patients with wide QRS and non-LBBB morphology, the evidence for this subgroup is weaker.[5]

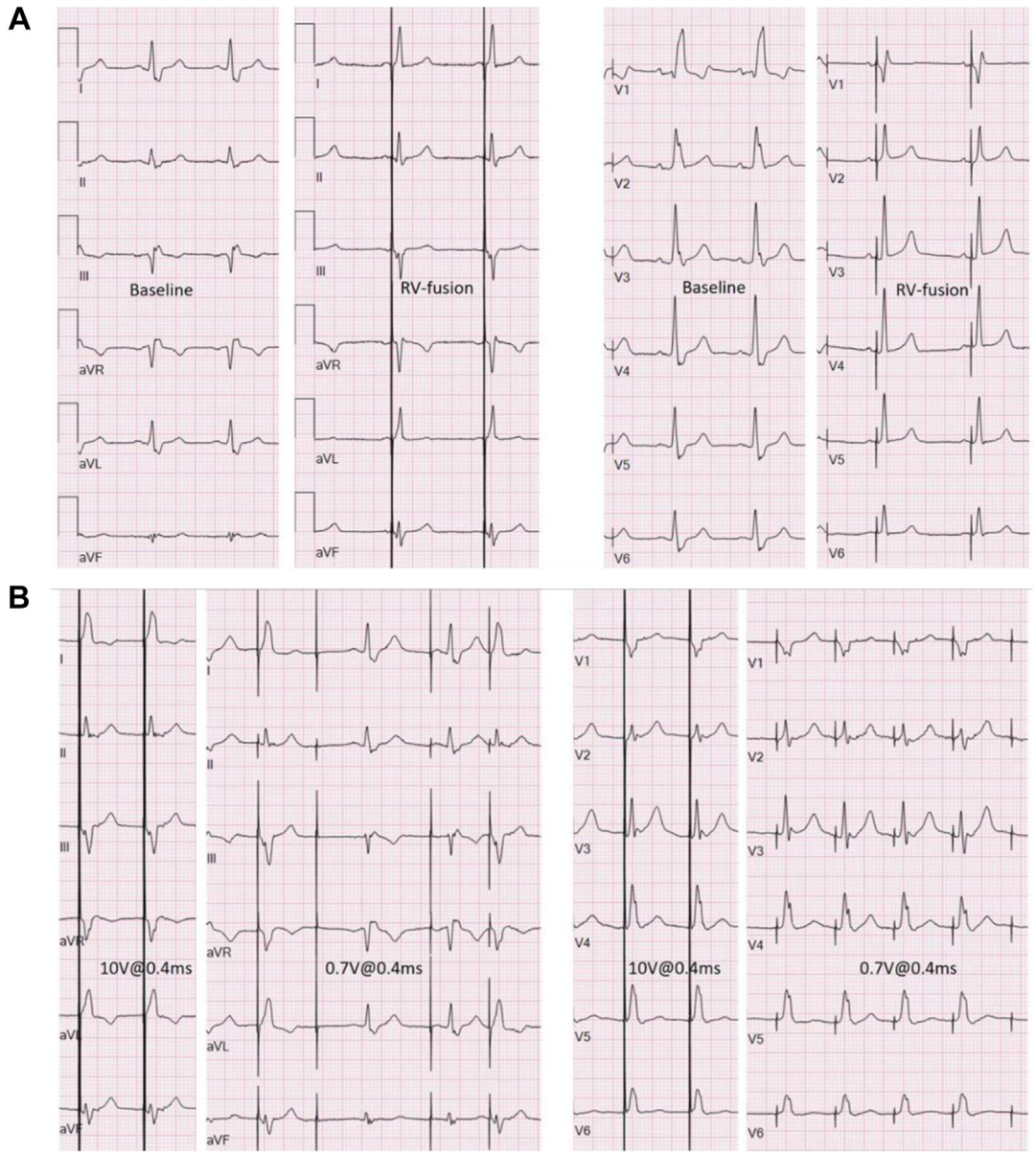

Figure 2 **A:** Comparison of baseline electrocardiogram with right ventricular (RV)-synchronized cardiac resynchronization therapy by fusion of intrinsic conduction with RV septal pacing at 90 ms sensed atrioventricular delay. **B:** Pacing at the RV septum without evidence of capture of the conduction system by voltage stepdown.

It has been shown that non-LBBB patients are more likely to respond to CRT in the presence of intraventricular dyssynchrony.[1] Although LBBB is known to be a possible cause of LV dysfunction, the contribution of non-LBBB conduction delays to LV dyssynchrony and systolic dysfunction is less established. However, a significant association between RBBB and LV mechanical dyssynchrony has been described by multiple studies.[6] Accordingly, traditional CRT delivered by a coronary sinus lead in HF patients with RBBB shows greater efficacy when a concomitant LV activation delay is present.[4]

CSP may be an alternative to conventional CRT, especially in cases of unsuccessful coronary sinus lead implantation, potentially enabling a nearly physiological biventricular activation by direct recruitment of the His-Purkinje system at different levels,[1] and can be considered in RBBB patients.[7]

Our case proves the effectiveness of a 2-lead resynchronization therapy enabled by septal stimulation in an HF patient with wide QRS and complete isolated RBBB. By activating the RV septum with fusion to intrinsic conduction along the His-Purkinje system (Figure 2), correction of electrical dyssynchrony was achieved, and improvement of both systolic and diastolic LV function eventually occurred (Figure 1).

The remarkable improvement of biventricular systolic function that we observed during follow-up may be explained, at least partially, by the association of RBBB with ventricular dyssynchrony, underlining the importance of restoring intraventricular synchrony also in the setting of delays involving the right side of the conduction system.

The ECG of our patient shows that the lead placed in the interventricular septum engages the myocardium and

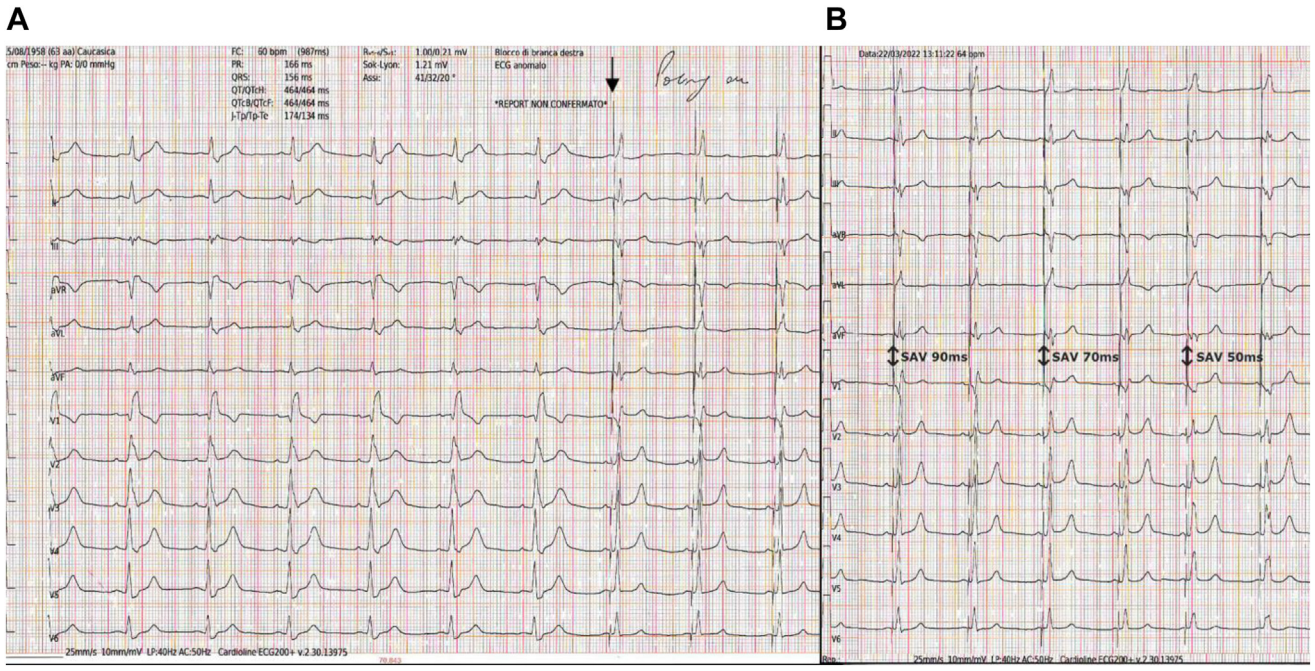

Figure 3 **A:** Electrocardiogram showing normal sinus rhythm with complete right bundle branch block (RBBB): as pacing is switched on, a change of ventricular conduction pattern from RBBB with near normalization is observed and is dependent on fusion with intrinsic conduction in the His-Purkinje network. **B:** Tailoring of the sensed atrioventricular interval (SAV) causes nearly complete RBBB correction when fusion is achieved (90 ms SAV), resembling the left bundle branch area pacing morphology, while pre-excitation of the right ventricular septum (50 ms SAV) causes a left bundle branch block–like paced complex.

possibly the Purkinje network distal to the block in the right septum, while preserving an unchanged LV activation via the His–left bundle system, thereby restoring a nearly physiological ventricular activation, as shown by QRS narrowing, at no trade-off with LV activation pattern (Supplemental Figure 4). Shortening of the QRS duration after CRT is indeed associated with a favorable CRT response.

As outlined in Figure 3, QRS narrowing is possible only by optimization of the SAV: when pacing is off the ECG shows complete RBBB; when pacing is turned on and the SAV programmed at 90 ms an almost complete correction of RV delay is observed, as the r′ in V_1 becomes less evident and the S wave in leads I, II, aVL, and V_4–V_6 disappears. Indeed, tailoring the SAV to achieve fusion of the intrinsic conduction to the left ventricle with correction of the RBBB is the key to resynchronization, as already reported for CRT recipients with LBBB.[8] Shortening the AV interval to 50 ms, therefore reducing fusion with spontaneous AV conduction (Figure 3B), shifts the activation pattern to an LBBB-like one that would rather disrupt biventricular synchronicity. The pattern shift caused by progressive septal pre-excitation (Figure 3B) proves that the septal lead is located closer to the right than to the left bundle branch area (see also Supplemental Figures 1, 2, and 3). The improvement of cardiac synchronicity and biventricular function observed by pacing the RV inflow tract in this patient with RBBB mimics the observations by Curila and colleagues[9] with LV septal pacing in patients with LBBB: pacing the RV septum at the inflow tract has been shown to cause less dyssynchrony than other RV sites, and may ensure correction of RBBB when fusion with intrinsic conduction via the left bundle branch is achieved. The fast conduction from the septal lead location to the RV free wall in our patients was enabled by the absence of septal scar, which would have rather impaired cardiac resynchronization and negatively impacted on prognosis, as reported by Leyva and colleagues.[10] We believe that pacing the RV septum distal to the site of RBBB with fusion to intrinsic conduction is an effective treatment in patients with a PR interval within normal range, as it enables ventricular synchronization at no trade-off with ventricular preload, and can be considered a feasible alternative when CSP fails to correct the RBBB or causes too much energy drain. Indeed, AlTurki and colleagues[11] reported that biventricular pacing with fusion significantly improved LVEF compared to conventional CRT in a small group of CRT recipients with RBBB. Siliste and colleagues[12] observed an optimized RV function owing to resynchronization by RV fusion pacing in a patient with normal LV function, sinus node disease, and first-degree AV block: RBBB was completely corrected by RV fusion pacing at no trade-off with ventricular preload. The fusion pacing concept may also be broadened to multipoint stimulation in patients with coexistent peripheral intraventricular conduction delay, as reported in literature.[13] One key aspect of fusion pacing is the AV interval: excessively long PR intervals may in fact cause ventricular unloading and reduced stroke volume,[1,8] thus limiting the adoption of fusion pacing. Correction of a coexistent very long PR interval by biventricular pacing has proven effective in CRT recipients irrespective of QRS morphology,[14] though CSP has the potential to achieve

superior resynchronization by correcting both AV and interventricular conduction delays. CSP-optimized CRT with and without fusion to intrinsic conduction has already proven to be effective, and is gaining wide clinical adoption to maximize cardiac resynchronization.[15]

Conclusion

In biventricular HF associated with RBBB, stimulating the LV by a coronary vein is not advisable owing to the absence of intraventricular LV conduction delay amenable to correction.[5] In this specific subgroup of patients, the combination of optimized medical therapy and CSP to correct the RBBB may represent an appealing option.[7]

Understanding the importance of the PR interval remains a key step for resynchronization therapy also in the setting of RBBB, as RV-synchronized CRT with capture of the myocardium and possibly of the Purkinje network downstream to the site of block can restore normal activation without creating a contralateral delay, similarly to LV-synchronized CRT in LBBB patients.[8] However, aside from our single patient experience, randomized controlled studies in RBBB patients are warranted to prove that correction of ventricular activation can enable reverse cardiac remodeling.

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Appendix

Supplementary Data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrcr.2023.06.010.

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