



Letter to the Editor

Usefulness of cardiac resynchronisation therapy in patients with right bundle branch block: Is viability an important piece of the puzzle?

K. O'Connor^a, M. Sénéchal^{a,*}, P. Lancellotti^b, M. Dubois^a, J. Magne^a, J. Champagne^a,
F. Philippon^a, L. Pierard^b, G. O'Hara^a

^a Institut de Cardiologie de Québec, Hôpital Laval, Department of Cardiology, Québec, Canada

^b CHU de Liège, Department of Cardiology, University Hospital, Sart Tilman, Liège, Belgium

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Abstract

Background: Benefits of cardiac resynchronisation therapy (CRT) in patients with heart failure (HF) and left bundle branch block (LBBB) have been well established. The presence of asynchronism and viability predicts response to CRT with good accuracy. Viability in the region of the pacing lead as predictor of response to CRT in patients with HF, intraventricular asynchrony and right bundle branch block (RBBB) has never been evaluated.

Methods: We studied 4 consecutive patients with RBBB (QRS>120 ms) advanced ischemic HF, low ejection fraction ($\leq 35\%$) and intraventricular asynchrony ≥ 50 ms scheduled for CRT. Dobutamine stress echocardiography (DSE) was performed within the week before CRT. Viability was defined as increased wall thickening during DSE. Viability in the region of left ventricular (LV) pacing lead was defined as the presence of viability in 2 contiguous segments. Response was defined by LV reverse remodeling (i.e. $\geq 15\%$ reduction in LV end-systolic volume) 3–6 months after CRT.

Results: Three patients demonstrated LV reverse remodeling at follow-up. Responders showed LV end-systolic volume decrease of $-31 \pm 16\%$ from baseline to follow-up whereas no change was observed in the non responder patient. Similar LV asynchronism was found in all patients. All responders had viability in ≥ 2 segments in the region of LV pacing.

Conclusion: This preliminary report suggests that similar reverse remodeling can be observed in RBBB patients as patients with LBBB after CRT. Intraventricular asynchrony and RBBB, viability in the region of pacing lead may help to predict response to CRT in patients with HF. © 2008 Elsevier Ireland Ltd. All rights reserved.

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1. Introduction

ACC/AHA Guidelines recommended cardiac resynchronisation therapy (CRT) in patients with heart failure (HF) with New York Heart Association (NYHA) class III to IV, low ejection fraction ($\leq 35\%$) and QRS duration > 120 ms, regardless of intraventricular delay pattern [1]. Despite these

criteria, up to 40% of patients failed to demonstrate a response to CRT [2]. Over 90% of patients enrolled in CRT studies have left bundle branch block (LBBB). In those patients, LV dyssynchrony helps to predict response to CRT [3]. Presence of viability has also gained growing acceptance as a predictor of response to CRT in patients with HF [2,4–6].

Less than 10% of patients with advanced systolic HF and abnormal ventricular conduction have RBBB. Consequently, patients with RBBB represent a small proportion of patients enrolled in CRT studies and limited data are available in this particular population [7]. In 2001, Garrigue et al. showed in 12 patients that only patients with RBBB associated with

* Corresponding author. Institut de Cardiologie de Québec, Hôpital Laval, 2725, Chemin Sainte-Foy, Québec, Québec Canada G1V 4G5. Tel.: +1 418 656 8711; fax: +1 418 656 4581.

E-mail address: mario.senechal@crhl.ulaval.ca (M. Sénéchal).

major intraventricular asynchrony are likely to respond to CRT [8]. However recently, Egoavil et al. analyzed the combined results of MIRACLE and Contak CD trials, which provided the largest cohort of patients with RBBB and HF [9]. With the exception of NYHA class, patients in these trials did not derive any clear significant benefit from CRT. Authors, thereby, concluded that there is few data supporting the use of CRT in patients with RBBB. Since RBBB was proved to be an important predictor of mortality in HF patients as much as LBBB, it seems important to clarify the place of CRT in patients with RBBB and HF. Numerous small studies have evaluated the presence of viability as a predictor of response to CRT in ischemic and non ischemic failing hearts [5,6]. Long term response to CRT may be explained by the presence of myocardial viability in patients with LV dysfunction. Moreover, presence of viability in the region of the pacing lead has been recently showed to be a predictor of acute response to CRT [10]. This factor has never been evaluated in patients with RBBB. This preliminary report describes our experience in such patients.

2. Methods

From June 2006 to September 2007, we studied 4 consecutive patients with RBBB underwent CRT implantation. The study was approved by our local ethics committee. Inclusion criteria were as follow: (1) RBBB (QRS > 120 ms), (2) NYHA functional class III and IV, (3) chronic LV systolic dysfunction (LV ejection fraction $\leq 35\%$), (4) basal LV dyssynchrony ≥ 50 ms, and (5) optimal medical treatment for HF including angiotensin-converting enzyme inhibitors or AT1 receptor antagonists diuretics, beta-receptor blockers and spironolactone when tolerated. Patients with recent myocardial infarction (<6 months), coronary revascularization procedure (<6 months) and presenting standard contraindications to DSE were excluded. All patients provided informed consent and were prospectively enrolled. One day after CRT implantation, the LV lead position was assessed from a chest X-ray. Using lateral views (anterior, lateral or posterior), we determined the LV lead location. Standard 2-dimensional echocardiography studies were performed within the week before CRT implantation. Echocardiographic measurements were performed by two observers blinded to patient's status using Philips Sonos 5500 or 7500 instrument with a 2.5-MHz transducer (Philips Medical Systems, Amsterdam, The Netherlands). LV volumes and ejection fraction were measured using the modified biplane Simpson's rule. Proximal isovelocity surface area (PISA) method was used to assess MR severity and to measure the effective regurgitant orifice (ERO) area. Intraventricular delay tissue Doppler imaging (TDI) was performed from apical view analyzing septal, inferior, lateral, posterior and anterior walls. Intraventricular electromechanical asynchrony was defined as the time between the shortest and the longest electromechanical delays among the five walls. Interventricular electromechanical asynchrony was defined

as the difference between the aortic and pulmonary ejection delays. All patients underwent DSE according to a low-dose infusion protocol. Patients received 5, 10, 15, and 20 $\mu\text{g/kg/min}$ of dobutamine in 3-minute stage, with echocardiographic images recorded at each stage [11,12]. Heart rate and blood pressure were monitored during each stage. Criteria for stopping the dobutamine infusion included (1) hypotension (systolic blood pressure <90 mmHg), (2) angina, (3) significant arrhythmias (atrial fibrillation, bigeminy, ventricular tachycardia), (4) attainment of 85% maximal predicted heart rate. The regional wall motion was assessed by the 16-segments model recommended by the American Society of Echocardiography [13]. Thus, a normal or hyperkinetic segment was graded as 1, mild hypokinetic as 2, severe hypokinetic as 3, akinetic as 4. Stress images during dobutamine infusion showing the maximum augmentation of wall motion were compared to baseline images. A segment was considered to have contractile reserve if the wall motion improved by one grade during DSE. Viability in the region of the LV pacing lead was defined as the presence of viability in 2 contiguous segments. Response to CRT was defined by evidence of LV reverse remodeling ($\geq 15\%$ reduction in LV end-systolic volume) 3–6 months after CRT.

3. Results

Table 1 lists the individual baseline characteristics of enrolled patients. The four patients (mean age 75 ± 6 years, 2 males) had ischemic HF, were in sinus rhythm and NYHA functional III. MR was observed in 2 patients (mean

Table 1
Population demographic and echocardiographic characteristics

	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	77	68	81	73
Sex (M/F)	M	F	F	M
NYHA pre CRT	III	III	III	III
NYHA post CRT	II	II	II	III
QRS (ms)	172	150	164	150
LV asynchronism (ms)	80	75	160	135
LVEF pre CRT (%)	28	23	23	19
LVEF post CRT (%)	33	28	51	19
ERO pre CRT (mm^2)	–	18	10	–
ERO post CRT (mm^2)	–	13	8	–
Akinetic segments rest (n)	9	8	10	8
Akinetic segments dobu (n)	8	8	7	8
WMSI rest	3.6	3.3	2.6	3.2
WMSI dobu	3.1	2.7	2.3	3.1
Viable segments (n)	6	6	4	1
≥ 4 viable segments (y/n)	Yes	Yes	Yes	No
Viability pacing lead (y/n)	Yes	Yes	Yes	No
LVSF rest (ml)	171	200	150	172
LVSF follow up (ml)	119	170	80	174
LVSF reduction (%)	30	15	47	–

NYHA: New York Heart Association; CRT: cardiac resynchronization therapy; LV: left ventricular; LVEF: left ventricular ejection fraction; ERO: effective regurgitant orifice; WMSI: wall motion score index; LVSF: left ventricular systolic volume.

ERO = 14 ± 6 mm²). Three patients were responders after CRT. In these patients, mean LV end-systolic volume decreased was $31 \pm 16\%$ (from 174 ± 25 ml to 123 ± 45 ml). There was no change in LV end-systolic volume in the non responder patient. With regard to LV asynchronism, no clinical significant difference was found between responders and non responder 105 ± 48 ms vs. 135 ms respectively. Patients with pre CRT MR had a change in ERO of 25% (14 mm² to 10.5 mm²).

All responders demonstrated viability in ≥ 4 segments (5 ± 1 segments). Moreover, those patients had viability in ≥ 2 segments in the region of the pacing lead which was not the case in the non responder patient. The pacing lead was in the posterior region for all patients. At peak DSE responders showed reduction of WMSI of 13% in comparison to 3% for the non responder patient.

4. Discussion

To the best of our knowledge, this preliminary report is the first to address viability, particularly in the region of the pacing lead, as a predictor of response to CRT in patients with RBBB. Our results show that 3 patients had a response to CRT defined by $\geq 15\%$ reduction in LV end-systolic volume. Of interest, all responders had local viability, i.e. myocardial viability in the region of pacing lead, contrasting with the non responder patient who had neither viability in the region of the pacing lead or substantial global viability. Significant electrical conduction delay (QRS ≥ 120 ms) is encountered in about 30% of patients with severe systolic dysfunction. Of these patients $\geq 90\%$ have LBBB. Companion trial reveals that only 10% of the 1520 patients studied had RBBB [14]. In subgroup analysis of Companion trial, the addition of CRT in patients with bundle branch block other than LBBB did not result in significant reduction of hazard ratios of primary end-point (death or hospitalization). The few studies examining the role of CRT in RBBB patients have yielded conflicting results supporting or lacking support for CRT in this setting. Other studies, however, have found that patients with RBBB and significant intraventricular mechanical delay respond to CRT [8]. Recently, Byrne et al. reported in an animal model that the magnitude of cardiac dyssynchrony in a failing heart with a pure RBBB is considerably less than in hearts with an LBBB, despite similar prolongation of the QRS [15]. In the same line, Haghjoo reported that significant intraventricular dyssynchrony was found in 63% of patients in the LBBB group as opposed to 31% of patient in the RBBB group [16]. The mechanisms explaining CRT beneficence in patient with HF is related to reduction of LV dyssynchrony and corresponding stress–strain disparities and inefficient contraction of the ventricle; it is not surprising that in presence of less LV asynchrony, patients with RBBB show less benefit from CRT than patients with LBBB.

Because regional wall thickening is influenced by the extent of myocardial fibrosis, it has been hypothesized that

myocardial viability could help to predict response to CRT. Using nuclear myocardial perfusion, magnetic resonance imaging and DSE, studies have demonstrated the importance of viability in predicting response to CRT [5,6,17]. Furthermore, in patients with transmural scar tissue in the region of the LV pacing lead, CRT did not demonstrate clinical or LV remodeling improvement at follow-up [18]. Studies evaluating the role of viability to predict response to CRT have involved a majority of patients with LBBB. This is the first report regarding viability as a predictor of response in patients with RBBB. Some studies have suggested that ischemic dilated cardiomyopathy is less likely to respond to CRT than non ischemic dilated cardiomyopathy, whereas other studies have not. However, these studies only examined outcomes based on the presence or absence of coronary artery disease as the cause of systolic heart failure. These studies did not consider, for example, the more specific possibility that infarct location influences CRT response. Whether CRT is “wide right” in RBBB remains to be determined [7]. Insufficient clinical evidences are available to reach definitive conclusions, and this will be difficult to overcome because of the underrepresentation of RBBB in systolic HF. Although CRT “non response” is likely a diverse phenomenon, there is emerging consensus that inadequate patient selection is a key element. This preliminary report suggests that patients with RBBB do not derive the same degree of benefit from CRT unless intraventricular dyssynchrony and viability in the region of the pacing lead are present. A study designed to specifically enroll patients with RBBB, congestive HF and significant LV asynchrony is required. Moreover, in such population, evidence of myocardial viability by DSE or any other valuable method (MRI, PET scan) should also be evaluated to find out if the criterion of viability in the region of the pacing lead is as important in patients with RBBB than in patients with LBBB. Such a study may identify which patients with RBBB will derive the greatest benefit from left-sided resynchronization.

5. Conclusion

Prospective randomized trials concluded that patients with RBBB do not derive significant benefit from CRT. However, in these studies, significant LV asynchrony was not an inclusion criterion and viability in the region of the pacing lead was not assessed. Our preliminary report suggests that in presence of significant LV asynchrony and viability in the region of the pacing lead, patients with RBBB and HF may show similar LV reverse remodeling as patients with LBBB after CRT.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [19].

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