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Original Article

Comparison of hemodynamic effects of biventricular versus left ventricular only pacing in patients receiving cardiac resynchronization therapy: A before–after clinical trial

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ABSTRACT

Background: Biventricular (BiV) pacing is the most common mode of delivering cardiac resynchronization therapy (CRT). However, initial clinical studies have indicated that left ventricular (LV) pacing is not inferior to BiV pacing. This study was conducted to address whether LV only pacing can provide the same hemodynamic response as BiV pacing.

Methods: This before–after clinical trial was conducted at Ekbatan Hospital, from July 2012 to November 2014. Patients with a LV ejection fraction $\leq 35\%$ and a QRS duration ≥ 0.12 s who had a standard indication for ventricular pacing were enrolled. The CRT devices of all patients had already been set for BiV pacing. Therefore, their CRT devices were set for LV only pacing for 3 months. The hemodynamic status of the patients was assessed by echocardiography before setting the CRT device to LV only pacing (as a control) and 3 months after (as an intervention).

Results: There was no statistically significant difference between the effect of BiV pacing and LV only pacing on the hemodynamic responses including LV ejection fraction, LV end diastolic and systolic volume, and velocity time integral of the aortic valve. Moreover, no significant difference was seen between men and women either.

Conclusions: LV only pacing is not inferior to BiV pacing, and the hemodynamic response was similar in the two groups. However, the LV mode has a number of advantages over the BiV mode. More evidence, based on large clinical trials, is needed to confirm our results.

1. Introduction

The prevalence of heart failure prevalence is increasing throughout the world. The reasons for this pandemic include the aging populations of both industrialized and developing nations and a growing incidence of obesity, diabetes, and hypertension [1]. Several conduction abnormalities are commonly seen in association with chronic heart failure. Among these are abnormalities of ventricular conduction, such as bundle branch blocks that alter the timing and pattern of ventricular contraction, so as to place the already failing heart at a further mechanical disadvantage [2]. These ventricular conduction delays produce suboptimal ventricular filling, a reduction in left ventricular (LV) contractility, prolonged duration of mitral regurgitation, and paradoxical septal wall motion. Taken together, these mechanical manifestations of altered ventricular conduction have been termed ventricular dyssynchrony [2,3]. Ventricular dyssynchrony has been defined by a prolonged QRS duration, generally longer than 120 ms, on a surface electrocardiogram [3]. By this definition, about one third of patients with systolic heart failure have ventricular dyssynchrony [4].

In patients with heart failure, cardiac resynchronization therapy (CRT) for 6 months was associated with reduced end-diastolic and end-systolic volume, reduced LV mass, increased ejection fraction, reduced mitral regurgitant blood flow, and improved myocardial performance index as compared with controls [5–8].

Biventricular pacing (BiV) is the most common mode of delivering CRT [9]. However, initial clinical studies comparing BiV pacing with LV only pacing indicated that BiV and LV pacing may provide a

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similar systolic function [10–15]. Nonetheless, more evidence is required based on clinical trials conducted in different settings, to confirm this issue. The present study addressed this important question by comparing the hemodynamic responses of BiV versus LV only pacing in patients with a standard indication for ventricular pacing.

2. Materials and methods

This before–after clinical trial was conducted at Ekbatan Hospital, affiliated with Hamadan University of Medical Sciences, West of Iran, from July 2012 to November 2014. Written informed consent was obtained from all parents. The present study was approved by the Ethic Committee of the university (D-3-16-35-9-4026 on 26 June 2012). The protocol was registered in the Iranian Registry of Clinical Trials (IRCT201203169014N7) accepted on 3 July 2012.

The patients with CRT, who were referred to the electrophysiological clinic of Ekbatan (Farshchian) Hospital, were enrolled if they fulfilled the following criteria: (a) LV ejection fraction less than or equal to 35%; (b) a QRS duration greater than or equal to 0.12 s; (c) sinus rhythm; (d) indication for the treatment of New York Heart Association (NYHA) functional Class III or ambulatory Class IV heart failure symptoms with optimal recommended medical therapy; and (e) had received CRT at least 3 months previously. Patient characteristics were as follows: etiology (non-ischemic, 24 patients; ischemic, 20 patients); morphology (LBBB, 38 patients; non-LBBB, 7 patients); QRS interval (LBBB group, 158 ± 32 ms; non-LBBB group, 185 ± 38 ms). All patients were on full medical treatments including loop diuretic (furosemide), beta blocker (long acting metoprolol or carvedilol) and angiotensin converting enzyme inhibitors or angiotensin receptor blockers. Spironolactone was administered to all patients with a creatinine level less than 2.2 mg/dL and potassium level less than 5.5 mEq/dL. The dosage of all drugs was adjusted according to the patients' conditions.

The CRT devices of all patients had already been set for BiV pacing. Therefore, their CRT devices were set for LV only pacing for 3 months. The hemodynamic status of the patients was assessed by echocardiography before setting (as control) and three months later (as an intervention). After setting, the mean QRS width was 148 ± 34 ms. A decrease of 0–80 ms in QRS width was observed. An atrioventricular (AV) delay was described as nominal in all patients, and echo-guided optimization was used in non-responsive patients. At the end of the study, patients' pacemakers were set back to the initial BiV pacing.

The hemodynamic response of interest included: (a) LV end diastolic volume per ml; (b) LV end systolic volume per ml; (c) LV ejection fraction per percent; and (d) velocity time integral of the aortic valve per cm.

In order to minimize possible errors, all patients were evaluated with a specific echocardiography machine (MY LAB 60, Esaote, Italy). The paired *t*-test was used for analysis of continuous variables. All statistical analyses were performed at a significance level of 0.05 using statistical software Stata 11 (Stata Corp, College Station, TX, USA).

3. Results

We identified 45 patients who fulfilled the entry criteria; one patient was excluded because of LV lead malfunction. All patients presented with at least NYHA function Class II or III. Clinical response to CRT was defined as improvement in the NYHA classification by one class after CRT implantation. The study was based on the 44 patients, regardless of the clinical response.

Twenty seven (61%) patients were female and 17 (39%) were male. The mean $\pm$ SD age of the patients was 63.0 ± 12.0 years with a minimum and a maximum of 26 and 83 years, respectively. During the study, no deaths and no serious ventricular arrhythmias or worsening clinical condition leading to hospitalization occurred.

The effect of BiV pacing and LV only pacing on hemodynamic responses is shown in Table 1. According to these results, no statistically significant differences in hemodynamic responses were seen in the two groups. Given that the end diastolic and systolic volume is different in men and women, the results were analyzed by sex. However, no statistically significant differences in the hemodynamic responses were seen between the two groups.

4. Discussion

The main objective of this study was to compare the hemodynamic responses of BiV pacing with those of LV pacing alone. The benefits of LV pacing include (1) the transition from BiV to LV pacing increases the longevity of the device and decreases the

Table 1
Comparison of the left ventricular systolic function among patients with biventricular pacing versus patients with left ventricular pacing alone.

Left ventricular systolic function	Biventricular pacing		Left ventricular pacing alone		*P* value
	Mean	SD	Mean	SD	
Total (44 patients)					
Left ventricular ejection fraction (%)	19.98	7.05	19.41	6.84	0.176
Left ventricular end diastolic volume (ml)	175.50	62.28	173.30	62.95	0.156
Left ventricular end systolic volume (ml)	141.00	53.49	139.93	53.88	0.489
Velocity time integral of aorta (cm)	16.84	5.34	16.95	4.31	0.847
Females (27 patients)					
Left ventricular ejection fraction (%)	18.89	6.23	18.11	5.58	0.225
Left ventricular end diastolic volume (ml)	160.00	12.76	158.11	66.62	0.434
Left ventricular end systolic volume (ml)	131.30	59.29	130.41	59.01	0.714
Velocity time integral of aorta (cm)	17.44	5.85	17.37	4.40	0.933
Males (17 patients)					
Left ventricular ejection fraction (%)	21.71	8.08	21.47	8.23	0.571
Left ventricular end diastolic volume (ml)	200.12	47.24	197.41	49.32	0.046
Left ventricular end systolic volume (ml)	156.41	39.55	155.06	41.80	0.276
Velocity time integral of aorta (cm)	15.88	4.40	16.29	4.21	0.519

costs of repeated surgery; (2) if the right ventricular (RV) threshold increases or RV lead is displaced, with maintaining an acceptable sensitivity, repeated surgery can be avoided by changing the pacing mode from BiV to LV only pacing; (3) in countries with limited resources where the cost of acquiring a pace and triple-chamber implantable cardioverter defibrillator (CRT) is high, dual-chamber devices can be used on the right atrium and left ventricle position, which is cost efficient. The results indicated that the benefits of the two procedures are similar. According to the European Society of Cardiology (ESC) guidelines on cardiac pacing and CRT, LV pacing alone may be considered as an alternative mode for BiV pacing. Furthermore, a respective 21% of patients who did not respond clinically or echocardiographically to BiV pacing responded to LV pacing mode [9]. Moreover, a recently conducted meta-analysis has demonstrated that in patients with moderate-to-severe heart failure, these two pacing modalities did not differ with regard to death/heart transplantation or need for hospitalizations [16].

In 2011, Thibault et al. conducted a multicenter, double-blind, crossover trial and compared the effects of LV and BiV pacing on exercise tolerance and LV remodeling in 211 patients with an LV ejection fraction $\leq 35\%$, QRS ≥ 120 ms, and symptoms of heart failure. They concluded that LV pacing was not superior to BiV pacing. Moreover, non-responders to BiV pacing may respond favorably to LV pacing [17]. The LV mode may have number advantages. First, in patients with severe heart failure who need three-chamber CRT, based on the guideline, using the LV mode may reduce the cost. Second, the time of implanting the LV mode is less than that of the BiV mode. Thus, using the first approach can reduce the harmful exposure to radiation in both the patient and physician. Third, in cases where the right ventricular lead placement is difficult or even impossible for any reason, the LV mode can be considered as an alternative approach.

5. Conclusion

Understanding the mechanism responsible for the lack of difference between LV and BiV pacing was not an objective of this study. As desynchronizing mostly affects the left ventricle [18–22], using LV pacing alone may be similar to BiV pacing. We conclude that LV pacing alone is not inferior to BiV pacing, and the hemodynamic response was similar in the two groups. However, more evidence, based on large clinical trials, is warranted in order to confirm our results.

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Conflict of interest

The authors declare that they have no conflicts of interest in relation to this work.

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