



Comparison of Benefits from Cardiac Resynchronization Therapy between Patients with Ischemic Cardiomyopathy and Patients with Idiopathic Dilated Cardiomyopathy

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Received 10 December 2008; Accepted 24 January 2009

Abstract

Background: Cardiac resynchronization therapy (CRT) is an effective treatment for patients with moderate to severe heart failure. However, 20-30% of patients remain non-responders to CRT. We sought to identify which patients benefit the most from CRT in regard to the etiology of heart failure.

Methods: Eighty-three consecutive patients (62 men) who had a biventricular pacemaker inserted at Tehran Heart Center between May 2004 and March 2007 were evaluated retrospectively. The inclusion criteria were comprised of New York Heart Association (NYHA) class III or IV, left ventricular ejection fraction <35%, and QRS >120ms. After 6 months, response was defined as being alive, no hospitalization for cardiac decompensation, and an improvement in NYHA class >1 grade.

Results: After 6 months, 60 patients out of the 83 patients were responders. Amongst the 83 patients, 48 had ischemic cardiomyopathy and 35 had non-ischemic cardiomyopathy. A cross-tabulation of response versus etiology showed no significant difference between ischemic versus non-ischemic cardiomyopathy with regard to response to CRT ($P=0.322$).

Conclusion: According to our study, there was no difference in response to CRT between ischemic versus non-ischemic cardiomyopathy at six months' follow-up.

J Teh Univ Heart Ctr 2 (2009) 115-118

Keywords: Cardiomyopathies • Heart failure • Pacemaker, artificial

Introduction

Synchronized ventricular contraction in normal hearts results in an optimal mechanical output in ejection time. Significant delays in conduction time through ventricles change the synchronized ventricular contraction and decrease the ability of the optimal output. Desynchronized ventricles can be resynchronized by cardiac resynchronization therapy (CRT) devices, designed for improving the parameters of the left ventricle function electrically and mechanically.¹⁻³

CRT is an effective treatment for patients with moderate to severe heart failure and left ventricular dyssynchrony and is considered a major breakthrough in the treatment of patients with advanced heart failure.^{4,5} However, between 20% and 30% of patients do not respond to CRT with respect to the definition of responding.^{6,7}

Identifying reliable predictors of effectiveness and the characteristics of patients who do respond to CRT remain a major challenge in clinical practice, particularly from the perspective of patient selection.

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It would be more efficient if clinicians could identify prospectively the patients likely to respond to CRT. Many studies have evaluated multiple factors in order to find electrical, demographical, mechanical, and etiological characteristics of responding and non-responding patients.⁸⁻¹⁰

Given that the etiology of heart failure could affect the outcome of CRT, we aimed at evaluating the role of etiology in the response to CRT. If etiology can indeed influence the response to CRT, it would be advisable to consider it in patients scheduled for CRT.

Methods

In total, 83 consecutive patients who had a biventricular pacemaker implanted at Tehran Heart Center between May 2004 and March 2007 were evaluated retrospectively (male/female ratio 62/21; mean age: 58±9.2).

The inclusion criteria consisted of the following: 1. Moderate to severe heart failure (NYHA class III or IV), 2. Left ventricular ejection fraction (LVEF) <35%, 3. QRS duration >125ms with a left-bundle-branch-block (LBBB) pattern, and 4. Optimal medication, including beta blockers, diuretics, and angiotensin converting enzyme inhibitors (ACE).

In the presence of significant known coronary artery disease (single-vessel, two-vessel, and three-vessel) confirmed by conventional angiography, the patients were categorized as those with ischemic cardiomyopathy; and the patients with normal coronary arteries were categorized as those with idiopathic dilated cardiomyopathy.

Six months after implantation, response was defined as being alive, no hospitalization for cardiac compensation, and improvement in New York Heart Association (NYHA) class ≥ 1 grade.

The study was approved by the institutional ethics committee, and informed consent was obtained from all the patients.

For electrocardiographic evaluations, all the patients' EKGs were recorded with a standard 12-lead electrocardiography machine (Hellige) at regular speed and voltage. The QRS configuration and duration were measured and confirmed by 2 cardiologists.

All the patients underwent 2D and tissue Doppler imaging (TDI) echocardiography using a Vingmed / Vivid 7 GE-System.

The echocardiographic images and hemodynamic parameters were obtained and measured in 4- and 5-chamber views in the left lateral position. LVEF, velocity time integral, mitral regurgitation severity, and electrical delays were evaluated. LVEF was calculated via Simpson's technique and global calculating methods. The dyssynchronization index was measured using TDI.

The patients received biventricular pacemakers with or without the implantable cardioverter-defibrillator (ICD); and the devices used were Insync III, Insync Marquis by Medtronic, and Frontier and Epic HF by St. Jude's.

The right ventricle (RV) leads were positioned at the apex of the RV, and the right atrium (RA) leads were placed at the right atria appendage or lateral wall. After coronary sinus angiography, the left ventricular (LV) leads were implanted in the lateral or posterolateral veins and when it was unattainable it would be inserted in the middle or great cardiac vein. There were 4 patients whose LV lead was implanted intra-operatively through thoracoscopy in the LV epicardial lateral wall. All the patients were in normal sinus rhythm.

One day after implantation, AV and V-V optimizations were performed using echo-guide and the echo findings were recalculated one month after implantation. The findings were used for the statistical study.

The data were analyzed with SPSS 15 Software. The quantitative data were presented as mean±SD, and a P value < 0.05 was considered significant.

Results

The clinical outcome of CRT after 6 months can be summarized as having 60 responders (72.3%) out of the total 83 (62 male) patients according to aforementioned criteria.

Amongst the 83 patients, 48 (58%) had ischemic cardiomyopathy and 35 (42%) had non-ischemic or dilated cardiomyopathy. Regarding the inclusion criteria, all the patients had a wide QRS complex with an LBBB configuration, which was shortened significantly in both groups (mean=24 ms). The mean NYHA class was 3.2, which was decreased by one grade on average (2.2) in the responders and by less than 1 grade in the non-responders (Table 1).

At 6 months' follow-up of the 83 patients, the cross tabulation of response versus etiology showed no significant

Table 1. Characteristics of patients with ischemic cardiomyopathy (group I) and patient with non-ischemic cardiomyopathy (group II) before and after CRT*

	Male	Age (y)	FC before	FC after	EF before	EF after	QRS before (ms)	QRS after (ms)	Δ QRS
group I	85%	59.4 (±10.4)	3.25 (±0.44)	2.1 (±0.95)	20.6% (±5.5)	26% (±7.2)	164.69 (±28.24)	137.14 (±22.1)	27.54 (±26.45)
group II	60%	55.65 (±10.66)	3.34 (±0.48)	2.37 (±0.97)	19.28 (±5.09)	26.87 (±8.3)	159.46 (±24.39)	137.15 (±22.10)	19.68 (±22.7)

*Data are presented as mean±SD

CRT, Cardiac resynchronization therapy; FC, Functional class; EF, Ejection Fraction; Δ QRS, QRS before CRT- QRS after CRT



difference between ischemic versus dilated cardiomyopathy in regard to response to CRT ($P=0.32$).

Discussion

Since the first report in 1994 of the implantation of a biventricular cardiac stimulator to improve the hemodynamic status,¹¹ this adjunctive treatment of refractory congestive heart failure has markedly evolved.

Several studies have demonstrated the efficacy of this new form of the management of advanced congestive heart failure.¹² However, %20-%30 non-responders to CRT are reported consistently.² Controversy still abounds over the factors that play a role in the results amongst the non-responders to CRT.

The etiology of heart failure is supposed to affect the response to CRT. The Molhock et al. study showed that the etiology of heart failure (ischemic cardiomyopathy versus dilated cardiomyopathy) did not affect the response to CRT.¹³ The Hua W. et al. study compared the short-term effect of CRT in both ischemic and non-ischemic cardiomyopathy and proved no statistically significant difference.¹⁴

There is little evidence in the literature showing that ischemic patients have a better outcome after CRT. Diaz et al. maintained that patients with ischemic heart disease had a lower probability of non-response.¹⁵ Be that as it may, there is increasing evidence indicating that non-ischemic patients fare better with CRT. As shown in an Italian registry, patients without ischemic disease have a greater improvement with CRT (From the Insync / Insync ICD Italian Registry. *Pacing and clinical electrophysiology* 2006;24:S2-10). Conversely, Leclercq et al. demonstrated that the underlying etiology, whether ischemic or otherwise, did not affect the improvement in the results of CRT implanted patients (Leclercq C, Eras D, Tang A. Comparative effects of ventricular resynchronization therapy in heart failure patients with or without coronary artery disease. *Annual of Cardiology Angiology* 2004;53:171-176). The non-ischemic patients had a greater increase in LVEF and decrease in NYHA functional class than did the patients with coronary artery disease in the Gasparini study.¹⁶

The sub-analysis of the MIRACLE trial was in parallel with more benefit and significant improvement in LV systolic function in dilated cardiomyopathy rather than ischemic cardiomyopathy.

Our study showed no difference in the CRT response with regard to etiology at six months' follow-up. Our results are compatible with those in the Zardookhi et al. study, which demonstrated that the CRT outcome appeared independent of age, gender, and heart failure etiology.¹⁷

In the CARE-HF study, when compared with the ischemic patients, the non-ischemic patients showed a greater extent of reduction in the estimated absolute risk of death or unplanned hospitalization after receiving CRT, although the etiology of

heart failure was not found to be and independent predictor for the outcome measure of CRT.¹⁸

Finally, we believe that despite the similar percentage of non-responders in both groups of our study population, there must be different reasons for non-response between the two groups. In our ischemic patients, non-response must have been related to the extension of the scar tissue, whereas in dilated cardiomyopathy it must have been related to right ventricular dysfunction.

The present study being retrospective, we did not have access to some data in all the patients. In addition, we did not perform the 6-minute walk test for all the patients; our definition of response was, therefore, based on hospitalization and subjective findings.

Conclusion

Our study is compatible with studies that show no difference in the response rate in regard to etiology. There is an explanation for the discrepancy amongst various studies. It seems that in studies with a longer period of follow-up, ischemic patients have a worse outcome in comparison with non-ischemic patients. In may be in consequence of the bad nature of coronary artery disease itself, which begets more vascular events, disease progression, and hospitalization.

Acknowledgments

This study was approved and was supported by Tehran Heart Center, Tehran University of Medical Sciences.

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