



Evaluation of Response to Cardiac Resynchronization Therapy in Patients with Non-Ischemic Cardiomyopathy Based on Echocardiographic Features Including Sphericity Index and Global Longitudinal Strain

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ABSTRACT

Background: In patients with Non-Ischemic Cardiomyopathy (NICM), Cardiac Resynchronization Therapy (CRT) has been shown to improve Left Ventricular Ejection Fraction (LVEF) and NYHA functional class. However, in some patients who received CRT, the results were not satisfying.

Objectives: This study aimed to evaluate echocardiographic features as a predictor of positive response to CRT in patients with NICM.

Methods: This case series study was conducted on 11 consecutive patients with NICM who were eligible for CRT at Imam Khomeini Hospital Complex. The patients' basic demographic and echocardiographic data including Septal Flash (SF), Sphericity Index (SI), and Global Longitudinal Strain (GLS) were recorded and followed for six months. Data analysis was done using the SPSS software, and paired t-test was used for comparison of the study variables.

Results: The results revealed an improvement in the median NYHA functional class from 3 (interquartile range: 2 - 4) to 1 (interquartile range: 1 - 2) ($P < 0.001$) at the follow-up. Assessment of LVEF through the Simpson method also showed a significant improvement from 28.25% to 39.31% ($P < 0.001$). Moreover, GLS improved and SI and SF decreased post CRT implantation.

Conclusions: The results demonstrated that a GLS of less than -10.48 before device implantation, but not SI or SF, might be a predictor of a positive response to CRT in patients with NICM. In these patients, higher GLS at baseline might add data to the existing criteria for selecting suitable patients for CRT implantation.

1. Background

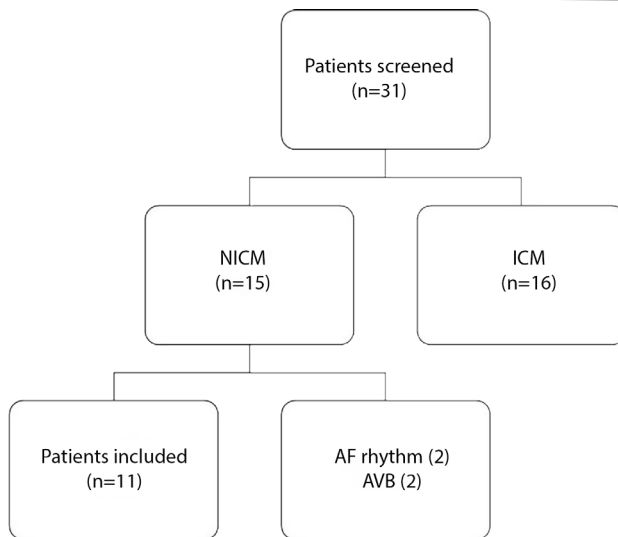
Heart Failure (HF) has been recognized as a major cause of morbidity and mortality in all communities. Cardiac Resynchronization Therapy (CRT) is the most promising treatment modality for patients with New York Heart Association (NYHA) Functional Class (FC) II-IV with reduced Left Ventricular Ejection Fraction (LVEF) and Left Bundle Branch Block (LBBB) morphology in Electrocardiogram (ECG) (1). Several clinical trials have

shown that CRT improved symptoms, Quality of Life (QoL), LVEF, and mortality rates in these patients (2, 3). Despite these impressive results, up to 30% of patients did not improve or even got worse after receiving CRT and were thus labeled as 'non-responders'. Identification of clinical and echocardiographic parameters that predict response using noninvasive tools prior to CRT may result in cost saving and fewer adverse events for patients. As previously illustrated (4), patients with Non-Ischemic Cardiomyopathy (NICM) benefit more than patients with ischemic cardiomyopathy.

2. Objectives

Therefore, the present study aims to evaluate the

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Figure 1. The Case Selection Algorithm

AF, atrial fibrillation; AVB, atrioventricular block; ICM, ischemic cardiomyopathy; NICM, non-ischemic cardiomyopathy.

echocardiographic parameters of patients with NICM before and after CRT implantation and to determine the parameters that can predict positive response to CRT.

3. Patients and Methods

From March 2015 until March 2017, 11 consecutive patients with NICM scheduled for receiving CRT at Imam Khomeini Hospital Complex, Tehran, Iran were prospectively followed. The inclusion criteria were suffering from NICM (documented with normal coronary angiography results), NYHA FC class II or more, QRS ≥ 150 msec, LBBB morphology in ECG, and LVEF $\leq 35\%$. Patients with different types of atrioventricular block, right bundle branch block, and atrial fibrillation rhythm were excluded from the study (Figure 1). Echocardiographic examination was performed for all patients prior to and six months after CRT implantation. LVEF, Left Ventricular End Systolic Volume (LVESV), Left Ventricular End Diastolic Volume (LVEDV), Sphericity Index (SI), Septal Flash (SF), and Global Longitudinal Strain (GLS) were recorded. CRT implantation was performed in the catheterization laboratory with multimodal analgesia (intravenous acetaminophen and

local lidocaine) (5) and known techniques (6). Response to CRT at the six-month follow-up was assessed through clinical and echocardiographic parameters. Reverse remodeling was defined as improvement in LVEF $\geq 5\%$ and a reduction of LVESV $\geq 15\%$.

This study complied with the tenets of the Declaration of Helsinki and was approved by the institutional ethical board of Tehran University of Medical Sciences (IR.TUMS.VCR.REC.1395.1326).

3.1. Statistical Analysis

The data have been expressed as mean + standard deviation or percentage, as appropriated. Data analysis was performed using the SPSS software (version 16.0) for both descriptive and comparative variables. The variables were compared using Pearson's test and paired t-test. $P < 0.05$ was considered statistically significant.

4. Results

The study population included seven females and four males with the mean age of 63.27 years (SD = 7.39). During the six-month period prior to CRT implantation, all patients were hospitalized at least once. At the time of device implantation, QRS duration ranged from 150 to 162 msec (mean 156). The baseline and follow-up characteristics of the patients have been presented in Table 1.

Right after CRT implantation, all patients showed q wave in lead I and a decrease in QRS width in ECG. Assessment of LVEF through eyeball and Simpson methods six months after CRT implantation showed a significant improvement from 23.18% to 35% ($P < 0.001$) and from 28.25% to 39.31% ($P < 0.001$), respectively. Moreover, the results revealed a significant reduction in LVESV, LVEDV, and SF and an improvement in LVEF and GLS after six months.

In univariate analysis, only GLS less than -10.48 was associated with response to CRT in patients with NICM. Furthermore, the patients with SF at baseline that was corrected after CRT were more likely to respond in comparison to the patients without SF. However, the difference was not statistically significant.

5. Discussion

According to the results, GLS less than -10.48 before

Table 1. Baseline and Follow-up Clinical Characteristics and Echocardiographic Parameters of the Patients with Non-Ischemic Cardiomyopathy

Variable	Prior to CRT Implantation	Post CRT Implantation	P value
NYHA class (percent)			< 0.001
I/II		100	
III/IV	100		
Hospital admission (percent)	100	9.9	< 0.001
No hospital admission (percent)		90.91	
QRS duration (ms ,SD)	156 \pm 6	110.64 \pm 7.13	< 0.001
LVEF with Eyeball method	23.17% \pm 7.16	35% \pm 7.41	< 0.001
LVEF with Simpson method	28.25% \pm 7.7	39.31% \pm 7.29	< 0.001
LVESV (mL)	141.15 \pm 61.01	99.81 \pm 59.19	0.009
LVEDV (mL)	149.71 \pm 73.59	115.98 \pm 57.48	0.01
GLS (%)	-9.02 \pm 2.81	-11.45 \pm 2.33	0.007
Sphericity index (%)	0.64 \pm 0.07	0.54 \pm 0.12	0.004
Septal flash (%)	54	30.56	0.08

Abbreviations: GLS, global longitudinal strain; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end systolic volume; NYHA, New York Heart Association.

implantation might be the predictor of a positive response to CRT in patients with NICM (sensitivity = 85% and specificity = 50%). Additionally, SI = 0.59 with a sensitivity of 83.3% and specificity of 50% was associated with better response in patients receiving CRT.

Based on the results, CRT responders comprised 63.34% of the patients under the present investigation. Similarly, Gabriel et al. (7) conducted a study in 2014 and reported that the response rate was equal to 59%.

In the current study, improvement in NYHA FC was accompanied by a significant increase in LVEF ($P < 0.001$) and a reduction in LVEDV ($P = 0.01$). These findings were comparable with those obtained by Carluccio et al. However, in contrast to their results, those of the present study revealed no significant correlation between the presence of SF at baseline and CRT response. This might be due to the small number of patients enrolled into the current study.

The principal finding of this study was that the presence of GLS less than -10.48 (with more absolute values) at baseline was an independent predictor of CRT response. Chun-Yan et al. (8) demonstrated that with the sensitivity of 73.0% and specificity of 73.4%, GLS of -13% predicted response to CRT in patients with ischemic cardiomyopathy. Recently, another study by Bijl et al. (9) indicated that improvement in GLS was associated with better response to CRT. These findings have not been studied yet among patients with NICM.

It is well-known that as the heart remodels, the SI declines (9). In addition, increase in remodeling decreases the chance of response to CRT. In the current study, SI less than 0.59 was associated with better response to CRT in patients with NICM. However, this was a trend and did not reach statistical significance.

5.1. Conclusion

In conclusion, the present study results indicated that echocardiographic parameters including GLS and SI might help in selecting patients for CRT.

5.2. Limitation of Study

This was a single center study with a limited number of patients, in which multivariate analysis was not performed. Hence, the power of the study was low despite the statistically significant p-values. For drawing more exclusive conclusions, these parameters are recommended to be evaluated in further studies with larger sample sizes and longer follow-up periods.

5.3. Ethical Approval

IR.TUMS.VCR.REC.1395.1326

5.4. Informed Consent

Written informed consent forms were obtained from all patients.

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Authors' Contribution

R.V. collected the data. M.E. made the initial idea. R.SB. performed the echocardiographic examinations. E.S. carried out the literature research and wrote the initial draft of the manuscript. MR helped with the initial draft. R.M. implanted the CRT, corrected and improved the draft, and submitted the manuscript. All authors read and approved the final manuscript.

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