A Study To Assess Major Adverse Cardiovascular Events In Heart Failure With Reduced Ejection Fraction After Cardiac Resynchronization Therapy

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Abstract

Objective

Cardiac resynchronization therapy (CRT) is an established treatment for heart failure patients with left ventricular dysfunction. However, the degree of major adverse cardiovascular events (MACE) post-CRT varies among patients. This study aims to compare MACE on follow-up after cardiac resynchronization therapy.

Methods

This observational study was conducted over one year, including 72 patients with heart failure and reduced ejection fraction after CRT in a tertiary care institute. Major adverse cardiovascular events were defined as heart failure hospitalization, recurrent myocardial infarction, and cardiovascular death on follow-up.

Results

Heart failure hospitalization occurred in 65.28% (47 cases) at 3 months and 47.22% (34 cases) at 6 months, while no cases of recurrent myocardial infarction, cardiovascular death, or all-cause mortality were observed during follow-up. Univariate regression identified key predictors of MACE on follow-up. Higher pre-CRT TAPSE was significantly associated with reduced MACE risk (3-month odds ratio: 0.764; 6-month odds ratio: 0.577); while longer QRS duration and elevated NT-ProBNP levels, were associated with increased MACE at both 3 months (odds ratios were 1.107 and 1.0004 respectively) and 6 months (odds ratios: 1.089 and 1.0003 respectively). Patients with LV-ESV reduction ≥15%, LVEF increase ≥5%, and non-ischemic etiology had the lowest MACE risk at 3 and 6-months follow-up. The multivariate logistic regression analysis revealed the NT-proBNP as a significant independent factor predicting MACE both at 3 and 6 months with an adjusted odds ratio of 1.0003 (1.0001-1.0006) and 1.0002 (1.0004-1.0004) respectively.

Conclusions

Cardiac resynchronization therapy (CRT) effectively reduces heart failure hospitalizations on follow-up. NT-proBNP emerged as a robust independent predictor of MACE at 3 and 6 months, emphasizing its role in pre and post-CRT risk assessment.

INTRODUCTION

Heart failure with reduced ejection fraction (HFrEF) remains a major global health concern, with high morbidity and mortality despite advancements in medical therapy. Cardiac resynchronization therapy (CRT) has emerged as an effective intervention to improve cardiac function and reduce symptoms in patients with left ventricular dysfunction and electrical dyssynchrony. However, the degree of clinical benefit varies among patients, with some experiencing major adverse cardiovascular events (MACE) post-CRT, including heart failure hospitalizations, recurrent myocardial infarction, and cardiovascular death. Identifying key predictors of MACE is crucial for optimizing patient selection and improving post-CRT outcomes. This study aims to evaluate the occurrence of MACE, including heart failure hospitalization, recurrent myocardial infarction, and cardiovascular death, in patients with HFrEF following CRT. By analyzing patient characteristics and echocardiographic parameters,

this study seeks to identify potential predictors of adverse outcomes, contributing to improved risk stratification and patient management post-CRT.

METHODS

This observational study was conducted in the cardiology department of a tertiary care institute after receiving approval from the institutional ethics committee. The study spanned 12 months and included 72 cases of HFrEF treated with CRT. Patients were eligible for inclusion if they had symptomatic heart failure classified as New York Heart Association (NYHA) class II or higher, a left ventricular ejection fraction (LVEF) of <35% despite receiving optimal medical therapy, and a QRS duration >130 ms on electrocardiography. Only patients in sinus rhythm before inclusion and during follow-up echocardiography were enrolled.

Patients were excluded if they refused to provide written informed consent. Those with organic valvular heart disease, a prior pacemaker or implantable cardioverter-defibrillator, right bundle branch block (RBBB), or atrial fibrillation on electrocardiogram (ECG) were also excluded. A target sample size of 70 cases was required to predict MACE following CRT. Detailed clinical history, baseline characteristics including demographics, clinical examination findings, routine investigations, electrocardiography, and two-dimensional transthoracic echocardiography were recorded. Tricuspid annular plane systolic excursion (TAPSE) was measured using M-mode recordings of the lateral tricuspid annulus in a right ventricular-focused view. The patients were followed-up for 6 months to assess MACE (major adverse cardiovascular events).

Statistical Analysis

MACE-related statistical analysis was conducted using the Chi-square test or Fisher's exact test for categorical variables and ANOVA for continuous variables, depending on data distribution. Univariate and multivariate logistic regression analyses were performed to identify significant MACE risk factors. Data analysis was conducted using SPSS version 25.0, with $p < 0.05$ considered statistically significant.

RESULTS

In this study, out of 72 patients, 62.50% were males (45 cases) and 37.50% were females (27 cases). The baseline mean ± SD values for key clinical and biochemical parameters were as follows: age 57.96 ± 11.8 years, BMI 23.68 ± 2.91 kg/m², QRS duration 161.61 ± 9.88 ms, and NT-ProBNP 10,269.76 ± 10,658.14 ng/L.

Regarding risk factors and comorbidities, diabetes mellitus was observed in 35 cases (49.30%), arterial hypertension in 26 cases (36.62%), dyslipidemia in 22 cases (30.56%), active smoking in 22 cases (30.56%), and ischemic heart failure etiology in 21 cases (29.17%). All patients received guideline-directed optimal medical therapy. At baseline, NYHA class III/IV symptoms were present in 68 cases (94.44%), including NYHA class III in 45 cases (62.50%), ambulatory class IV symptoms in 23 cases (31.94%), and NYHA class II in 4 cases (5.56%).

Heart failure hospitalization occurred in 65.28% (47 cases) at 3 months and 47.22% (34 cases) at 6 months, while no cases of recurrent myocardial infarction, cardiovascular death, or all-cause mortality were observed during follow-up. Univariate regression identified key predictors of MACE on follow-up. Higher pre-CRT TAPSE was significantly associated with reduced MACE risk (3-month odds ratio: 0.764; 6-month odds ratio: 0.577); while longer QRS duration and elevated NT-ProBNP levels, were associated with increased MACE at both 3 months (odds ratios were 1.107 and 1.0004 respectively) and 6 months (odds ratios: 1.089 and 1.0003 respectively) (table 1,3). Patients with LV-ESV reduction ≥15%, LVEF increase ≥5%, and non-ischemic etiology had the lowest MACE risk at 3 and 6-months follow-up (table 1,3). The multivariate logistic regression analysis revealed the NT-proBNP as a significant independent factor predicting MACE both at 3 and 6 months with an adjusted odds ratio of 1.0003 (1.0001-1.0006) and 1.0002 (1.0004-1.0004) respectively (table 2,4). With rising NT-ProBNP levels, the risk of MACE during follow-up increases significantly.

DISCUSSION

Cardiac resynchronization therapy (CRT) is an established treatment for patients with heart failure with reduced ejection fraction (HFrEF) and left ventricular dyssynchrony. Despite its therapeutic benefits, some patients continue to experience major adverse cardiovascular events (MACE) after CRT. Identifying factors that contribute to adverse outcomes remains essential for improving patient selection and optimizing therapeutic strategies.

NT-ProBNP serves as a reliable indicator of myocardial strain and volume overload in heart failure patients. In this study, elevated NT-ProBNP levels before CRT implantation were associated with a higher likelihood of MACE at 3-month and 6-month follow-ups. These findings are consistent with previous research demonstrating that NT-ProBNP is closely related to heart failure severity and response to CRT[1,2]. Persistently high NT-ProBNP levels may indicate ongoing myocardial dysfunction and a limited response to CRT, reinforcing its value as a predictor of adverse outcomes.

QRS duration is a well-established marker of electrical dyssynchrony and response to CRT. The present study observed a significant association between prolonged QRS duration and increased MACE risk. This finding is supported by previous studies indicating that patients with QRS duration exceeding 150 ms tend to benefit more from CRT, whereas those with shorter QRS durations may experience a less favourable response[3,4]. The persistence of electrical dyssynchrony despite CRT may contribute to unfavourable cardiac remodeling and an increased risk of adverse events in these patients.

Right ventricular (RV) function is an important determinant of heart failure prognosis. In this study, tricuspid annular plane systolic excursion (TAPSE) was inversely associated with MACE, suggesting that patients with preserved RV function had better post-CRT outcomes. These results are in agreement with earlier studies emphasizing the role of RV function in predicting heart failure progression and hospitalization rates following CRT[5]. The findings highlight the need to incorporate RV function assessment into CRT eligibility criteria to improve patient outcomes.

Patients who exhibited significant reductions in LV end-systolic volume (LV-ESV) and improvements in LVEF had a lower incidence of MACE in this study. These observations are consistent with prior research demonstrating that CRT responders who experience substantial structural remodeling achieve better long-term clinical outcomes, including reduced hospitalization rates and improved survival[6,7]. The assessment of early echocardiographic changes post-CRT may provide useful insights into long-term prognosis and guide clinical management decisions.

Several studies have reported that patients with non-ischemic cardiomyopathy exhibit greater reverse remodeling and better survival following CRT compared to those with ischemic etiology. However, in this study, ischemic etiology did not emerge as a significant determinant of MACE. Previous research has suggested that non-ischemic patients may have greater myocardial viability and a more favourable response to CRT[1]. The variations observed in this study may be influenced by differences in patient characteristics and adherence to guideline-directed medical therapy.

These findings emphasize the need for a comprehensive pre-CRT evaluation incorporating NT-ProBNP, QRS duration, and RV function to refine patient selection and improve outcomes. The strong association between left ventricular structural changes and reduced MACE further highlights the importance of post-CRT monitoring to identify

responders early. Future studies with larger cohorts and extended follow-up durations are needed to further refine CRT response criteria and validate the identified prognostic markers.

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Table 1. Univariate logistic regression to assess significant risk factors of MACE at 3 months.

Variables	Beta coefficient	Standard error	P value	Odds ratio	Odds ratio Lower bound (95%)	Odds ratio Upper bound (95%)
Age (years)	0.006	0.021	0.775	1.006	0.965	1.048
ECG (LBBB/QRS Duration)	0.102	0.035	0.003	1.107	1.035	1.185

Pre-CRT (ms)						
NT-ProBNP (ng/L)	0.0004	0.0001	0.002	1.0004	1.0002	1.0007
TAPSE (mm) Pre-CRT	-0.269	0.091	0.003	0.764	0.640	0.913
Gender						
Female				1.000		
Male	0.415	0.506	0.412	1.514	0.562	4.082
Ischemic etiology	-0.492	0.534	0.357	0.612	0.215	1.740
NYHA class III/IV	1.484	1.103	0.179	4.409	0.507	38.330
LV-ESV reduction >=15%	-1.943	0.604	0.001	0.143	0.044	0.468
Absolute increase in LVEF >=5%	-1.955	0.928	0.035	0.142	0.023	0.873

Table 2. Multivariate logistic regression to assess significant risk factors of MACE at 3 months.

Variables	**Beta coefficient**	**Standard error**	**P value**	**Odds ratio**	**Odds ratio Lower bound (95%)**	**Odds ratio Upper bound (95%)**
ECG (LBBB/QRS Duration) Pre-CRT (ms)	0.030	0.062	0.626	1.031	0.912	1.165
NT-ProBNP (ng/L)	0.0003	0.0001	0.009	1.0003	1.0001	1.0006
TAPSE (mm) Pre-CRT	0.211	0.181	0.244	1.234	0.866	1.759
LV-ESV reduction >=15%	-0.129	1.097	0.907	0.879	0.102	7.552
Absolute increase in LVEF >=5%	-1.035	1.609	0.520	0.355	0.015	8.312

Table 3. Univariate logistic regression to assess significant risk factors of MACE at 6 months.

Variables	**Beta coefficient**	**Standard error**	**P value**	**Odds ratio**	**Odds ratio Lower bound (95%)**	**Odds ratio Upper bound (95%)**
Age (years)	0.002	0.020	0.931	1.002	0.963	1.042

ECG (LBBB/QRS Duration) pre-CRT (ms)	0.085	0.029	0.004	1.089	1.028	1.153
NT-ProBNP (ng/L)	0.0003	0.0001	<0.0001	1.0003	1.0002	1.0005
TAPSE (mm) Pre-CRT	-0.550	0.130	<0.0001	0.577	0.447	0.745
Gender						
Female				1.000		
Male	-0.059	0.487	0.903	0.943	0.363	2.450
Ischemic etiology	-1.091	0.556	0.049	0.336	0.113	1.000
NYHA class III/IV	3.341	2.663	0.210	28.253	0.153	5220.881
LV-ESV reduction >=15%	-2.985	0.926	0.001	0.051	0.008	0.310
Absolute increase in LVEF >=5%	-3.789	3.472	0.275	0.023	0.000	20.404

Table 4. Multivariate logistic regression to assess significant risk factors of MACE at 6 months.

Variables	**Beta coefficient**	**Standard error**	**P value**	**Odds ratio**	**Odds ratio Lower bound (95%)**	**Odds ratio Upper bound (95%)**
ECG (LBBB/QRS Duration) Pre-CRT (ms)	-0.018	0.062	0.767	0.982	0.869	1.109
NT-ProBNP (ng/L)	0.0002	0.0001	0.015	1.0002	1.00004	1.0004
TAPSE (mm) Pre-CRT	-0.252	0.174	0.147	0.777	0.553	1.093
Ischemic etiology	-1.789	1.277	0.161	0.167	0.014	2.042
LV-ESV reduction >=15%	-1.594	1.412	0.259	0.203	0.013	3.233