



ORIGINAL ARTICLE

What happens to non-responders in cardiac resynchronization therapy?



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KEYWORDS

Heart failure;
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Abstract

Introduction and Objectives: Left ventricular reverse remodeling (LVRR) is strongly related to the long-term prognosis of patients undergoing cardiac resynchronization therapy (CRT). The aim of this study was to assess the long-term clinical outcome of patients without LVRR at six months after CRT implantation and to determine the prognostic impact of clinical response in this population.

Methods: We analyzed 178 consecutive patients who underwent successful CRT device implantation (age 64 ± 11 years; 69% male; 89% in New York Heart Association [NYHA] functional class III; 35% with ischemic cardiomyopathy). Clinical status and echocardiographic parameters were determined before and six months after CRT implantation. We identified those without criteria for LVRR ($\geq 10\%$ increase in left ventricular ejection fraction with $\geq 15\%$ reduction in left ventricular end-systolic diameter compared to baseline). Clinical responders were defined by a sustained improvement of at least one NYHA functional class.

Results: At six-month assessment after CRT, 109 (61%) patients showed LVRR. During a mean follow-up of 56 ± 21 months, 47 (26%) patients died, with higher mortality in the group without LVRR (36% vs. 20%, $p=0.023$). Clinical response was greater in patients with LVRR (88% vs. 55%, $p<0.001$). In patients without LVRR, clinical response to CRT was the strongest independent predictor of survival (hazard ratio: 0.120; 95% confidence interval: 0.039-0.366; $p<0.001$).

Conclusion: Although patients without LVRR six months after CRT implantation had a worse prognosis, with higher all-cause mortality, clinical response can be an independent predictor of survival in this population.

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PALAVRAS-CHAVE

Insuficiência cardíaca;
Terapia de ressincronização cardíaca;
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Prognóstico

O que acontece aos não respondedores na terapia de ressincronização cardíaca?**Resumo**

Introdução e objetivos: A remodelagem reversa do ventrículo esquerdo (RRVE) tem sido fortemente relacionada com o prognóstico em longo prazo de doentes submetidos à terapia de ressincronização cardíaca (TRC). O objetivo deste estudo foi avaliar o desfecho clínico a longo prazo de doentes sem RRVE aos seis meses após a implantação de TRC e definir o impacto prognóstico da resposta clínica nessa população.

Métodos: Foram analisados 178 doentes submetidos à implantação de TRC (64 ± 11 anos, 69% do sexo masculino, 89% da classe funcional III da *New York Heart Association* (NYHA), 35% com cardiomiopatia isquêmica). O estadió clínico e a avaliação ecocardiográfica foram feitos antes e após seis meses de TRC. Foram identificados aqueles que não tinham critérios de RRVE (aumento $\geq 10\%$ na fração de ejeção com uma redução de $\geq 15\%$ na dimensão sistólica do ventrículo esquerdo). Os respondedores clínicos foram definidos por uma melhoria sustentada de pelo menos uma classe funcional NYHA.

Resultados: Aos seis meses de avaliação após TRC, 109 (61%) doentes apresentaram RRVE. Durante um seguimento médio de 56 ± 21 meses, 47 (26%) doentes morreram, com maior mortalidade no grupo sem RRVE (36% versus 20%, $p = 0,023$). A resposta clínica foi maior no grupo de doentes com RRVE (88% versus 55%, $p < 0,001$). Em doentes sem RRVE, a resposta clínica à TRC foi o maior preditor independente de sobrevida (*hazard ratio*: 0,120; IC95%: 0,039-0,366; $p < 0,001$).

Conclusão: Embora doentes sem RRVE seis meses após a implantação da TRC apresentem um pior prognóstico com maior taxa de mortalidade por todas as causas, a resposta clínica pode ser um preditor independente de sobrevida nessa população.

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List of abbreviations

AV	atrioventricular
BMI	body mass index
CRT	cardiac resynchronization therapy
HF	heart failure
LBBS	left bundle branch block
LVEDD	left ventricular end-diastolic diameter
LVEF	left ventricular ejection fraction
LVESV	left ventricular end-systolic volume
LVRR	left ventricular reverse remodeling
NYHA	New York Heart Association
VV	interventricular

Introduction

Cardiac resynchronization therapy (CRT) is recommended by current guidelines for symptomatic heart failure (HF) with left ventricular ejection fraction (LVEF) $\leq 35\%$ and prolonged QRS interval.^{1,2} CRT is effective in improving HF symptoms, exercise capacity, quality of life and cardiac function, as well as reducing HF hospitalizations and death.³⁻⁸ Trials have assessed the efficacy of CRT by means of improvement in clinical status and/or reduction in left ventricular end-systolic volume (LVESV) at mid-term follow-up.⁹⁻¹² Clinical and echocardiographic responses to CRT may not coincide,

but left ventricular reverse remodeling (LVRR) is considered a powerful indicator of clinical outcomes.¹³⁻¹⁵ Up to 40% of patients will not experience significant reduction in left ventricular chamber size and are defined as CRT non-responders.¹⁶ Although this population has a poor prognosis, little is known about the factors that influence their outcomes. The aim of this study was to assess the long-term clinical outcome of patients without LVRR at six months after CRT implantation and to determine the prognostic impact of clinical response in this population.

Methods

This was a single-center study of patients who underwent successful CRT defibrillator device implantation between 2004 and 2012, a total of 178 consecutive CRT recipients. Patient data were prospectively collected in our cardiology department's information system and analyzed retrospectively. Patients were selected for CRT if they met currently recommended criteria: (1) LVEF $\leq 35\%$; (2) symptoms of HF, defined as New York Heart Association (NYHA) class II-IV despite optimal medical therapy; and (3) QRS duration ≥ 120 ms. Patients were classified as ischemic in the presence of significant coronary artery disease ($>50\%$ stenosis of two or more epicardial vessels or the left main, or $>50\%$ stenosis of the proximal left anterior descending coronary artery on coronary angiography, and/or a history of previous myocardial infarction or myocardial revascularization). All other patients were classified as non-ischemic. Leads were placed

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