



ORIGINAL ARTICLE

## Time to left ventricular reverse remodeling after cardiac resynchronization therapy: Better late than never



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### KEYWORDS

Cardiac resynchronization therapy;  
Left ventricular reverse remodeling;  
Time course

### Abstract

**Introduction:** Left ventricular reverse remodeling (LVRR), defined as reduction of end-diastolic and end-systolic dimensions and improvement of ejection fraction, is associated with the prognostic implications of cardiac resynchronization therapy (CRT). The time course of LVRR remains poorly characterized. Nevertheless, it has been suggested that it occurs  $\leq 6$  months after CRT.

**Objective:** To characterize the long-term echocardiographic and clinical evolution of patients with LVRR occurring  $>6$  months after CRT and to identify predictors of a delayed LVRR response.  
**Methods:** A total of 127 consecutive patients after successful CRT implantation were divided into three groups according to LVRR response: Group A, 19 patients (15%) with LVRR after  $>6$  months (late LVRR); Group B, 58 patients (46%) with LVRR before 6 months (early LVRR); and Group C, 50 patients (39%) without LVRR during follow-up (no LVRR).

**Results:** The late LVRR group was older, more often had ischemic etiology and fewer patients were in NYHA class  $\leq$  II. Overall, group A presented LVRR between group B and C. This was also the case with the percentage of clinical response (68.4% vs. 94.8% vs. 38.3%, respectively,  $p < 0.001$ ), and hospital readmissions due to decompensated heart failure (31.6% vs. 12.1% vs. 57.1%, respectively,  $p < 0.001$ ). Ischemic etiology (OR 0.044;  $p = 0.013$ ) and NYHA functional class  $<$  III (OR 0.056;  $p = 0.063$ ) were the variables with the highest predictive value for late LVRR.

**Conclusions:** Late LVRR has better clinical and echocardiographic outcomes than no LVRR, although with a suboptimal response compared to the early LVRR population. Ischemic etiology and NYHA functional class  $<$  III are predictors of late LVRR.

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**PALAVRAS-CHAVE**

Terapêutica  
de ressincronização  
cardíaca;  
Remodelagem inversa  
do ventrículo  
esquerdo;  
Evolução temporal

**Tempo para a remodelagem inversa do ventrículo esquerdo: mais vale tarde do que nunca****Resumo**

**Introdução:** A remodelagem inversa do ventrículo esquerdo (RIVE), definida pela redução das dimensões telediastólicas e telessistólicas e pela melhoria da fração de ejeção, tem sido associada às implicações prognósticas da terapia de ressincronização cardíaca (TRC). A evolução temporal da RIVE permanece um processo pouco caracterizado. No entanto, tem sido sugerido que ocorrerá num período  $\leq 6$  meses após TRC.

**Objetivos:** Caracterizar a longo prazo a evolução ecocardiográfica e clínica dos pacientes (P) com evidência de RIVE, num período  $>6$  meses após TRC, e identificar preditores de uma resposta de RIVE tardia.

**Métodos:** Cento e vinte e sete P consecutivos, após implantação bem-sucedida de TRC, foram divididos em três grupos, de acordo com a resposta de RIVE: grupo A, 19P (15%) com RIVE após seis meses (RIVE tardia); grupo B, 58P (46%) com RIVE antes dos seis meses (RIVE precoce) e grupo C, 50P (39%) sem RIVE durante o *follow-up* (sem RIVE).

**Resultados:** O grupo da RIVE tardia era mais velho, tinha mais etiologia isquémica e menos P em classe NYHA  $\geq$  III. Globalmente, o grupo A apresentou um grau de RIVE entre os grupos B e C. O mesmo ocorreu em relação ao grau da resposta clínica (68,4 versus 94,8 versus 38,3%, respetivamente,  $p < 0,001$ ) e às readmissões hospitalares por descompensação da insuficiência cardíaca (31,6 versus 12,1 versus 57,1%, respetivamente,  $p < 0,001$ ). A etiologia isquémica (OR 0,044;  $p = 0,013$ ) e a classe funcional  $<$  III (OR 0,056;  $p = 0,063$ ) foram as variáveis com maior valor preditor para a ocorrência de RIVE tardia.

**Conclusões:** A RIVE tardia tem uma melhor resposta clínica e ecocardiográfica do que a ausência de RIVE, embora com uma resposta subótima, quando comparada com a população com RIVE precoce. A etiologia isquémica e uma classe NYHA  $<$  III foram preditores de RIVE tardia.

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**Introduction**

Cardiac resynchronization therapy (CRT) has become an effective non-pharmacological treatment for patients with impaired left ventricular ejection fraction (LVEF), prolonged QRS duration and New York Heart Association (NYHA) functional class  $\geq$  III symptoms of heart failure (HF) despite optimal medical therapy. Large multicenter clinical trials have shown that CRT can mitigate HF symptoms, improve exercise capacity and quality of life, reduce the incidence of hospitalizations due to HF and decrease mortality.<sup>1-4</sup> Most of these benefits are thought to be related to left ventricular (LV) reverse remodeling (LVRR), a response characterized by a reduction in LV end-diastolic (LVEDD) and end-systolic (LVESD) dimensions and volumes and improvement of LV ejection fraction (LVEF).<sup>5-7</sup> The time course of this phenomenon remains poorly characterized. It has been suggested that the structural and functional changes associated with LVRR occur early after CRT and are more pronounced before the six-month landmark, a time by which the extent of reverse remodeling has been shown to predict long-term prognosis in these patients.<sup>6-9</sup> Nevertheless, a variable proportion of eligible patients fail to respond initially but appear to develop LVRR after six months following CRT implantation. This population with late LVRR, who are not included in the already known proportion (around 30%) of non-responders to CRT, correspond to a different spectrum of individuals that, to the best of our knowledge, has

never been directly analyzed in a prospective study. To overcome this limitation, the present study characterizes the timing of LVRR occurrence and assesses the long-term echocardiographic and clinical evolution of patients with LVRR occurring  $>6$  months after CRT implantation. We also sought to identify potentially related clinical characteristics that might predict a late response to CRT.

**Methods**

This is a single-center analysis of patients who underwent successful CRT device implantation. A total of 127 consecutive CRT recipients were included and patient data were prospectively collected in the information system of our cardiology department and analyzed. Patients were selected for CRT if they met currently recommended criteria: (1) LVEF  $<35\%$ ; (2) symptoms of HF, defined as NYHA class II-IV despite optimal medical therapy; and (3) QRS duration  $\geq 120$  ms. Patients were classified as ischemic in the presence of significant coronary artery disease ( $>50\%$  stenosis of two or more epicardial vessels or  $>50\%$  left main or proximal left anterior descending coronary artery stenosis on coronary angiography and/or a history of previous myocardial infarction or revascularization). Other patients were classified as non-ischemic. All leads were placed transvenously via the subclavian and cephalic route using fluoroscopy. The right ventricular lead was positioned in the apex or mid septum. The LV lead was placed with an over-the-wire

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