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ORIGINAL ARTICLE

## Does permanent atrial fibrillation modify response to cardiac resynchronization therapy in heart failure patients?

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### KEYWORDS

Heart failure;  
Cardiac  
resynchronization;  
Atrial fibrillation;  
Responder

### Abstract

**Introduction:** The benefits of cardiac resynchronization therapy (CRT) documented in heart failure (HF) may be influenced by atrial fibrillation (AF). We aimed to compare CRT response in patients in AF and in sinus rhythm (SR).

**Methods:** We prospectively studied 101 HF patients treated by CRT. Rates of clinical, echocardiographic and functional response, baseline NYHA class and variation, left ventricular ejection fraction, volumes and mass, atrial volumes, cardiopulmonary exercise test (CPET) duration (CPET dur), peak oxygen consumption (VO<sub>2</sub>max) and ventilatory efficiency (VE/VCO<sub>2</sub> slope) were compared between AF and SR patients, before and at three and six months after implantation of a CRT device.

**Results:** All patients achieved  $\geq 95\%$  biventricular pacing, and 5.7% underwent atrioventricular junction ablation. Patients were divided into AF (n=35) and SR (n=66) groups; AF patients were older, with larger atrial volumes and lower CPET dur and VO<sub>2</sub>max before CRT. The percentages of clinical and echocardiographic responders were similar in the two groups, but there were more functional responders in the AF group (71% vs. 39% in SR patients; p=0.012). In SR patients, left atrial volume and left ventricular mass were significantly reduced (p=0.015 and p=0.021, respectively), whereas in AF patients, CPET dur (p=0.003) and VO<sub>2</sub>max (p=0.001; 0.083 age-adjusted) showed larger increases.

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## PALAVRAS-CHAVE

Insuficiência cardíaca;  
Ressincronização cardíaca;  
Fibrilhação auricular;  
Respondedor

**Conclusion:** Clinical and echocardiographic response rates were similar in SR and AF patients, with a better functional response in AF. Improvement in left ventricular function and volumes occurred in both groups, but left ventricular mass reduction and left atrial reverse remodeling were seen exclusively in SR patients (ClinicalTrials.gov identifier: NCT02413151; FCT code: PTDC/DES/120249/2010).

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## A fibrilhação auricular modifica a resposta à terapêutica de ressincronização cardíaca em doentes com insuficiência cardíaca?

### Resumo

**Introdução:** Os benefícios da terapêutica de ressincronização cardíaca (TRC), documentados na insuficiência cardíaca (IC), poderão ser influenciados pela fibrilhação auricular (FA). Pretendemos avaliar comparativamente efeitos TRC em doentes em FA e em ritmo sinusal (RS).

**Métodos:** Foram estudados prospetivamente 101 doentes submetidos a TRC. Percentagens de respondedores clínicos, ecocardiográficos e funcionais, valores basais e variação de classe NYHA, fração de ejeção, volumes e massa ventriculares esquerdos, volumes auriculares, duração da prova de esforço cardiorrespiratória (PECR dur), consumo pico de oxigénio (VO2p) e eficiência ventilatória de esforço (VE/VCO2) foram comparados entre grupos FA e RS, pré-implantação TRC e nos seis meses após implantação.

**Resultados:** Os doentes tiveram percentagens de *pacing* biventricular  $\geq 95\%$ , com 5,7% de ablação auriculoventricular juncional. Definimos grupo FA (n=35) e grupo RS (n=66), tendo os doentes com FA idade superior, maiores volumes auriculares, menores PECR dur e VO2p pré-CRT. Percentagens de respondedores clínicos e ecocardiográficos foram idênticas nos dois grupos, mas de respondedores funcionais foram superiores nos doentes FA (71 *versus* 39% no grupo RS; p=0,012). Nos doentes RS verificou-se a redução significativa do volume auricular esquerdo e da massa ventricular esquerda (p=0,015 e p=0,021, respetivamente) e nos doentes com FA maior aumento da PECR dur (p=0,003) e VO2p (p=0,001; p=0,083 ajustado para idade).

**Conclusão:** As respostas clínica e ecocardiográfica à TRC foram semelhantes nos doentes FA e RS, com resposta funcional superior em FA. A melhoria de função e dimensões ventriculares esquerdas foi idêntica nos dois grupos, contudo redução de massa ventricular esquerda e remodelagem inversa auricular esquerda foram exclusivas de doentes RS (ClinicalTrials.gov Identifier: NCT02413151; FCT code: PTDC/DES/120249/2010).

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## Introduction

Cardiac resynchronization therapy (CRT) is an important device-based, non-pharmacological treatment for chronic heart failure (HF). The multiple benefits of CRT in selected HF patients under optimized pharmacologic therapy include improvement in symptoms and quality of life, left ventricular (LV) remodeling and decreased mortality and hospital admissions for HF, and have been established by multiple large trials,<sup>1-5</sup> leading to its recommendation in current guidelines.<sup>6</sup> An important feature in HF is the presence of atrial fibrillation (AF), the arrhythmia most frequently associated with HF, which affects up to 45%-50% of patients, depending on the severity of HF.<sup>7,8</sup> For HF patients still in sinus rhythm (SR), the annual incidence of AF is approximately 5%.<sup>9</sup> AF is negatively related to prognosis, although some authors do not consider it an

independent prognostic predictive factor after correction for age and comorbidities.<sup>10</sup> Atrial arrhythmias, if not appropriately managed, may have a negative impact on the clinical benefits of CRT,<sup>11</sup> since, in AF patients, CRT can only correct intra- and interventricular dyssynchrony. CRT is also hampered by high intrinsic ventricular rates and irregularity, leading to reduced capture, fusion and pseudo-fusion, and hence less effective biventricular pacing.<sup>12</sup>

Although the evidence from large randomized controlled trials is weak,<sup>13,14</sup> and some authors have argued that HF patients in AF may respond less well to CRT,<sup>15-20</sup> the European Society of Cardiology (ESC) guidelines recommend that this therapy should also be used for AF patients, as long as atrioventricular (AV) junction ablation is added in patients in whom continuous biventricular pacing is lost.<sup>6</sup> Recently, the CERTIFY study<sup>21</sup> showed that long-term survival after CRT among patients with AF and AV junction ablation is similar to

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