



REVIEW ARTICLE

## Cardiac resynchronization therapy in patients with atrial fibrillation: A meta-analysis



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### KEYWORDS

Atrial fibrillation;  
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Atrioventricular  
nodal ablation;  
Meta-analysis

### Abstract

**Background and Objective:** To combine the results of the best scientific evidence in order to compare the effects of cardiac resynchronization therapy (CRT) in heart failure patients with atrial fibrillation (AF) and in sinus rhythm (SR) and to determine the effect of atrioventricular nodal ablation in AF patients.

**Methods:** The electronic databases PubMed, B-On and Cochrane CENTRAL were searched, and manual searches were performed, for randomized controlled trials and cohort studies up to November 2012. The endpoints analyzed were all-cause and cardiovascular mortality and response to CRT.

**Results:** We included 19 studies involving 5324 patients: 1399 in AF and 3925 in SR. All-cause mortality was more likely in patients with AF compared to patients in SR ( $OR=1.69$ ; 95% CI: 1.20–2.37;  $p=0.002$ ). There were no statistically significant differences in cardiovascular mortality ( $OR=1.36$ ; 95% CI: 0.92–2.01;  $p=0.12$ ). AF was associated with an increased likelihood of lack of response to CRT ( $OR=1.41$ ; 95% CI: 1.15–1.73;  $p=0.001$ ). Among subjects with AF, ablation of the atrioventricular node was associated with a reduction in all-cause mortality ( $OR=0.42$ ; 95% CI: 0.22–0.80;  $p=0.008$ ), cardiovascular death ( $OR=0.39$ ; 95% CI: 0.20–0.75;  $p=0.005$ ) and the number of non-responders to CRT ( $OR=0.30$ ; 95% CI: 0.10–0.90;  $p=0.03$ ).

**Conclusions:** The presence of AF is associated with increased likelihood of all-cause death and non-response to CRT, compared to patients in SR. However, many patients with AF benefit from CRT. Atrioventricular nodal ablation appears to increase the benefits of CRT in patients with AF.  
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**PALAVRAS-CHAVE**

Fibrilhação auricular;  
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cardíaca;  
Ablação  
auriculoventricular;  
Metanálise

**Terapêutica de ressincronização cardíaca em doentes com fibrilhação auricular: uma metanálise****Resumo**

**Introdução e objetivos:** Combinar os resultados da melhor evidência científica de forma a comparar os efeitos da terapêutica de ressincronização cardíaca (TRC) em doentes com insuficiência cardíaca em fibrilhação auricular (FA) e em ritmo sinusal (RS) e determinar a influência da ablação auriculoventricular (AV) no grupo de doentes em FA.

**Métodos:** A pesquisa realizou-se nas bases de dados eletrónicas da PubMed, B-On e CENTRAL e de forma manual, incluindo ensaios clínicos controlados aleatorizados e estudos de coorte até novembro de 2012. Analisou-se a mortalidade total e cardiovascular e a resposta à TRC.

**Resultados:** Foram incluídos 19 estudos que envolveram 5324 pacientes: 1399 em FA e 3925 em RS. O grupo com doentes em FA apresenta maior risco de mortalidade total, comparativamente ao grupo de doentes em RS ( $OR=1,69$ ; IC 1,20–2,37,  $p=0,002$ ). Não foram verificadas diferenças estatisticamente significativas quanto à mortalidade cardiovascular ( $OR=1,36$ , IC 0,92–2,01,  $p=0,12$ ). A não resposta à TRC foi maior no grupo em FA ( $OR=1,41$ ; IC 1,15–1,73;  $p=0,001$ ). Entre os indivíduos em FA, a ablação do nódulo auriculoventricular foi associada à redução da mortalidade total ( $OR=0,42$ ; IC 0,22–0,80;  $p=0,008$ ), mortalidade cardiovascular ( $OR=0,39$ ; IC 0,20–0,75;  $p=0,005$ ) e número de não respondedores à TRC ( $OR=0,30$ ; IC 0,10–0,90;  $p=0,03$ ).

**Conclusões:** A presença de FA está associada a maior probabilidade de morte por todas as causas e de não resposta à TRC, comparativamente aos doentes em RS. Contudo, um número significativo de doentes em FA beneficia da TRC. A ablação AV parece aumentar os benefícios da TRC nos doentes com FA.

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## Introduction

Atrial fibrillation (AF) is the most common arrhythmia in patients with heart failure (HF) and is associated with increased mortality and morbidity.<sup>1</sup> About 20% of patients treated with cardiac resynchronization therapy (CRT) are in AF.<sup>2,3</sup> Despite the high prevalence of AF in patients with HF and the fact that many meet the criteria for CRT, randomized controlled trials have excluded these patients in most cases.<sup>4</sup> Thus, the effect of this therapy in patients with AF is still controversial.

Notwithstanding this controversy, according to the American Heart Association, American College of Cardiology and Heart Rhythm Society guidelines, CRT is a class IIa recommendation (level of evidence B) for patients with AF, left ventricular ejection fraction (LVEF)  $\leq 35\%$  and ventricular dyssynchrony, since a high percentage of biventricular capture can be ensured. Atrioventricular (AV) nodal ablation should be performed in cases of incomplete biventricular capture.<sup>5</sup>

AV nodal ablation offers the most effective method for rate control in AF patients, by creating a complete heart block and regularizing cardiac rhythm through permanent pacing. This approach enables complete biventricular pacing.<sup>6</sup> Nevertheless, the importance of AV nodal ablation (compared to pharmacologic therapy) in achieving an optimized response to CRT in AF patients remains unclear.

The meta-analyses published by Upadhyay et al. in 2008<sup>7</sup> and by Wilton et al. in 2011<sup>8</sup> suggested significant

differences in outcomes between patients in SR and those in AF, highlighting the need for further research.<sup>6</sup>

The aim of this meta-analysis was to investigate the effects of CRT in patients with AF compared with patients in SR, and to evaluate the effect of AV nodal ablation in the former group. To the best of our knowledge, this is the most recent and up-to-date meta-analysis on this subject.

## Methods

### Search strategy

Searches were conducted in the electronic databases PubMed, B-On, and Cochrane Central Register of Controlled Trials, and included the following terms: "atrial fibrillation", "heart failure", "congestive heart failure", "congestive cardiac failure", "chronic heart failure", "chronic cardiac failure", "resynchronization therapy", "cardiac resynchronization therapy", "cardiac resynchronization", "heart resynchronization", "artificial biventricular pacemaker", "biventricular pacemaker", "biventricular pacing", "biv", "dual-chamber pacing", "dual-chamber pacemaker", "atrioventricular nodal ablation", "atrioventricular junction ablation", "ablation pacing", "ablation techniques", "ablation", "AV nodal ablation", "AVJ ablation".

We considered studies in humans, published and unpublished, written in English or Portuguese, up to November 2012. In addition, we performed a manual search of

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