Atrial Fibrillation During Cardiac Resynchronization Therapy

Mariëlle Kloosterman, BSc, Alexander H. Maass, MD, PhD, Michiel Rienstra, MD, PhD, Isabelle C. Van Gelder, MD, PhD*

KEYWORDS

• Implantation • Biventricular pacing • Heart failure • Atrioventricular junction ablation

KEY POINTS

- Atrial fibrillation (AF) has a high prevalence (20%–40%) among patients with heart failure (HF) receiving cardiac resynchronization therapy (CRT).
- Randomized data on success of CRT in patients with AF are sparse and in part come from patients undergoing atrioventricular junction (AVJ) ablation for untreatable AF rather than from patients with HF and AF.
- Every effort should be made to assess success of biventricular (BiV) pacing.

INTRODUCTION

More than 2 decades of research has established CRT as one of the most exciting advancements in HF treatment. CRT improves left ventricular (LV) function by restoring intraventricular, interventricular, and atrioventricular dyssynchrony thereby conferring symptomatic relief and survival benefits to most recipients.[1–5] CRT has an established role as an efficacious and safe device-based, nonpharmacologic approach for patients with HF, impaired LV function (left ventricular ejection fraction [LVEF] $\leq$35%), electrical dyssynchrony (QRS duration $\geq$120 ms), sinus rhythm, and optimal medical therapy. However, optimal CRT use in patients with HF and AF, an important subgroup of patients, remains uncertain.

AF and HF can be characterized as the twin epidemics of modern cardiovascular medicine. AF is the most common arrhythmia in patients with HF, with the prevalence of AF in patients with HF ranging from 10% to 15% in New York Heart Association (NYHA) class II to up to 50% in NYHA class IV[6] and with the incidence of new-onset atrial tachyarrhythmias (ATs) and AF ranging from 20% to 40% according to CRT device diagnostics.[7] The latest European Society of Cardiology (ESC) guidelines and American College of Cardiology Foundation/American Heart Association/Heart Rhythm Society (ACCF/AHA/HRS) guidelines consider patients with permanent AF as eligible to receive CRT (class II A, level of evidence B) (**Table 1**).[8,9] However, guidelines about heart rate control during AF, that is, drug therapy, or ablation in the heterogeneous group of patients with AF undergoing CRT, and recommendations about nonpermanent AF, are missing.

This review gives an overview of the barriers during CRT and the current literature (**Table 2**) on the effect of CRT in patients with AF. These barriers include the occurrence of new or recurrent

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Department of Cardiology, Thoraxcenter, University Medical Center Groningen, PO Box 30.001, 9700 RB Groningen, The Netherlands
* Corresponding author.
E-mail address: i.c.van.gelder@umcg.nl

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Table 1
Clinical practice recommendations to CRT in patients with permanent atrial fibrillation issued by the European Society of Cardiology in collaboration with the European Heart Rhythm Association

Recommendations	Class	Level
Patients with HF, wide QRS, and reduced LVEF		
CRT should be considered in patients with chronic HF, intrinsic QRS ≥120 ms, and LVEF ≤35% who remain in NYHA functional class III and ambulatory IV despite adequate medical treatment, provided that a BiV pacing as close to 100% as possible can be achieved	IIa	B
AV junction ablation should be added in case of incomplete BiV pacing	IIa	B
Patients with uncontrolled heart rate who are candidates for AV junction ablation		
CRT should be considered in patients with reduced LVEF who are candidates for AV junction ablation for rate control	IIa	B

Abbreviations: AV, atrioventricular; BiV, biventricular; CRT, cardiac resynchronization therapy; HF, heart failure; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

From European Society of Cardiology (ESC), European Heart Rhythm Association (EHRA), Brignole M, et al. 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy. Europace 2013;15(8):1097; with permission of Oxford University Press (UK) (c) European Society of Cardiology, www.escardio.org.

AF and other ATs that hamper CRT response due to the inability to continuously pace the ventricles. Finally, the role of AVJ ablation is discussed.

DETRIMENTAL EFFECT OF ATRIAL FIBRILLATION ON RESPONSE TO CARDIAC RESYNCHRONIZATION THERAPY

AF and ATs have a high prevalence in real-world patients with CRT. In recent CRT trials, the cumulative incidence of new-onset AF/ATs ranged between 20% and 40% according to device interrogations[10–15] (**Table 3**).

The incidence of new-onset AT/AF is important because it can be associated with less response to CRT and more cardiac adverse events during long-term follow-up. Buck and colleagues[16] showed that in 114 consecutive patients of whom 56 (49%) had (prior) AF (23 AF present at implantation of CRT and 33 a prior history of AF) and 58 who had no history of AF, new-onset AF occurred in 14 (24%) patients during a median follow-up of 18 months. New-onset AF was associated with a lower response (4 [29%] responders versus 10 [71%] nonresponders, $P = .02$), with response being defined as a decrease in LV end-systolic volume greater than or equal to 10%.

Episodes with AT/AF are regularly recurring phenomena. During a median follow-up of 13 months, AT/AF episodes of greater than 10 min occurred in 361 (30%) of 1193 patients.[17] Device-detected AT/AF lead to a higher risk of all-cause mortality (ACM) or HF hospitalizations (hazard ratio [HR], 2.16; $P = .032$) (**Fig. 1**). These AT/AF episodes can also lead to uncontrolled ventricular rates. During a median follow-up of 18 months, 443 of 1404 patients with HF experienced episodes of AF, being uncontrolled in 34% (**Fig. 2**).[14] Suboptimal CRT delivery with BiV pacing less than 95% was significantly and inversely correlated to ventricular heart rate, decreasing by 7% for each 10-beats-per-minute increase in ventricular rate. Uncontrolled ventricular rate was associated with HF hospitalizations and ACM (HR, 1.69; 95% confidence interval [CI], 1.01–2.83; $P = .046$).

A large retrospective, cross-sectional analysis of 80,768 patients, using the Medtronic Discovery Link database, showed that BiV pacing less than 98% was observed in 40.7% of patients.[18] Among those with suboptimal pacing, AT/AF was the most common reason for loss of BiV pacing, with the contribution of AT/AF to the loss of CRT increasing with lesser percentages of BiV pacing (**Fig. 3**). Comparably, in another retrospective, observational analysis of the Discovery Link database including only patients with an atrial lead for AF diagnostics and device programming with the intent of achieving continuous BiV pacing, 8686 (8%) of 54,019 patients included had persistent or permanent AF. Nearly half (47%) of the patients with persistent AF had less than 90% BiV pacing during AF. Relative to patients with high BiV pacing, patients with moderate (90%–98%) BiV pacing had a 20% increase in mortality rate (HR, 1.20; 95% CI, 1.15–1.26; $P<.001$), and the patients who received low (<90%) BiV pacing had a 32% increase in mortality rate (HR, 1.32, 95% CI, 1.23–1.41; $P<.001$).

Hayes and colleagues[19] observed that patients with AF were able to experience only similar survival rates as patients in sinus rhythm if the ventricular heart rate could be successfully suppressed and the BiV pacing rates exceeded 98.5%.

But how can the effective percentage of BiV pacing be assessed? There is often discrepancy