

An aggressive solution for patients with heart failure and atrial fibrillation: nodal ablation and cardiac resynchronization therapy

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Heart failure and atrial fibrillation are two diseases that often coexist and contribute to worsening the prognosis and quality of life of patients. Managing this situation is still a challenge today. The ablation of the atrioventricular node associated with cardiac resynchronization therapy (CRT) fits into this context as a definitive but effective solution. Indeed, long-term positive results have been demonstrated in patients with atrial fibrillation ineligible for ablation and refractory to medical therapy in terms of symptom reduction and, more recently, also mortality. Furthermore, the role of this strategy in obtaining adequate biventricular pacing in patients who may benefit from CRT but are ineligible due to the presence of atrial fibrillation is being highlighted.

Introduction

Heart failure and atrial fibrillation are two closely related cardiovascular diseases that often coexist and complicate each other, exerting a negative effect on the cardiovascular system and the well-being of patients. Heart failure can favour the development of atrial fibrillation through numerous mechanisms, such as the increase in atrial pressures, the activation of neuro-hormonal systems and the consequent cardiac remodelling, which contribute to creating a proarrhythmic environment.

In turn, atrial fibrillation causes a reduction in cardiac output through an increase in heart rate, the loss of the contribution of atrial systole to ventricular filling, and the irregularity of the cardiac cycle. Thus, heart failure and atrial fibrillation have a synergistic negative impact on quality of life, functional capacity, and hospitalization rate.

Atrial fibrillation can not only cause a flare-up of heart failure, but it can also be the *primum movens* for the development of left-ventricular dysfunction in the context of what is commonly referred to as tachycardiomyopathy. It

is a condition defined by the presence of atrial or ventricular dysfunction secondary to a persistent tachyarrhythmia and the prognosis tends to be benign as it resolves in most cases with treatment of the underlying tachyarrhythmia.

Conversely, the onset of atrial fibrillation in heart failure patients is associated with increased mortality. Indeed, even short episodes of atrial fibrillation may be sufficient to cause a significant worsening of left-ventricular function when the loss of atrioventricular synchrony is aggravated by variable and shortened ventricular filling times. In turn, the progression of heart failure can exacerbate further episodes of atrial fibrillation, thus triggering a vicious cycle.

Precisely for this reason, the prevalence of atrial fibrillation increases with the progression of heart failure, ranging from <5% in patients in NYHA functional Class I to 50% in patients in NYHA functional Class IV.^{1,2}

An aggressive solution for the management of atrial fibrillation

The choice to pursue a rhythm control strategy rather than a rate control strategy is mainly based on symptoms

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and aimed at obtaining a benefit in terms of quality of life, since to date, there is insufficient evidence to favour either of the two strategies over the other. In 2008, the AF-CHF trial showed that in patients with heart failure and atrial fibrillation, drug therapy for rhythm control is not superior to that for rate control in terms of prevention of cardiovascular mortality and progression of heart failure.³ On the contrary, transcatheter ablation of atrial fibrillation would seem to be superior to medical therapy for the control of rhythm or heart rate. The literature on the subject seems to agree in affirming that this strategy allows to obtain a benefit in terms of symptoms; while as regards the effect on mortality and the hospitalization rate, there are still not enough data to reach definitive conclusions.

The CASTLE-AF trial demonstrated that transcatheter ablation of atrial fibrillation, when compared with medical therapy, in heart failure patients with reduced ejection fraction is associated not only with a significant reduction in mortality and hospitalizations for heart failure, but also an increase in functional capacity and left-ventricular ejection fraction.⁴ The latter figure was, however, disproved by a subsequent randomized study, the AMICA trial, which did not show any differences in terms of the increase in the ejection fraction between the two study groups.⁵

On the opposite side with respect to transcatheter ablation, the range of therapeutic choices available for the management of atrial fibrillation includes ablation of the atrioventricular node with permanent pacemaker implantation. This is a valid non-drug option for rate control in patients who cannot undergo transcatheter ablation for atrial fibrillation and who do not respond to or do not tolerate rate and rhythm therapy (class of recommendation IIa, level of evidence B according to the ESC 2020 guidelines for the management of atrial fibrillation).⁶

This approach is called 'ablate and pace' and, compared with drug therapy alone, offers the possibility of regulating the ventricular response and obtaining more efficient rate control.¹ The consequence is a significant reduction in dyspnoea, palpitations, and fatigue, as well as an improvement in exercise tolerance.⁷

In a large prospective registry, only 3.5% of patients re-experienced atrioventricular conduction during long-term follow up.⁸ Hence, it is an effective and long lasting but irreversible rate control strategy as it is accepted that the patient becomes pacemaker dependent.

However, this is a fairly safe procedure: according to a meta-analysis, the incidence of surgery-related deaths is 0.27% and the rate of other complications, such as haematomas, malignant arrhythmias, and lead malfunction, is always <1%.¹

Most studies on the ablation of the atrioventricular node as a therapeutic option for atrial fibrillation do not distinguish between right pacing and biventricular pacing. Despite this, it has been widely demonstrated that this strategy, when compared with drug therapy alone, leads to a significant improvement in symptoms and quality of life; moreover, in patients with a reduced systolic function of the left ventricle, a minimal but significant increase of the same has been shown.^{1,9}

Although right pacing causes left-ventricular dyssynchrony in about half of patients, the reason why left-ventricular ejection fraction improves in most cases is likely to be due to the positive effect of ablation of the atrioventricular node has on the dysfunction induced by tachycardia, which is often present in this context.

However, there is ample evidence that biventricular vs. right pacing improves quality of life, functional capacity, and hospitalization rate in patients undergoing atrioventricular node ablation.¹⁰ The ablate and pace for atrial fibrillation (APAF) trial has shown that these benefits in terms of reducing the clinical manifestations of heart failure are not evident only in patients with ejection fraction <35%, NYHA functional Class III or more, and with a longer QRS duration at 120 ms, but also in those that do not fall into this category.¹¹

In addition, the APAF-cardiac resynchronization therapy (CRT) trial, which considered patients with QRS \leq 110 ms, permanent atrial fibrillation, and at least one hospitalization for heart failure in the year prior to randomization, demonstrated a reduction in mortality in the ablation group of the atrioventricular node and CRT, compared with the group treated with rate control drugs. After 4 years of follow up, the relative and absolute risk reduction were, respectively, 74 and 27%, and the interesting fact is that this benefit was present regardless of the initial ejection fraction.¹²

In contrast, the benefits of sinus rhythm had already been highlighted by the PABA-CHF trial, which demonstrated the superiority of catheter ablation of atrial fibrillation over the ablate and pace strategy with biventricular pacing in terms of increased ejection fraction of the left ventricle and improvement of functional capacity and quality of life.¹³

Therefore, the ablation of the atrioventricular node associated with CRT constitutes a valid therapeutic option, but according to current evidence, it should be considered only when the alternatives that can be used for rhythm or rate control are not applicable or fail.

A definitive solution to optimize cardiac resynchronization therapy

The role of CRT in heart failure patients with ventricular dyssynchrony and persistent atrial fibrillation is still under study. In fact, most of the multicentre studies that have supported the use of CRT in patients with heart failure had excluded patients with atrial fibrillation. Precisely for this reason, according to current guidelines, this type of treatment is aimed almost exclusively at subjects in sinus rhythm, with the only exception of patients suffering from heart failure with reduced ejection fraction who need a pacemaker for an advanced atrioventricular block.¹⁴

The benefits of CRT are attributable to the reduction of left-ventricular dyssynchrony, with consequent improvement of the ejection fraction, and to the reverse remodelling that occurs in the long term.¹⁵ But the main determinant of the success of this therapy is a high rate of biventricular pacing and the presence of an atrial

fibrillation rhythm, which is irregular and characterized by a rapid ventricular rate, can interfere with this goal. In fact, in about two-thirds of patients with permanent or persistent atrial fibrillation, a high percentage of effective capture by the device is not achieved because, if the atrioventricular conduction is intact, spontaneous beats often occur. In addition, fusions or pseudofusions can occur and are recorded by the device as paced beats, causing an overestimation of the percentage of biventricular pacing which can lead to erroneous classification of the patient as a 'non-responder'.¹⁶

Therefore, in most patients with atrial fibrillation and preserved atrioventricular conduction, adequate biventricular pacing can only be achieved through ablation of the atrioventricular node. Although its application in this context is still a matter of debate, several studies have shown that ablation of the atrioventricular node, in patients in whom the indication for CRT is limited by the presence of atrial fibrillation, induces an improvement in left-ventricular function, functional capacity, and survival, reaching results similar to those obtained in patients in sinus rhythm.¹⁷

A meta-analysis found that among patients with <90% biventricular pacing rate, those who underwent atrioventricular node ablation achieved a 59% reduction in non-responder rate and a 37% reduction in mortality. Importantly, these positive effects are only achieved when adequate biventricular pacing cannot be achieved despite maximal rate control therapy. Furthermore, before evaluating the ablation of the atrioventricular node, other possible causes that can interfere with CRT, such as frequent ventricular extrasystoles, must be excluded.

In conclusion, although there is not much evidence in this regard, the opinion of the experts is in favour of the usefulness of CRT in patients with permanent atrial fibrillation in NYHA functional Class III or IV with the same indications provided for patients in sinus rhythm, provided that ablation of the atrioventricular node is also performed in cases of incomplete capture by the device (<90-95%) caused by atrial fibrillation.¹⁸

Conflict of interest: None declared.

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