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EDITORIAL

Catheter Ablation for Atrial Fibrillation in Heart Failure: Ready for Mainstream Adoption, or Is More Evidence Needed?

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The incidence of atrial fibrillation (AF) is approaching epidemic proportions, as our ageing population accumulate risk factors [1]. Adverse effects of arrhythmia on myocardial function, even in the absence of rapid ventricular rates, have now been well described [2]. Conversely, structural, haemodynamic and neuro-hormonal changes in heart failure predispose to AF [3]. Establishing the direction of causality can prove challenging. Catheter ablation is more effective than medical therapy in ameliorating symptoms of AF in patients with preserved systolic function [4]. The role of ablation in improving *clinical outcomes* in heart failure, however, is still under investigation.

In this issue of *Heart Lung Circulation*, Virk et al. [5] perform a meta-analysis of randomised controlled trials comparing ablation to medical therapy for AF in the setting of systolic heart failure, with the primary endpoint being change in left ventricular ejection fraction (LVEF). Ablation resulted in a small, but significant, improvement in LVEF above medical therapy alone (mean baseline LVEF was 30% with mean additional increase of 5.7%). In secondary analyses, ablation was found to be superior to medical therapy in improving 6-minute walk time, quality of life and mid-term mortality. The mortality endpoint included three studies with a minimum follow-up of one year [6–8].

The publication of Catheter Ablation for Atrial Fibrillation for Heart Failure (CASTLE-AF) [8] and Catheter Ablation Versus Medical Rate Control in Atrial Fibrillation and Systolic Dysfunction (CAMERA-MRI) [9] has shed new light on the clinical implications of AF ablation in heart failure. Their inclusion differentiates this study from prior meta-analyses. CASTLE-AF, a randomised trial of 363 patients, found ablation reduced death and hospitalisation due to heart failure, compared to medical therapy alone. Indeed, CASTLE-AF contributes the majority of the data to the mid-term mortality endpoint in Virk et al.'s meta-analysis [5]. Sub-analyses of CASTLE-AF suggested younger patients with less severely impaired ventricles (LVEF 25–35%, compared to LVEF < 25%) benefited more from ablation. CAMERA-MRI carefully selected a population with idiopathic cardiomyopathies, finding ablation significantly improved LVEF compared to rate control. The benefit was more marked in those without late gadolinium enhancement on cardiac magnetic resonance imaging (MRI), increasing LVEF by an average of 22%. The impressive magnitude of improvement perhaps reflected selection of true "arrhythmia-mediated" cardiomyopathies, by exclusion of other obvious pathologies. Therefore, further studies are required to define the subset of patients that are most likely to benefit from ablation. Several clinical factors predictive of ablation success have been identified in patients with preserved systolic function–these include low volume of left atrial fibrosis on delayed enhancement MRI [10,11] and duration of long-standing persistent AF less than 2 years (compared to >2 years) [12]. Their role in selecting heart failure patients for AF ablation has not been investigated.

Balanced against the clinical benefits of ablating AF in heart failure are the complexity and risk of these procedures. Most trials in this meta-analysis [5] included persistent AF only, with a mean continuous AF duration of 24 months pre-ablation [7,9,13]. Expectations of success therefore need to be tempered, with an average of 1.3–1.7 procedures per patient to achieve rhythm control, and a subset of patients where rhythm control

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was not achievable despite multiple procedures. Additional linear ablation outside the pulmonary veins was standard protocol, although evidence to guide this strategy is lacking [14]. The pooled rate of major complications was surprisingly high, at 8.2%. Given LVEF is a surrogate clinical endpoint, the risk-benefit ratio of achieving a modest improvement warrants careful consideration in each patient. Complication rates of AF ablation in populations with preserved systolic function range from 2.3–4.5% in registry datasets [15–17], although this may underestimate the true incidence. The combination of pre-existing ventricular impairment, intravenous fluid administration during irrigated ablation, and impaired immunity in heart failure may predispose to pulmonary oedema and post-operative pneumonia respectively. Furthermore, vascular comorbidities, bleeding diatheses and prolonged substrate ablation may increase risk of access site complications, tamponade and thrombo-embolic complications.

Moreover, it is important to recognise the inherent limitations of meta-analysis. The included trials, aside from CASTLE-AF, typically had small numbers of patients; and these small trials are vulnerable to positive publication bias. Interestingly, the rate of patient attrition during screening was substantial and unique to this field, predisposing to attrition bias. CASTLE-AF, for example, randomised 363 patients of 3,013 screened. This is predominantly driven by strict inclusion criteria for an interventional trial in highly comorbid patients. Operators could not be blinded to intervention and thus performance bias may result; no trial has yet been conducted with a ''sham-procedure'' in AF ablation.

Catheter ablation offers a promising therapy for heart failure patients with atrial fibrillation. The magnitude of benefit may be dependent on underlying cardiac substrate, and careful patient selection is required. Atrial fibrillation ablation in this population remains a complex procedure with moderate complication rates. Furthermore, the optimal ablation set outside of the pulmonary veins has not been defined in this population. Therefore, we would argue that additional randomised trials powered to detect meaningful clinical endpoints are required (such as mortality, stroke or re-hospitalisation for heart failure), before ablation can be considered a mainstream intervention in patients with heart failure and AF.

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Declarations of Interest

Nil.

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