

# Who benefit most from catheter ablation of persistent atrial fibrillation?

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Atrial fibrillation (AF) and heart failure (HF) frequently coexist and are associated with common etiologies such as hypertension, diabetes mellitus, coronary heart disease, valvular disease, and sleep apnea. Both AF and HF affect each other negatively. AF may cause impaired left ventricular (LV) systolic function (1) and increase the incidence of HF by three fold (2). It is therefore expected that restoration of sinus rhythm should be associated with improvement of cardiac function and consequently better prognosis. However, previous studies have shown that pharmacological rhythm control strategy is not superior to rate control (3,4), due to limited efficacy to sinus rhythm restoration and potential toxicity of antiarrhythmic drugs.

Catheter ablation targeting isolation of the pulmonary veins has become an effective treatment of choice for drug-refractory AF (5,6). Several studies have shown that LV systolic dysfunction is at least partially reversible after restoration of sinus rhythm by catheter ablation. Furthermore, successful ablation of persistent AF may yield other prognostic benefits such as improvement in quality of life and exercise performance (7-10). Recent studies demonstrated that rhythm control strategy pursued by catheter ablation is superior to both rate control and pharmacological rhythm control (9-12). However, these recent studies had enrolled a heterogeneous group of patients including ischemic heart disease, non-ischemic cardiomyopathy, and valvular heart disease. AF in patients with these structural heart diseases responsible for LV

dysfunction may be the consequence rather than the cause of cardiomyopathy, which limits the optimal assessment of effect of catheter ablation. Furthermore, achievement of durable sinus rhythm after ablation of persistent AF is more challenging compared to paroxysmal AF, presumably due to the larger arrhythmia substrates contributing to its initiation and perpetuation (13-15). Current guidelines have no specific recommendation of rhythm control strategy with catheter ablation in patients with persistent AF and LV dysfunction (16). The 2016 European Society of Cardiology Guideline for the management of AF describes that rhythm control therapy is indicated for the purpose of symptom improvement in patients with AF. If the impact of AF on clinical symptom is less certain, rhythm control strategy pursued by cardioversion with antiarrhythmic drugs may be therapeutic option to determine whether patients benefits most from aggressive strategy of rhythm control or not. Based on these limitations, clinical applications to select patients with persistent AF and HF who are eligible for ablation still remains a challenging task.

The multicenter, randomized clinical trial by Prabhu *et al.* in the issue of *Journal of American College of Cardiology* (17) enrolled patients with persistent AF and idiopathic cardiomyopathy. The etiology of the underlying cardiomyopathy was otherwise unexplained, apart from the presence of AF. This well-designed study compared the improvement of LV systolic function after the restoration of sinus rhythm with catheter ablation versus ongoing

AF with rate control. All patients underwent cardiac magnetic resonance imaging (CMR) to assess LV ejection fraction and the extent of late gadolinium enhancement indicating myocardial fibrosis. The LV ejection fraction improved by  $18\% \pm 13\%$  in the catheter ablation group compared with  $4.4\% \pm 13\%$  in the rate control group ( $P < 0.0001$ ) and normalized [left ventricular ejection fraction (LVEF)  $\geq 50\%$ ] in 58% *vs.* 9% ( $P = 0.0002$ ). Importantly, the improvement of LV ejection fraction was marked especially in patients without late gadolinium enhancement on CMR. Patients without late gadolinium enhancement had a significantly greater improvement in LV ejection fraction ( $22.3\%$  *vs.*  $11.6\%$ ,  $P = 0.0069$ ) and were more likely to normalize LV ejection fraction ( $73\%$  *vs.*  $21\%$ ,  $P = 0.0093$ ) than those with delayed enhancement. Pre-procedural assessment of late gadolinium enhancement on CMR improves the identification of patients with a high likelihood for a better prognosis after ablation.

Even when the ventricular rate is well controlled, AF may be the cause of LV systolic dysfunction that is reversible after restoration of sinus rhythm with catheter ablation in patients with no LV fibrosis. This observation supports the concept that AF-related cardiomyopathy may occur in spite of adequate rate control. Contrary to these outcomes, a recent clinical data demonstrated that an impaired myocardial energetics and LV dysfunction in patients with lone AF did not normalize after ablation, suggesting that lone AF may be the consequence of an occult cardiomyopathy process rather than the cause of cardiomyopathy (18). There is a possibility that LV dysfunction with the late gadolinium enhancement on CMR may reflect the progression of occult cardiomyopathy process, which may be hard to be improved even after the restoration of sinus rhythm with catheter ablation. However, the study by Prabhu provides an encouraging outcome that sinus rhythm restoration in patients without late gadolinium enhancement yields prognostic benefit of a significant improvement of cardiac function. This result suggests that AF significantly contributes to adverse hemodynamics, and ablation of AF could favorably affect cardiac function in patients with no LV scar at that time.

The study by Prabhu *et al.* has several limitations. Their results were limited by the small number of patients. The data of HF hospitalization and mortality were not described. Lack of these clinical data underpowered the study. Presumably, successful rhythm controls that results in improvement of cardiac function should be associated with consequently better prognosis at least for a meaningful

period of time in the clinical practice. The investigators ought to be congratulated in achieving very high rates of ablation success and freedom from AF recurrence. Pulmonary vein isolation was achieved in 100% and posterior wall isolation was achieved in 85% with ablation time of  $43 \pm 12$  minutes. AF burden as assessed by using an implanted loop recorder was only  $1.6\% \pm 5.0\%$ . All patients maintained sinus rhythm at the time of CMR post-ablation. It remains to be seen whether these excellent results with low rate of complications can be replicated. Even with these limitations, the study by Prabhu provides important information that pre-procedural assessment of delayed enhancement on CMR serves as valuable prognostic tool by which to better stratify patients with persistent AF and idiopathic cardiomyopathy for rhythm control strategy pursued by catheter ablation. This study provides the grounds for reconsider the current guideline for the indication of catheter ablation of persistent AF in patients with HF. Further studies with larger sample size and long-term follow-up duration are warranted to replicate these positive outcomes.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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