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EDITORIAL COMMENT

Atrial Fibrillation in Patients With Hypertrophic Cardiomyopathy

Caveat Ablator*

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Hypertrophic cardiomyopathy (HCM) is a cardiac disease characterized by abnormal left ventricular (LV) wall thickening (often asymmetric) not explained by other causes associated with a non-dilated LV and preserved ejection fraction.[1] Myocyte disarray and hypertrophy, systolic anterior motion of the mitral valve, and mitral regurgitation are often seen. Atrial fibrillation (AF) is a commonly associated arrhythmia seen in roughly 20 to 30% of patients in specialty centers.[2] HCM patients with AF may be more prone to symptoms due to impaired LV filling and increase in mitral valve abnormalities, especially when ventricular rate is poorly controlled. Stroke risk is elevated independent of CHA_2DS_2-VASc score. Antiarrhythmic agents generally have modest efficacy in this population, with care needed to prevent cardiac and extracardiac adverse effects.[3]

Catheter ablation has become a widely applied therapy for AF, particularly for patients with little structural heart disease and in those with systolic heart failure caused or exacerbated by AF. Randomized clinical trials in general AF populations have shown improved efficacy of ablation therapy over antiarrhythmic drug (AAD) therapy, with improved maintenance of sinus rhythm, lower AF burden, reduced symptoms, improved quality of life, and reduced hospitalizations.[4]

Data on efficacy of AF ablation for patients with HCM are sparser, and no randomized clinical trials exist. Information is limited to cohort studies with a mix of prospective and retrospective designs. One recent meta-analysis and systematic review of 19 such studies with 1,183 HCM patients found a single-procedure success rate of 39%, with a 34% rate of repeat procedure and a 41% rate of continuation of AADs.[5] Another recent analysis comparing AF ablation in 262 HCM patients with 642 patients without HCM confirms the impression that HCM patients have higher rates of recurrent AF, repeat ablation, and use of AADs after ablation, with a pooled relative risk of 1.6 for recurrent atrial arrhythmias after the last AF ablation.[6] Little data exist for other clinical endpoints, such as hospitalization, stroke, and mortality.

In this issue of *JACC: Advances*, Pierri et al[7] report on their retrospective multicenter cohort study of 555 HCM patients with nonpermanent AF, of whom 140 underwent catheter ablation and 415 were treated medically. From this cohort, the authors selected 113 patients undergoing ablation and 113 propensity score matched (PSM) medical therapy controls and compared outcomes over a median follow-up of nearly 5 years. They found no significant difference in a composite outcome of all-cause mortality, heart transplant, and acute heart failure exacerbation. Fewer patients in the ablation group experienced AF recurrences (63.7% vs 84.1%) and transition to permanent AF (20.4% vs 33.6%).

Strengths of the report include the large cohort size (the largest yet of HCM patients with AF), inclusion of multiple expert HCM referral centers, and relative long follow-up. Weaknesses include retrospective design, inability to match and control for all variables, lack of a protocolized ablation technique, little detailed information on left atrial (LA) structural disease, and no data on total hospitalizations, AF

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burden, or quality of life. Patients undergoing ablation had numerically longer time from diagnosis, higher prevalence of implantable cardioverter defibrillators, higher rates of longstanding-persistent AF, and larger LA size. As the authors note, confounding by indication may be present, with AF patients being perhaps more symptomatic and prone to worse clinical outcomes. Important differences in LA function may not have been captured by the variables included in the PSM. It has been shown that impaired LA strain is associated with worse clinical outcomes, even after adjusting for diastolic function.[8,9] Both LA volume and strain have been shown to improve the prediction of new-onset AF in HCM patients, regardless of LA diameter.[10] Among non-HCM patients, LA strain has been reported to predict arrhythmia recurrence following catheter ablation of AF.[11] Therefore, it is possible that more detailed assessment of LA function and inclusion in the PSM process may have altered the study findings. Overall, the study provides important information to clinicians caring for patients with AF and HCM while challenging practitioners of AF ablation to improve patient selection and clinical outcomes.

With this new information in hand, where does the field stand today regarding catheter ablation of AF in HCM patients? Firstly, appropriate stroke prevention therapy should be maintained for all patients. It is notable that only 45% of all medically treated AF patients were treated with oral anticoagulants at baseline, with a high use of vitamin K antagonist over direct oral anticoagulants. As with all other AF patients, those with HCM should undergo comprehensive risk factor management according to current guidelines.[4,12] A particular emphasis is placed on rhythm control in HCM patients with poorly tolerated AF.[3] Worse outcomes have been reported for HCM patients with a combination of AF and outflow obstruction.[13] These patients may depend more on LV filling during LA contraction in sinus rhythm and could therefore derive greater clinical benefit from rhythm control. The present study included ~20% of patients with obstructive HCM; however, evaluating catheter ablation in a larger group with obstructive physiology would be important to determine its clinical utility in this scenario.

Another important observation in the present study is that the median time from diagnosis to ablation in the intervention group was over 3 years (and over 5 years in a quarter of patients). With recent data showing better outcomes for early AF rhythm control, it is possible that outcomes would have been better had AF ablation been applied earlier in the course of disease, particularly when AF is paroxysmal and less LA structural disease has developed.[14,15] Other studies have shown improved outcomes for catheter ablation when lifestyle modification and risk reduction are undertaken.[4,12] Application of preprocedure cardiac magnetic resonance imaging may improve outcomes through selection of patients with less LA scarring, who are more likely to respond. Whether newer ablation technologies such as pulse-field ablation or more extensive ablation techniques improve outcomes in HCM patients remains to be determined.

Overall, catheter ablation of AF in HCM patients should still be considered, particularly in patients with paroxysmal AF, higher degree of symptoms, and less structural LA disease. For other patients, careful risk-benefit assessment and shared decision-making should take place, with patients apprised of the limited evidence for favorable outcomes. Patients undergoing cardiac surgery for outflow tract obstruction or mitral valve disease should be considered for surgical AF ablation. Finally, we hope that more HCM centers performing AF ablation will prospectively gather detailed baseline data and report outcomes to collectively advance the field.

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