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EDITORIAL

Ablation of Atrial Fibrillation in Hypertrophic Cardiomyopathy: Semper Discere (Always Learning)

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Atrial fibrillation (AF) represents the most common sustained arrhythmia in patients with hypertrophic cardiomyopathy (HCM).[1–4] Overt symptomatic episodes of AF occur in ≈20% of patients with HCM.[1–4] Asymptomatic, clinically silent AF is detected in up to 25% of patients with HCM by using cardiac implantable electronic devices[1–4] AF is more common and the risk of thromboembolic stroke is higher in patients with HCM than in the general population.[1–4] Anticoagulation reduces the risk of stroke in both symptomatic and asymptomatic AF and is indicated in all patients with HCM, independent of the CHA2DS2-VASc score.[1–3] Historically, development of AF has been regarded as a significant turning point for patients with HCM and has been associated with hemodynamic deterioration with worsening functional status and heart failure.[5,6] However, recent observations provide robust evidence that AF no longer results in deterioration of clinical status, noted in early reports of patients with HCM.[1–4,7–9] Contemporary studies demonstrate that paroxysmal AF infrequently progresses to permanent AF in patients with HCM.[1–4] These studies also provide robust evidence that AF does not contribute to heart failure progression or arrhythmic sudden death in HCM.[1–4] Patients with HCM who have AF currently have a low disease-related mortality, similar to patients with HCM who do not have AF.[1–4]

See Article by Dinshaw et al.

The recommended management strategy for asymptomatic AF in patients with HCM is rate control using oral ß blockers or nondihydropyridine calcium channel antagonists and anticoagulation.[7–9] Maintaining normal sinus rhythm with continued anticoagulation is the preferred approach for patients with HCM who have symptomatic AF.[7–9] Options for maintaining sinus rhythm are recommended in an incremental manner with lifestyle modification, antiarrhythmic drugs, catheter ablation, or surgical or thoracoscopic ablation.[9,10] Guidelines for rhythm control in all patients with symptomatic AF now include the class I recommendation for lifestyle modification with weight loss, strict control of risk factors, and avoidance of triggers as part of the rhythm control strategy.[9] Recent observations on efficacy and adverse effects of antiarrhythmic medications for rhythm control of AF in HCM indicate that the probability of remaining on a single antiarrhythmic drug is 62% at 1 year and 42% at 3 years.[4] Sinus rhythm is maintained in 74% of patients at 1 year and 50% of patients at 3 years for those taking sotalol.[4] Discontinuation of sotalol because of adverse effects was necessary in only 2% of patients.[4] At 3 years, only 8.5% of patients had amiodarone discontinued because of inefficacy. However, it was discontinued in 19% of patients with HCM because of adverse effects.[4] Although the absence of prospective randomized trials of antiarrhythmic drugs versus ablation represents a limitation of all publications on AF management in patients with HCM, the best available registry data indicate that the initial

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attempt to maintain sinus rhythm with lifestyle modification and antiarrhythmic drugs is a moderately successful approach.

Contemporary guidelines for rhythm control with catheter ablation of paroxysmal or persistent AF include the class I recommendation with level of evidence (LOE) A, indicating that AF catheter ablation for pulmonary vein isolation (PVI) for rhythm control is useful after one failure of a class I or III antiarrhythmic drug, attributable to lack of efficacy or adverse effects, to improve symptoms in patients with AF (class I, LOE A).[9,10] Catheter ablation as first-line therapy for PVI may be considered for rhythm control to improve symptoms in selected patients with paroxysmal AF (class IIa, LOE B) or persistent AF without major risk factors for AF recurrence (class IIb, LOE C). Complete isolation of the pulmonary veins is recommended during the procedure (class I, LOE A).[9,10] The use of additional ablation lesions beyond PVI (complex fractioned atrial electrograms, low-voltage areas, fragmented areas, ectopic foci, rotors, and others) may be considered but is not well established (class IIb, LOE B).[9,10]

In this issue of the *Journal of the American Heart Association* (*JAHA*), Dinshaw and colleagues report the outcome of 65 patients with HCM who underwent AF ablation using a strategy that included PVI in all patients and selective ablation of complex fractionated electrograms or subsequent atrial tachycardias (ATs).[11] At baseline, paroxysmal, persistent, and primary AT was present in 13 (20%), 51 (78.5%), and 1 (1.5%) of patients, respectively.[11] Notably, 50% of the patients in this cohort underwent ablation without a prior trial of an antiarrhythmic drug. Of the patients, 25 (38.4%) developed AT, including 54 separate ATs. Detailed assessment of arrhythmia mechanisms demonstrated macroreentry in 37 (68.5%), localized reentry in 12 (22.2%), a focal mechanism in 1 (1.9%), and an unclassified mechanism in 4 (7.4%).[11] After 1.9+1.2 ablation procedures, freedom from overall AF/AT recurrence was demonstrated in 60% of patients, with no recurrence in 84.6% of procedures with paroxysmal AF and 52.9% of patients with persistent AF ($P<0.01$).[11] Notably, antiarrhythmic drug therapy was continued in 24 patients (36.9%).[11] On the basis of these observations, the authors conclude that AF ablation in patients with HCM is effective for long-term control.[11] ATs are frequently observed in patients with HCM after ablation.[11] The authors also conclude that there is freedom from atrial arrhythmia in a reasonable number of patients, with continued use of antiarrhythmic drugs in many patients.

The observations by Dinshaw and colleagues confirm prior observations while adding new information on longer-term follow-up and arrhythmia mechanisms after AF ablation in patients with HCM.[11] The single-center, retrospective, observational report by Dinshaw et al extends observations to 4 years in 65 patients, with 78.5% having persistent AF. The observation that 38% of patients developed AT after the ablation, a 38% recurrence rate at 4 years after 1.9+1.2 procedures, with 37% of patients on antiarrhythmic therapy, is consistent with prior reports. Of note, the cohort studied herein demonstrated body mass index averaging in the nonobese range (<30 kg/m^2), which may affect the generalizability of the findings. Obesity is highly prevalent among patients with HCM and is associated with worse AF outcomes.[12] The authors compare 6 prior publications on AF ablation in patients with HCM, including 3 prospective and 3 retrospective observational reports between 2006 and 2015.[11] These have included 26 to 79 patients with HCM undergoing 1.2+1.9 procedures and followed up from 0.9 to 2.9 years. AT developed in 8% to 37% of patients after ablation, and antiarrhythmic drugs were in use at last follow-up in 24% to 54% of patients. Overall, freedom from AT or AF was reported in 46% to 94% of patients.[11]

The clinical implications of this investigation by Dinshaw and colleagues merit consideration in the context of other contemporary publications on outcomes of AF ablation in patients with HCM.[13–15] Three meta-analyses of catheter ablation of AF in patients with HCM have been published.[13–15] One included 5 studies with 403 patients with HCM and 393 controls.[13] Freedom from AF/AT relapse was higher in patients without HCM after a single procedure: 38.7% patients with HCM versus 49.8% controls (odds ratio [OR], 2.25; $P=0.03$); and after ≥1 procedure: 51.8% patients with HCM versus 71.2% controls (OR, 2.62; $P=0.0006$).[13] Repeated procedures and antiarrhythmic drugs (OR, 4.70; $P<0.0001$) were more frequently needed in patients with HCM.[13] Overall, the risk of relapse was 2-fold higher after ablation in patients with HCM compared with controls.[13] The conclusions were similar from another meta-analysis that included 15 studies with 531 patients.[14] A final meta-analysis included 8 observational studies, with 7 case series with no control groups and 1 case-matched study.[15] This analysis reached similar conclusions, with detailed subgroup analysis, and showed improved outcomes in patients with HCM who had paroxysmal compared with persistent AF.[15]

Understanding the pathophysiologic mechanisms of AF in HCM is fundamental to improving ablation outcomes. Anatomic factors, such as atrial fibrosis and myofibrillary disarray, are potential substrates for conduction delay and intra-atrial reentry. Increased thickness of the atrial wall could result in nontransmural lesions with both radiofrequency and cryoablation. Sarcomeric gene mutations, which account for ≈60% of HCM cases, may have a more direct role.[16] The β-myosin heavy chain missense mutation increases

AF risk, with 47% of carriers developing AF over long-term follow-up.[16] Angiotensin receptor gene polymorphyisms have been implicated in the development of AF in HCM.[17] Abnormal calcium handling has been proposed as a pathophysiological mechanism in HCM, accounting for triggered activity causing AF.[18] Other proposed mechanisms include autonomic influences, mitral regurgitation, and ischemia.

Patients with HCM may have non–pulmonary vein triggers more commonly than the general population, accounting for late recurrences.[19] Some investigators have advocated extensive ablation beyond pulmonary vein isolation.[19] However, there is no consensus on the optimal approach for AF ablation in patients with HCM. It is unclear if performing pulmonary vein isolation and targeting sustained ATs is superior to using a more aggressive approach with extensive lesion sets, including lines, targeting complex fractionated electrograms and non–pulmonary vein triggers in both atria. Current guidelines for catheter ablation recommend complete isolation of the pulmonary vein as the primary objective (class I, LOE A). Additional ablation lesions beyond PVI (complex fractioned atrial electrograms, low-voltage areas, fragmented areas, ectopic foci, rotors, and others) may be considered but are not well established (class IIb, LOE B).[9,10]

In the absence of robust data from randomized controlled trials specifically in patients with AF who have HCM, clinicians should rely on the best available data and current guidelines.[9,10] These include the class I recommendation with LOE A, recommending AF catheter ablation for PVI for rhythm control after one failure of a class I or III antiarrhythmic drug in patients with symptomatic AF.[9,10] Catheter ablation as first-line therapy for PVI may be considered for rhythm control to improve symptoms in selected patients with symptomatic paroxysmal AF (class IIa, LOE B) or persistent AF without major risk factors for AF recurrence (class IIb, LOE C). Although there has been considerable progress in improving outcomes of patients with HCM who have AF, it is evident that much remains unknown.

ARTICLE INFORMATION

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Disclosures

None.

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