Apical Hypertrophic Cardiomyopathy: The Variant Less Known

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Hypertrophic cardiomyopathy (HCM) is an umbrella term for a heterogeneous heart muscle disease that was historically (and still is) defined by the detection of left ventricular (LV) hypertrophy (LVH) in the absence of abnormal cardiac loading conditions. Long after this morphological definition was established, the genetic basis of HCM was discovered, and we now know it is predominantly caused by autosomal dominant mutations in sarcomeric protein genes.

Several patterns of LVH have been described in HCM: asymmetric septal (here referred to as “classic” HCM), concentric, reverse septal, neutral, and apical (ApHCM), as well as other, rarer LVH variants such as isolated lateral LVH and isolated inferoseptal LVH. Distinguishing between morphological HCM subtypes has conferred little in terms of personalized management strategies, with one distinctive exception: ApHCM. Compared with classic HCM, ApHCM is more sporadic, sarcomere mutations are detected less frequently, there is more atrial fibrillation (AF) and sudden cardiac death (SCD) risk factors differ. No authoritative ApHCM-specific recommendations to guide diagnosis, family screening, and patient stratification currently exist.

First described in Japan in 1976, ApHCM is exemplified by “giant” negative precordial T-waves on electrocardiography and by “spadelike” configuration of its LV cavity in end diastole. This review summarizes the epidemiology, clinical expression, genetics, and prognosis of ApHCM, while also highlighting knowledge gaps.

Pathophysiology and Clinical Characteristics

Epidemiology

ApHCM is not as rare as first thought, accounting for up to 25% of HCM in Asian populations and 1% to 10% in non-Asians. Ethnic variation influences prevalence, natural history, and prognosis, and Western sufferers may exhibit a more malignant form.

Genetics

Fewer ApHCM patients report a positive family history compared with classic HCM, potentially suggesting differences in ascertainment screening and/or different etiological (genetic, environmental) factors. In this context, the applicability of conventional HCM risk stratification can be challenged given that family history of SCD is heavily weighted (Table 1).

In terms of identifiable sarcomere gene mutations, one study that used a 9-gene panel, 25% of 71 ApHCM versus 34% of 1053 all-cause HCM patients had detectable genetic defects: ACTC1 (cardiac α-actin), MYBPC3 (myosin-binding protein C), MYH7 (β-myosin heavy chain), MYL2 (myosin regulatory light chain), MYL3 (myosin essential light chain), TNNT2 (cardiac troponin T2), TNNI3 (cardiac troponin I3), TNNC1 (troponin C1, slow skeletal and cardiac type), and TPM1 (α-tropomyosin 1). The phenotype and clinical outcomes of these ApHCM patients did not differ between genotype-positive or -negative subjects. Other studies confirm reduced mutation rates in ApHCM versus all-cause HCM (13% versus 40% with an 8-gene panel, plus 3 metabolic cardiomyopathy genes: GLA (α-galactosidase A) for Fabry disease; LAMP2 (lysosomal associated membrane protein-2) for Danon disease; and PRKAG2 (protein kinase, AMP-activated, noncatalytic, gamma-2) for PRKAG2 cardiomyopathy.

As with classic HCM, identified genetic mutations in ApHCM are mainly sarcomeric, autosomal dominant, and influenced by environmental and ethnic/demographic factors including sex. Specific data regarding genetic profiling in the different ApHCM morphologies or ethnicities are lacking. In a
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Histopathology

Myocardial biopsies from the LV apex in ApHCM have been compared with those from the septum in classic HCM and show less myocyte disorganization (10% versus 86%, \( P<0.0001 \)), although severity and extent of interstitial fibrosis was equivalent (100% versus 93%; \( P=\text{ns} \)).

Diagnostic Criteria and Subtypes

Characterized by lack of apical tapering and the presence of precordial T-wave inversion, the diagnostic criteria for ApHCM have evolved over time; originally contingent on left ventriculography demonstrating “unique spade-like configuration and marked apical obliteration” together with electrocardiographic “giant” negative T-waves and high QRS voltage. With imaging advances, definition now relies on demonstrating LVH predominating in the LV apex, with wall thickness in the apex ≥15 mm and a ratio of maximal apical to posterior wall thickness ≥1.5, based on echocardiography or cardiovascular magnetic resonance (CMR). Of note, this diagnostic criterion was not included in the 2014 ESC HCM guideline. The American Heart Association also lacks specific diagnostic criteria for ApHCM and similarly uses wall thickness of ≥15 mm as their threshold for diagnosis of HCM; however, a recent study assessing the reliability of sudden cardiac death recommendations used diagnostic criteria as unexplained hypertrophy in a nondilated LV with wall thickness ≥13 mm by CMR or transthoracic echocardiography, highlighting an emerging trend toward using a lower diagnostic cutoff.

In ApHCM, there is typically no LV outflow tract obstruction from systolic anterior motion of the anterior mitral valve leaflet and therefore no associated mitral regurgitation. ApHCM can exist with or without midventricular obstruction and cavity obliteration (MVOCO) and with or without apical aneurysm formation. It can be subclassified into 3 forms: (1) “pure,” with isolated apical hypertrophy; (2) “mixed,” with both apical and septal hypertrophy but with the apex thickest; and (3) “relative” ApHCM, believed to be an early ApHCM phenotype. Individuals with relative ApHCM do not meet conventional diagnostic criteria for ApHCM but share imaging findings with the pure group. Relative ApHCM is diagnosed when electrocardiography shows characteristic precordial T-wave inversion and CMR shows loss of the usual apical wall thickness tapering due to apical wall thickness exceeding basal wall thickness, although failing to reach the ApHCM diagnostic cutoff of wall thickness ≥15 mm. As the normal heart exhibits tapering of wall thickness towards the apex, loss of this is abnormal. One CMR study reported 22 subjects, 95% of whom had additional

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Table 1. Genetic and Phenotypic Differences and Similarities Between Classic HCM and ApHCM

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<tr>
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<th>Classic (ASH) HCM</th>
<th>ApHCM</th>
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<tr>
<td>% Of all HCM cases</td>
<td>46%</td>
<td>8%</td>
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<td>Mean age at diagnosis, y</td>
<td>46 (all subtypes)</td>
<td>41.41</td>
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<td>ECG</td>
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<td>Voltage criteria for LVH</td>
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<td>Nonspecific ST-segment and T-wave abnormalities</td>
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<td>Deep, narrow Q-waves in the lateral and inferior leads</td>
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<td>Giant negative T-waves characteristic</td>
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<td>Voltage criteria for LVH, T-wave inversion</td>
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<td>AF relatively common; NSVT</td>
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<td>Genetics</td>
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<td>Autosomal dominant sarcomere protein gene mutations</td>
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<td>Identifiable pathogenic gene mutations in 34%–40%</td>
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<td>Majority of gene mutations in MYBPC3 and MYH7</td>
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<td>Majority of gene mutations in MYBPC3 and MYH7</td>
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<td>Associated morbidity</td>
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<td>Atrial fibrillation</td>
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<td>LVOTO</td>
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<td>Diastolic dysfunction</td>
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<td>Chest pain</td>
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<td>Pulmonary hypertension</td>
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<td>Ventricular arrhythmias</td>
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<tr>
<td>All-cause mortality rate</td>
<td>1.3% (all subgroups combined)</td>
<td>0.5%-4% (but much lower patient numbers)–likely equivalent</td>
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ApHCM indicates apical hypertrophic cardiomyopathy; ASH, asymmetrical septal hypertrophy; HCM, hypertrophic cardiomyopathy; LVH, left ventricular hypertrophy; LVOTO, left ventricular outflow tract obstruction; MYBPC3, myosin-binding protein C; MYH7, β-myosin heavy chain; NSVT, nonsustained ventricular tachycardia.
cardiac structural abnormalities including left atrial (LA) dilatation, apical aneurysm, myocardial scar, and ≥20 mm apical systolic cavity obliteration. In another study, relative apical hypertrophy appeared to be the only explanation for giant T-wave inversion, given the absence of other causes of this abnormality.

Relative ApHCM was originally considered entirely benign, but recent data suggest associated pathology with LA dilatation, apical aneurysm, and myocardial scar (Figure 1). Relative ApHCM may simply represent early disease that with time progresses to overt ApHCM, eventually meeting conventional criteria, as with other HCM variants where penetrance is age dependent.

Natural History and Prognosis
ApHCM is more prevalent in men than women, with male-to-female ratios typically 1.6 to 2.8:1. The average age at presentation is 41.4±14.5 years, with mixed ApHCM tending to be more symptomatic and have a greater likelihood of LA enlargement, increased LV filling pressures, and elevated blood cardiac protein biomarkers in the absence of acute coronary syndrome. ApHCM was originally thought to carry no increased mortality risk, but recent data suggest annual cardiac death rates of 0.5% to 4%, approaching those for classic HCM. Increased mortality in women was reported, possibly due to more AF and pulmonary hypertension (Table 1). Patients with mixed ApHCM, younger age at presentation (<41 years), complete end-systolic cavity obliteration at the level of the papillary muscles, paradoxical diastolic flow jet by echocardiography, and apical asynergy have been shown to have higher cardiovascular morbidity. Malignant ventricular arrhythmias and mortality has been linked to apical aneurysms, but only in Western sufferers.

In terms of small-vessel disease and microvascular obstruction, a feature recognized in HCM, there may be an increased role related to reentry around the aneurysm. LA enlargement secondary to LV diastolic dysfunction at the time of first ApHCM presentation predicts later AF, which is commoner in females and prognostically adverse.

Serum Biomarkers
Comparing high-sensitivity cardiac troponin T levels between different HCM morphological subtypes found rates in ApHCM versus nonobstructive versus obstructive classical HCM of 14%, 47%, and 57%, respectively. High-sensitivity cardiac troponin T correlated with age, LA area, and maximum LV wall thickness in mixed subtypes. In another study, cardiac troponin I was significantly lower in ApHCM compared with classic HCM, and it correlated with maximum LV wall thickness, LV dysfunction, and male sex when considering all subtypes.

Cavity Obliteration
Apical systolic cavity obliteration occurs in pure, and to a lesser extent, relative ApHCM. A measure of the degree of apical cavity obliteration is provided by the ratio of the end-systolic length of apical obliteration to the end-systolic length of the LV cavity. A systolic obliteration-to-cavity ratio >0.5 is associated with increased incidence of AF, stroke, heart failure, and cardiovascular death. Degree of obliteration rather than apical wall thickness influences prognosis.

MVOCO may occur as a consequence of midapical lateral and septal hypertrophy and therefore a complication of mixed rather than pure ApHCM. In severe cases, midventricular cavity obliteration persists in diastole and is often associated with a paradoxical midcavity diastolic flow jet, which indicates the associated presence of an apical aneurysm. In contrast, the pathophysiology behind midventricular obstruction in classic HCM is attributable to the basal-to-midseptal hypertrophy coming into contact with a hypercontractile but nonhypertrophied LV free wall, often with the interposition of hypertrophied papillary muscle.

Apical Aneurysms
Apical aneurysms are defined as a discrete, thin-walled, dyskinetic/akineti c segment of the most distal portion of the
LV with a relatively wide communication to the main cavity in diastole. They occur in 2% of patients with HCM and 13% to 15% with ApHCM (Figure 3). A cue to their presence is the persistence of apical blood pooling distal to the point of apical systolic cavity obliteration and/or a paradoxical diastolic jet. Small aneurysms are often overlooked on echocardiography and may be difficult to delineate without advanced imaging.

In ApHCM, it is hypothesized that apical aneurysms and obstructive physiology arise from regional myocardial scarring caused by repeatedly exposing the apical myocardium to increased LV wall stress and high systolic pressures, leading to pressure overload, increased oxygen demand, impaired coronary perfusion, and ischemia. The dyskinetic/ akinetic aneurysm confers risk of apical thrombus formation and thromboembolic stroke. Apical aneurysms have been associated with LVH severity, SCD, monomorphic VT, LV systolic dysfunction, and heart failure.

It is important to distinguish apical aneurysms arising from ApHCM from those arising from midcavity obstruction in classic HCM. One study investigating outcomes in patients with apical aneurysms irrespective of the HCM morphological subtype, identified aneurysms in 4.8%. Authors identified 2 distinct patterns of LVH in those with aneurysms: segmental thickening confined to the distal LV in 51%, and in the remaining 49% diffuse thickening of the septum and free wall, resulting in an “hourglass” configuration with midventricular muscular narrowing, creating discrete proximal and distal chambers. Thromboembolic events were 2-fold more common (P=0.06) in those with apical aneurysms compared with those without, and this subgroup also experienced a 3-fold greater adverse event rate, at 6.4%/year.

**Phenotypic Mimics**

Fabry disease causes progressive LVH that potentially mimics ApHCM. Up to 23% of patients with Fabry disease with LVH have ApHCM pattern by CMR.
Long-term athletic training produces cardiac structural changes, namely, increased diastolic dimensions of the LV cavity, LVH, and increased LV mass. In athletes with LVH, distinguishing the physiological “athlete’s heart” from HCM may be challenging. An overlapping “gray zone” is described when absolute LV wall thickness is between 13 and 15 mm, observed in 2% of highly trained male athletes. Highly trained female athletes rarely show >11 mm of LVH, suggesting that athletic females presenting within the “gray zone” are more likely to have HCM. One study exploring LVH ≥13 mm on echocardiography, 3 had pure apical LVH (range 15–18 mm), and 2 had LVH basally, as well as in the apex. Native T1 and extracellular volume values using CMR are lower in athletes than in HCM, which is a useful differentiator. Furthermore, as LVH increases in athletes, extracellular volume continues to decrease, whereas in HCM it continues to increase.

Athletes with pure apical LVH had normal ECGs (no T-wave inversion), and the phenotype was postulated to reflect athletic training, rather than true HCM. Another study demonstrated that athletes with HCM were 3 times likelier to exhibit ApHCM than their sedentary HCM counterparts (35.8% versus 11.9%). It is difficult to distinguish apical LVH attributable to athletic remodeling from ApHCM; however, an ApHCM-pattern ECG is regarded as unequivocally abnormal. The increased frequency of ApHCM in athletes may itself reflect an ascertainment bias resulting from screening programs, but as mentioned above, the difficulty in assessing SCD risk remains.

**Imaging**

**Echocardiography**

Transthoracic echocardiography can reveal apical hypertrophy, differentiate between pure and mixed forms, and identify additional prognostic features that could influence outcome such as the presence of diastolic dysfunction, MVOCO, or apical aneurysms. However, imaging the apex remains a potential challenge, particularly for subtle prognostic features such as apical akinesis or sequestration caused by massive hypertrophy. Early phenotypes and relative ApHCM could be missed by echocardiography; thus, those with deep T-wave inversion and noncontributory echocardiography should undergo additional imaging. Although global LV systolic function may appear normal or supranormal in ApHCM, LV peak systolic mitral annular velocity (S') is commonly reduced, more so in the mixed rather than in the pure form. Interstitial fibrosis of the subendocardium (where muscle bundles aligned along the LV driving long-axis function), commonly seen in ApHCM, may partly account for this impairment. Furthermore, end-systolic MVOCO and paradoxical diastolic flow jets predict apical asynergy and apical aneurysms, and are associated with increased morbidity.

Two-dimensional strain or speckle tracking demonstrate regional apical dyskinesis and reduced LV “twist,” which can be attributable to cavity obliteration negating the effect of apical twist in systolic contraction.

**Cardiovascular Magnetic Resonance**

CMR may detect early ApHCM phenotypes better than echocardiography. Apical hypertrophy was missed by echocardiography in 40% of cases, later detected by CMR. CMR is more sensitive at detecting apical aneurysms and can identify 25% to 43% of those missed by echocardiography. CMR has advantages in confounding patient populations, such as athletes. Late gadolinium enhancement (LGE) is common in HCM; the presence and amount of LGE may be associated with the severity of hypertrophy as well as increased risk of heart failure and SCD. LGE patterns in ApHCM are characteristic: apical and subendocardial – patterns that are uncommon in other HCM variants in the absence of coexisting coronary disease. This “MI pattern” of LGE adds credence to the hypothesis that apical myocardial ischemia is key in ApHCM. HCM registry data showed LGE in ApHCM in 45.8% of subjects. Aneurysms are considered the arrhythmogenic substrate, but it may be the intra-aneurysm scar that matters most. Of note, extent/presence of (apical or any) LGE does not contribute to cavity obliteration negating the effect of apical twist in systolic contraction.
versus healthy controls, values consistently correlate with wall thickness and LGE and can also be elevated in LGE-negative apical segments.41 Areas of T2 elevation (indicating myocardial edema) are also seen in HCM.

Rest and stress perfusion data are missing for ApHCM (Figure 5). Rest perfusion abnormalities have been well described in classic HCM, correlating with severity of LGE, degree of hypertrophy and myocardial fibrosis.42 The clinical significance of perfusion abnormalities is not yet explored.

**Cardiac Computerized Tomography**

Computerized tomography (CT) using iodine-based contrast detects late enhancement consistent with the presence of myocardial fibrosis. While the segment-based sensitivity of
computerized tomography for HCM fibrosis detection is lower than for CMR, patient-based sensitivity is similar offering a viable alternative for those unable to undergo CMR. As it is not uncommon for ApHCM to open clinically with chest pain and T-wave inversion, computerized tomography reporters should be alert to the possibility of discovering ApHCM in such referrals.

**Nuclear Scintigraphy**

Perfusion imaging using single photon emission computed tomography (SPECT) unveils the characteristic (but not pathognomonic) “solar polar” perfusion map of ApHCM: an intensely bright apical spot of counts surrounded by a circumferential ring of decreasing counts. Other findings...
include increased apical tracer uptake at rest and the spadelike configuration of the LV. Fixed and reversible stress perfusion defects are reported in the context of unobstructed epicardial coronary arteries, but again, the significance of these findings is unexplored. Single photon emission computed tomography can miss ApHCM because dense apical fibrosis normalizes apical tracer counts so single photon emission computed tomography and other findings (ECG, wall thickness) do not correlate.

Angiography
Left ventriculography identifies the characteristic “ace of spades” LV cavity configuration in end diastole in 69% of cases and aids the detection of apical aneurysms.

Management Strategies
Management in HCM involves symptom assessment and determination of likely mechanisms of symptoms, risk

Figure 5. Quantitative perfusion mapping in ApHCM. CMR pixelwise inline perfusion maps at rest (A), stress (B) in (i) basal, (ii) mid, (iii) apical short axis and (iv) 2-chamber views in a patient with ApHCM and MVOCO. Stress perfusion defects are seen in the hypertrophied apex. Bull’s-eye plots are shown (rest C, stress D). There is 37% MBF reduction at stress (D) apically (1.47 mL/g per minute) vs 2.35 mL/g per minute in remote, non-hypertrophied segments. Rest MBF(C) is 0.74 and 0.85 mL/g per minute, respectively. MPR is 1.99 in the apex and 2.76 in remote myocardium, indicating microvascular disease in the hypertrophied apex. Healthy volunteer stress MBF is 2 to 4 mL/g per minute. ApHCM indicates apical hypertrophic cardiomyopathy; CMR, cardiovascular magnetic resonance; MBF, myocardial blood flow; MPR, myocardial perfusion reserve; MVOCO, midventricular obstruction and cavity obliteration.
**Table 2. Management Differences and Similarities Between Classic HCM and ApHCM**

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<th>Classical (ASH) HCM</th>
<th>ApHCM</th>
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<tr>
<td><strong>Medical</strong></td>
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<tr>
<td>β-Blockers</td>
<td>- First-line treatment to reduce LVOT and burden of ventricular arrhythmias</td>
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<tr>
<td></td>
<td>- Nondihydropyridine calcium channel blockers – second line</td>
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<tr>
<td></td>
<td>- Atrial fibrillation and thromboembolism less common than in ApHCM but if present, anticoagulant indicated</td>
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<tr>
<td>VT ablation</td>
<td>- Also first line (symptom improvement in MVOCO and reduce burden of ventricular arrhythmias)</td>
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<td></td>
<td>- Nondihydropyridine calcium channel blockers also second line</td>
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<td></td>
<td>- Anticoagulants in the case of atrial fibrillation or thromboembolism</td>
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<tr>
<td><strong>Ablation</strong></td>
<td>Alcohol septal ablation of hypertrophied basal septum in symptomatic LVOT</td>
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<td></td>
<td>VT ablation considered</td>
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<td></td>
<td>Potential role of alcohol ablation in symptomatic ApHCM with MVOCO (no randomized control data)</td>
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<tr>
<td></td>
<td>- No role for alcohol septal ablation</td>
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<td></td>
<td>- VT ablation in rare cases</td>
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<tr>
<td><strong>Devices</strong></td>
<td>ICD implantation (ESC 5-y HCM SCD risk score tailored more specifically to ASH risk factors than other morphological variants)</td>
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<tr>
<td></td>
<td>- AHA guidance on ICD implantation broader</td>
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<td></td>
<td>ICDs may be underutilized because of current scoring criteria if using ESC algorithm</td>
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<tr>
<td></td>
<td>- Current prospective trial of distal ventricular pacing for ApHCM with drug refractory symptoms and MVOCO</td>
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<tr>
<td><strong>Surgical</strong></td>
<td>Septal myectomy (reduces symptoms and risks associated with LVOT)</td>
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<tr>
<td></td>
<td>Few case reports detailing symptomatic improvement following apical myectomy. No randomized control data</td>
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AHA indicates American Heart Association; ApHCM, apical hypertrophic cardiomyopathy; ESC, European Society of Cardiology; ICD, implantable cardiac defibrillator; LVOT, left ventricular outflow tract obstruction; MVOCO, midventricular obstruction and cavity obliteration; SCD, sudden cardiac death; VT, ventricular tachycardia.

assessment and its mitigation, family screening, and chronic symptom/risk management. Treatment options for ApHCM are based on classic HCM approaches aiming to minimize any heart failure, AF, or MVOCO symptoms and reduce/mitigate ventricular arrhythmias and sudden death. Therapy is medical or electrophysiological (device/ablation), but as LV outflow tract obstruction is typically absent in ApHCM, therapeutic benefits may be lower than in classic HCM, and myectomy-type approaches are exploratory rather than routine (Table 2).

**Medical**

β-Blockers reduce rest and exercise-induced LV outflow tract obstruction in classic HCM, and the negative inotropic and chronotropic effects of nondihydropyridine calcium channel blockers prolong LV filling, reduce gradients, and improve subendocardial blood flow in classic HCM, but data for ApHCM are missing.

**Catheter Ablation**

Although sustained monomorphic VT is uncommon in classic HCM, a case series reported monomorphic VT in ApHCM from reentry in a region of apical scar. Circuits were varied (endocardial, epicardial, intramural) and successfully ablated using endocardial/epicardial/transcoronary approaches.

**Devices**

There are currently no trials or predictive models to guide implantable cardiac defibrillator (ICD) insertion specifically for ApHCM. The ESC 5-year HCM SCD risk score was based on all HCM morphological subtypes without breakdown for ApHCM. Potential risk markers for SCD in ApHCM (apical aneurysm, MVOCO, midcavity gradient, paradoxical diastolic flow jet) were not shortlisted predictors. ApHCM patients tend to score negative for family history of SCD, and there is concern that risk may be underestimated. For intermediate-risk patients, the ESC guideline suggests that the presence of “other” potentially relevant associated adverse markers like apical aneurysms (alluding to ApHCM) may also be taken into account when planning implantable cardiac defibrillators. In contrast, Maron’s group have recently sought to evolve the American Heart Association guidance for implanting cardiac defibrillators by proposing new criteria for HCM patients fulfilling one or more major risk factors for SCD. These include novel high-risk markers such as CMR LGE demonstration of extensive fibrosis comprising ≥15% of LV mass by quantification or “extensive and diffuse” by visual estimation, and also the presence of LV apical aneurysm, independent of size, with associated regional scarring. This risk stratification is more sensitive at predicting those at risk of SCD than the ESC guidance and demonstrates progression toward understanding more individualized risk factors.

Dual-chamber pacing with short atrioventricular delay has been proposed as a treatment for symptomatic HCM with apical LVH where there are detectable midapical LV...
obstructive gradients.\textsuperscript{49} This is thought to work by reducing the extent of regional LV cavity obliteration through the introduction of contractile dysynchrony. Our group is currently conducting a randomized placebo-controlled trial of distal ventricular pacing in patients with drug-refractory symptoms and MVOCO (Clinicaltrials.gov NCT03450252).

Alcohol Septal Ablation and Apical Myectomy

The absence of overt septal hypertrophy causing LV outflow tract obstruction may render septal ablation/myectomy in ApHCM unwarranted, but single case studies have highlighted a potential role in those with symptomatic MVOCO, as it may reduce gradients and improve heart failure symptoms. Additionally, apical myectomy has been reported to increase end-diastolic dimensions and improve symptoms.

Conclusions

ApHCM poses specific etiological, diagnostic, prognostic, and therapeutic challenges compared with more commonly detected and better understood morphological HCM variants. The phenotypic spectrum and natural history of ApHCM ("pure," "mixed," and "relative") is being clarified, as is the impact of sarcomere gene mutations, sex, and other clinical and environmental factors on phenotype expression. Further research is needed to understand why some patients develop mixed ApHCM with a higher risk of arrhythmias, heart failure, and SCD, while others go on to manifest the pure form with a relatively more benign course. ApHCM-specific treatments are needed to halt or regress the LV mid-to-apical hypertrophy and its ensuing complications and multicenter longitudinal outcome data needed to robustly inform on an SCD risk stratification tool appropriate for ApHCM.

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Disclosures

None.

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