Caso clínico Dr Guillermo Centurion Villegas GUILLECV35@HOTMAIL.COM

Masculino 51 años deportista de natación de largos trayectos. Nada 4-5 km en travesías. Asintomático.

Motivo de la consulta: esclarecimiento de problemas detectados por ocasión de control para la práctica de deportes

Antecedentes familiares: Padre tuvo muerte súbita a los 45 años (Al parecer por infarto agudo del miocardio(IAM)?. Era obeso, tabaquista, alcohólico).

Examen cardiovascular normal. PA en consultorio 130/90 mmHg

En 2007 por ocasión de un control deportivo, se detectó un ECG patológico que motivó la realización de tomografía computadorizada del corazón que reveló apenas hipertrofia apical del VI y coronarias normales. ECG: Bradicardia sinusal 54 lpm, onda T negativas profundas en pared antero lateral y en II.

Ecocardiograma ventrículo izquierdo de diámetros máximos normales, espesor de paredes normales.

FEVI conservada. VD s/p. Dilatación biauricular y de la raíz aórtica. Función diastólica normal

Ergometría en cicloergómetro CF IA (PP+)

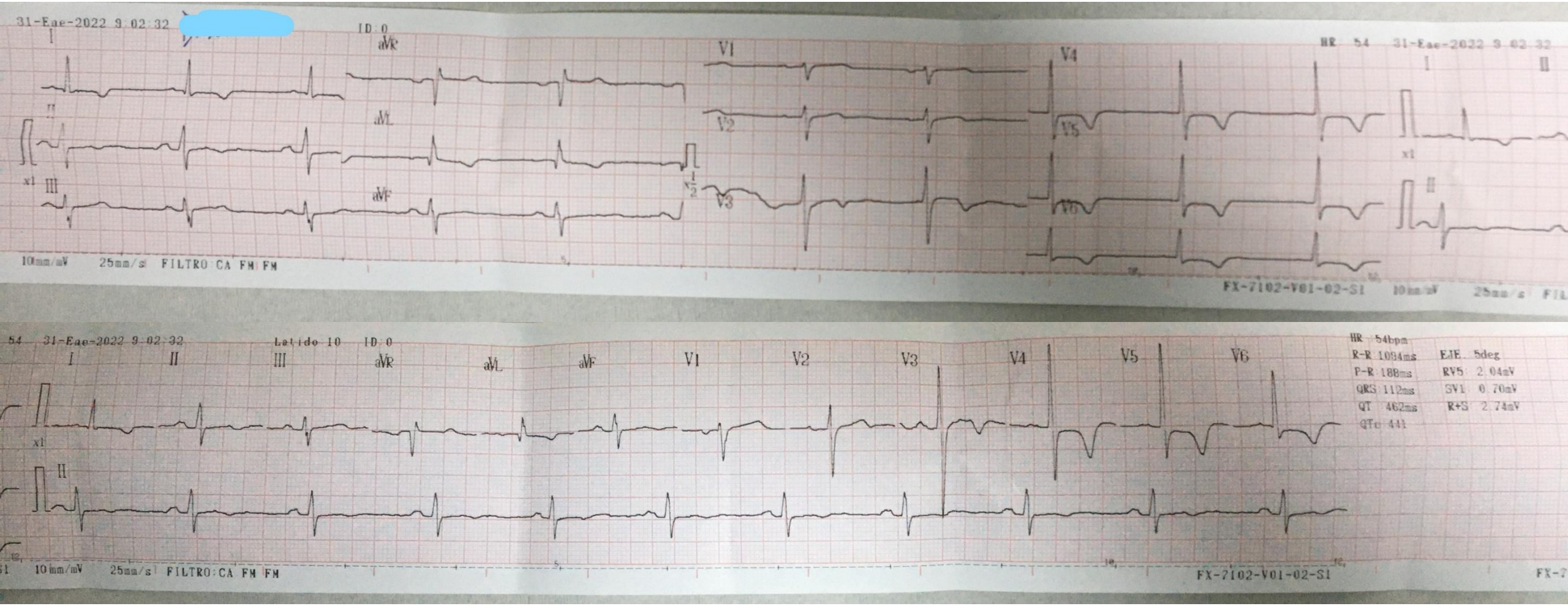
Case report

51-year-old male long-distance swimming athlete. Swim 4-5km on trails. Asymptomatic

Reason for consultation: clarification of problems detected by control occasion for the practice of sports.

Family bacground: Father had sudden death at age 45 (Apparently due to acute myocardial infarction (AMI)? . He was obese, smoker, alcoholic).FE: Normal cardiovascular exam. BP 130/90 mmHg

In 2007, during a sports check-up, a pathological ECG was detected that prompted a computed tomography scan of the heart that revealed Left ventricular hypertrophy (LVH)confined on apical region: Apical Hypertrophic Cardiomyopathy (ApHCM) and normal coronary arteries. ECG: sinus bradycardia (54 bpm), deep negative T waves in the anterolateral wall and in II. Transthoracic echocardiogram Left ventricular normal maximum diameters, normal wall thickness. preserved LVEF. Normal RV. Biatrial and aortic root dilatation. normal diastolic function. Ergometer in cycle ergometer CF IA (PP+)

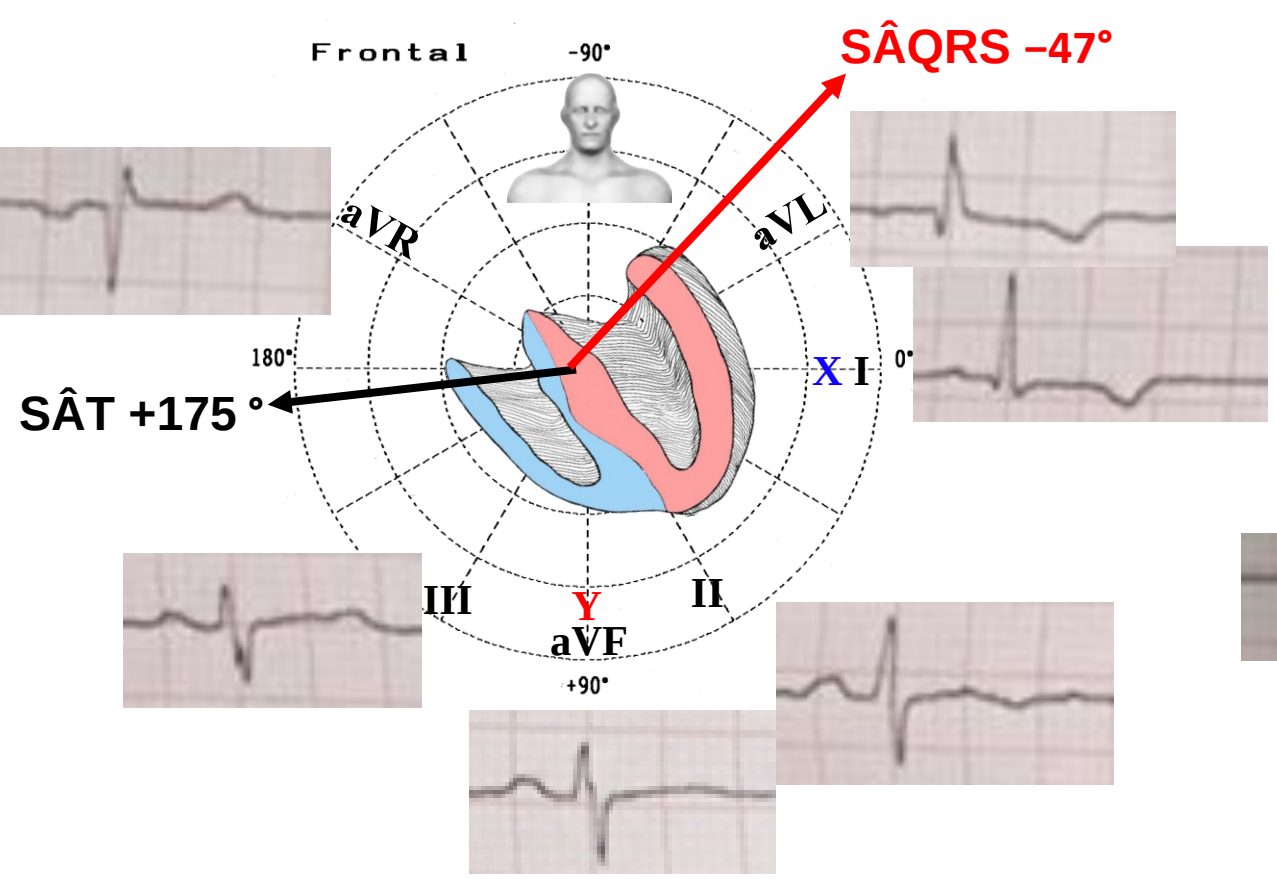


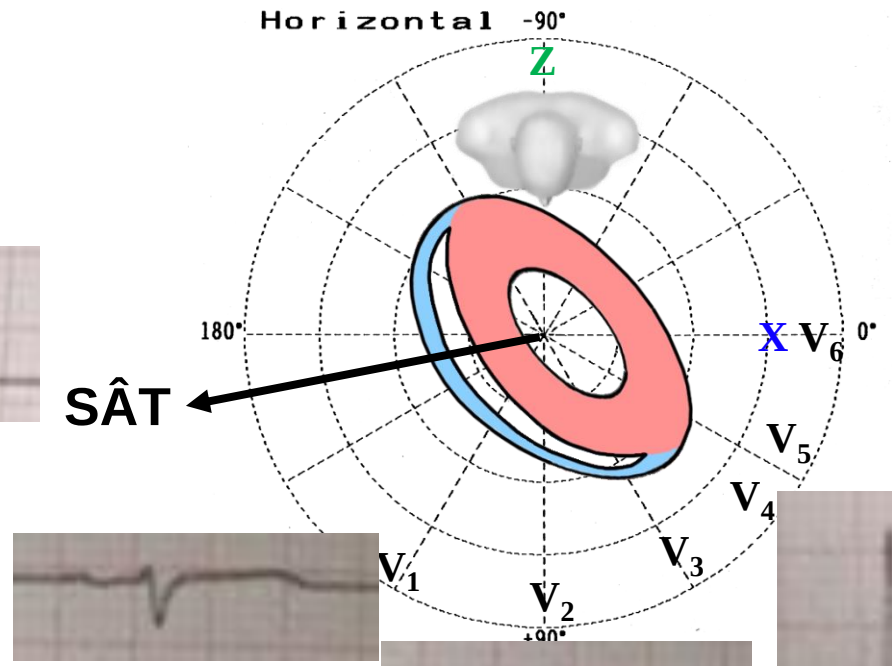
Let's see ECG analyze no next slide

Vejamos ECG analise no proximo slide

Veamos análisis del ECG en la siguiente diapositiva

Wide QRS-T angle >90° A wide frontal QRS-T angle greater than 90° was associated with an increased risk of SCA independent of demographic characteristics, baseline comorbidities, prolonged intraventricular conduction, ECG LVH and LVEF in this population. This simple ECG tool should be evaluated as a measurement that could potentially enhance clinical risk stratification for SCA. (1)



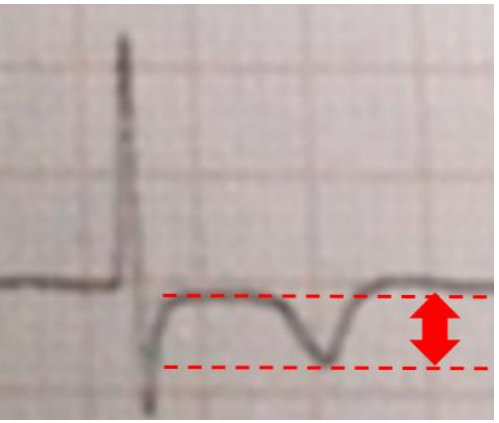


Negative T-waves Not giant !

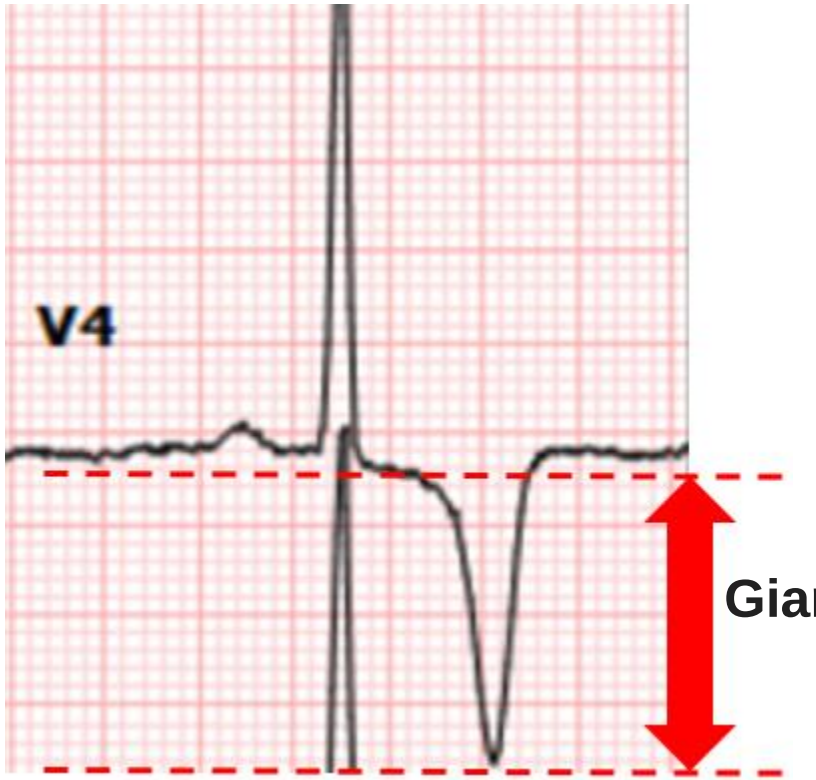
1. Kelvin C.M. Chua, et al.,QRS-T angle on the 12-lead ECG as a Predictor of Sudden Death beyond the LV Ejection Fraction.J Cardiovasc Electrophysiol. 2016 Jul; 27(7): 833–839.doi: 10.1111/jce.12989

Giant negative T-waves defined as negative voltage of ≥1 mV (≥10 mm)[1] are characteristic but not are but not pathognomonic nor mandatory for diagnosis. In one ApHCM study of 105 patients, 94% had abnormal ECGs with voltage criteria for LVH (65%) and T-wave inversion (93%), but **only 47% had Giant negative T-waves**.[1]

ECG of
Dr Guillermo Centurion Villegas patient



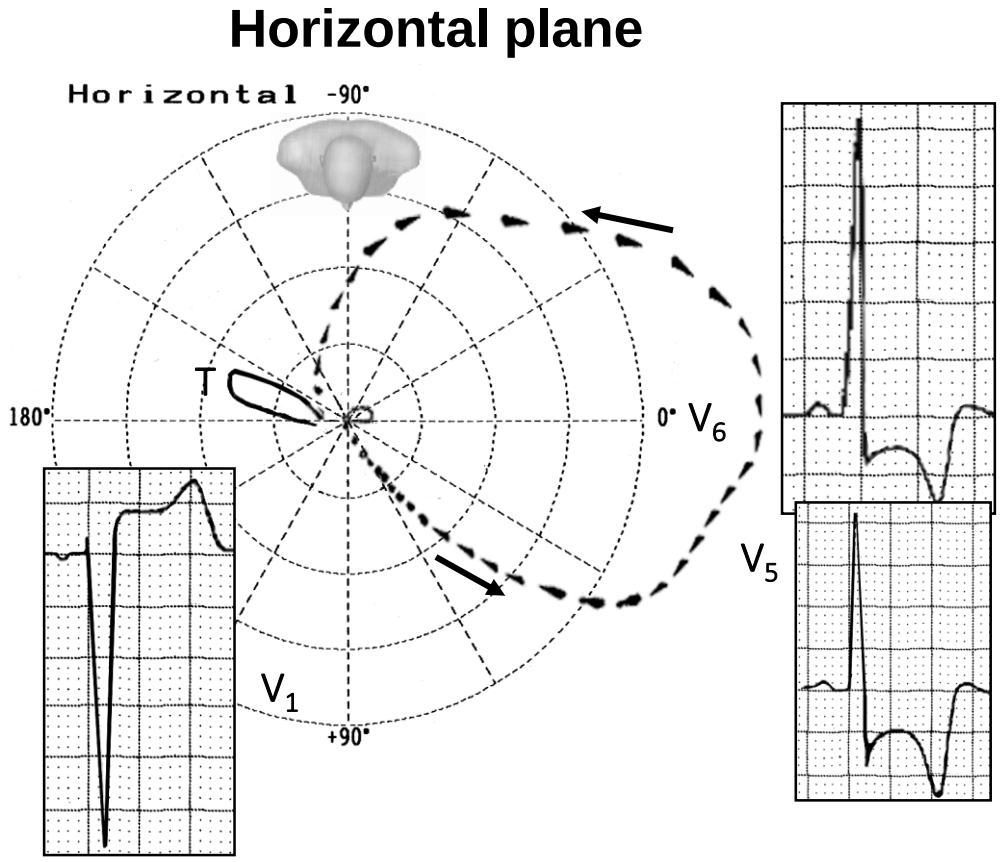
Negative T-waves
No Giant



Giant negative T-waves
≥1 mV (≥10 mm)

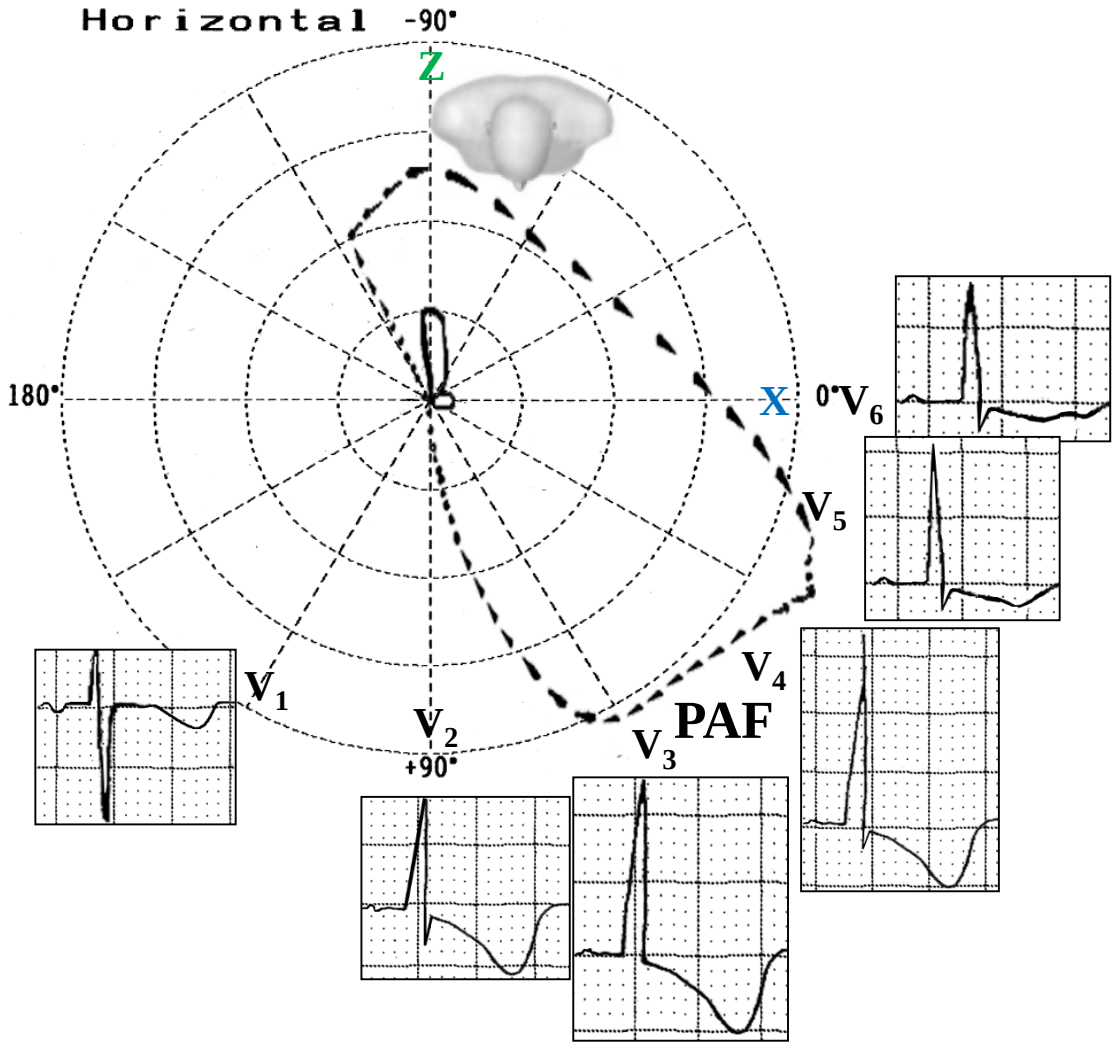
1. **Eriksson MJ, Sonnenberg B, Woo A, Rakowski P, Parker TG, Wigle ED, Rakowski H, Douglas Wigle E, Rakowski H, Toronto F. Long-term outcome in patients with apical hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 2002;39:638–645**

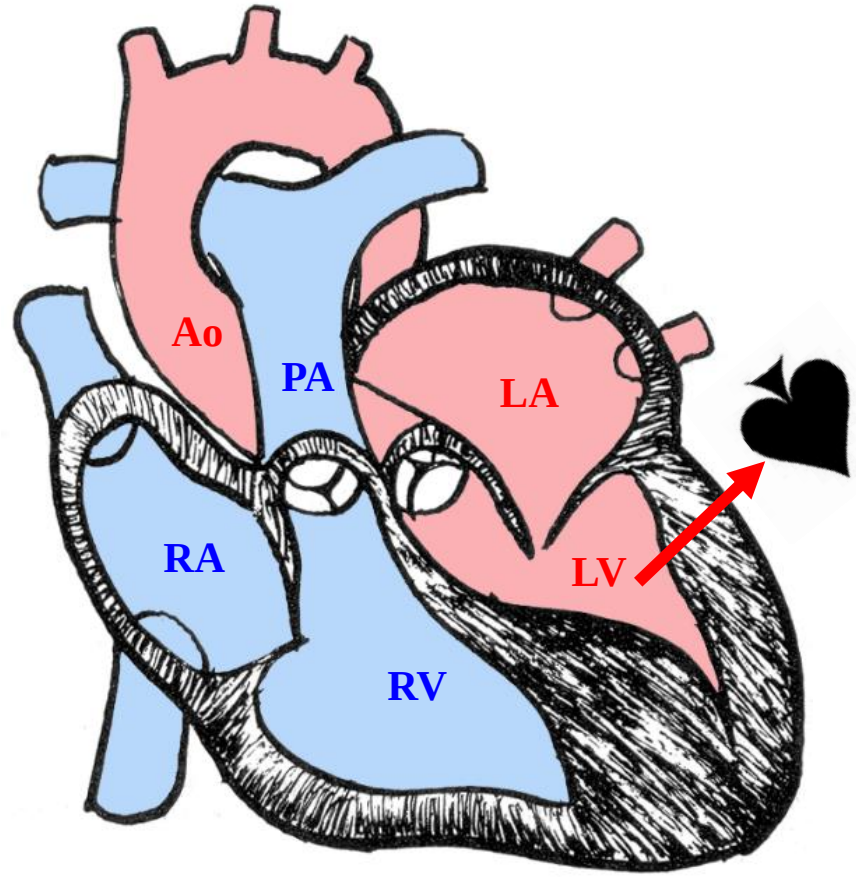
Vectocardiogram of apical NO-HCM: vectorcardiographic LVH type IV of our classification



- Initial vectors of QRS loop heading forward and to the left;
- Anteriorization of QRS loop predominantly located in the left anterior quadrant;
- Maximal vector that increases voltage;
- Final vectors located to the right and backward with ST/T vector in the right posterior quadrant;
- E point that does not match the 0 point and is located backward and rightward from the latter.

Left Ventricular Hypertrophy, vectorcardiographic type IV



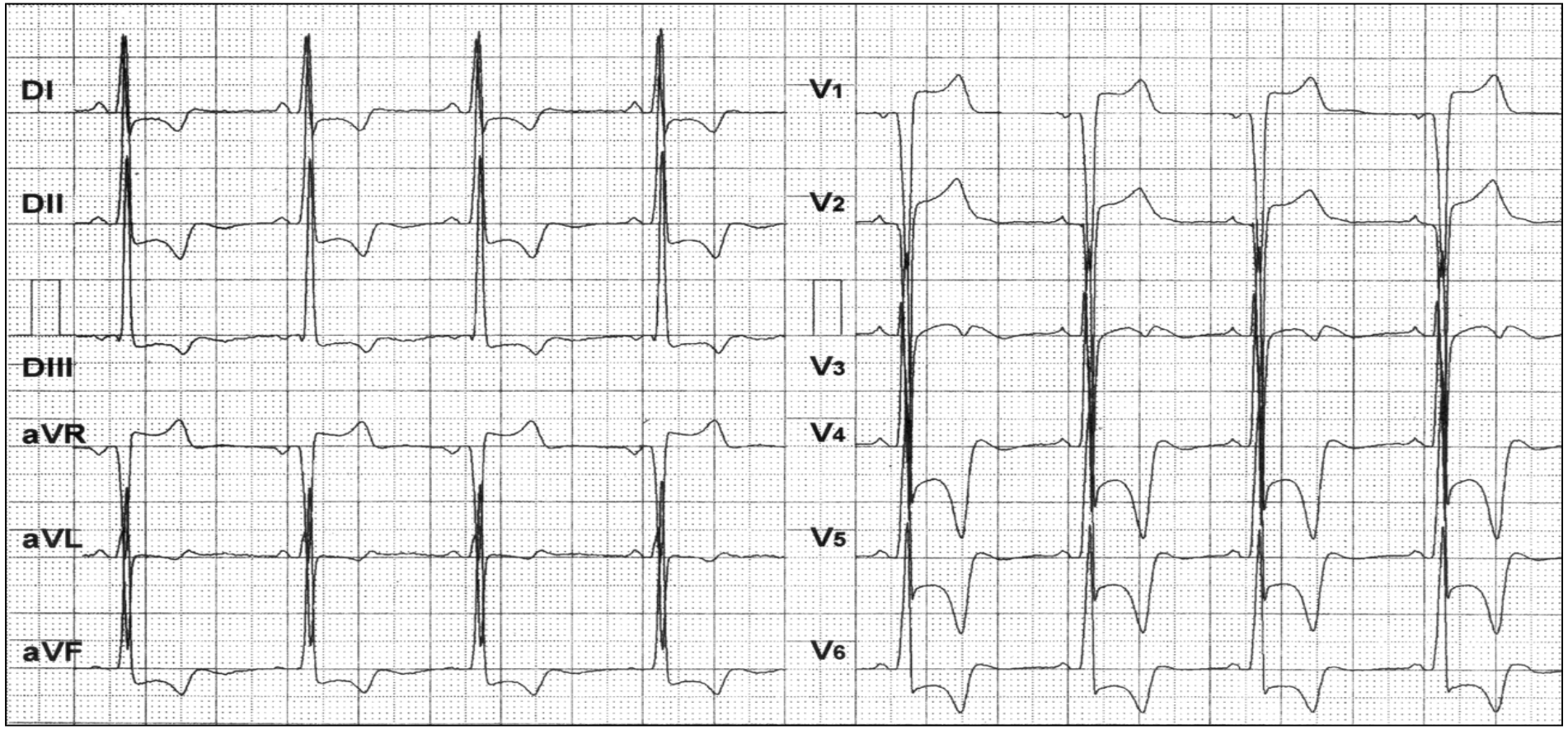


The "ace-of-spades" sign

Clinical diagnosis: non-obstructive apical hypertrophic cardiomyopathy of the inferior and apical region of the septum.

ECG/VCG diagnosis: LVH type IV: Prominent QRS loop Anterior Forces (**PAF**). The QRS-loop is located predominantly in the left anterior quadrant. The initial 10 to 20 ms forces without convexity to the right. The R waves are predominant across precordial leads. The T loop is located in the posterior quadrants on orthogonal Z line; consequently, T waves are negative, deep and giant in precordial leads.

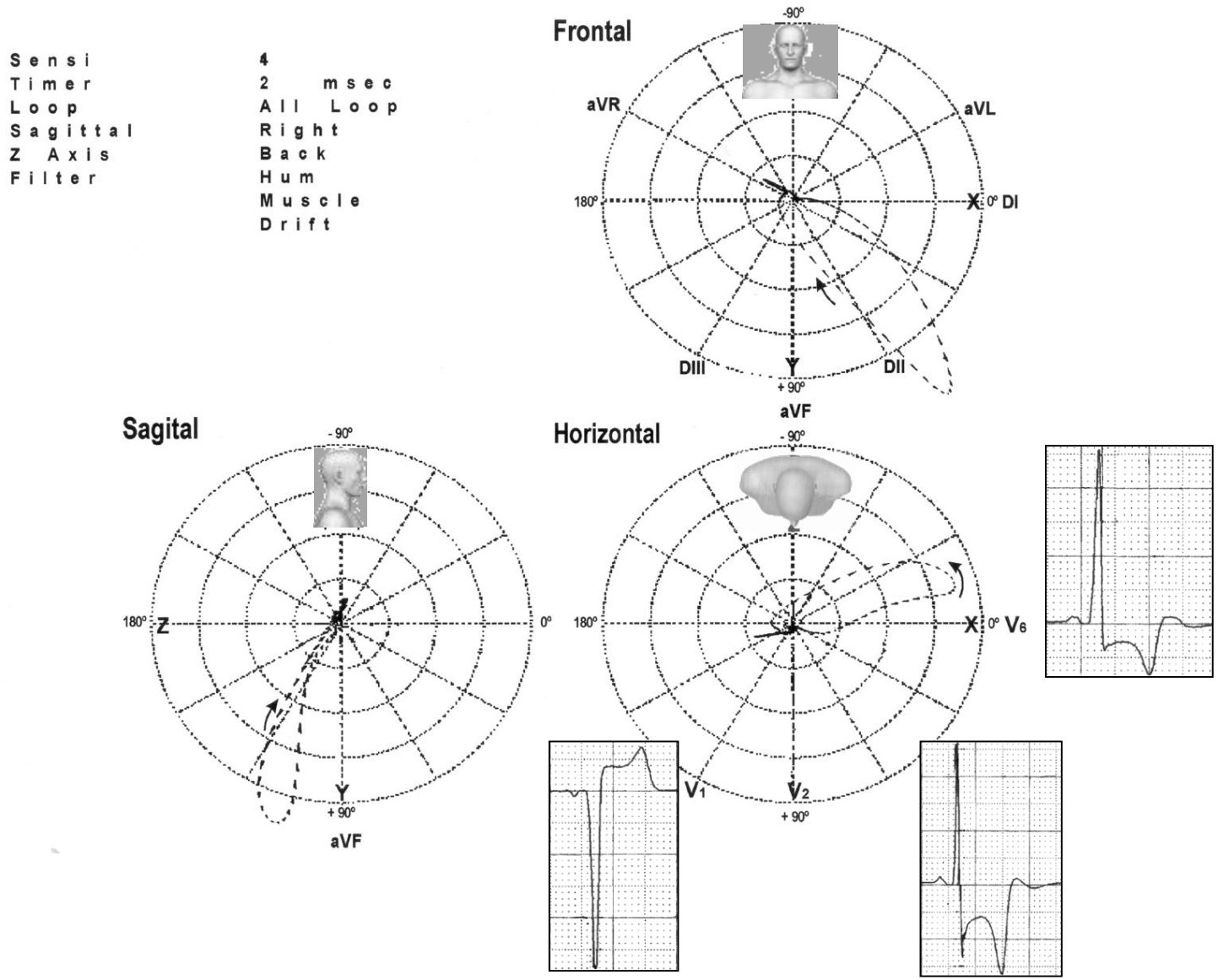
Name: SFS; **Age**: 15 y/o; **Sex**: M; **Race:** W; **Weight**: 70 Kg; **Height**: 1.72 m; **Date**: 03/31/98;**Medication in use**: beta blockers.



Clinical/echocardiographic diagnosis: Non-obstructive hypertrophic cardiomyopathy. Diastolic thickness of interventricular septum in the apical region greatly increased (32 mm): Ap-HCM.

ECG diagnosis: sinus rhythm, LAE, normal QRS axis on frontal plane (+50º), LVH (positive Sokolow-Lyon index: S of V1 + R of V5 ≥ 35 mm or 3.5 mV in adults older than 30, 40 mm or 4.0 mV between 20 and 30 years (Sokolow-Rapaport) and > 60 mm between 16 and 20 years and > 65 mm between 11 and 16 years), QS pattern in V1-V2 contrasting with abruptly prominent QRS anterior forces in intermediate leads (V3-V4), R wave of V5 or V6 > 26 mm and strain pattern of ventricular repolarization from V4-V6, high lateral (I aVL), and inferior wall (II-III-aVF) leads (wide QRS/ST/T angle: near 180º).

ECG/VCG correlation



Vectorcardiogram diagnosis: The main body of the QRS loop located in the left, inferior, and posterior quadrant and the magnitude of maximal QRS vector clearly increased (>2.2 mV.): LVH. Giant negative T wave from V4 to V6 (Ap-HCM)

Hypertrophic cardiomyopathy (HCM) is a cardiomyopathy genetically determined that constitutes the main cause of SCD in young athletes.[1] Its most frequent form derives from heterogenic mutations of sarcomeric proteins.[1,2] HCM is associated with a variable degree of penetrance and clinical expression.[1,3]

LVH with diastolic dysfunction and no other known cause, such as essential hypertension or severe aortic stenosis, is the main feature of the disease.[3,4]]

Wall thickness ≥ 15 mm in any segment of the LV is diagnostic for HCM.[1,3] This is associated with heart failure (HF) and increased risk of SCD.[1,3,4] Hypertrophied myocytes displayed in a core of interstitial fibrosis may justify a substrate for an increased arrhythmic risk, therefore indicating the need for an implantable cardiac defibrillator (ICD) in some cases.[5] LVH is not usually present at birth, but instead develops gradually in adolescence and has a progressive behaviour.[1]

Main risk factors establish as higher risk for SCD

1) Cardiac Arrest
2. Higher LV maximum thickness
3. Larger left atria
4. Higher left ventricular outflow tract gradient
5. Family history of SCD
6. Prior history of complex arrhythmic events or cardiac arrest (CA).[2,6]
7. Recurrent unexplained (not neurally mediated) syncope particulary in young people
8. History of recovery from SCD
9. Blood pressure decrease or inadequate increase during upright exercise
10. Hereditary genetic defect, associated to unfavorable prognosis
11. Presence of NS-VT in Holter in patient with alteration of conscience

Apical HCM (ApHCM) represents a complex subset of patients with a non-obstructive variant of HCM, whose risk of SCD seems not negligible.[7]

All patients must undergo risk stratification for SCD, albeit most applied scores likely underestimate the risk of heart events.[8,9] It is not yet fully established if this lower score represents a lower arrhythmic risk of the variant itself or if it shows a lower capability on predicting the risk of events in these patients.

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.[4]

Ethnic variation influences prevalence, natural history, and prognosis, and Western sufferers may exhibit a more malignant form.[1]

Genetics

Fewer ApHCM patients report a positive family history compared with classic HCM,[5] 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 [6], [7].[1], [2], [4], [8], [9], [10], [11]

Genetic and phenotypic differences and similarities between Classic HCM and ApHCM

	Classic HCM	ApHCM
% Of all HCM cases	**46%**	**8%**
Mean age at diagnosis	**46 (all subtypes)**	**41.(41)**
ECG	➢ Voltage criteria for LVH ➢ Nonspecific ST-segment ➢ T-wave abnormalities ➢ Deep, narrow Q-waves in the lateral and inferior leads	• Giant negative T-waves • Characteristic voltage criteria for LVH, • T-wave inversion • AF relatively common; • NSVT
Genetics	✓ Autosomal dominant sarcomere protein gene mutations ✓ Identifiable pathogenic gene mutations in 34%–40% ✓ Majority of gene mutations in MYBPC3 and MYH7	❑ Autosomal dominant sarcomere protein gene mutations ❑ Identifiable pathogenic gene mutations in 13%–25% ❑ Majority of gene mutations in MYBPC3 and MYH711

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.

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[11]: *ACTC1* (cardiac α-actin 1), *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.[11] 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.[12]As with classic HCM, identified genetic mutations in ApHCM are mainly sarcomeric, autosomal dominant, and influenced by

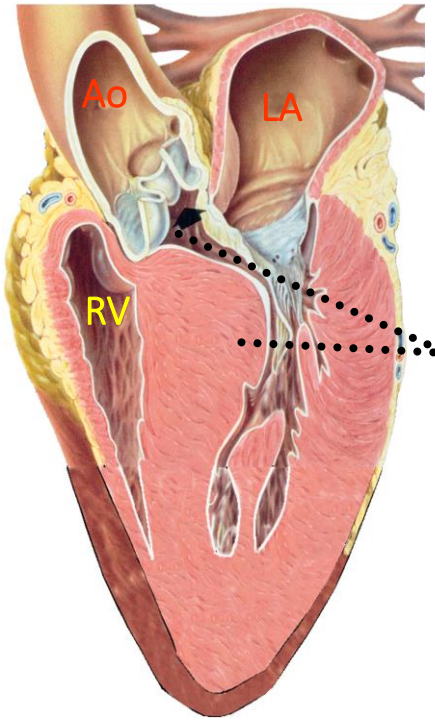
Hypertrophyc cardiomyopathy classification

1) **Obstructive forms (O-HCM)**
   - ❑ Septal asymmetrical with resting LVOT obstruction (obstruction at subaortic level): is found in approximately 20% of the patients, classically occurs at the, and is associated with mitral valve systolic anterior motion (SAM).
   - ❑ Mid-ventricular obstructive HCM (MVO-HCM): asymmetrical LVH with MVO and elevated intraventricular pressure gradients (1%).

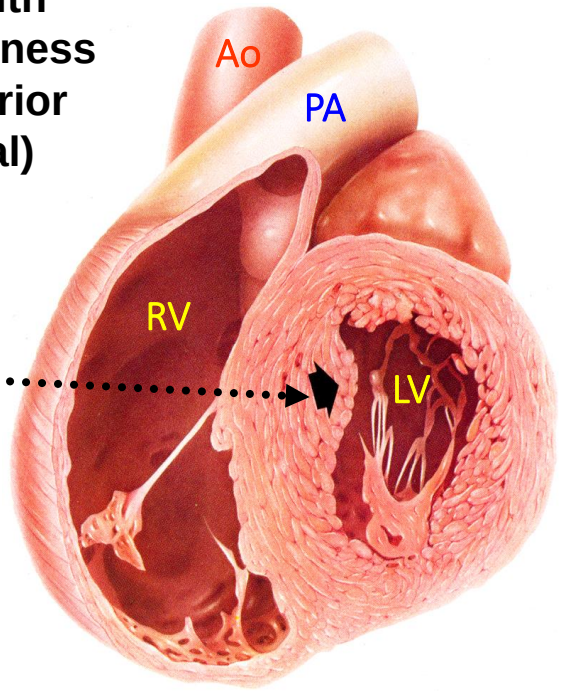
2) **Non-obstructive forms (NO-HCM)**
   - ❑ Septal asymmetrical with no obstruction;
   - ❑ **Apical Hypertrophic Cardiomiopathy (Ap HCM): 2%, 3% to 8%;**
   - ❑ Lateral and/or posterolateral;
   - ❑ Concentric or symmetrical, or homogeneous hypertrophic: 5%;
   - ❑ Right ventricle: 2%.

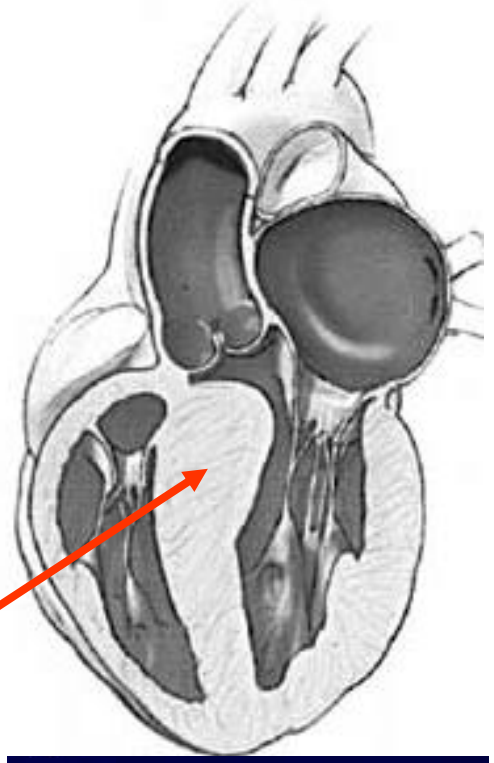
Obstructive form (O-HCM)	Non-obstructive form (NO-HCM)
Septum with greater thickness in the superior part (basal) (20% or in the middle portion) (1%).	Septum with greater thickness in the inferior part (apical).
Free wall with progressive decrease of thickness from the base to the apex (the same as normal).	Free wall with no or normal decrease of the thickness from the base to the apex.

Classical obstructive form of hypertrophic cardiomyopathy (O-HCM)

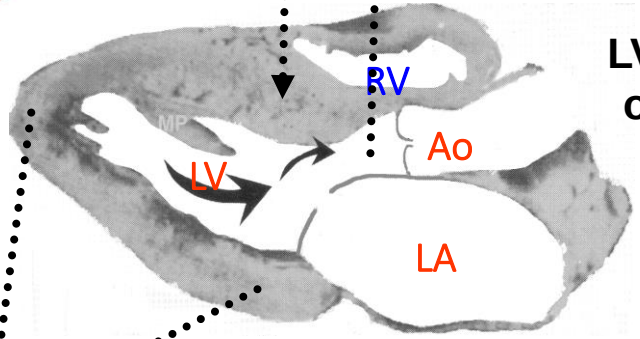


Septum with greater thickness in the superior part (basal)

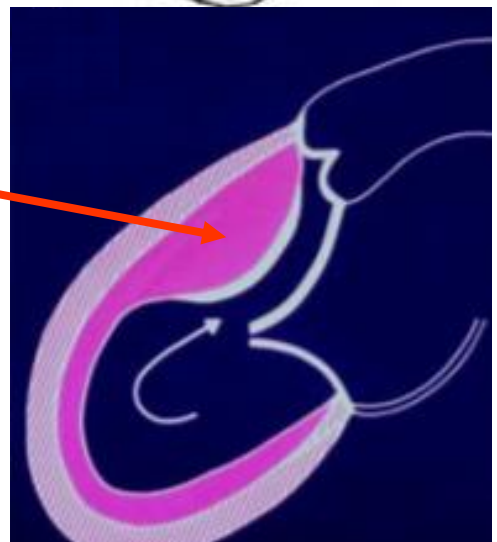




LVOT



LVOT: LV outflow tract

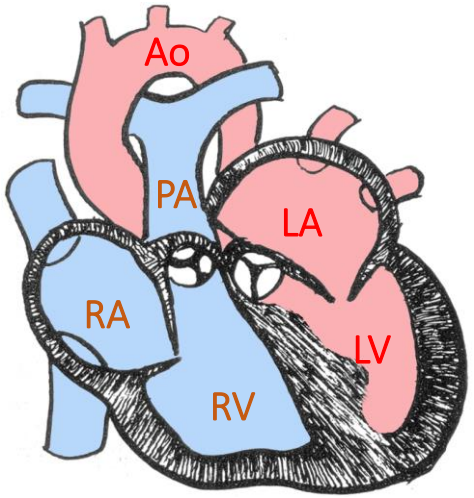


Free wall with progressive decrease of thickness from the base to the apex

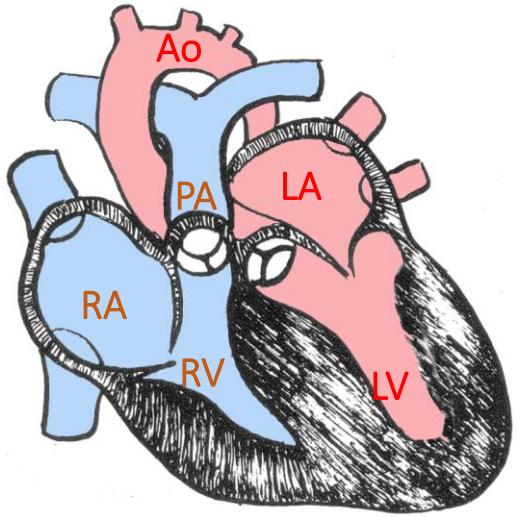
Outline of Non-Obstructive forms of HCM

NON OBSTRUCTIVE FORMS

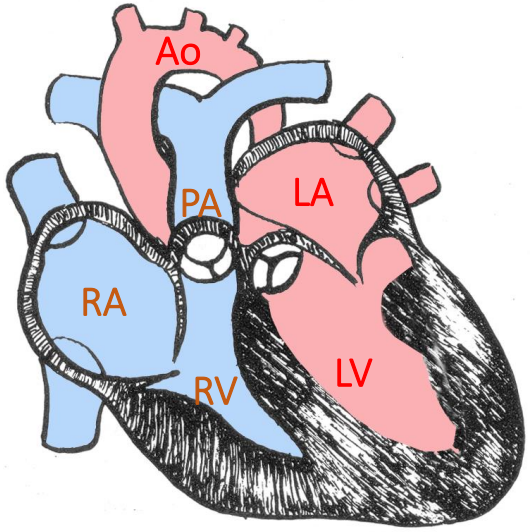
Septal asymmetrical without obstruction



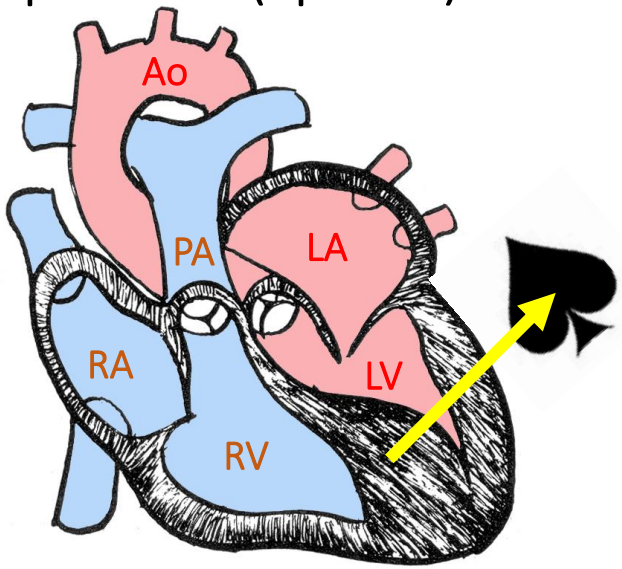
Symmetrical



Lateral and/or laterobasal



Apical HCM (Ap-HCM)



The "ace-of-spades" sign

environmental and ethnic/demographic factors including sex.[5]

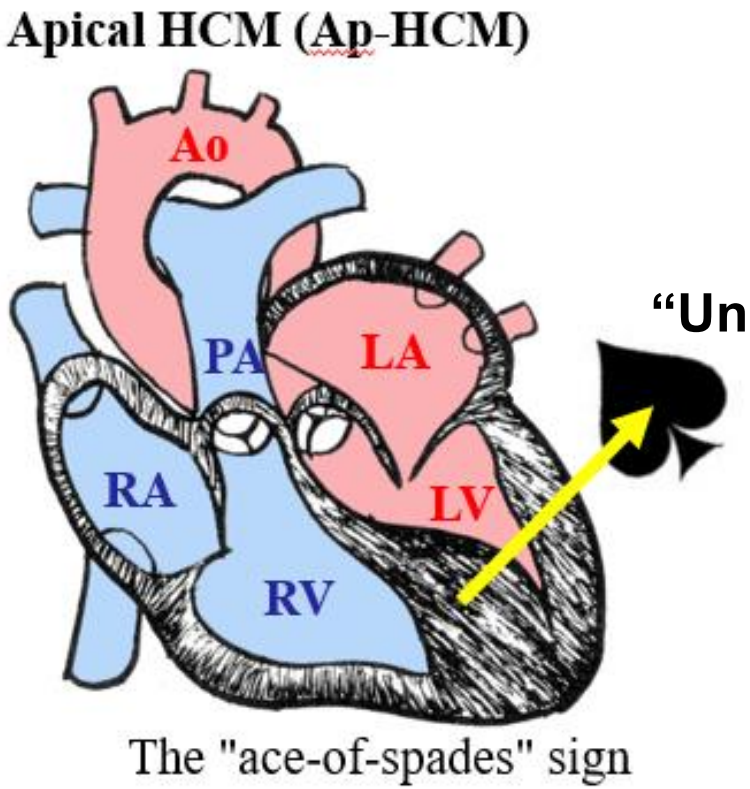
Specific data regarding genetic profiling in the different ApHCM morphologies or ethnicities are lacking. In a study looking at genotype-phenotype correlations in ApHCM, those that carried a pathogenic sarcomere gene mutation had a stronger family history of HCM (39% versus 26%; *P*=0.4) but no phenotypic features were not significantly different.[11] European Society of Cardiology (ESC) and American College of Cardiology Foundation/American Heart Association HCM guidelines provide no ApHCM-specific genotyping or family screening recommendations.

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),[13] although severity and extent of interstitial fibrosis was equivalent (100% versus 93%; *P*=ns).[13]

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 shape and marked apical obliteration” together with ECG “giant” negative T-waves and high QRS voltage.[14]



“Unique spade-like shape and marked apical obliteration”

14. Yamaguchi H, Ishimura T, Nishiyama S, Nagasaki F, Nakanishi S, Takatsu F, Nishijo T, Umeda T, Machii K. Hypertrophic nonobstructive cardiomyopathy with giant negative T waves (apical hypertrophy): ventriculographic and echocardiographic features in 30 patients. *Am J Cardiol*. 1979;44:401–412.

Disorders that may involve the left ventricular apex

There are many disorders that may involve the left ventricular apex; however, they are sometimes difficult to differentiate. The spectrum of diseases that most frequently affect the apex of the left ventricle include:

1. **Takotsubo cardiomyopathy ("octopus trap"):** transient apical ballooning syndrome, apical ballooning cardiomyopathy, stress-induced cardiomyopathy, Gebrochenes-Herz-Syndrome, broken heart, and simply stress cardiomyopathy. A bulging out of the LV apex with a hypercontractile base of the LV is often noted. Its hallmark is bulging out of the apex of the heart with preserved function of the base.
2. **Left ventricular aneurysms and pseudoaneurysms**
3. **Apical diverticula**
4. **Apical ventricular remodelling**
5. **Apical hypertrophic cardiomyopathy (ApHCM)** (**Cisneros 2011**)
6. **Left ventricular non-compaction**
7. **Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D)** with LV involvement
8. **Left ventricular false tendons:** fibrous or fibromuscular bands that stretch across the LV from the septum to the free wall. They can also tether to a papillary muscle, but unlike the chordae tendineae, do not connect to the mitral leaflets. They are anatomic variants that should not be mistaken for abnormalities such as tumors, subaortic membranes, thrombus borders, septal hypertrophy.
9. **Chronic chagasic myocardiopathy**

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).1 Of note, this diagnostic criterion was not included in the 2014 ESC HCM guideline. The **AHA** also lacks specific diagnostic criteria for ApHCM and similarly uses wall thickness of ≥15 mm as their threshold for diagnosis of HCM; however, an study assessing the reliability of SCD recommendations used diagnostic criteria as unexplained hypertrophy in a nondilated LV with wall thickness ≥13 mm by CMR or transthoracic echocardiography,10 highlighting an emerging trend toward using a lower diagnostic cutoff. With an emphasis on the diagnostic criteria and imaging features. In this setting cardiac imaging methods can provide the clue to obtaining the diagnosis.

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.15 It can be subclassified into 3 forms:

I. **“Pure,” with isolated apical hypertrophy;**

II. **“Mixed,” with both apical and septal hypertrophy16 but with the apex thickest1; and**

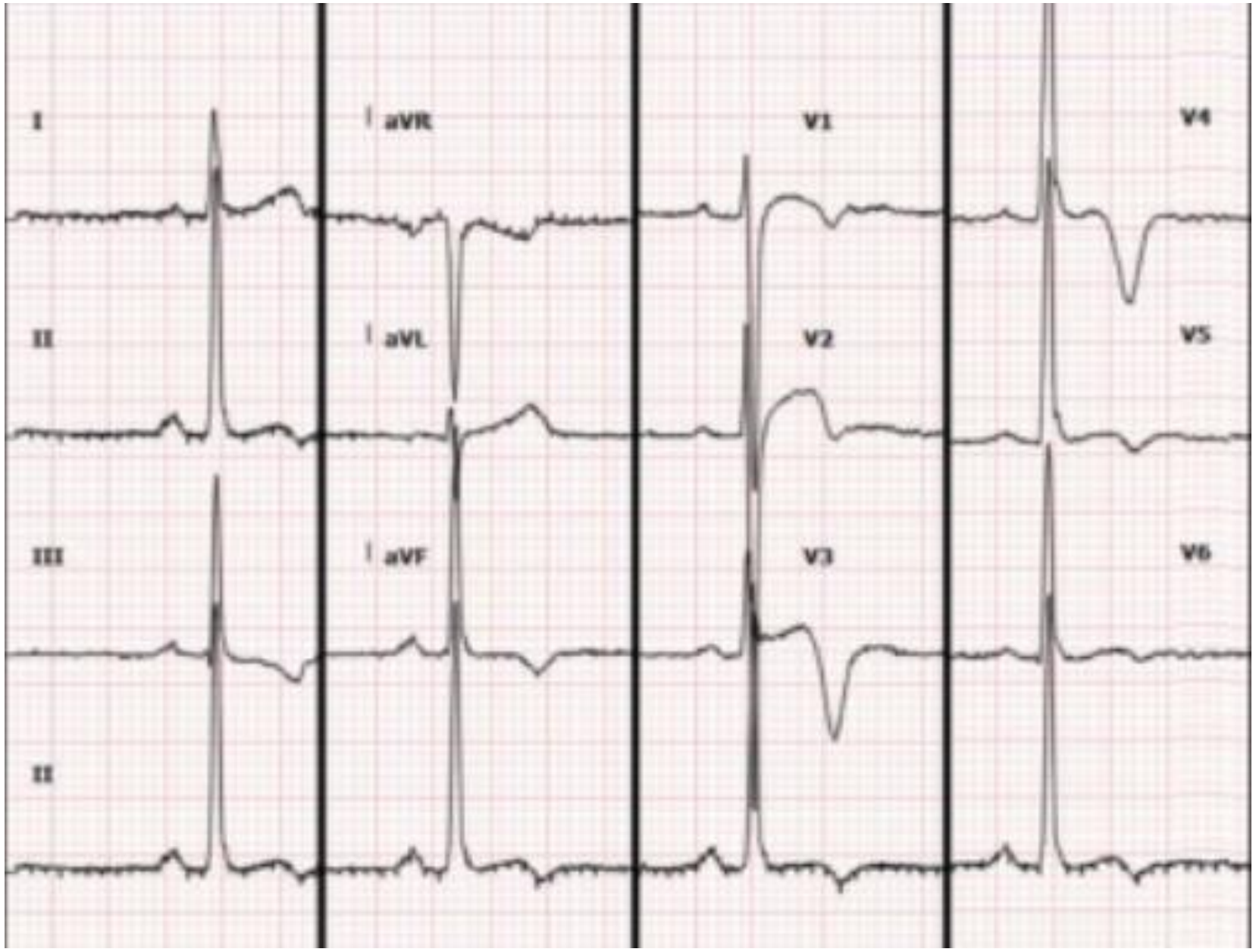
III. **“Relative” ApHCM, believed to be an early ApHCM phenotype.**

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 ECG shows characteristic precordial T-wave inversion and CMR shows loss of the usual apical wall thickness tapering due to apical wallthickness exceeding basal wall thickness, although failing to reach the ApHCM diagnostic cutoff of wall

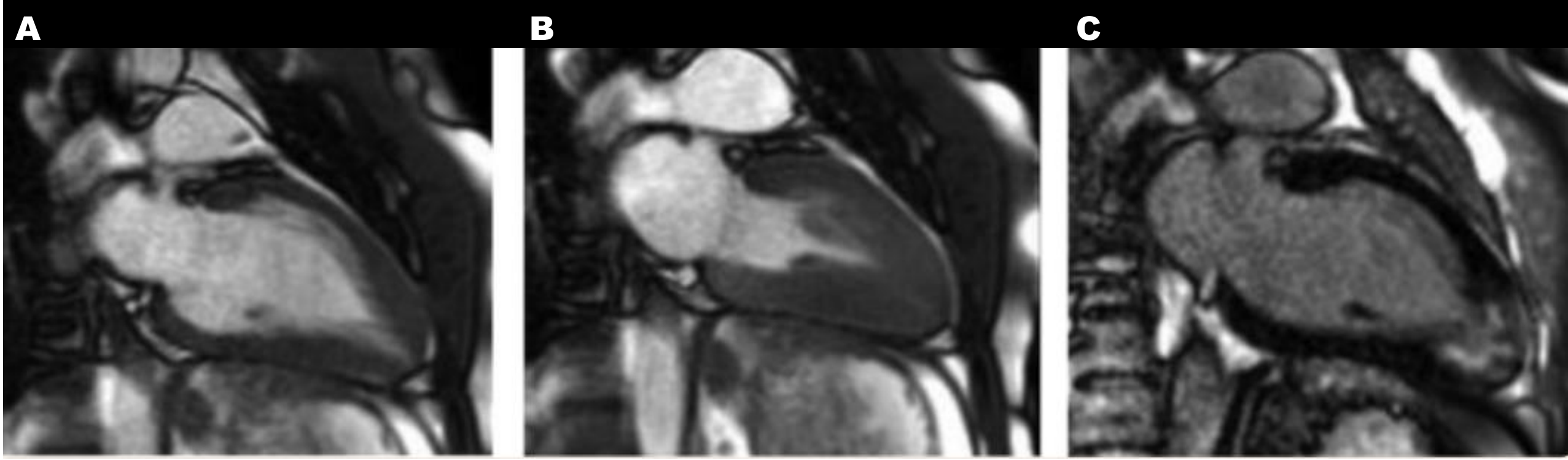
thickness ≥15 mm.17

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 cardiac structural abnormalities including left atrial (LA) dilatation, apical aneurysm, myocardial scar, and ≥20 mm apical systolic cavity obliteration.17 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.18

Relative ApHCM was originally considered entirely benign, but recent data suggest associated pathology with LA dilatation, apical aneurysm, and myocardial scar17 (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.



ECG in relative ApHCM. **A**, ECG demonstrates precordial T-wave inversion and voltage criteria for LVH.



Two-chamber CMR demonstrates loss of apical tapering with relative but not absolute apical hypertrophy in diastole

(**A**) Systolic apical cavity obliteration

(**B**) Late Gadolinium Enhancement (LGE) in the hypertrophied apex

(**C**). ApHCM indicates apical hypertrophic cardiomyopathy;

CMR, cardiovascular magnetic resonance; LVH, left ventricular hypertrophy.

Natural History and Prognosis

ApHCM is more prevalent in men than women, with male-to-female ratios typically 1.6 to 2.8:1.[1], [4]

The average age at presentation is 41.4±14.5 years,[1] 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.[1]

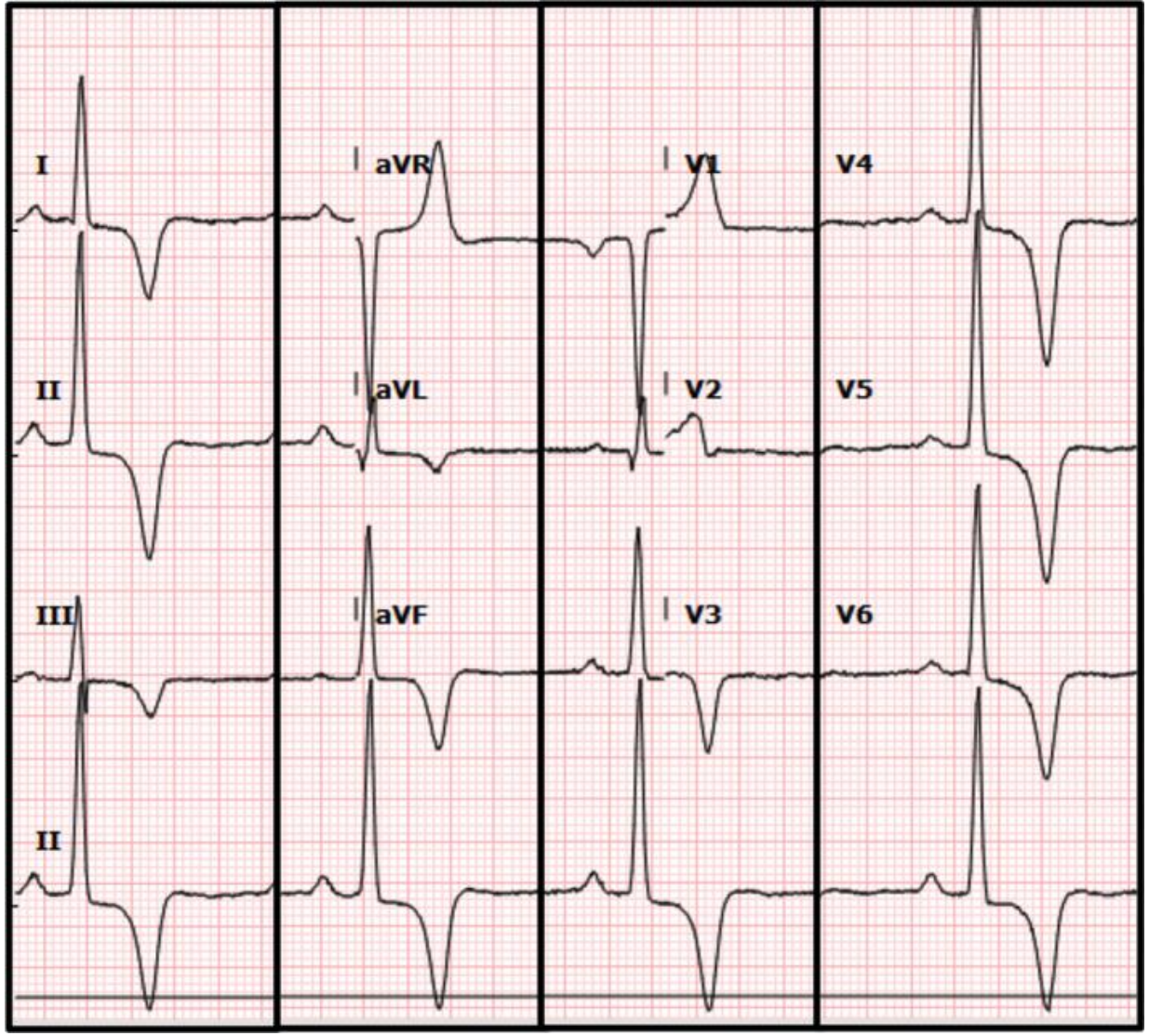
ApHCM was originally thought to carry no increased mortality risk,[1] but recent data suggest annual cardiac death rates of 0.5% to 4%, approaching those for classic HCM.[4], [11] Increased mortality in women was reported, possibly due to more AF and pulmonary hypertension[4] (Table [1]). Patients with mixed ApHCM, younger age at presentation (<41 years),[1] complete end-systolic cavity obliteration at the level of the papillary muscles, paradoxical diastolic flow jet by echocardiography, and apical asynergy[16] have been shown to have higher cardiovascular morbidity. Malignant ventricular arrhythmias and mortality has been

linked to apical aneurysms, but only in Western sufferers.16

In terms of small-vessel disease and microvascular obstruction, a feature recognized in HCM, there may be an increased role for ischemia in ApHCM from cavity obliteration and the persistence of apical contraction into early-mid diastole, resulting in dynamic small-vessel obstruction in the apical segments, regional myocardial perfusion defects, and chest pain.19 Impaired myocyte relaxation and increased energetic cost of early hypercontractility may contribute, particularly in early disease.

Electrocardiography and Arrhythmias

Giant negative T-waves defined as negative voltage of ≥1 mV (≥10 mm)1 are characteristic but not mandatory for diagnosis (Figure 2). In one ApHCM study of 105 patients, 94% had abnormal ECGs with voltage criteria for LVH (65%) and T-wave inversion (93%), but only 47% had giant negative T-waves.1 Maximal T-wave negativity weakly correlated with apical wall thickness, and electrocardiography does not well differentiate mixed and pure ApHCM variants.1 Giant negative T-waves have also been identified in other types of HCM and consequently they are not not a pathognomonic feature The giant T-wave inversion appears as a manifestation of ventricular repolarization abnormalities, and are associated with various clinical conditions such as myocardial infarction, pericarditis, hypertrophic cardiomyopathy, central nervous system diseases, electrolyte imbalance (potassium or calcium deficiency), LQTS, -wave inversion appears as a manifestation of ventricular repolarization abnormalities,



ECG in pure ApHCM. Voltage criteria for LVH and giant negative T-wave inversion in precordial and inferolateral leads. ApHCM indicates apical hypertrophic cardiomyopathy; LVH, left ventricular hypertrophy.

Holter monitoring in ApHCM detected asymptomatic and symptomatic NSVT in 18% and 5%, respectively1; AF in 12%; VT in 3%; and VF in 1%.1 AF prevalence in other studies was at 20% to 28%.3 MVT occurs in ApHCM with aneurysms, possibly related to reentry around the aneurysm. LAE secondary to LV diastolic dysfunction at the time of first ApHCM presentation predicts later AF,20 which is commoner in females and prognostically adverse.4, 20

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.[21] High-sensitivity cardiac troponin T correlated with age, LA area, and maximum LV wall thickness when considering all subtypes.[21] 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.[22]

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.[23] A systolic obliteration-to-cavity ratio >0.5 is associated with increased incidence of AF, stroke, heart failure, and cardiovascular death.[24] Degree of obliteration rather than apical wall thickness influences prognosis.[23]

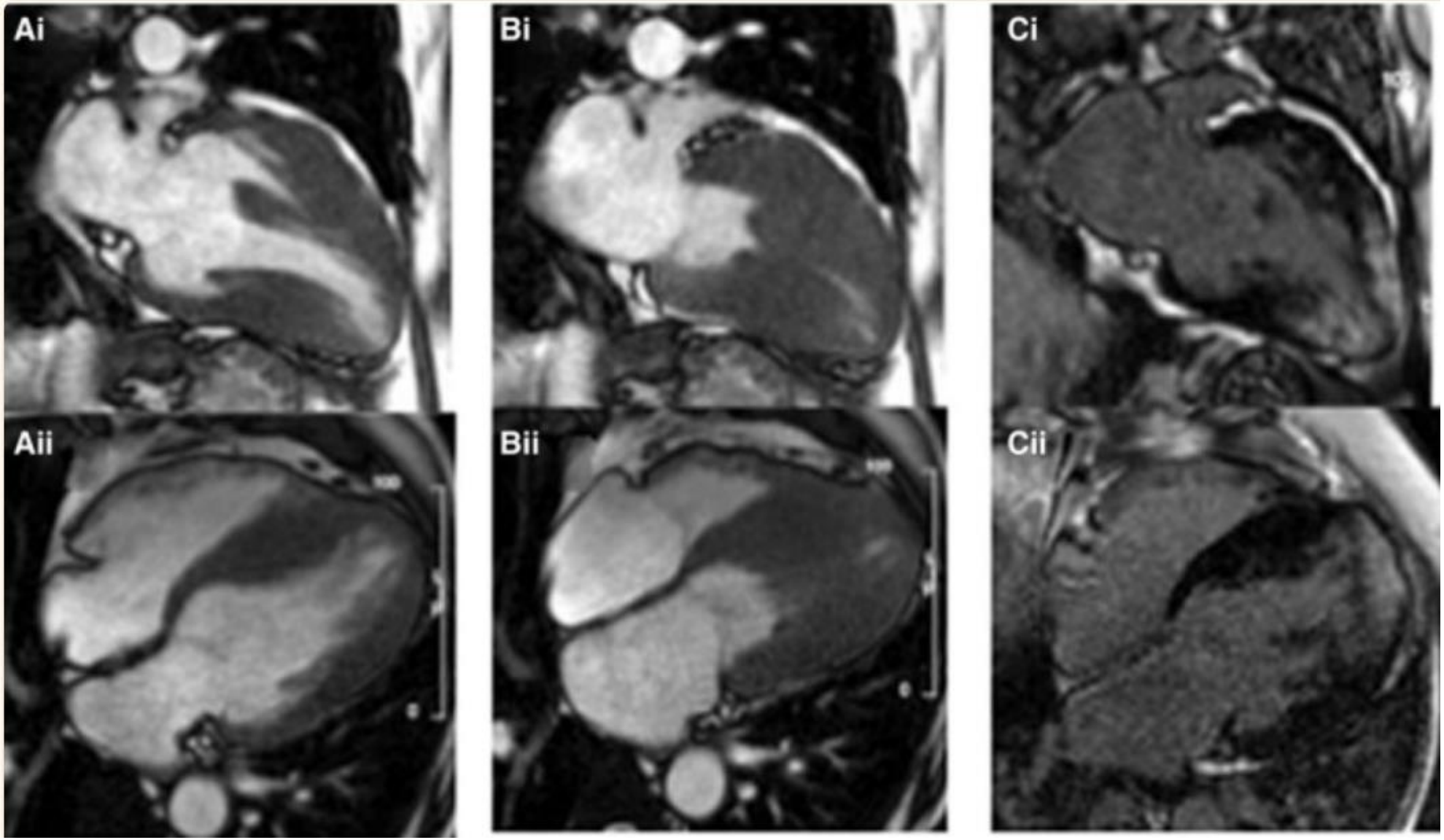
MVOCO may occur as a consequence of midapical lateral and septal hypertrophy[15] and therefore a complication of mixed rather than pure ApHCM. In severe cases, midventricular cavity obliteration persists in diastole and is often associated with a paradoxical midcavity diastolic flow jet, which indicates the associated presence of an apical aneurysm.[16] 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.

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.16 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.

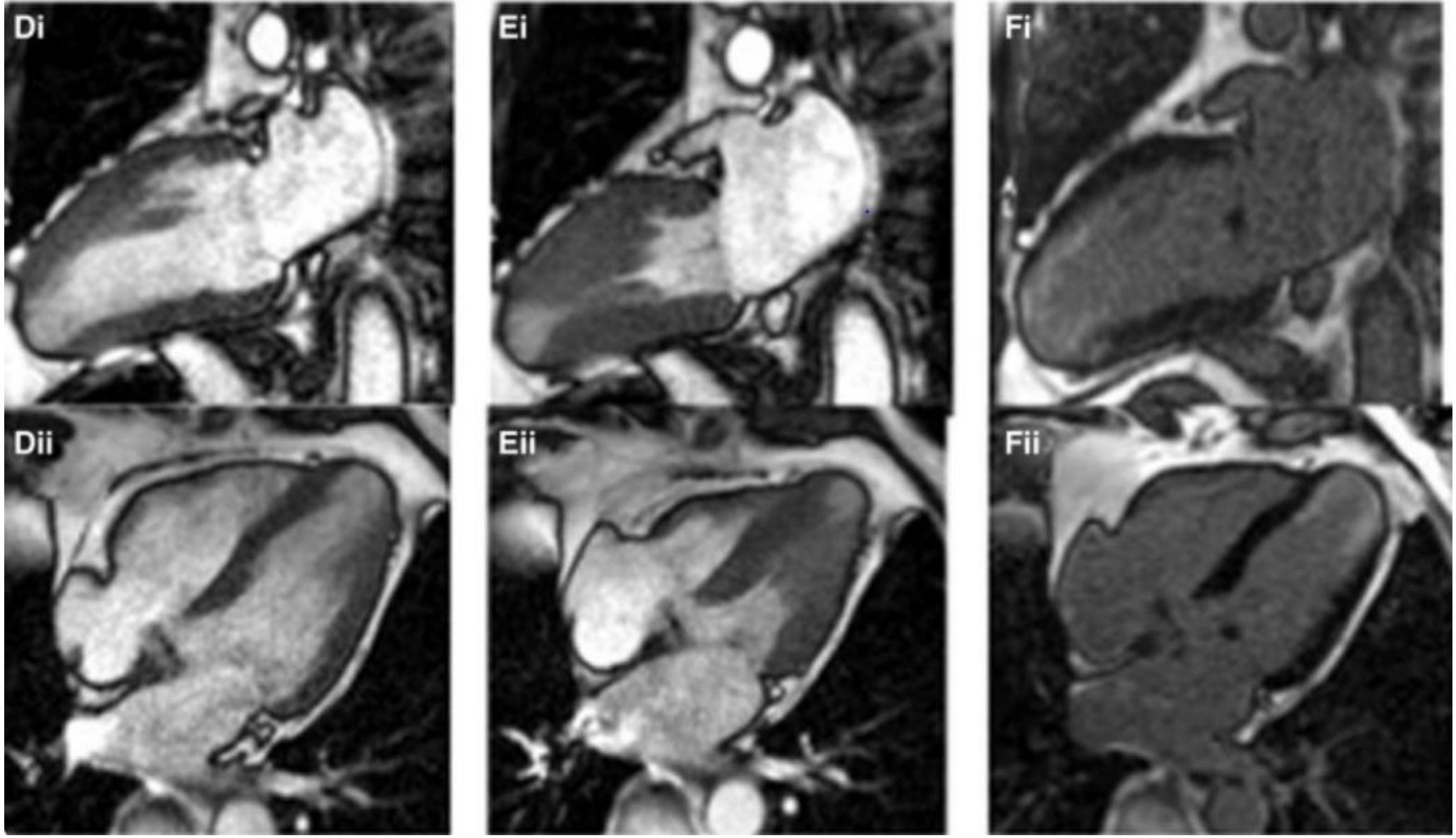
Apical Aneurysms

Apical aneurysms are defined as a discrete, thin-walled, dyskinetic/akinetic segment of the most distal portion of the LV with a relatively wide communication to the main cavity in diastole.[16] They occur in 2% of patients with HCM and 13% to 15% with ApHCM[16], [25] (Figure 3). A cue to their presence is the persistence of apical blood pooling distal to the point of apical systolic cavity obliteration[17] and/or a paradoxical diastolic jet. Small aneurysms are often overlooked on echocardiography and may be difficult to delineate without advanced imaging.[15] 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.25 The dyskinetic/akinetic aneurysm confers risk of apical thrombus formation and thromboembolic stroke.25 Apical aneurysms have been associated with LVH severity, SCD, monomorphic VT,24 LV systolic dysfunction, and heart failure.25



CMR comparison of mixed ApHCM (**A** through **C**) and pure ApHCM (**D** through **F**), both with apical aneurysm formation. Long-axis views of a patient with mixed ApHCM in diastole in 2-chamber (**Ai**) and 4-chamber (**Aii**), which in systole demonstrate midventricular obstruction but not total cavity obliteration due to persistence of apical chamber (**Bi**; **Bii**). The apical aneurysm contains LGE (**Ci**; **Cii**).



A different patient with pure ApHCM has a thinned aneurysmal apex demonstrated in diastole on 2- (**Di**) and 4-chamber views (**Dii**). In systole, the apical aneurysm becomes apparent (**Ei**; **Eii**) and contains LGE (**Fi**; **Fii**). ApHCM indicates apical hypertrophic cardiomyopathy; LGE, late gadolinium enhancement.

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%.[26] 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.[26] Thromboembolic events were 2-fold more common. 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.[27]

Long-term athletic training produces cardiac structural changes, namely, increased diastolic dimensions of the LV cavity, LVH, and increased LV mass.[28] 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.[29] 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.[29]

In one athletes 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.28 Native T1 and extracellular volume values using CMR are lower in athletes than in HCM, which is a useful differentiator.30 Furthermore, as LVH increases in athletes, extracellular volume continues to decrease, whereas in HCM it continues to increase.

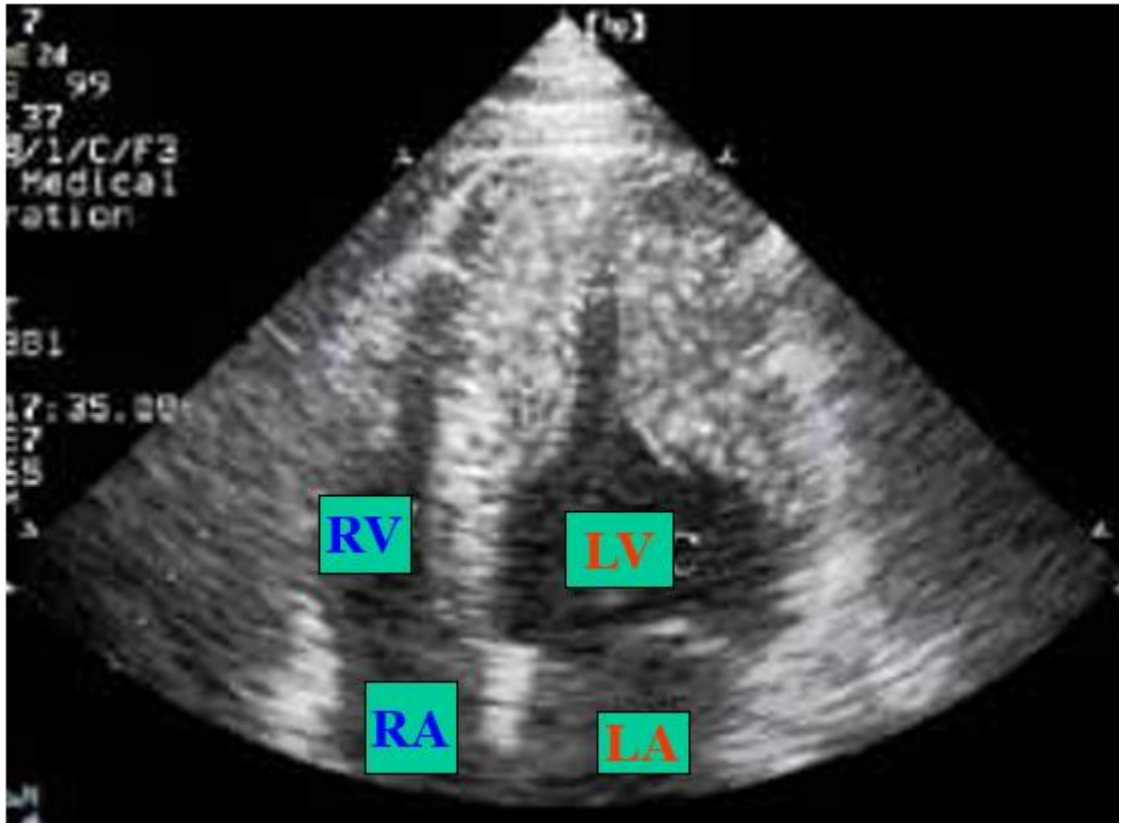
Athletes with pure apical LVH had normal ECGs (no T-wave inversion28), and the phenotype was postulated to reflect athletic training, rather than true HCM. Another study demonstrated that athletes with HCM were 3 times likelier to exhibit ApHCM than their sedentary HCM counterparts (35.8% versus 11.9%).31 It is difficult to distinguish apical LVH attributable to athletic remodeling from ApHCM; however, an ApHCM-pattern ECG is regarded as unequivocally abnormal.31 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

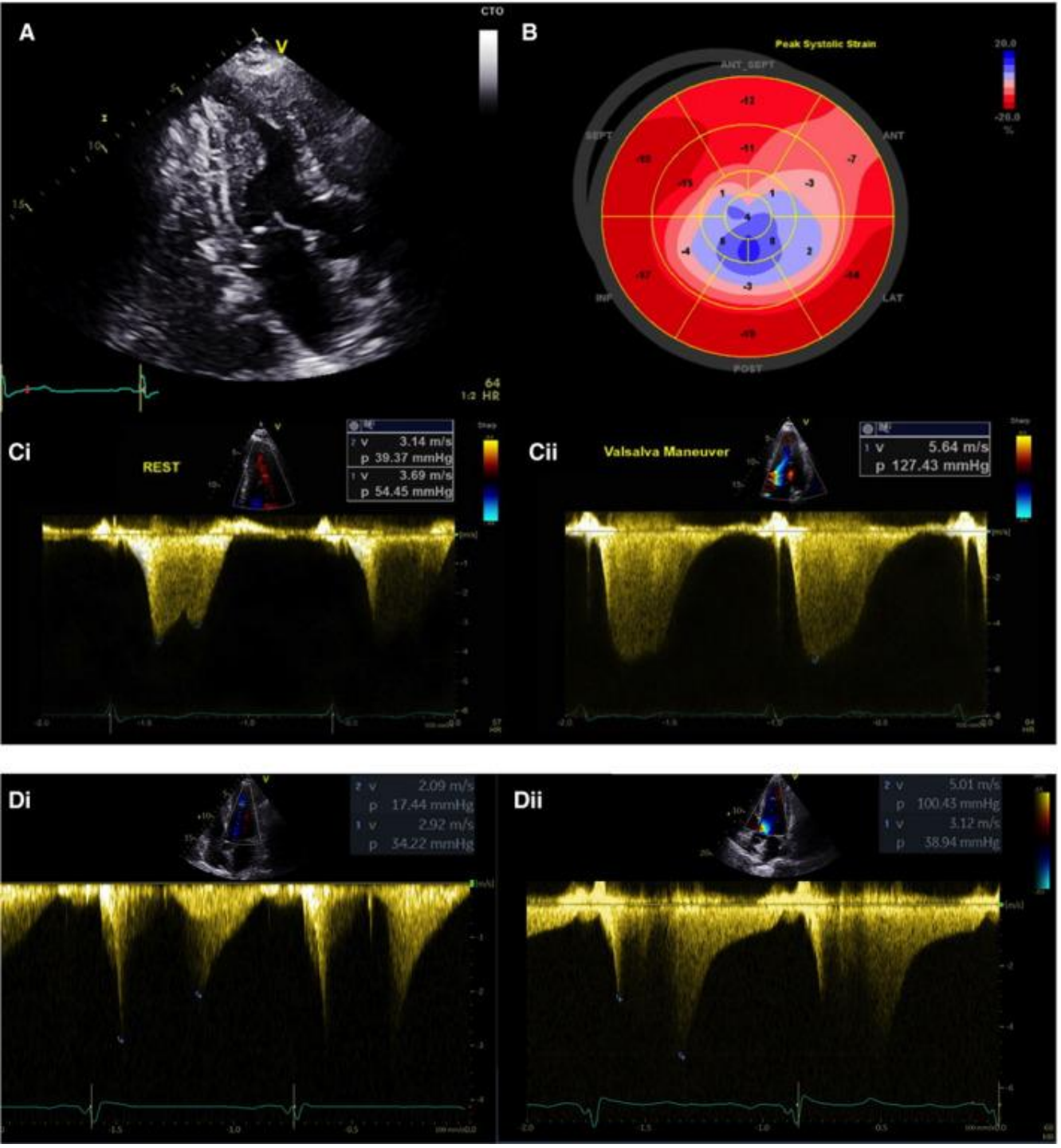
Transthoracic echocardiography can reveal apical hypertrophy, differentiate between pure and mixed forms, and identify additional prognostic features that could influence outcome such as the presence of diastolic dysfunction, MVOCO, or apical aneurysms.[23], [32], [33] However, imaging the apex remains a potential challenge, particularly for subtle prognostic features such as apical akinesis or sequestration caused by massive hypertrophy.[16] Early phenotypes and relative ApHCM could be missed by echocardiography; thus, those with deep T-wave inversion and noncontributory echocardiography should undergo additional imaging.[34] 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.[32] 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[16] (Figure).

Transthoracic two-dimensional echocardiography



Two-dimensional echocardiogram. Apical 4-chamber view shows apical hypertrophy in the apical one third of the ventricle, with apical left ventricle cavity obliteration.
RV = right ventricle **RA** = right atrium **LA** = left atrium **LV**= left ventricular cavity



Transthoracic echocardiography in ApHCM. ApHCM with a small discrete apical chamber visible in the apical 3-chamber view (**A**) and corresponding polar plot showing loss of longitudinal strain apically (**B**). At rest, continuous wave Doppler across the point of distal ventricular obstruction demonstrates a midsystolic peaking jet, followed by a drop in velocity prior to second peak representing paradoxical early diastolic jet flow, with gradients of 54 and 39 mm Hg, respectively (**Ci**). During Valsalva, systolic and diastolic jets merge, with a systolic intracavity gradient of 127 mm Hg, and a lengthening of the diastolic “tail” toward late diastole (**Cii**). By contrast,

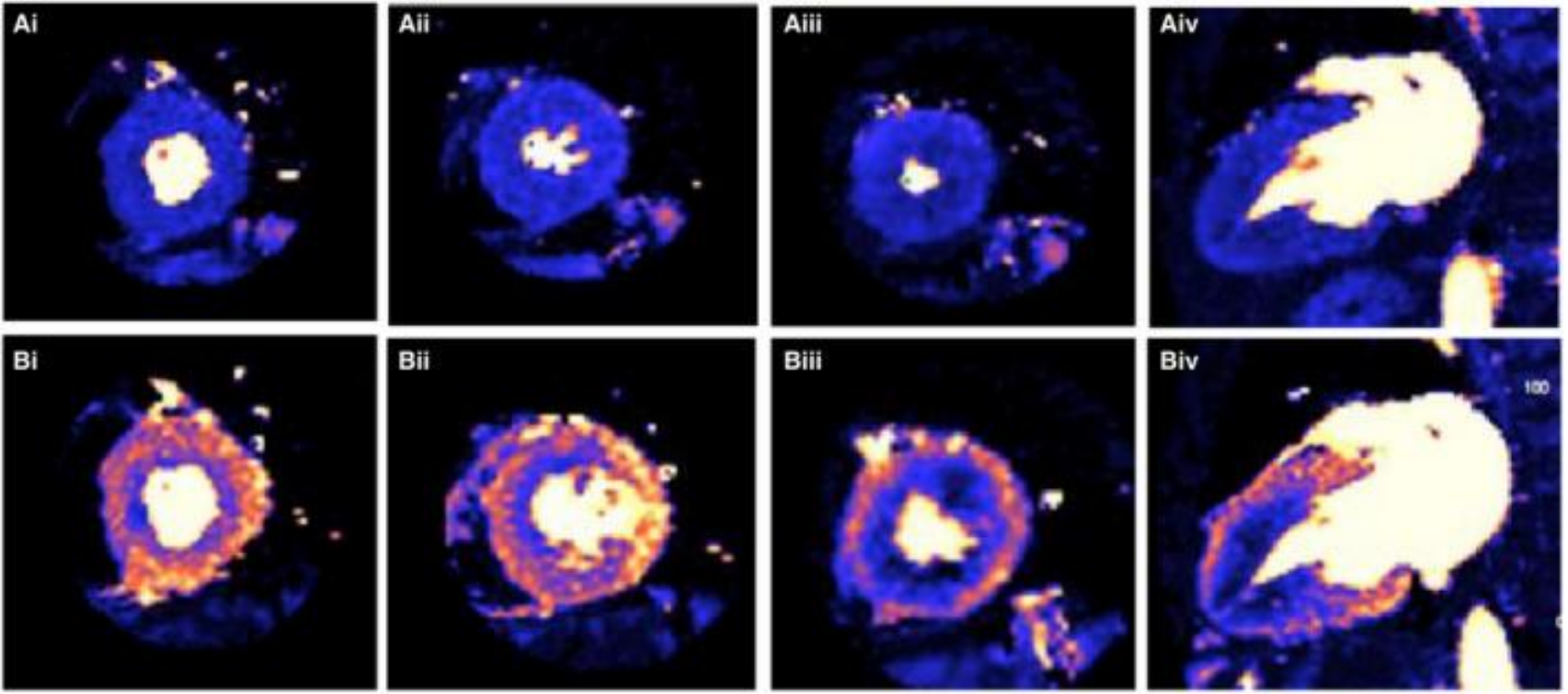
(**D**) demonstrates continuous wave Doppler traces from a patient with ApHCM and midcavity obstruction.

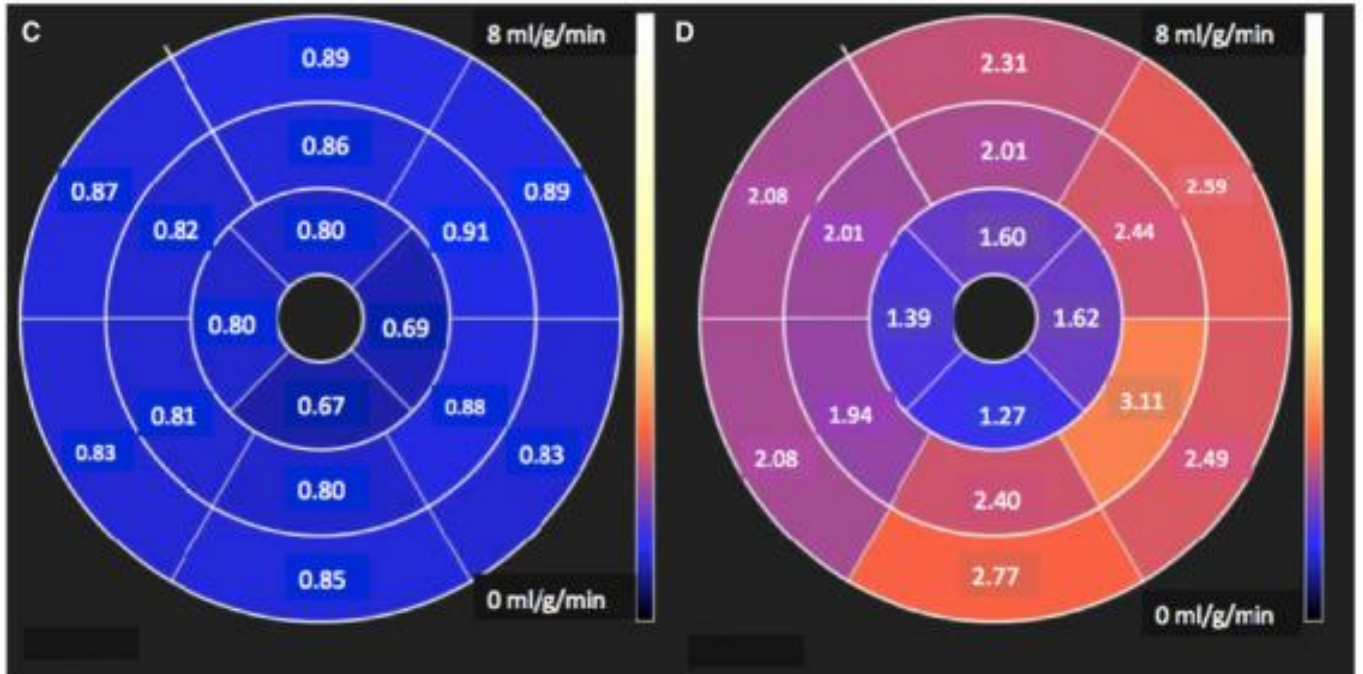
At rest, there is midsystolic loss of Doppler alignment due to cavity obliteration, with corresponding Doppler dropout before paradoxical diastolic jet (**Di**). During Valsalva, the measured systolic gradient is unchanged, but the paradoxical diastolic jet gradient now exceeds 100 mm Hg with extension in duration to the end of diastole (**Dii**). ApHCM indicates apical hypertrophic cardiomyopathy.

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.[35] CMR is more sensitive at detecting apical aneurysms and can identify 25% to 43% of those missed by echocardiography.[25], [36] 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.[37] LGE patterns in ApHCM are characteristically apical and subendocardial[37], [38], [39]–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.[40] 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 feature in the ESC HCM risk-stratification algorithm.

Despite heterogeneity in reported native T1 values (indicating diffuse myocardial fibrosis) in classic and ApHCM 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 Next slide). 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.





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

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[43] 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.[44] Other findings include increased apical tracer uptake at rest and the spadelike configuration of the LV.[45] Fixed and reversible stress perfusion defects are reported in the context of unobstructed epicardial coronary arteries,[45] 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.[1, 45]

Angiography

Left ventriculography identifies the characteristic “ace of spades” LV cavity configuration in end diastole in 69% of cases[1] and aids the detection of apical aneurysms.[16]

Management ApHCM

Medical

- β-blockers also first line (symptom improvement in MVOCO and reduce burden of ventricular arrhythmias)
- Nondihydropyridine calcium channel blockers also second line
- Anticoagulants in the case of atrial fibrillation or thromboembolism

Ablation

- Potential role of alcohol ablation in symptomatic ApHCM with MVOCO (no randomized control data)
- No role for alcohol septal ablation
- VT ablation in rare cases

Devices

- ICDs may be underutilized because of current scoring criteria if using ESC algorithm
- Current prospective trial of distal ventricular pacing for ApHCM with drug refractory symptoms and MVOCO

Surgical

- Few case reports detailing symptomatic improvement following apical myectomy. No randomized control data

Learning points

I. Risk scores for sudden cardiac death (SCD/SCA) show that apical hypertrophic cardiomyopathy (ApHCM) patients have an overall low probability of rhythmic events.

II. Patients with ApHCM are still at higher risk for cardiac events and attention should be taken to determine the need for a cardiac device.

III. Wide QRS-T angle >90° A wide frontal QRS-T angle greater than 90° was associated with an increased risk of SCA

IV. Large-scale registries are needed to define variables to segregate patients with ApHCM in risk groups for SCD.

References

1. Eriksson MJ, Sonnenberg B, Woo A, Rakowski P, Parker TG, Wigle ED, Rakowski H, Douglas Wigle E, Rakowski H, Toronto F. Long-term outcome in patients with apical hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 2002;39:638–645. [PubMed] [Google Scholar]
2. Sakamoto T, Tei C, Murayama M, Ichiyasu H, Hada Y. Giant T wave inversion as a manifestation of asymmetrical apical hypertrophy (AAH) of the left ventricle. Echocardiographic and ultrasono-cardiotomographic study. *Jpn Heart J*. 1976;17:611–629. [PubMed] [Google Scholar]
3. Kubo T, Kitaoka H, Okawa M, Hirota THE. Clinical profiles of hypertrophic cardiomyopathy with apical phenotype. *Circulation*. 2009;73:2330–2336. [PubMed] [Google Scholar]
4. Klarich KW, Jost CHA, Binder J, Connolly HM, Scott CG, Freeman WK, Ackerman MJ, Nishimura RA, Tajik AJ, Ommen SR. Risk of death in long-term follow-up of patients with apical hypertrophic cardiomyopathy. *Am J Cardiol*. 2013;111:1784–1791. [PubMed] [Google Scholar]
5. Arad M, Penas-Lado M, Monserrat L, Maron BJ, Sherrid M, Ho CY, Barr S, Karim A, Olson TM, Kamisago M, Seidman JG, Seidman CE. Gene mutations in apical hypertrophic cardiomyopathy. *Circulation*. 2005;112:2805–2811. [PubMed] [Google Scholar]
6. O'Mahony C, Jichi F, Pavlou M, Monserrat L, Anastasakis A, Rapezzi C, Biagini E, Gimeno JR, Limongelli G, McKenna WJ, Omar RZ, Elliott PM; Hypertrophic Cardiomyopathy Outcomes Investigators . A novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCM risk-SCD). *Eur Heart J*. 2014;35:2010–2020. [PubMed] [Google Scholar]

7. O'Mahony C, Jichi F, Ommen SR, Christiaans I, Arbustini E, Garcia-Pavia P, Cecchi F, Olivotto I, Kitaoka H, Gotsman I, Carr-White G, Mogensen J, Antoniades L, Mohiddin SA, Maurer MS, Tang HC, Geske JB, Siontis KC, Mahmoud KD, Vermeer A, Wilde A, Favalli V, Guttmann OP, Gallego-Delgado M, Dominguez F, Tanini I, Kubo T, Keren A, Bueser T, Waters S, Issa IF, Malcolmson J, Burns T, Sekhri N, Hoeger CW, Omar RZ, Elliott PM. International external validation study of the 2014 European Society of Cardiology guidelines on sudden cardiac death prevention in hypertrophic cardiomyopathy (EVIDENCE-HCM). *Circulation*. 2018;137:1015–1023. [PubMed] [Google Scholar]
8. Patten M, Pecha S, Aydin A. Atrial fibrillation in hypertrophic cardiomyopathy: diagnosis and considerations for management. *J Atr Fibrillation*. 2018;10:1–6. [PMC free article] [PubMed] [Google Scholar]
9. Spirito P, Ferrazzi P. Pulmonary hypertension in hypertrophic cardiomyopathy: a forgotten marker in the identification of candidates to surgical myectomy? *Eur Heart J Cardiovasc Imaging*. 2016;17:611–612. [PubMed] [Google Scholar]
10. Maron MS, Rowin EJ, Wessler BS, Mooney PJ, Fatima A, Patel P, Koethe BC, Romashko M, Link MS, Maron BJ. Enhanced American College of Cardiology/American Heart Association strategy for prevention of sudden cardiac death in high-risk patients with hypertrophic cardiomyopathy. *JAMA Cardiol*. 2019;4:644–657. [PMC free article] [PubMed] [Google Scholar]
11. Towe EC, Bos JM, Ommen SR, Gersh BJ, Ackerman MJ. Genotype-phenotype correlations in apical variant hypertrophic cardiomyopathy. *Congenit Heart Dis*. 2015;10:E139–E145. [PubMed] [Google Scholar]

12. Gruner C, Care M, Siminovitch K, Moravsky G, Wigle ED, Woo A, Rakowski H. Sarcomere protein gene mutations in patients with apical hypertrophic cardiomyopathy. *Circ Cardiovasc Genet*. 2011;4:288–295. [PubMed] [Google Scholar]
13. Morimoto S, Sekiguchi M, Uemura A, Hiramitsu S, Kimura K, Ohtsuki M, Ishii J, Kato S, Kasanuki H, Hishida H. Cardiac muscle cell disorganization in apical hypertrophic cardiomyopathy a cardiac biopsy study. *Jpn Heart J*. 2003;44:506–513. [PubMed] [Google Scholar]
14. Yamaguchi H, Ishimura T, Nishiyama S, Nagasaki F, Nakanishi S, Takatsu F, Nishijo T, Umeda T, Machii K. Hypertrophic nonobstructive cardiomyopathy with giant negative T waves (apical hypertrophy): ventriculographic and echocardiographic features in 30 patients. *Am J Cardiol*. 1979;44:401–412. [PubMed] [Google Scholar]
15. Jan MF, Todaro MC, Oreto L, Tajik AJ. Apical hypertrophic cardiomyopathy: present status. *Int J Cardiol*. 2016;222:745–759. [PubMed] [Google Scholar]
16. Chen CC, Lei MH, Hsu YC, Chung SL, Sung YJ. Apical hypertrophic cardiomyopathy: correlations between echocardiographic parameters, angiographic left ventricular morphology, and clinical outcomes. *Clin Cardiol*. 2011;34:233–238. [PMC free article] [PubMed] [Google Scholar]
17. Flett AS, Maestrini V, Milliken D, Fontana M, Treibel TA, Harb R, Sado DM, Quarta G, Herrey A, Sneddon J, Elliott P, McKenna W, Moon JC. Diagnosis of apical hypertrophic cardiomyopathy: T-wave inversion and relative but not absolute apical left ventricular hypertrophy. *Int J Cardiol*. 2015;183:143–148. [PMC free article] [PubMed] [Google Scholar]

18. Wu B, Lu M, Zhang Y, Song B, Ling J, Huang J, Yin G, Lan T, Dai L, Song L, Jiang Y, Wang H, He Z, Lee J, Yong HS, Patel MB, Zhao S. CMR assessment of the left ventricle apical morphology in subjects with unexplainable giant T-wave inversion and without apical wall thickness >/=15 mm. *Eur Heart J Cardiovasc Imaging*. 2016;18:186–194. [PubMed] [Google Scholar]

19. Stephenson E, Monney P, Pugliese F, Malcolmson J, Petersen SE, Knight C, Mills P, Wragg A, O'Mahony C, Sekhri N, Mohiddin SA. Ineffective and prolonged apical contraction is associated with chest pain and ischaemia in apical hypertrophic cardiomyopathy. *Int J Cardiol*. 2018;251:65–70. [PubMed] [Google Scholar]

20. Roh S-Y, Kim D-H, Ahn J, Lee KN, Lee DI, Shim J, Choi J-I, Park S-W, Kim Y-H. Long-term outcome of catheter ablation for atrial fibrillation in patients with apical hypertrophic cardiomyopathy. *J Cardiovasc Electrophysiol*. 2016;27:788–795. [PubMed] [Google Scholar]

21. Jenab Y, Pourjafari M, Darabi F, Boroumand MA, Zoroufian A, Jalali A. Prevalence and determinants of elevated high-sensitivity cardiac troponin T in hypertrophic cardiomyopathy. *J Cardiol*. 2014;63:140–144. [PubMed] [Google Scholar]

22. Kubo T, Kitaoka H, Okawa M, Yamanaka S, Hirota T, Hoshikawa E, Hayato K, Yamasaki N, Matsumura Y, Yasuda N, Sugiura T, Doi YL. Serum cardiac troponin I is related to increased left ventricular wall thickness, left ventricular dysfunction, and male gender in hypertrophic cardiomyopathy. *Clin Cardiol*. 2010;33:E1–E7. [PMC free article] [PubMed] [Google Scholar]

23. Kim H, Park J-H, Won K-B, Yoon H-J, Park H-S, Cho Y-K, Nam C-W, Han S, Hur S-H, Kim Y-N, Kim K-B. Significance of apical cavity obliteration in apical hypertrophic cardiomyopathy. *Heart*. 2016;102:1215–1220. [PubMed] [Google Scholar]

24. Wilson P, Marks A, Rastegar H, Manous AS, Mark Estes NA. Apical hypertrophic cardiomyopathy presenting with sustained monomorphic ventricular tachycardia and electrocardiographic changes simulating coronary artery disease and left ventricular aneurysm. *Clin Cardiol*. 1990;13:885–887. [PubMed] [Google Scholar]

25. Maron MS, Finley JJ, Bos JM, Hauser TH, Manning WJ, Haas TS, Lesser JR, Udelson JE, Ackerman MJ, Maron BJ. Prevalence, clinical significance, and natural history of left ventricular apical aneurysms in hypertrophic cardiomyopathy. *Circulation*. 2008;118:1541–1549. [PubMed] [Google Scholar]

26. Rowin EJ, Maron BJ, Haas TS, Garberich RF, Wang W, Link MS, Maron MS. Hypertrophic cardiomyopathy with left ventricular apical aneurysm: implications for risk stratification and management. *J Am Coll Cardiol*. 2017;69:761–773. [PubMed] [Google Scholar]

27. Deva DP, Hanneman K, Li Q, Ng MY, Wasim S, Morel C, Iwanochko RM, Thavendiranathan P, Crean AM. Cardiovascular magnetic resonance demonstration of the spectrum of morphological phenotypes and patterns of myocardial scarring in Anderson-Fabry disease. *J Cardiovasc Magn Reson*. 2016;18:14. [PMC free article] [PubMed] [Google Scholar]

28. Pelliccia A, Maron BJ, Spataro A, Proschan MA, Spirito P. The upper limit of physiologic cardiac hypertrophy in highly trained elite athletes. *N Engl J Med*. 1991;324:295–301. [PubMed] [Google Scholar]

29. Maron BJ. Distinguishing hypertrophic cardiomyopathy from athlete's heart: a clinical problem of increasing magnitude and significance. *Heart*. 2005;91:1380–1382. [PMC free article] [PubMed] [Google Scholar]

30. Swoboda PP, McDiarmid AK, Erhayiem B, Broadbent DA, Dobson LE, Garg P, Ferguson C, Page SP, Greenwood JP, Plein S. Assessing myocardial extracellular volume by T1 mapping to distinguish hypertrophic cardiomyopathy from athlete's heart. *J Am Coll Cardiol*. 2016;67:2189–2190. [PubMed] [Google Scholar]

31. Sheikh N, Papadakis M, Schnell F, Panoulas V, Malhotra A, Wilson M, Carré F, Sharma S. Clinical profile of athletes with hypertrophic cardiomyopathy. *Circ Cardiovasc Imaging*. 2015;8:e003454. [PubMed] [Google Scholar]

32. Choi EY, Rim SJ, Ha J-W, Kim YJ, Lee SC, Kang DH, Park SW, Song JK, Sohn DW, Chung N. Phenotypic spectrum and clinical characteristics of apical hypertrophic cardiomyopathy: multicenter echo-Doppler study. *Cardiology*. 2008;110:53–61. [PubMed] [Google Scholar]

33. Moon J, Shim CY, Ha J-W, Cho IJ, Kang MK, Yang W-I, Jang Y, Chung N, Cho S-Y. Clinical and echocardiographic predictors of outcomes in patients with apical hypertrophic cardiomyopathy. *Am J Cardiol*. 2011;108:1614–1619. [PubMed] [Google Scholar]

34. Moon JCC, Fisher NG, Mckenna WJ, Pennell DJ, Pennell DJ. Detection of apical hypertrophic cardiomyopathy by cardiovascular magnetic resonance in patients with non-diagnostic echocardiography. *Heart*. 2004;90:645–649. [PMC free article] [PubMed] [Google Scholar]

35. Pons-Lladó G, Carreras F, Borrás X, Palmer J, Llauger J, Bayés De Luna A. Comparison of morphologic assessment of hypertrophic cardiomyopathy by magnetic resonance versus echocardiographic imaging. *Am J Cardiol*. 1997;79:1651–1656. [PubMed] [Google Scholar]

36. Fattori R, Biagini E, Lorenzini M, Buttazzi K, Lovato L, Rapezzi C. Significance of magnetic resonance imaging in apical hypertrophic cardiomyopathy. *Am J Cardiol*. 2010;105:1592–1596. [PubMed] [Google Scholar]

37. Yamada M, Teraoka K, Kawade M, Hirano M, Yamashina A. Frequency and distribution of late gadolinium enhancement in magnetic resonance imaging of patients with apical hypertrophic cardiomyopathy and patients with asymmetrical hypertrophic cardiomyopathy: a comparative study. *Int J Cardiovasc Imaging*. 2009;25:131–138. [PubMed] [Google Scholar]

38. Choudhury L, Mahrholdt H, Wagner A, Choi KM, Elliott MD, Klocke FJ, Bonow RO, Judd RM, Kim RJ. Myocardial scarring in asymptomatic or mildly symptomatic patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 2002;40:2156–2164. [PubMed] [Google Scholar

39. Kebed KY, Al Adham RI, Bishu K, Askew JW, Klarich KW, Araoz PA, Foley TA, Glockner JF, Nishimura RA, Anavekar NS. Evaluation of apical subtype of hypertrophic cardiomyopathy using cardiac magnetic resonance imaging with gadolinium enhancement. *Am J Cardiol*. 2014;114:777–782. [PubMed] [Google

40. Neubauer S, Kolm P, Ho CY, Kwong RY, Desai MY, Dolman SF, Appelbaum E, Desvigne-Nickens P, DiMarco JP, Friedrich MG, Geller N, Harper AR, Jarolim P, Jerosch-Herold M, Kim DY, Maron MS, Schulz-Menger J, Piechnik SK, Thomson K, Zhang C, Watkins H, Weintraub WS, Kramer CM; HCMR Investigators . Distinct subgroups in hypertrophic cardiomyopathy in the NHLBI HCM Registry. *J Am Coll Cardiol*. 2019;74:2333–2345. [PMC free article] [PubMed] [Google Scholar]

41. Kato S, Nakamori S, Bellm S, Jang J, Basha T, Maron M, Manning WJ, Nezafat R. Myocardial native T1 time in patients with hypertrophic cardiomyopathy. *Am J Cardiol*. 2016;118:1057–1062. [PMC free article] [PubMed] [Google Scholar]

42. Chiribiri A, Leuzzi S, Conte MR, Bongioanni S, Bratis K, Olivotti L, De Rosa C, Lardone E, Di Donna P, Villa ADM, Cesarani F, Nagel E, Gaita F, Bonamini R. Rest perfusion abnormalities in hypertrophic cardiomyopathy: correlation with myocardial fibrosis and risk factors for sudden cardiac death. *Clin Radiol*. 2015;70:495–501. [PMC free article] [PubMed] [Google Scholar]

43. Langer C, Lutz M, Eden M, Lüdde M, Hohnhorst M, Gierloff C, Both M, Burchert W, Faber L, Horstkotte D, Frey N, Prinz C. Hypertrophic cardiomyopathy in cardiac CT: a validation study on the detection of intramyocardial fibrosis in consecutive patients. *Int J Cardiovasc Imaging*. 2014;30:659–667. [PubMed] [Google Scholar]
44. Parker Ward R, Hemlata MD, Pokharna K, Lang RM, Williams KA. Resting “Solar Polar” map pattern and reduced apical flow reserve: characteristics of apical hypertrophic cardiomyopathy on SPECT myocardial perfusion imaging. *J Nucl Cardiol*. 2003;10:506–512. [PubMed] [Google Scholar]
45. Cianciulli TF, Saccheri MC, Masoli OH, Redruello MF, Lax JA, Morita LA, Gagliardi JA, Dorelle AN, Prezioso HA, Vidal LA. Myocardial perfusion SPECT in the diagnosis of apical hypertrophic cardiomyopathy. *J Nucl Cardiol*. 2009;16:391–395. [PubMed] [Google Scholar]
46. Spoladore R, Maron MS, D'Amato R, Camici PG, Olivotto I. Pharmacological treatment options for hypertrophic cardiomyopathy: high time for evidence. *Eur Heart J*. 2012;33:1724–1733. [PubMed] [Google Scholar]
47. Inada K, Seiler J, Roberts-Thomson KC, Steven D, Rosman J, John RM, Sobieszczyk P, Stevenson WG, Tedrow UB. Substrate characterization and catheter ablation for monomorphic ventricular tachycardia in patients with apical hypertrophic cardiomyopathy. *J Cardiovasc Electrophysiol*. 2011;22:41–48. [PubMed] [Google Scholar]
48. Elliott PM, Anastasakis A, Borger M, Borggrefe M, Cecchi F, Charron P, Hagege A, Lafont A. 2014 ESC guidelines on diagnosis and management of hypertrophic cardiomyopathy. *Eur Heart J*. 2014;35:2733–2779. [PubMed] [Google Scholar]
49. Begley D, Mohiddin S, Fananapazir L. Dual chamber pacemaker therapy for mid-cavity obstructive hypertrophic cardiomyopathy. *Pacing Clin Electrophysiol*. 2001;24:1639–1644. [PubMed] [Google