Ap-HCM or Yamaguchi syndrome and Overview: Invigorating the value of the Electro-Vectorcardiogram

Apical hypertrophic cardiomyopathy (Ap-HCM) or Yamaguchi syndrome is a non-obstructive subtype of hypertrophic cardiomyopathy (HCM) which predominantly affects the left ventricular (LV) apex of the heart. The apex (the most inferior, anterior, and lateral part as the heart lies in situ) is located on the midclavicular line, in the fifth intercostal space. It is formed by the left ventricle. The base of the heart, the posterior part, is formed by both atria, but mainly the left. Ap-HCM is a rare form of HCM which usually involves the apex of the LV and rarely involves the right ventricle (RV) apex or both (**Albanesi Filho FM, Castier MB, Lopes AS, Ginefra P. Is the apical hypertrophic cardiomyopathy seen in one population in Rio de Janeiro city similar to that found in the East? Arq Bras Cardiol. 1997; 69:117–123**.) Ap-HCM was thought to be confined to the Japanese population but it is also found in other populations. Of all the HCM patients in Japan the prevalence of Ap-HCM was 15%, whereas in USA the prevalence was only 3% (**Kitaoka H, Doi Y, Casey SA, Hitomi N, Furuno T, Maron BJComparison of prevalence of apical hypertrophic cardiomyopathy in Japan and the United States.Am J Cardiol. 2003 Nov 15; 92(10):1183-6**.*)*. Due to the nature of its presentation that mimics acute coronary syndrome (ACS) and also to the unfamiliarity of the condition by some physicians, the diagnosis of ApHCM is frequently missed or delayed (from: https://www.jmedscindmc.com/text.asp?2019/39/4/197/257755) **(Payus AO, Sholeh FM, Mustafa N. Yamaguchi syndrome – A pseudoacute coronary syndrome of the young: A case report on apical hypertrophic cardiomyopathy. J Med Sci 2019; 39:197-9**)(**Abdin A, Eitel I, de Waha S, Thiele H. Apical hypertrophic cardiomyopathy presenting as acute coronary syndrome. Eur Heart J Acute**

Cardiovasc Care 2016; 5:289-91). This variant causes in 2%, 3% to 8%; obliteration of LV cavity at the apex together with an apical wall thickness > 15 mm or a ratio between apical and basal LV wall thicknesses ≥1.3-1.5 cm.(**Betocchi S, Hess OM, Losi MA, *et al.* Regional left ventricular mechanics in hypertrophic cardiomyopathy. Circulation. 1993; 88:2206-2214**). This variant has a better prognosis than the other variants, although it has been more associated with ischemia and apical myocardial infarction. (**Wigle ED. Cardiomyopathy: The diagnosis of hypertrophic cardiomyopathy. Heart. 2001; 86:709-714.)**

The relevance of the ECG VCG in Ap-HCM

Apical Hypertrophic Cardiomyopathy Electrocardiogram relevant features

- Giant negative T waves in the precordial ECG leads: Giant negative T waves negativity ≥ 1.0 mV (10 mm). Giant negative T waves are more common in Japanese patients than in American patients: 15% in Japan vs. 3% in the US (**Kitaoka H, Doi Y, Casey SA, *et al.* Comparison of prevalence of apical hypertrophic cardiomyopathy in Japan and the United States. Am J Cardiol. 2003; 92:1183-1186**.). The significant posterior and rightward shift of the ST/T vector is responsible for the characteristic giant negative T wave (>10 mm) in the leads of the horizontal plane from V2 to V5. T waves at the onset, may not present a significant voltage and may appear later with the evolution of the disease. (**Bielli M, Parravicini U, Zanetta M, *et al.* [Apical hypertrophic cardiomyopathy: description of a case in advanced age with documentation of electrocardiographic course]. G Ital Cardiol. 1991; 21:1325-1329**.)
- The depth of negative T waves is related to craniocaudally asymmetry and apical late enhancement (**Dumont CA, Monserrat L, Soler R, *et al.***

Interpretation of electrocardiographic abnormalities in hypertrophic cardiomyopathy with cardiac magnetic resonance. Eur Heart J. 2006; 27:1725-1731).

- Stress test may decrease the depth of T waves (**Tilmant PY, Lablanche JM, Laurent JM, *et al.* [Non-obstructive hypertrophic myocardiopathy. Apropos of 5 cases]. Arch Mal Coeur Vaiss. 1980; 73:1269-1278**).
- Three hypotheses emerged to explain these negative T waves: 1) apical subendocardial ischemia.; 2) apical cell disorder; 3) greater duration of action potential of hypertrophied cells, thus conditioning the area to have a slower repolarization. (**Maron BJ. The giant negative T wave revisited ... in hypertrophic cardiomyopathy. J Am Coll Cardiol. 1990; 15:972-973**.)
- The prevalence in the western world of Ap-HCM is approximately 0.02 to 0.2% and it constitutes 8% of the cases of the entity. In Japan, the apical form of HCM constitutes 25% of HCM. (**Maron BJ. The giant negative T wave revisited ... in hypertrophic cardiomyopathy. J Am Coll Cardiol. 1990; 15:972-973.**)
- Prominent R waves in intermediate precordial leads are observed in ≈80% of cases of Ap-HCM subtype.
- Sometimes R-wave voltage and T-wave negativity progressively decreased in magnitude in serial ECGs.
- NS-VT can be observed in patients that developed apical aneurysm with normal coronary arteries; to clarify the mechanisms of ECG abnormalities in HCM, 102 patients were examined with CMR. Distribution and magnitude of hypertrophy and late enhancement were correlated with ECG abnormalities: Abnormal Q waves reflect the interrelation between upper anterior septal

thickness and other regions of the LV and RVs, and wider Q waves are associated with late enhancement. Conduction disturbances and absent septal Q waves are associated with late enhancement;

- The depth of negative T waves is related to craniocaudally asymmetry and apical late enhancement. (**Dumont CA, Monserrat L, Soler R, *et al.* Interpretation of electrocardiographic abnormalities in hypertrophic cardiomyopathy with cardiac magnetic resonance. Eur Heart J. 2006; 27:1725-1731**.)

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

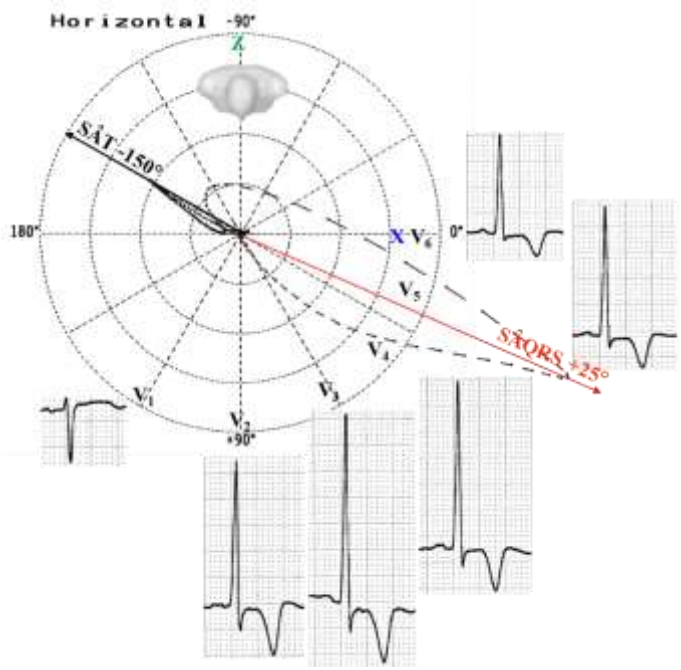
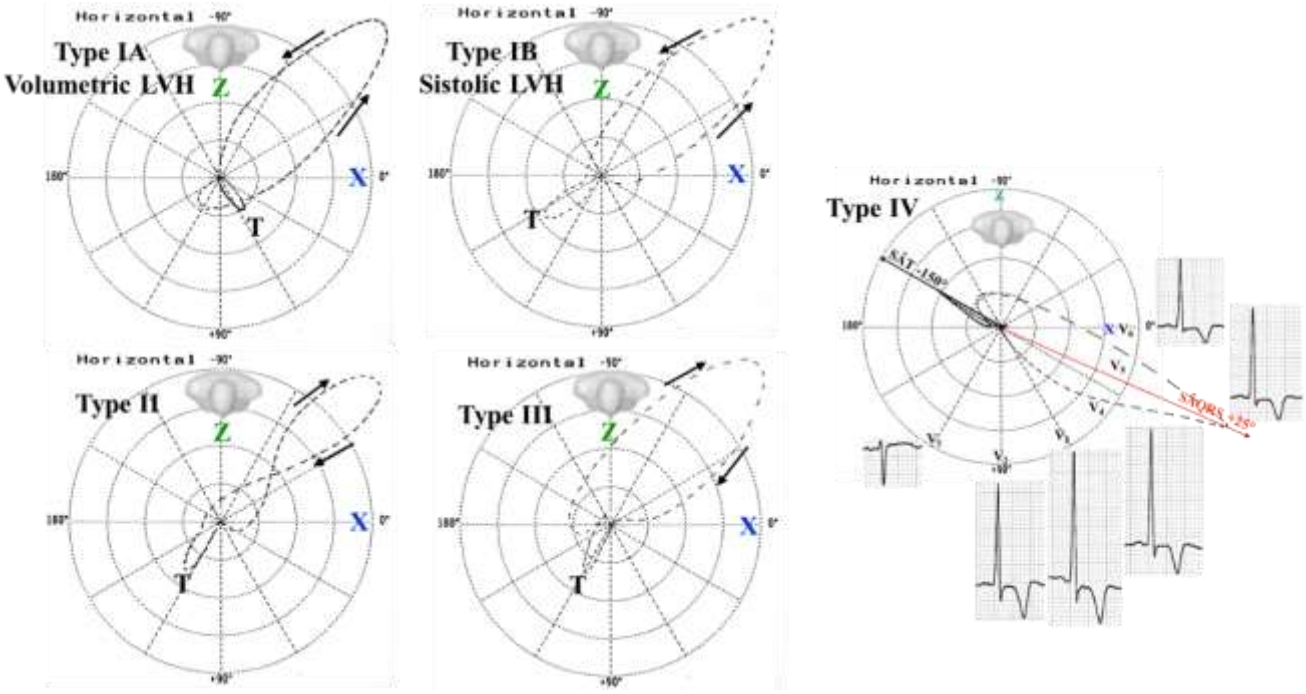


Figure 31. Vectocardiogram of apical NO-HCM: vectorcardiographic LVH type IV.

- Initial vectors of QRS loop heading forward and to the left;
- QRS loop predominantly located in the left anterior quadrant;
- Maximal vector that increases voltage;
- Final vectors located in the right posterior quadrant;
- **E** point (beginning of the QRS loop) that does not match the **0** point (end of the QRS loop) and is located backward and rightward from the latter.

This pattern is considered for us a vectorcardiographic LVH type IV. Vectorcardiographically we divided LVH in the following variants,

The five VCG left ventricular hypertrophic (LVH) types in the HP modified from Varrriale. (**Wigle ED. Cardiomyopathy: The diagnosis of hypertrophic cardiomyopathy. Heart. 2001; 86:709-714.**)

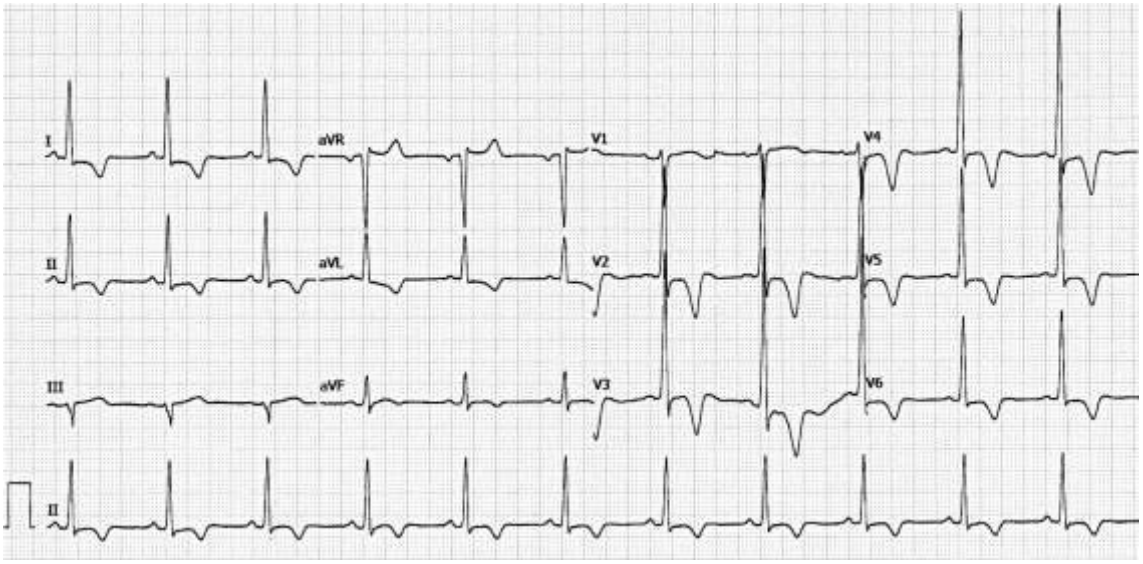


The diagnosis is based on the following elements in Ap-HCM: Type IV LVH

- Giant (≥10mm) and negative T waves from V2 to V4;
- Prominent R waves in intermediate precordial leads: QRS-loop predominantly located on anterior left quadrant (HP)
- T-wave axis on to right posterior quadrant Horizontal Plane) and in top right quadrant in the Frontal Plane: Extreme Axis Deviation = QRS axis between -- 90° and ±180° (AKA "Northwest Axis"). (**Andrés RicardoPérez-Riera. Electrocardiographic "Northwest QRS Axis" in the Brugada Syndrome: A Potential Marker to Predict Poor Outcome. JACC: Case Reports Volume 2, Issue 14, 18 November 2020, Pages 2230-2234 Mini-Focus Issue: Electrophysiology**)
- Mild symptoms and benign course;
- Aspect of spade cards in left ventriculography(pathognomonic?);
- Absence of ventricular gradient

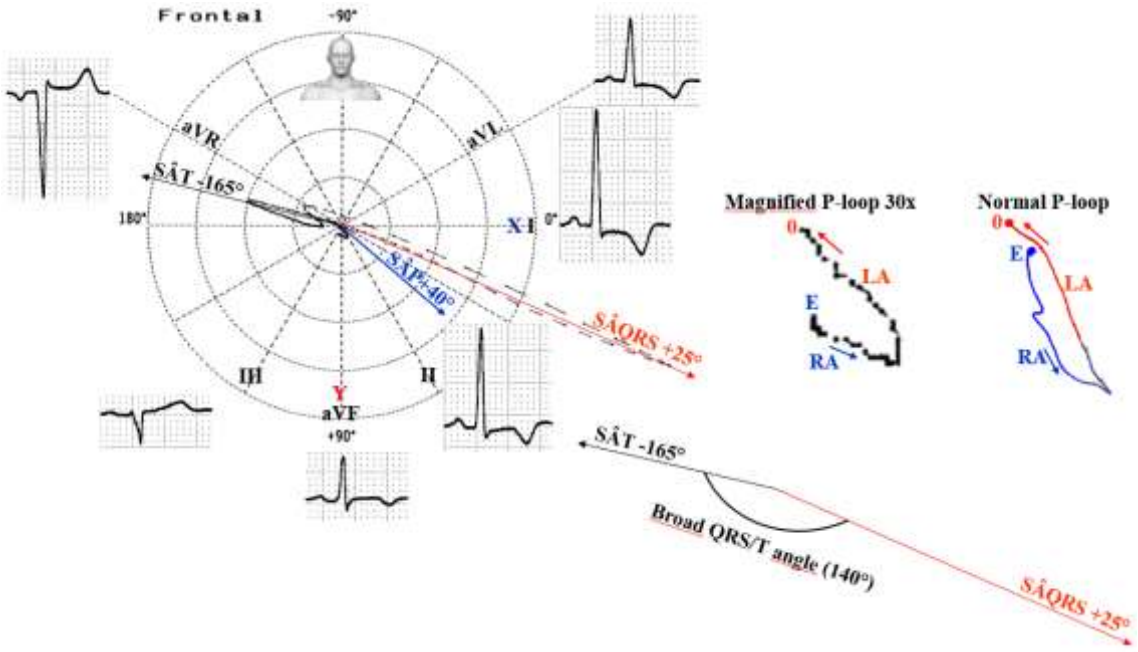
- It is very important to highlight that incidence increases significantly the more advanced the age of the group under study, since typical ECG manifestations may appear late and with evolution.

Typical examples of ECG/VCG in Ap-HCM



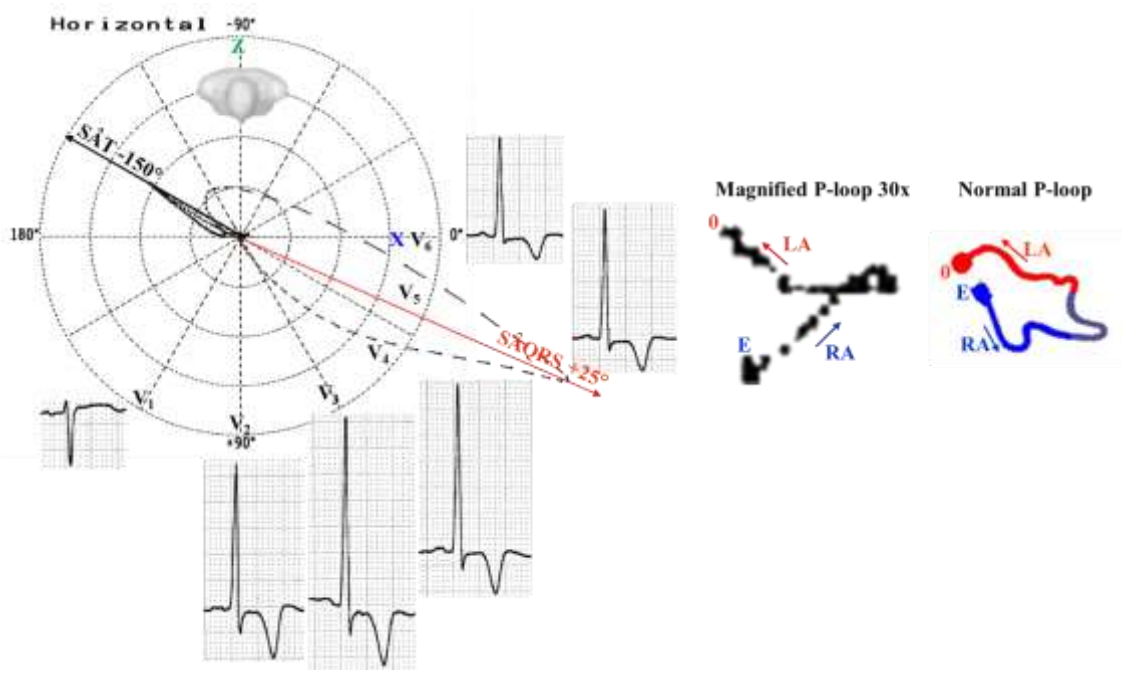
Prominent R waves in intermediate precordial leads, giant negative T waves only in V3 (T-wave ≥10mm deep). By definition giant negative T wave is considered when ≥ 10 mm deep. In the present case only V3 meets this criterion. T wave is negative in I, II, aVL, and from V1 to V6. LVH criteria based on increase of amplitude or voltage of the QRS complexes. Positive Sokolow-Lyon index: S of V1 + R of V5 ≥35 mm in adults. Positive point score system for LVH or Romhilt-Estes Score = 6 points. ST-T vector opposite to QRS without digitalis. R wave in V5 or V6 ≥30 mm. 5 or more points: certain LVH.

ECGVCG correlation Frontal plane



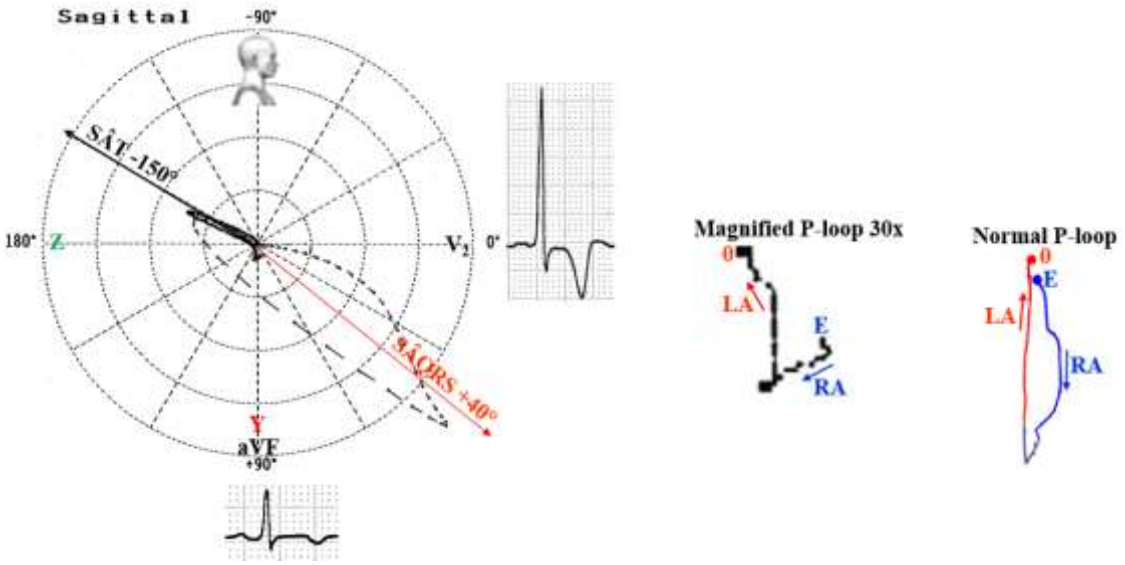
Normal P- wave/loop, very broad QRS/T angle (140°): SÂQRS + 25°/ SÂT -165°.

ECGVCG correlation Horizontal o Transverse plane



QRS-loop predominantly located on anterior left quadrant (=25 degree, clockwise rotation. Giant R wave form V2 to V5, and deep negative T-waves from V2 to V6. T-loop located on posterior right quadrant (SÂT -165°.). Very broad QRS/T angle near160°.). A wide QRS-T angle > 90° in 12-leads ECG is associated with an increased risk of SCA independent of the left ventricular ejection fraction. (**Kelvin C.M. Chua, M.D., Wide 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**.)

ECG/VCG correlation on Right Sagittal Plane



Magnified P-loop shows normal (or near normal) P- wave/loop, very broad QRS/T angle (140°): SÂQRS + 40°/ SÂT -150°. Negative T-wave in V2 because T loop is directed to back and upward.

ECG/VCG Example of Ap-HCM

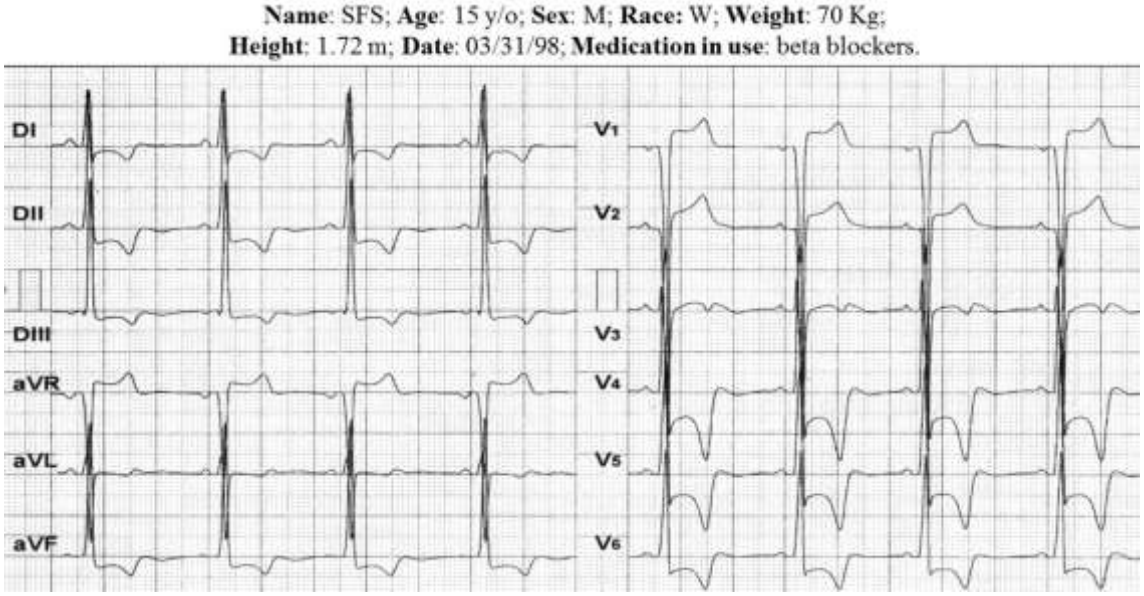


Figure. Clinical/echocardiographic diagnosis: Ap-HCM Non-obstructive HCM. Diastolic thickness of interventricular septum in the apical region greatly increased (32 mm): Ap-HCM.

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 QRS 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

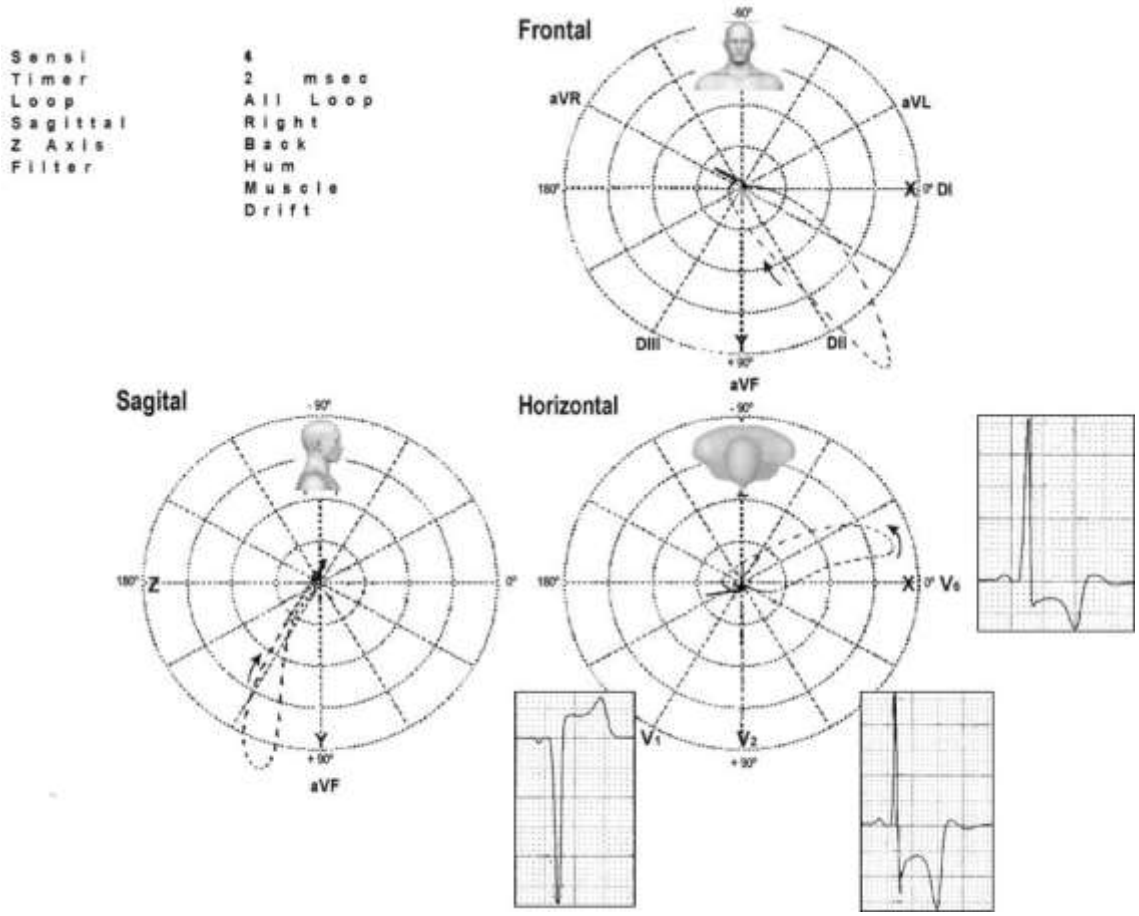


Figure x. ECG/VCG correlation of the same patient: The main body of the QRS loop located in the left, inferior, and posterior quadrant and the magnitude of maximal QRS vector clearly increased (>2.2 mV.): LVH. Giant negative T wave from V4 to V6 (Ap-HCM).

Clinical case

Male patient, with 41 years of age, with history of chest pain and exhaustion in strain. He mentions systemic hypertension without treatment currently. He doesn't smoke or have diabetes. His father died with 77 years of age due to AMI? His brother died suddenly when he was 37 y/o in his sleep.

Cardiac auscultation: regular heart rhythm; HR=68 bpm + fourth heart sound without murmur; Normal pulmonary artery and limbs. BP=140/100 mmHg

After the ECG was performed we also suggested TTE to rule out Ap-HCM. Supplementary tests. Several ECGs with the same morphology.

Echo: LV end diastolic diameter: 49 mm. LV end systolic diameter: 26 mm. Septal diastolic thickness: 14 mm; LV posterior wall diastolic diameter: 14 mm; aorta: 29 mm; LA: 40 mm; EF=78%; mass: 355 g

Conclusion: moderate LV concentric hypertrophy. Moderate LV diastolic dysfunction. Heart valves with normal morphological aspect. Absence of gradient in the LVOT. Mild mitral reflux.

Holter monitoring: Sinus rhythm predominates, asymptomatic isolated ventricular ectopic beats (210), absence of NS-VT.

Left heart catheterization:

Presence of myocardial bridge in the proximal $^{1}/_{3}$ of the LAD

LV with ap-HCM with apical predominance (ventriculography shows spade-like morphology)

Normal coronary arteries

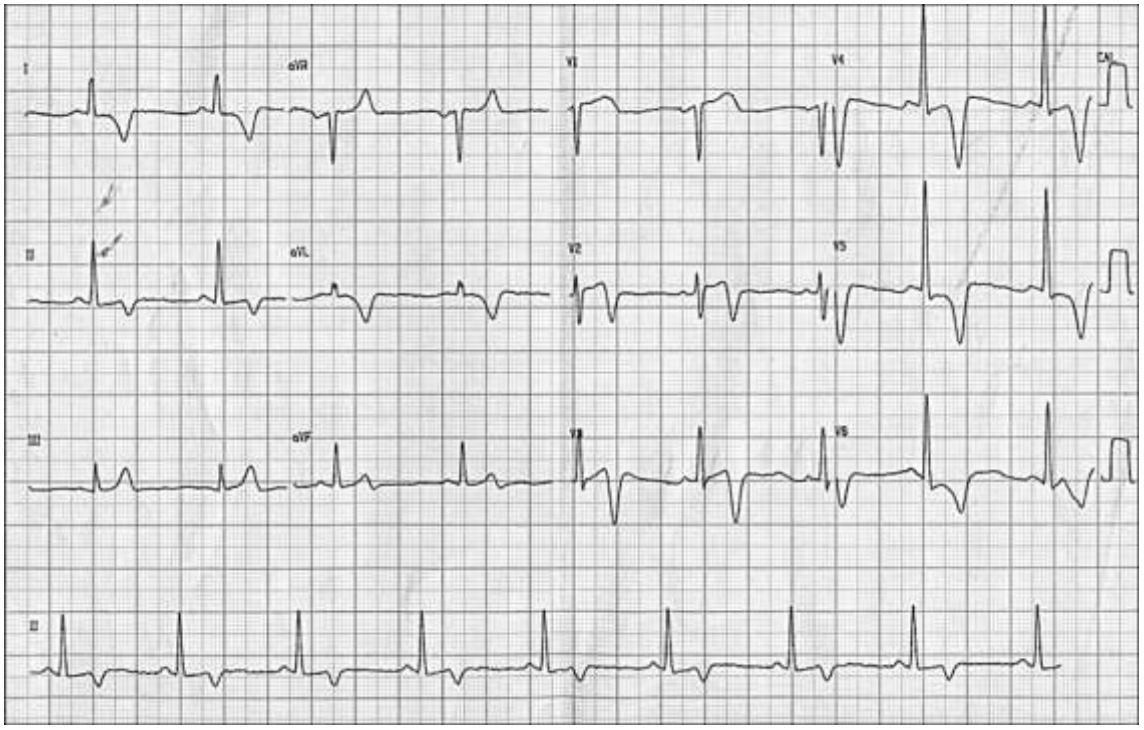


Figure. Deep T-wave inversion (TWI) asymmetric T-wave in I, aVL and from V2 to V6 In the inferior leads. Biphasic-T-waves in aVF Negative Symmetric T-wave in II, V2-V3

Vectorcardiogram of Ap-HCM

In the apical form we find Type IV vectorcardiographic loop of LVH of our classification; nevertheless, it is not exclusive, since other non-apical forms of HCM may display this pattern.

This curious form of HCM is characterized by presenting:

- Initial vectors of QRS loop heading to the front and the left;
- 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. This is the only case of LVH without CAD associated to T loop in this quadrant. A curious fact is constituted by the association of apical infarction and T loop in right posterior position.

- E point that does not match the 0 point of the QRS-loop, and located backward and to the right from the latter.

Note: The important posterior and rightward shift of the ST/T vector is responsible for the characteristic giant negative T wave (> 10 mm) in the anterolateral leads of the horizontal plane from V2 to V6. T waves at the onset, may not present a significant voltage and may appear later with the evolution of the disease.

Stress test may decrease the depth of T waves [31]. Note: The important posterior and rightward shift of the ST/T vector is responsible for the characteristic giant negative T wave (> 10 mm) in the leads of the horizontal plane from V2 to V5. T waves at the onset, may not present a significant voltage and may appear later with the evolution of the disease. (**Bielli M, Parravicini U, Zanetta M, *et al.* [Apical hypertrophic cardiomyopathy: description of a case in advanced age with documentation of electrocardiographic course]. G Ital Cardiol. 1991; 21:1325-1329**.).

Note: The important posterior and rightward shift of the ST/T vector is responsible for the characteristic giant negative T wave (> 10 mm) in the leads of the horizontal plane from V2 to V5. T waves at the onset, may not present a significant voltage and may appear later with the evolution of the disease. (**Bielli M, Parravicini U, Zanetta M, *et al.* [Apical hypertrophic cardiomyopathy: description of a case in advanced age with documentation of electrocardiographic course]. G Ital Cardiol. 1991; 21:1325-1329**.).

Genetic

HCM is inherited as an autosomal dominant trait and is attributed to mutations in one of a number of genes that encode for one of the sarcomere proteins.

About 50-60% of patients with a high index of clinical suspicion for HCM will have a mutation identified in at least 1 of 9 sarcomeric genes. Approximately 45% of these mutations occur in the β myosin heavy chain gene on chromosome 14 q11.2-3, while approximately 35% involve the cardiac myosin binding protein C gene. Since HCM is typically an autosomal dominant trait, children of an HCM parent have 50% chance of inheriting the disease-causing mutation. Whenever a mutation is identified through genetic testing, family-specific genetic testing can be used to identify relatives at risk for the disease. In individuals without a family history of HCM, the most common cause of the disease is a de novo mutation of the gene that produces the β-myosin heavy chain. HCM is a myocardial disease with variable phenotypes and genotype. Non-obstructive HCM localized to the cardiac apex (wall thickening is confined to the most distal region at the apex)

Ap-HCM is an specific variant of HCM. This variant has been first described in Japan where the prevalence is much higher than in the western world.

Ap- HCM, occurs in only 1 to 2% of the non-Japanese population.

Only a limited number of sarcomere gene defects (e.g., cardiac actin Glu101Lys) are consistently produce Ap-HCM (**Arad M, Penas-Lado M, Monserrat L, *et al.* Gene mutations in apical hypertrophic cardiomyopathy. Circulation. 2005; 112:2805-281**)

De novo cases are frequent.

A single amino acid substitution in actin causes either CHF or maladaptive cardiac hypertrophy, depending on its effect on actin structure and function. De novo mutations in cardiac actin gene were identified in two patients with sporadic HCM who presented

with syncope in early childhood. Patients were heterozygous for missense mutations resulting in Pro164Ala and Ala331Pro amino acid substitutions, adjacent to regions of actin-actin and actin-myosin interaction, respectively. A mutation that cosegregated with familial HCM was also found, causing a Glu99Lys substitution in a weak actomyosin binding domain. The cardiac phenotype in many affected patients was characterized by an Ap-HCM (**Olson TM, Doan TP, Kishimoto NY, *et al.* Inherited and de novo mutations in the cardiac actin gene cause hypertrophic cardiomyopathy. J Mol Cell Cardiol. 2000; 32:1687-1694**)

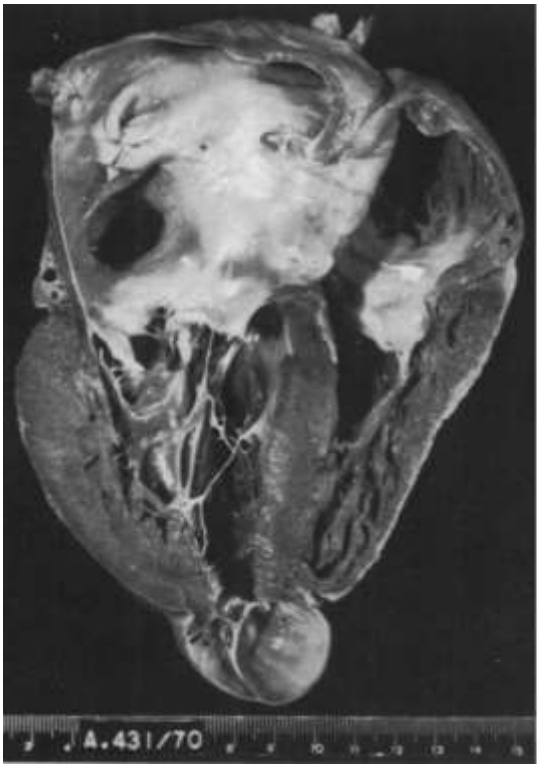
Differential Diagnosis with Disorders that may involve the left ventricular apex

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:

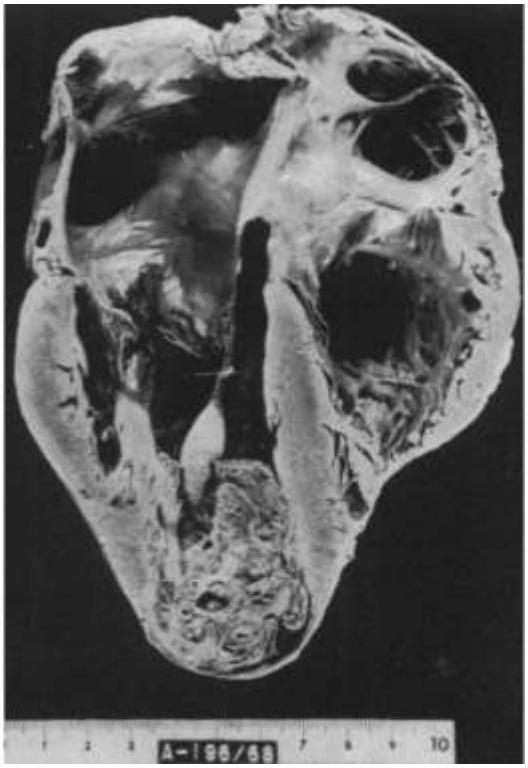
1. **LV apical cardiac tumors:** Primary tumors of the heart are rare, with an incidence of between 1.7 and 190 per 100 000 at unselected necropsy, the majority of which are benign. (**Reynen K. Cardiac myxomas. N Engl J Med 1995; 333:1610–7**) Cardiac myxomata account for approximately half of these, occurring most frequently in the atria (75% LA and 20% RA), and rarely in the LV or RV (3–4% on either side). Other benign primary cardiac tumors include papillary fibroelastomas, fibromas and lipomas. Diagnostic tool to establish diagnosis Transthoracic Echocardiography (TTE) with contrast/ CCT: Cardiac Computed Tomography/ Cardiovascular Magnetic Resonance Imaging (CCT/CMRI).
2. **LV apical thrombus:** Mobility of LV apical thrombi was the most important parameter associated with early thrombus resolution. Late resolution of LV apical thrombi was associated with poor long-term clinical outcomes. (**Jin Kyung Oh, Shape and Mobility of a Left Ventricular Thrombus Are Predictors of Thrombus Resolution. Korean Circ J. 2019 Sep; 49(9): 829–837.Published online 2019 Apr 9. doi: 10.4070/kcj.2018.0346**) Diagnostic tool to establish diagnosis: **TTE with contrast/CCT/CMRI.**

3. **Isolated ventricular non-compaction (LVNC):** is a very unusual congenital cardiomyopathy. It is a disease of endomyocardial trabeculations that increase in number and prominence. This cardiomyopathy carries a high risk of malignant arrhythmias, thromboembolic phenomenon and LV dysfunction. Diagnostic tool to establish diagnosis CMRI/CCT **(Spirito P, Autore C. Apical hypertrophic cardiomyopathy or left ventricular non-compaction? A difficult differential diagnosis.Eur Heart J. 2007 Aug; 28(16):1923-4.)**
4. **Endomyocardial fibrosis (EMF):** It is an idiopathic disorder of the tropical and subtropical regions of the world that is characterized by the development of restrictive cardiomyopathy and fibrotic changes in the endocardium, usually limited to the cardiac apex Diagnostic tool to establish diagnosis: CMRI/CCT A LV angiogram shows apical obliteration during both systole and diastole in EMF, whereas in Ap-HCM obliteration occurs only in systole and also there is an absence of significant ventricular hypertrophy in EMF patients (**Al Helaly S, Hegazy H, Malik S Pitfalls in diagnosis and clinical, echocardiographic, and hemodynamic findings in endomyocardial fibrosis: a 25-year experience. Hassan WM, Fawzy ME, Chest. 2005 Dec; 128(6):3985-92**.).
5. **Coronary Artery Disease (CAD):** Physicians caring for patients with chest pain should consider Ap-HCM in their differential diagnosis in case of a patient with chest pain and ECG changes suggestive of CAD. (**Hamza Duygu, Apical hypertrophic cardiomyopathy might lead to misdiagnosis of ischaemic heart disease. Int J Cardiovasc Imaging. 2008 Oct;24(7):675-81. doi: 10.1007/s10554-008-9311-7**.) Diagnostic tool to establish diagnosis: TTE/coronary angiogram and LVG
6. **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 left ventricular 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.
7. LV aneurysms
8. LV pseudo aneurysms
9. Apical diverticula
10. Apical ventricular remodeling

11. ARVC/D with LV involvement
12. LV 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.
13. Chronic Chagasic myocardiopathy: the apical aneurysm with thrombus in it is a frequent and distinctive finding. (**M V Elizari 1Chagasic myocardiopathy: historical perspective. 1999;59 Suppl 2:25-40**.). The apical aneurysm more frequent in men, unrelated to age, and heart weight. Patients dying of the cardiac consequences of Chagas's cardiomyopathy were more likely to have an apical aneurysm than those whose death was unrelated to the disease but the mode of death (SCD or with CHF) was unconnected with its presence. Transillumination from within the ventricle at necropsy was not only useful in demonstrating the aneurysm but also showed areas of myocardial thinning elsewhere. Thrombosis within the lesion are frequent. (**J S Oliveira, et al Apical aneurysm of Chagas's heart disease. Br Heart J. 1981 Oct;46(4):432-7. doi: 10.1136/hrt.46.4.432**.)



Chronic Chagasic cardiomyopathy with apical aneurysm.



Thrombosis of the apical aneurysm.

14. **Ap-HCM (Cisneros S, Duarte R, Fernandez-Perez GC, *et al.* Left ventricular apical diseases. Insights Imaging. 2011; 2:471-482.)** With an emphasis on the diagnostic criteria and imaging features. In this setting cardiac imaging methods can provide the clue to obtaining the diagnosis.

Figure Pathognomonic left ventriculography

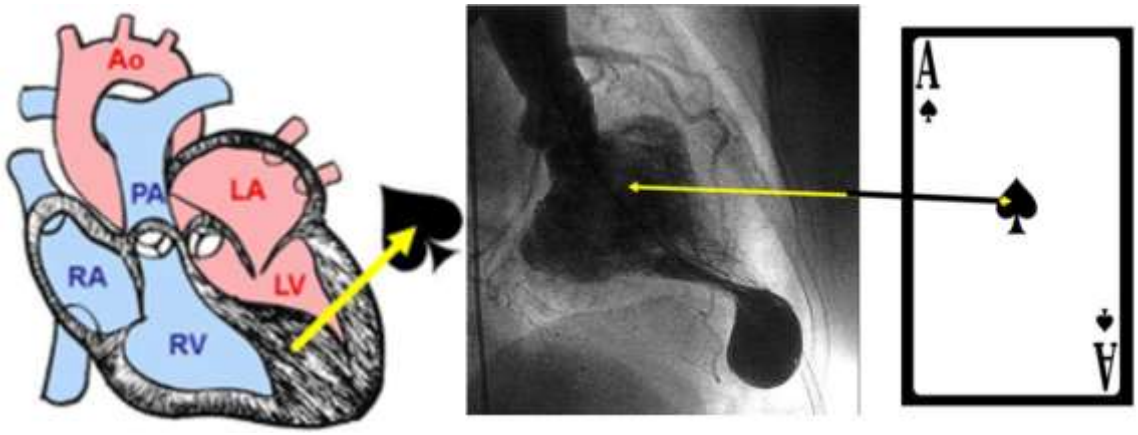


Figure . Left Ventriculography pathognomonic of Ap-HCM: Ace-of-spades sign refers to the pathognomonic configuration of the LV as seen in Ap-HCM.

15. **Differential diagnosis (Yusuf SW, Bathina JD, Banchs J, *et al.* Apical hypertrophic cardiomyopathy. World J Cardiol. 2011; 3:256-259.)**

Ap-HCM complications

Specific complications of apical HCM include

1) Apical infarctions with resultant aneurysm formation, the so called burned-out apex. An apical aneurysm further increases the risk of
2) Thrombi formation and thromboembolic phenomena.
3) Major Adverse Cardiac Events (MACE): The presence of apical aneurysms or a significant amount of delayed enhancement (>5%) are major predictors of MACE and survival in Ap-HCM.

4) Atrial Fibrillation: AF is common in HCM with a prevalence of 22-32 %. The impact of AF on overall survival, LV function, thromboembolic stroke and quality of life is crucial.

Prognosis

The prognosis of Ap-HCM with regard to SCD is believed to be better than that of O-HCM. Patients with the Ap-HCM had a benign clinical course. However, the mutation Arg719Trp in the cardiac beta-myosin heavy chain (beta MHC) gene is a high risk factor for sudden death and can be associated with an unusual Ap-HC. (**Dohlemann C, Hebe J, Meitinger T, *et al.* Apical hypertrophic cardiomyopathy due to a de novo mutation Arg719Trp of the beta-myosin heavy chain gene and cardiac arrest in childhood. A case report and family study. Z Kardiol. 2000; 89:612-619**.). Current evidence suggests that these patients experience severe symptoms and are at increased risk of ventricular arrhythmias and death, especially in the presence of an apical akinetic chamber. A large LV end diastolic dimension may predict cardiac events in Ap-HCM patients (**Suganuma Y, Shinmura K, Hasegawa H, Tani M, Nakamura Y. Clinical characteristics and cardiac events in elderly patients with apical hypertrophic cardiomyopathy. Nippon Ronen Igakkai Zasshi. 1997; 34:474–481**)

Morbid sequel, and other extra-cardiac disorders such as: AF, diastolic dysfunction, LAE, apical thrombi, ventricular aneurysms/apical akinetic chamber, myocardial infarction, CHF, high incidence of coronary fistulae and morbid AF. (**Chung T, Yiannikas J, Freedman SB, *et al.* Unusual features of apical hypertrophic cardiomyopathy. Am J Cardiol. 2010; 105:879-883**.)

Neuromuscular disorders (NMDs): Ap-HCM is rarely associated with NMDs, such as limb girdle muscular dystrophy, glycogen storage disease, metabolic myopathy, myopathy of unknown significance, or eosinophilia-myalgia syndrome. The rare

association of NMDs with Ap-HCM might be due to absence of systematic neurological investigations of patients with Ap=HCM and vice versa. (**Yan GX, Antzelevitch C. Cellular basis for the electrocardiographic J wave. Circulation. 1996; 93:372-379**)

The probability of survival without morbid events at 10 years was 77±4%.

Three independent predictors of cardiovascular morbidity were identified: age at diagnosis ≥60 years, LA diameter ≥36 mm, and New York Heart Association class ≥III at baseline. (**Yan L, Wang Z, Xu Z, *et al.* Two hundred eight patients with apical hypertrophic cardiomyopathy in china: clinical feature, prognosis, and comparison of pure and mixed forms. Clin Cardiol. 2012; 35:101-106**.)

ICD has been was used in Ap-HCM patients with cardiac arrest and NS-VT[(**Noureldin RA, Liu S, Nacif MS, *et al.* The diagnosis of hypertrophic cardiomyopathy by cardiovascular magnetic resonance. J Cardiovasc Magn Reson. 2012;14:17**.).

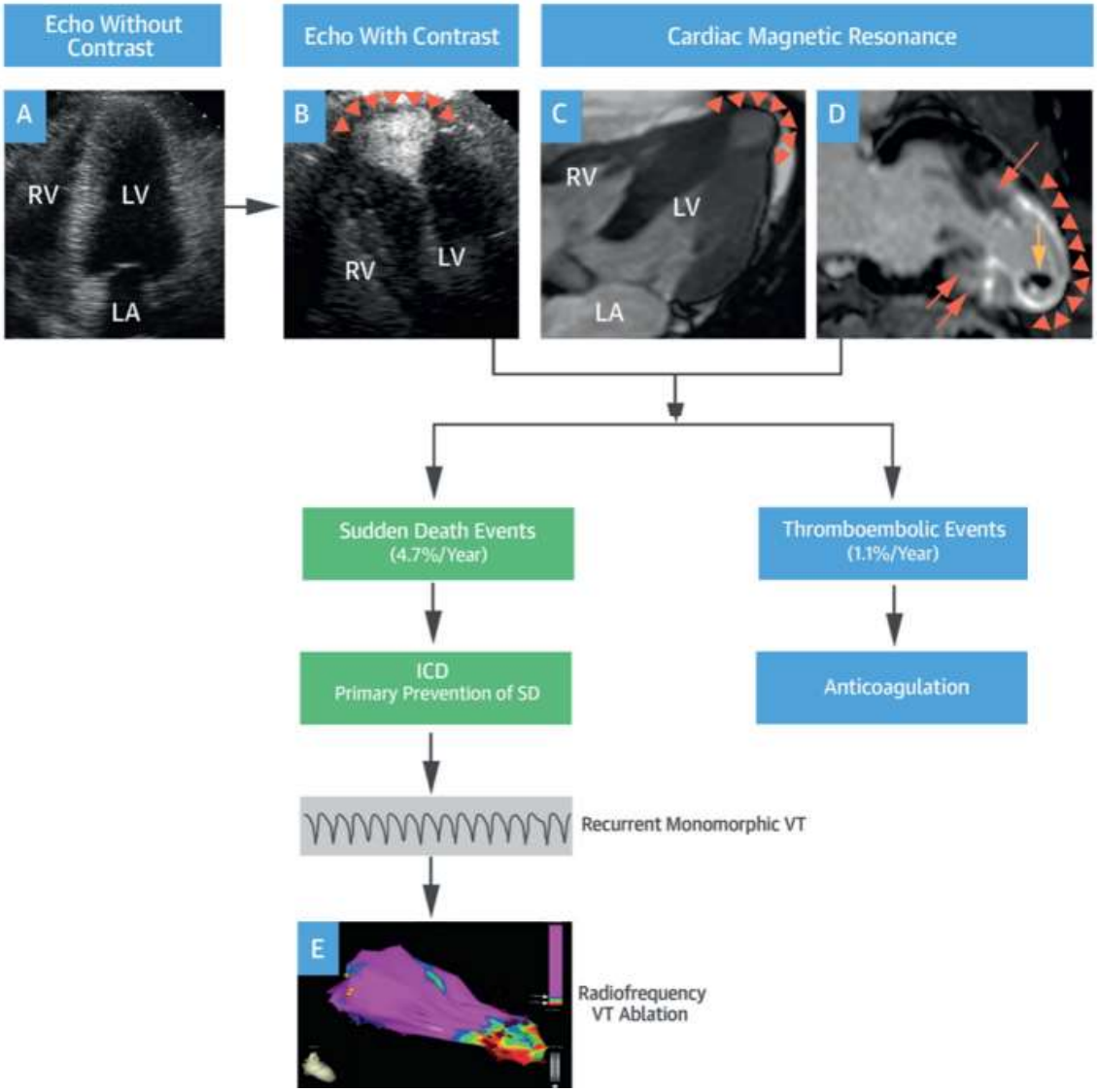
Unlike other variants of HCM, the prognosis of ApHCM is relatively benign. The overall mortality rate of Ap-HCM patients was 10.5% and cardiovascular mortality was 1.9% after a follow-up of 13.6 ± 8.3 years. (**Eriksson MJ, Sonnenberg B, Woo A, Rakowski P, Parker TG, Wigle ED, Rakowski H. Long-term outcome in patients with apical hypertrophic cardiomyopathy. J Am Coll Cardiol. 2002; 39:638–645.**)

Management

Currently available therapies for HCM have been effective in reducing morbidity, there remain important unmet needs in the treatment of both the obstructive and non-obstructive phenotypes. Novel pharmacotherapies directly target the molecular underpinnings of HCM. The recent developments in the treatment of HCM including pharmacotherapy. Medications used to treat symptomatic patients with Ap-HCM include verapamil, beta-blockers and antiarrhythmic agents such as amiodarone and procainamide.

Implantable cardioverter defibrillator: HCM patients with LV apical aneurysms are at high risk for arrhythmic sudden death and thromboembolic events. Identification of this phenotype expands risk stratification and can lead to effective treatment interventions for potentially life-threatening complications (**Ethan J Rowin et al Hypertrophic Cardiomyopathy With Left Ventricular Apical Aneurysm: Implications for Risk Stratification and Management. J Am Coll Cardiol. 2017 Feb 21;69(7):761-773. doi: 10.1016/j.jacc.2016.11.063**.). An ICD is recommended for high risk patients In HCM, unlike CAD, prevention of SCD with ICD therapy is unassociated with significant increase in cardiovascular morbidity or mortality, or transformation to CHF deterioration. ICD therapy does not substantially impair overall psychological and physical well-being. (**Barry J Maron 1Clinical Course and Quality of Life in High-Risk Patients With Hypertrophic Cardiomyopathy and Implantable Cardioverter-Defibrillators. Circ Arrhythm Electrophysiol. 2018 Apr;11(4):e005820. doi: 10.1161/CIRCEP.117.005820**.). Ap-HMC, VTs of which are usually NS-VT. This difference makes more severe, which indicates the need of implanting automatic ICD as a secondary prevention for SCD, in association to β-blockers. The latter are aimed at decreasing the number of shocks by the device.

Diagnosis, Expanded Risk Stratification, and Management Implications in HCM Patients with High-Risk LV Apical Aneurysms



(A to D) Aneurysms more reliably identified by CMR and contrast with TTE. (A) in 4-chamber view shows normal apical contour without evidence of apical aneurysm, whereas TTE (Echo) with contrast (B) and CMR (C) in the same patient demonstrates medium-sized, thin-wall apical aneurysm (arrowheads) with associated hour-glass–shaped LV chamber (D). Aneurysms can raise risk of SD. (D) In another patient, contrast-enhanced CMR image shows transmural LGE of aneurysm rim (arrowheads) with contiguous cho into the inferior (short arrows) and anterior LV walls (long arrow), a potential nidus of MVT. Aneurysms are sources of thromboemboli. Marked signal intensity contrast between the bright aneurysm rim and hypointense mass (yellow arrow) confirms presence of a thrombus in the apical aneurysm. Below are management implications and effect of treatment interventions, including prevention of SD with ICDs, radiofrequency ablation of arrhythmic focus for refractory monomorphic VT (E). and stroke prophylaxis with anticoagulation. (E) Electroanatomic endocardial voltage map in the right anterior oblique view of an apical aneurysm patient with recurrent VT. The red dots represent the ablation lesions delivered around the rim of the scarred aneurysm. ICD ¼ implantable cardioverter defibrillator; LA ¼; LV ¼; RV ¼; SD ¼ sudden death; VT ¼ ventricular tachycardia. (**Rowin, E. J., Maron, B. J. et al. (2017). *Hypertrophic Cardiomyopathy With Left Ventricular Apical Aneurysm. Journal of the American College of Cardiology, 69(7), 761–773.* doi: 10.1016/j.jacc.2016.11.063**).

Ablation: Patients with Ap-HCM or non-Ap-HCM had similar success rate of AF ablation after single procedure and lower success rate after multiple procedure compared with the control group. **(Xuan Chen et al. Long-term outcome of catheter ablation for atrial fibrillation in patients with apical hypertrophic cardiomyopathy. J Cardiovasc Electrophysiol. 2018 Jul;29(7):951-957. doi: 10.1111/jce.13645.**); Long-term outcome of catheter ablation for AF was worse in patients with Ap-HCM, as compared to controls, but was similar to patients with asymmetric septal obstructive HCM (**Seung-Young Roh et al. Long-Term Outcome of Catheter Ablation for Atrial Fibrillation in Patients With Apical Hypertrophic Cardiomyopathy. J Cardiovasc Electrophysiol. 2016 Jul;27(7):788-95. doi: 10.1111/jce.12985**.). Ap-HCM has a better prognosis than asymmetric septal HCM. However, the outcome of catheter ablation for AF in patients with Ap-HCM is similar. In patients with Ap-HCM, AF Is frequent and associated with a substantial risk for strokes and mortality suggesting that AF should be carefully managed in Ap-HCM. (**Lee SE, et al. Impact of atrial fibrillation on the clinical course of apical hypertrophic cardiomyopathy. Heart. 2017 Oct;103(19):1496-1501. doi: 10.1136/heartjnl-2016-310720**).

Monomorphic VT in a Ap-HCM can be due to endocardial, epicardial or intramural reentry in areas of apical scar. ICD indications in HCM if one or more of the acknowledged SCD risk factors were present: Family history of premature HCM-related death particularly if sudden, in a close relative, or multiple in occurrence, unexplained syncope, particularly in young patients, or if demonstrated to be arrhythmia-based, frequent, multiple, or prolonged episodes of NSVT documented in serial ambulatory, Holter monitoring and hypotensive or attenuated blood pressure response to exercise