Middle age man with high blood pressure, moderate symmetrical left ventricular hypertrophy, normal coronary arteries and pathognomonic left ventricular shape: The "ace-of-spades" sign on left ventriculography

Hombre de mediana hipertenso con moderada hipertrofia simétrica ventricular izquierda, arterias coronarias normales y ventrículo izquierdo con aspecto patognomónico: El señal del "as de espadas" en la ventriculografía izquierda

Homem de meia idade, hipertenso e com hipertrofia simétrica moderada do ventrículo esquerdo, artérias coronárias normais e ventrículo esquerdo com aspecto patognomônico: O sinal do "ás de espadas" na ventriculografia esquerda

From Raimundo Barbosa Barros M.D.
Coronary Center Hospital de Messejana Dr. Carlos Alberto Studart Gomes Fortaleza-Ceará-Brazil

Finals comments Andrés Ricardo Pérez-Riera M.D. Ph.D.
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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 made (annex) we suggested performing Echo to rule out apical hypertrophic cardiomyopathy.
- Supplementary tests
- Several ECGs with the same morphology. See the next slide.

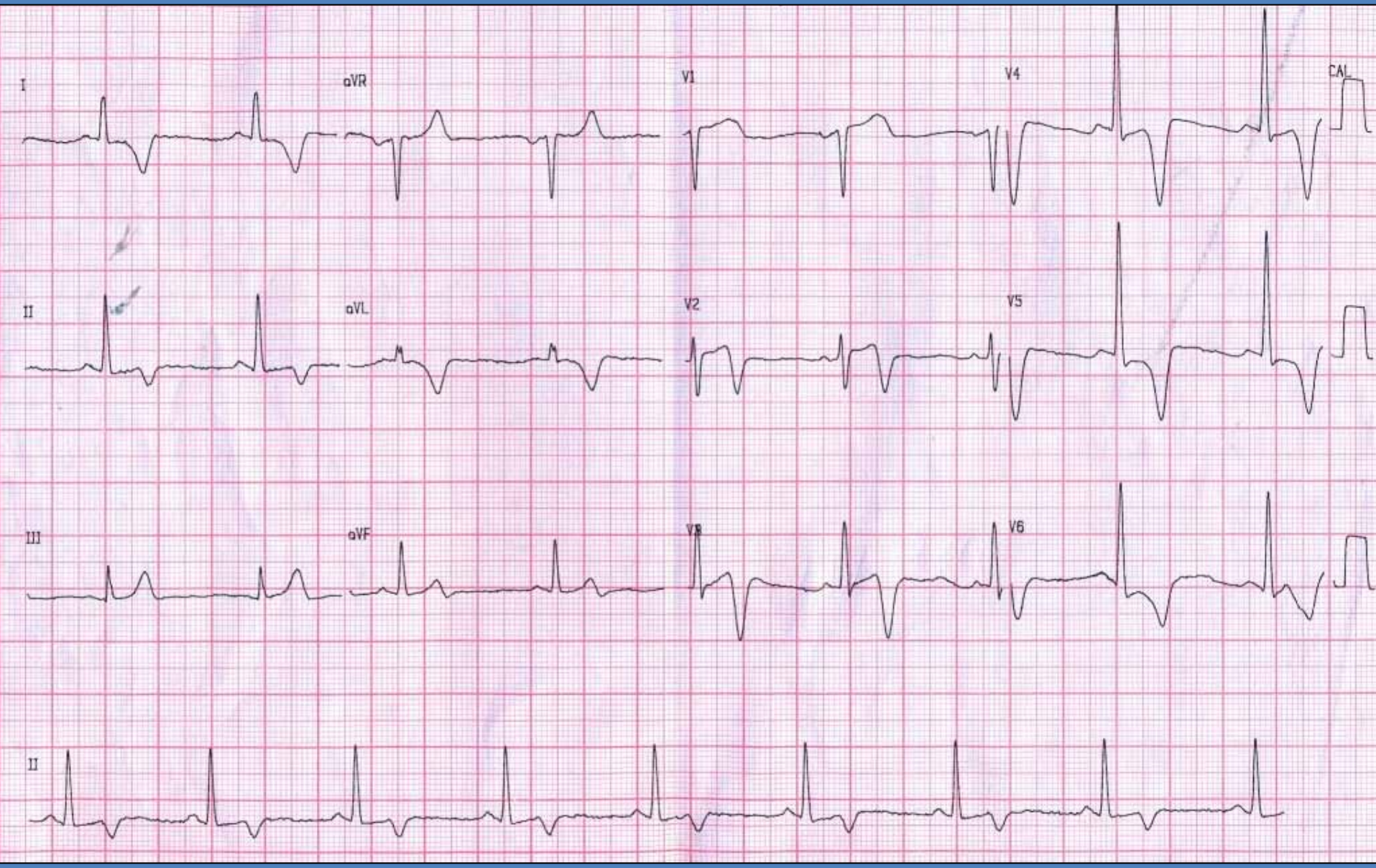
Echo: LV end diastolic diameter: 49 mm. LV end systolic diameter: 26 mm. Septal diastolic thickness: 14 mm. LV posterior wall diastolic diameter: 14 mm. Aorta: 29 mm; LA: 40 mm EF=78% Mass: 355 g
Conclusion: moderate LV concentric hypertrophy. Moderate LV diastolic dysfunction. Heart valves with normal morphological aspect. Absence of gradient in the LVOT. Mild mitral reflux.

Holter monitoring:
Sinus rhythm predominates
Asymptomatic isolated ventricular ectopic beats (210)
Absence of NSVT

Left heart catheterization:
Presence of myocardial bridge in the proximal $^{1}/_{3}$ of the LAD
LV with asymmetrical hypertrophy with apical predominance (ventriculography shows spade-like morphology)
Normal coronary arteries
Any comments?

Portuguese

Masc.,41 anos com história de pontadas no peito e cansaço aos esforços.
Relata H.A.S. sem tratamento atualmente.Nega fumo e diabetes.
Pai faleceu aos 77 anos de IAM?Irmão faleceu súbitamente aos 37 anos enquanto dormia.
AC:Ritmo cardíaco regular FC=68 bpm+ quarta bulha sem sopro
A.pulmonar e extremidades normais
PA=140/100mmHg
Após realização do ECG(anexo) sugerimos realizar ECO para afastar cardiomiopatia hipertrófica apical.Vários ECGs com a mesma morfologia
ECO: Diametro diastólico final do VE:49mm Diametro sistólico final do VE:26mm.Espessura diast. do septo:14mm. Diametro diastolico da parede posterior do VE:14mm. Aorta: 29mm;AE:40mm.FE=78% Massa:355g Conclusão: Hipertrofia moderada concêntrica do VE; Disfunção diastólica moderada do VE.; Valvas cardíacas com aspecto morfologico normal.Ausência de gradiente na via de saída do VE. Refluxo mitral leve.
HOLTER:
Predomina ritmo sinusal
Ectopias ventriculares isoladas(210) assintomáticas
Ausência de de TVNS
CATE:
Presença de ponte miocárdica no 1/3 proximal da DA
VE com hipertrofia assimétrica com predomínio apical(ventriculografia mostra morfologia “spade-like”
“Coronárias normais”


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

Estimado Raimundo, interesante vuestro caso.
Se cerraria como una MCH concentrica o apical? Aunque esto no cambia el riesgo del paciente.
saludos
Alberto

Dear Raimundo:
Your case report is very interesting.
It is a concentric or apical HCM (.?) However these diagnosis does not change the risk for the patient

Estimado Alberto:

Entiendo que dices que siendo una cardiomiopatia concêntrica o apical este hecho no influencia en el pronóstico.
En realidad el pronóstico depende de su base genética, pero en general se considera que la forma apical es de curso mas benigno, a menos que obedezca a la mutación Arg719Trp de la beta miosina de cadena pesada. Caso contrario, el pronóstico siendo apical es mejor.(1)
Dear Alberto: The prognosis of ApHCM with regard to SCD is believed to be better than that of common HCM. Patients with the ApHCM 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 ApHCM (1);
Andrés.

1. **Dohlemann C, Hebe J, Meitinger T, 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 Jul;89:612-619.**

Early repolarization is seen in all leads, usually isoproterenol deminishes the early repolarization

Repolarização precoce é vista em todas as derivações. Isoproterenol usualmente diminui a repolarização precoce

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Dear Professor Melvin very cleaver and acute your Electrocardiographic observation related diffuse ST segment elevation in this case report. However, I think that in this case ST segment elevation is not seen in all leads, but only on right precordial leads. Please see again the ECG in third Slides before.Do you think that the present case could correspond to early repolarization pattern (ERP) type 3 of Antzelevich and Yan concept? These researches postulated that ERS and Brugada Syndrome (BrS) share similar ECG characteristics, clinical outcomes, risk factors, as well as a common arrhythmic platform related to amplification of I(to)-mediated J waves. Although BrS and ERS differ with respect to the magnitude and lead location of abnormal J wave manifestation, following Antzeletich and Yan concept (1) all represent a continuous spectrum of phenotypic expression, termed J-wave syndromes. These authors proposed divided ERP into three subtypes:

Type 1: ERP observed predominantly in the lateral precordial leads. It is prevalent among healthy male athletes and rarely seen in IVF survivors;

Type 2: ERP predominantly in the inferior or inferolateral leads. It is associated with a higher level of risk;

Type 3: ERP globally in the inferior, lateral, and right precordial leads, is associated with the highest level of risk for development of malignant arrhythmias and is often associated with IVF storms.

1. Antzelevitch C, Yan GX. J-wave syndromes. from cell to bedside. J Electrocardiol. 2011 Nov-Dec; 44:656-661.

Ventricular myocardium is composed of at least three electrophysiologically distinct cell types: epicardial, endocardial, and M cells. In ERP the ST segment elevation is attributed to shortening of ventricular action potentials in epicardial regions that are responsible by the potential differences resulting in a current similar to the subepicardial injury current, BrS and IVF. ST-segment elevation in a structurally normal heart is associated with an ECG J wave, which can be observed in the early repolarization, IVF, and the BrS. A transmural voltage gradient during initial ventricular repolarization, which results from the presence of a prominent action potential notch (spike and dome) mediated by the transient outward potassium current (I(to)) in epicardium but not endocardium, is responsible for the registration of the J wave on the ECG. (1; 2) This explains partially why the exercise and isoproterenol infusion abolish the ST segment elevation in "benign" ERP like in BrS and IVF patients. (3)

1. **Yan GX, Antzelevitch C. Cellular basis for the electrocardiographic J wave. Circulation. 1996 Jan 15;93:372-379.**
2. **Hlaing T, DiMino T, Kowey PR, Yan GX. ECG repolarization waves: their genesis and clinical implications. Ann Noninvasive Electrocardiol. 2005 Apr;10:211-223.**
3. **Bernard A, Genée O, Grimard C, Sacher F, Fauchier L, Babuty D. Electrical storm reversible by isoproterenol infusion in a striking case of early repolarization. J Interv Card Electrophysiol. 2009 Aug; 25: 123-127.**

Andrés Ricardo Pérez-Riera M.D. Ph.D.

Professor Pérez- Riera and Raimundo Barbosa Barros "The Fox"
One question: Is the isoproterenol indicated from patients with CMH?
My best
Adail - Bahia - Brasil
Queridos El Potro e The Fox
O ECG sob Isoproterenol é da paciente com Cardiomiopatia Hipertrófica?
Grato pela atenção
Adail - Bahia – Brasil

Dear Adail: Isoproterenol is a beta-adrenergic receptor agonist used only in punctual situations in HCM. Cardiac catheterization with isoproterenol challenge may identify patients with HCM who may benefit from septal reduction therapy for whom the initial noninvasive evaluation does not show severe obstruction.(1) In HCM the ST/T modifications are secondary eventually following features:

1. Microcirculation disease
2. Decrease of vasodilator capacity
3. Systemic compression of septal and subepicardial vessels: ST segment elevation
4. Fall of pressure in aorta root
5. Difficulty in coronary filling by hypertrophy
6. Coronary atherosclerosis in patients older than 50 years old
7. Excessive increase of mass and subsequent offer/demand disproportion.

Raimundo&Andrés

1. Elesber A, Nishimura RA, Rihal CS, Ommen SR, Schaff HV, Holmes DR Jr. Utility of isoproterenol to provoke outflow tract gradients in patients with hypertrophic cardiomyopathy. Am J Cardiol. 2008 Feb 15; 101:516-520.

Spanish

Estimado Adail isoproterenol es un agonista del receptor beta-adrenérgico utilizado sólo en situaciones puntuales en la miocardiopatía hipertrófica. El cateterismo cardíaco con el reto de isoproterenol puede identificar a los pacientes con miocardiopatía hipertrófica, que pueden beneficiarse de la terapia de reducción septal para los que la evaluación no invasiva inicial no se presenta obstrucción severa. (1)
Isoproterenol está contraindicado en HMC ya que el medicamento causa inducción de la hipertrofia ventricular, fibrosis y disfunción cardiaca a través de la estimulación de la fosfatidilinositol 3-quinasa (PI 3-quinasas o PI3Ks). Estos son una familia de enzimas que participan en las funciones celulares, tales como el crecimiento celular, proliferación, diferenciación, motilidad supervivencia, y el tráfico intracelular, que a su vez están implicados en el cáncer
En la CMH las modificaciones del segmento ST/T son secundárias eventualmente a los siguientes problemas:
Enfermedad de microcirculación
Disminución de a capacidad de vasodilatación
Compresion de los vasos epicãrdicos
Caida de la presión en el tronco de la aorta
Dificultad para el llenado coronario por la hipertrofia
Eventual presencia de arteroesclerosis em pacientes mayores de 50 años
Desproporcional aumento de la masa con inbalance oferta/demanda.

Raimundo&Andrés.

QUERIDOS AMIGOS DEL FORUM

El trazado de los amigos del brasil, es de extraordinaria rareza El primer vector se depolariza normalmente ,pero después de los 50 ms , dura 120ms Todas las ondas T estan aplanadas

Me parece nunca haver visto una imagen parecida. Podria ser un caso de hibernación , que es frecuente con la reducción de la temperature del cuerpo en sobrevivientes de muerte subita con lesion cerebral

Seria interesante que analizen los amigos profe Andres y Dr Raimundo las bases electrofisiologicas y patológicas de este extremadamente extraño caso

Un fraternal abrazo

Samuel Sclarovsky from Israel.

Dear forum´s friends

The ECG of my friends from Brazil, is of extraordinary rarity. The dpolarization of the first vector is normal, but after 50sm(duration 120ms) all T waves are flattened.

I think that I had never seen a similar pattern.

Could be a case of hibernation, which is common with the reduction of body temperature in survivors of sudden death with brain injury.

It would be interesting that our friends Andrés and Dr Raimundo analized the electrophysiological and pathological basis of this extremely rare case.

A fraternal embrace

Samuel Sclarovsky Israel

FINAL COMMENTS

Which is the definition of pathognomonic? The word is an adjective of Greek origin from + fit to judge, from interpreter; akin to Greek to know specifically distinctive or characteristic of a disease or pathologic condition; denoting a sign or symptom on which a diagnosis can be made. (of a sign or symptom) specific to a disease or condition, such as Koplik's spots on the buccal and lingual mucosa, which are indicative of measles. In others words when the signal is present is not possible other diagnosis.

Pathognomonic (often misspelled as *pathognomic* and sometimes as *pathomnemonic*, homophone to *pathopneumonic*) is a term, often used in medicine, that means *characteristic for a particular disease*. A pathognomonic sign is a particular sign whose presence means that a particular disease is present beyond any doubt. Labelling a sign or symptom "pathognomonic" represents a marked intensification of a "diagnostic" sign or symptom.While some findings may be classic, typical or highly suggestive in a certain condition, they may not occur *uniquely* in this condition and therefore may not directly imply a specific diagnosis. A pathognomonic sign or symptom has very high specificity but does not need to have high sensitivity: for example it can sometimes be absent in a certain disease, since the term only implies that, when it is present, the doctor instantly knows the patient's illness. The presence of a pathognomonic finding, on the other hand, allows immediate diagnosis, since there are no other conditions in the differential diagnosis.Singular pathognomonic signs are relatively uncommon. Examples of pathognomonic findings include Koplik's spots inside the mouth in measles, the palmar xanthomata seen on the hands of people suffering from hyperlipoproteinemia, or a tetrad of rash, arthralgia, abdominal pain and kidney disease in a child with Henoch-Schönlein purpura.As opposed to symptoms (reported subjectively by the patient and not measured) and signs (observed by the physician at the bedside on physical exam, without need for a report) a larger number of medical test results are pathognomonic. A example is the hypersegmented neutrophil, which is seen only in megaloblastic anemias (not a single disease, but a set of closely related disease states). More often a test result is "pathognomonic" only because there has been a consensus to define the disease state in terms of the test result (such as diabetes mellitus being defined in terms of chronic fasting blood glucose levels).In contrast, a test with very high sensitivity rarely misses a condition, so a negative result should be reassuring (the disease tested for is absent). A sign or symptom with very high sensitivity is often termed *sine qua non* An example of such test is a genetic test to find an underlying mutation in certain types of hereditary colon cancer.

Hypertrophic cardiomyopathy(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 phenotpype and genotype. Non-obstructive hypertrophy localized to the cardiac apex (wall thickening is confined to the most distal region at the apex,) or apical hypertrophic cardiomyopathy (ApHCM) is a specific variant of HCM. This disease has been first described in Japan where the prevalence is much higher than in the western world.

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

Only a limited number of sarcomere gene defects (eg, cardiac actin Glu101Lys) consistently produce ApHCM (1). 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 ApHCM (2). The typical features of ApHCM include:

1. **Arad M, Penas-Lado M, Monserrat L, et al. Gene mutations in apical hypertrophic cardiomyopathy. Circulation. 2005; 112:2805-2811.**
2. **Olson TM, Doan TO, 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.**

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 including:

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 left ventricular apex with a hypercontractile base of the LV is often noted. It is the hallmark bulging out of the apex of the heart with preserved function of the base that earned
2. Left ventricular aneurysms and pseudoaneurysms
3. Apical diverticula
4. Apical ventricular remodelling
5. **Apical hypertrophic cardiomyopathy (ApHCM)**
6. Left ventricular non-compaction
7. Arrhythmogenic right ventricular cardiomyopathy/dysplasia(ARVC/D with left ventricular involvement
8. Left ventricular false tendons: are 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 an emphasis on the diagnostic criteria and imaging features. In this setting cardiac imaging methods can provide the clue to obtaining the diagnosis.

1. Cisneros S, Duarte R, Fernandez-Perez GC, et al. Left ventricular apical diseases. Insights Imaging. 2011 Aug;2:471-482.

HYPERTROPHYC CARDIOMYOPATHY CLASSIFICATION

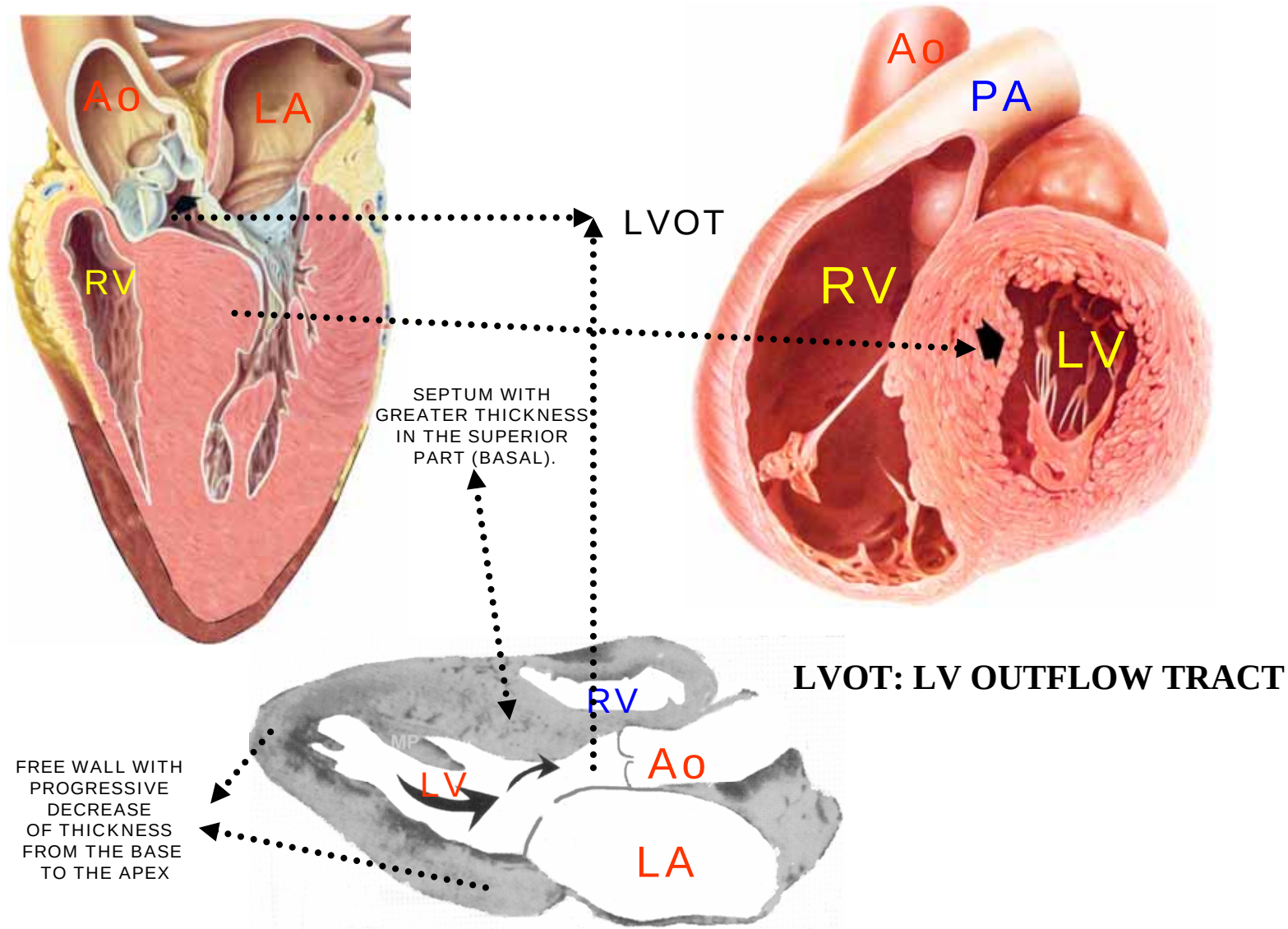
1) **OBSTRUCTIVE FORM (OHCM)**
Septal asymetrical with obstruction with gradient

2) **NON-OBSTRUCTIVE FORM (NO-HCM)**
2A) Septal asymetrical with no obstruction;
2B) Apical Hypertrophic Cardiomiopathy (Ap HCM): 2%, 3% to 8%.
2C) Lateral and/or postero-lateral;
2D) Concentrical or symmetrical, or homogeneous hypertrophic: 5%.
2E) Right ventricle: 2%.

OBSTRUCTIVE FORM (OHCM)	NONOBSTRUCTIVE FORM (NOHCM)
Septum with greater thickness in the superior part (basal).	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.

Classification and differences of obstructive and nonobstructive forms of Hypertrophic Cardiomyopathy.

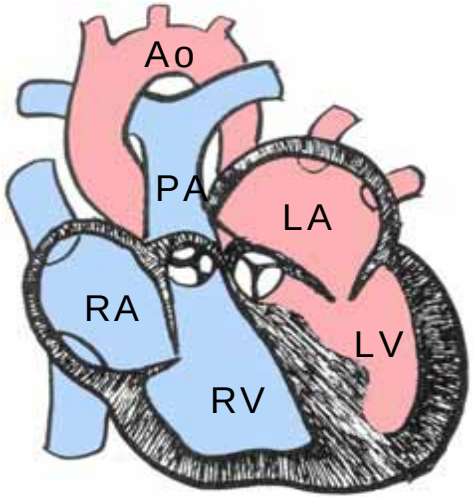
OBSTRUCTIVE FORM OF HYPERTROPHIC CARDIOMYOPATHY (OHCM)



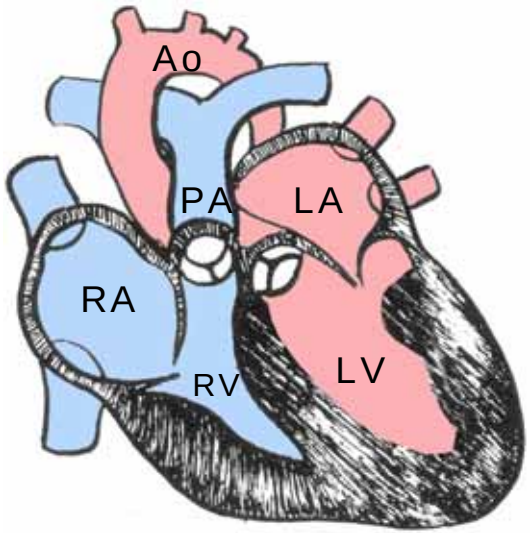
Outline of obstructive form of Hypertrophic Cardiomyopathy.

NONOBSTRUCTIVE FORMS

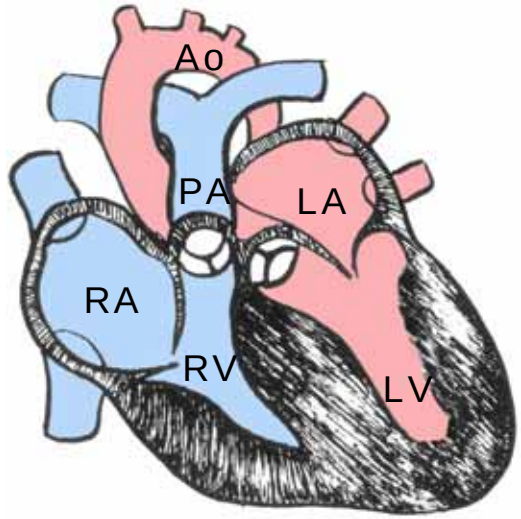
SEPTAL ASYMMETRICAL WITHOUT OBSTRUCTION



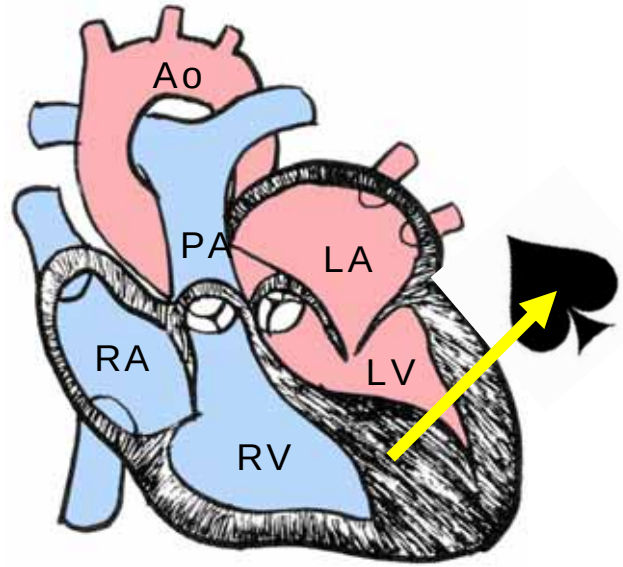
LATERAL AND/OR POSTERO-LATERAL



SYMMETRICAL



APICAL HYPERTROPHIC CARDIOMYOPATHY



The "ace-of-spades" sign

Outline of nonobstructive form of Hypertrophic Cardiomyopathy.

Apical Hypertrophic cardiomyopathy Electrocardiogram 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 American patients: 15% in Japan vs 3% in US (1). The singnificative 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.(2)

The depth of negative T waves is related to craniocaudal asymmetry and apical late-enhancement (3)

Stress test may decrease the depth of T waves.(4)

Three hypotheses aroused 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.(5)

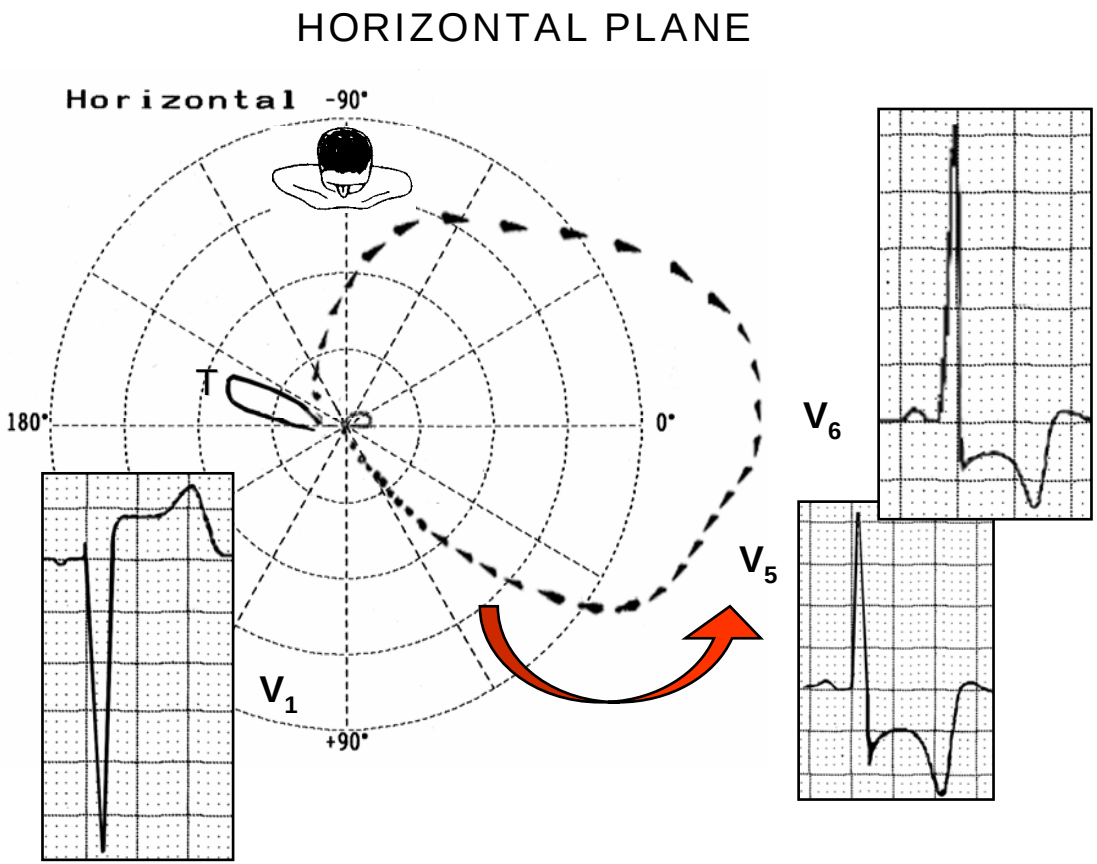
The prevalence in the western world of this form of HCM is approximately 0.02 to 0.2% and it constitutes 8% of the cases of the entity. In Japan, the apical form of HCM constitutes 25% of HCM.(6)

1. Kitaoka H, Doi Y, Casey SA, Comparison of prevalence of apical hypertrophic cardiomyopathy in Japan and the United States. Am J Cardiol. 2003;92:1183-1186.
2. Bielli M, Parravicini U, Zanetta M, Zenone F. . G Ital Cardiol. Apical hypertrophic cardiomyopathy: description of a case in advanced age with documentation of electrocardiographic course 1991;21:1325-1329.
3. 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.
4. Tilmant PY, Lablanche JM, Laurent JM, Héthuin JP, Folliot JP, Bertrand ME. . Non-obstructive hypertrophic myocardiopathy. Apropos of 5 cases Arch Mal Coeur Vaiss. 1980;73:1269-1278.
5. Tsunakawa H, Wei D, Mashima S, Harumi K. . Study on the genesis of giant negative T wave in apical hypertrophic cardiomyopathy using a three-dimensional computer model. Jpn Heart J. 1991;32:799-809.
6. Maron BJ. The giant negative T wave revisited ... in hypertrophic cardiomyopathy. J Am Coll Cardiol. 1990 Apr;15:972-973.

Sometimes R-wave voltage and T-wave negativity progressively decreased in magnitude at serial ECGs
Non-sustained or sustained VT can be observed in patients that developed apical aneurysm with normal coronary arteries;To clarify the mechanisms of ECG abnormalities in hypertrophic cardiomyopathy, 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 left and right ventricles, 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 craniocaudal asymmetry and apical late-enhancement (1)

1. 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.

VECTOCARDIOGRAM OF APICAL NOHCM: VECTOCARDIOGRAPHIC IV TYPE LVE



1) Initial vectors of QRS loop heading forward and to the left;

2) Anteriorization of QRS loop predominantly located in the left anterior quadrant;

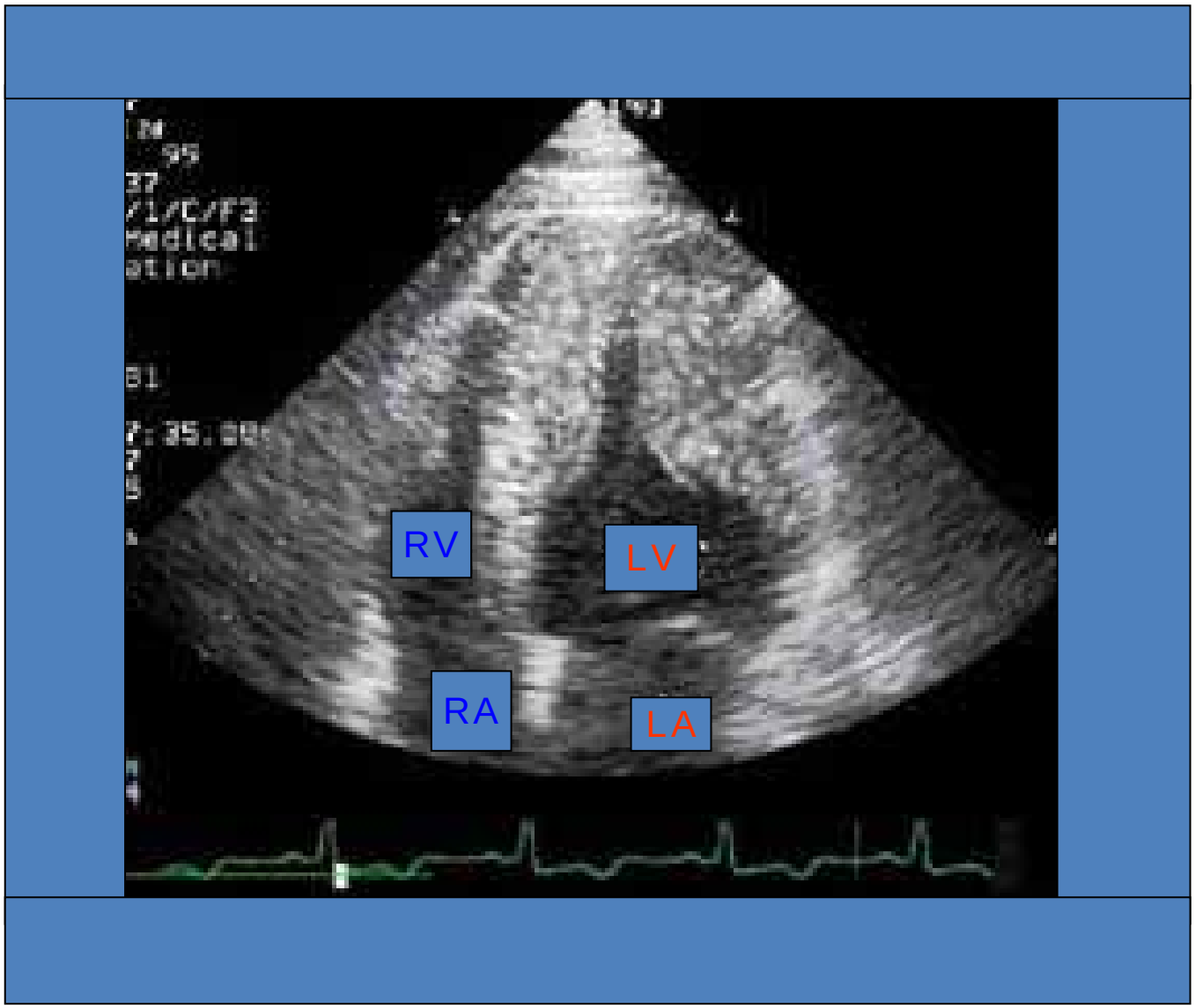
3) Maximal vector that increases voltage;

4) Final vectors located to the right and backward with ST/T vector in the right posterior quadrant;

5) E point that does not match the 0 point and is located backward and rightward from the latter.

Vectocardiogram features in Apical Hypertrophic Cardiomyopathy.

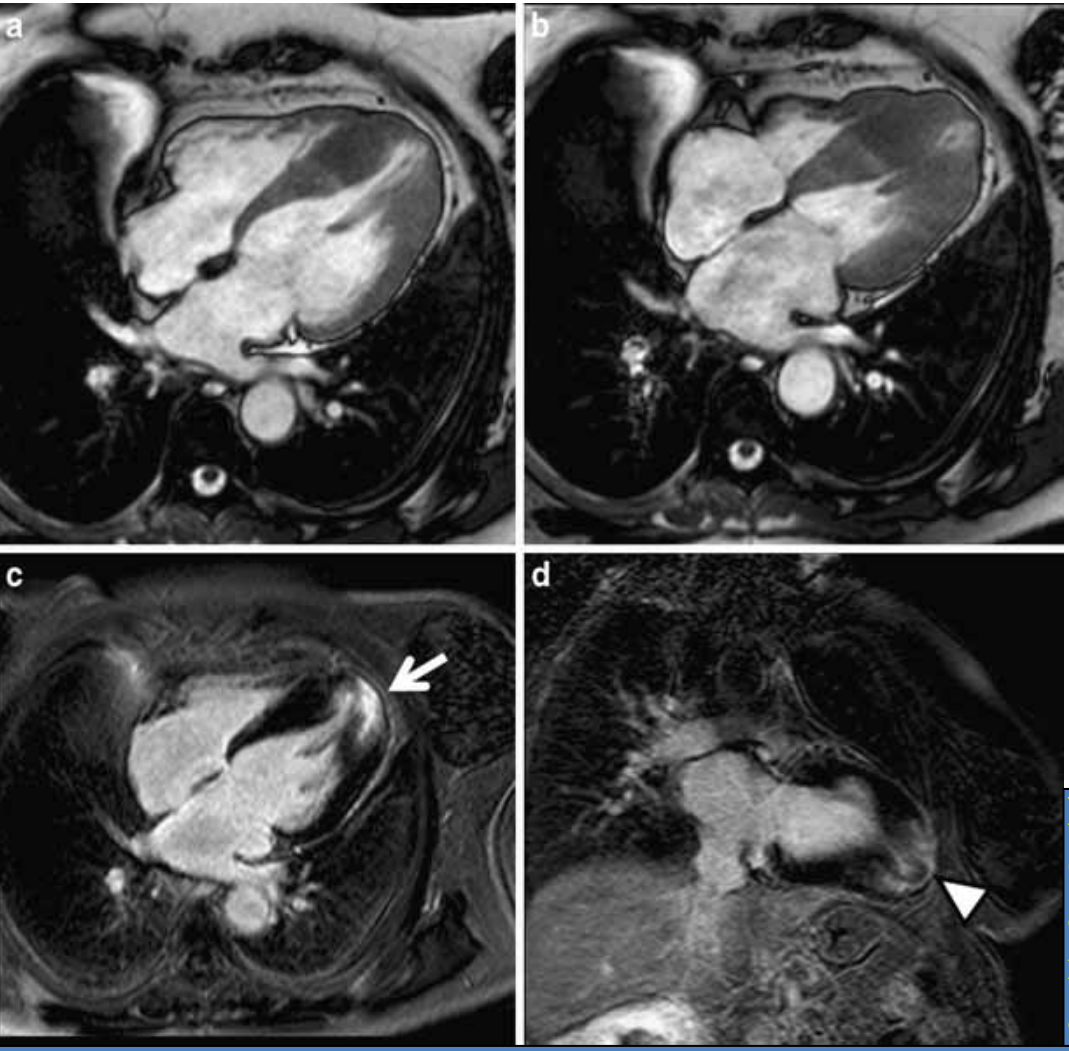
Transtoracic two-dimensional echocardiography



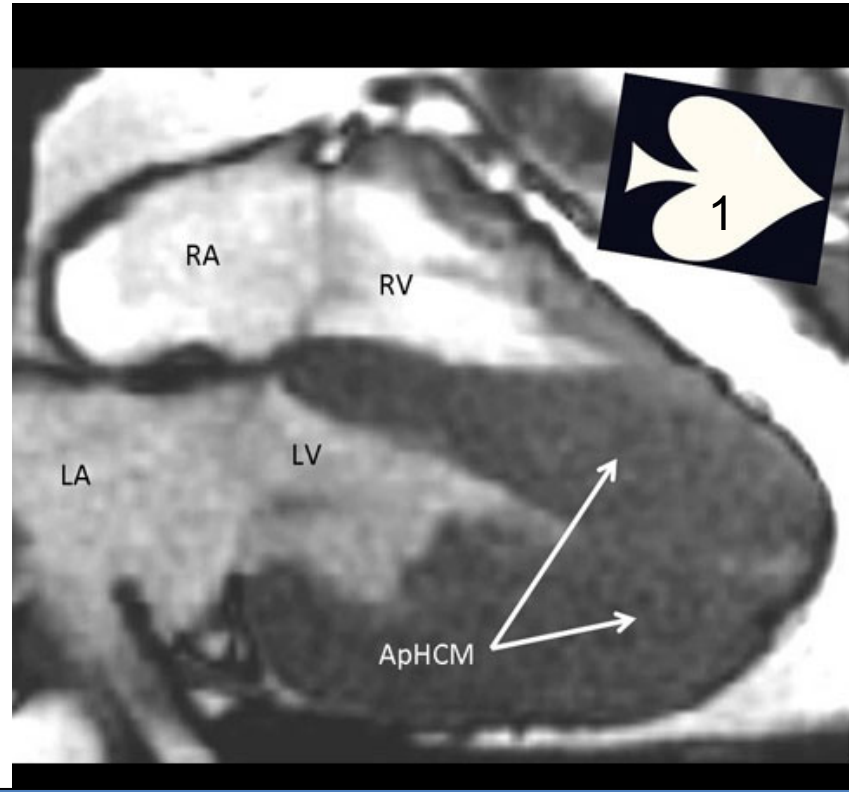
Two dimensional echocardiogram. Apical 4-chamber view shows apical hypertrophy in the apical one third of the ventricle, with apical left ventricle cavity obliteration.

RV = right ventricle **RA** = right atrium **LA** = left atrium **LV**= left ventricular cavity

Cardiovascular magnetic resonance (CMR) or Cine MRI



Apical form of hypertrophic cardiomyopathy. Cine MRI in the four-chamber view shows progressive thickening of the ventricular walls towards the apex in diastole (**a**) and systole (**b**). Late enhancement in a four-chamber view (**c**) and vertical long axis (**d**) demonstrates strong enhancement in the hypertrophied myocardium (arrow). Note the presence of “pseudo diverticulum” in the most apical myocardium (arrowhead)



Four-chamber CMR SSFP image demonstrates asymmetrical left ventricular apical thickening. (LV = left ventricle; RV = right ventricle; LA = left atrium; RA = right atrium; ApHCM = apical hypertrophy).

The "ace-of-spades" sign on left ventriculography and CMR being pathognomonic of Ap HCM.

HCM is characterized by substantial genetic and phenotypic heterogeneity, leading to considerable diversity in clinical course including the most common cause of SCD in young athletes and a determinant of HF symptoms in patients of any age.

Two-dimensional echocardiography has been the most reliable method for establishing a clinical diagnosis of HCM. However, CMR, with its high spatial resolution and tomographic imaging capability, has emerged as a technique particularly well suited to characterize the diverse phenotypic expression of this complex disease.

CMR is often superior to echocardiography for HCM diagnosis, by identifying areas of segmental hypertrophy (ie., anterolateral wall or apex) not reliably visualized by echocardiography (or underestimated in terms of extent).

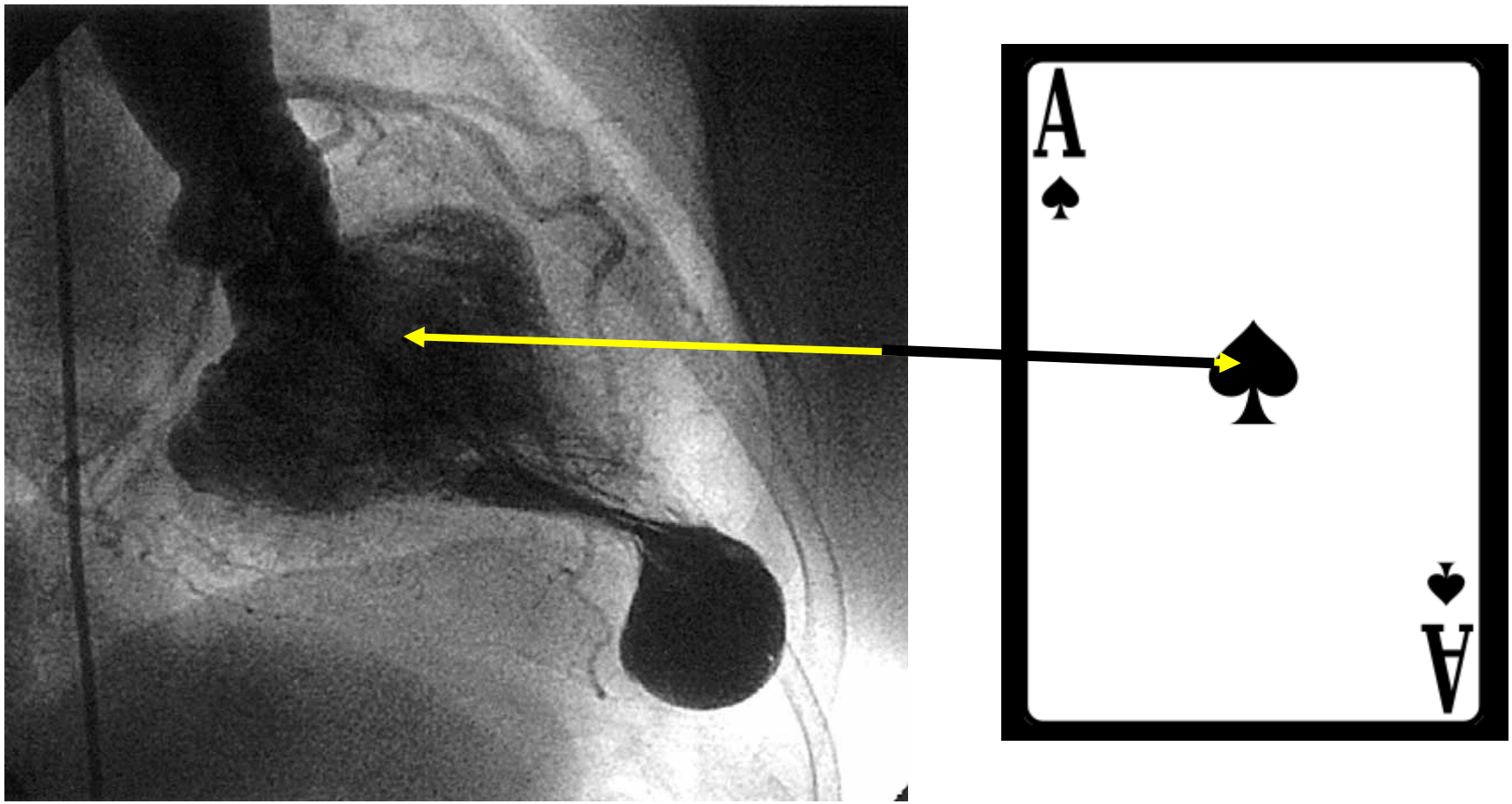
High-risk HCM patient subgroups identified with CMR include those with thin-walled scarred LV apical aneurysms (which prior to CMR imaging in HCM remained largely undetected)

End-stage systolic dysfunction, and massive LV hypertrophy. CMR observations also suggest that the cardiomyopathic process in HCM is more diffuse than previously regarded, extending beyond the LV myocardium to include thickening of the RV wall as well as substantial morphologic diversity with regard to papillary muscles and mitral valve. These findings have implications for management strategies in patients undergoing invasive septal reduction therapy.

Among HCM family members, CMR has identified unique phenotypic markers of affected genetic status in the absence of LVH including: **myocardial crypts, elongated mitral valve leaflets and late gadolinium enhancement.** The unique capability of contrast-enhanced CMR with late gadolinium enhancement to identify myocardial fibrosis has raised the expectation that this may represent a novel marker, which may enhance risk stratification. Late gadolinium enhancement(LGE) appears to be an important determinant of adverse LV remodeling associated with systolic dysfunction. However, the predictive significance of LGE for SCD is incompletely resolved and ultimately future large prospective studies may provide greater insights into this issue. These observations underscore an important role for CMR in the contemporary assessment of patients with HCM, providing important information impacting diagnosis and clinical management strategies.

Left Ventriculography

The "ace-of-spades" sign on left ventriculography being pathognomonic. (1)



1. **Olearczyk B, Gollol-Raju N, Menzies DJ. Apical hypertrophic cardiomyopathy mimicking acute coronary syndrome: a case report and review of the literature. Angiology. 2008 Oct-Nov;59:629-631**.

The diagnosis is based on the following elements in ApHCM

1. Giant and negative T waves from V2 to V4;
2. Mild symptoms and benign course;
3. Aspect of spade cards in left ventriculography;
4. 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.

Differential diagnosis(1)

1. LV apical cardiac tumors
2. LV apical thrombus
3. Isolated ventricular non-compaction
4. Endomyocardial fibrosis
5. Coronary artery disease.

1. Yusuf SW, Bathina JD, Banchs J, Mouhayar EN, Daher IN. Apical hypertrophic cardiomyopathy**.** World J Cardiol. 2011 Jul 26;3:256-259.

Prognosis

The prognosis of ApHCM with regard to SCD is believed to be better than that of common HCM. Patients with the ApHCM 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 ApHCM(1). 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.

Morbid sequel, and others extra-cardiac disorders such as:

Atrial fibrilation, diastolic dysfunction, left atrial enlargement, apical thrombi, ventricular aneurysms/ apical akinetic chamber, myocardial infarction, progressive heart failure, high incidence of coronary fistulae and morbid atrial fibrillation.(2)

Neuromuscular disorders ApHCM is only 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 ApHC might be due to absence of systematic neurologic investigations of patients with AHC and vice versa.(3)

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, left atrial diameter ≥36 mm, and New York Heart Association class ≥III at baseline.(4)

1. Dohlemann C, Hebe J, Meitinger T, 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.
2. Chung T, Yiannikas J, Freedman SB, Kritharides L. Unusual features of apical hypertrophiccardiomyopathy**.** Am J Cardiol. 2010 Mar 15;105:879-883.
3. Yan Lm Wang Z, Xu Z et al. Finsterer J Stöllberger C. Neuromuscular disorders associated with apical hypertrophic cardiomyopathy. Acta Cardiol. 2009 Feb;64:85-89.
4. Two hundred eight patients with apical hypertrophic cardiomyopathy in china: clinical feature, prognosis, and comparison of pure and mixed forms.ClinCardiol 2012 Feb;35:101-106.

Mangement

1. **Drugs** Medications used to treat symptomatic patients with ApHCM include verapamil, beta-blockers and antiarrhythmic agents such as amiodarone and procainamide.

2. **Implantable cardioverter defibrillator:** An ICD is recommended for high risk patients. (See next slide)

3. **Ablation:** Monomorphic VT in a ApHCM can be due to endocardial, epicardial or intramural reentry in areas of apical scar. Epicardial ablation or transcoronary alcohol ablation is required in some cases.(1)

4. **Apical myectomy** improves functional status by decreasing left ventricular end-diastolic pressure, improving operative compliance, and increasing stroke volume. This procedure might be of value in other patients with HCM who have severe hypertrophy and small LV end-diastolic volume.(1)

5. **Heart transplantation:** ApHCM is a morphologic variant in which the hypertrophy is primarily localized to the apex of the LV. A subset of patients have progressive, drug-refractory diastolic heart failure with severely limiting symptoms caused by low cardiac output. Heart transplantation has been the only therapeutic option available for such patients.

1. Inada K, Seiler J, Roberts-Thomson KC, et al. Substrate characterization and catheter ablation for monomorphic ventricular tachycardia in patients with apical hypertrophic cardiomyopathy. J Cardiovasc Electrophysiol. 2011 Jan;22:41-48.
2. Schaff HV, Brown ML, Dearani JA, et al. Apical myectomy: a new surgical technique for management of severely symptomatic patients with apical hypertrophic cardiomyopathy. J Thorac Cardiovasc Surg. 2010 Mar;139:634-640.

ICD indications in HCM if one or more of the acknowledged SCD risk factors were present:

1. Family history of premature HCM-related death particularly if sudden, in a close relative, or multiple in occurrence
2. Unexplained syncope, particularly in young patients , or if demonstrated to be arrhythmia-based
3. Frequent, multiple, or prolonged episodes of NSVT documented on serial ambulatory Holter monitoring
4. Hypotensive or attenuated blood pressure response to exercise
5. Extreme left ventricular hypertrophy(≥30mm) particularly in young patients.