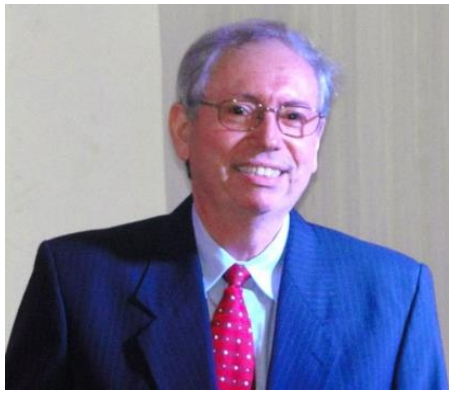
Would it be possible an ECG/VCG like this, in the absence of structural heart disease? unexplainable giant T-wave inversion



https://ekgvcg.wordpress.com/

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2. Chief of the Coronary Center of the Hospital de Messejana Dr. Carlos Alberto Studart Gomes. Fortaleza - Brazil
3. Visiting Scientist at Program in Molecular and Integrative Physiological Sciences (MIPS), Department of Environmental Health | Harvard T.H. Chan School of Public Health.

Portuguese: Reporte de caso

Seria possível um eletrocardiograma como este, na ausência de doença cardíaca estrutural?

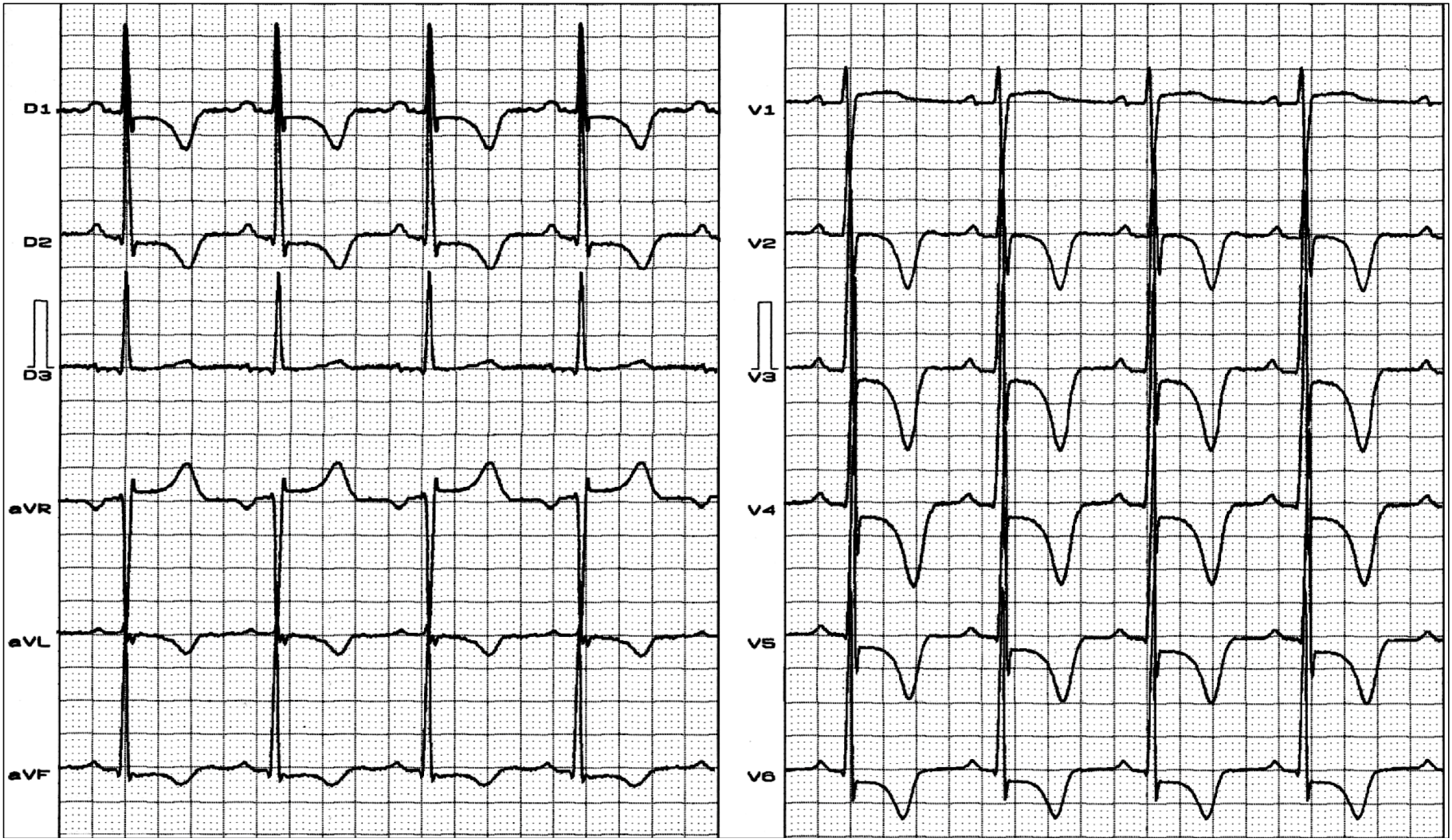
Identificação: Caucasiano, 38 anos, arquiteto, normolíneo.
Motivo da consulta: avaliação clínica para iniciar prática esportiva em academia. Assintomático, nega vícios, ou antecedentes pessoais de importância. Sempre hígido.
Antecedentes familiares: negativos.
Exame físico: nada digno de nota. Altura: 1.80m; Peso 83kg; PA 130/80mmHg; FC 62bpm; pulsos periféricos presentes.
ECG/VCG: próximos slides.
Ecocardiografia transtorácica (ETT):
Câmaras cardíacas de dimensões normais: Diâmetro diastólico do VE = 47 mm (VN 38-52); Diâmetro sistólico do VE = 30mm (VN 26-34); átrio esquerdo = 36mm (VN 28-40).
Espessura miocárdica normal: septo = 9mm, parede posterior do VE = 9 mm
Desempenho ventricular preservado, sem alterações de contractilidade segmentar.
Função diastólica do ventrículo esquerdo preservada (Doppler tecidual).
Fração de ejeção do ventrículo esquerdo = 0,66 % (VN 0,55-080).
Valvas cardíacas com textura e mobilidade normais.
Fluxos transvalvares ao estudo com Doppler e mapeamento de fluxo em cores: normais.
Aorta torácica sem alterações anatômicas. Diâmetro da aorta = 34 mm (VN 28-40).
Pericárdio normal.
Conclusão: Exame dentro dos parâmetros da normalidade.

Solicitamos ressonância magnética do coração com realce tardio para avaliação de fibrose / infarto e viabilidade miocárdica.

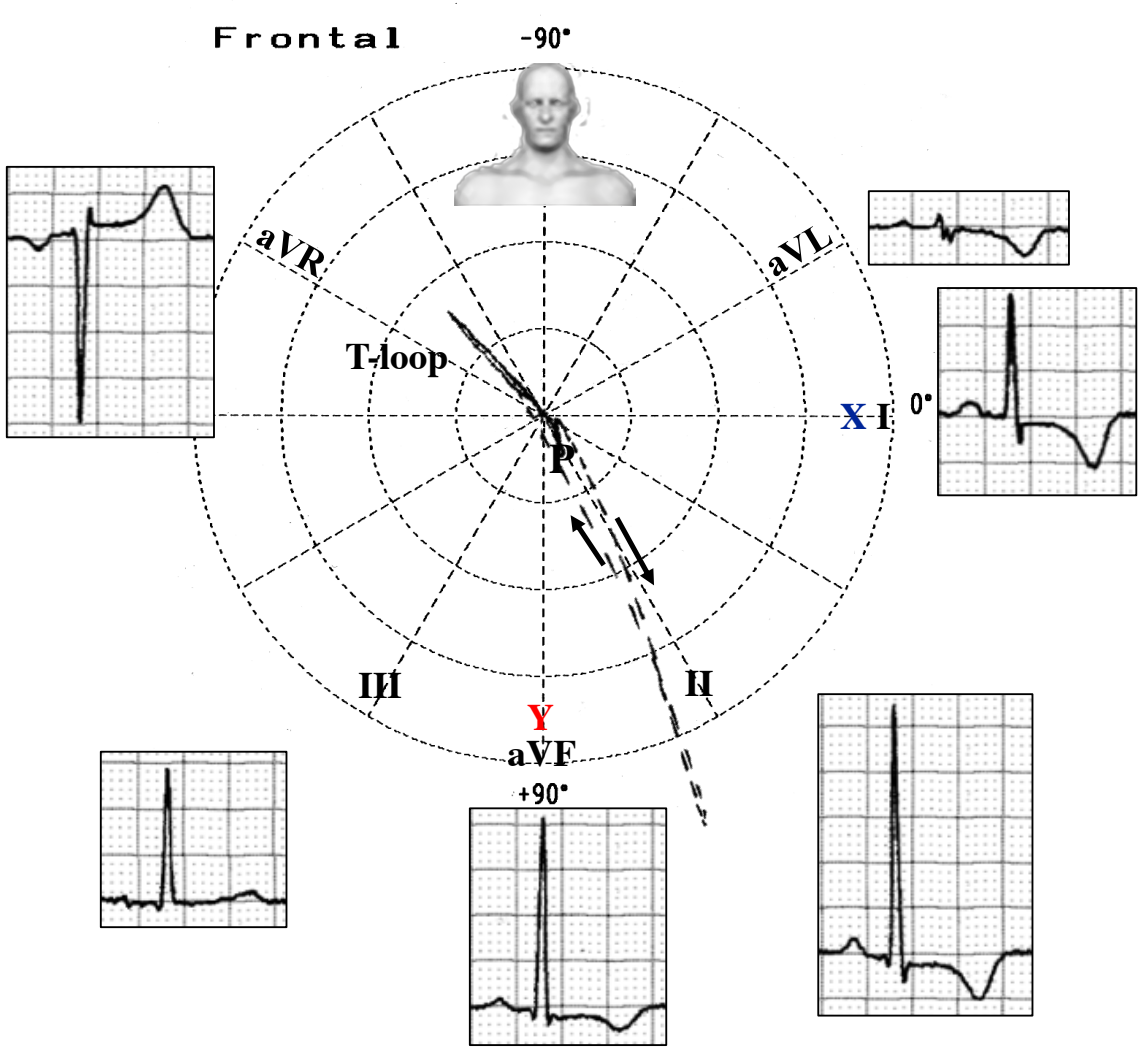
English: Case Report

Would it be possible an ECG/VCG like this, in the absence of structural heart disease?

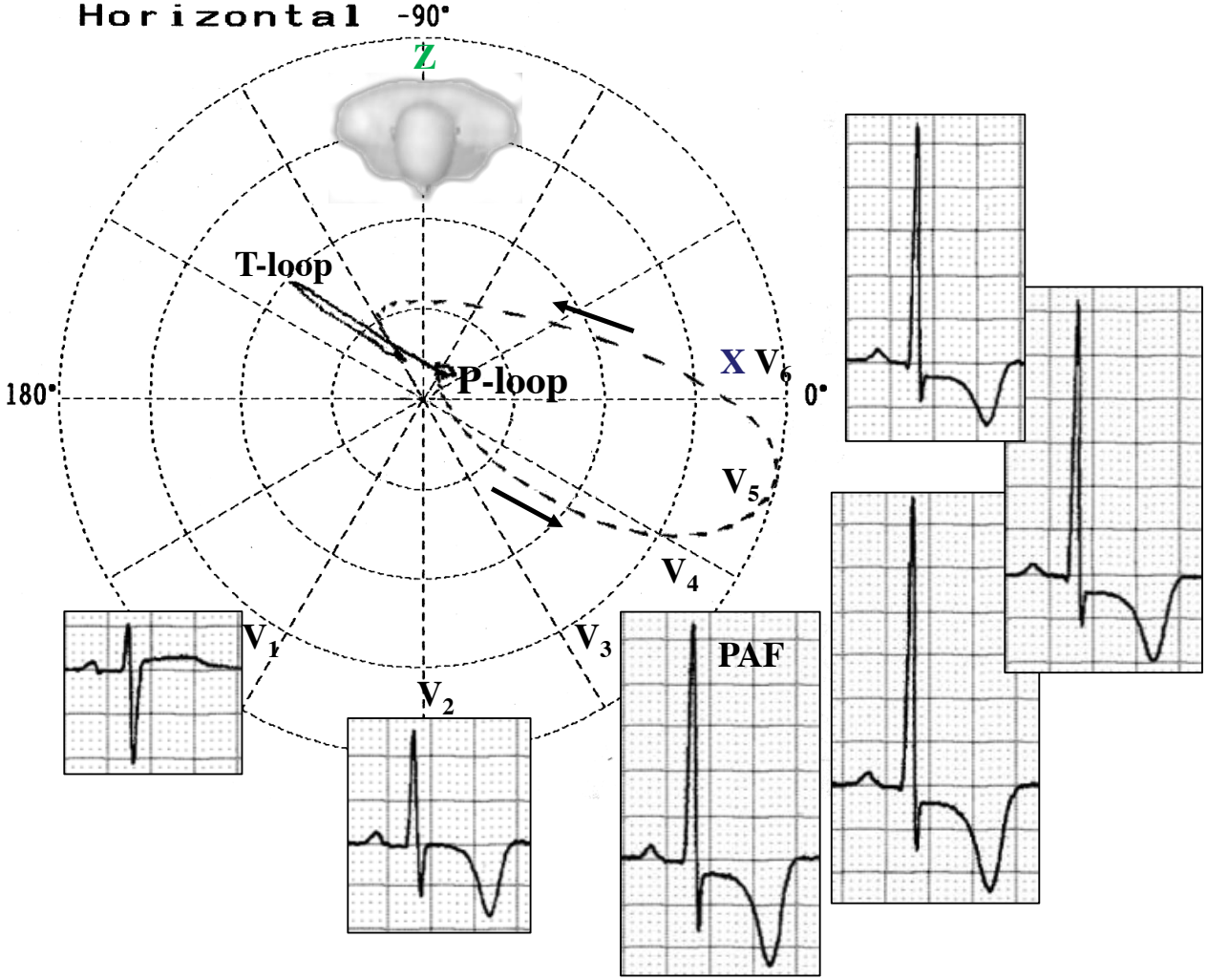
Identification: Caucasian, 38 years old, architect, normoline.
Reason for consultation: clinical evaluation to start practicing sports in the gym. Asymptomatic, denies addictions or personal history of importance. Always healthy.
Negative family background for hereditary diseases.
Physical examination: nothing worthy of note. Height 1.80m; Weight 83kg.; BP 130/80mmHg, HR 62bpm, peripheral pulses present and regular.
ECG/VCG
Transthoracic echocardiography:
Normal dimensions of cardiac chambers: LV diastolic diameter= 47 mm (NV 38-52); LV systolic diameter 30mm (NV 26-34); left atrium= 36mm (NV 28-40).
Diastolic thickness of septum and LV posterior wall 9 mm each (normal myocardial thickness)
Preserved ventricular performance without segment contractility alterations
Preserved LV diastolic function (Tissue Doppler)
Normal Left Ventricular Ejection Fraction = 0.66% (NVs from 0.55 to 080)
Heart valves with normal texture and mobility
Normal Doppler color flow mapping
Normal thoracic aorta diameter =34 mm (NV 28-40)
Normal pericardium
Conclusion
Examination within normal parameters.
We request cardiovascular magnetic resonance (CMR) with late gadolinium enhancement for evaluation of fibrosis / infarction and myocardial viability.


D1
D2
D3
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6

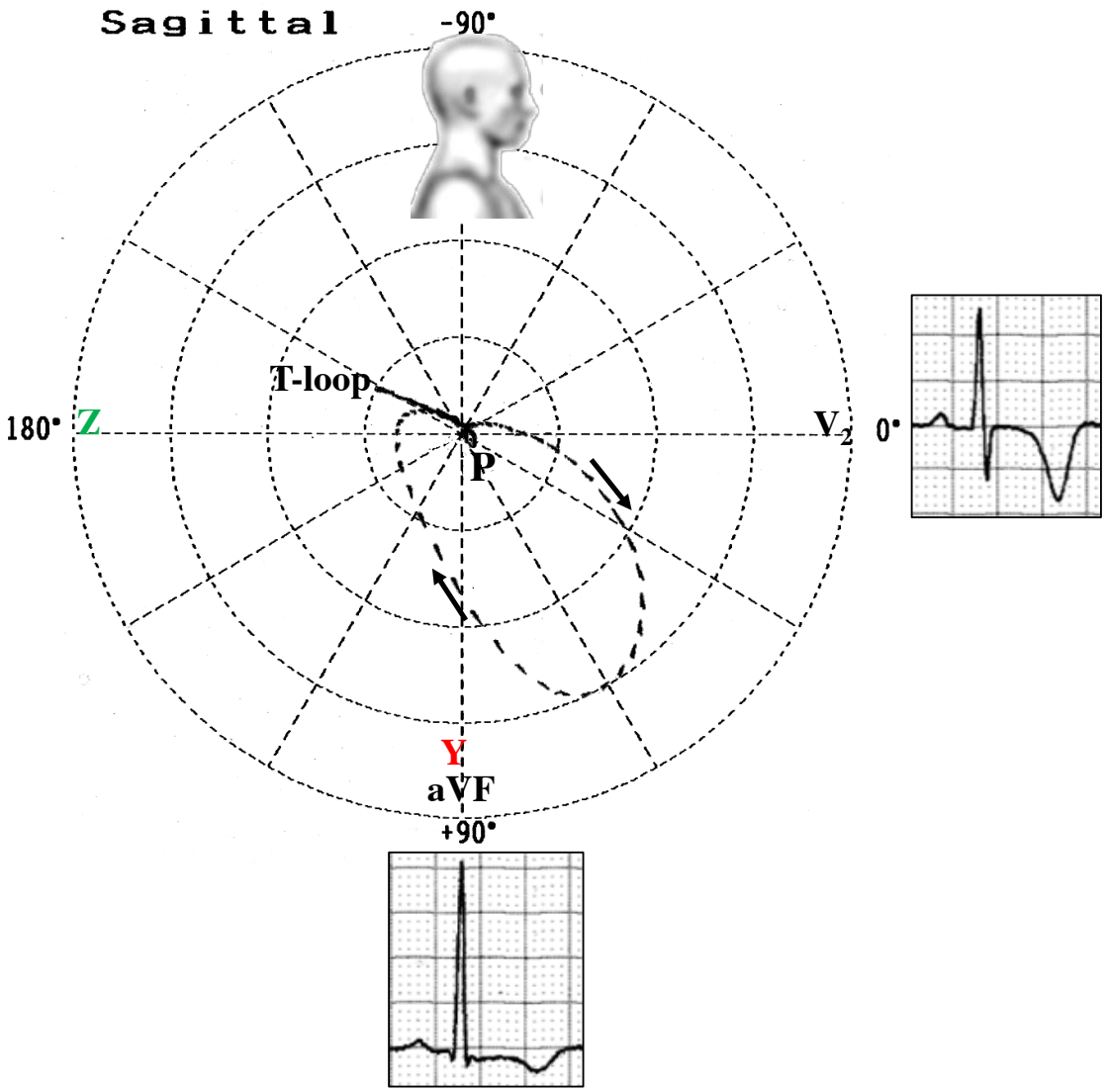
ECG/VCG correlation in the Frontal Plane



ECG/VCG correlation in the Horizontal Plane



ECG/VCG correlation in the Right Sagittal Plane



Colleagues opinions

Dear Andrés

Although there is no clear heart disease by Echo and physical exam. , there is clear electrical LV changes compatible with ST segment depression in anterolateral and high lateral regions. Sokolow-Lyon close to 50 mm; intrinsecoid deflexion in V5 around 0.06 second; QRST angle = 140 degrees (planar); T peak-Tend interval 100 ms. Can't rule out hypertrophyc cardiomyopathy of some degree (although echo is normal). In my opinion there is clear LV electrical remodeling. Need some other investigation, like NMR searching for delayed enhancement. Cannot release for sports participation until finish the investigation.

Dalmo Antônio **Ribeiro-Moreira M.D.Ph.D**. São Paulo Brazil

Chief Medical Electrophysiology and Cardiac Arrhythmia Dante Pazzanese Institute of Cardiology Sao Paulo Brazil

This is probably apical hypertrophic cardiomyopathy, which can be difficult to diagnose with echocardiography. MRI should show the changes.
Kind regards

Kjell Nikus, MD, PhD
Tampere, Finland

Spanish
Hola amigos Mi opinión
La clínica no dice nada relevante y a pesar de que el ecocardiograma no decir nada a nivel apical de VI (a veces no se tiene una buena ventana apical o no ser realiza una sub-xifoidea), el ECG muestra ondas T profundas negativas en las derivaciones precordiales de mas de 10 mm lo que sugieren fuertemente una miocardiopatía hipertrófica apical o forma japonesa de Yamaguchi.
La ventriculografía mostraría la típica imagen de "as de pique" y coronarias normales; pero como la clínica y examen físico no orientan hacia enfermedad coronaria, por consecuencia el paso inmediato seria una RNM con realce tardío con gadolinio que podría demostrar la hipertrofia del segmento apical.
Se descarto miocarditis chagásica con serología? vNo pienso en cardiopatía isquémica
Saludos cordiales
Dr. Juan José Sirena Santiago del Estero Argentina
English
Hello friends My opinion
The clinic says nothing relevant and although the echocardiogram did not say anything to apical level VI (sometimes you do not have a good apical window or not makes a sub-xiphoid), the ECG shows deep negative T waves in precordial leads (more than 10 mm) which strongly suggest apical hypertrophic cardiomyopathy or Japanese form of Yamaguchi.
Ventriculography will show the typical image of "ace of spades" and normal coronary arteries; but as clinical and physical examination not oriented towards coronary artery disease, consequently immediate step would be an MRI with late gadolinium enhancement that could prove apical hypertrophy segment.
myocarditis Chagas serology was discarded?. I do not think of Coronary heart disease
Best regards
Juan Jose **Sirena MD Santiago del Estero Argentina**

Spanish

Le haría un buen Eco con un buen equipo. Si es normal, lo dudo (a veces no se aprecia bien la verdadera punta) le solicitó una Resonancia magnética.
Me cuesta creer que el eco sea normal.
Saludos a todos, y gracias por este fabuloso espacio
Miguel Amor MD

English
I would do an echocardiogram with good equipment. If results normal - which I doubt- (sometimes it is not easy to analyze the tip of the heart by transthoracic echocardiography)
Is hard to believe that the echocardiogram is normal. In this case, I would request a Cardiac Magnetic Resonance
Greetings to all and thanks for this fabulous space
Miguel Amor MD

Estimado profesor:
Este paciente con un ECG que muestra ondas T negativas y con un ecocardiograma dentro de la normalidad, puede que mas adelante desarrolle una miocardiopatia hipertrofica como se ha demostrado en estudios anteriores.
Saludo afectuosamente

Dear Professor:
This patient with an ECG showing T waves negatives and with an echocardiogram within normal limits, may later develop hypertrophic cardiomyopathy as demonstrated in previous studies

Your truly
Eduardo Quiñones MD

Spanish

Hola querido Andrés: El ECG no es normal para un paciente caucasiano deportista.
Presenta un BAV de 1er grado con signos de HVI (R peak time en V2 y V3 anormales y criterios ECG de HVI (índice de Sokolov positivo).
El infra desnivel del segmento ST es máximo de V3 a V6 hasta de 1,5 mm no es habitual en caucásicos y se registra además en DI, DII y aVF, además de las derivaciones precordiales de V2 a V6.
La onda T negativa gigante en precordiales de V2 a V6 máxima de V3 a V6 simétricas que simulan una T de origen isquémico. En las derivaciones de los miembros también presenta onda T negativa pero asimétrica sugestiva de HVI.
En aVR presenta supra desnivel del segmento ST que expresa el incremento de las presiones interventriculares.
El intervalo QTc se encuentra prolongado, lo que no es habitual en la HVI fisiológica del deportista.
En la ecocardiografía el diámetro diastólico VI no es el habitual de un deportista con estos cambios ECG (47 mm). No refieren alteraciones del llenado diastólico VI ni crecimiento auricular izquierdo.
Descartado los trastornos hidroelectrolíticos como la hipocalcemia severa (no me impresiona) y la hipertensión endocraneana de la cual no puedo sospechar ya que no presenta sintomatología.
El diagnóstico es el de una miocardiopatía hipertrófica por los cambios electrocardiográficos. Dado que los espesores parietales no concuerdan con la misma, sería interesante además de la RNM cardiaca con realce tardío con gadolinio.
La realización de un ecuestres con ejercicio y descartar una forma de miocardiopatía hipertrófica obstructiva dinámica, en la cual no obtendrá gradientes intraventriculares en reposo pero si en el esfuerzo, y que traerán HVI concéntrica a predominio apical y lateral como evidencia el trazado del paciente.
Un cordial saludo
Martín Ibarrola

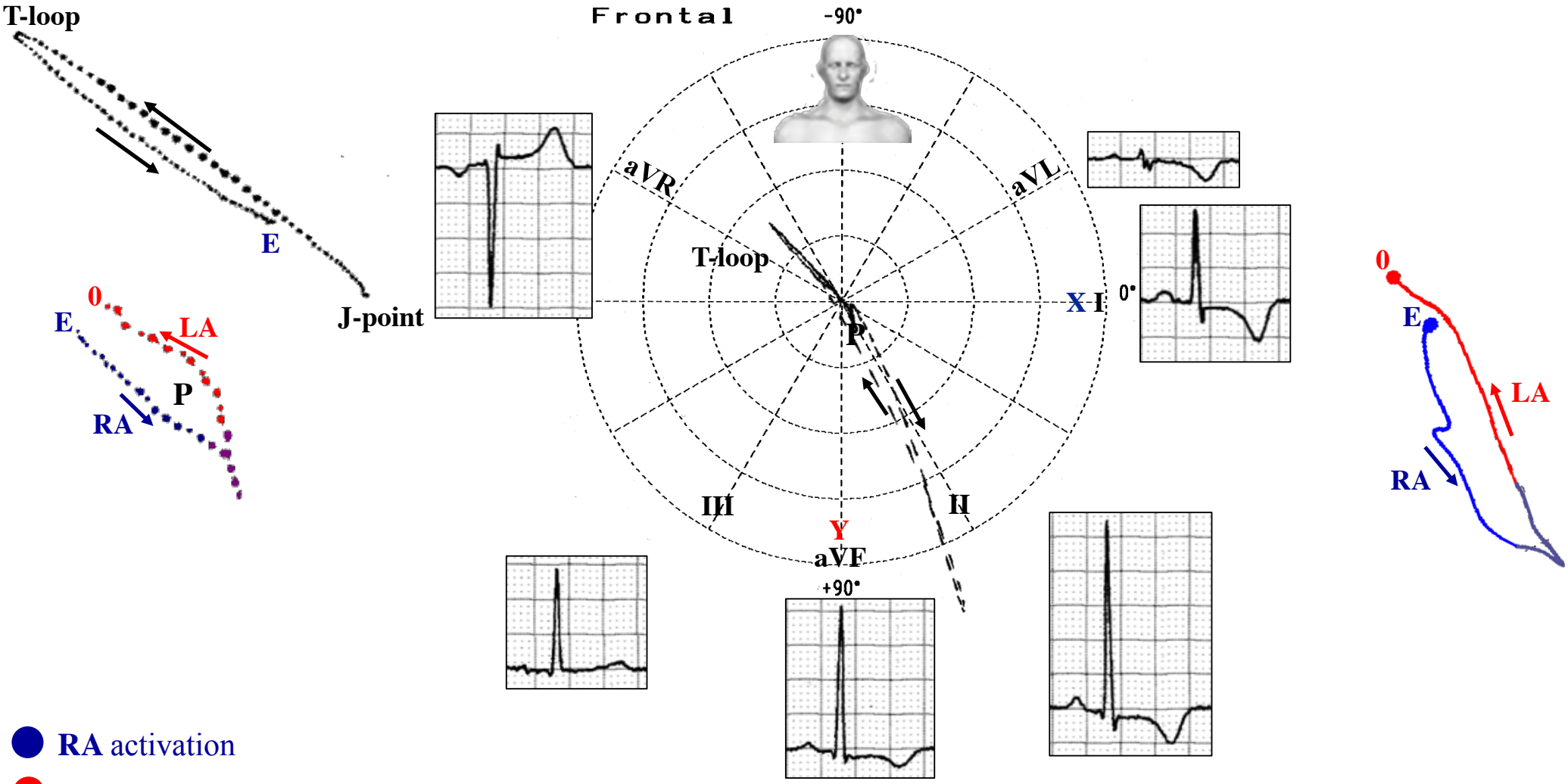
English: Hello dear Andrés: The ECG is not normal for a Caucasian athlete.
It has a 1st degree AV block with signs of LVH (prolonged R peak time in V2 and V3 and abnormal Sokolov-Lyon voltage criteria of LVH.
The ST segment depression of 1.5 mm from V3 to V6 is not common in Caucasians and is also recorded in I, II and aVF, plus precordial leads from V2 to V6.
Giant negative T wave in precordial leads V2 to V6 (deeper in V3-V4 that simulate symmetric ischemic T wave.
In the limb leads have negative asymmetric T wave suggestive of LVH.
In aVR ST-segment elevation that expresses the increase in ventricular pressures.
The QTc interval is prolonged, which is not usual in the physiological athlete LVH.
Echocardiography LV diastolic diameter is not the usual sportsman with these ECG changes (47 mm).
No alterations refer LV diastolic filling or left atrial enlargement.
Discarded electrolyte disturbances such as severe hypocalcemia (not impress me) and intracranial hypertension which I can not suspect as it has no symptoms.
The diagnosis is a hypertrophic cardiomyopathy by the electrocardiographic changes. Since the parietal thicknesses do not agree with it, it would be interesting addition to the cardiac MRI with late gadolinium enhancement.
Conducting a stress test could unmask latent dynamic obstructive cardiomyopathy, which will not get intraventricular gradients at rest but in the effort, and that will bring concentric LVH and lateral apical dominance as evidence tracing the patient.
A cordial greeting
Martín Ibarrola
MD

The ECG suggests apical hypertrophic cardiomyopathy that is often missed by echo, unless contrast is used . Cardiac MRI is a good choice.

Yochai Birnbaum
Professor
Medicine-Cardiology
Baylor College of Medicine
Houston, TX, US

Final comments

ECG/VCG correlation in the Frontal Plane



- **RA** activation
- **LA** activation
- Biatrial activation

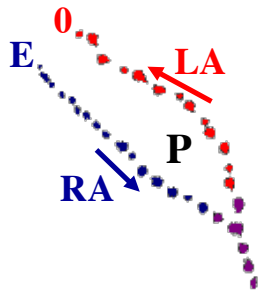
Normal P -oop. Normal QRS-loop axis + 65°, T-loop axis on right superior quadrant close -135°.

The normal P loop in the Frontal Plane

RA activation in FP

LA activation

Biatrial activation



E point: it constitutes the zero point of VCG and it remains stationary before the onset of the P loop. It corresponds to the isoelectric line between the T wave and the P wave of ECG. The **E** letter corresponds to the cardiac dipole.

0 point: it corresponds to the end of "biatrial" chamber activation, QRS loop onset (because PR segment does not exist, it is only a point) and the end of ventricular repolarization (T loop).

J point: in vectorcardiography, it corresponds to 3 elements: end of ventricular depolarization (QRS complex); beginning of repolarization (ST segment) when it does not present depression or elevation, and T wave onset. In situations where there is depression or elevation of ST segment, the J point does not coincide with the **0** point, and the greater or lesser distance between both points indicate the greater or lesser ST segment elevation or depression. The phenomenon is observed in early repolarization, acute phase of infarction, variant angina, pericarditis, Brugada syndrome, arrhythmogenic right ventricular dysplasia, channelopaties etc.

P loop: loop of small voltage corresponding to the depolarization of the biatrial chamber. The initial part corresponds to the right atrium **RA** (between 0 and 70 ms), next the interatrial septum (between 20 and 45 ms), and finally the left atrium **LA** (between 30 and 90 ms). To make an analysis possible, it is necessary to amplify: 1 mV = 30 cm.

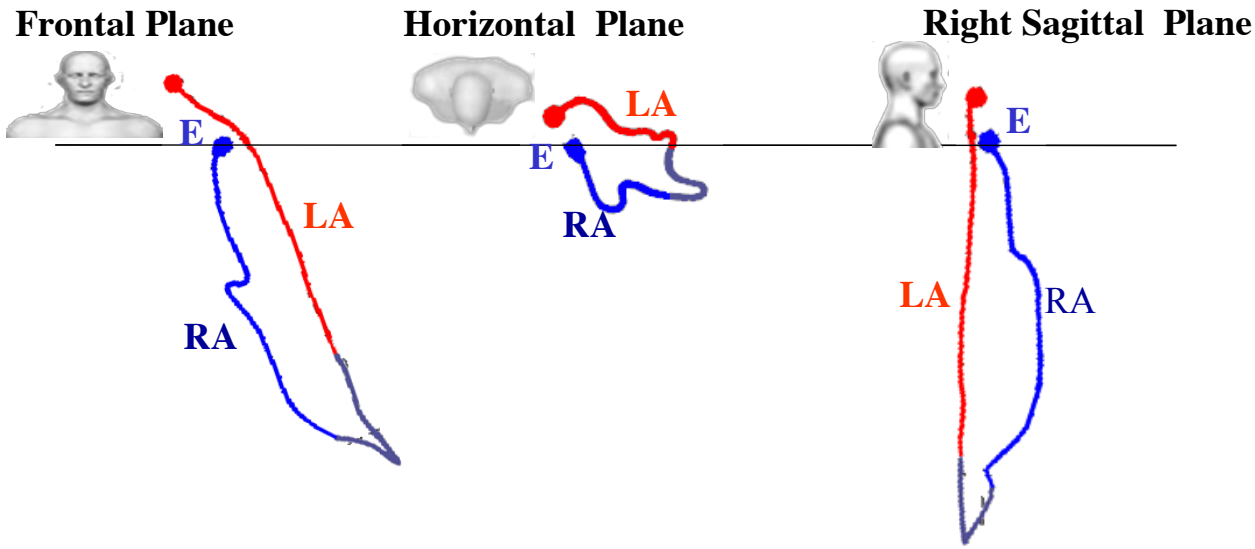
The P loop begins in the **E** point and ends in the so-called **0** point. The former has an anterior and inferior location in relation to the latter. The P loop is open because atrial repolarization (Tp loop) is diametrically opposite to the P loop.

Items to be studied in the P-loop

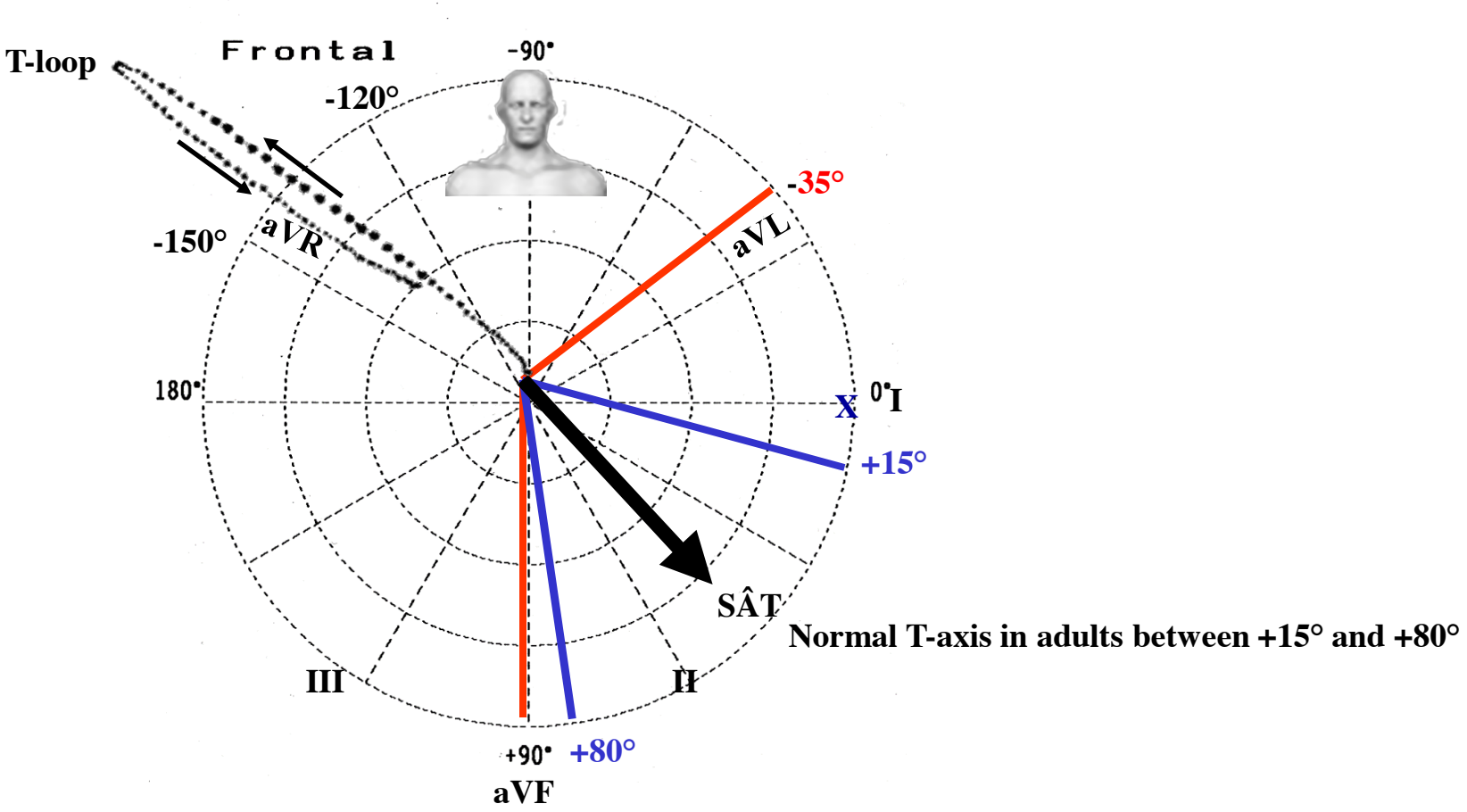
Magnitude and direction of maximal vector: P vector;
Location of the greatest part of the P loop;
Morphology;
Aspect: presence of notches;
P-loop rotation: FP: counterclockwise; in the HP: counterclockwise or in eight; and RSP: clockwise.
Location of the **E** (initial) and **0** points (final).

The P loop has a short slow conduction in the onset, in at least 2 planes.

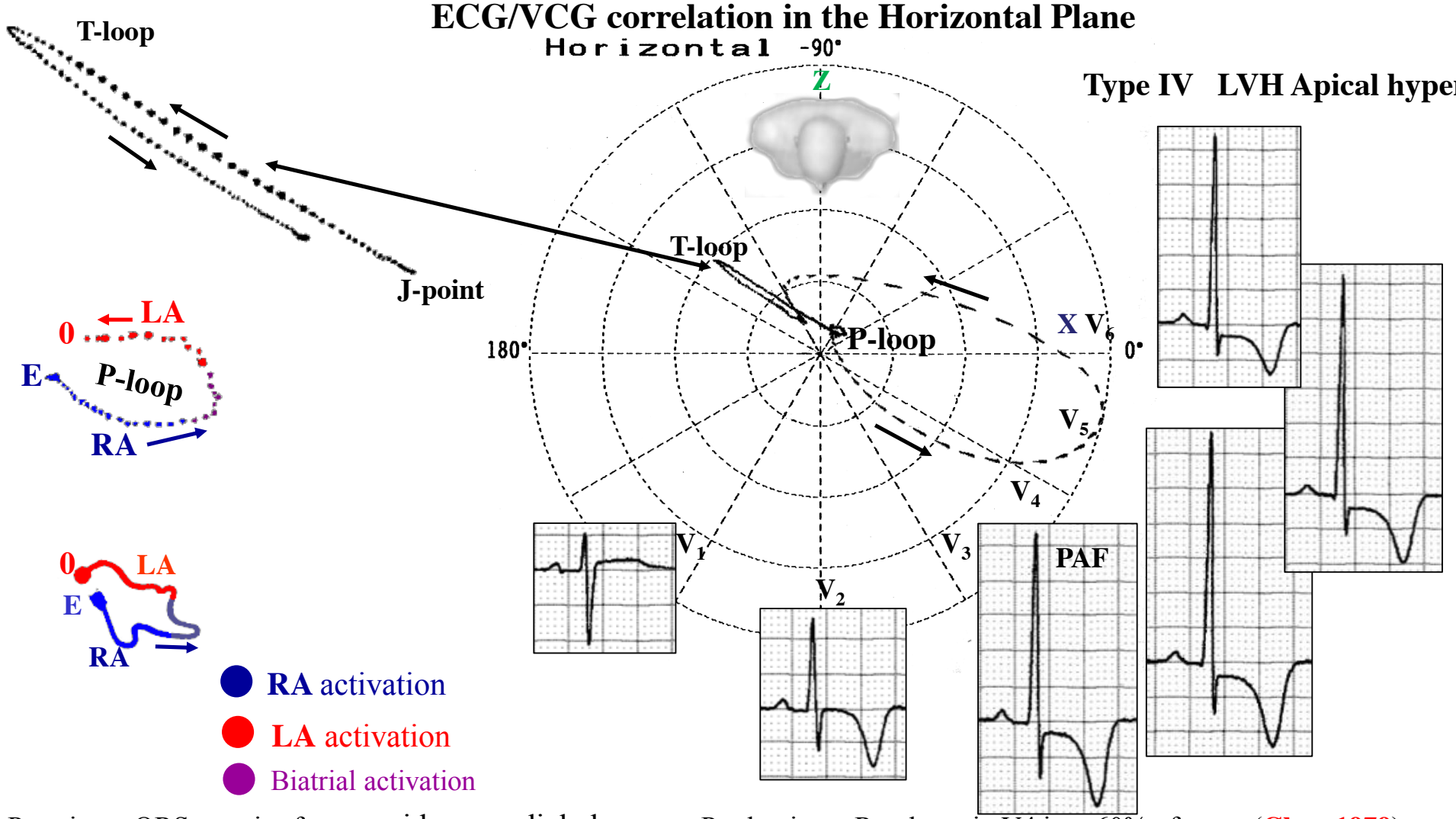
Two small notches are usually observed: one in the efferent limb and another in the afferent limb.



Location of the normal T-loop/normal T-wave axis in Frontal Plane in the normal adults



In the normal adult > 95% of cases T-loop/T-wave axis is located between **+15°** to **+80°** in the frontal plane. Tolerance of extreme values ranges between **-35°** to +**90°.** In the present case T axis is located on top right quadrant between -120° to -150°.

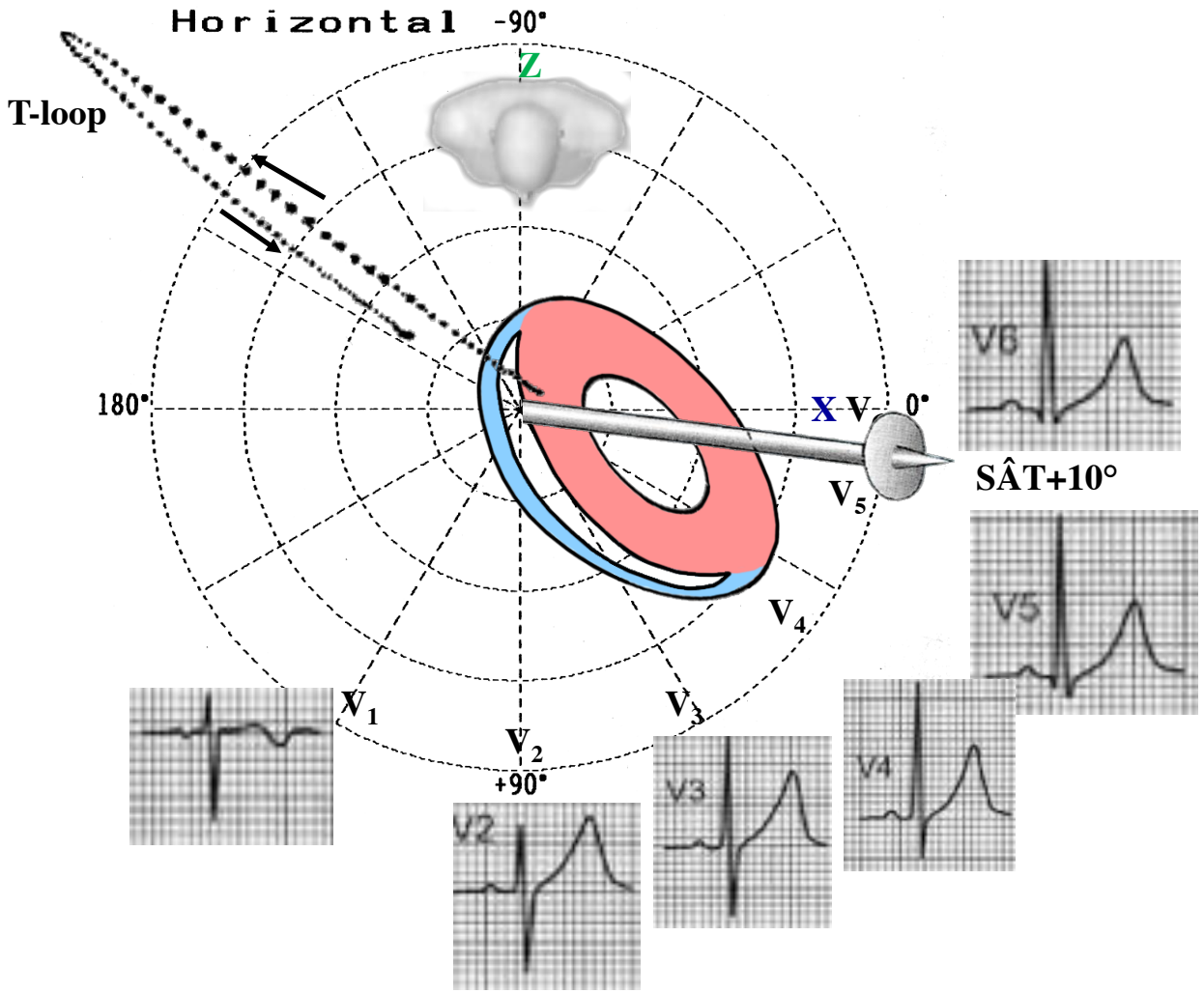


PAF: Prominent QRS anterior forces: mid-precordial changes. Predominant R voltage in V4 in ≈ 60% of cases (**Chen 1979**)

Initial vectors of QRS-loop heading to the front and the left, QRS-loop, predominantly located in the left anterior quadrant, increase voltage of Maximal QRS-vector, final QRS-vectors located to the right and backward quadrant and ST/T vector located in the right posterior quadrant.

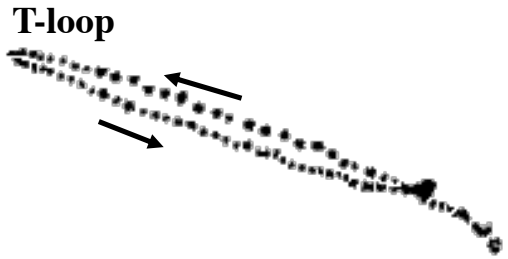
Positive Sokolow and Lyon index: S of V_1 + R of $V_5 \geq 35$ mm or 3.5 mV in adults older than 30 years old.

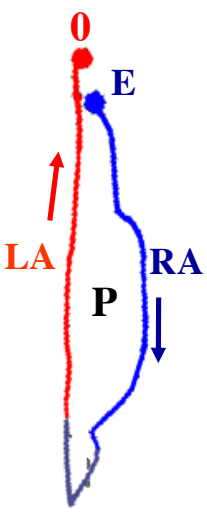
Location of the normal T-loop/normal T-wave axis in Frontal Plane in the normal adults

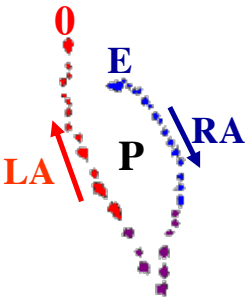


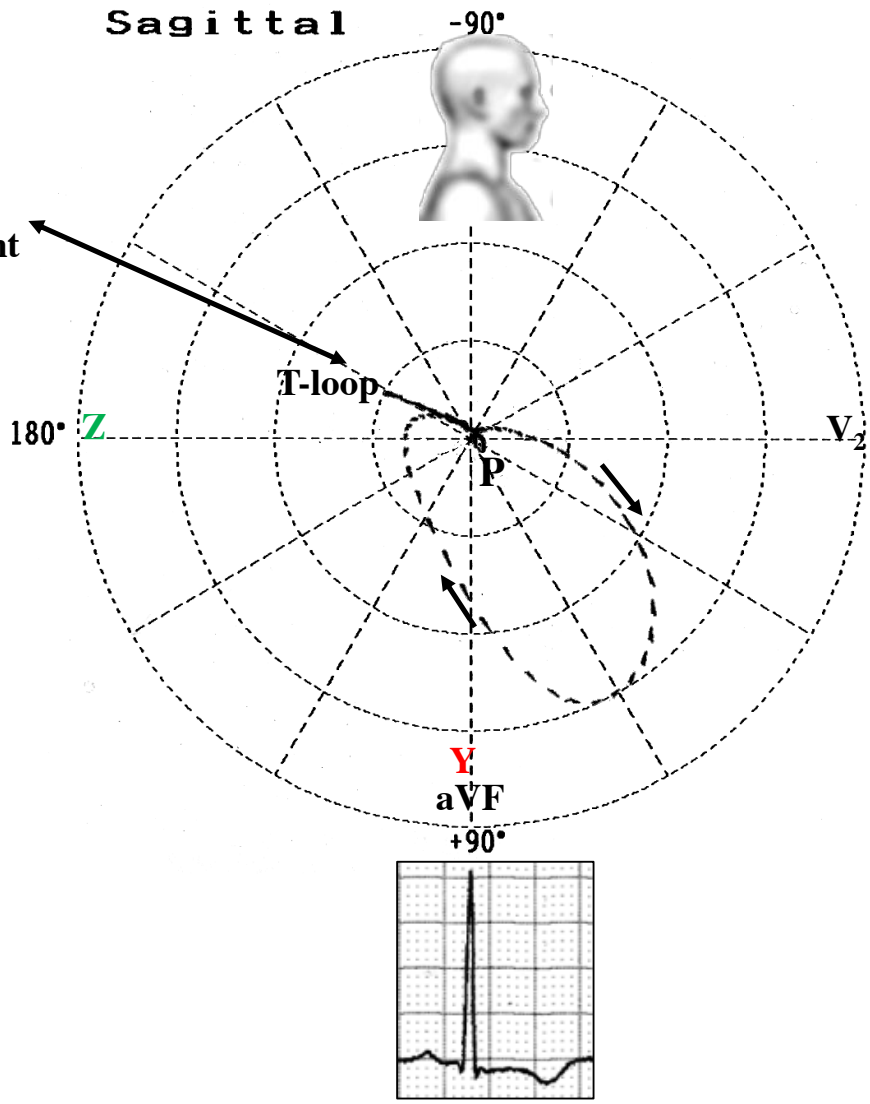
T-waves polarity is always positive from V_3 to V_6; generally positive in V_2 and frequently negative in V_1. In normal adults, invariably the ventricular repolarization vector (T vector SÂT) in the horizontal plane is heading to the left and usually discretely to the front near the +10° very close to V6. In the present case T-loop is located on right back quadrant.

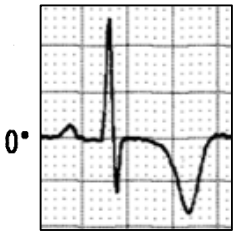
ECG/VCG correlation in the Right Sagittal Plane







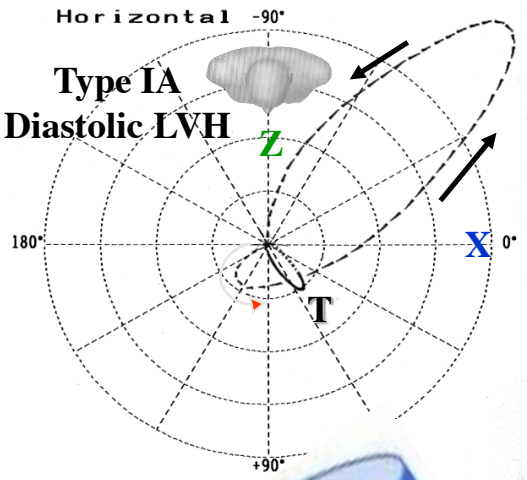


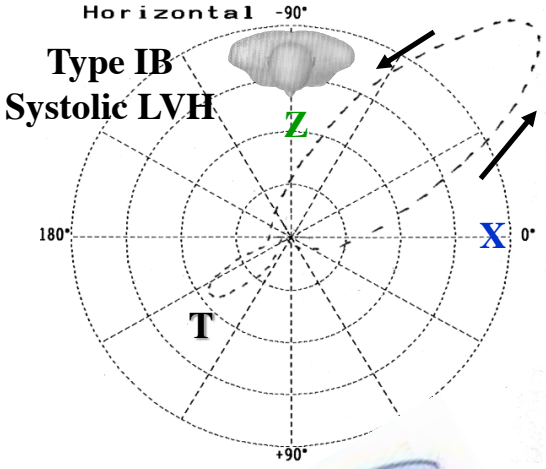


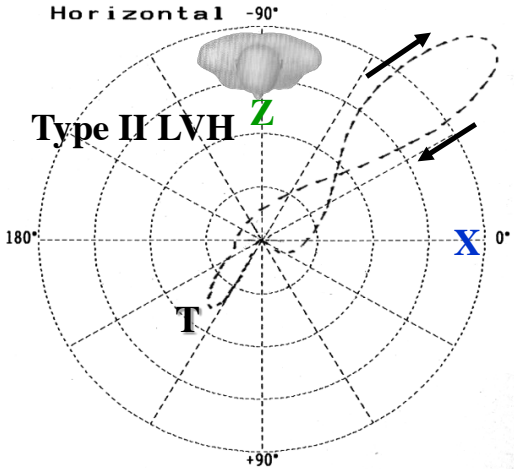
PAF: Prominent QRS anterior forces

- **RA** activation
- **LA** activation
- Biatrial activation

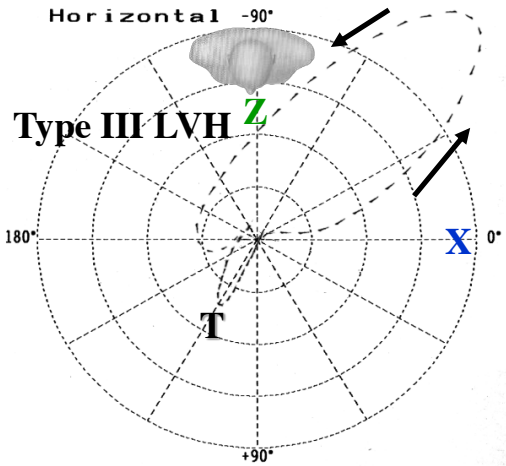
The five VCG types of LVH in the Horizontal Plane: IA, IB, II, III and IV

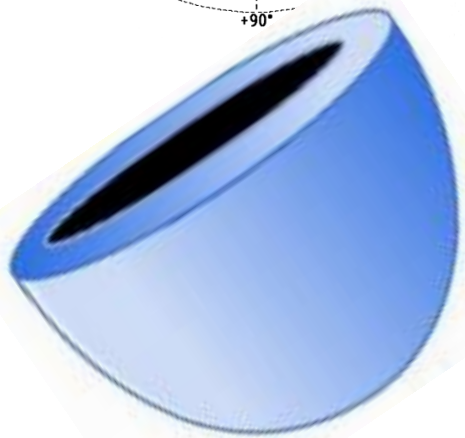




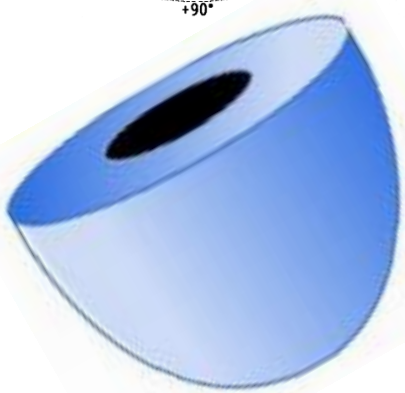


Pseudo LBBB



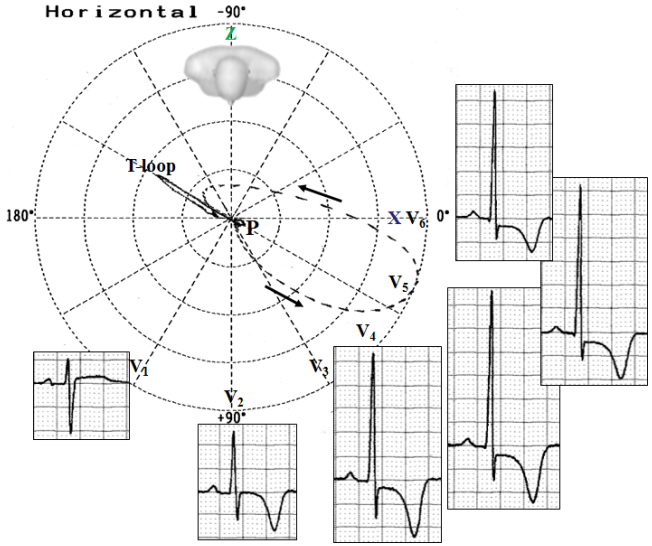


Eccentric LVH
Type IA
Diastolic LVH



Concentric LVH
Type IB
Systolic LVH
Strain pattern of repolarization

This is the pattern of the present case



Type IV LVH (Apical hypertrophy)

Vectocardiogram of apical non-obstructive hypertrophic cardiomyopathy

In the apical form we find type IV vectorcardiographic LVH loop 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(anteriorization);
- Increase voltage of Maximal QRS-vector;
- Final vectors located to the right and backward, with ST/T vector in the right posterior quadrant. This is the only case of LVE without coronary insufficiency 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, and located backward and to the right from the latter (**Pérez-Riera 2013**).
- T-loop is characteristically discordant related QRS-loop, elongated, assimetric and situated in the right posterior quadrant (**Abinader 1982**).

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 1991**).

Stress test may decrease the depth of T waves (**Tilmant 1980**).

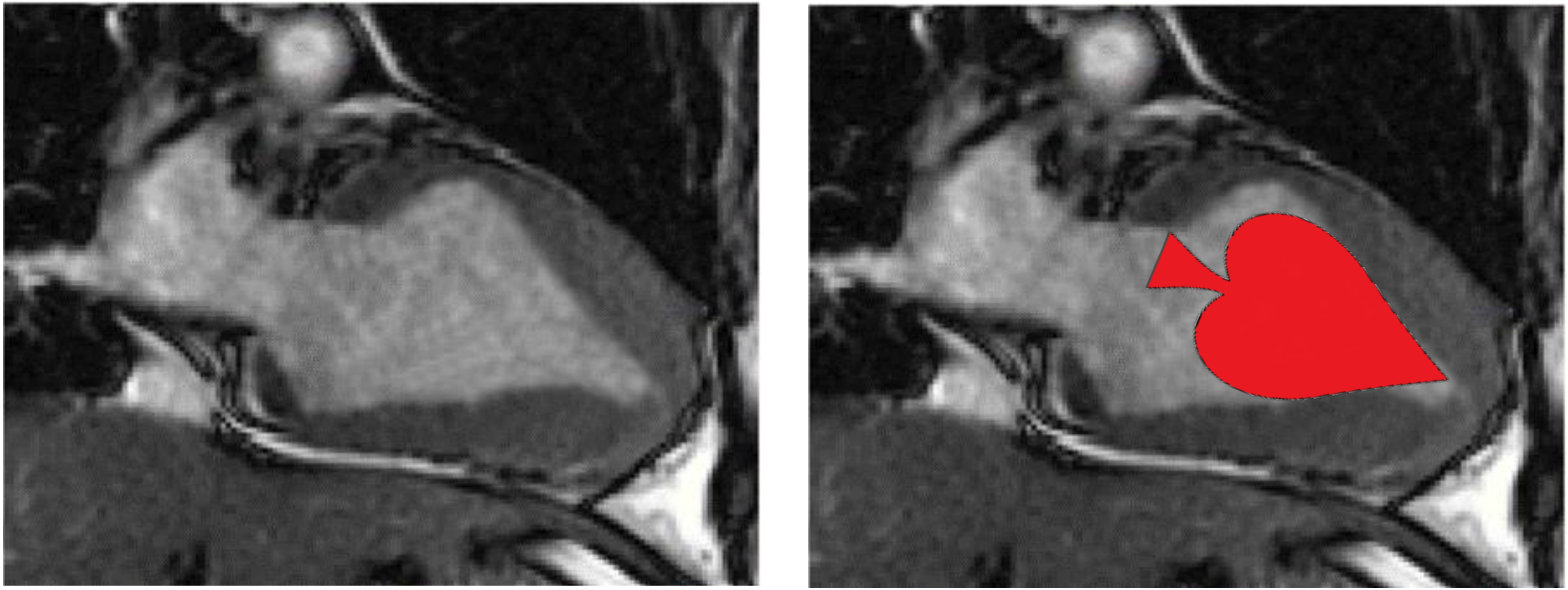
Cardiovascular magnetic resonance (CMR). Cardiac–magnetic resonance cine image for the global assessment and target heart.
Late gadolinium enhancement for evaluation of fibrosis / infarction and myocardial viability.

Comments

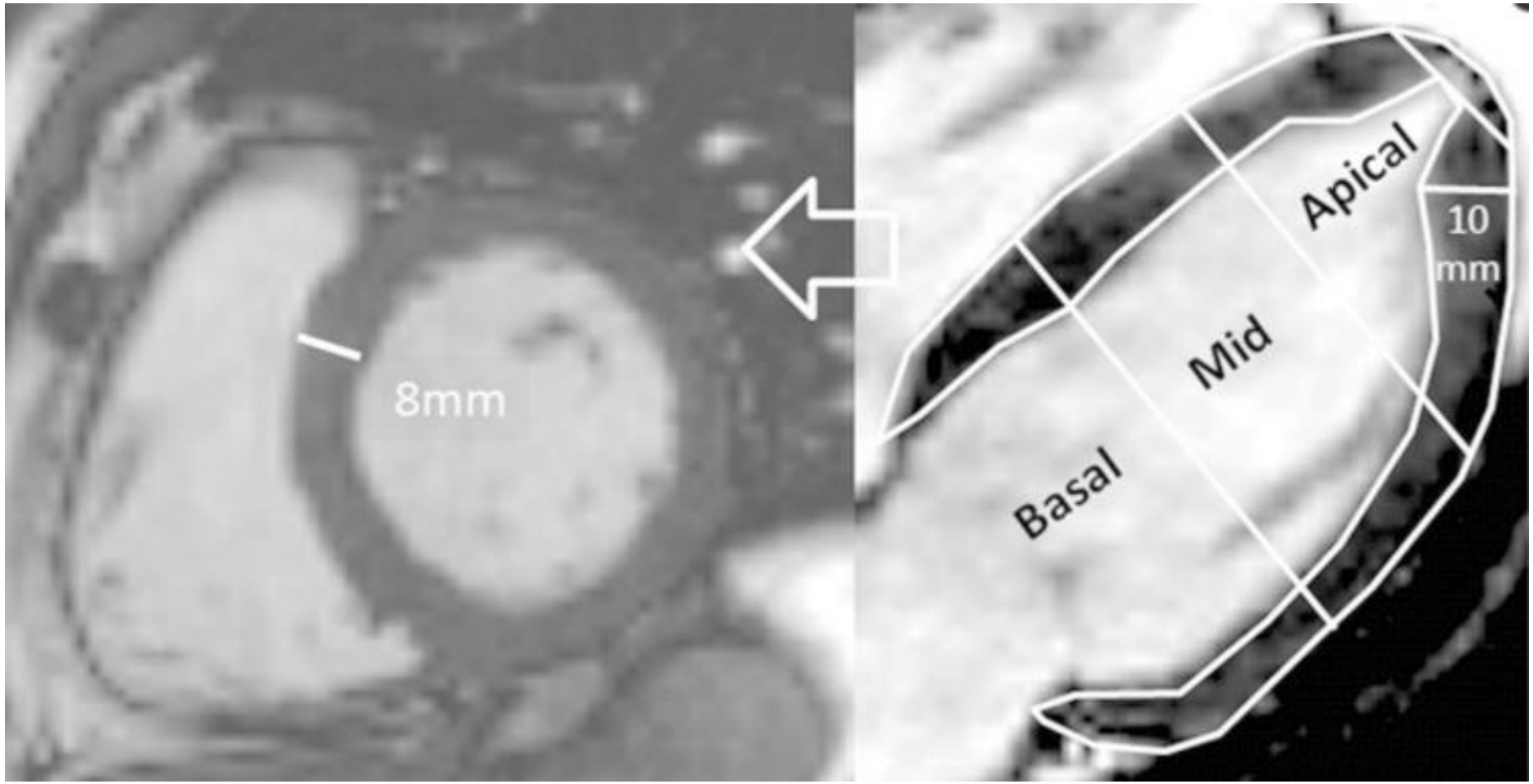
Right atrium of preserved dimensions
Left atrial dimensions preserved
Right ventricle with preserved dimensions
Preserved systolic function of the right ventricle
LVH with apical predominance, with a maximum thickness of **21 mm** (Absolute apical wall thickness > 15 mm is diagnosis of Ap-HCM)
Preserved left ventricular dimensions, global and segmental systolic function preserved left ventricle = 72%.
absence of obstruction of in the left ventricular outflow tract.
Absence. thrombi

Diagnostic impression

Normal biventricular systolic function
Left ventricular hypertrophy of apical predominance.
Absence of obstruction in the left ventricular outflow tract
Ap-HCM it may be frequently missed by transthoracic 2-dimensional cardiac echocardiography because of poor image quality of left ventricular apex. The diagnostic accuracy of echocardiography for Ap-HCM is limited without using contrast or 3-dimensional echocardiography, MRI has an important role in diagnosis. The diagnostic criteria for Ap-HCM: Absolute apical wall thickness > 15 mm, or a ratio of apical to basal left ventricular wall thicknesses of 1.3–1.5 (**Chun 2010**).
A characteristic spade-like shape of the left ventricular cavity can be seen at end diastole on vertical long-axis views and on ventriculography. This configuration is caused by localized apical hypertrophy.
Other findings on MRI include apical aneurysms and delayed enhancement in the hypertrophic or non-hypertrophic segments. The vertical long-axis image above shows circumferential increased wall thickness in the apical portion of the left ventricle, measuring up to 16 mm. This results in a spade-like appearance of the left ventricular cavity. Delayed enhancement at the cardiac apex is compatible with myocardial fibrosis.



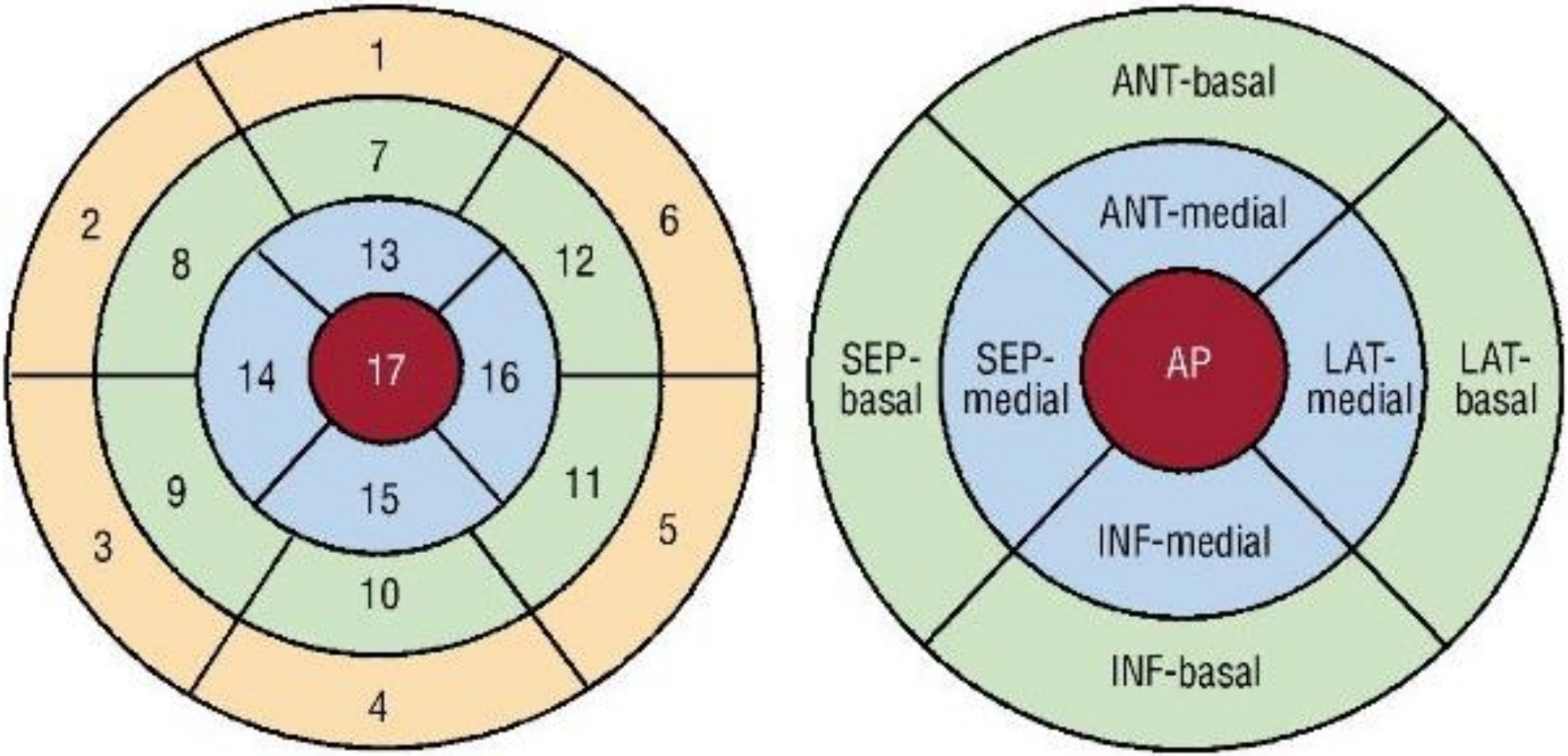
Cardiac–magnetic resonance cine image demonstrating hypertrophy of the apex in an "ace-of-spades" configuration Ap-HCM. Patients with unexplainable giant T-wave inversion in the precordial leads and apical wall thickness <15 mm cannot be diagnosed as apical hypertrophic cardiomyopathy (Ap-CM) according to the current criteria. When the absolute thickness of apical is was below the current diagnostic criteria of Ap-CM, the apical morphological features of subjects with unexplainable giant T-wave inversion are significantly different from normal. Whether these subjects should be included into a preclinical scope of Ap-HCM needs further investigations (**Wu 2016**). A total of 60 subjects with unexplainable giant T-wave inversion and 76 healthy volunteers were prospectively enrolled. The segmented LV wall thickness was measured according to the AHA 17-segmented model. The apical angle (apA) as well as the regional variations in LV wall thickness was analyzed. Considerable variation in LV wall.



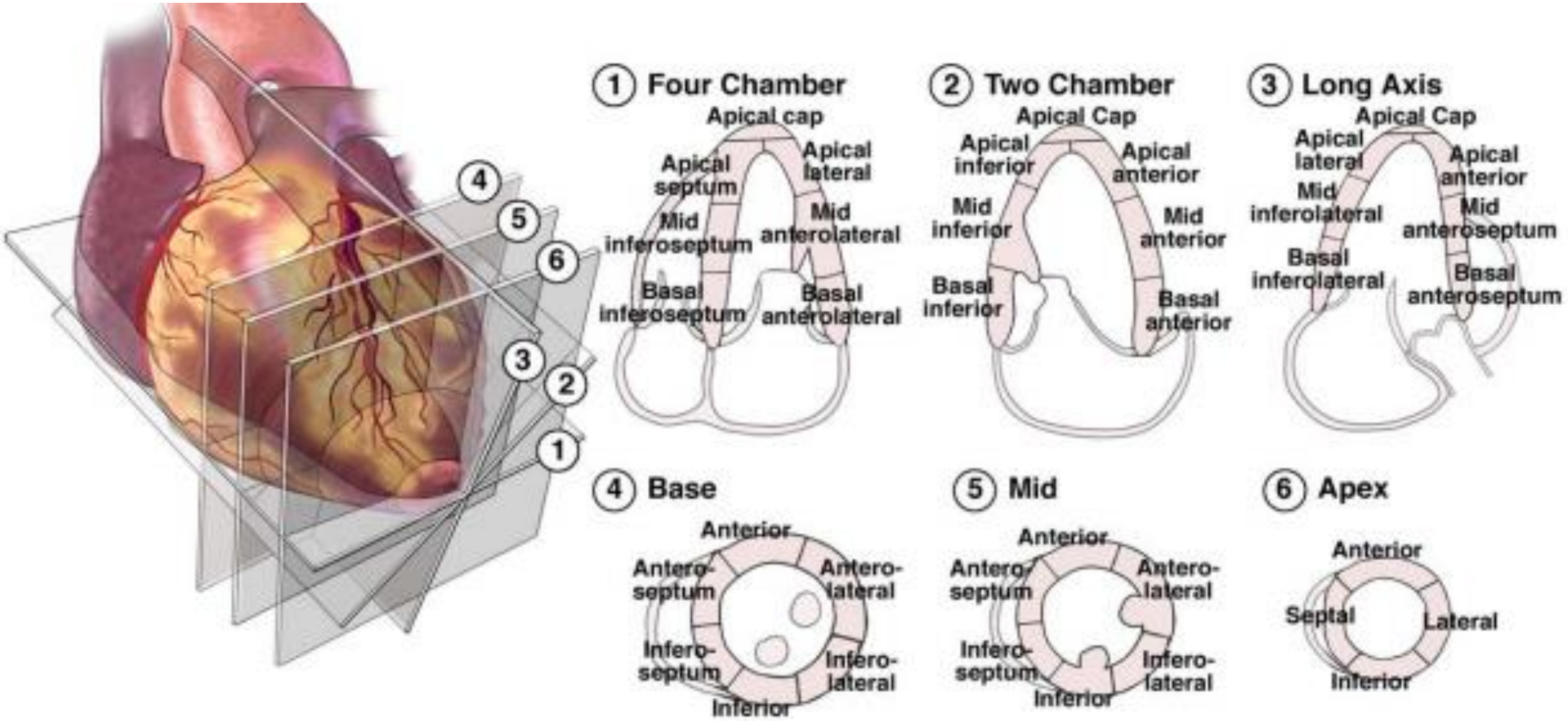
Measuring apical wall thickness

Left: short axis slice near the base of the heart with max wall thickness of 8 mm. Middle: four chamber view. The left ventricle is divided into thirds: Basal, mid and apical, the apical cap makes up only the most apical 6% of the ventricle. At the base the short axis slice is truly perpendicular to the wall. Towards the distal ventricle — as the cavity tapers, the short axis slice is not perpendicular to the wall — this complicates wall thickness measurement and it should be performed on multiple long axis views, perpendicular to the true septal axis and with careful exclusion of papillary muscle origins and trabeculation.

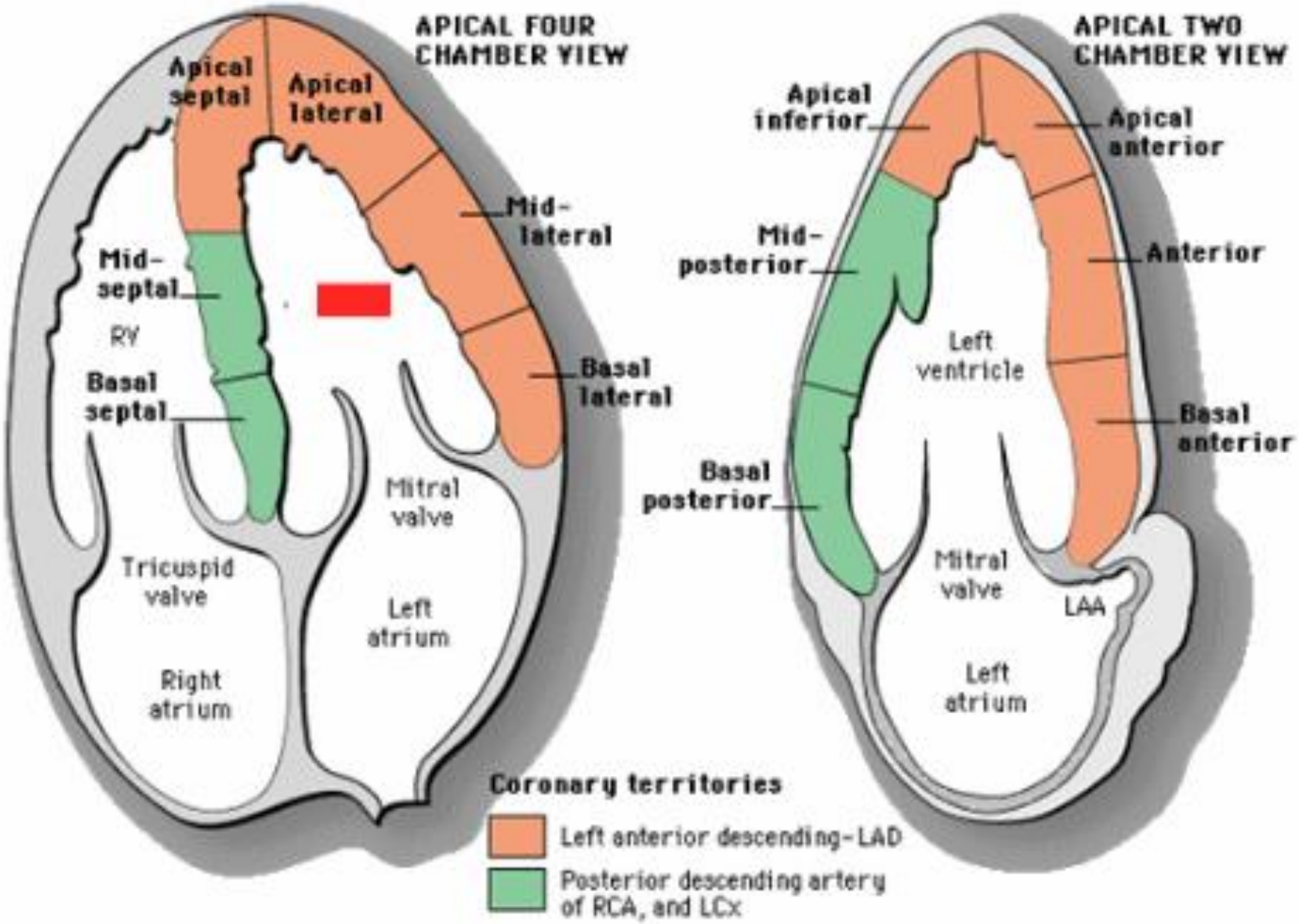
A 17 segment cardiac model, including the apical cap, suggested by the American Heart Association Writing Group on Myocardial Segmentation and Registration for Cardiac Imaging (**Cerqueira 2002**).



Afected segment in Ap-HCM number 17/AP apical cap



Segmental analysis of LV walls based on schematic views, in a parasternal short and long axis orientation, at three different levels. The ‘‘apex segments’’ are usually visualized from apical four-chamber, apical two- and three-chamber views. The apical cap can only be appreciated on some contrast studies. A 16 segment model can be used, without the apical cap, as described in an ASE 1989 document.(**Schiller 1989**) A 17 segment model, including the apical cap, has been suggested by the American Heart Association Writing Group on Myocardial Segmentation and Registration for Cardiac Imaging (**Cerqueira 2002**).


APICAL FOUR CHAMBER VIEW
Apical septal
Apical lateral
Mid-lateral
Mid-septal
RV
Basal lateral
Basal septal
Mitral valve
Tricuspid valve
Left atrium
Right atrium
APICAL TWO CHAMBER VIEW
Apical inferior
Apical anterior
Mid-posterior
Anterior
Left ventricle
Basal anterior
Basal posterior
Mitral valve
LAA
Left atrium
Coronary territories
Left anterior descending-LAD
Posterior descending artery of RCA, and LCx

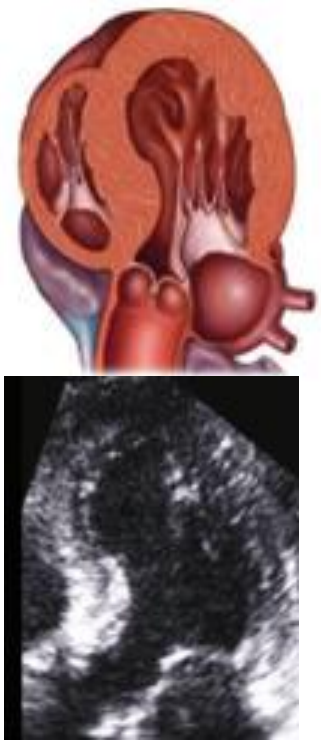
Characteristics of Ap-HCM

Compared with normals, the apex decreased significantly in male and female subjects, respectively. CMR is often superior to echocardiography for HCM diagnosis, by identifying areas of segmental hypertrophy (ie., anterolateral wall or apex) not reliably visualized by echo (or underestimated). 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 LVH. 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. 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 appears to be an important determinant of adverse LV remodeling associated with systolic dysfunction. However, the predictive significance of LGE for sudden death 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. Ap-HCM (**Yamaguchi 1979**) is a phenotypic variant of nonobstructive HCM, in which hypertrophy of the myocardium predominantly involves the left ventricular apex (**Gupta 20016**). It is most common in Japan but also seen in western populations. This apical variant constitutes ≈25% of cases of HCM in Japan but only 1% to 2% of the cases of HCM in the non-Japanese population. Apical thrombus, left-ventricular non-compaction and endomyocardial fibrosis may create a similar echocardiographic appearance, which can be distinguished from Ap-HCM using cardiac–magnetic resonance imaging (**Noureldin 2012; Moon 2004**). Patients are typically male and present in middle age with symptoms of palpitations, chest pain or dyspnea. Although autosomal-dominant inheritance has been reported in a few families, the condition is usually sporadic (**Arad 2005**). The ECG typically shows giant precordial T-wave inversions. SCD from ventricular arrhythmia has been described, and prophylactic ICD is occasionally performed. However, the prognosis is generally more benign than other types of HCM (**Eriksson 2005**).

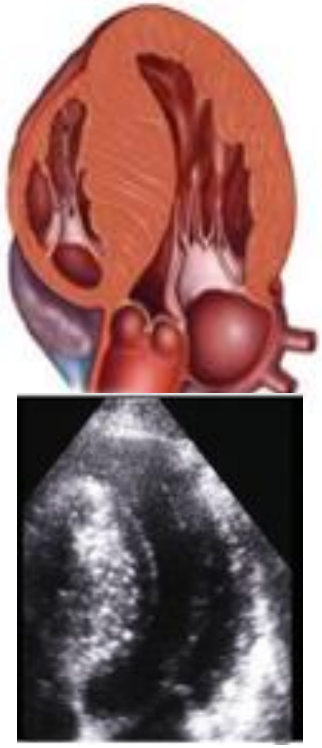
Genotype-Phenotype Correlations in Apical Hypertrophic Cardiomyopathy

HCM is underscored by profound phenotypic and genotypic heterogeneity. Little is known about the spectrum and prevalence of mutations and genotype-phenotype correlations in Ap-HCM. Between 1999 and 2007, Researches from the Mayo Clinic, Rochester, Minn, USA (**Towe 2015**) studied 1053 patients with the diagnosis of HCM underwent sarcomeric genetic testing. Blinded to the genetic test results, each echocardiogram was scored for septal morphology and phenotyping was performed using the patient's medical record. Echocardiographically, HCM where categorized into four morphological subtypes: reverse curve, sigmoidal, neutral contour, and Ap-HCM. The reverse curve HCM is the strongest predictor of a positive genetic test.

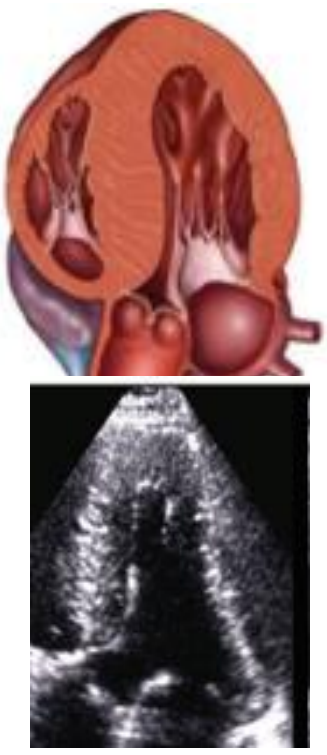
Deformation patterns in genotyped patients. echocardiographic depiction of ventricular septal morphologies in HCM



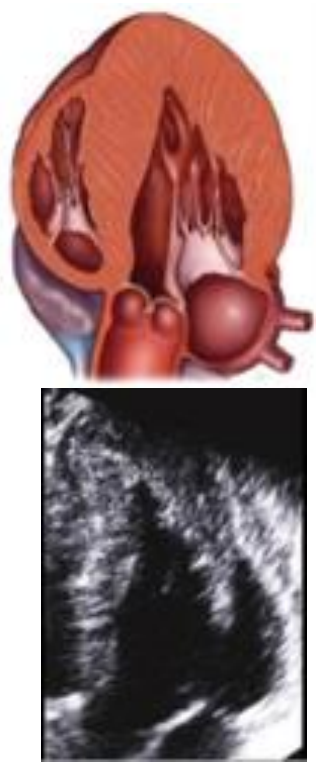
Sigmoidal



Reverse curve



Neutral



Apical

Subset analysis was performed to elucidate the genotype, phenotype, and outcome of Ap-HCM. Overall, 71 patients (7%) had Ap-HCM by echocardiography (63% male, mean age 47.8 ± 15 years, mean left ventricular wall thickness 19.8 ± 6 mm). Left ventricular outflow tract obstruction was uncommon (seven patients; 10%).18 patients (25%) had a positive genetic test, with the majority of mutations found in MYBPC3 (six; 35%) and MYH7 (six; 35%). Follow-up was available on 68 patients (96%) with a median age of 57.3 years (range 19.3-82 years). Mean follow-up was 5.5 years (range 0.1-18.2 years). There was no statistical difference between the occurrence rates of adverse events between genotype-positive and genotype-negative groups.

In this largest cohort of patients with genetic testing for HCM, 7% exhibited Ap-HCM. This subtype is associated with a negative genetic test in 75% of the cases.

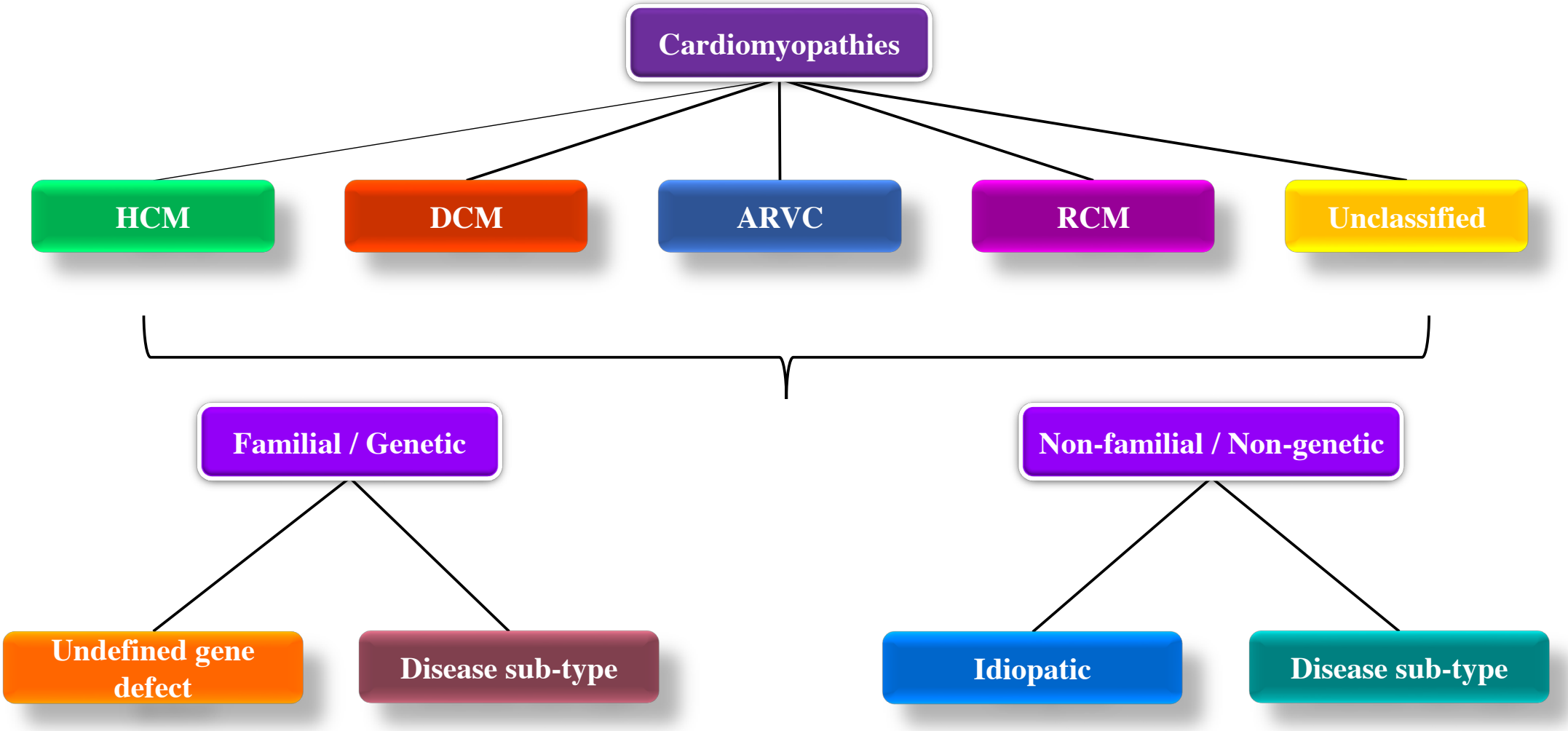
In patients with Ap-HCM the two more common mutations were (MYBPC3-HCM and MYH7-HCM) remained most common among patients who had a positive genetic test.

Mutations in HCM (in red color mutations of Ap-HCM)

Gene	Gene name
ACTC	α-Cardiac Actin
ACTN2	α-Actinin2
ANKRD1	Cardiac Ankyrin Repeat, Domain 1
CAV3	Caveolin 3
COX15	COX 15 homolog. Cytochrome C oxidase assembly protein
CRYAB	Crystallin αB
CSRP3	Cysteine and Glycine-rich Protein 3
GLA	α-Galactosidase
LAMP-2	Lysomal-Associated Membrane Protein 2
MYBPC3	Myosin Binding Protein C (Ap-HCM)
MYH6	β-Myosin Heavy Chain 6
MYH7	β-Myosin Heavy Chain 7 (Ap-HCM)
MYL2	Myosin Regulatory Light Chain 2, slow
MYL3	Myosin Light Chain 3, slow
MYLK2	Myosin Light Chain kinase 2

Gene	Gene name
MYO6	Unconventional Myosin VI
MYOZ2	Myozenin 2
NEXN	Nexilin (F actin binding protein)
PLN	Phospholamban
PRKAG2	AMP = activated Protein kinase, y2, non-catalytic subunit
TNNC1	Cardiac Troponin C, type 1
TAZ	Tafazzin
TCAP	Titin-cap (Telethonin)
TNNI3	Cardiac Troponin I, type 3
TNNT2	Cardiac Troponin T, type 2
TPM1	α-Tropomyosin 1
TTN	Titin
TTR	Transthyretin
VCL	Vinculin

Summary of proposed classification system. ARVC, arrhythmogenic right ventricular cardiomyopathy; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; RCM, restrictive cardiomyopathy



There are various forms of cardiomyopathy, each with different underlying causes for the insufficient circulation.

1. **Dilated cardiomyopathy (DCM):** one or both of the ventricles (in most cases only the left one) become enlarged with a thin, weakened muscle wall unable to generate enough pumping force during contractions;
2. **Arrhythmogenic right ventricular cardiomyopathy (ARVC):** the replacement of the degenerating myocardium with scar (fibrofatty) tissue results in disturbed electrical signals and conduction in the heart (arrhythmia);
3. **Hypertrophic cardiomyopathy (HCM):** a thickened myocardium due to abnormal growth and arrangement (hypertrophy and disarray) of muscle fibers results in smaller chamber volume and sometimes blocks the blood flow (obstruction);
4. **Restrictive cardiomyopathy (RCM):** due to their stiffness, the ventricles do not get refilled with enough blood during relaxation, hence the heart cannot supply the organs with sufficient circulation during contraction;
5. **Left-ventricular non-compaction cardiomyopathy (LVNC**): the wall of the left ventricle is spongiform, characterized by a meshwork of muscle fibers;
6. **Peripartum cardiomyopathy (PPCM):** a special form of dilated cardiomyopathy that becomes manifest towards the end of pregnancy or within a few months following delivery;
7. **Paediatric cardiomyopathy:** this type of cardiomyopathy becomes manifest in infancy or early childhood, and is usually characterized by more severe symptoms and worse outcomes than when the disease manifests in adulthood (from a structural-functional point of view, most frequently it is DCM>HCM>RCM>ARVC).

The MOGE(S) classification for a phenotype-genotype nomenclature of cardiomyopathy: endorsed by the World Heart Federation (Arbustini 2013)

The recently proposed MOGE(S) for classification of cardiomyopathies was proposed, but its clinical use has not been described. Nosology system embodies all of these characteristics, and describes the

1. Morphofunctional phenotype (M),
2. **O**rgan(s) involvement (O)
3. **G**enetic inheritance pattern (G)
4. **E**tiological annotation (E) including genetic defect or underlying disease/substrate, and
5. **S**tatus: Functional status (S) of the disease using both the ACC/AHA stage and NYHA functional class.

The proposed nomenclature is supported by a web-assisted application and assists in the description of cardiomyopathy in symptomatic or asymptomatic patients and family members in the context of genetic testing. It is expected that such a nomenclature would help group cardiomyopathies on their etiological basis, describe complex genetics, and create collaborative registries.

This recent propose for classification attempt to harmonize these competing systems named the MOGE(S) system, based on descriptive logical nosology, currently remains unproven as a fully practical solution.

Hypertrophic cardiomyopathy classification

Classification and differences of obstructive and non-obstructive forms of Hypertrophic Cardiomyopathy.

1) Obstructive form (OHCM)

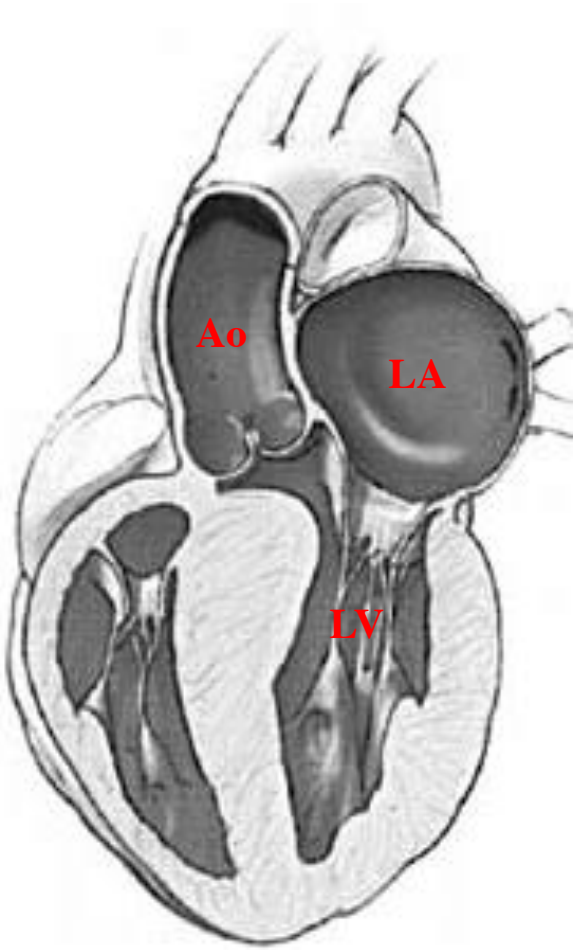
- Septal asymmetrical with resting left ventricular outflow obstruction (obstruction at subaortic level): is found in approximately 20% of the patients, classically occurs at the, and is associated with mitral valve systolic anterior motion (SAM).
- Mid-ventricular obstructive HCM HCM(MVO-HCM) asymmetric LV hypertrophy with MVO and elevated intraventricular pressure gradients (1%).

2) Non-obstructive Form (NO-HCM)

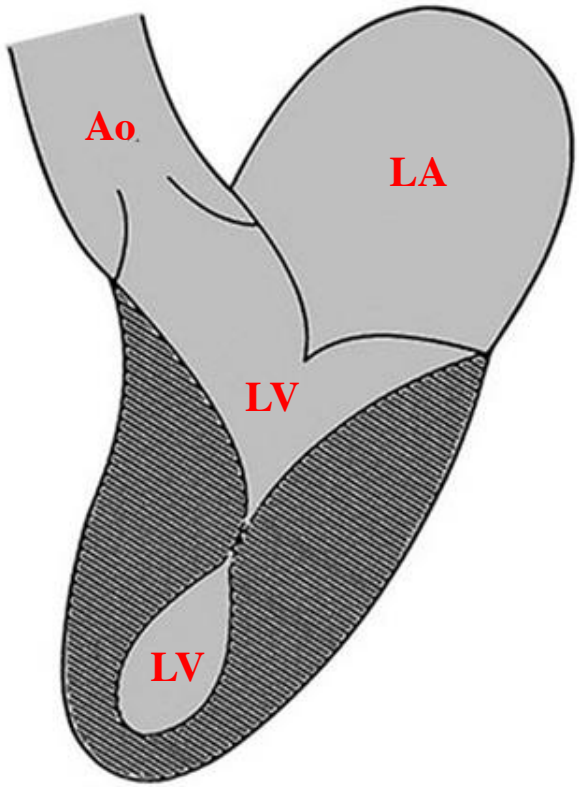
- Septal asymmetric with no obstruction;
- Mid-septal hypertrophic cardiomyopathy
- **Apical Hypertrophic Cardiomyopathy (Ap-HCM): 2%, 3% to 8%.**
- Lateral and/or posterolateral;
- Concentric, symmetrical, or homogeneous hypertrophic: 5%.
- Right ventricle: 2%.

Obstructive form (OHCM)	Non-obstructive form (NOHCM)
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.

I. Obstructive forms of Hypertrophic Cardiomyopathy (OHCM)



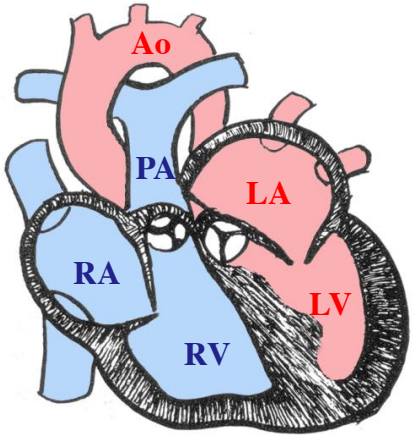
Septal asymmetrical with resting left ventricular outflow obstruction (obstruction at subaortic level): is found in approximately 20% of the patients, classically occurs at the, and is associated with mitral valve systolic anterior motion (SAM).



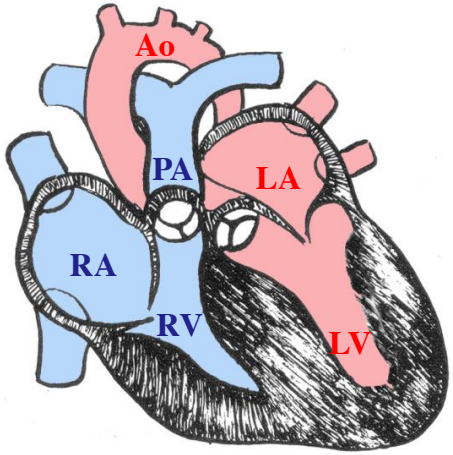
Mid-ventricular obstructive HCM HCM(MVO-HCM) asymmetric LV hypertrophy with MVO and elevated intraventricular pressure gradients.(1%).

II. Non-obstructive forms of Hypertrophic Cardiomyopathy (NO-HCM)

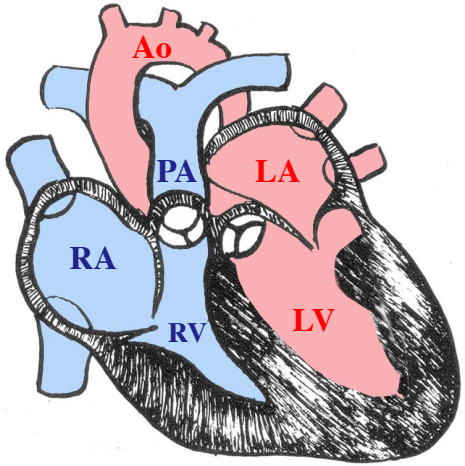
Septal asymmetrical without obstruction



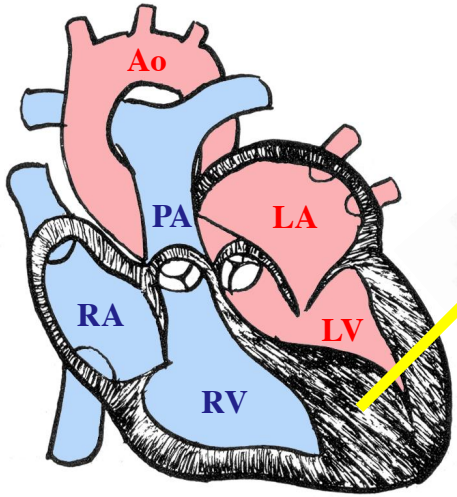
Symmetrical



Lateral and/or posterolateral



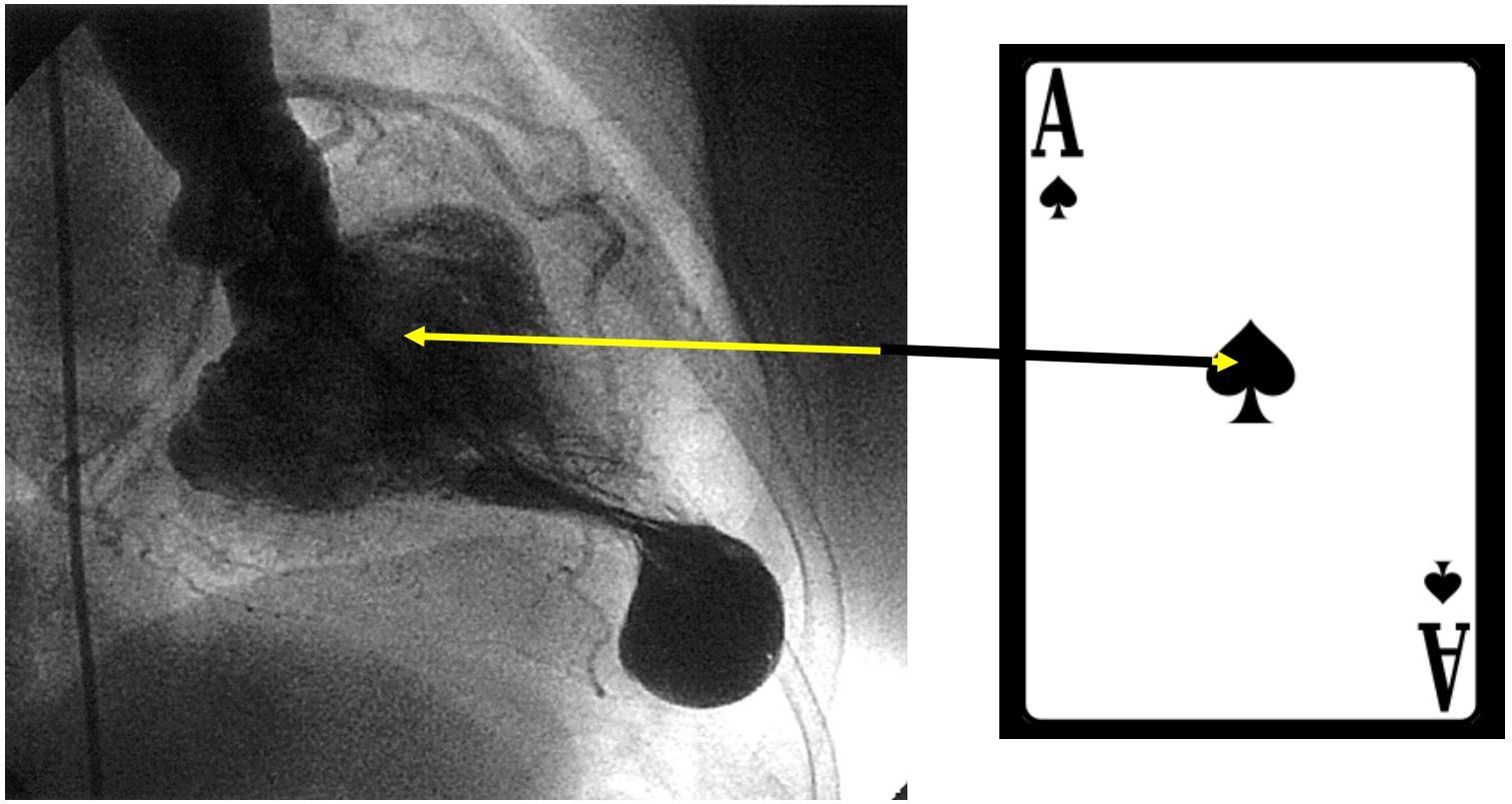
Apical hypertrophic cardiomyopathy



The "ace-of-spades" sign

Left Ventriculography in Ap-HCM

The "ace-of-spades" sign on left ventriculography being pathognomonic (**Olearczyk 2008**)



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;
5. Transition from normal T wave to negative T wave required several years and remained usually unchanged thereafter. This change may occur rather abruptly on rare occasions. Disappearance of giant negative T-waves may also occur slowly and progressively in patients, in whom apical aneurysm had developed (**Sakamoto 2001**).

Observation: The following ECG changes are indicative of apical aneurysm in Ap-HCM patients (Observation: An apical aneurysm is defined as persistence of apical blood pool distal to cavity obliteration in systole).

I. Increase in QRS-complex duration
II. QRS-complex fragmentation
III. Decrease in QRS-complex amplitude
IV. ST-segment elevation(STE) form V4 to V6 (j-point in V5) are statistically more frequent in patients with apical aneurysm compared to those without aneurysm (93% vs 7%, $p<0.001$). There are a positive correlation between the presence of the STE in V4-6 derivations and the presence of the apical aneurysm (Spearman's $\rho=0.895$, $p<0.001$) (**Ozeke 2015**).
V. Positivisation of negative T waves in V3-V6 (deep t-wave in V5) (**Pennacchini 2015**).

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 of Ap-HCM (Yusuf 2011)

Disease	Diagnostic tool to establish diagnosis of Ap-HCM
1. LV apical cardiac tumors	Echocardiogram with contrast/CCT/CMRI
2. LV apical thrombus	Echocardiogram with contrast/CCT/CMRI
3. Isolated ventricular non-compaction	CMRI/CCT
4. Endomyocardial fibrosis	LVG/CMRI
5. Coronary artery disease	Echocardiogram/coronary angiogram and LVG

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, pseudoaneurysms and congenital apical diverticula (see differential diagnosis in the next slide)
3. Apical ventricular remodelling
4. **Apical hypertrophic cardiomyopathy (ApHCM) (Cisneros 2011)**
5. Left ventricular non-compaction
6. Arrhythmogenic right ventricular cardiomyopathy/dysplasia(ARVC/D with left ventricular involvement
7. 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.
8. 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.

Differences among aneurysms, pseudo-aneurysms and congenital diverticula

	Aneurysms	Pseudoaneurysms	Congenital diverticula
Layers	All layers of the ventricular myocardium	Organized hematoma and pericardium	All layers of the ventricular myocardium
Cine	Akinetic dyskinetic segment	Akinetic or dyskinetic segment	Slow contraction during systole
Myocardial late enhancement	Yes	No, only the border of the pseudoaneurysm will show enhancement	No
Pericardial late enhancement	No or faint	Marked	No

Relative merits of each non-invasive imaging technique for the assessment of HCM

Factor assessed	Echocardiography	Multi-detector CT	MR iaging
LV volume	+++	++	++++
Ejection fraction	+++	+++	++++
LV filling pressure	+++	-	++
Dynamic obstruction	+++	+	+++
Ischemial CFR	+	-	++
Tissue characterization	++	+	++++

Prognosis of Ap-HCM

The prognosis of Ap-HCM with regard to SCD is believed to be better than that of common 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-HCM (**Dohlemann 2000**). 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. Ap-HCM show a relatively small burden of myocardial fibrosis and less severe diastolic dysfunction and subsequently more favorable clinical manifestations in comparison with other HCMs. This may be one explanation of why most patients with Ap-HCM show a benign course of disease compared with non-Ap-HCM (**Kim 2015**). Morbid sequel, and others extra-cardiac disorders such as: Atrial fibrillation, diastolic dysfunction, left atrial enlargement, apical thrombi, stroke, ventricular aneurysms/apical akinetic chamber, myocardial infarction, progressive heart failure, high incidence of coronary fistulae and morbid atrial fibrillation (**Chung 2010**). cardiovascular death. Neuromuscular disorders Ap-HCM 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 (**Finsterer 2009**). The probability of survival without morbid events at 10 years was 77 ± 4%. Several independent predictors of cardiovascular morbidity are identified: 1. Age at diagnosis ≥ 60 years.; 2. Left atrial diameter ≥ 36 mm.; 3. Atrial fibrillation.; 4. New York heart association class ≥ III at baseline (**Yan 2012**); 5. Ventricular aneurysms.; 6. Apical thrombi.; 7. Diastolic dysfunction and 8. Myocardial infarction. The most frequent morbid events in patients with Ap-HCM are atrial fibrillation (10% of patients) and myocardial infarction (**Eriksson 2002**). Patients with apical aneurysm have a largely unfavorable clinical course, and are often unrecognized because echocardiography is limited in the assessment of the left ventricular (LV) apex. Apical aneurysm is not rare in patients with HCM and it confers an extremely poor prognosis. Early aggressive therapies should be considered for this entity and prophylactic aneurysmectomy may be an option (**Xiao 2016**). Ap-HCM patients, the aneurism presence and the extent of quantification of late gadolinium enhancement (LGE) identified by cardiac MRI are both significant predictors of major adverse clinical events. Thus, patients with both apical aneurysm and >5% LGE are at highest risk for major adverse events. **The rate of apical obliteration** is defined as the net obliteration to end-diastolic apical cap thickness (**Hanneman 2014**). Abnormal systolic apical cavity obliteration is graded as > 20 mm or > 10 mm. Measured in the 5 mm long axis cine crosscuts in the 3 views (4ch, 2ch, LVOT view) from the apical cap to the blood cavity in systole. The minimum of the three measurements is used.

The ratio of obliteration to cavity is defined as the end-systolic obliteration to cavity height. The ratio of obliteration to cavity could provide useful information to predict the occurrence of adverse events in Ap- HCM (**Kim 2015**).

Events were defined as a composite of new onset of AF, stroke, HF, and cardiovascular (CV) death.

Management

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 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;
   - Prior cardiac arrest
   - Sustained VT and Non-SVT
   - Unexplained syncope, particularly in young patients , or if demonstrated to be arrhythmia-based;
   - Frequent, multiple, or prolonged episodes of NSVT documented on serial ambulatory Holter monitoring;
   - Hypotensive or attenuated blood pressure response to exercise;
   - Extreme left ventricular hypertrophy (≥ 30mm) particularly in young patients.
   - An abnormal blood pressure response to exercise
   - possible risk factors included: atrial fibrillation, myocardial ischaemia, left ventricular outflow obstruction, high risk mutations, and intense (competitive) physical exertion.
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 (**Inada 2011**).

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 (**Schaff 2010**).

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.

References

1. Abinader EG, Rauchfleisch S, Naschitz J. Hypertrophic apical cardiomyopathy: a subtype of hypertrophic cardiomyopathy. Isr J Med Sci. 1982;18(10):1005-9.
2. Arad M, Penas-Lado M, Monserrat L, Maron BJ, Sherrid M, Ho CY, et al. Gene mutations in apical hypertrophic cardiomyopathy. Circulation 2005;112(18):2805-11.
3. Arbustini E, Narula N, Dec GW, et al. The MOGE(S) Classification for a Phenotype-Genotype Nomenclature of Cardiomyopathy: Endorsed by the World Heart Federation. Glob Heart. 2013;8(4):355-82.
4. Bielli M, Parravicini U, Zanetta M, Zenone F. [Apical hypertrophic cardiomyopathy: description of a case in advanced age with documentation of electrocardiographic course]. G Ital Cardiol. 1991;21(12):1325-9.
5. Cerqueira MD, Weissman NJ, Dilsizian V, et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: a statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. Circulation 2002;105(4):539-42.
6. Chun EJ, Choi SI, Jin KN, et al. Hypertrophic cardiomyopathy: assessment with MR imaging and multidetector CT. Radiographics. 2010;30(5):1309-28.
7. Chen CH, Nobuyoshi M, Kawai C. ECG pattern of left ventricular hypertrophy in nonobstructive hypertrophic cardiomyopathy: the significance of the mid-precordial changes. Am Heart J. 1979;97(6):687-95.
8. Chung T, Yiannikas J, Freedman SB, Kritharides L. Unusual features of apical hypertrophiccardiomyopathy. Am J Cardiol. 2010;105(6):879-83.
9. Cisneros S, Duarte R, Fernandez-Perez GC, et al. Left ventricular apical diseases. Insights Imaging. 2011;2(4):471-482.
10. Dohlemann C, Hebe J, Meitinger T, Vosberg HP. 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(7):612-9.
11. Eriksson MJ, Sonnenberg B, Woo A, et al. Long-term outcome in patients with apical hypertrophic cardiomyopathy. J Am Coll Cardiol 2002;39(4):638-45.
12. Finsterer J Stöllberger C. Neuromuscular disorders associated with apical hypertrophic cardiomyopathy. Acta Cardiol. 2009;64(1):85-9.
13. Gupta T, Paul N, Palaniswamy C, et al. Sudden Cardiac Arrest in a Patient With Apical Hypertrophic Cardiomyopathy: Case Report and a Brief Review of Literature. Am J Ther. 2016;23(1):e276-82.

14. 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;22(1):41-8.
15. Hanneman K, Crean AM, Williams L, et al. Cardiac magnetic resonance imaging findings predict major adverse events in apical hypertrophic cardiomyopathy. J Thorac Imaging. 2014;29(6):331-9.
16. Kim EK, Lee SC, Hwang JW, et al. Differences in apical and non-apical types of hypertrophic cardiomyopathy: a prospective analysis of clinical, echocardiographic, and cardiac magnetic resonance findings and outcome from 350 patients. Eur Heart J Cardiovasc Imaging. 2015 Aug 4. pii: jev192. [Epub ahead of print]
17. Kim H, Park JH, Won KB, et al. Significance of apical cavity obliteration in apical hypertrophic cardiomyopathy. Heart. 2016 Mar 11. pii: heartjnl-2015-309121. doi: 10.1136/heartjnl-2015-309121. [Epub ahead of print]
18. Moon JC, Fisher NG, McKenna WJ, Pennell DJ. Detection of apical hypertrophic cardiomyopathy by cardiovascular magnetic resonance in patients with non-diagnostic echocardiography. Heart 2004;90(6):645-9.
19. Noureldin RA, Liu S, Nacif MS, Judge DP, Halushka MK, Abraham TP, et al. The diagnosis of hypertrophic cardiomyopathy by cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2012;14:17.
20. Olearczyk B, Gollol-Raju N, Menzies DJ. Apical hypertrophic cardiomyopathy mimicking acute coronary syndrome: a case report and review of the literature. Angiology. 2008;59(6):629-31.
21. Ozeke O, Ertan C, Keskin G, et alAssociation of ST elevation with apical aneurysm in hypertrophic cardiomyopathy. Indian Heart J. 2015;67(5):434-9.
22. Pennacchini E, Musumeci MB, Conte MR, et al. Electrocardiographic evolution in patients with hypertrophic cardiomyopathy who develop a left ventricular apical aneurysm. J Electrocardiol. 2015;48(5):818-25.
23. Pérez-Riera AR, de Lucca AA, Barbosa-Barros R, et al. Value of electro-vectorcardiogram in hypertrophic cardiomyopathy.Ann Noninvasive Electrocardiol. 2013;18(4):311-26.
24. Sakamoto T. Apical hypertrophic cardiomyopathy (apical hypertrophy): an overview. J Cardiol. 2001;37 Suppl 1:161-78.
25. 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;139(3):634-40.
26. Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989;2(5):358-67.

27. 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(11):1269-78.
28. Towe EC1,.Bos JM, Ommen SR, Gersh BJ, Ackerman MJ Genotype-Phenotype Correlations in Apical Variant Hypertrophic Cardiomyopathy.Congenit Heart Dis. 2015;10(3):E139-45.
29. Wu B, Lu M, Zhang Y, et al. 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 Mar 29. pii: jew045. [Epub ahead of print]
30. Xiao Y, Wang LP, Yang YK, et al. Clinical Profile and Prognosis of Left Ventricular Apical Aneurysm in Hypertrophic Cardiomyopathy. Am J Med Sci. 2016;351(1):101-10.
31. Yamaguchi H, Ishimura T, Nishiyama S, et al. Hypertrophic nonobstructive cardiomyopathy with giant negative T waves (apical hypertrophy): ventriculographic and echocardiographic features in 30 patients. Am J Cardiol 1979;44(3):401-12.
32. Yan L, Wang Z, Xu Z, Li Y, Tao Y, Fan C. Two hundred eight patients with apical hypertrophic cardiomyopathy in china: clinical feature, prognosis, and comparison of pure and mixed forms. Clin Cardiol. 2012;35(2):101-6.
33. Yusuf SW, Bathina JD, Banchs J, Mouhayar EN, Daher IN. Apical hypertrophic cardiomyopathy. World J Cardiol. 2011;3(7):256-9.

Thank you very much! This is my wife and I in the typical Japanese restaurant.


My food
Japanese food