SYMPTOMATIC YOUNG MAN CARRYING
SYMMETRICAL HYPERTROPHIC CARDIOMYOPATHY
AND STRONG FAMILIAL HISTORY OF SUDDEN
DEATH IN HIS SIBLINGS

HOMEM JOVEM SINTOMÁTICO PORTADOR DE
CARDIOMIOPATIA HIPERTRÓFICA SIMÉTRICA E
FORTES ANTECEDENTES DE MORTE SÚBITA EM
SEUS IRMÃOS

From Raimundo Barbosa Barros MD
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Comments
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ABC Faculty- ABC Foundation - Cardiology discipline - Santo André - SP - Brazil
Identification: C.B.N., male 32 years of age

Complain: palpitations and fainting sensation

Histórico: History

1) Forte relato de morte súbita familiar:
   Strong background of sudden death in his family members
   21 irmãos
   21 siblings
   08 mortes inexplicadas na infância
   8 of them with unexplained sudden death during infancy
   06 irmãos com morte súbita na faixa de 20 a 50 anos
   6 siblings with sudden death occurred between 20 and 50 years of age.
   07 irmãos vivos sem relato do acompanhamento médico
   7 alive siblings without report of medical accompaniment
2) He does medical accompaniment (medical care) since at least 2008

Relato de cardiopatia hipertrófica

There are reports of Hypertrophic Cardiomyopathy (HCM)

3) Development of High blood pressure since 2009.
He is actually using losartan potassium

4) One event of near-syncope
Atrial fibrillation episodes

Atual: encaminhado como candidato a implante de CDI
Referred to our service as candidate to implantable of a cardioverter-defibrillator (ICD)
Atrial fibrillation with an uncontrolled, rapid ventricular heart rate response
Left ventricular hypertrophy with strain pattern of repolarization.
AF with appropriated ventricular response. Prominent QRS Intermediate Anterior Forces. LVH with strain or systolic pattern of repolarization.
Atrial fibrillation (AF) is strongly associated with the following risk factors:

1. **Hemodynamic stress**: Increased intra-atrial pressure results in atrial electrical and structural remodeling and predisposes to AF. The most common causes of increased atrial pressure are mitral or tricuspid valve disease and LV dysfunction. Systemic or pulmonary hypertension also commonly predisposes to atrial pressure overload, and intracardiac tumors or thrombi are rare causes.

2. **Atrial ischemia**: Myocardial ischemia in HCM and another element present in the disease secondary to: 1) microcirculation disease; 2) decrease of vasodilator capacity; 3) systemic compression of septal and subepicardial vessels; 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.

3. **Inflammation**

4. **Noncardiovascular respiratory causes**: Pulmonary embolism, pneumonia, lung cancer, and hypothermia have been associated with AF.

5. **Alcohol and drug use**

6. **Endocrine disorders**: Stimulants, alcohol, and cocaine can trigger AF. Acute or chronic alcohol use (ie, holiday or Saturday night heart, also known as alcohol-related cardiomyopathy) and illicit drug use (ie, stimulants, methamphetamines, cocaine) have been specifically found to be related to AF.

7. **Neurologic disorders**: Intracranial processes such as subarachnoid hemorrhage or stroke can precipitate AF.

8. **Genetic factors**: A history of parental AF appears to confer increased likelihood of AF (and occasional family pedigrees of AF are associated with defined ion channel abnormalities, especially sodium channels).(1) One cohort study suggests that familial AF is associated with an increased risk of AF. This increase was not lessened by adjustment for genetic variants and other AF risk factors.

9. **Advancing age**: AF is strongly age-dependent, affecting 4% of individuals older than 60 years and 8% of persons older than 80 years.

In the present case factors 1, 2, and 8 are present.

Is atrial fibrillation common with HCM and what's the best way to treat it?

AF is very common in HCM. It is present in five per cent of people at diagnosis and develops in approximately five to ten per cent of people in the five years following diagnosis. The best way to treat it is to try to prevent it with the use of medication such as betablockers and amiodarone. If someone goes into atrial fibrillation, normal rhythm can be restored using DC cardioversion. This requires a brief general anaesthetic and the heart is shocked back into a normal rhythm. If AF is frequent or prolonged it is generally advised that people take warfarin to prevent clot formation in the atria. In some people it is not possible to restore normal rhythm. In this instance we try to control the heart rate with drugs such as betablockers or calcium antagonists. Olivotto et al (1) analyzed the prognostic implications of AF in a large, community-based HCM population assembled from Italian and US cohorts. Occurrence of AF and outcome were assessed in 480 consecutive HCM patients (age at diagnosis, 45±20 years; 61% male) who were followed up for 9.1±6.4 years. AF occurred in 107 patients (22%; incidence, 2%) and was independently predicted by advancing age, congestive symptoms, and increased LA size at diagnosis. Patients with AF had increased risk for HCM-related death because of excess HF–related mortality but not sudden, unexpected death. This risk associated with AF was substantially greater in patients with outflow obstruction or with earlier development of AF (≤50 years of age). AF patients were also at increased risk for stroke and severe NYHA class III or IV. Compared with those with exclusively paroxysmal AF, patients developing chronic AF showed higher combined probability of HCM-related death, functional impairment, and stroke. In a subgroup of 37 patients with AF (35%), the clinical course was largely benign in the absence of stroke and severe symptoms. The authors concluded that in a community-based HCM population, AF (1) was common, with 22% prevalence over 9 years; (2) was associated with substantial risk for HF–related mortality, stroke, and severe functional disability, particularly in patients with outflow obstruction, those ≤50 years of age, or those developing chronic AF; and (3) was nevertheless compatible with benign outcome in 35% of patients.

AF) is the most common sustained arrhythmia in patients with HCM, and it bears numerous pathophysiologic consequences that potentially affect patient outcome and symptoms. However, studies regarding the impact of AF on the long-term prognosis of HCM patients have been limited in number, with sometimes conflicting results. Olivotto, study on community-based patient populations showed that AF is associated with long-term clinical deterioration, embolic complications, and increased cardiovascular mortality due to HF and stroke. The consequences of AF on the long-term prognosis of HCM patients are not uniformly unfavorable, however, and in about 33% of patients the arrhythmia is compatible with an uneventful course.

AF is present in ≈ 5% of HCM patients at the time of diagnosis. Ostial pulmonary vein (PV) diameter is increased in patients with AF as well as hypertensive patients (as the present case). These findings support the theory that the cascade of events leading to diastolic dysfunction might predispose a person to AF by stretching the PVs. This mechanism is likely relevant to AF in HCM as well. The recognition that AF often times arises from the PVs has led to innovation of ablation techniques that target this zone to electrically isolate the PVs from the LA. Anticoagulation is the cornerstone of AF treatment. HCM is a common and complex heterogeneous cardiovascular entity. Its relationship to ischaemic stroke and AF is under-recognized and consequently, many patients who should be on oral anticoagulation for stroke prevention go untreated. Additional AF treatment in HCM patients depends on the initial decision regarding need for surgical intervention, whether or not AF is permanent, and the severity of symptoms in patients with non-permanent AF. If surgery is planned, correction of the arrhythmia with MAZE procedure, which isolates the arrhythmogenic foci, at the time of myectomy is an option to consider. The goal in HCM patients with permanent AF is to control the HR whether by chronic medications or through ablate + pace procedure. Based on the severity of symptoms, HCM patients with non-permanent AF will be treated with either the rate control strategy (beta-blockers/calcium channel blocker) or the rhythm control strategy (PV ablation, antiarrhythmic drugs, or RFCA of the LA). This is because adverse effects of antiarrhythmics and complications after invasive procedures are justifiable only in HCM patients who experience severe symptoms.
Sinus rhythm, short PR interval: pseudo or true pre-excitation WPW?, QRS axis -20°, LVH with systolic or strain pattern of repolarization with wide QRS/T angle >100° may approach near 180° by significant secondary ventricular repolarization alteration in anterolateral and inferior wall. Prominent R waves in intermediary precordial leads $V_2$ to $V_4$. 
Short PR interval: Familial pseudo-Wolff-Parkinson-White syndrome?

Mutation in the PRKAG2 gene is responsible for a familial syndrome of ventricular preexcitation, AF, conduction defects, and cardiac hypertrophy. Gollob et al. (1) identified a novel mutation (Arg531Gly) in the gamma-2 regulatory subunit (PRKAG2) of AMP-activated protein kinase (AMPK) to be responsible for a syndrome associated with ventricular preexcitation and early onset of AF and conduction disease. The identification of the cardiac ion channel(s) serving as substrate for AMPK not only would provide insight into the molecular basis of AF and heart block but also may suggest targets for the development of more specific therapy for these common rhythm disturbances.

Clinico-pathologic and experimental data suggest the hypothesis of a glycogen storage disease. Sternick et al(2) from Brazil, studied two large families and found a total of 20 affected individuals showing a combination of sinus bradycardia, short PR interval, RBBB, intra and infrahsian conduction disturbances often requiring a pacemaker, and atrial tachyarrhythmias. Three individuals died suddenly at a young age. No patient had the Wolff-Parkinson-White (WPW) syndrome, and only two patients (10%) had myocardial hypertrophy. The authors performed screening of the exons and exon-intron boundaries of PRKAG2. Genetic analysis revealed a missense mutation (Arg302Gln) in the affected individuals from both families. This mutation had been described before and has been associated with the familial form of the WPW syndrome and with a high prevalence of LVH.

PRKAG2 mutations are responsible for a diverse phenotype and not only the familial form of the WPW syndrome. Familial occurrence of RBBB, sinus bradycardia, and short PR interval should raise suspicion of a mutant PRKAG2 gene.

Prominent R waves in intermediary precordial leads.

Systolic or strain pattern of repolarization with wide QRS/T angle >100° may approach near 180°.
Bifid T wave with two distinct peaks was found in 39 cases (24.84%) of highly trained athletes, 5 of them with mild prolonged QTc and KCN genes mutations. (1)

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<tr>
<th>Medida</th>
<th>Normal LV dimensions</th>
<th>Mass&gt; ++++</th>
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<tr>
<td>VE Diâmetro Diastólico Final</td>
<td>Diastolic LV final diameter</td>
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<td>VE Diâmetro Sistólico Final</td>
<td>Systolic LV diameter</td>
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<td>Átrio Esquerdo</td>
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<td>Aorta</td>
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<td>Relação Átrio Esquerdo / Aorta</td>
<td>LA/Ao</td>
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<td>Espessura do Septo</td>
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<td>Espessura da Parede Posterior</td>
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<td>(mulher até 110g/ m² e homem até 134g/m²)</td>
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<td>FUNÇÃO DE VE</td>
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<tr>
<td>Fração de Ejeição</td>
<td>(53% - 77%)</td>
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<td>Fração de Encurtamento</td>
<td>(24% - 46%)</td>
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**Ventriculo Esquerdo:**
- Normal LV dimensions
- Mass> ++++
- Preserved LV Systolic function
- Diastolic dysfunction
ATRI E VENTRICULO DIREITOS:
Cavidades com diminuição normal
Função sistólica do VD preservada

AORTA:
Com calibre e dimensões normais

VALVA AORTA:
Gradiente na Via de Saída do VE de 13 mmHg
Regurgitação mitral leve

VALVA MITRAL:
Normal
Regurgitação mitral leve

ARTÉRIA E VALVA PULMONARES:
Artéria pulmonar com calibre normal
Valva pulmonar sem alterações

VALVA TRICUSPIDÉ:
Normal

PERICÁRDIO:
Normal

OBSERVAÇÕES

CONCLUSÃO: Miocardiopatia hipertrófica
Epessura do Septo de 1.6 cm com gradiente de repouso de 13 mmHg
Câmaras cardíacas com diâmetro cavitários normais
Função sistólica do VE preservada
Alteração na função diastólica do VE tipo I
Hipertensão pulmonar leve, Pressão sistólica na artéria pulmonar de 30 mmHg

Minimal gradient LV/Ao

Minimal mitral regurgitation

Septum thickness and free posterior wall 16mm.
Minimal gradient at rest 13mmHg
Non-sustained VT run?

Very short PR interval
DATA DO INICIO DA GRAVAÇÃO
7/5/2011

RELATÓRIO DE ECG DINÂMICO (HOLTER)

Nome do Paciente:
Endereço:
Tarja/Passaporte:
Supervisor:
Técnico:
Indicações:

FREQUÊNCIA CARDÍACA
- Limite PF-1 Intermitente:
- Limite PF-1 Intervalo:
- Média das 24 Horas:
- Limite PF-Horário:
- Limite PF-Intermitente:
- Limite PF-Intergem:

ARRITMIA VENTRICULAR
- EV Total:
- EV Por Total:
- TV Total:
- TV-V mas longa:
- TV-V - Máxima FC:
- TV-V - Maior Intergem:
- TV-Vs por 1000 por Hora:

VARIABILIDADE DE R-R
- ONN-24 Horas:
- Índice SDNN:
- Índice SDNN:
- Índice ONN:
- Não Houve:
- Não Houve:
- Não Houve:
- Não Houve:
- Não Houve:

NÁLISE DO SEGMENTO ST
- Oito da Idade de ST Célula:
- Total de Minutos de ST Célula:
- Oito da Idade de ST Célula:
- Início ST-Max Elevation:
- Taxa de Episódio de ST:
- Taxa de Episódio de ST:

ARRITMIA SUPRAVENTRICULAR
- PJJ:
- Maio Poás:

BRADICARDIA
- Nível de QT:
- Nível de QT:
- Nível de QT:
- Nível de QT:
- Nível de QT:
- Nível de QT:

EVENTOS SIGNIFICATIVOS DE ECG
ESTUDO ELETROFISIOLOGICO INVASIVO

Electrophysiology study (EP test or EP study)

CONCLUSÕES

Exame realizado sob boas condições técnicas e sem intercorrências;
Ritmo de base sinusal propagado para os ventrículos pelo sistema de normal condução, sob a relação 1:1;
Condução atrioventricular preservada em todos os níveis
Ausência de pré-excitación de câmaras cardíacas em qualquer direção;
Ausência de taquicardias supraventriculares frente à estimulação atrial programada.
Ausência de taquicardias ventriculares frente à estimulação programada.

Fortaleza, 17 de outubro de 2011.

Normal AV conduction. Absence of pre-excitation, absence of supraventricular tachycardia with Atrial programmed stimulation, and absence of ventricular tachycardia with programmed ventricular stimulation.
Colleagues opinions
 Increible y muy lindo caso Dr Raimundo y Prof Mustang Presenta en los primeros ECG FA de ARV y luego FA, esta se presenta en un 10% de la evolucion de las MCH. No encuentro criterios para TV. En el ECG posterior es muy interesante en RS presenta desviacion del eje electrico a la izquierda y signos de HVI con indice de Sokolovpositivo. Injuria subendocardica con T negativas que son por el insuficiente aporte de O2 en las zonas subendocardicas por el severo incremento de las presiones intraventriculares. El eco confirma el diagnostico, dada la HVI y la disfuncion diastolica, el strain rate nos podria contribuir a cuales zonas son las mas afectadas por fibrosis, al igual que la RMN con realce tardio. De los criterios diagnosticos de MCH para familiares de primer grado de pacientes afectados presenta Criterios mayores
 Ecocardiograficos: Hipertrofia ventricular  13 mm septo anterior o pared posterior o 16 mm en el septo posterior o la pared lateral. (si) SAM con contacto septal (no)
 Electrocardiograficos: Criterios de hipertrofia ventricular con alteraciones de la repolarizacion (Romhilt & Estes). (si)
 Ondas T negativas (3mm en cara anterolateral o  5mm en cara inferior). (si)
 Ondas Q patologicas (> 40 ms o > 25% onda R) (no)
 De los criterios menores:
 Alteraciones leves repolarizacion en precordiales. (si)
 Onda S en V2 > 25 mm (si)
 Sintomas (sincope, dolor precordial o disnea) no explicadas
 El diagnostico de la enfermedad debe realizarse en un familiar de primer grado si existe un criterio mayor ó 2 Criterios ecocardiograficos menores o 1 criterio ecocardiografico menor junto a 2 criterios electrocardiograficos menores Obviamente presenta criterios positivos de MCH de origen familiar o genetica. Por la edad 30 años podria pensarse en un mejor pronostico y seguimiento, pero ha presentado FA y antecedentes muy pesadosfamiliares.Se podria utilizar Beta-bloqueadores, Antagonistas del calcio, Antiarritmos. A pesar de no referir sintomatologia de angor o sincopes ni registro de TV en el Holter esta plenamente justificada la colocacion de un CDI profilactico.
 Esa es mi humilde interpretacion de este interesante caso. me encantaria escuchar la palabras de los electrofisiologos que son los que en definitiva dan la ultima palabra acerca de la indicacion de CDI.
 Saludos
 Martin Ibarrola
Incredible and very nice case of Raimundo and Prof Mustang
In the first an second ECGs AF is observed. This arrhythmia occurs in ≈ 10% of the evolution of the HCM. I don’t see criteria for TV. In the subsequent ECG (third) the rhythm is sinus. The QRS electric axis has deviation to the left and there are signs of LVH with positive Sokolov index. Additionally, a subendocardial injury with negative T waves are observed consequence of the insufficient supply of O₂ in the subendocardial layers by severe augmentation of intraventricular pressure.
The echo confirmed the diagnosis, given the LVH and diastolic dysfunction, strain rate which could contribute to the most affected areas of fibrosis, as well as delayed enhancement MRI.
Strong diagnostic criteria of HCM in first-degree relatives of patients are presented.

MAJOR CRITERIA

ECHOCARDIOGRAPHIC

Septal ventricular hypertrophy 16 mm and free wall. (Yes)
SAM septal contact (no)

ELECTROCARDIOGRAPHIC

Criteria for ventricular hypertrophy with repolarization abnormalities (Romhilt & Estes). (Yes)
Negative T waves (3mm or 5mm on anterolateral and inferior walls). (Yes)
Pathological Q waves (> 40 ms or> 25% R wave) (no)

MINOR CRITERIA

Slight alterations in precordial ECG repolarization. (Yes)
S wave in V2> 25 mm (Yes)
Symptoms (syncope, chest pain or dyspnea) unrelated
Diagnosis of the disease should be performed in a first degree if there is a major criterion or 2 echocardiographic criteria or 1 minor echocardiographic criterion with 2 minor electrocardiographic criteria
Obviously has a positive criterion of familial HCM or genetic origin.
By age 32 years could think of a better prognosis and monitoring, but has submitted heavy AF and background family.
We could use beta-blockers, calcium antagonists, antiarrhythmics
Although not referring angina or syncope or record VT on the Holter monitoring is fully justified the placement of an ICD prophylactically.
That is my humble interpretation of this interesting case.
I would love to hear the words of the electrophysiological ultimately are the ones giving the last word on the indication of ICD.
Regards.
Martin Ibarrola Nickname “The gallant”
Queridos amigos del forum trataré de analizar el material que nos envían estos extraordinariños colegas Dr Raimundo Barbosa Barros y Profesor Andrés Ricardo Pérez Riera M.D. Ph.D.

Los tres trazados tienen un común denominador: los vectores basales muy aumentados manifestados por ondas S muy profundas en DIII y R muy altas en aVL y DI y desvío no extremo del eje del QRS hacia la izquierda (menos de - 30°).

Se observan ondas R de gran voltaje en V2 lo que expresa los potenciales del septo superior izquierdo, vecino a la base anterior del ventrículo izquierdo.

Las ondas T profundas negativas en las precordiales izquierdas expresan los potenciales epicárdicos de la base cardiaca, sugiriendo que los potenciales electrotonícos epicárdicos en las base son muy hipertróficos y más cortos, que los de la punta y cara lateral.

Los segmentos ST deprimidos indican alta tensión intracavitaria, debido a alteración en la relajación diastólica, responsable por el agrandamiento de la aurícula izquierda y la tendencia a la aparición de fibrilación auricular

Un fraternal abrazo
Samuel Sclarovsky

Dear friends of the forum will try to analyze the material that send to us these extraordinaries colleagues Dr Raimundo Barros Barbosa and Professor Andrés Ricardo Pérez Riera MD Ph.D.

The three ECGs have a common denominator: the greatly increased basal vectors manifested deep S wave in DIII and very high R waves DI and aVL and deviation of the QRS axis to the left (Non extreme: less than - 30 °). R waves have high voltage V2 which expresses the potential of the upper septum left neighbor to the anterior base of the LV.

Deep negative T waves in left leads express epicardial potentials of the cardiac base, suggesting that epicardial electrotonic potential at the base are very hypertrophic and shorter, than the apex and lateral wall one. Depressed ST segments indicate high intracavitary pressure due to impaired diastolic relaxation, responsible for the enlargement of the LA and the tendency to AF.

A fraternal embrace
Samuel Sclarovsky
HYPERTROPHIC CARDIOMYOPATHY (HCM)

CONCEPT: complex heart disease, which is characterized by hypertrophy of variable location in the LV and/or RV, in most cases heredo-familial, autosomal polygenic dominant, with a high degree of penetrance (60% reveal familial relationship and 40% sporadic). To this date, Over 27 genetic types are known. These encode the sarcomere proteins by alteration in the chromosomes with the numbers: 1, 3, 11, 12, 14, 15, 19 and gene of actin with a great morphological diversity, and which is characterized in most cases by asymmetrical septum hypertrophy, obstructive or non obstructive (90%), in comparison to LV free wall (there are concentrically or symmetrical forms, characterized by nonselective hypertrophy, both in the septum and the free wall like the present case), with small or normal size of ventricular cavity (95%), hypodistole, by increase of ventricular mass and rigidity responsible of distensibility involvement with a subsequent LV diastolic dysfunction. in 5% to 10% of patients, in the late phase, they evolve into dilatation and systolic dysfunction resulting from myocardial fibrosis secondary to microinfarctions and possible associated coronary artery disease.

Myocardial ischemia and another element present in the disease secondary to:

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

The anatomopathological substrate is an important septal cell disorder (95%) and hypertrophy of the middle layer with narrowing of light of the intramural branches responsible of ventricular dysfunction as well as arrhythmias.

HCM is one of the archetypal monogenic cardiovascular disorders to be understood at the molecular level. Twenty years after the discovery of the first HCM disease gene, genetic studies still confirm that HCM is principally a disease of the sarcomere. At the biophysical level, myofilament mutations generally enhance Ca(2+) sensitivity, maximal force production, and ATPase activity(1). These defects ultimately appear to converge on energy deficiency and altered Ca(2+) handling as major common paths leading to the anatomic (hypertrophy, myofiber disarray, and fibrosis) and functional features (pathological signaling and diastolic dysfunction) characteristic of HCM. Most of these genes encode sarcomeric proteins, such as myosin-7 (also known as cardiac muscle β-myosin heavy chain; MYH7), cardiac myosin-binding protein C (MYBPC3), and cardiac muscle troponin T (TNNT2). MYH7 and MYBPC3 mutations account for about 50% of cases. However, the molecular events that ultimately lead to the clinical phenotype of HCM are still unclear. There are several potential pathways, which include altered calcium cycling and sarcomeric calcium sensitivity, increased fibrosis, disturbed biomechanical stress sensing, and impaired cardiac energy homeostasis. An improved understanding of the pathological mechanisms involved will result in greater specificity and success of therapies for patients with HCM.

RISK MARKERS USED TO ASSESS THE MAGNITUDE OF SUDDEN DEATH RISK

1. Extreme increase of septal thickness: extreme left ventricular (LV) hypertrophy (> 30 mm) in Young patients massive LV hypertrophy in a young patient,
2. Very increased estimation of myocardial mass
3. Progression of the disease to LV wall thinning and decrease of EF
4. History of recovery from SCD
5. Recurrent syncope in youngster
6. Unexplained (not neurally mediated) syncope, particularly in young patients
7. Nonsustained VT NS-VT on Holter monitoring in patient with alteration of conscience frequent and/or prolonged runs of nonsustained ventricular tachycardia on Holter, may also justify consideration of a prophylactic ICD.
8. S-VT induction in electrophysiological study
9. Significant bradyarrhythmia or concealed conduction
10. Atrial fibrillation
11. Abnormal blood pressure response: Blood pressure decrease or inadequate increase during upright exercise. (hypotension induced by strain)
12. Association with high blood pressure.
13. History of associated infarction or myocardial ischemia, especially in young patient that presents alteration of conscience
14. Family history of multiple sudden deaths,
15. Hereditary genetic defect, associated to unfavorable prognosis. **Type I HCM**: with genetic alteration with mutations in locus 1q of the long arm of chromosome 14, which alters the heavy chain of cardiac β-myosin (β-MyHC), high penetrance, severe hypertrophy and sudden cardiac death present in approximately 50% of affected patients. The locations Arg403 (substitution of the amino acid arginine by glycine in position 403), Arg453Cys (substitution of the amino acid arginine by cysteine in position 453), and Arg719Trp (substitution of the amino acid argynine by tryptophan in position 719) are considered malignant.
Type II HCM: (15%) alteration in chromosome 1: locus 1q3. It modifies cardiac troponin T (cTnT). These patients present little hypertrophy and high arrhythmic mortality in youngsters under 30 years old. To this moment, 8 mutations have been described.

NOTE: in patients in whom a genetic diagnosis has been made of malignant form, even in absence of symptoms and hypertrophy, implantable cardioverter defibrillator is indicated.

**Implantable Defibrillator indication in HCM**

Most of the data concerning the efficacy of the ICD in HCM comes from a large multicenter international register conducted by Maron et al.(1). The study analyzed the relationship between clinical risk profile and incidence and efficacy of ICD intervention in HCM. This Multicenter registry study of ICDs implanted between 1986 and 2003 in 506 unrelated patients with HCM. Patients were judged to be at high risk for SD; had received ICDs; underwent evaluation at 42 referral and nonreferral institutions in the US, Europe, and Australia; and had a mean follow-up of 3.7 years. Measured risk factors for SD included **family history of SD, massive LVH, NS-VT on Holter monitoring, and unexplained prior syncope**. The main outcome measure was appropriate ICD intervention terminating VT or VF. The 506 patients were predominately young (mean age, 42 yo) at implantation, and most (439) [87%] had no or only mildly limiting symptoms. ICD interventions appropriately terminated VT/VF in 103 patients (20%). Intervention rates were 10.6% per year for secondary prevention after cardiac arrest (5-year cumulative probability, 39%, and 3.6% per year for primary prevention (5-year probability, 17%). Time to first appropriate discharge was up to 10 years, with a 27% probability 5 years or more after implantation. For primary prevention, 18 of the 51 patients with appropriate ICD interventions (35%) had undergone implantation for only a single risk factor; likelihood of appropriate discharge was similar in patients with 1, 2, or 3 or more risk markers.

The single SD due to an arrhythmia (in the absence of advanced HF) resulted from ICD malfunction. ICD complications included inappropriate shocks in 136 patients (27%). In a high-risk HCM cohort, ICD interventions for life-threatening VT were frequent and highly effective in restoring normal rhythm. An important proportion of ICD discharges occurred in primary prevention patients who had undergone implantation for a single risk factor. Therefore, a single marker of high risk for SD may be sufficient to justify consideration for prophylactic ICD implantation in selected patients with HCM.

Flow diagram showing outcome for 506 high risk patients with HCM who had received ICDs for primary prevention (based on one or more risk factors) or secondary prevention in those who had experienced cardiac arrest or S-VT). Two patients not included here died of HCM with refractory HF and systolic dysfunction despite the ICD.
Seven years previously Maron et al (2) conducted a retrospective multicenter study of the efficacy of ICDs in preventing SD in 128 patients with HCM who were judged to be at high risk for SD. At the time of the implantation, the patients were 8 to 82 years old, and 69 patients (54%) were less than 41 years old. The average follow-up period was 3.1 years. ICDs were activated appropriately in 29 patients (23 %), by providing defibrillation shocks or antitachycardia pacing, with the restoration of sinus rhythm; the average age at the time of the intervention was 41 years. The rate of appropriate defibrillator discharge was 7% per year. 25% of patients had inappropriate discharges. In the group of 43 patients who received ICDs for secondary prevention (after cardiac arrest or S-VT), the devices were activated appropriately in 19 patients (11% per year).

From 85 patients who had prophylactic implants because of risk factors (i.e., for primary prevention), 10 had appropriate interventions (5 % per year). The interval between implantation and the first appropriate discharge was highly variable but was substantially prolonged (4 to 9 years) in six patients. In all 21 patients with stored electrographic data and appropriate interventions, the interventions were triggered by VT or VF. These arrhythmias appears to be the principal mechanism of SD in patients with HCM. In high-risk patients with HCM, ICDs are highly effective in terminating such arrhythmias, indicating that these devices have a role in the primary and secondary prevention of SD.

The clinical phenotype of HCM results from mutations in sarcomeric proteins and subsequent activation of multiple cellular constituents including signal transducers. HCM, despite its current recognition and management as a single disease entity, involves multiple partially independent mechanisms, despite similarity in the ensuing phenotype. To treat HCM effectively, it is necessary to delineate the underlying fundamental mechanisms that govern the pathogenesis of the phenotype and apply these principles to the treatment of each subset of clinically recognized HCM.

Here we need immediately genetic screening of this family. Recent trial conducted by O'Mahony C et al. (1) shows that HCM patients with an ICD have a significant cardiovascular mortality and are exposed to frequent inappropriate shocks and implant complications. Consequently, new strategies are required to improve patient selection for ICDs and to prevent disease progression in those that receive a device. They studied 334 HCM patients (median age 40 years, 62% male, 92% primary prevention) at risk of SCD treated with ICD. 36 patients (11%) received concurrent cardiac resynchronisation therapy for HF symptoms. Results During the 1286 patient-years of follow-up, cardiovascular mortality (including transplantation) occurred in 22 (7%) patients (1.7%/year) and was associated with NYHA class III/IV, percentage fractional shortening and implantation for secondary prevention. There were no SCD. 28 (8%) patients received appropriate shocks (2.3%/year), which were predicted by baseline fractional shortening. 56 (16%) patients received inappropriate shocks (4.6%/year). 60 (18%) patients experienced implant-related complications (5.1%/year), including two deaths. Adverse ICD-related events (inappropriate shocks and/or implant complications) were seen in 101 (30%) patients. Patients with cardiac resynchronization therapy were more likely to develop implant complications than those with single-chamber ICDs and had a higher 5-year cardiovascular mortality than did the rest of the cohort.

A family history of SD, like the present case, is an important risk marker in patients with HCM. Patients receiving ICDs for primary prevention because of a family history of HCM-related SD, whether as an isolated risk factor or combined with other markers, experienced rates of appropriate ICD discharge comparable to that of other patient subsets with increased risk. (1)

A near-normal life expectancy and a highly satisfactory quality of life are now realistic treatment goals for patients with HCM. Treatment strategies depend on appropriate patient selection, including drug treatment for exertional dyspnea (beta-blockers, verapamil, disopyramide) and the septal myotomy-myectomy operation, which is the standard of care for severe refractory symptoms associated with marked outflow obstruction; alcohol septal ablation and pacing are alternatives to surgery for selected patients. High-risk patients may be treated effectively for SD prevention with the ICD.

ICD therapy is effective in SCD prevention in patients with HCM, although the complication rate is significant. NS-VT seems to be the most predictive risk factor for appropriate device discharges. Number of risk factor did not impact the incidence of appropriate ICD interventions. (2)

LEFT VENTRICULAR ENLARGEMENT (LVE) / HYPERTROPHY (LVH) VECTORCARDIOGRAPHIC FEATURES
Vectorcardiographic types of LVH in the horizontal plane (IA, IB, II and III).
**LVH TYPE IA**

**DIASTOLIC, ECCENTRIC, OR VOLUME OVERLOAD**

**LVH TYPE IB**

**SYSTOLIC OR CONCENTRIC HYPERTROPHY**

**TYPES I:** vector of the initial 20 ms heading to the front and the right (Type IA) or to the front and the left (Type IB), oval morphology, counterclockwise rotation, and most of the QRS loop located in the left posterior quadrant. T loop matching QRS (IA) or not matching QRS (IB).
The septal vector may be magnified, originating a possible prominent R in V₁ and V₂.

Increased ventricular activation time (VAT) ≥55ms V₆, deep and clean Q waves can be observed, with a short duration, from V₄ to V₆. ST upwardly concave and elevated in V₅ - V₆.

T waves matching with QRS.

ECG/VCG correlation in the horizontal plane. LVH type IA of VCG.
LVH VCG TYPES IB

**TYPE IB**: vector of initial 20 ms of QRS loop heading to the front and the left, oval morphology, CCW rotation, location predominant in left posterior quadrant and maximal vector of increased magnitude: > 2 mV.

T loop opposite to QRS loop (not matching) heading to the front and the right: QRS/ST angle near 180°

ECG/VCG characterization of systolic LVH in the horizontal plane.
LVH VCG TYPES II

LVH TYPE IIA

- Proximal portion bigger than distal

LVH TYPE IIB

- Proximal and distal portion equal

LVH TYPE IIC

- Proximal portion smaller than distal

TYPE II: very similar to the QRS loop of Complete LBBB: vector of the initial 20 ms heading to the front and the left, (rare to the right), rotation in eight with counterclockwise proximal portion and clockwise distal portion, and E point that does not coincide with the 0 point, and located to the front and the right from the latter. T loop to the front and right, opposite to the QRS loop. In general types II correspond to severe left ventricular hypertrophy.
LVH VCG TYPE IIA

ECG/VCG correlation in the horizontal plane in severe systolic LVH type II of VCG (pseudo ILBBB).
LVH VCG TYPE III

TYPE II: very similar to QRS loop of CLBBB: vector of initial 20 ms heading to the front and the left (rarely to the right), rotation in eight with counterclockwise proximal portion and clockwise distal portion, and e point not matching 0 point and located to the front and the right of this. T loop to the front and the right, opposite to QRS loop.

NOTE: it differentiates from CLBBB by absence of middle-final delay.

ECG/VCG correlation in the horizontal plane type II of VCG.
LVH VCG TYPE IIC

Vector of initial 20 ms to the front and right, counterclockwise proximal portion and most of the loop is clockwise (inverted). Opposite T loop: to the front and the right.

TYPE IIC

PROXIMAL PORTION SMALLER THAN DISTAL
LVH VCG TYPE III

This is the variant frequently found in LVH and high blood pressure characterized by a QRS with the following characteristics:

- Initial vectors heading to the right and discretely to the front
- QRS loop with clockwise rotation (simulating anterolateral myocardial infarction)
- Narrow shape
- Maximal vector with increased voltage (>2mV)
- Located mostly in the left posterior quadrant
- T loop opposite, to the front and the right

VCG in the horizontal plane type III of VCG.
LVH VCG TYPE IV?

Final J point of QRS loop is not coincident with initial 0 point: located to back and rightward

ECG/VCG correlation in the horizontal plane type IV LVH VCG pattern Is this the present case?
VCG CRITERIA FOR DIAGNOSIS OF LVH

• QRS loop morphology: oval shape or figure in eight
• Initial forces to left and anteriorly
• Wide QRS/ST-T angle > 100°. May approach 180°
• The magnitude of the left maximal spatial QRS vector in the FP is ≥2mV
• The magnitude of the left maximal spatial QRS vector in the HP is ≥2.2mV below the age of 50 years and 1.8 above this age.
• The magnitude of the left maximal spatial QRS vector in the in the RSP and is ≥1.6mV
• The left maximal spatial QRS vector in HP directed to back and leftward

VCG features in Hypertrophic Cardiomyopathy

1. Initial conduction delay of QRS loop is the rule.
2. The 10 to 20ms vector is decreased
3. The Left Maximum Spatial Voltage (LMSV) is markedly augmented (averaging 3.8mV). This voltage relate quite well to the left muscle mass calculated from biplane angiogram. LMSV values of 3, 4 and 5 mV related to left ventricular weights of 150, 275 and 400 gm/M2, respectively
4. QRS loop has counterclockwise or figure in eight rotations in horizontal plane
5. QRS loop is located in left posterior quadrant in HP
6. T loop is discordant with QRS loop: QRS/ST/T angle greater than 100°