Hypertrophic Cardiomyopathy Challenging Questions

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- No disclosures

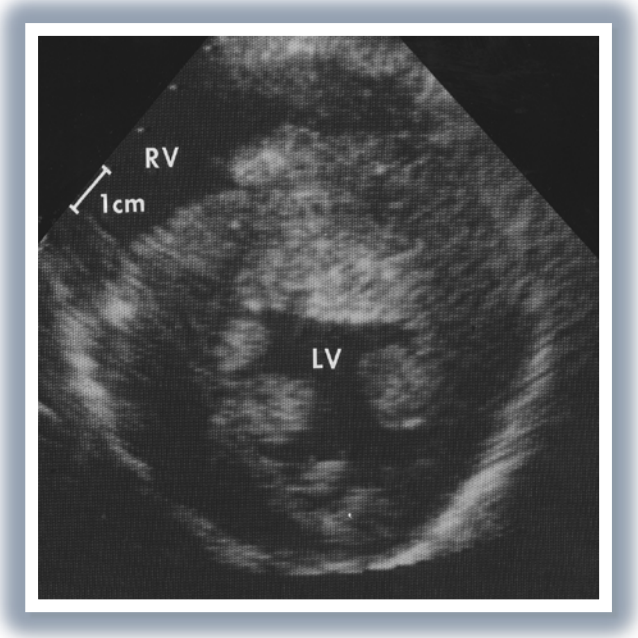
Hypertrophic Cardiomyopathy

- ? Genetics ?
- ? Myectomy ?
- ? Natural history ?
- ? ICD ?

Hypertrophic Cardiomyopathy

- Question 1 : what about genetics and HCM?

Hypertrophic Cardiomyopathy



Old Definition :
Severe hypertrophy of the myocardium in the absence of a known etiology

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"Essentially, HCM is always a genetic disorder..."

Marian and Roberts
Circ 1995: 92: 1336-1347

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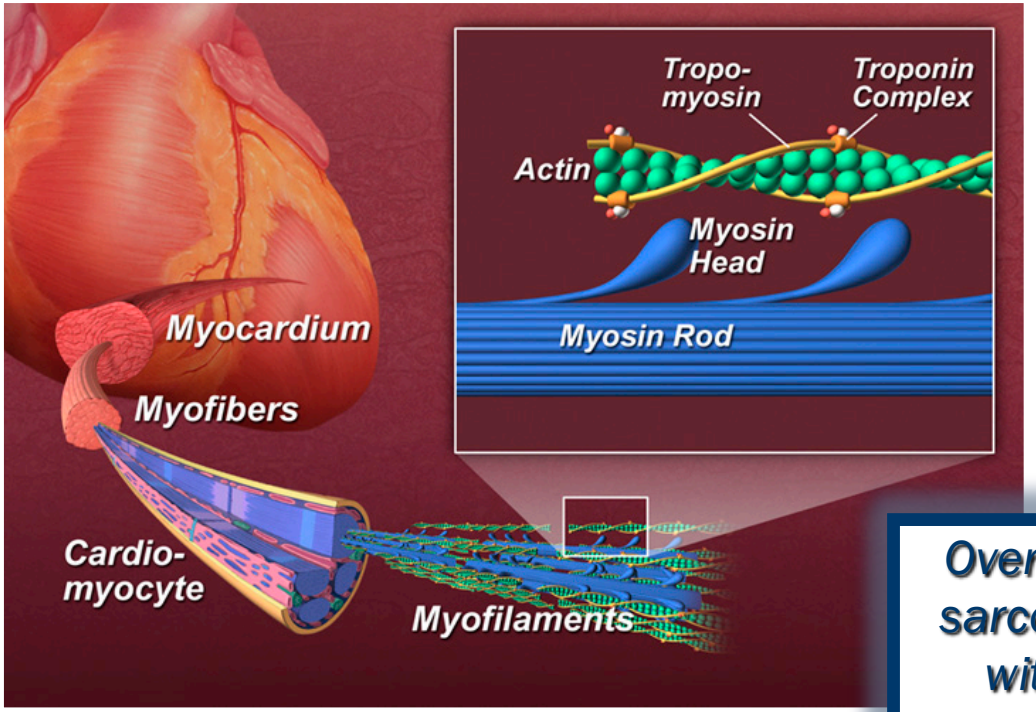

Over 16 defective sarcomeric genes with over 500 different mutations

2 nonsarcomeric genes
(PRKAG2 and LAMP2)

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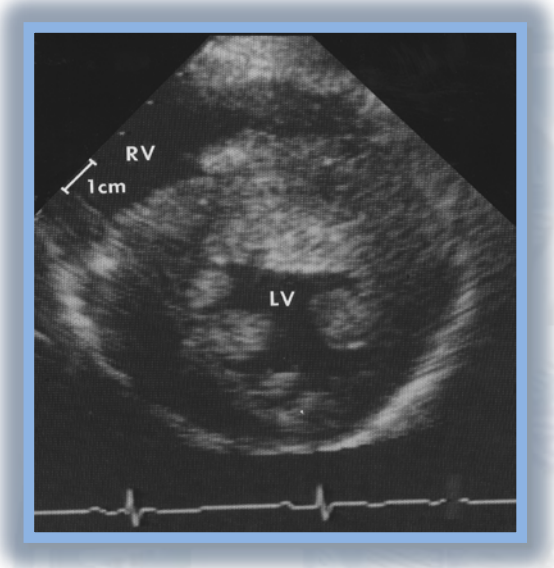
Mutation

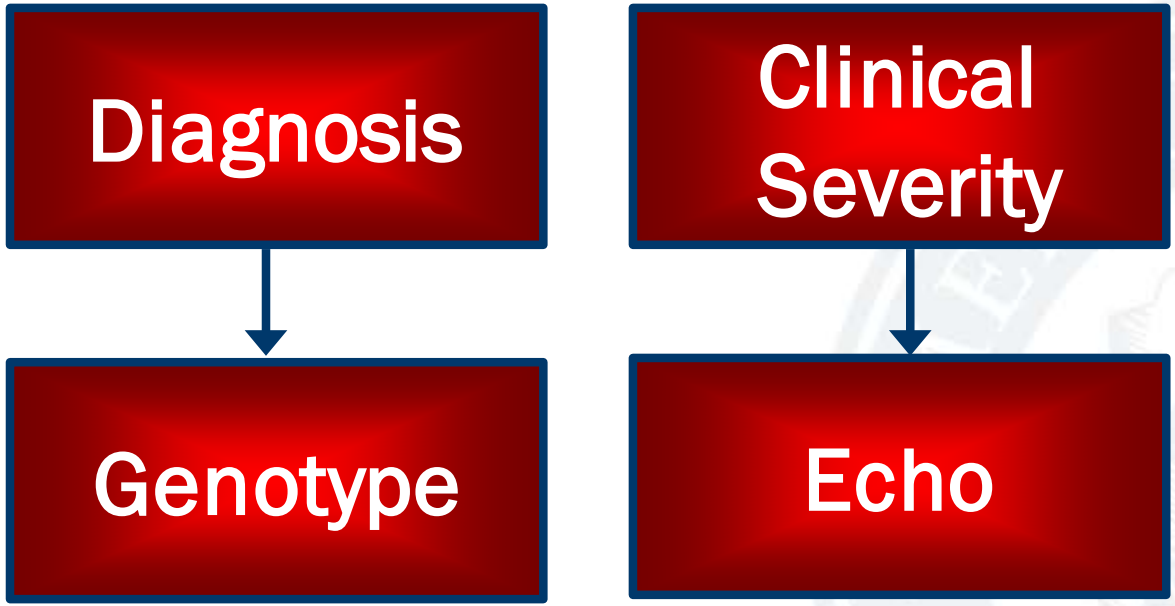
Poison polypeptide

Altered sarcomere structure and function



Compensatory Hypertrophy

Diagnosis of HCM - Year 2020



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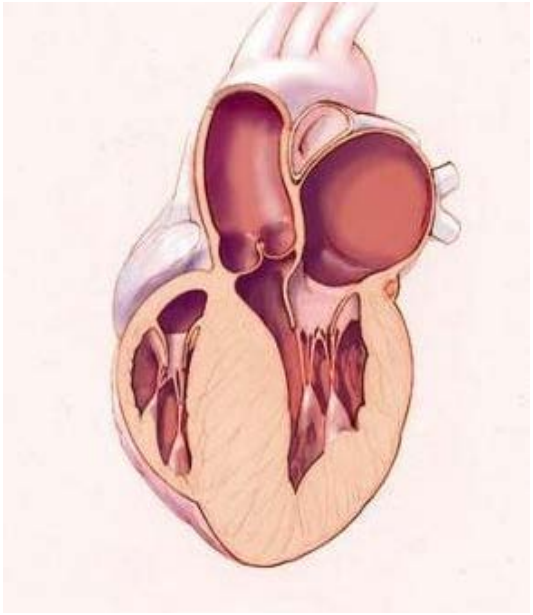
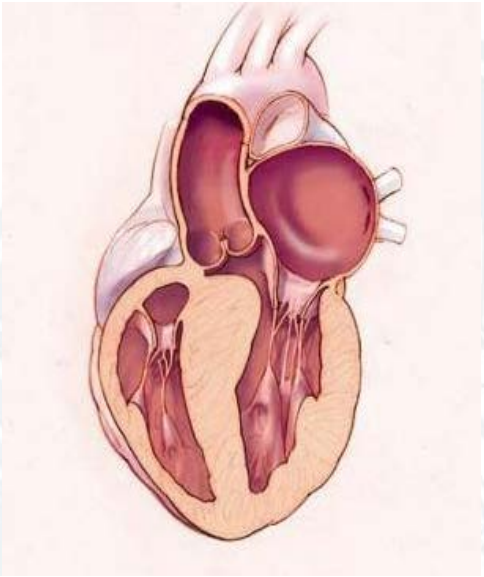
Early age
Spontaneous LVH



Massive LVH
Reverse curve septum
Sudden death

Age related

Later age
Triggered: HTN, AS



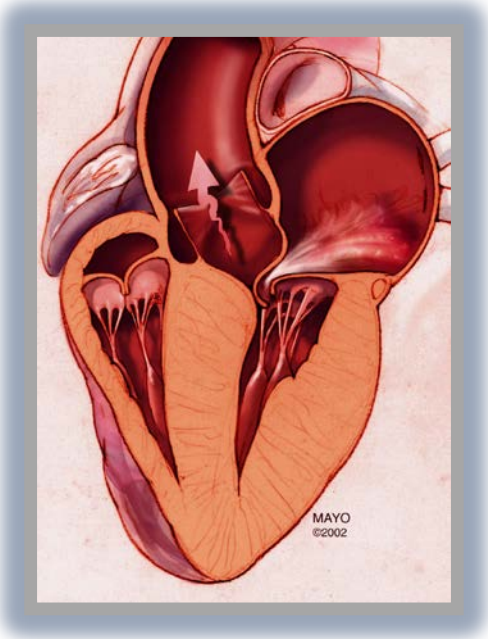
Mild LVH
Sigmoid septum
CHF, AF

Hypertrophic Cardiomyopathy

- Genetics - Clinical implications
  - Screen all first degree relatives
    - Adults every 5 years
    - Adolescents every year (especially athletes)
  - Obtain family history of HCM or sudden death

Hypertrophic Cardiomyopathy

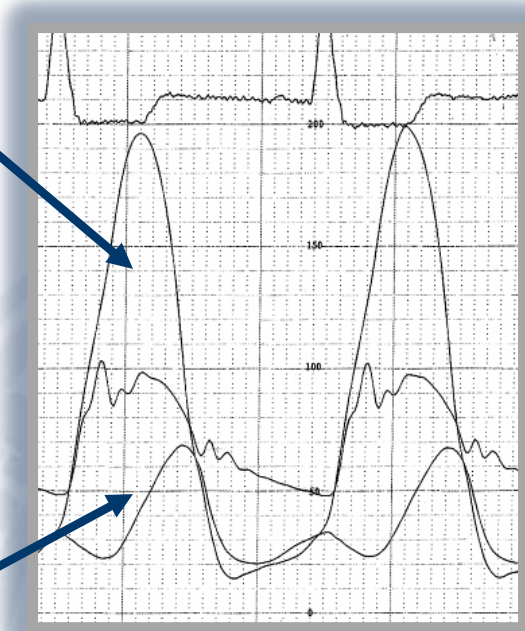
- Question 1 : what about genetics and HCM?
- Question 2 : what about different types of myectomy?



LVO obstruction

- Caused by SAM
- Present in 2/3 pts with HCM
- Major cause of symptoms
  - Ischemia
  - Diastolic dysfunction
  - Mitral regurgitation

Gradient
100 mmHg



LAP
45 mmHg

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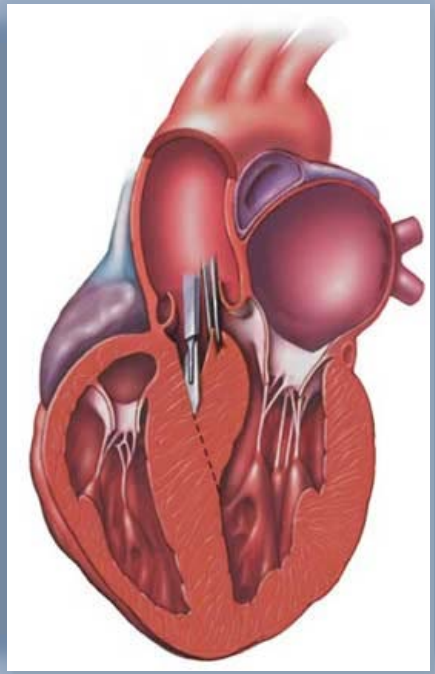
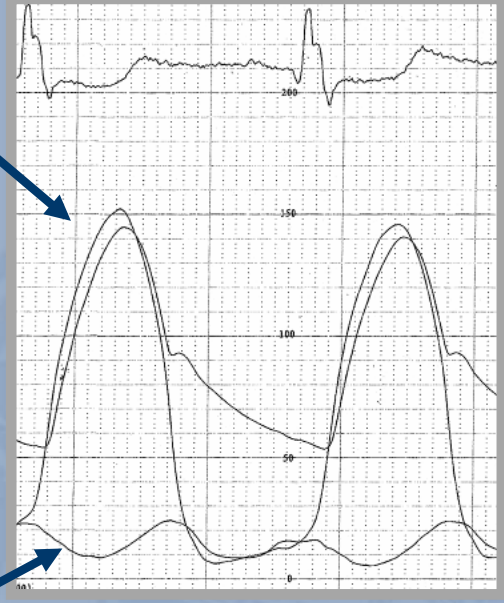


Relieve obstruction
Septal myectomy

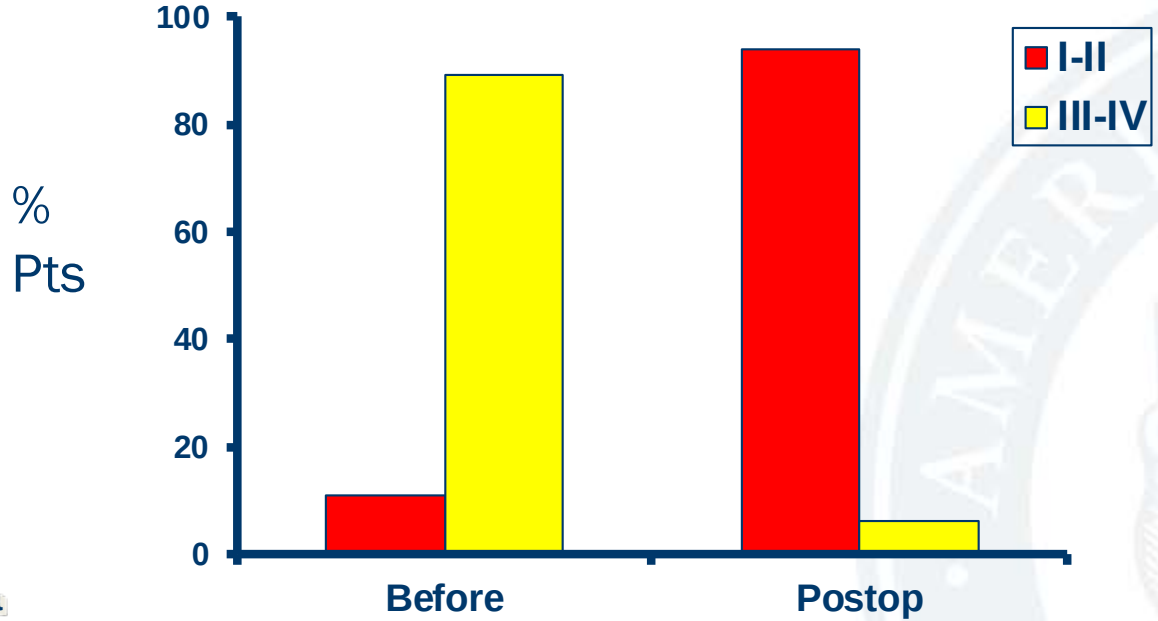
- Transaortic approach
- Operative risk < 1%
- Results
  - Gradient < 10 mmHg
  - No residual MR
  - Complete relief sx

Gradient
10 mmHg



LAP
12 mmHg

Septal Myectomy – 10 yr F/U
Symptomatic Improvement



Mayo Data
350 patients

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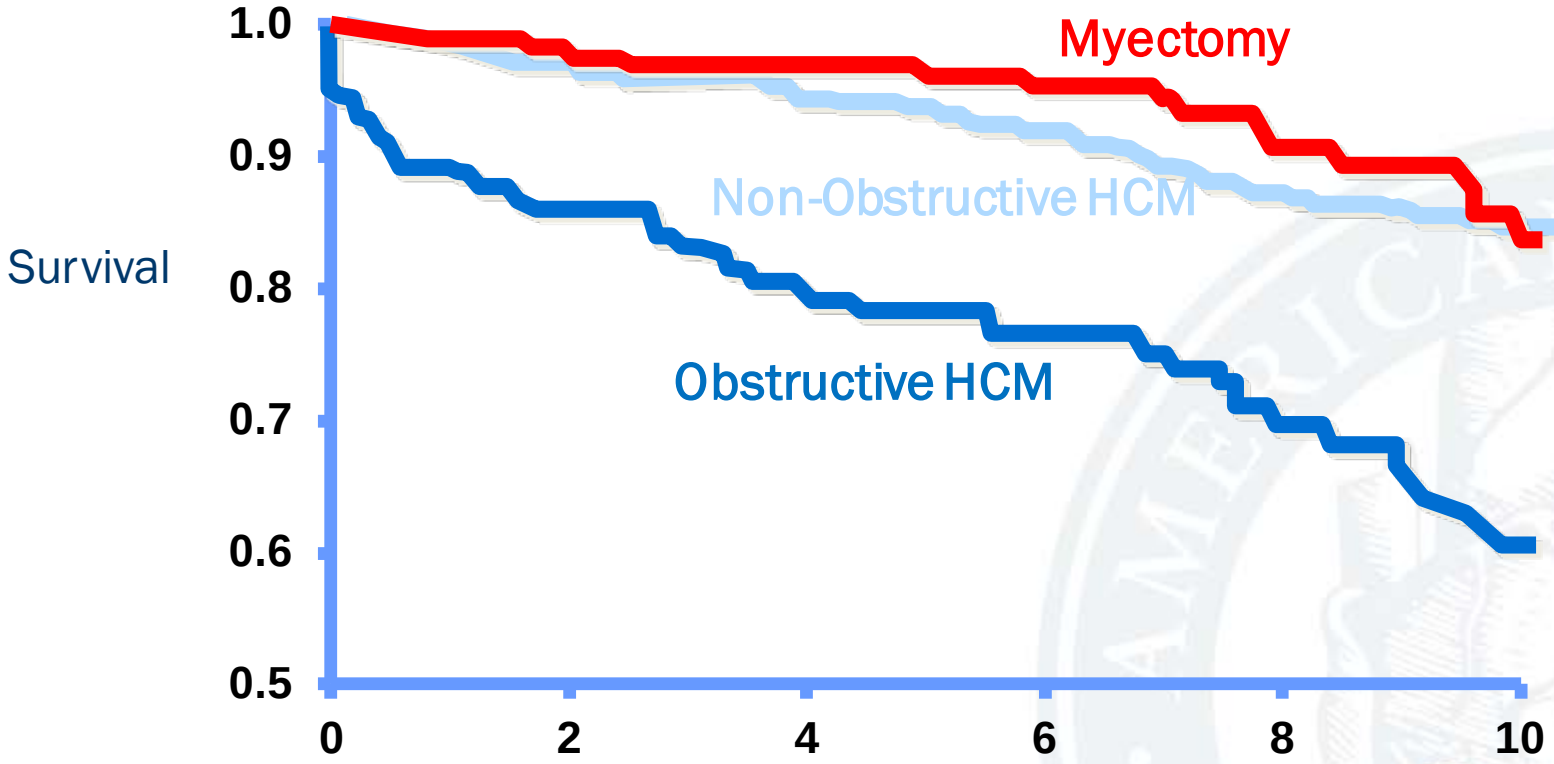
Hypertrophic Cardiomyopathy

It is clear that surgical myectomy will result in marked long-lasting symptomatic improvement in over 90% of patients with severe symptoms and obstruction

Septal Myectomy – Long term outcome



Ommen et al: JACC 2005
Maron et al: NEJM 2003

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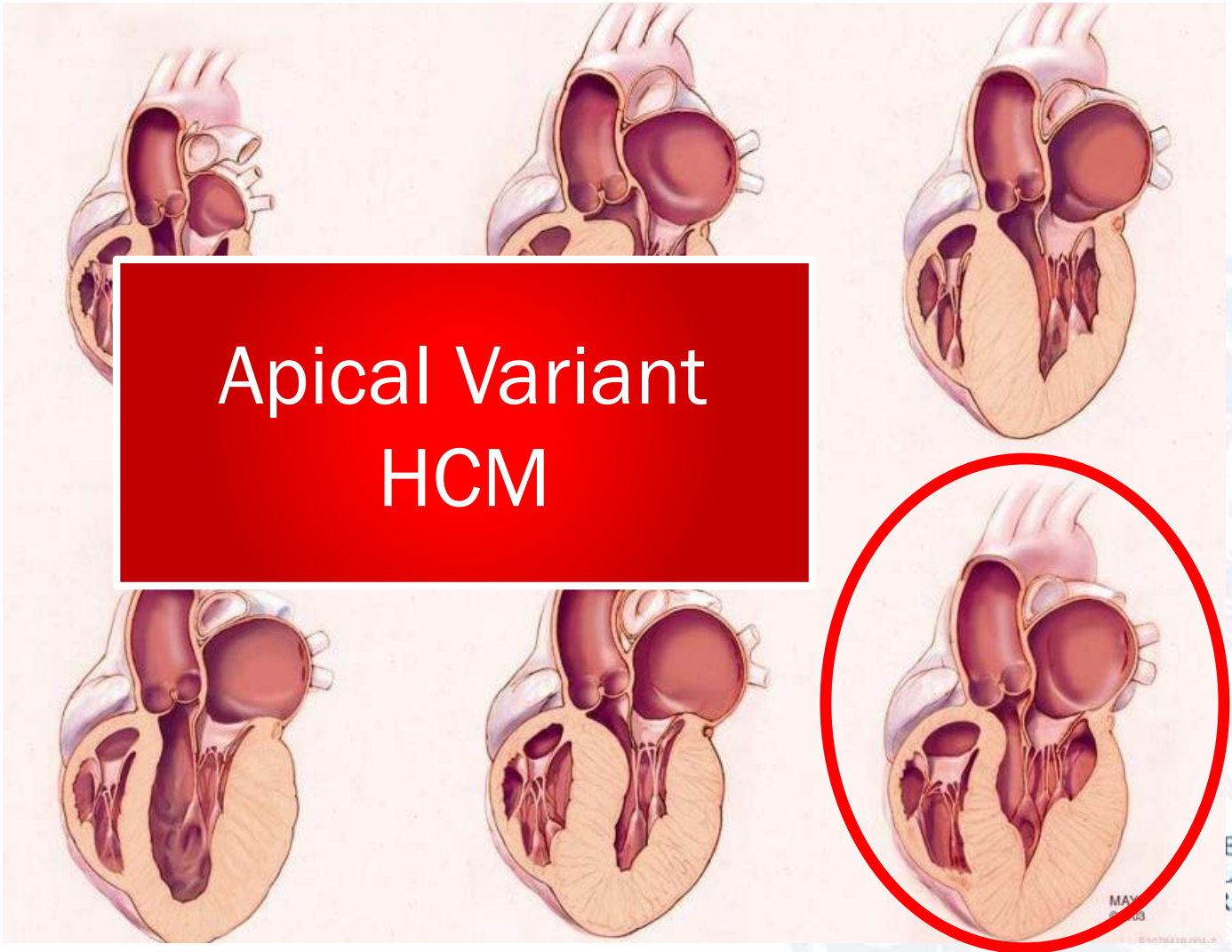
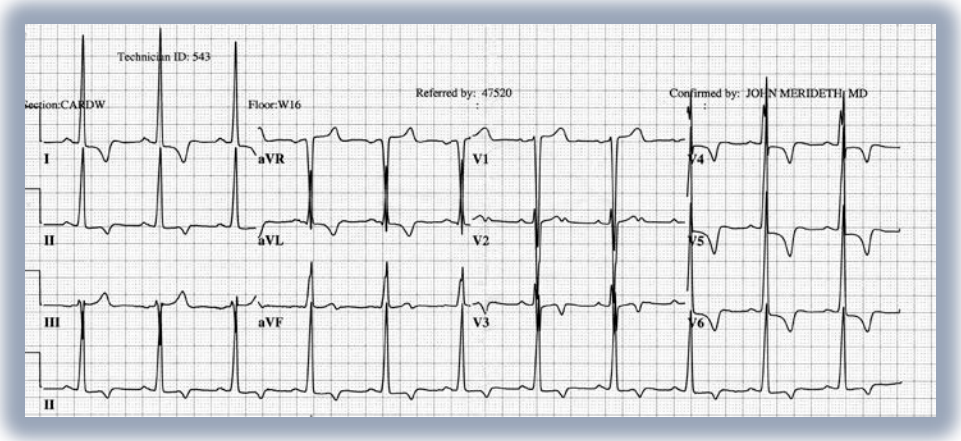

Apical Variant
HCM

Apical HCM

Diffuse symmetric T wave inversions

Disease of diastole

Abnormal effective operative compliance



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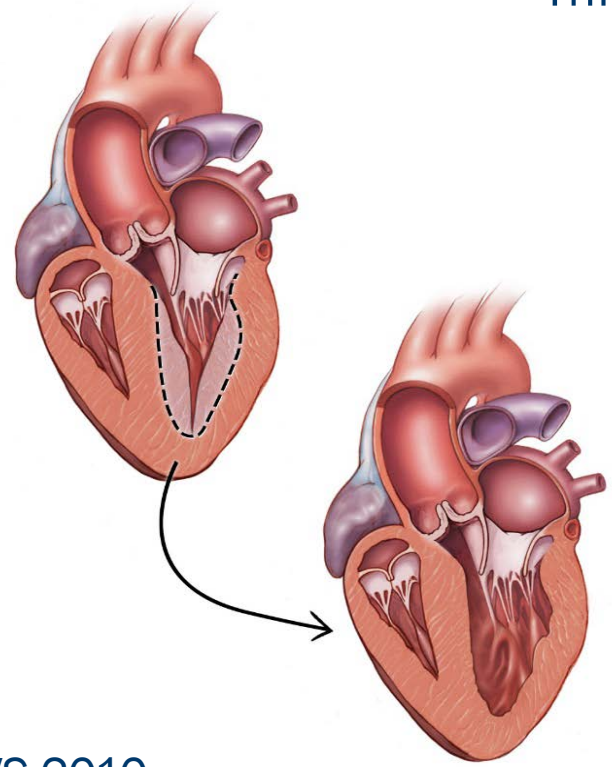
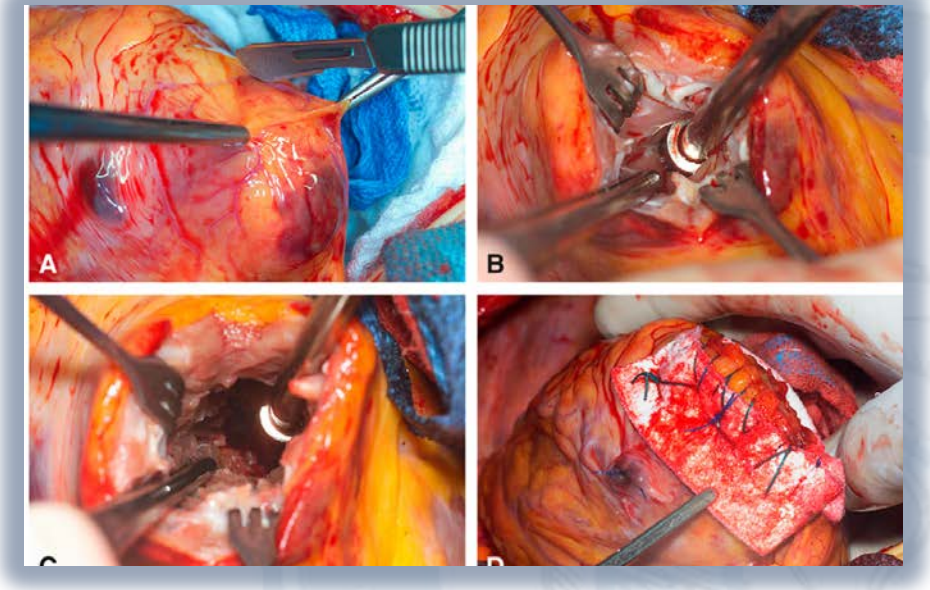
Novel “apical myectomy”
Remove massive myocardium
Through apical approach





JTCVS 2010

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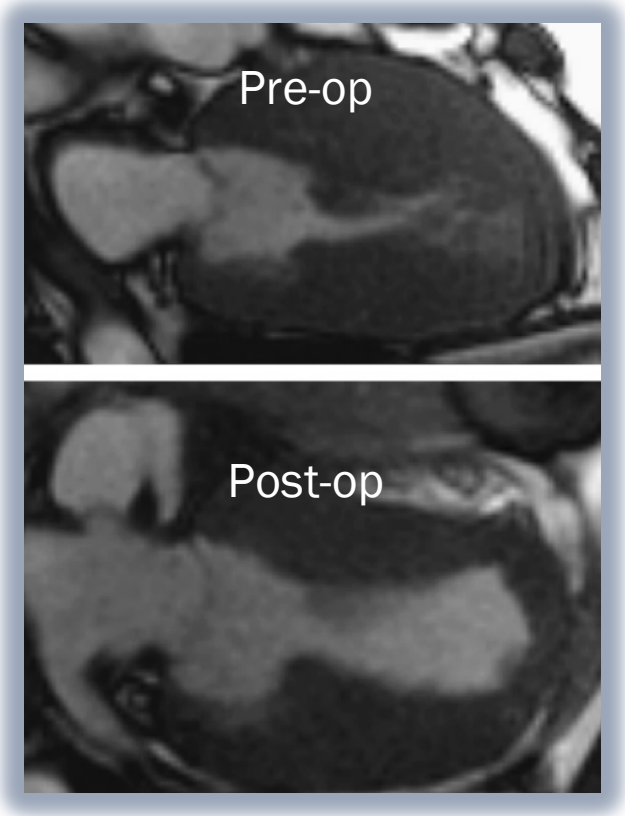
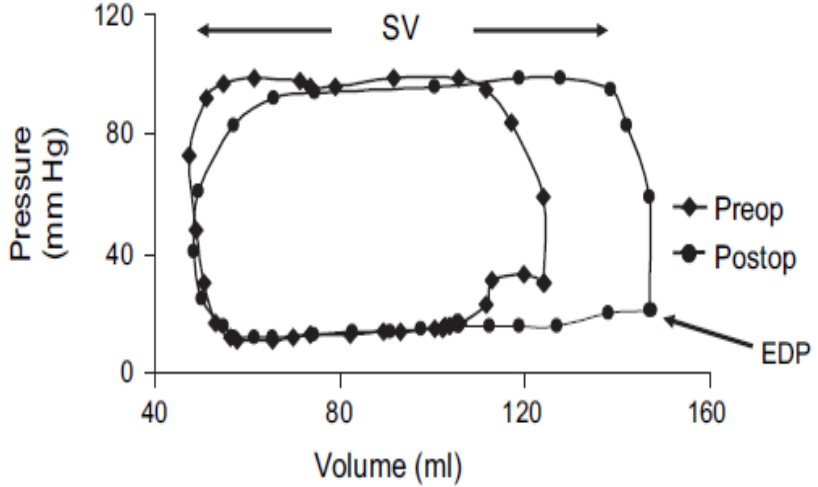


Increase LV volume
Improve effective operative compliance

Improve symptoms of dyspnea



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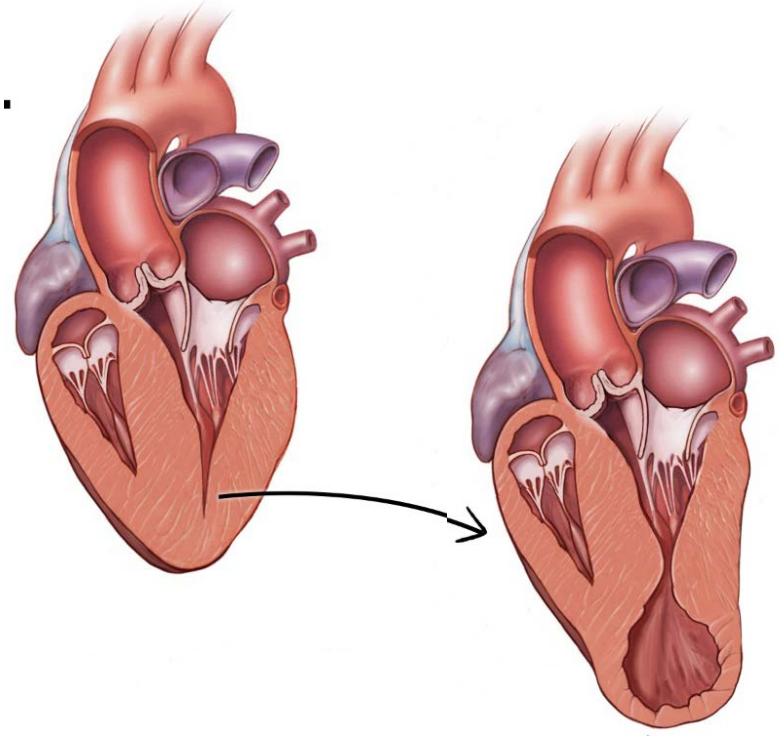


Adverse natural history apical HCM

↓

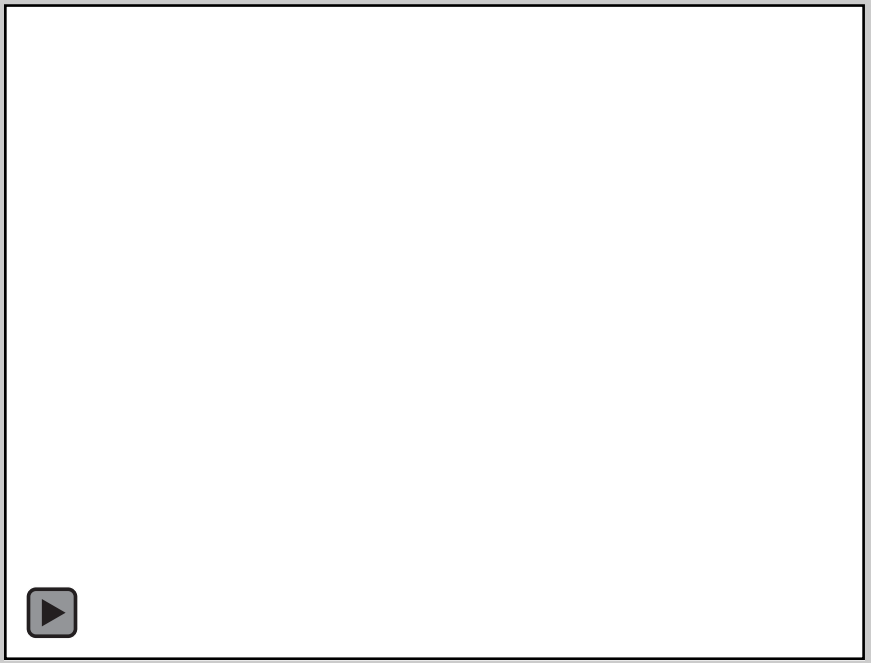
Apical ischemia

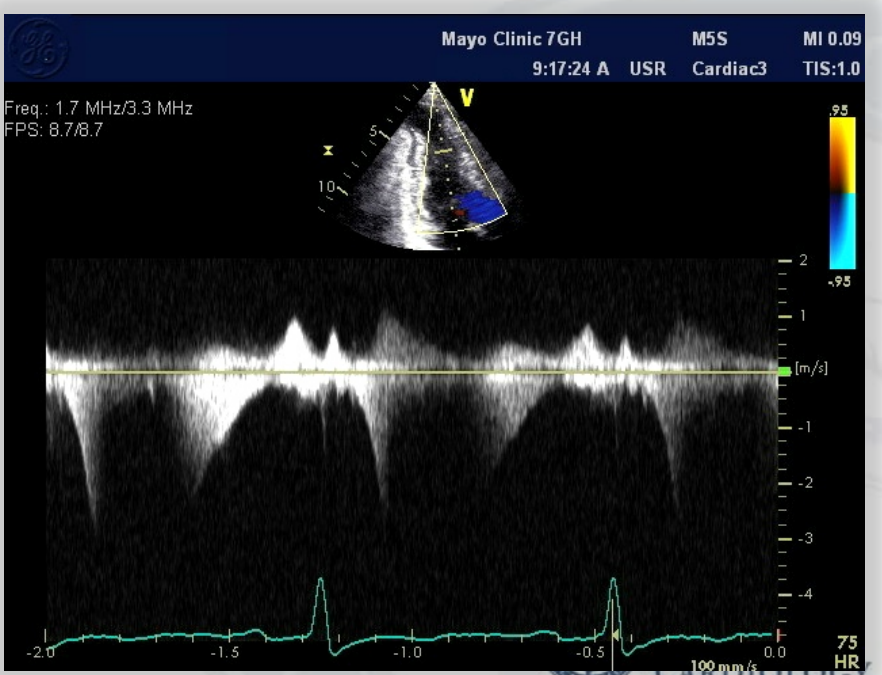
↓

Apical aneurysm + mid obstruction

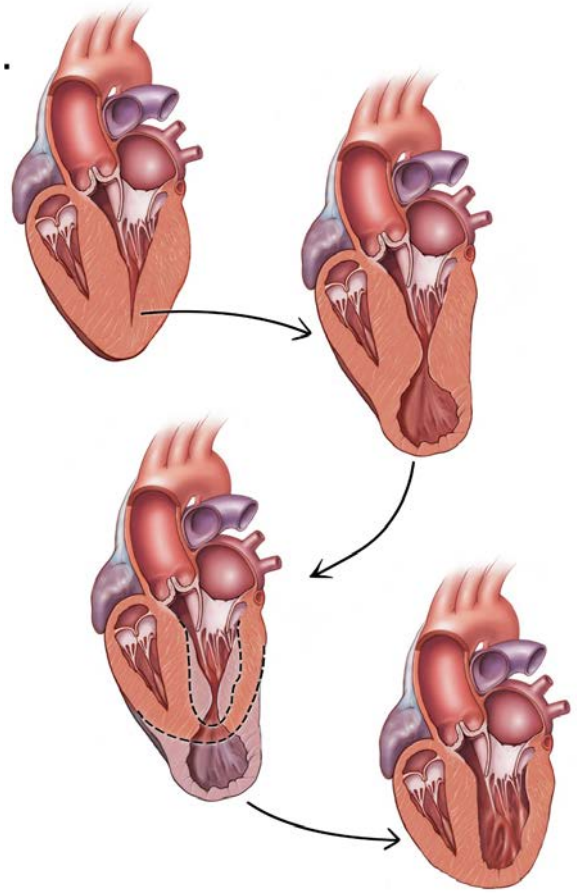
Once development of apical aneurysm

- More symptoms
- Higher risk VT
- Increased risk embolic events





May need contrast enhancement to identify apical aneurysms



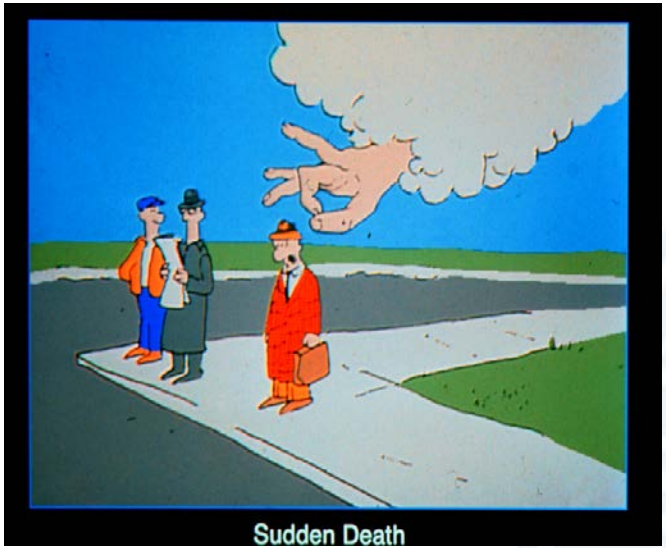
Another type of “myectomy”

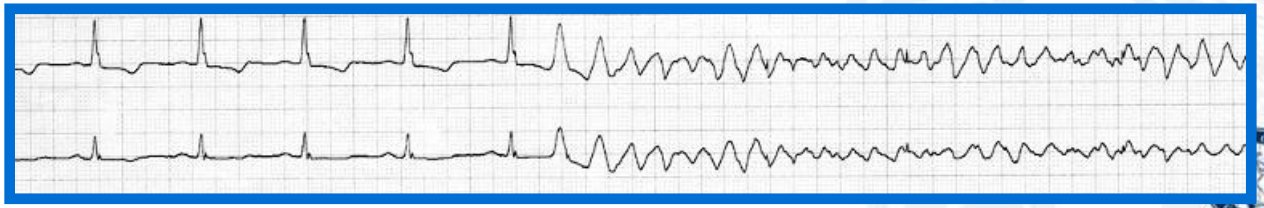
- Transapical approach
- Resect midventricular obstruction
- Resect apical aneurysm

Hypertrophic Cardiomyopathy

- Question 1 : what about genetics and HCM?
- Question 2 : what about different types of myectomy?
- Question 3 and 4: what about natural history and sudden death?

Sudden death in HCM pts





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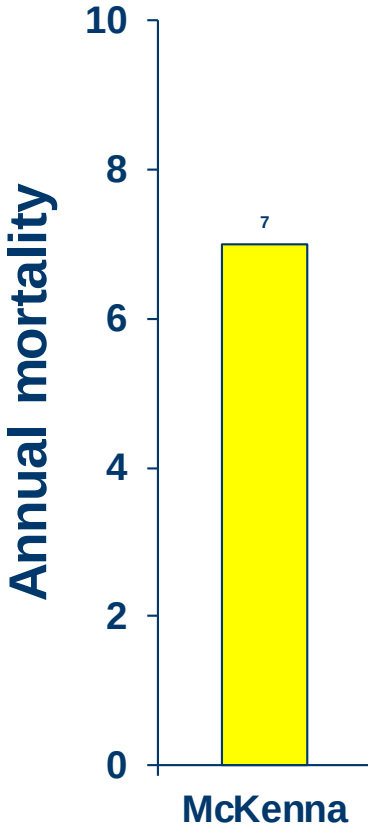
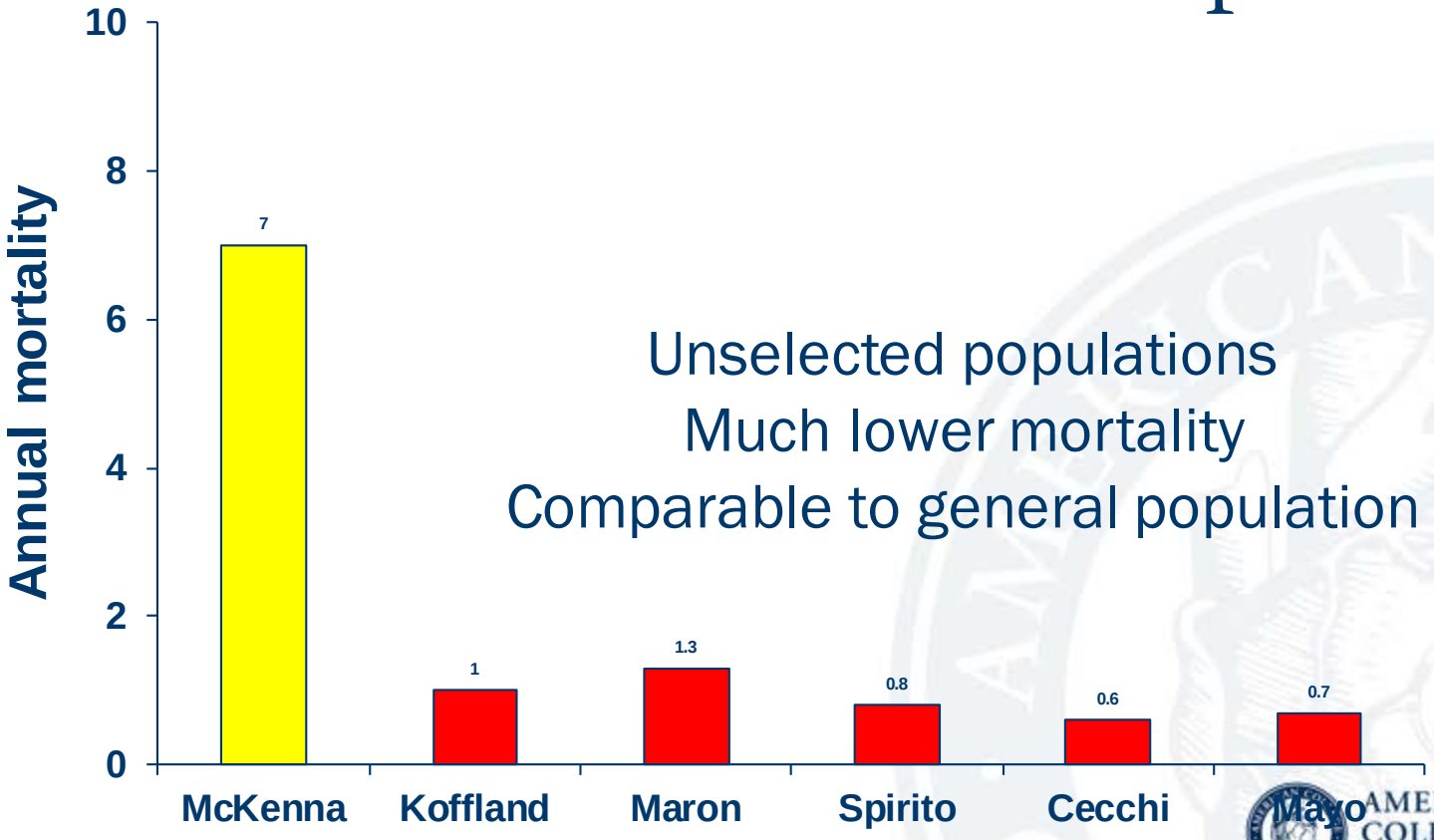
Sudden death in HCM pts



Initial studies at referral centers
High annual mortality (4-7%/yr)
Majority due to sudden death

Sudden death in HCM pts



Unselected populations
Much lower mortality
Comparable to general population

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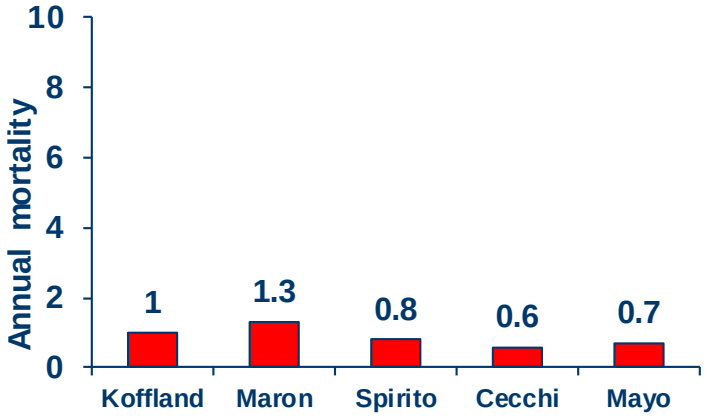
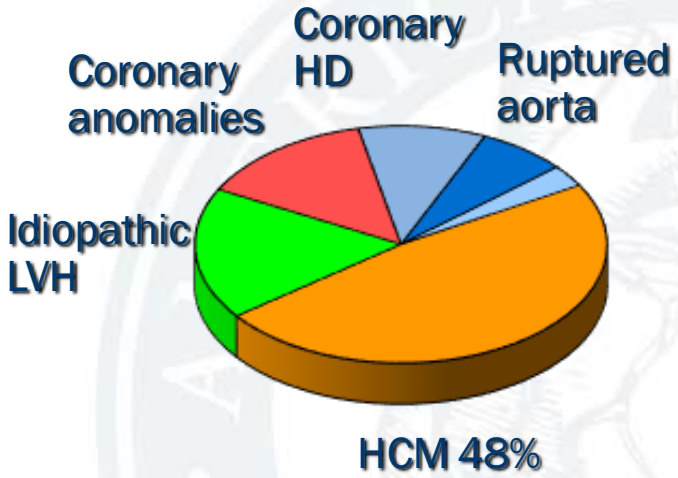
Sudden death in HCM pts

Low Annual Mortality Overall



Most Common Cause Sudden Death In Young



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Sudden death in HCM pts

- ✓ Unpredictable - years go by
- ✓ AICD can be lifesaving
- ✓ Can we predict who is at risk?

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PRACTICE GUIDELINE

2011 ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy

A Report of the American College of Cardiology Foundation/
American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons

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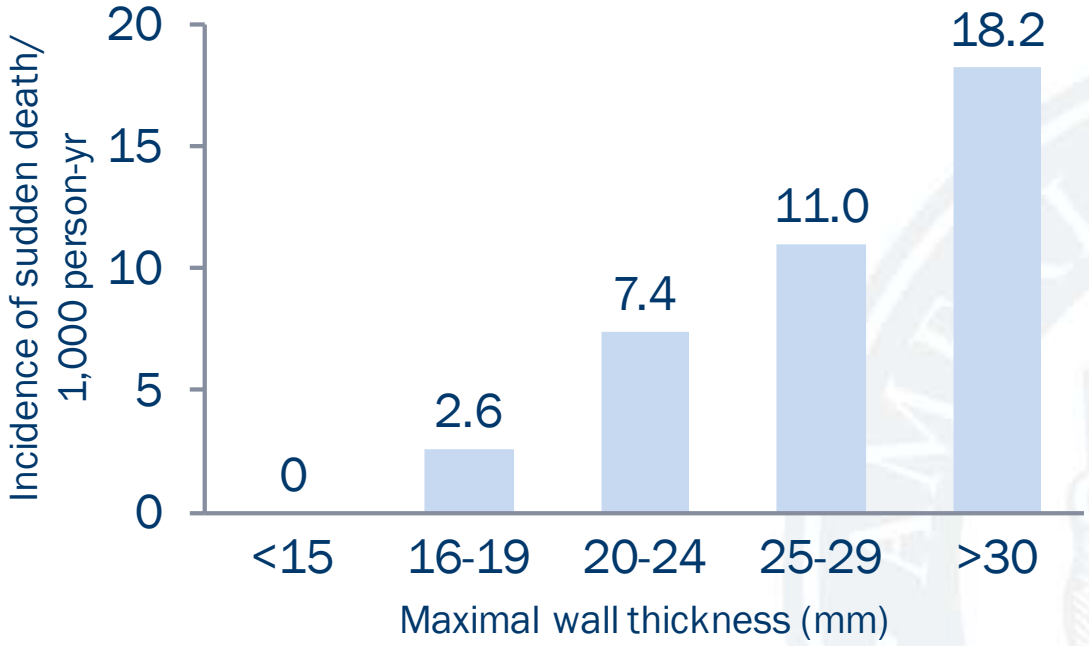
Risk Factors – Literature

- Out-of-hospital arrest
- Sustained VT
- Family history sudden death – HCM
- Massive hypertrophy
- Syncope
- NSVT on Holter
- TMET – VT or drop BP

Sudden death in HCM pts



NEJM 342:24:1778, Sept 19, 2000

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ACC/AHA Guidelines

Really Bad

Arrest
Sustained VT

Bad

FH HCM and Sudden death
LVH > 30 mm
Unexplained syncope

Somewhat Bad

NSVT
BP drop TMET
LVO
CAD

This is the best that we had..
But positive predictive accuracy < 15%

20-25% incidence
Inappropriate shocks
(younger active population of HCM)

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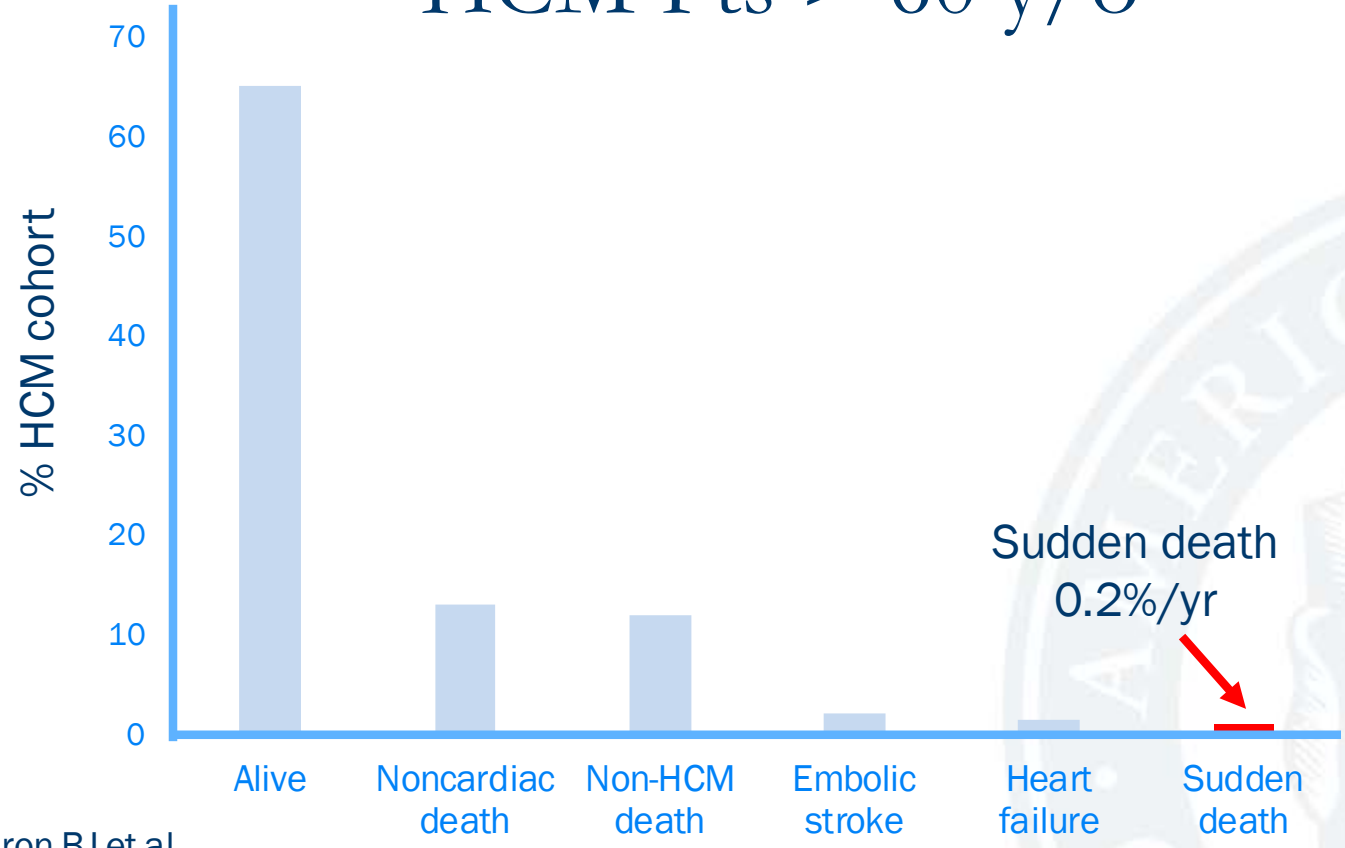
Sudden death in HCM pts
What's New?

- ✓ Age is important
- ✓ MRI with gadolinium
- ✓ Risk scores

HCM Pts > 60 y/o



Maron BJ et al
Circulation 2013:127:585

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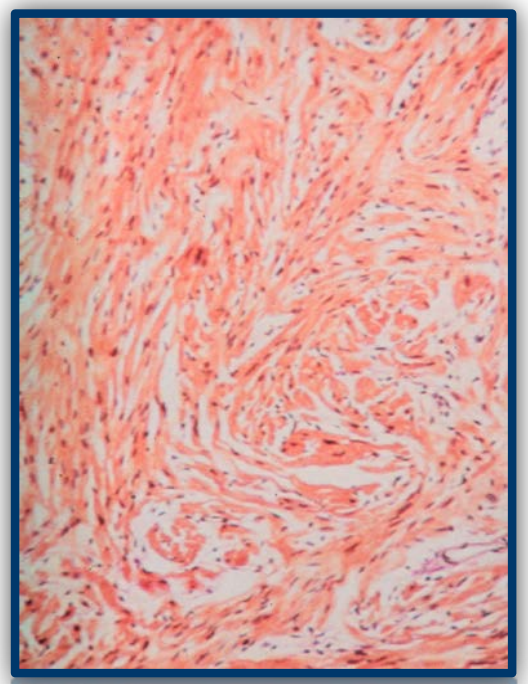
Sudden death in HCM pts
Age is important

- ✓ 76 y/o man with syncope after getting up in the middle of the night
- ✓ 23 y/o college student who suddenly passes out in class

Myocyte Disarray



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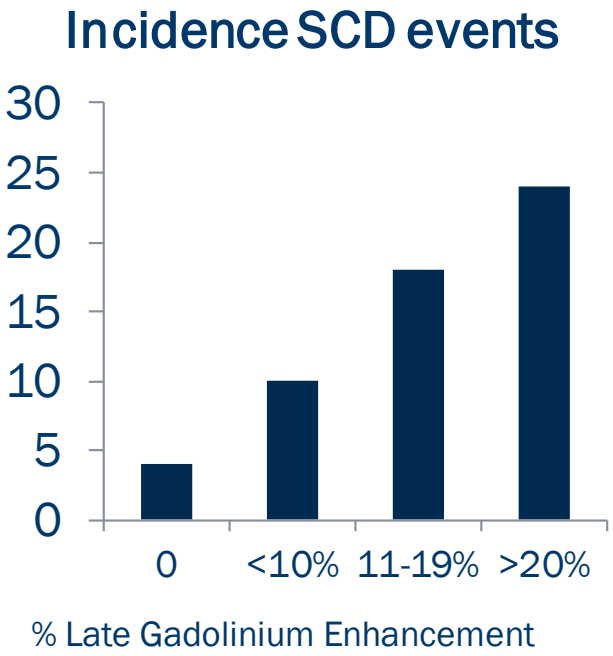
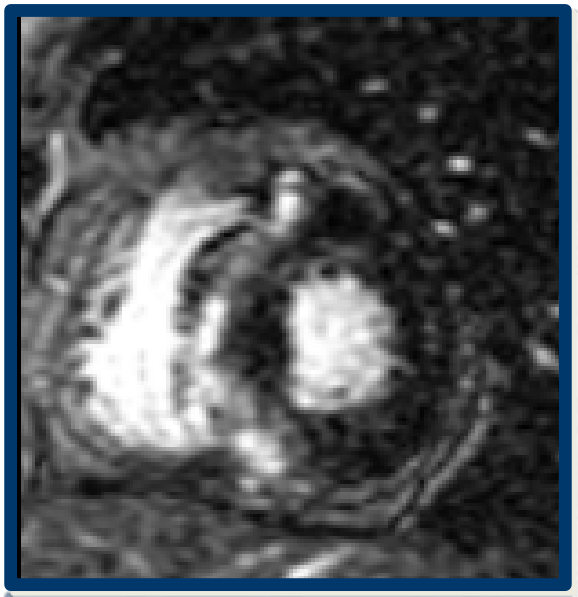
Gadolinium Enhancement Defects on MRI

1293 HCM pts – F/U 3.3 yrs





Chan et al: Circulation 2014:130:484-495

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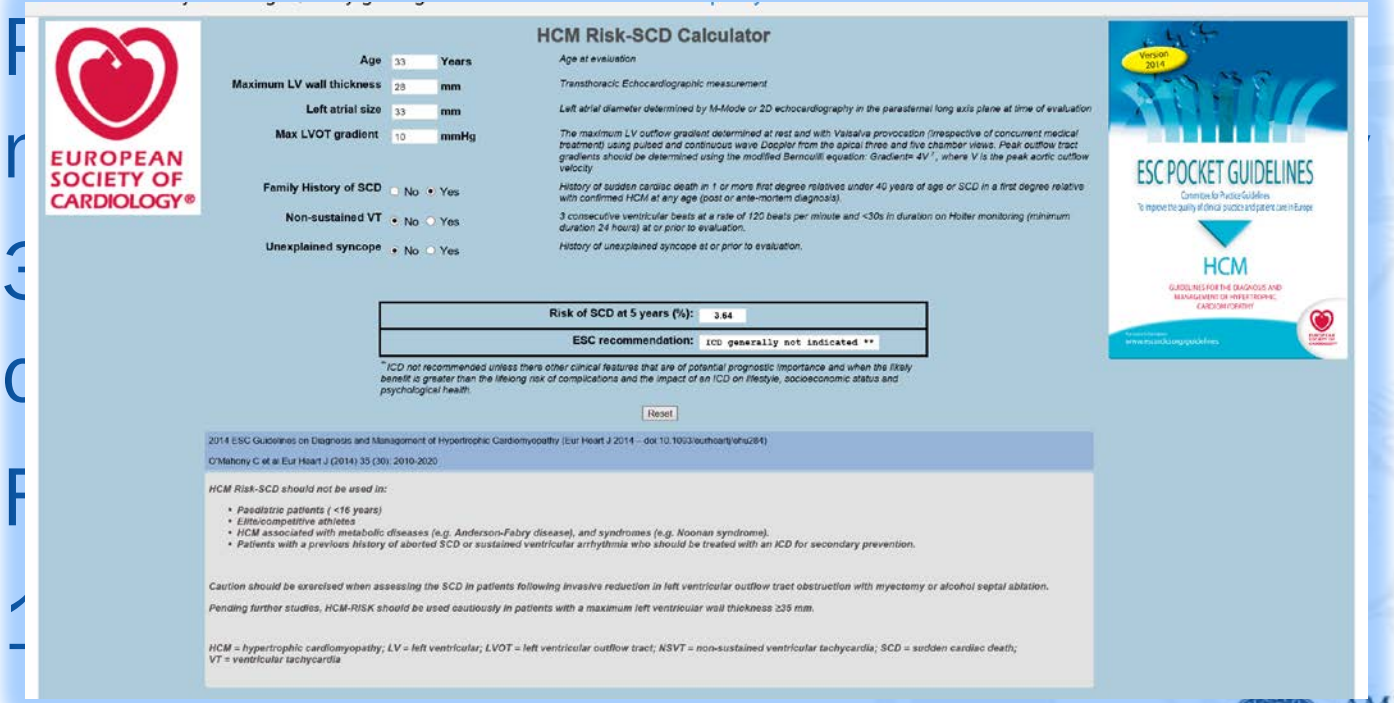
HCM Risk-SCD Calculator (ESC)

- F
- r
- 3
- C
- F
- 1



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HCM Risk-SCD Calculator

Age	33 Years	*Age at evaluation*
Maximum LV wall thickness	28 mm	*Transthoracic Echocardiographic measurement*
Left atrial size	33 mm	*Left atrial diameter determined by M-Mode or 2D echocardiography in the parasternal long axis plane at time of evaluation*
Max LVOT gradient	10 mmHg	*The maximum LV outflow gradient determined at rest and with Valsalva provocation (irrespective of concurrent medical treatment) using pulsed and continuous wave Doppler from the apical three and five chamber views. Peak outflow tract gradients should be determined using the modified Bernoulli equation: Gradient= 4V², where V is the peak aortic outflow velocity*
Family History of SCD	○ No ◉ Yes	*History of sudden cardiac death in 1 or more first degree relatives under 40 years of age or SCD in a first degree relative with confirmed HCM at any age (post or ante-mortem diagnosis).*
Non-sustained VT	◉ No ○ Yes	*3 consecutive ventricular beats at a rate of 120 beats per minute and <30s in duration on Holter monitoring (minimum duration 24 hours) at or prior to evaluation.*
Unexplained syncope	◉ No ○ Yes	*History of unexplained syncope at or prior to evaluation.*

Risk of SCD at 5 years (%):	3.64
ESC recommendation:	ICD generally not indicated **

** *ICD not recommended unless there other clinical features that are of potential prognostic importance and when the likely benefit is greater than the lifelong risk of complications and the impact of an ICD on lifestyle, socioeconomic status and psychological health.*

Reset

2014 ESC Guidelines on Diagnosis and Management of Hypertrophic Cardiomyopathy (Eur Heart J 2014 – doi:10.1093/eurheartj/ehu284)

O'Mahony C et al Eur Heart J (2014) 35 (30): 2010-2020

HCM Risk-SCD should not be used in:

- *Paediatric patients (<16 years)*
- *Elite/competitive athletes*
- *HCM associated with metabolic diseases (e.g. Anderson-Fabry disease), and syndromes (e.g. Noonan syndrome).*
- *Patients with a previous history of aborted SCD or sustained ventricular arrhythmia who should be treated with an ICD for secondary prevention.*

Caution should be exercised when assessing the SCD in patients following invasive reduction in left ventricular outflow tract obstruction with myectomy or alcohol septal ablation.

Pending further studies, HCM-RISK should be used cautiously in patients with a maximum left ventricular wall thickness ≥35 mm.

HCM = hypertrophic cardiomyopathy; LV = left ventricular; LVOT = left ventricular outflow tract; NSVT = non-sustained ventricular tachycardia; SCD = sudden cardiac death; VT = ventricular tachycardia

O'Mahony et al European Heart Journal 2014:35:2010

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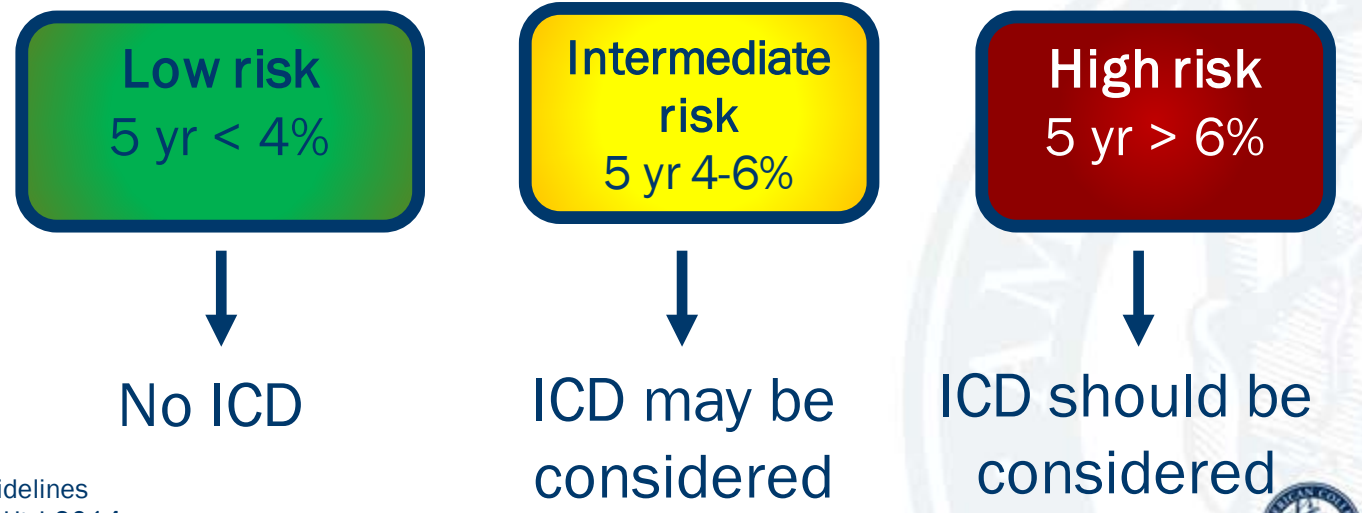
HCM Risk Score



ESC guidelines
European Ht J 2014

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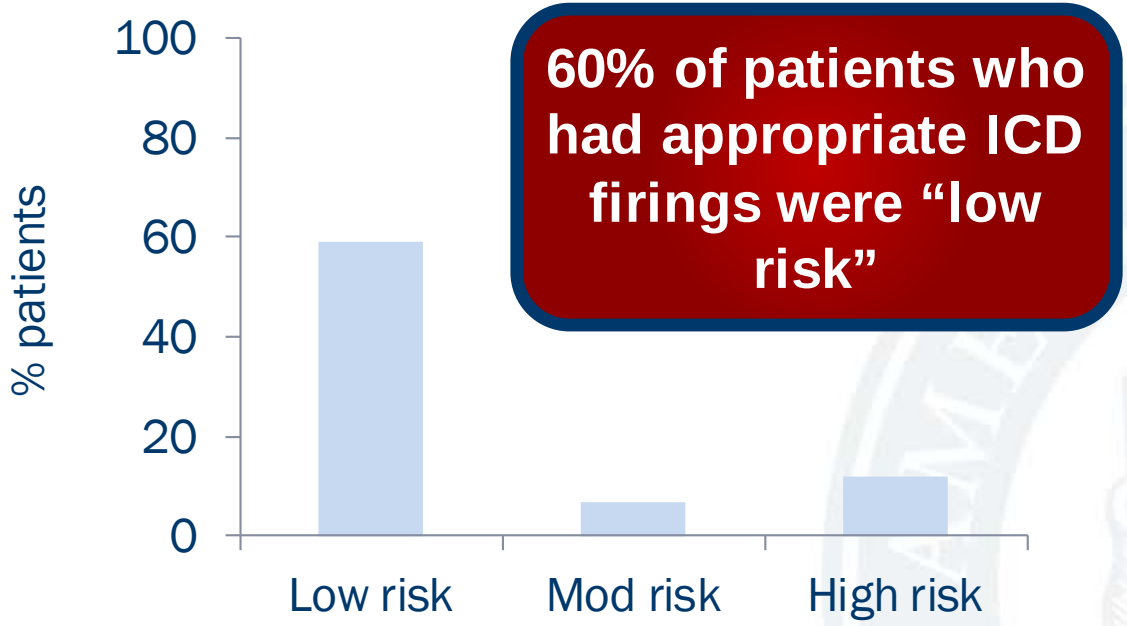
Patients who had appropriate firings from ICD vs ESC risk score



60% of patients who had appropriate ICD firings were "low risk"

Maron et al : AJC 2015

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Patients who had appropriate firings from ICD vs ESC risk score

“Missed”

22% of patients who had appropriate ICD firings were “low risk”

Young
Severe LVH

Young
Strong FH

Mayo Data

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Putting it altogether
Consideration of AICD in HCM

FH sudden death
1º relative
Sudden death < 40 y/o
Sudden death with HCM

Massive LVH
> 30 mm
> 25 mm*
*young age
*MRI GE

Syncope
Unexplained
Young
Recent

All others: Calculate ESC risk score
Consider AICD if 5 yr risk > 6%

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Putting it altogether
Consideration of AICD in HCM

This needs to be a shared decision making process involving the needs and preferences of the patient and resources available

Hypertrophic Cardiomyopathy

- ? Genetics ?
- ? Myectomy ?
- ? Natural history ?
- ? ICD ?

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48 y/o man with HCM– Asymptomatic

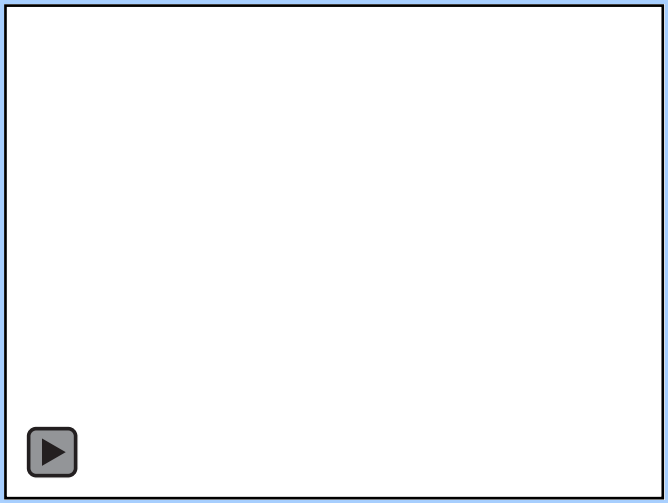
No FH HCM or sudden death

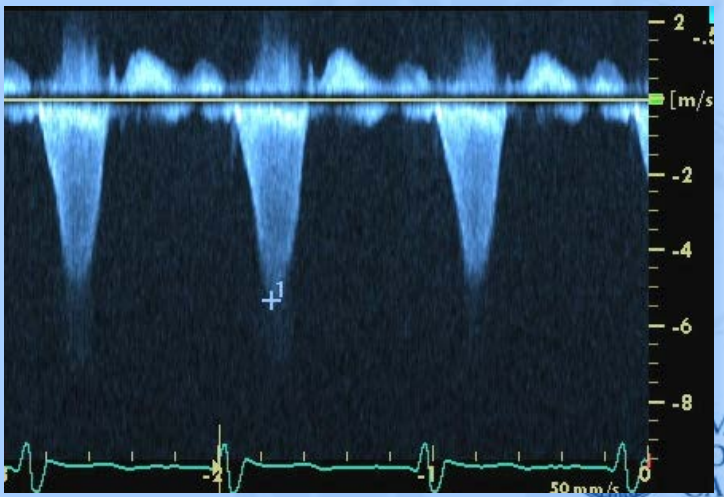
On lopressor 200 mg per day

Septal thickness 3.2 cm

LVO gradient 90 mmHg

Normal coronaries – 2 mm septal





What would you do now?

1. Implant ICD
2. Add disopyramide
3. Septal ablation
4. Septal myectomy

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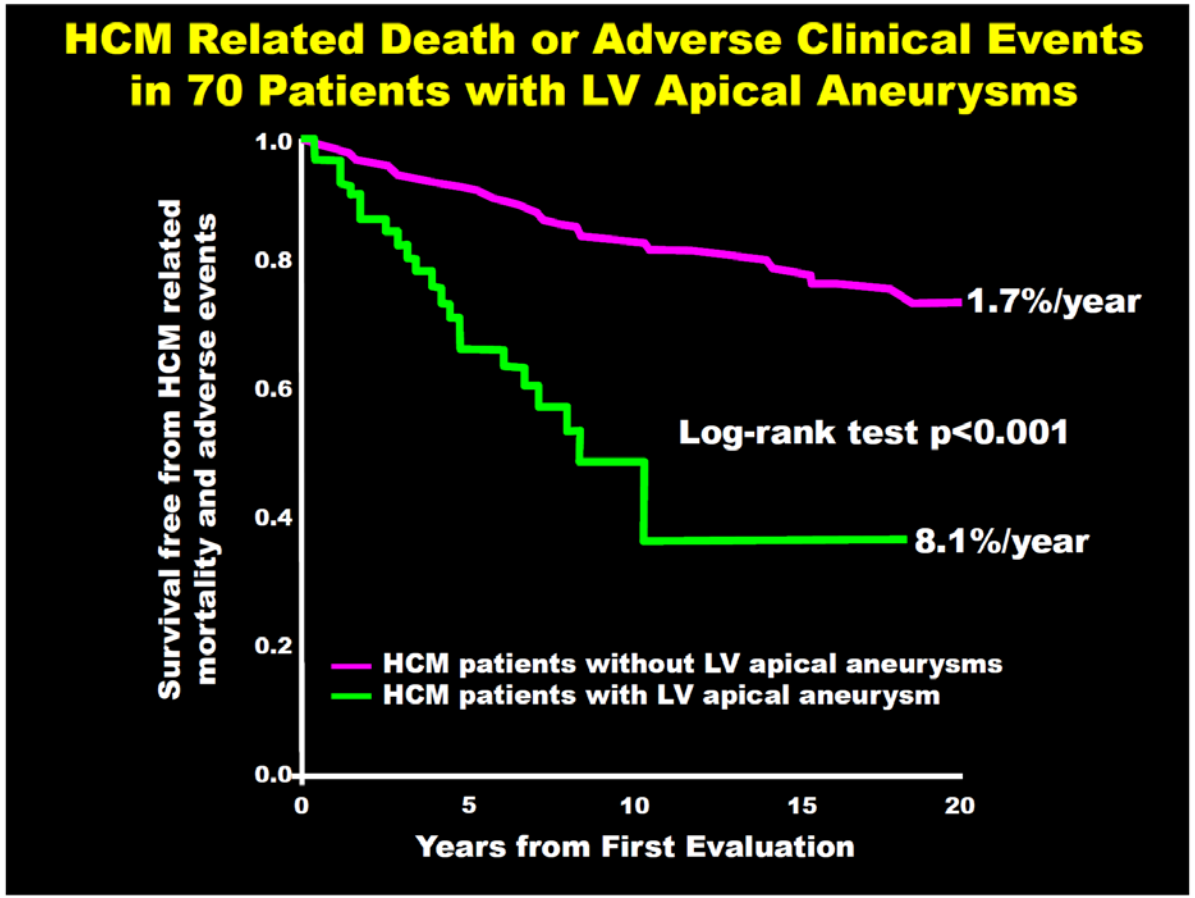
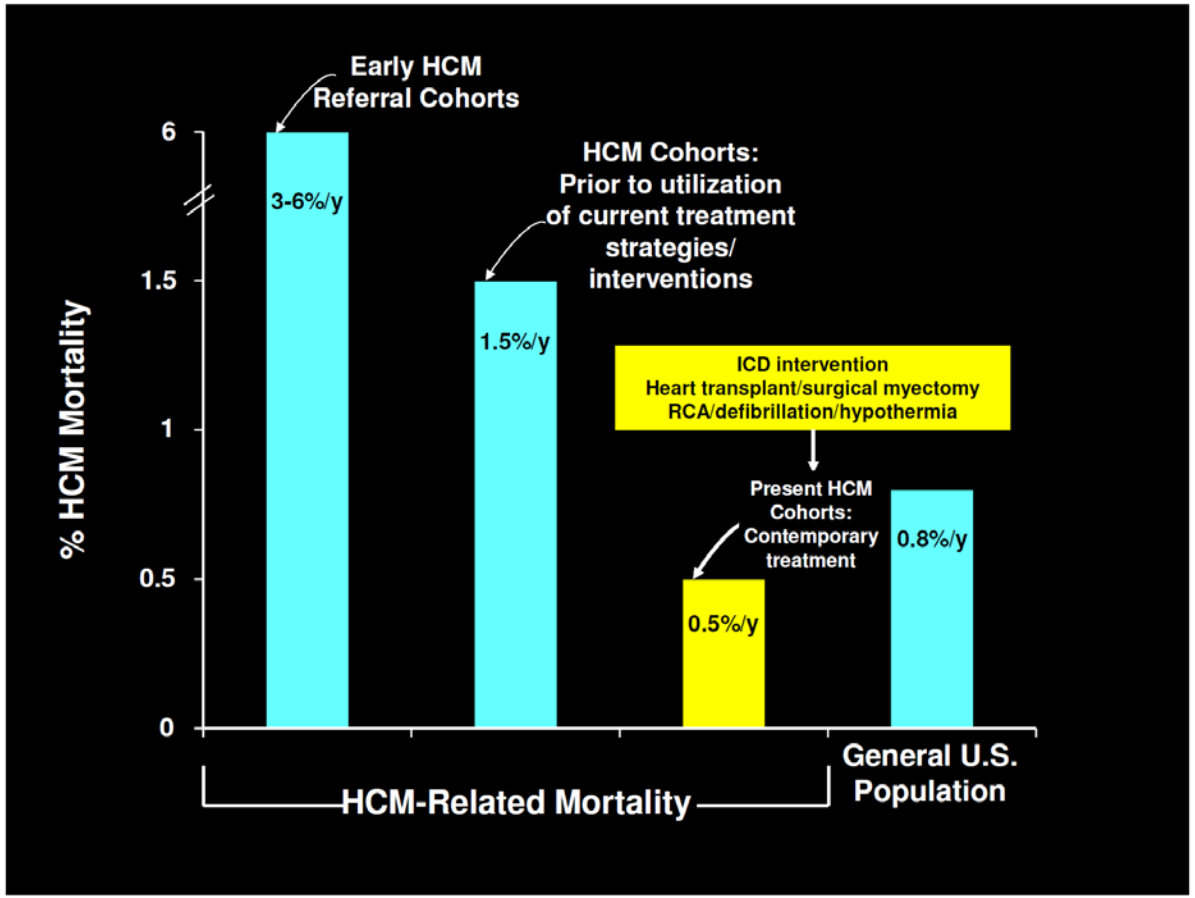

HCM Related Death or Adverse Clinical Events
in 70 Patients with LV Apical Aneurysms
Survival free from HCM related mortality and adverse events
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
Years from First Evaluation
1.7%/year
Log-rank test p<0.001
8.1%/year
HCM patients without LV apical aneurysms
HCM patients with LV apical aneurysm


Early HCM
Referral Cohorts
HCM Cohorts:
Prior to utilization
of current treatment
strategies/
interventions
ICD intervention
Heart transplant/surgical myectomy
RCA/defibrillation/hypothermia
Present HCM
Cohorts:
Contemporary
treatment
% HCM Mortality
6
1.5
1
0.5
0
3-6%/y
1.5%/y
0.5%/y
0.8%/y
HCM-Related Mortality
General U.S.
Population