Recognizing HCM and HF: making the diagnosis

Mariana Brandão, MD

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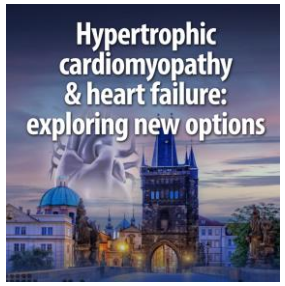
Hypertrophic cardiomyopathy & heart failure: exploring new options



Recognizing HCM and HF: making the diagnosis

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EACVI Web&Communication Committee

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Disclosures

Nothing to declare.

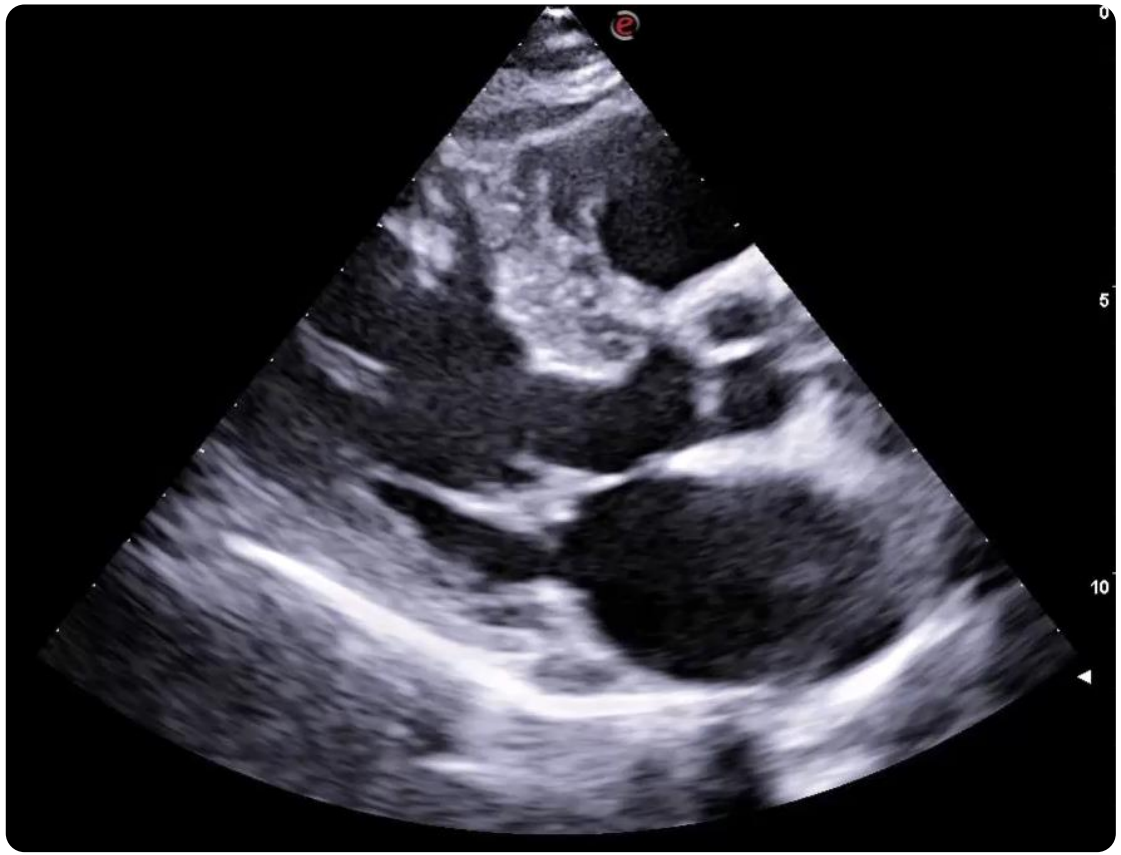
Hypertrophic cardiomyopathy

Unexplained hypertrophy (LV end-diastolic wall thickness of **≥15 mm**),

Ø of another disease capable of producing the magnitude of observed LVH

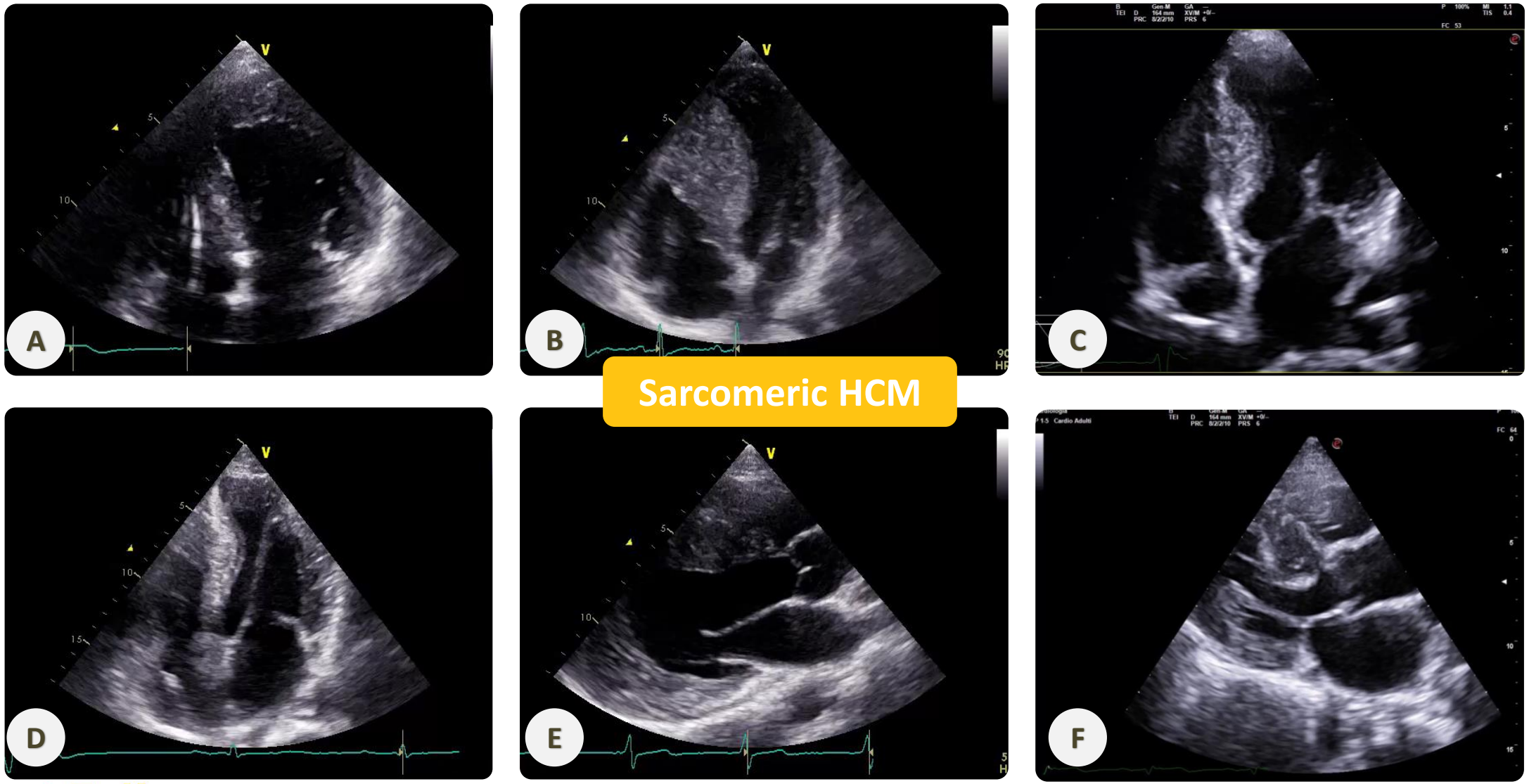
Unexplained hypertrophy (LV end-diastolic wall thickness of **≥13 mm**), in **family members** of HCM patients, or patients with a **positive genetic test**

- Prevalence 1:200 – 1:500
- Pattern of inheritance: autosomal dominant
- Incomplete penetrance, variable phenotypic expression

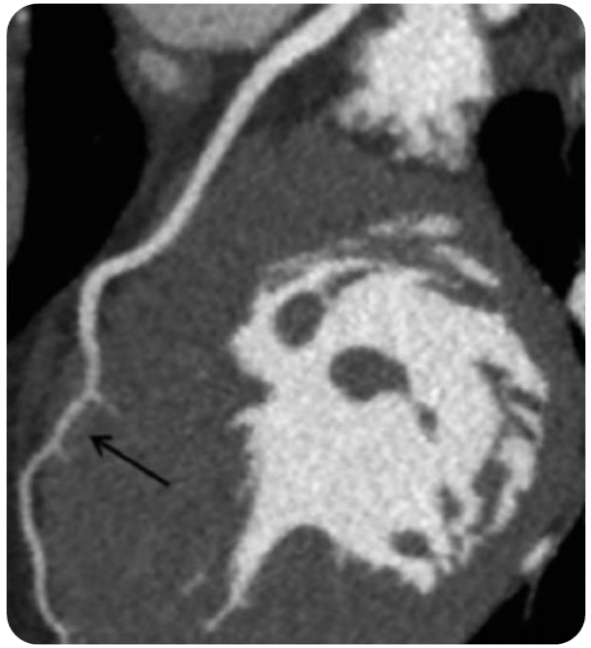


Ommen *et al.* Circulation. 2020

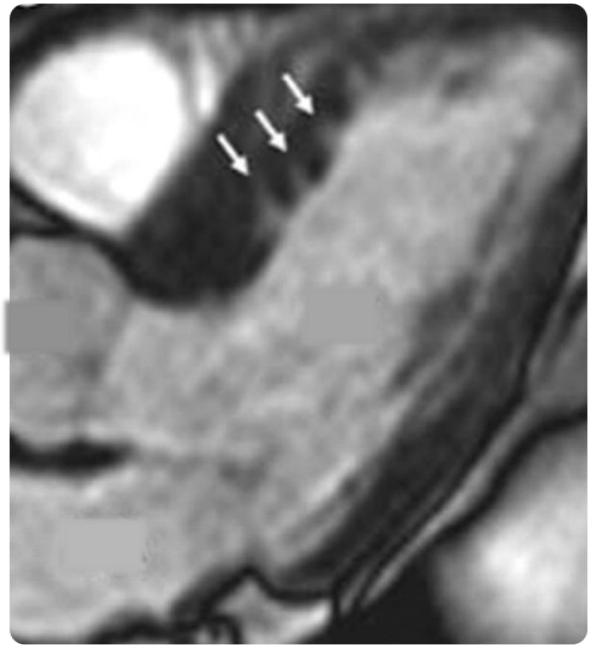
HCM: variable phenotypic expression



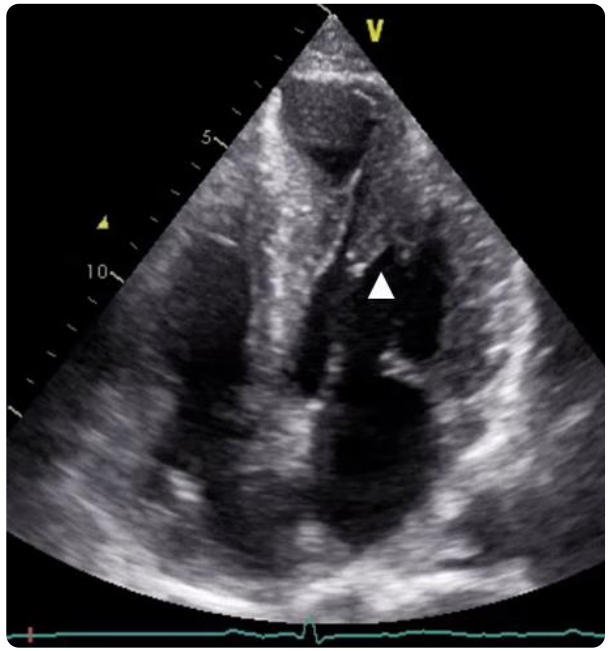
HCM is not only LVH!

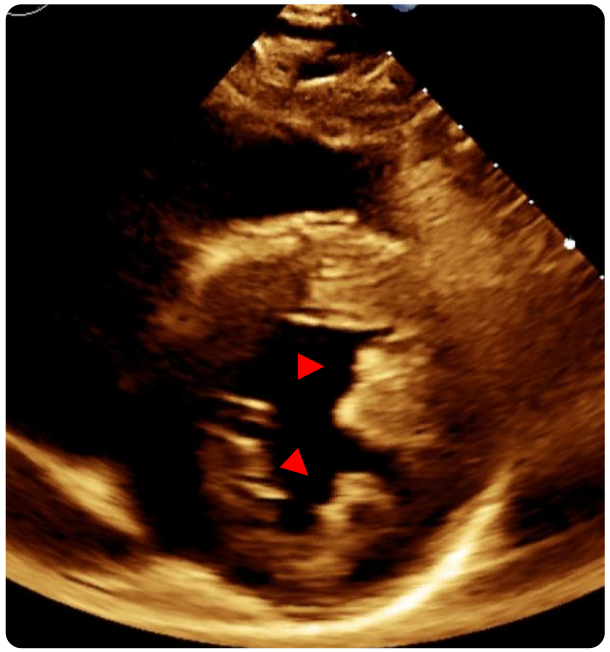


Myocardial bridging



Myocardial crypts



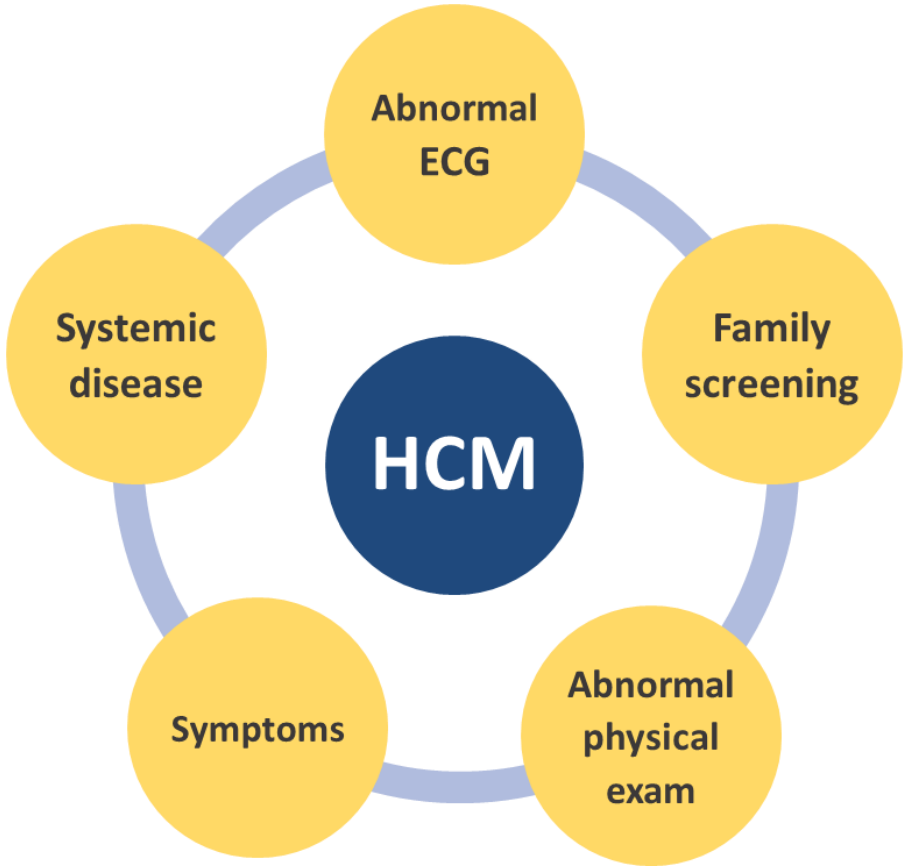


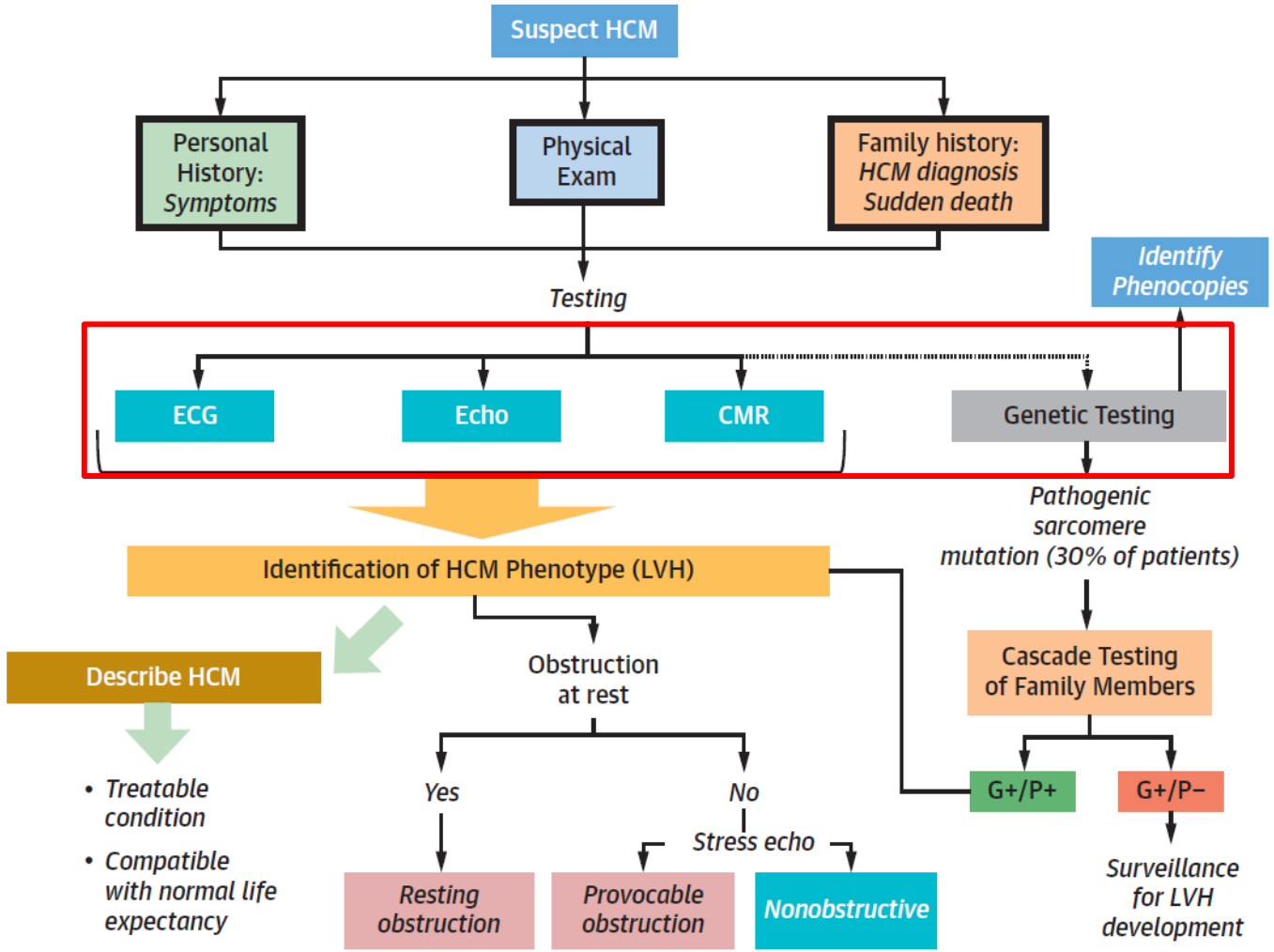
Papillary muscle abnormalities

Bifid, displaced, apically inserted papillary muscles

Non-diagnostic features!

HCM: clinical presentation

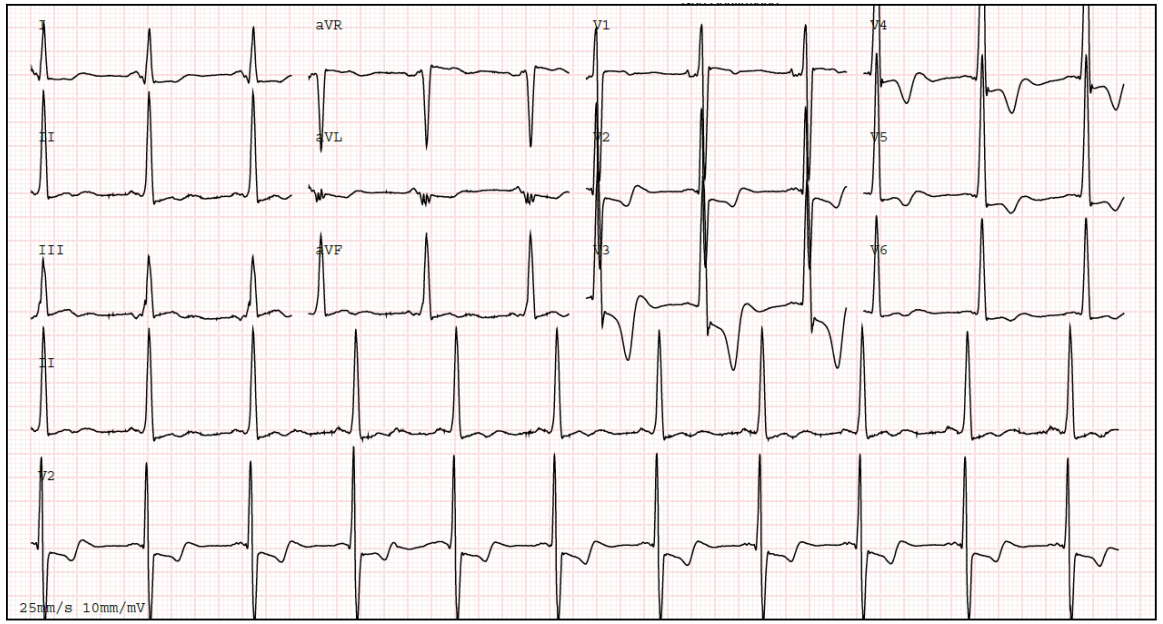




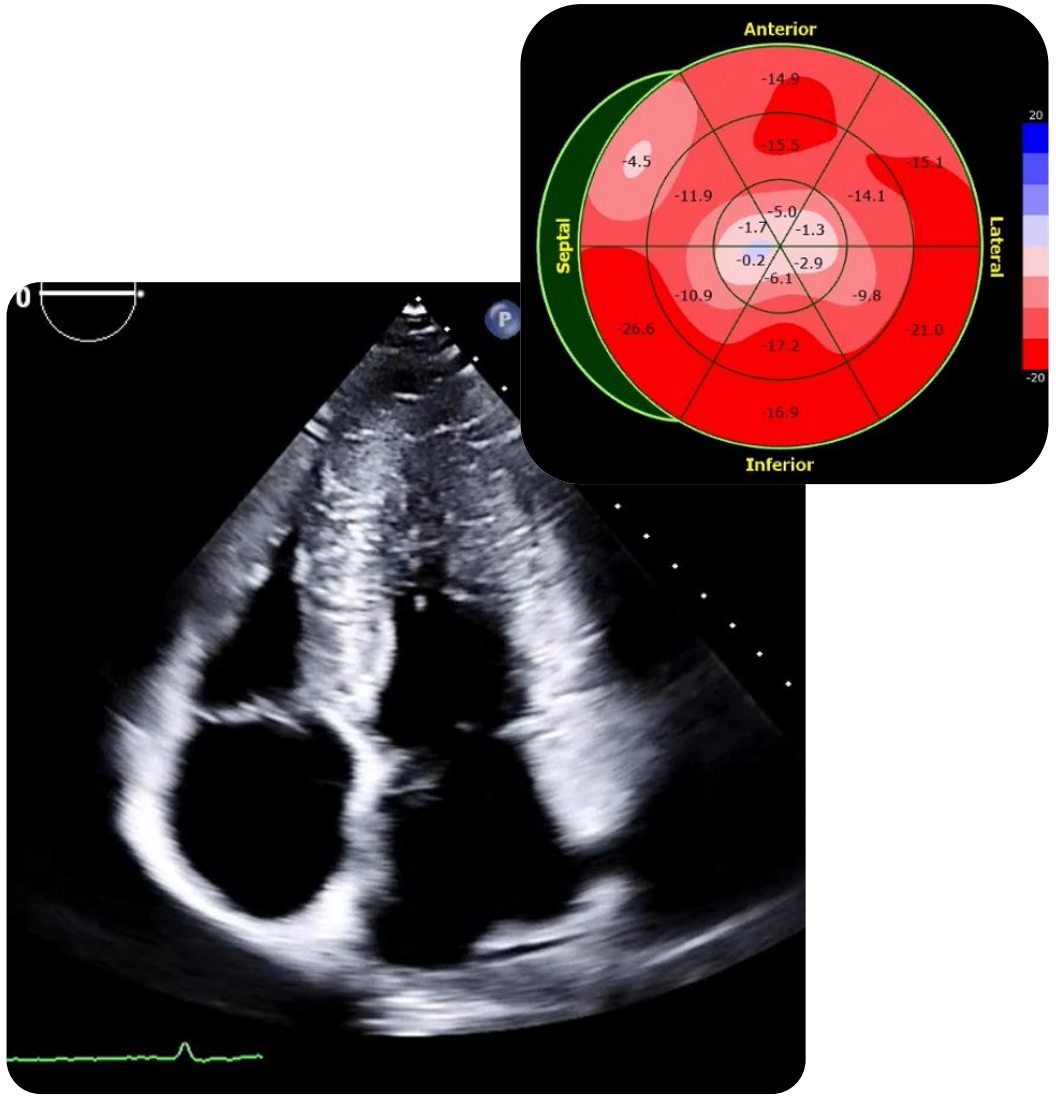
Maron et al. J Am Coll Cardiol. 2022

HCM: diagnostic pathway

ECG alterations



38-year-old male, engineer, high intensity recreational sports, asymptomatic, referred for abnormal ECG in routine screening

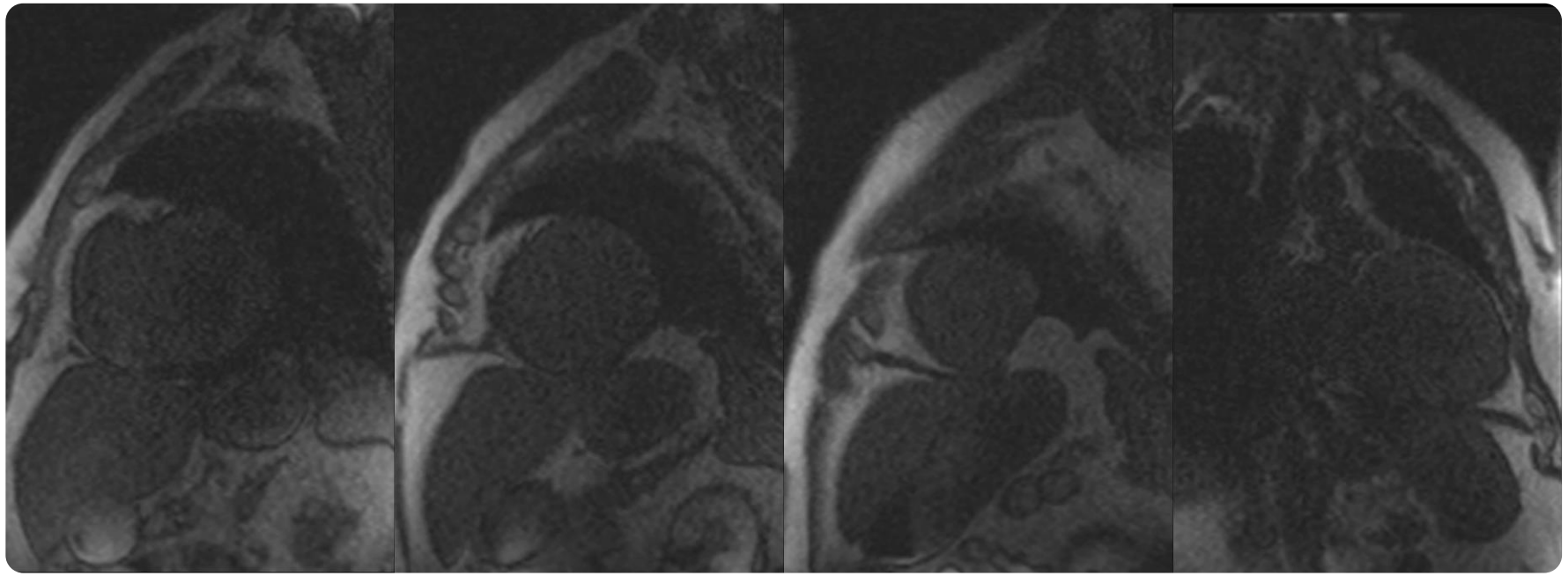


Apical variant of HCM: apical LVH with cavity obliteration

HCM: clinical presentation

Angina

- **Microvascular dysfunction** is part of the pathophysiology of HCM; may be present in asymptomatic patients
- The severity of coronary microvascular dysfunction is an independent predictor of long-term clinical deterioration and death



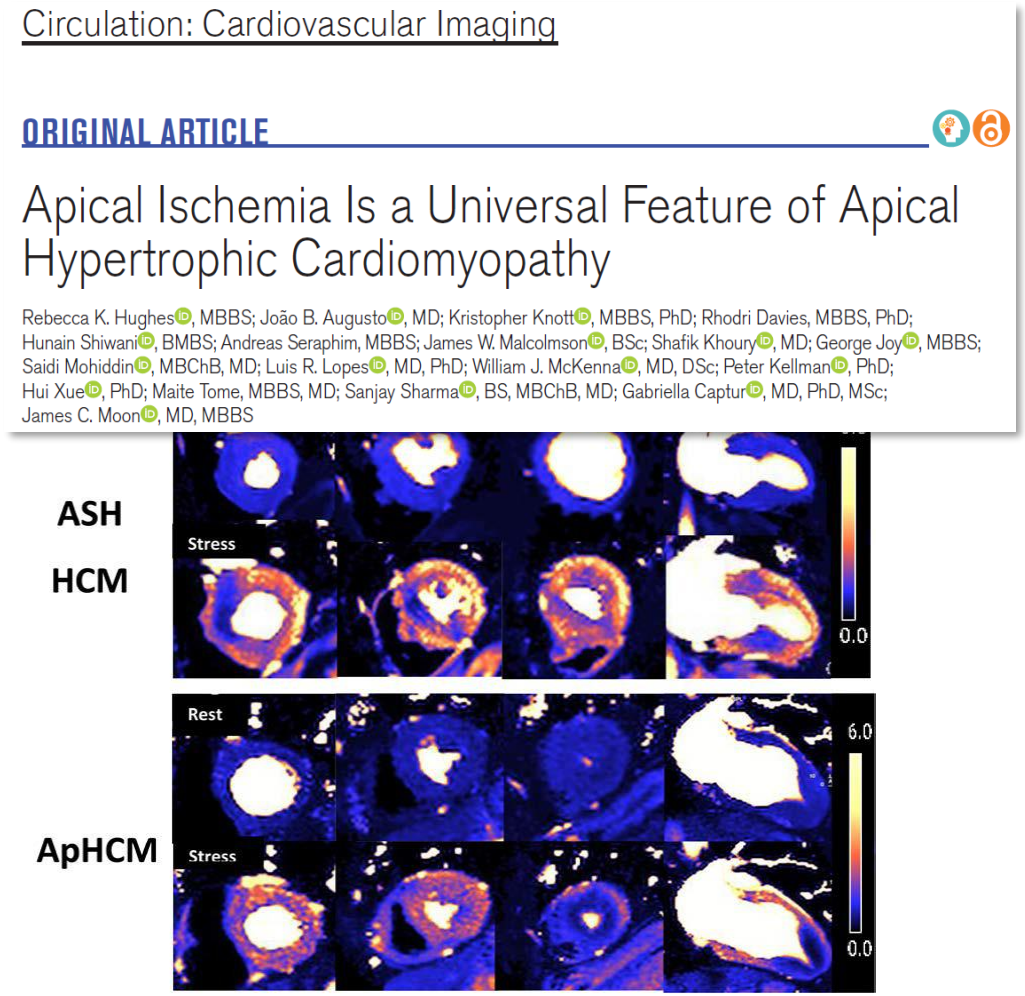
Cardiac magnetic resonance perfusion study showing extensive, diffuse, perfusion defect *(image credits: N. Dias Ferreira)*

Ommen et al. *Circulation.* 2020 | Cecchi et al. *N Engl J Med* 2003

HCM: clinical presentation

Angina

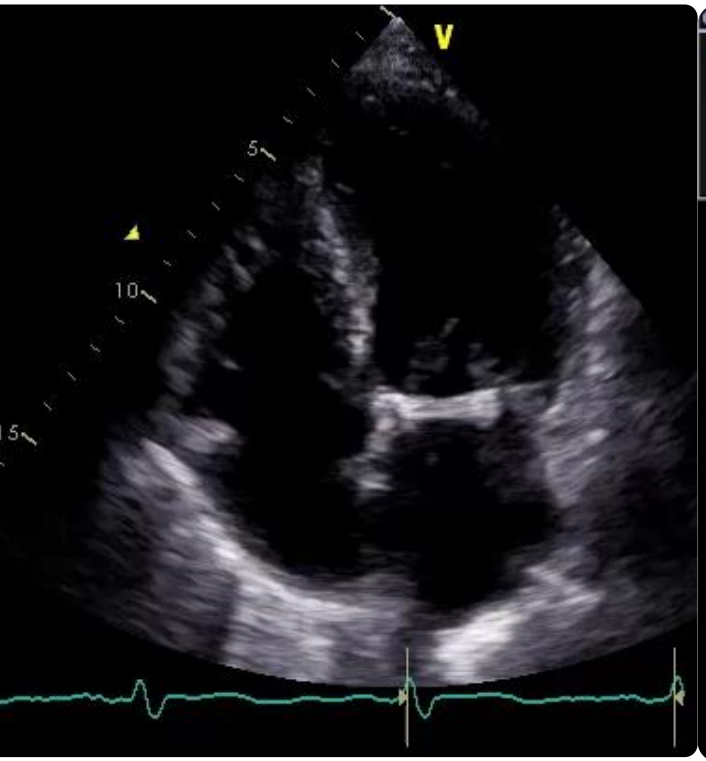
- **100%** patients with **apical HCM** (overt or relative) had apical **perfusion defects** on CMR
- Perfusion defects are likely to represent microvascular ischemia
- **Apical ischemia** may be one of the mechanisms that contributes to the development of **LV aneurysms**

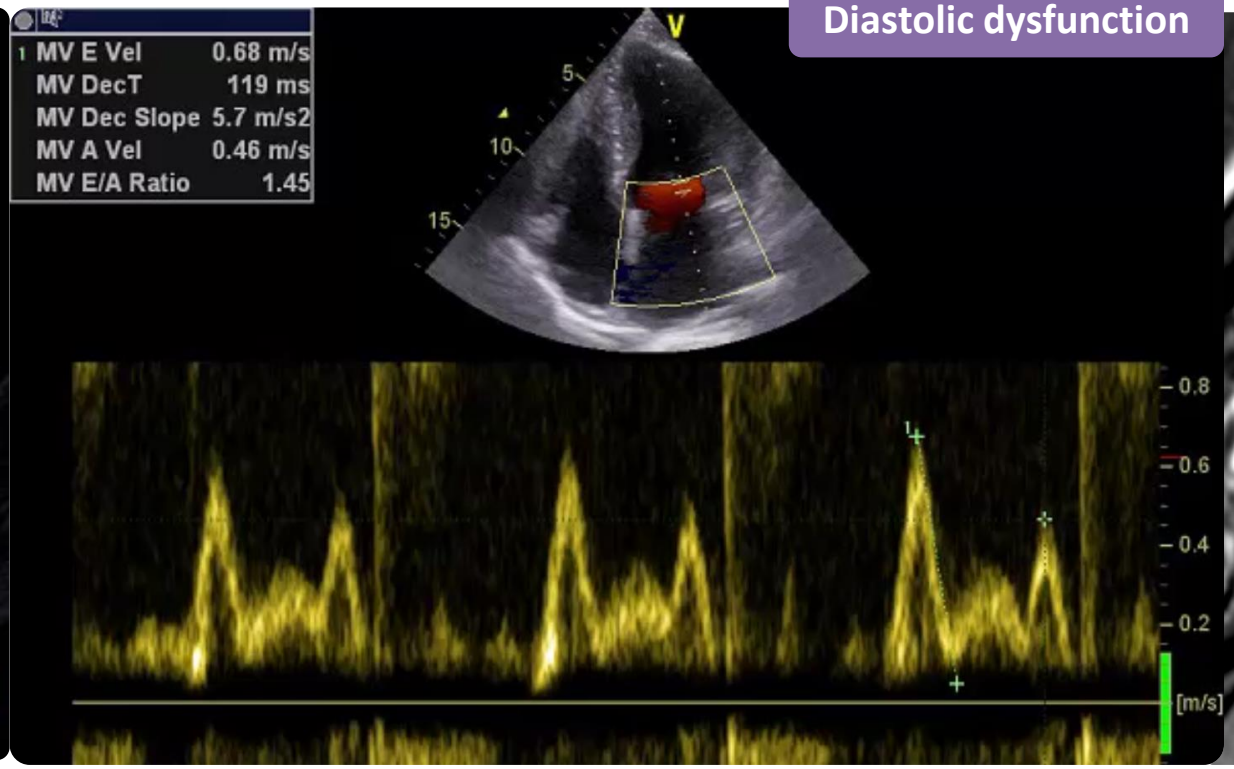


Ommen et al. *Circulation.* 2020 | Hughes et al. *Circ Cardiovasc Imaging*. 2023

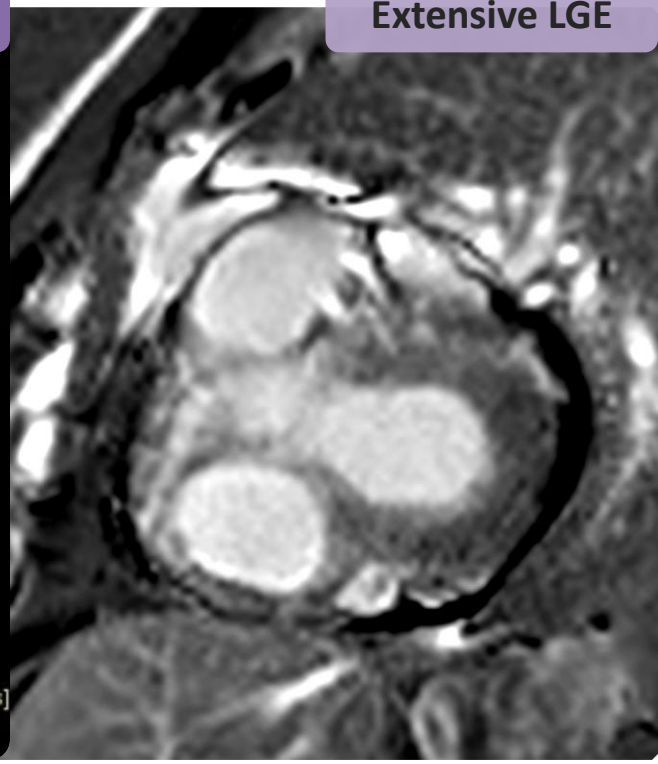
HCM: clinical presentation

Heart failure





Diastolic dysfunction



Extensive LGE

Female with TNNI3 gene variant with hypokinetic-restrictive form of HCM, severe diastolic dysfunction with triphasic filling pattern

HCM: clinical presentation

Heart failure

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 64, NO. 24, 2014
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Clinical Phenotype and Outcome of Hypertrophic Cardiomyopathy Associated With Thin-Filament Gene Mutations

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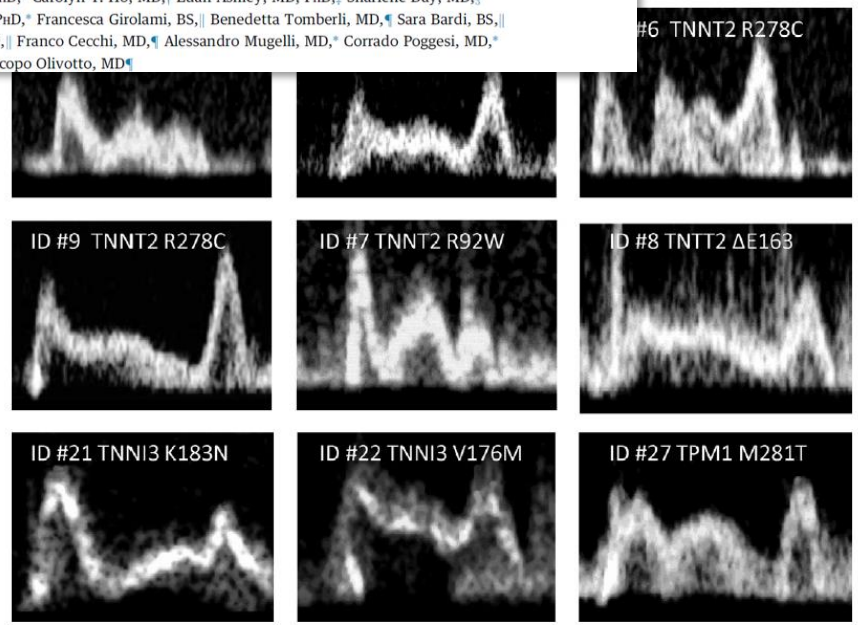
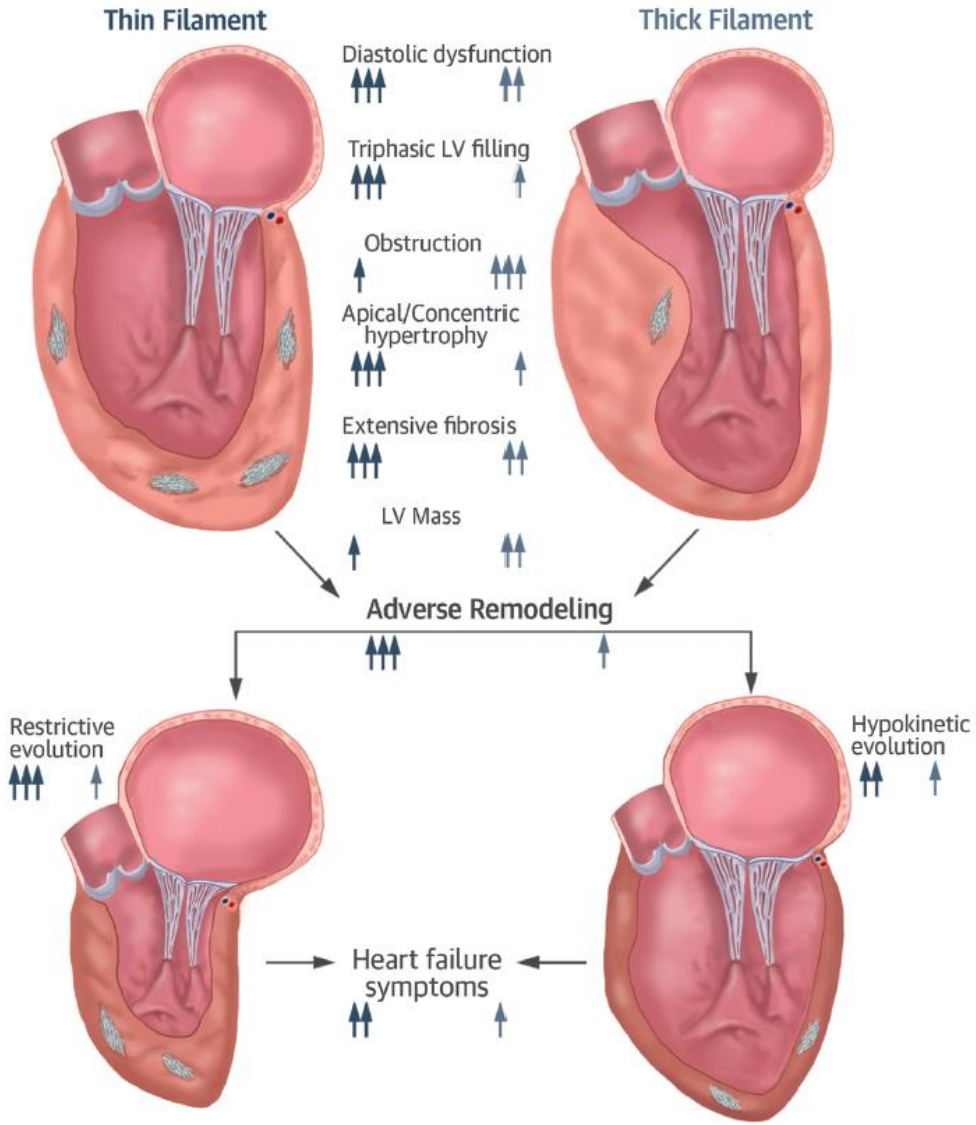
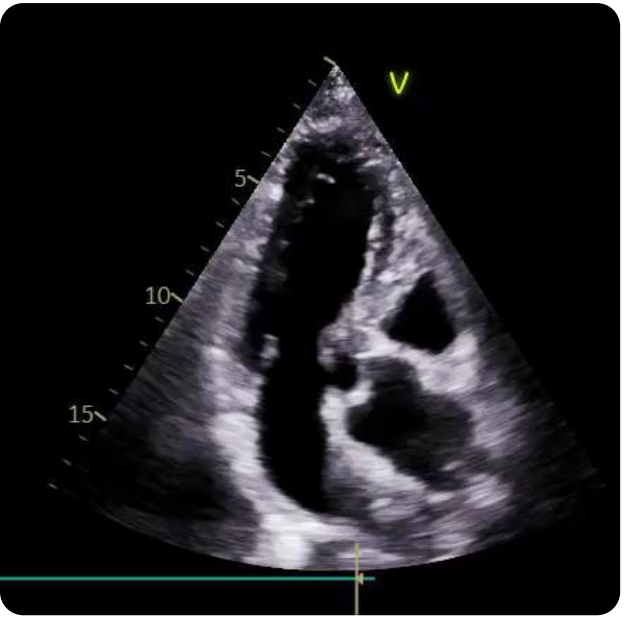


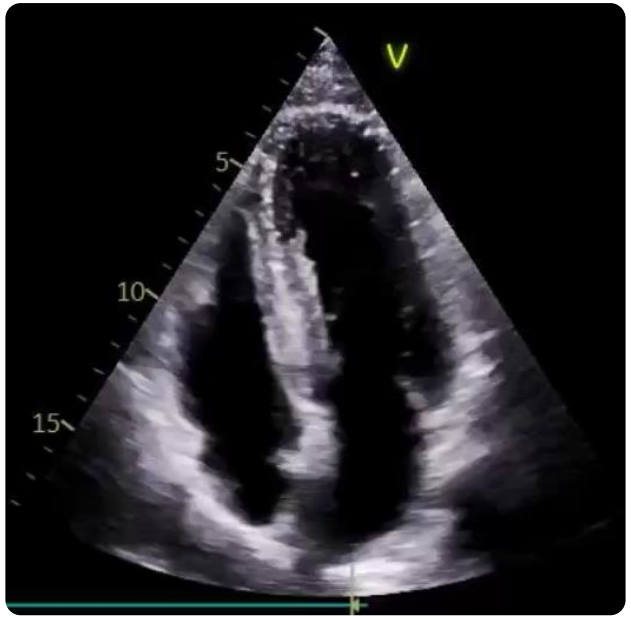


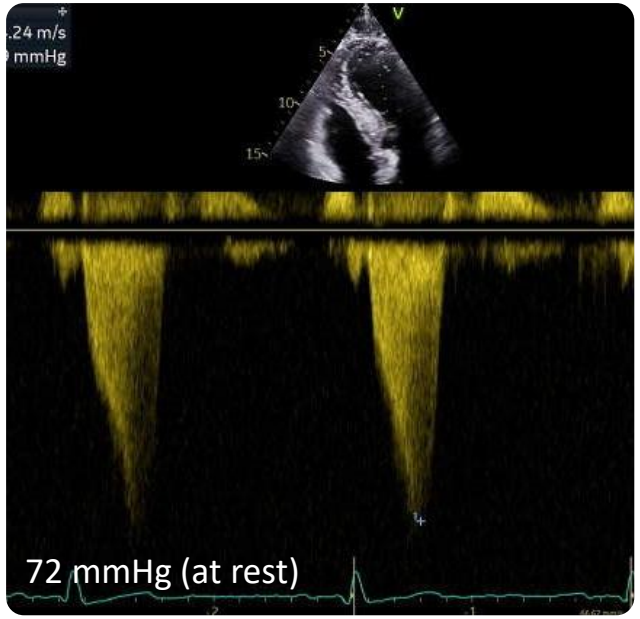
Coppini et al. J Am Coll Cardiol. 2014

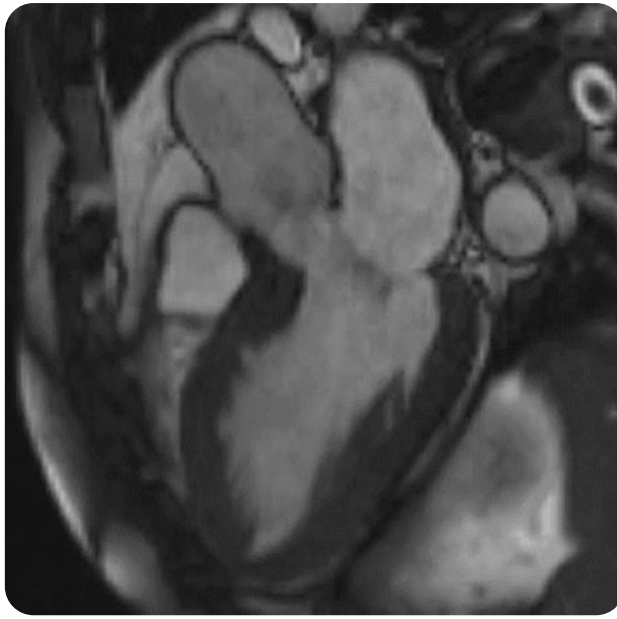
HCM: clinical presentation

Syncope







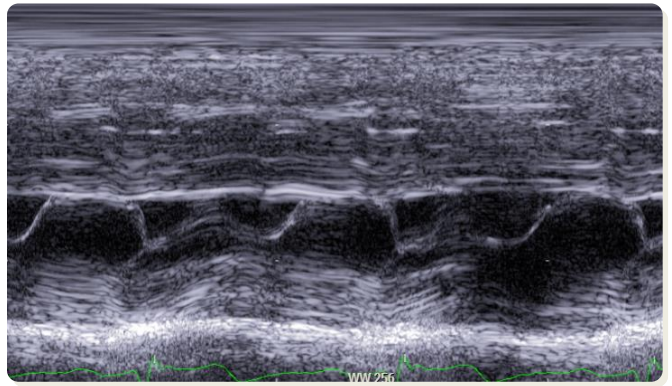


39-year-old female, presenting with recurrent episodes of syncope on exertion (carrying groceries, …); mid-ventricular and LVOT obstruction are noted.

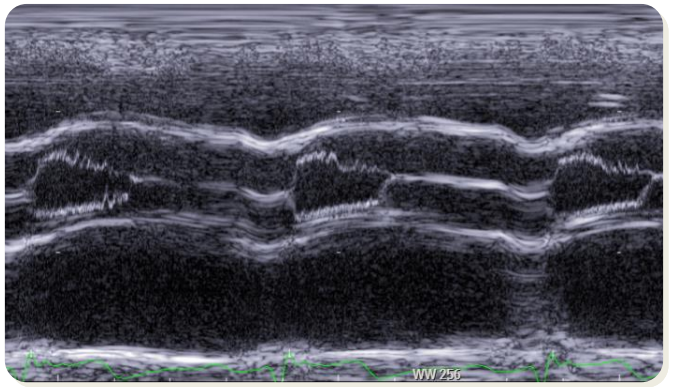
HCM with obstruction

LVOT obstruction

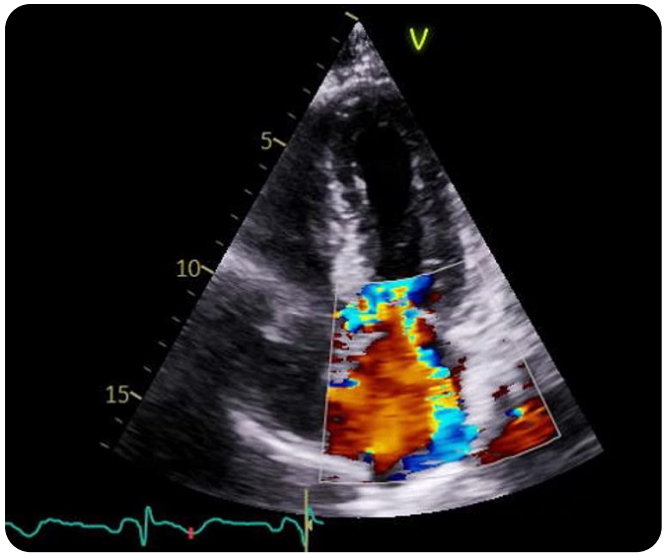
- LVOTO (at rest or provoked) is present in up to **75%** of patients with HCM



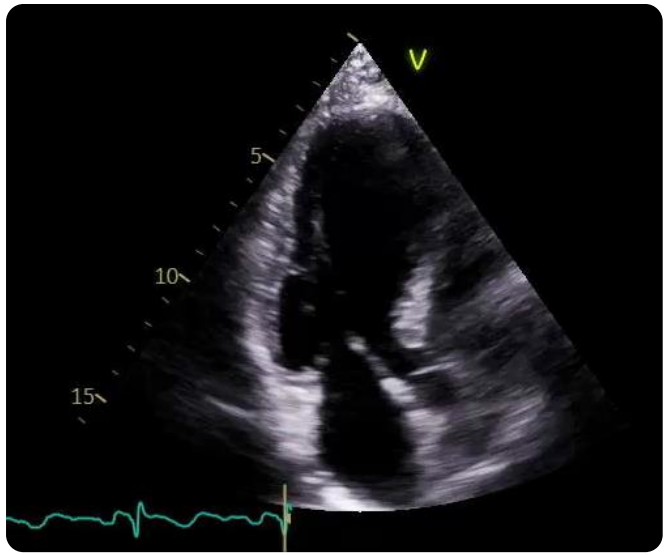
SAM of the anterior MV leaflet



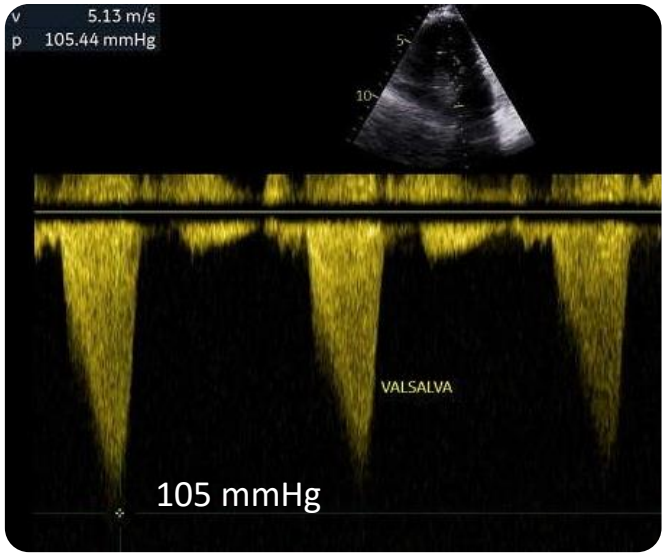
AV fluttering and mid-systolic closure



Eccentric MR jet due to SAM/Venturi forces



SAM of MV anterior and posterior leaflets



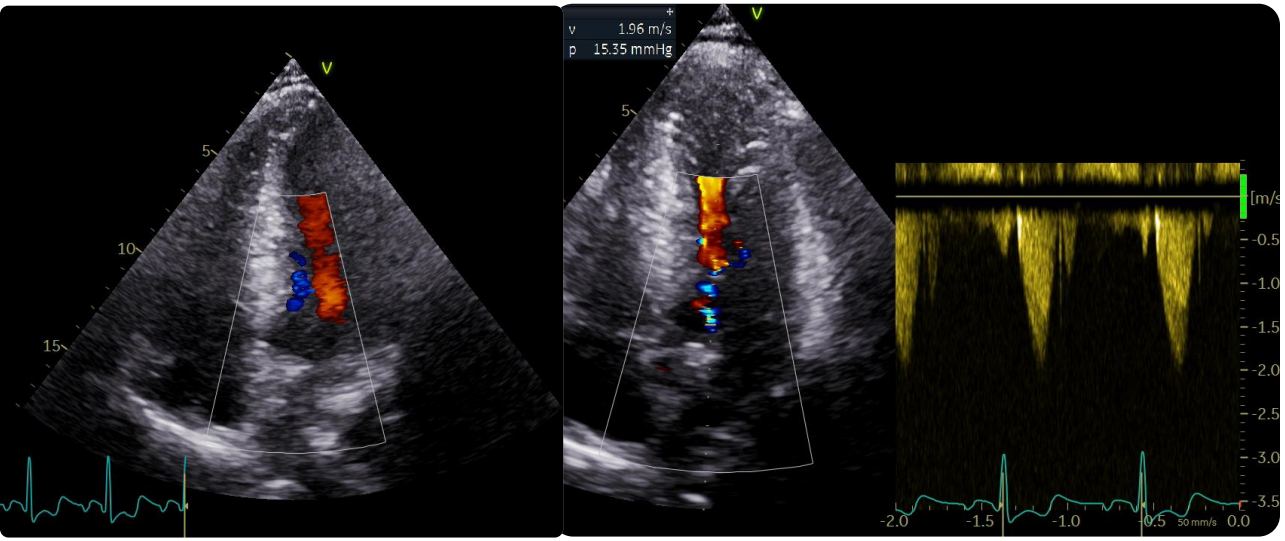
LVOT CW with “dagger-shaped” envelope

HCM with *latent* obstruction

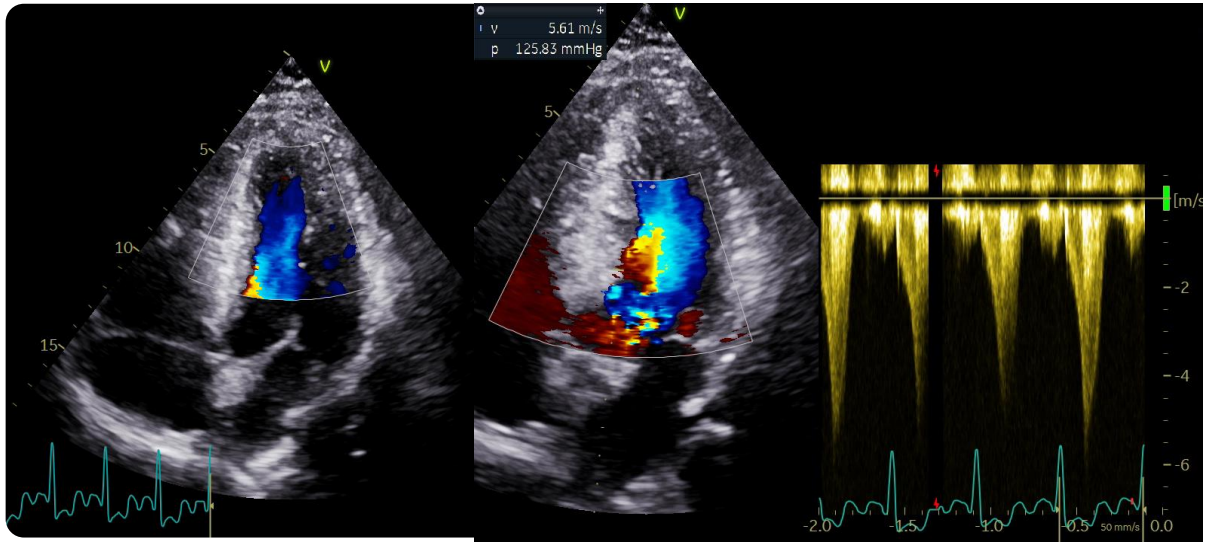
Stress exercise echocardiography

- LVOTO *can be missed on resting echocardiography* in up to **50%** of patients with **obstructive** physiology
- Stress exercise echocardiography represents the most physiological form of provocation and is useful to unmask latent LVOTO

Basal (LVOT gradient 15mmHg)



Peak exercise (LVOT gradient 126 mmHg)



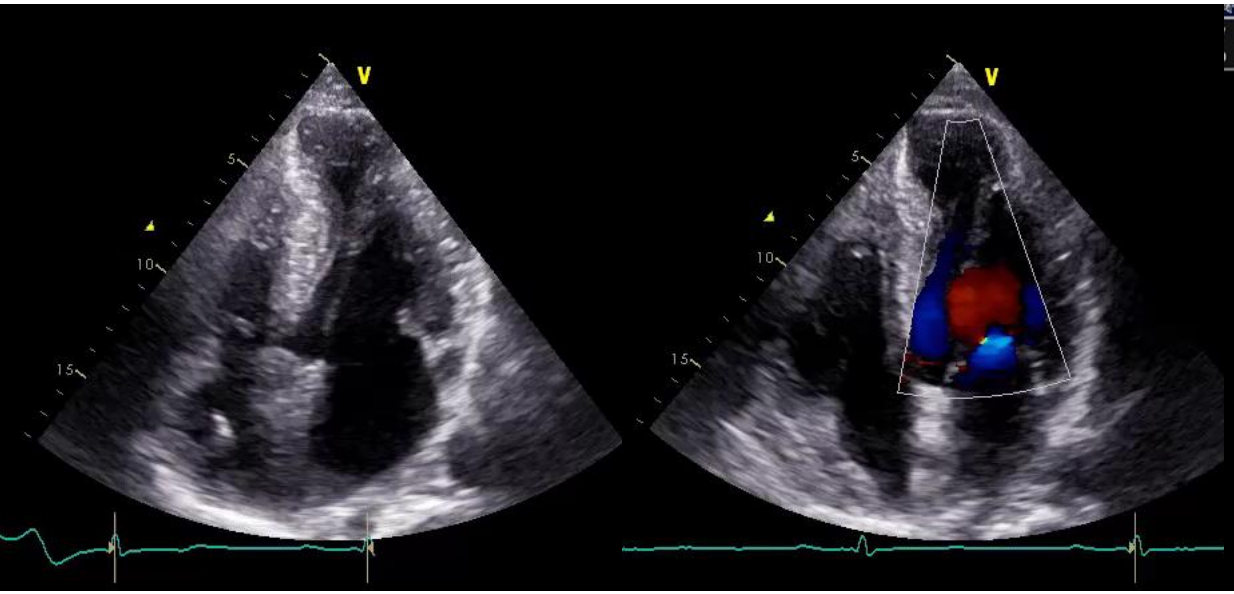
(image credits: E. Pálinkás, A. Oddo, Careggi University Hospital)

Ommen et al. *Circulation.* 2020

HCM with obstruction

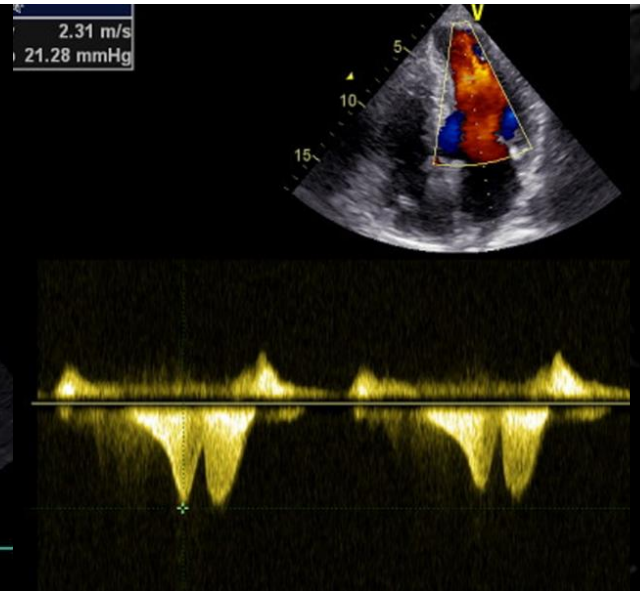
Midventricular obstruction

- Systolic obliteration of the LV that is unrelated to SAM, color Doppler demonstrates turbulence at the midventricular level
- Due to abrupt flow cessation across the obliterated ventricle in mid-systole, pressure gradient measure may be impossible: *signal void*

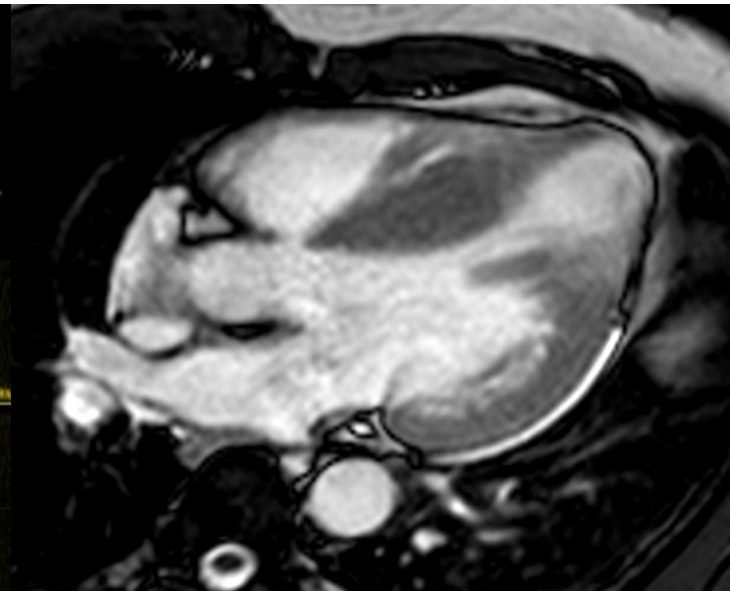


PM-septal contact during systole

Obstruction at **midventricular level**



"Lobster claw" / "signal void" CW sign



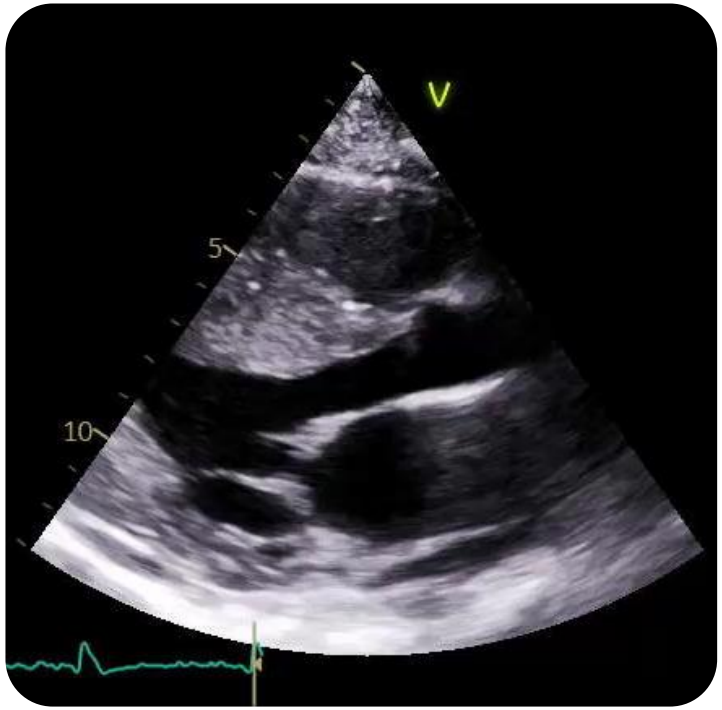
Apical aneurysm on CMR

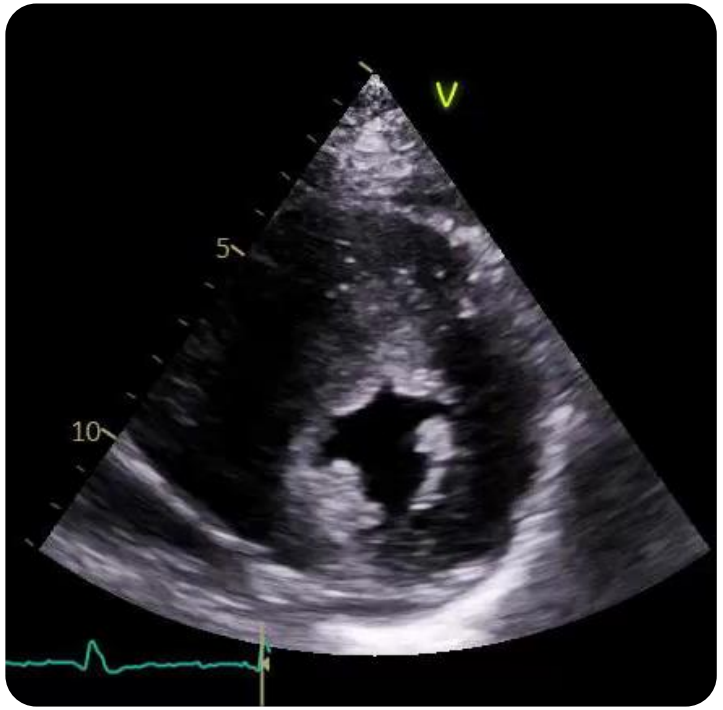
Brandão et al. *Rev Esp Cardiol.* 2022

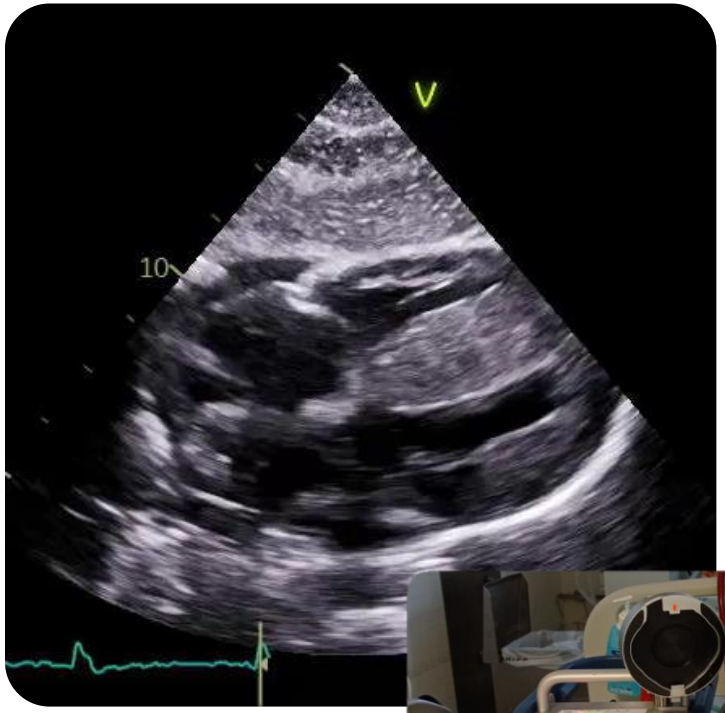
HCM: clinical presentation

Ventricular arrhythmias & sudden death

Sudden cardiac death may be the *first manifestation* of HCM!

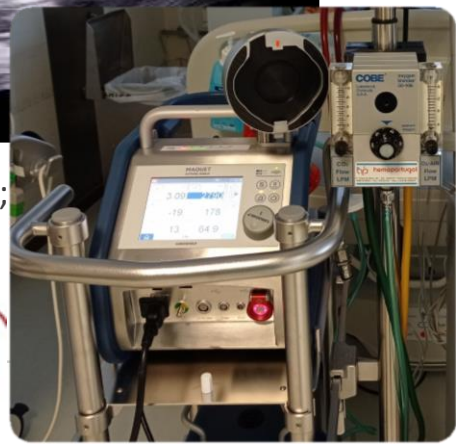






29-year-old female experienced aborted sudden death during immediate post-partum; eCPR, followed by 2-days under VA-ECMO;

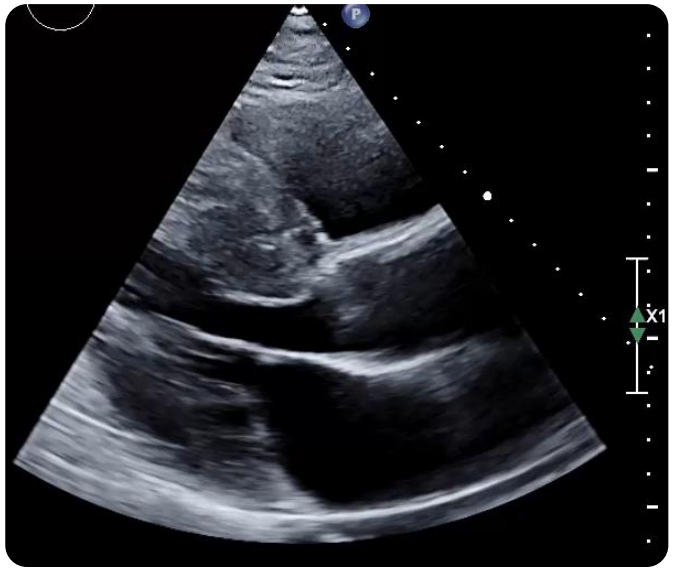
TTE revealed MWT 30mm; CMR revealed extensive LGE and perfusion defects; S-ICD was implanted before discharge

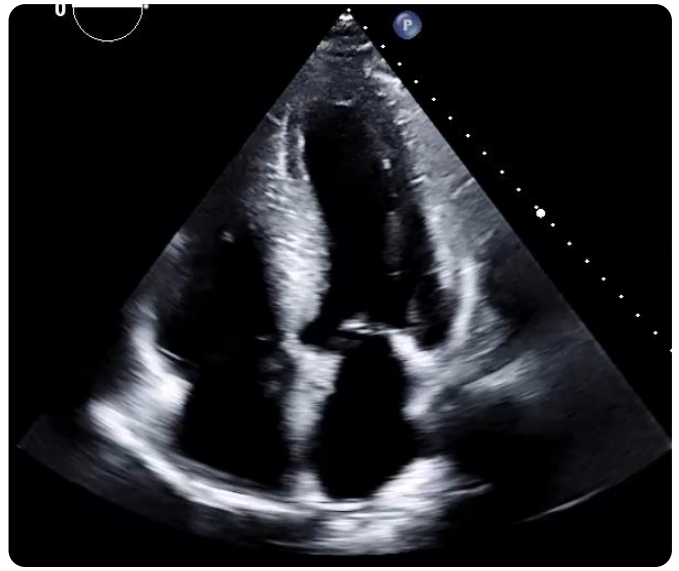


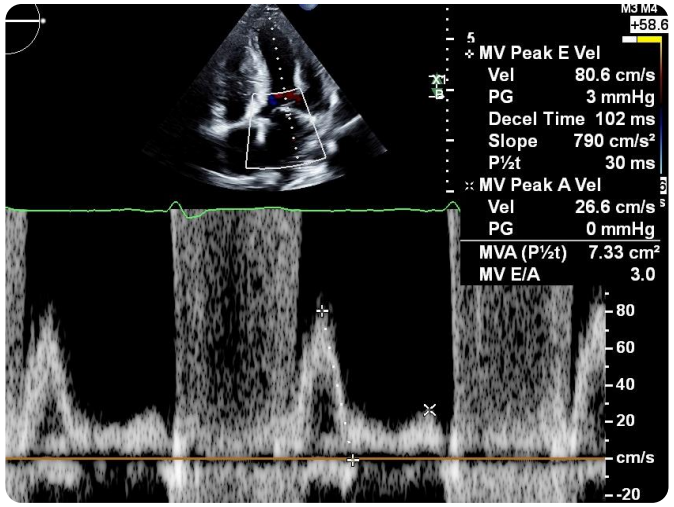
Not all LVH is HCM!

Case 1

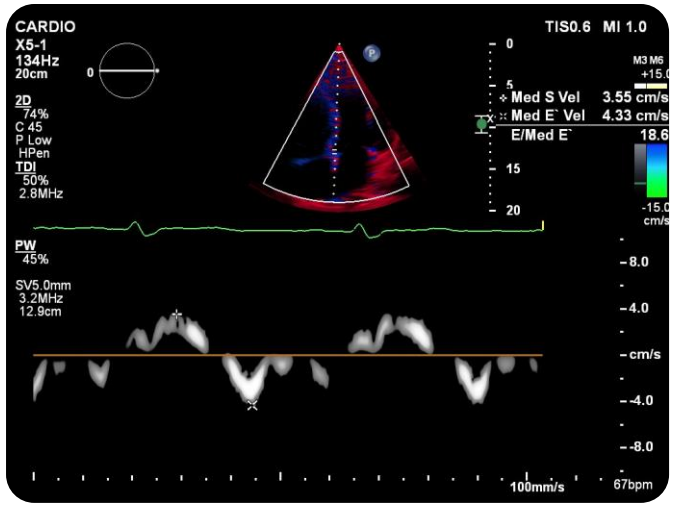
- 62-year-old **male**
- Family history SCD + (aunt)
- Mild **HF symptoms (NYHA I-II)**
- Systemic complaints: Ø



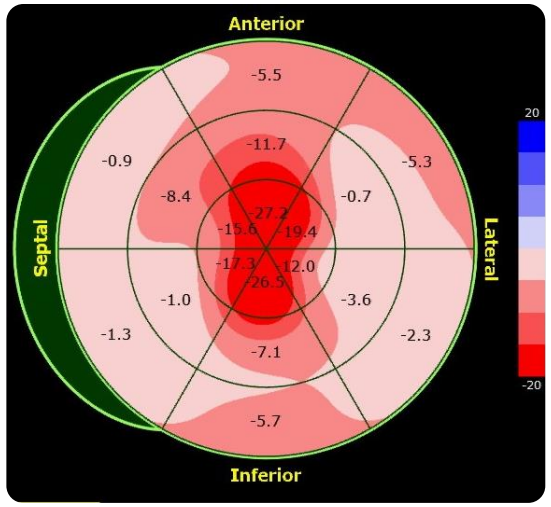




Restrictive filling pattern



Low mitral anular TDI velocities



Reduced GLS with apical sparing

Case 1

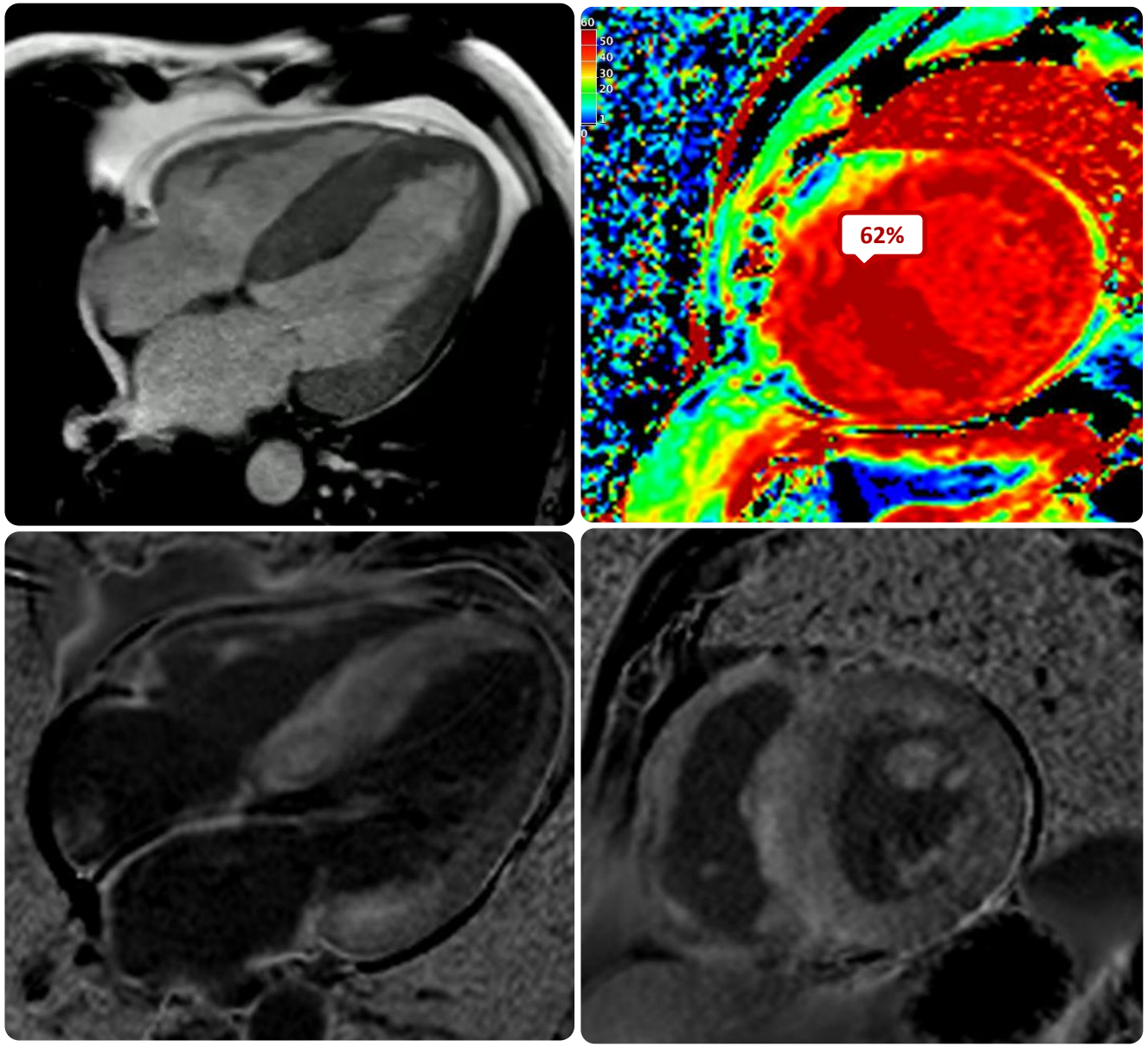
Parametric mapping

Siemens – 1.5T MOLLI

- ↑ **Native T1**: 1122 ms (885-1059 ms)
- ↑ **Extracellular volume:** 62%

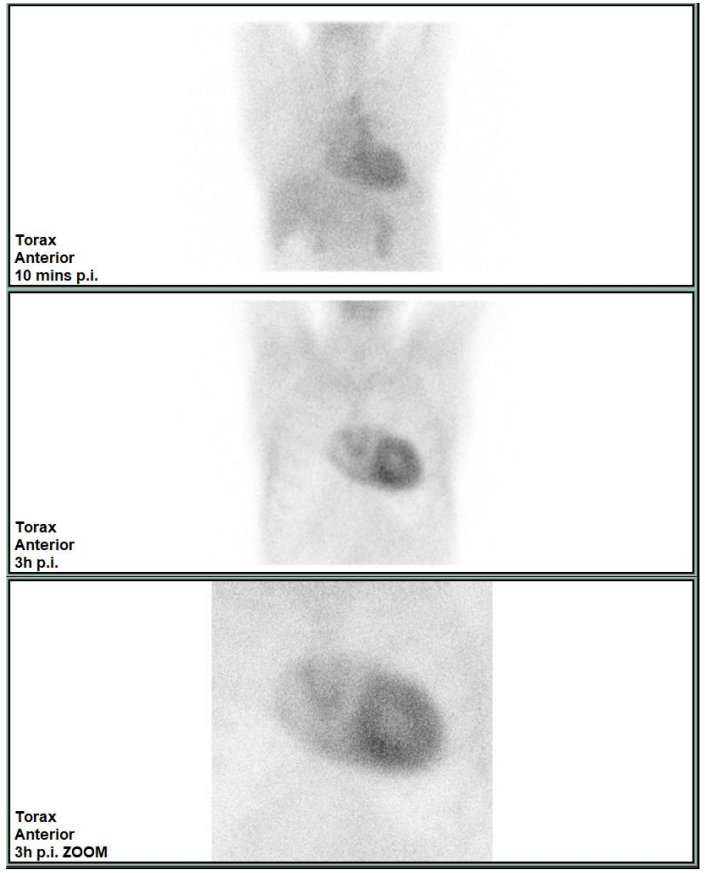
LGE

- Abnormal gadolinium kinetics/myocadial nulling
- **Extensive, diffuse, subendocardial** and **midmural LGE**, including all LV segments and RV free wall

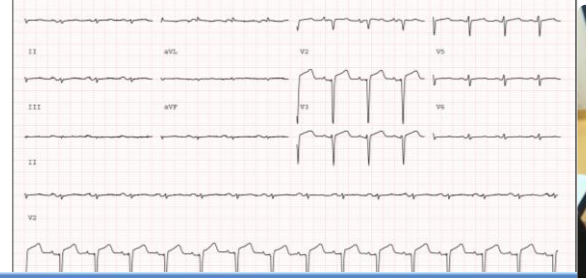


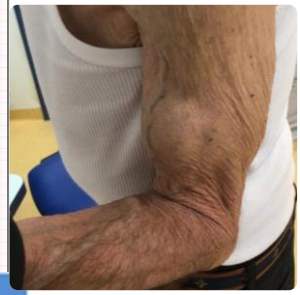
Markedly increased ECV (62%); diffuse subendocardial/midmural LGE in all LV segments

Case 1



99mTc-DPD scintigraphy showing myocardial>bone uptake, suggestive of **TTR amyloidosis**





Heart failure, syncope, or bradyarrhythmia, with echocardiogram and/or cardiac magnetic resonance imaging (CMR) suggesting/indicating cardiac amyloid

Bone scintigraphy with ^{99m}Tc-DPD/HMDP/PYP

Grade 0 | Grade 1 | Grade 2 to 3

Serum immunofixation + Urine immunofixation + serum free light chain assay (Freelite)
Monoclonal protein present?

No

Cardiac ATTR amyloidosis

TTR genotyping

Wild-Type ATTR amyloidosis

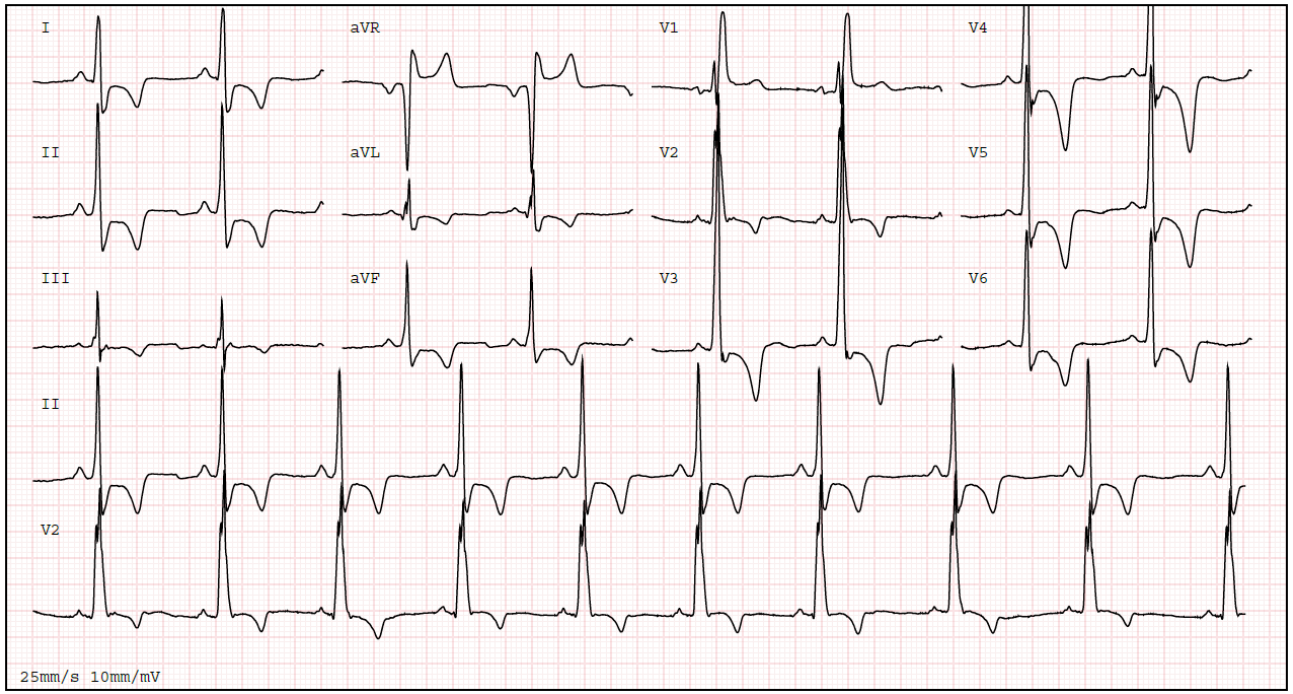
- **Bone scintigraphy**: Perugini score **3**
- Normal **hematologic tests**
- **Genetic test/ TTR gene sequencing:** negative
- Patient under treatment with **Tafamidis**

wtATTR-CM

Gilmore et al. *Circulation.* 2016

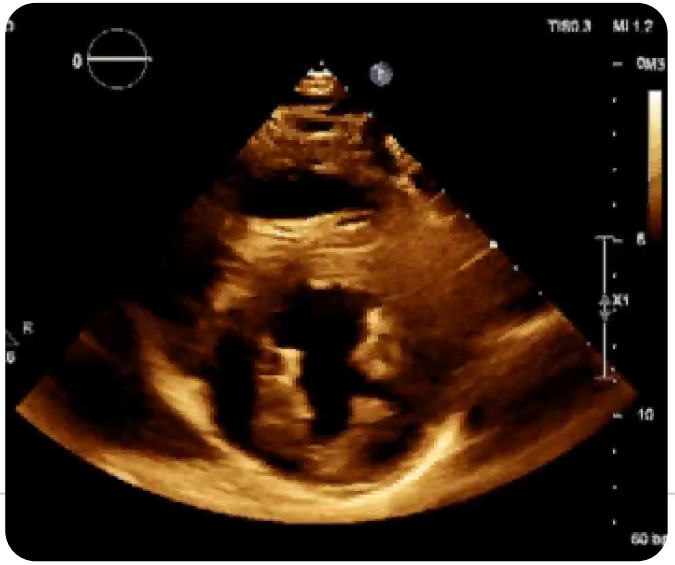
Case 2

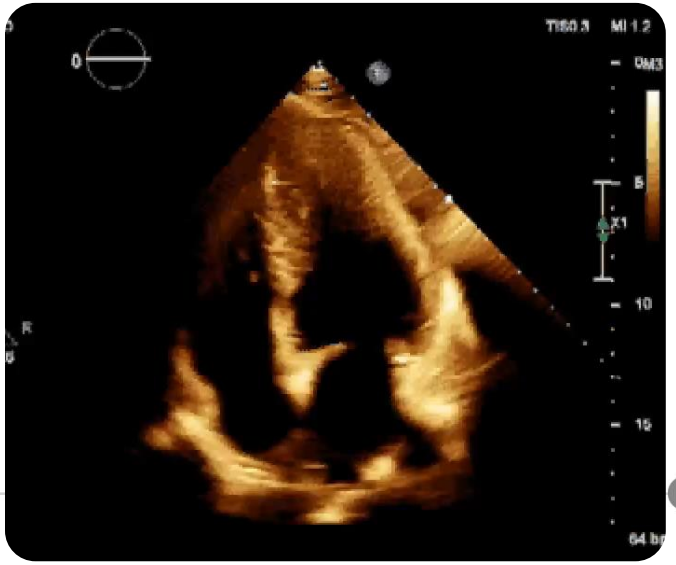
- **57**-year-old **male**
- Past medical history: Ø
- Family history CVD/SCD: : Ø
- Asymptomatic
- Unremarkable physical examination



Referred due to **ECG abnormalities**

Apical variant of HCM?





Case 2

CMR imaging

- Severe, concentric LV hypertrophy, preserved LVEF

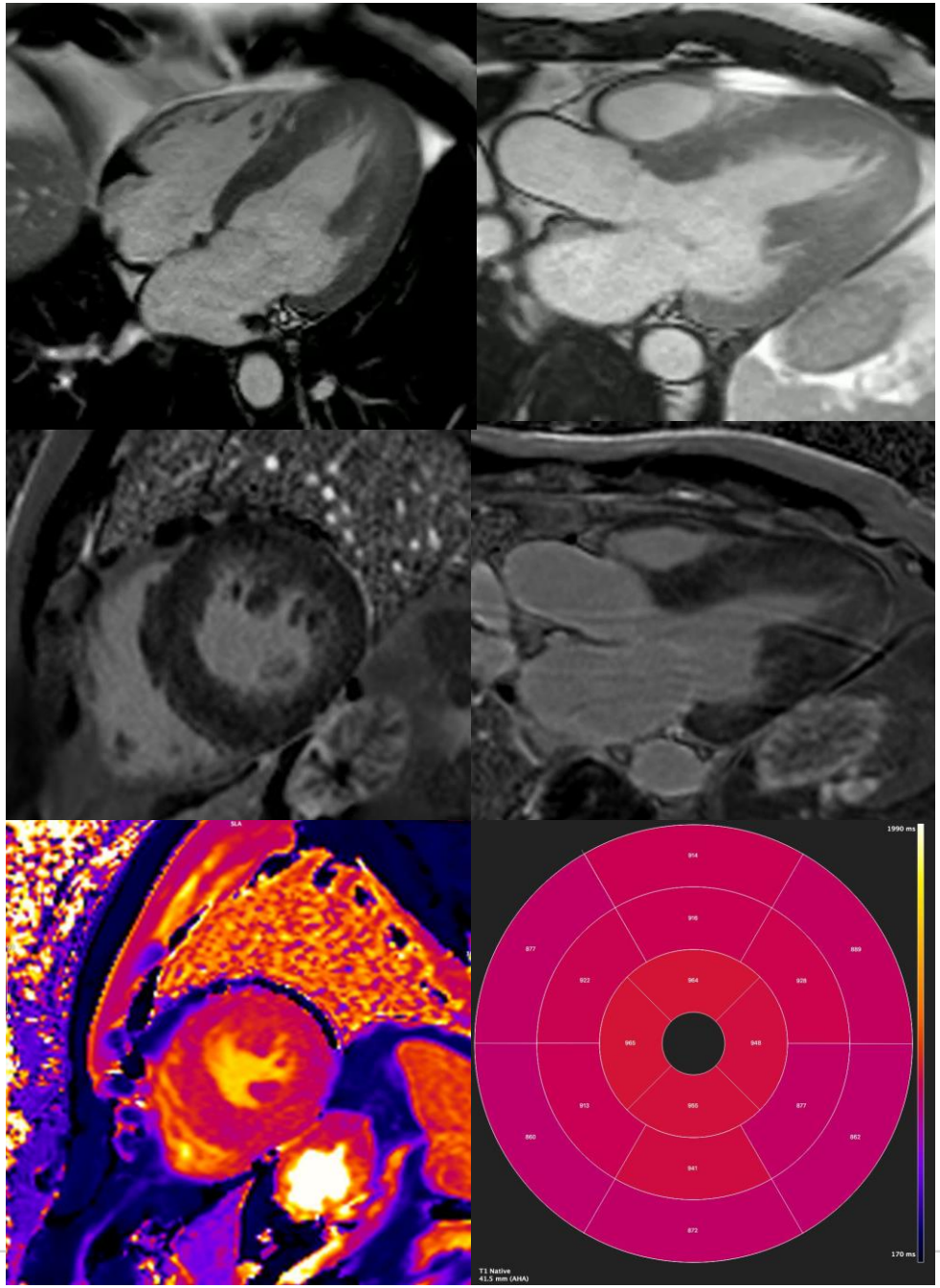
LGE

- **Intramural LGE** in distal (hypertrophied) LV segments

Parametric mapping

Siemens – 1.5T MOLLI

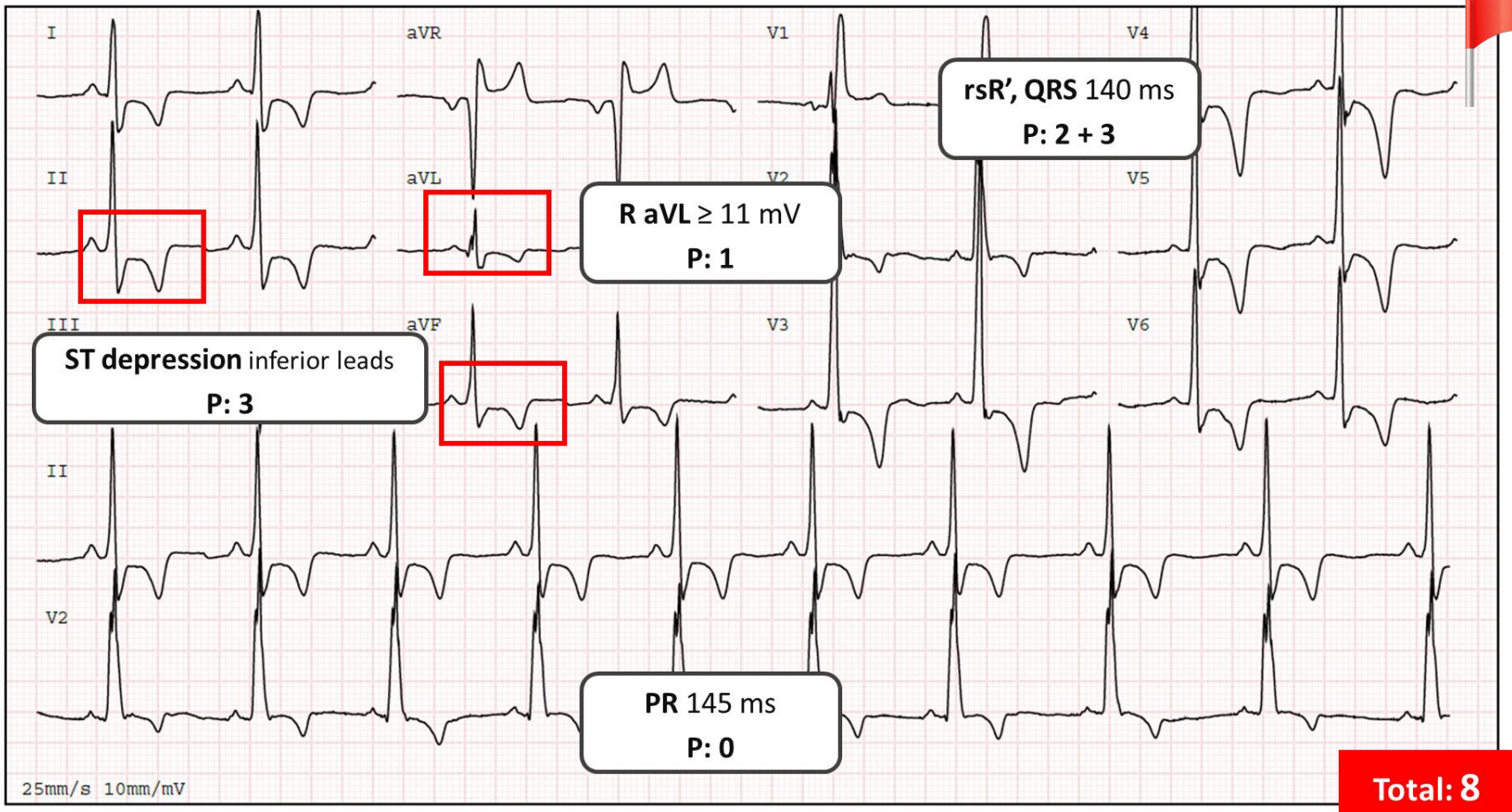
- ↓ **Native T1**: 826-894 ms (885-1059 ms) in LV basal and mid segments



Case 2

- Genetic test – HCM panel: **GLA pathogenic variant c.337T>C (p.Phe113Leu)**
- Low AGAL activity – plasma/ leucocyte (1 nmol/h/mg; reference value 6-19)
- Under treatment with **Migalastat**

Fabry disease



Total: 8

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HCM: differential diagnosis

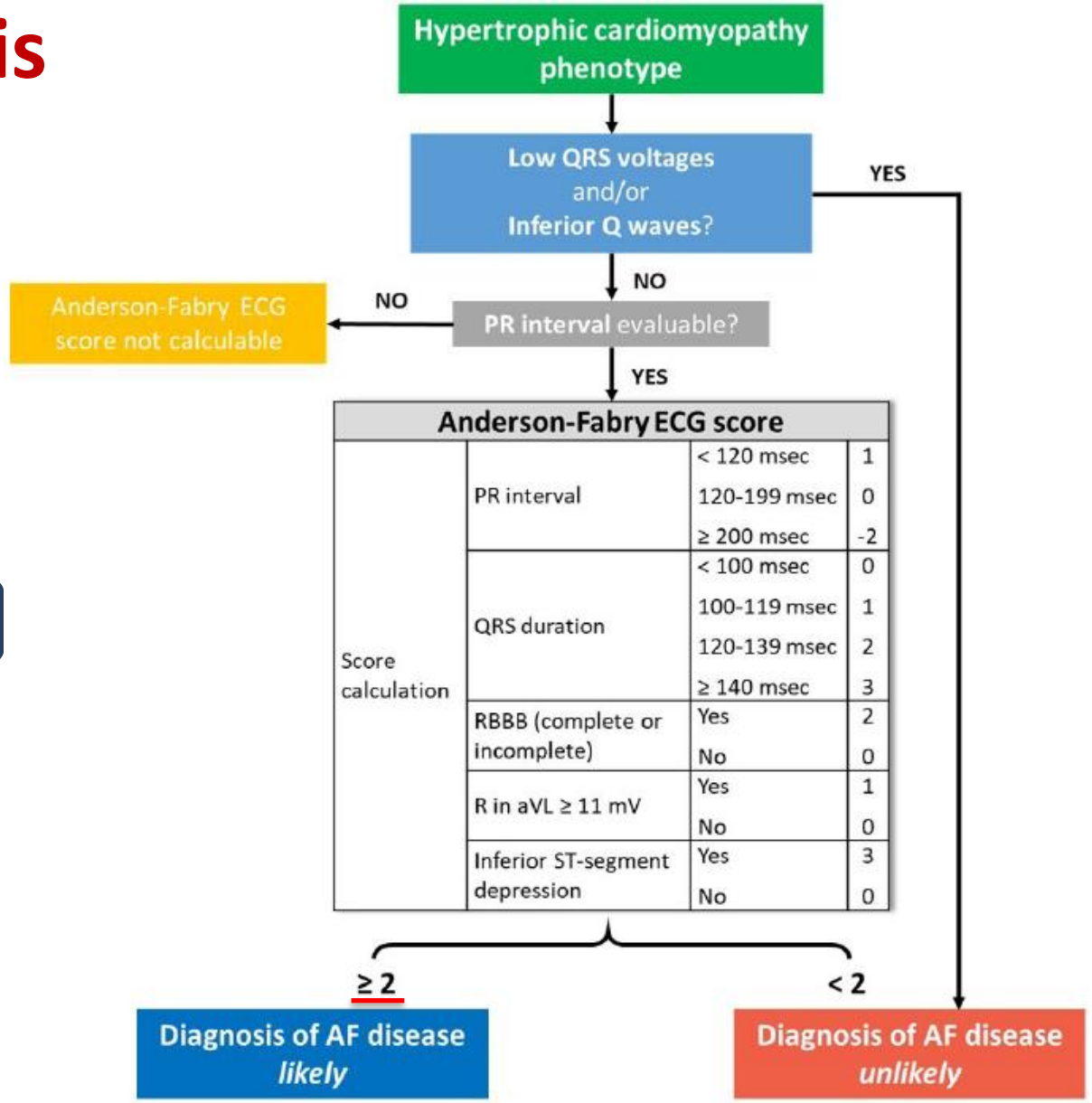
Original research

Standard ECG for differential diagnosis between Anderson-Fabry disease and hypertrophic cardiomyopathy

Giovanni Vitale ,[1] Raffaello Ditaranto ,[1] Francesca Graziani,[2] Ilaria Tanini,[3] Antonia Camporeale,[4] Rosa Lillo,[2] Marta Rubino,[5] Elena Panaioli,[2] Federico Di Nicola,[1] Valentina Ferrara,[1] Rossana Zanoni,[1] Angelo Giuseppe Caponetti,[1] Ferdinando Pasquale,[1] Maddalena Graziosi,[1] Alessandra Berardini,[1] Matteo Ziacchi,[1] Mauro Biffi,[1] Marisa Santostefano,[6] Rocco Liguori,[7,8] Nevio Taglieri,[1] Elena Nardi,[1] Ales Linhart ,[9] Iacopo Olivotto,[3] Claudio Rapezzi,[10,11] Elena Biagini[1]

ECG predictors of Anderson-Fabry disease

- **Short PR**
- **Prolonged QRS** duration
- **RBBB** pattern
- **R in aVL** ≥1.1 mV
- **Inferior ST-segment depression**



Vitale et al. *Heart*. 2022

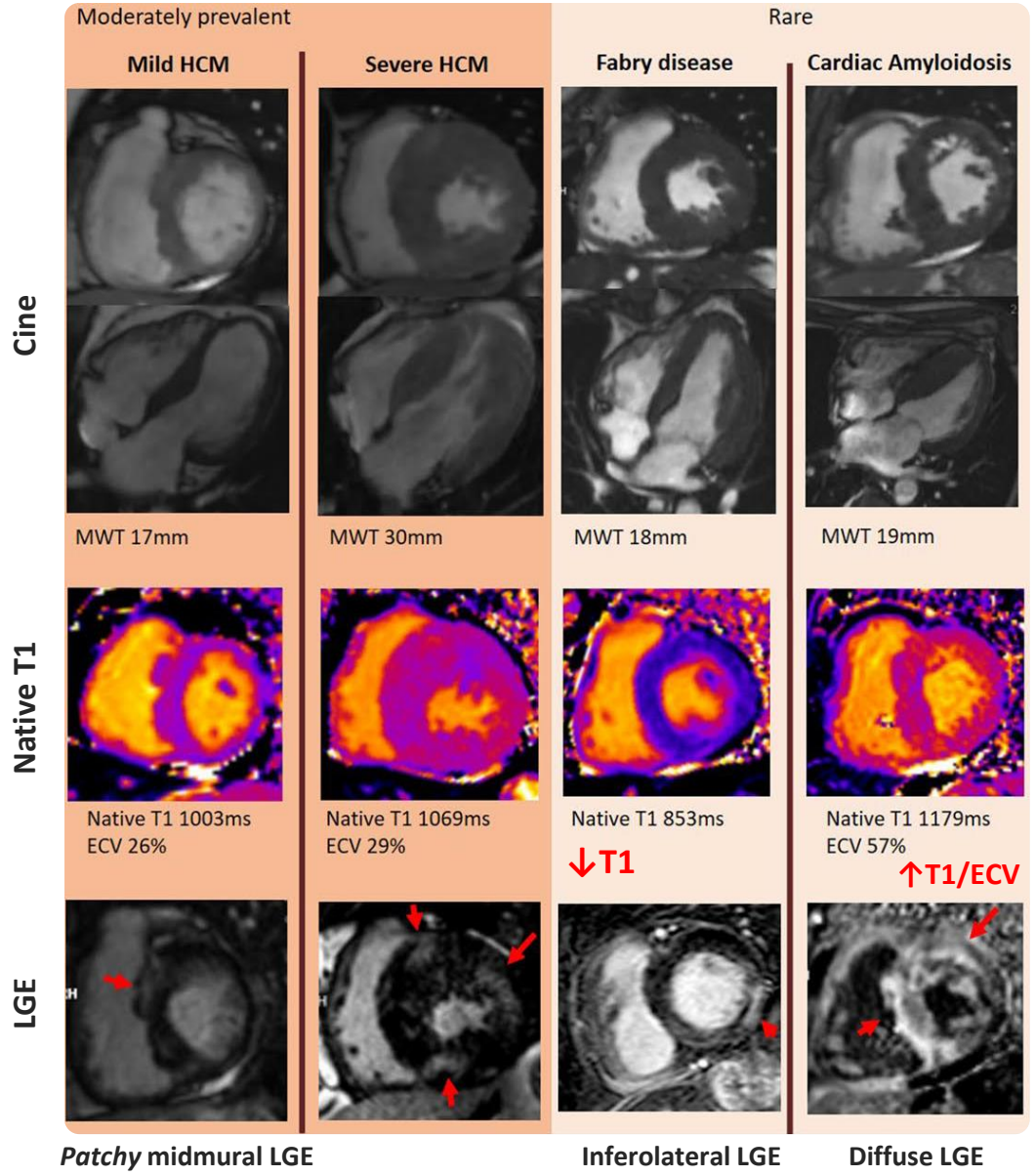
Role of CMR and genetics

CMR imaging

- **Sarcomeric HCM**
  - Enhanced diagnostic accuracy (MWT, variants, aneurysms)
  - Tissue characterization – **SCD risk stratification** *extensive* LGE (≥15%) ?
- **Differential diagnosis** with **phenocopies**
  - LGE pattern, parametric mapping

Genetics

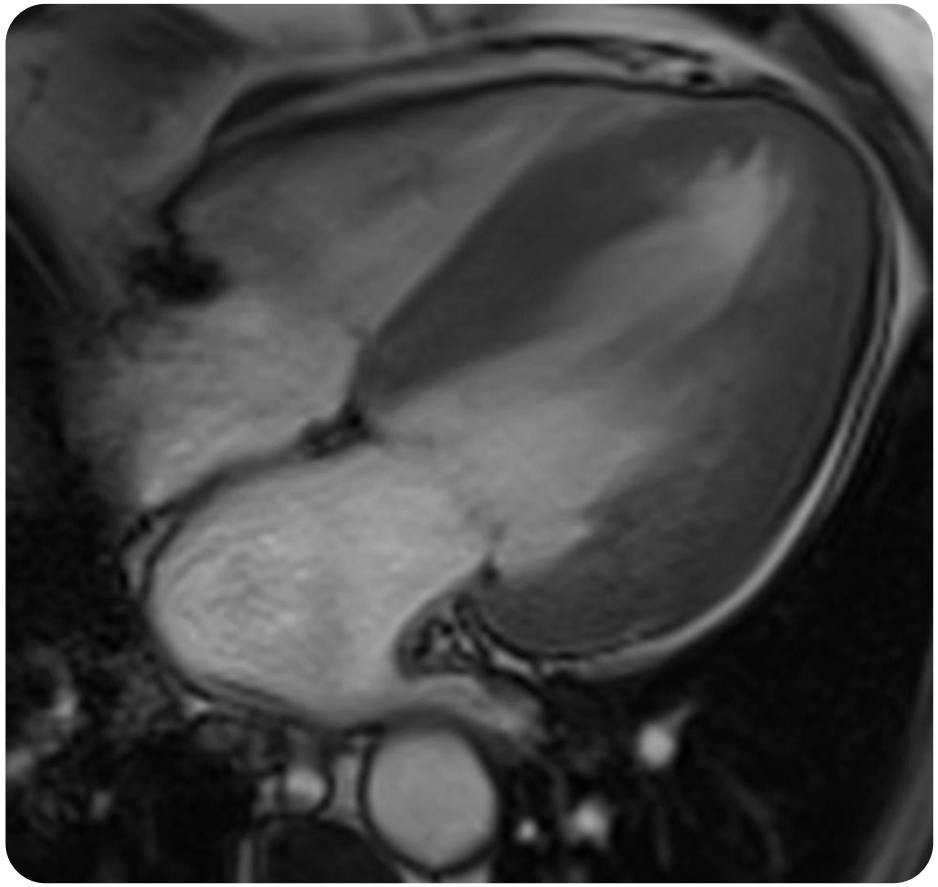
- Diagnostic confirmation; *prognostic value?*
- Family cascade screening
- Identification of **phenocopies**



Adapted from Aguiar Rosa et al. *Int Journ Cardiovasc Imaging.* 2022

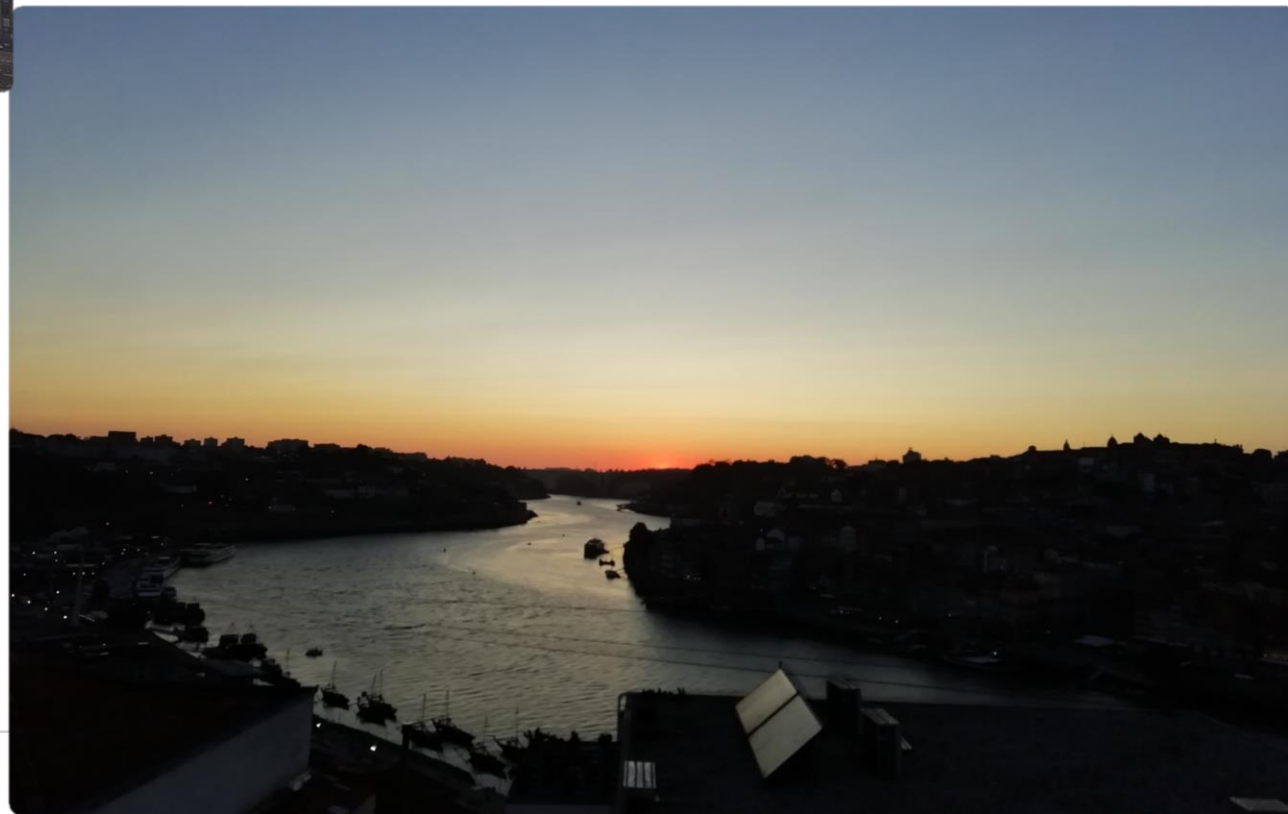
Final remarks

- Importance of history and physical examination: attention to **red flags!**
- Thorough **family history**: cardiomyopathies, SCD, devices, systemic disease…
- The importance of **ECG**: the devil is in the details
- **Echocardiogram** is **key***: look beyond LVH!*
- Role of **exercise echocardiography** for unmasking latent **LVOTO**
- Added value of **CMR** and **genetics** for **differential diagnosis**
- Importance of recognizing **phenocopies** with available targeted treatment



Thank you!

@MSBBrandao



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