

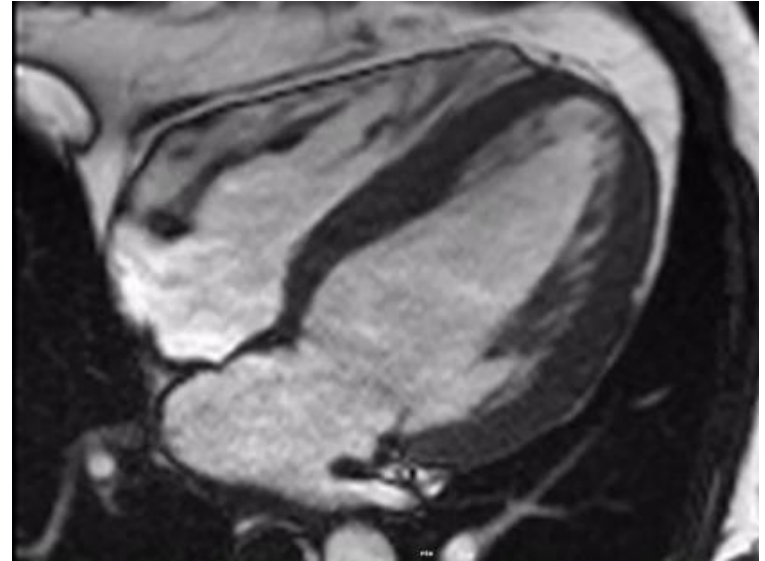


ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ
- 2025/ 2026 -

ΚΑΡΔΙΑΓΓΕΙΑΚΗ ΑΠΕΙΚΟΝΙΣΗ ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

ΓΡΗΓΟΡΙΟΣ ΧΑΤΖΑΝΤΩΝΗΣ, MD, PhD

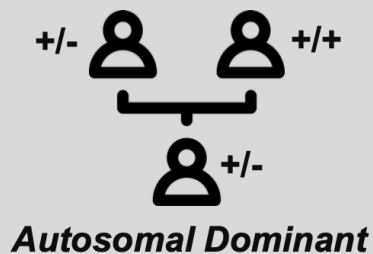
Ποια είναι η αιτία υπερτροφίας του μυοκαρδίου;



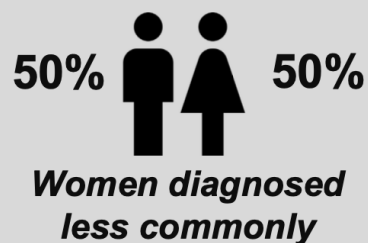
ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Hypertrophic Cardiomyopathy (HCM) is a Globally Prevalent & Common Genetic Heart Disease

Inheritance Pattern



Sex Distribution

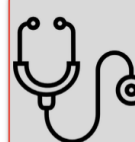


Disease Prevalence

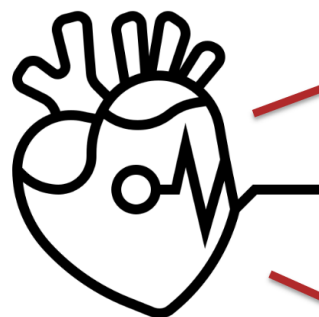


**Estimated
1:200 – 1:500**

Triggers for Evaluation



Symptoms
Cardiac Event
Heart Murmur
Abnormal EKG
Cardiac Imaging
Family Studies



HCM

**LV Outflow Tract
Obstruction
(LVOTO)**

$\frac{2}{3}$ have LVOTO

$\frac{1}{3}$ do not have LVOTO

Other non-HCM Causes of LV Hypertrophy

Metabolic & Multi-organ Syndromes

RASopathies
Mitochondrial myopathies
Glycogen / Lysosomal storage diseases
Amyloidosis
Sarcoidosis
Hemochromatosis
Danon disease

Secondary Causes

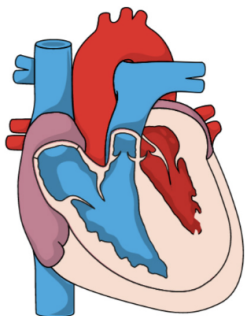
Athlete's heart
Hypertension
Valvular & subvalvular stenosis

Abbreviations: EKG, indicates electrocardiogram; RAS, reticular activating system.

Ommen, SR et al. 2020 ACC/AHA Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. *Circulation*. XXX:XX-XX.

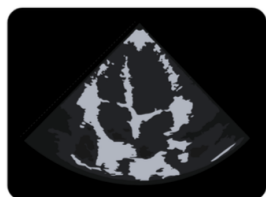
ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Defining Hypertrophic Cardiomyopathy in 2020



- Morphologic expression confined solely to the heart
- Characterized by left ventricular (LV) hypertrophy
Basal anterior septum in continuity with the anterior free wall = most common
- No other cardiac, systemic or metabolic disease capable of producing the magnitude of hypertrophy present
- Disease-causing sarcomere (or sarcomere-related) variant identified or genetic etiology unresolved

Diagnostic Criteria in Adults



2D echocardiography or cardiac MRI

Maximal end-diastolic LV wall thickness ≥ 15 mm

Maximal end-diastolic LV wall thickness 13-14 mm in family member of HCM pt. or in conjunction with positive genetic test

Other Nondiagnostic Morphologic Abnormalities Associated with HCM

- Systolic anterior motion (SAM) of the mitral valve
- Hyperdynamic LV function
- Hypertrophied & apically displaced papillary muscles
- Myocardial crypts
- Anomalous papillary muscle insertion in anterior MV leaflet
- Elongated mitral valve leaflets
- Myocardial bridging
- Right ventricular hypertrophy

Abbreviations: 2D, indicates two dimensional; MRI, magnetic resonance imaging; mm, millimeter; pt, patient.

Ommen, SR et al. 2020 ACC/AHA Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. *Circulation*. XXX:XX-XX.

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Adverse Event Associated Hypertrophic Cardiomyopathy

Majority of patients with HCM have a normal life expectancy without limiting symptoms or the need for major treatments



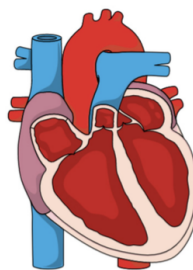
Sudden Death



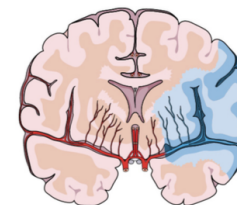
Progressive Functional Limitation



Atrial Fibrillation



Heart Failure

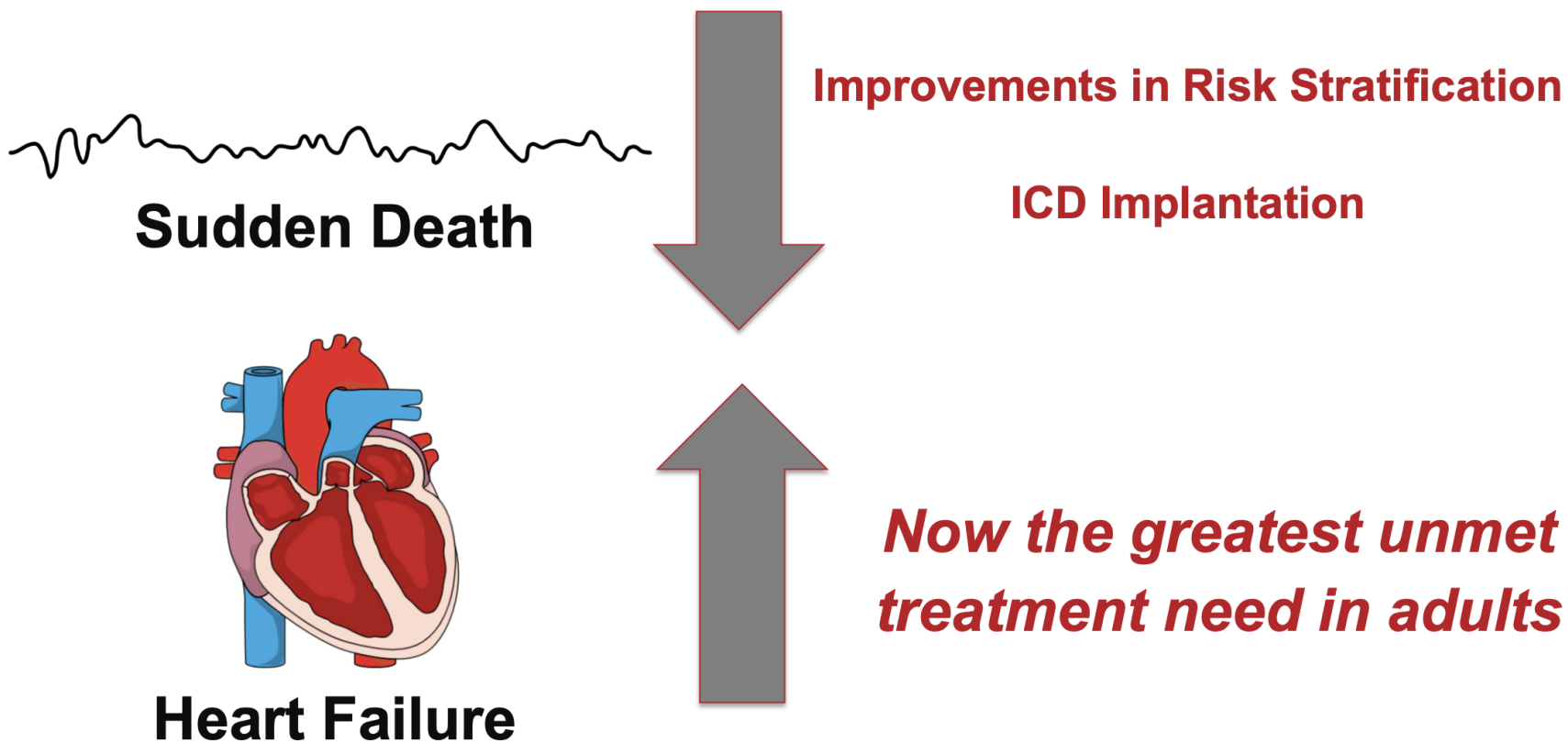


Thromboembolism

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ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Hypertrophic Cardiomyopathy Mortality Rates Now < 1% per Year

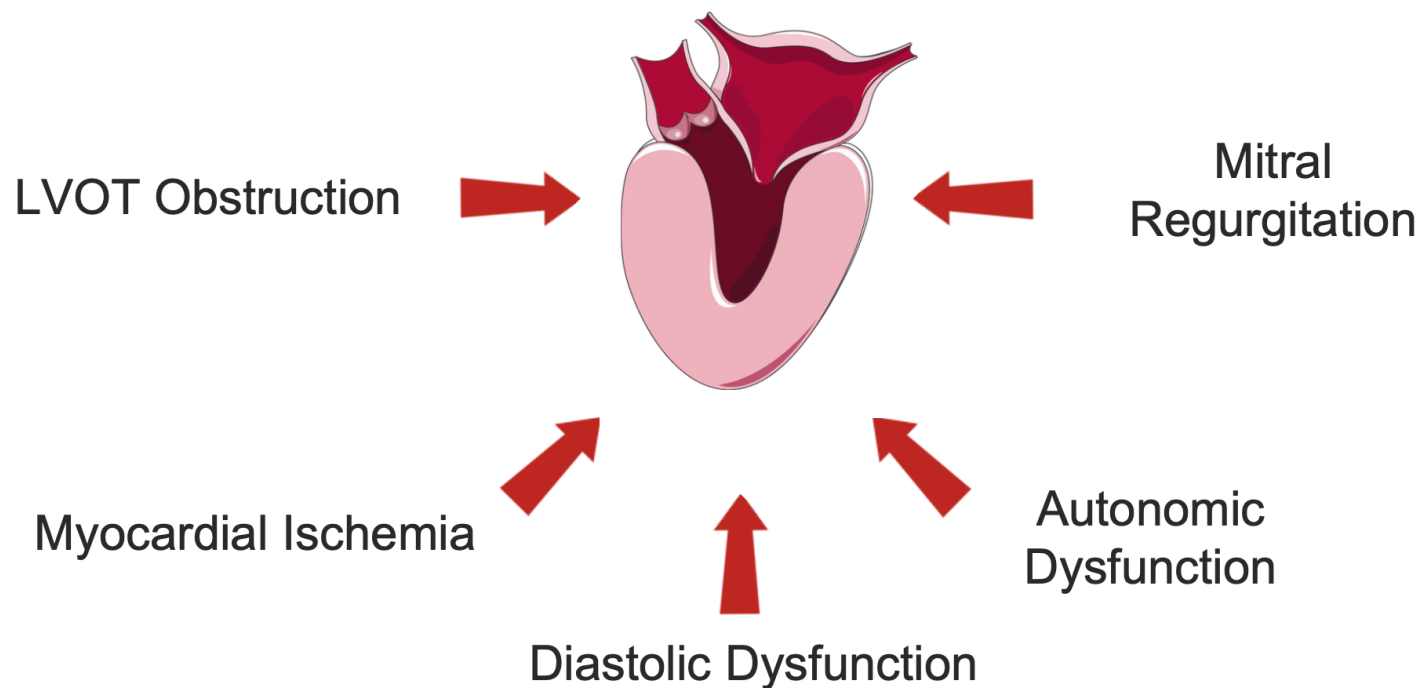


Abbreviations: ICD indicates implantable cardioverter-defibrillator.

Ommen, SR et al. 2020 ACC/AHA Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. *Circulation*. XXX:XX-XX.

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Pathophysiologic Myocardial Changes in Hypertrophic Cardiomyopathy



Abbreviations: LVOT indicates left ventricular outflow tract.

Ommen, SR et al. 2020 ACC/AHA Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. *Circulation*. XXX:XX-XX.

Hypertrophic Cardiomyopathy: Clinical Aspects

- Characterized by myocyte disarray, hypertrophy, and interstitial fibrosis
- 90% of pts have familial disease
- 10% *de novo* mutations
- Increased risk of SCD
- Adult prevalence 1:500 (Autosomal Dominant)
- 1st degree-relatives -1:2 risk gene carrier

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Genetic Etiology of Hypertrophic Cardiomyopathy (HCM)



~30-60% of HCM patients have an identifiable pathogenic or likely-pathogenic genetic variant

Sarcomere Genes Implicated in HCM

MYH7
MYBPC3
TNNI3
TNNT2
TPM1
MYL2
MYL3
ACTC1



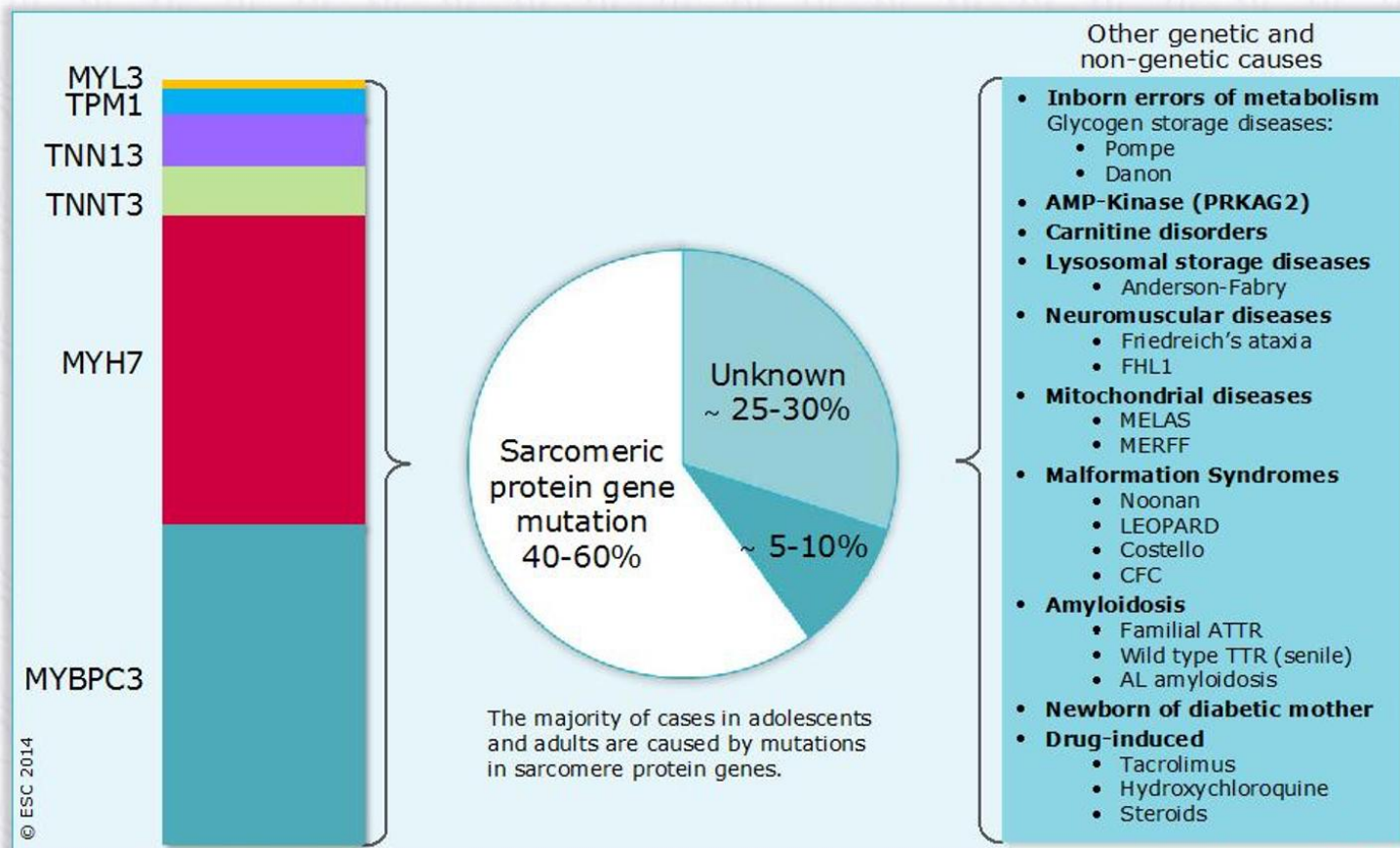
Many others have no genetic evidence of disease and / or no other affected family members

Two most common genes that harbor pathogenic variants in HCM (70%)

Ommen, SR et al. 2020 ACC/AHA Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. *Circulation*. XXX:XX-XX.

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Diverse aetiology of hypertrophic cardiomyopathy



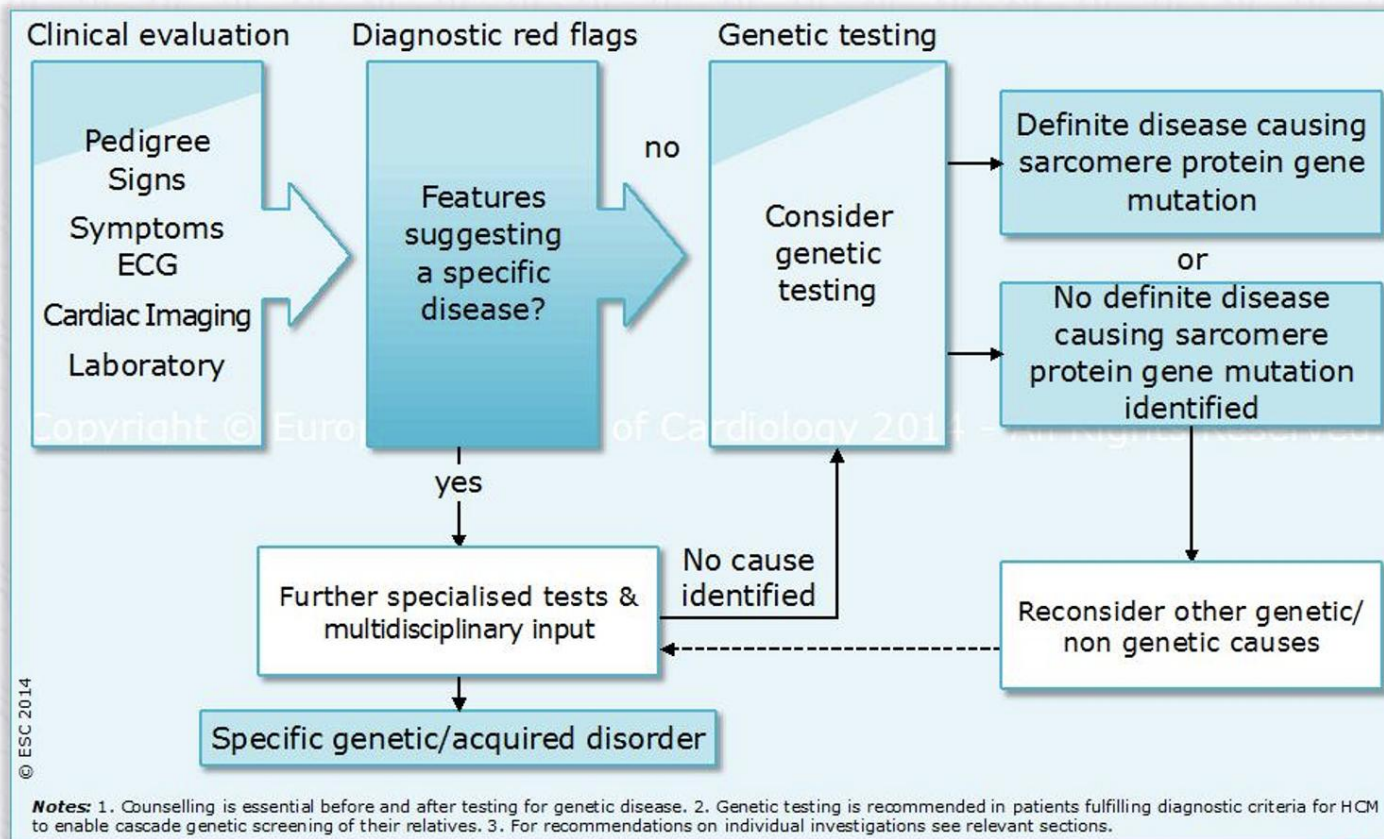
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European Heart Journal (2014);35:2733-2779 - doi:10.1093/eurheartj/ehu284

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ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Schematic summarising the general approach to the diagnosis of hypertrophic cardiomyopathy


www.escardio.org/guidelines

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

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Genetic counselling

Recommendations	Class	Level
Genetic counselling is recommended for all patients with HCM when their disease cannot be explained solely by a non-genetic cause, whether or not clinical or genetic testing will be used to screen family members.	I	B
Genetic counselling should be performed by professionals trained for this specific task working within a multidisciplinary specialist team.	IIa	C

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Genetic testing in probands

Recommendations	Class	Level
Genetic testing is recommended in patients fulfilling diagnostic criteria for HCM, when it enables cascade genetic screening of their relatives.	I	B
It is recommended that genetic testing be performed in certified diagnostic laboratories with expertise in the interpretation of cardiomyopathy-related mutations.	I	C
In the presence of symptoms and signs of disease suggestive of specific causes of HCM, genetic testing is recommended to confirm the diagnosis.	I	B
Genetic testing in patients with a borderline ^a diagnosis of HCM should be performed only after detailed assessment by specialist teams.	IIa	C
Post-mortem genetic analysis of stored tissue or DNA should be considered in deceased patients with pathologically confirmed HCM, to enable cascade genetic screening of their relatives.	IIa	C

^aBorderline: left ventricular wall thickness 12 – 13 mm in adults; left ventricular hypertrophy in the presence of hypertension, athletic training, valve disease.

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Genetic and clinical testing of adult relatives

Recommendations	Class	Level
Cascade genetic screening, after pre-test counselling, is recommended in first-degree adult relatives of patients with a definite disease-causing mutation.	I	B
Clinical evaluation, employing ECG and echocardiography and long-term follow-up, is recommended in first-degree relatives who have the same definite disease-causing mutation as the proband.	I	C
First-degree relatives who do not have the same definite disease-causing mutation as the proband should be discharged from further follow-up but advised to seek re-assessment if they develop symptoms or when new clinically relevant data emerge in the family.	IIa	B
When no definite genetic mutation is identified in the proband or genetic testing is not performed, clinical evaluation with ECG and echocardiography should be considered in first-degree adult relatives and repeated every 2-5 years (or 6-12 monthly if non-diagnostic abnormalities are present).	IIa	C

Proband = usually the first family member to be diagnosed with the condition.

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Clinical Features in Patients with “HCM Mimics”

Life Stage	Systemic Features	Possible Etiology	Diagnostic Approach
Infants (0-12 months) and toddlers	Dysmorphic features, failure to thrive, metabolic acidosis	- RASopathies - Glycogen storage diseases, other metabolic or mitochondrial diseases - Infant of a mother with diabetes	- Geneticist assessment - Newborn metabolic screening - Specific metabolic assays - Genetic testing
Early childhood	Delayed or abnormal cognitive development, visual or hearing impairment	- RASopathies - Mitochondrial diseases	- Biochemical screening - Genetic testing
School age and adolescence	Skeletal muscle weakness or movement disorder	- Friedrich ataxia, Danon disease - Mitochondrial disease	- Biochemical screening - Neuromuscular assessment - Genetic testing
Adulthood	Movement disorder, peripheral neuropathy, renal dysfunction	Anderson-Fabry disease, Friedrich ataxia, infiltrative disorders (e.g., amyloidosis), glycogen storage diseases	- Biochemical screening, - Neuromuscular assessment - Genetic testing

Abbreviations: RAS indicates reticular activating system.

Ommen, SR et al. 2020 ACC/AHA Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. *Circulation*. XXX:XX-XX.

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Examples of signs and symptoms suggestive of specific diagnoses

Symptom/sign	Diagnosis
Learning difficulties, mental retardation	• Mitochondrial diseases • Noonan/LEOPARD/Costello syndrome • Danon disease
Sensorineural deafness	• Mitochondrial diseases (particularly with diabetes) • Anderson-Fabry disease • LEOPARD syndrome
Visual impairment	• Mitochondrial diseases (retinal disease, optic nerve atrophy) • TTR-related amyloidosis (cotton wool type vitreous opacities) • Danon disease (retinitis pigmentosa) • Anderson-Fabry disease (cataracts, corneal opacities)

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Examples of signs and symptoms suggestive of specific diagnoses (Cont.)

Symptom/sign	Diagnosis
Gait disturbance	Friedreich's ataxia
Paraesthesia/sensory abnormalities/neuropathic pain	- Amyloidosis - Anderson-Fabry disease
Carpal tunnel syndrome	TTR-related amyloidosis (especially when bilateral and in male patients)
Muscle weakness	- Mitochondrial diseases - Glycogen storage disorders - FHL1 mutations - Friedreich's ataxia
Palpebral ptosis	- Mitochondrial diseases - Noonan/LEOPARD syndrome - Myotonic dystrophy
Lentigines/café au lait spots	LEOPARD/Noonan syndrome
Angiokeratomata, hypohidrosis	Anderson-Fabry disease

FHL1= four and a half LIM domains 1; LEOPARD = lentigines, ECG abnormalities, ocular hypertelorism, pulmonary stenosis, abnormal genitalia, retardation of growth and sensorineural deafness; TTR = transthyretin.



ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Echocardiography Recommendations in Hypertrophic Cardiomyopathy

COR	LOE	Recommendations
1	B-NR	1. In patients with suspected HCM, a TTE is recommended in the initial evaluation.
1	B-NR children	2. In patients with HCM with no change in clinical status or events, repeat TTE is recommended every 1 to 2 years to assess the degree of myocardial hypertrophy, dynamic LVOTO, MR, and myocardial function.
1	C-LD adults	2. In patients with HCM with no change in clinical status or events, repeat TTE is recommended every 1 to 2 years to assess the degree of myocardial hypertrophy, dynamic LVOTO, MR, and myocardial function.
1	B-NR	3. For patients with HCM who experience a change in clinical status or a new clinical event, repeat TTE is recommended.
1	B-NR	4. For patients with HCM and resting LVOT gradient <50 mm Hg, a TTE with provocative maneuvers is recommended.

Abbreviations: COR indicates classification of recommendation; LOE, level of evidence; B-NR, Level B nonrandomized; C-LD, Level C, limited data; TTE, transthoracic echocardiogram; LVOTO, left ventricular outflow tract obstruction; MR, mitral regurgitation; LVOT, left ventricular outflow tract.

Ommen, SR et al. 2020 ACC/AHA Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. *Circulation*. XXX:XX-XX.

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Transthoracic echocardiography evaluation in hypertrophic cardiomyopathy

Recommendations	Class	Level
In all patients with HCM at initial evaluation, transthoracic 2-D and Doppler echocardiography are recommended, at rest and during Valsalva manoeuvre in the sitting and semi-supine positions—and then on standing if no gradient is provoked.	I	B
Measurement of maximum diastolic wall thickness is recommended, using 2-D short-axis views in all LV segments, from base to apex.	I	C
A comprehensive evaluation of LV diastolic function is recommended, including pulsed Doppler of mitral valve inflow, tissue Doppler velocities at the mitral annulus, pulmonary vein flow velocities, pulmonary artery systolic pressure, and measurement of LA size and volume.	I	C
In <i>symptomatic</i> patients with a resting or provoked peak instantaneous LV outflow tract gradient <50 mm Hg, 2-D and Doppler echocardiography <i>during exercise</i> in the standing, sitting or semi-supine position is recommended to detect provokable LVOTO and exercise induced mitral regurgitation.	I	B

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Echocardiographic features that suggest specific aetiologies

Finding	Specific diseases to be considered
Increased interatrial septum thickness	Amyloidosis
Increased AV valve thickness	Amyloidosis; Anderson-Fabry disease
Increased RV free wall thickness	Amyloidosis, myocarditis, Anderson-Fabry disease, Noonan syndrome and related disorders
Mild to moderate pericardial effusion.	Amyloidosis, myocarditis
Ground-glass appearance of ventricular myocardium on 2-D echocardiography	Amyloidosis
Concentric LVH	Glycogen storage disease, Anderson-Fabry disease, PRKAG2 mutations
Extreme concentric LVH (wall thickness ≥ 30 mm)	Danon disease, Pompe disease
Global LV hypokinesia (with or without LV dilatation)	Mitochondrial disease, TTR-related amyloidosis, PRKAG2 mutations, Danon disease, myocarditis, advanced sarcomeric HCM, Anderson-Fabry disease
Right ventricular outflow tract obstruction	Noonan syndrome and associated disorders

PRKAG2 = gamma-2 subunit of the adenosine monophosphate-activated protein kinase;

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European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284



ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Transoesophageal echocardiography

Recommendations	Class	Level
Perioperative TOE is recommended in patients undergoing septal myectomy, to confirm the mechanism of LVOTO, to guide the surgical strategy, to assess post-surgical complications and to detect residual LV outflow tract obstruction.	I	C
TOE should be considered in patients with LVOTO if the mechanism is unclear, or when assessing the mitral valve apparatus before a septal reduction procedure, or when severe mitral regurgitation, caused by intrinsic valve abnormalities, is suspected.	IIa	C
TOE with intracoronary contrast injection of the candidate septal perforator artery should be considered to guide septal alcohol ablation when transthoracic windows are insufficient for proper visualization of echo-contrast within the myocardium.	IIa	C

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Nuclear scintigraphy

Recommendations	Class	Level
Bone scintigraphy (particularly with ^{99m}Tc -DPD) should be considered in patients with symptoms, signs and non-invasive tests consistent with TTR-related amyloidosis.	IIa	B
Cardiac CT should be considered in patients who have inadequate echocardiographic imaging and contra-indications for CMR.	IIa	C

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Cardiovascular Magnetic Resonance (CMR) Imaging Recommendations in HCM

COR	LOE	Recommendations
1	B-NR	1. For patients suspected to have HCM in whom echocardiography is inconclusive, CMR imaging is indicated for diagnostic clarification
1	B-NR	2. For patients with LVH in whom there is a suspicion of alternative diagnoses, including infiltrative or storage disease as well as athlete's heart, CMR imaging is useful.
1	B-NR	3. For patients with HCM who are not otherwise identified as high risk for SCD, or in whom a decision to proceed with ICD remains uncertain after clinical assessment that includes personal/family history, echocardiography, and ambulatory electrocardiographic monitoring, CMR imaging is beneficial to assess for maximum LV wall thickness, ejection fraction (EF), LV apical aneurysm, and extent of myocardial fibrosis with LGE.
1	B-NR	4. For patients with obstructive HCM in whom the anatomic mechanism of obstruction is inconclusive on echocardiography, CMR imaging is indicated to inform the selection and planning of SRT.

Abbreviations: SCD indicates sudden cardiac death; ICD, implanted cardioverter-defibrillator; LV, left ventricular; LGE, late gadolinium enhancement; SRT, septal reduction therapy; COR, classification of recommendation; LOE, level of evidence; B-NR, Level B nonrandomized.

Ommen, SR et al. 2020 ACC/AHA Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. *Circulation*. XXX:XX-XX.



ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Cardiovascular magnetic resonance evaluation in hypertrophic cardiomyopathy

Recommendations	Class	Level
It is recommended that CMR studies be performed and interpreted by teams experienced in cardiac imaging and in the evaluation of heart muscle disease.	I	C
In the absence of contra-indications, CMR with LGE is recommended in patients with suspected HCM who have inadequate echocardiographic windows, in order to confirm the diagnosis.	I	B
In the absence of contra-indications, CMR with LGE should be considered in patients fulfilling diagnostic criteria for HCM, to assess cardiac anatomy, ventricular function, and the presence and extent of myocardial fibrosis.	IIa	B
CMR with LGE imaging should be considered in patients with suspected apical hypertrophy or aneurysm.	IIa	C
CMR with LGE imaging should be considered in patients with suspected cardiac amyloidosis.	IIa	C
CMR with LGE may be considered before septal alcohol ablation or myectomy, to assess the extent and distribution of hypertrophy and myocardial fibrosis.	IIb	C

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Table 1 Added value of CMR in the evaluation of patients with increased left ventricular thickness.

Morphological visualization

Identification of the predominant morphologic phenotype
 Quantification of maximum thickness
 Differentiation between symmetric and asymmetric morphologies
 Assessment of the segments involved
 Evaluation of recesses, diverticula, aneurysms, clefts, and crypts
 Structural evaluation of the mitral and aortic valve apparatus
 Evaluation of the papillary muscles, and abnormalities of the tendinous chords
 Differentiation of the true interventricular septum from other adjacent structures

Functional evaluation

Biventricular volume quantification and function
 Assessment of global and segmental systolic thickening
 Presence of dynamic left ventricular outflow tract (LVOT) and its cause
 Valvular function
 Perfusion
 Strain

Risk stratification

Maximum thickness
 Presence of LVOT obstruction
 Presence of focal or diffuse fibrosis
 Quantification of total ventricular mass and fibrosis

Differential diagnosis

Athlete's heart
 Hypertensive heart disease
 Valvular heart disease
 Other pathologies with LVOT obstruction: membrane or subaortic ring
 Metabolic, deposit and infiltrative diseases
 Tumours (intramyocardial fibroma)



GLOBAL CARDIOLOGY
SCIENCE & PRACTICE

Review article

Cardiac magnetic resonance imaging in the evaluation of patients with hypertrophic cardiomyopathy

Juan Carlos Brenes¹, Adelina Doltra^{2*}, Susanna Prat²

Brenes et al., Global Cardiology Science and Practice, 2018

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Table 2 Technical advantages of CMR in the evaluation of patients with HCM over echo.

TECHNICAL ADVANTAGES OF CMR

Accurate delimitation of the endocardial rim

Possibility of obtaining infinite imaging planes

Coverage of both ventricles

Better estimation of ventricular volumes and function

Better estimation of the magnitude of hypertrophy as compared to echocardiography

Better identification of focal forms

Visualize and quantification of fibrosis

Brenes et al., Global Cardiology Science and Practice, 2018

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

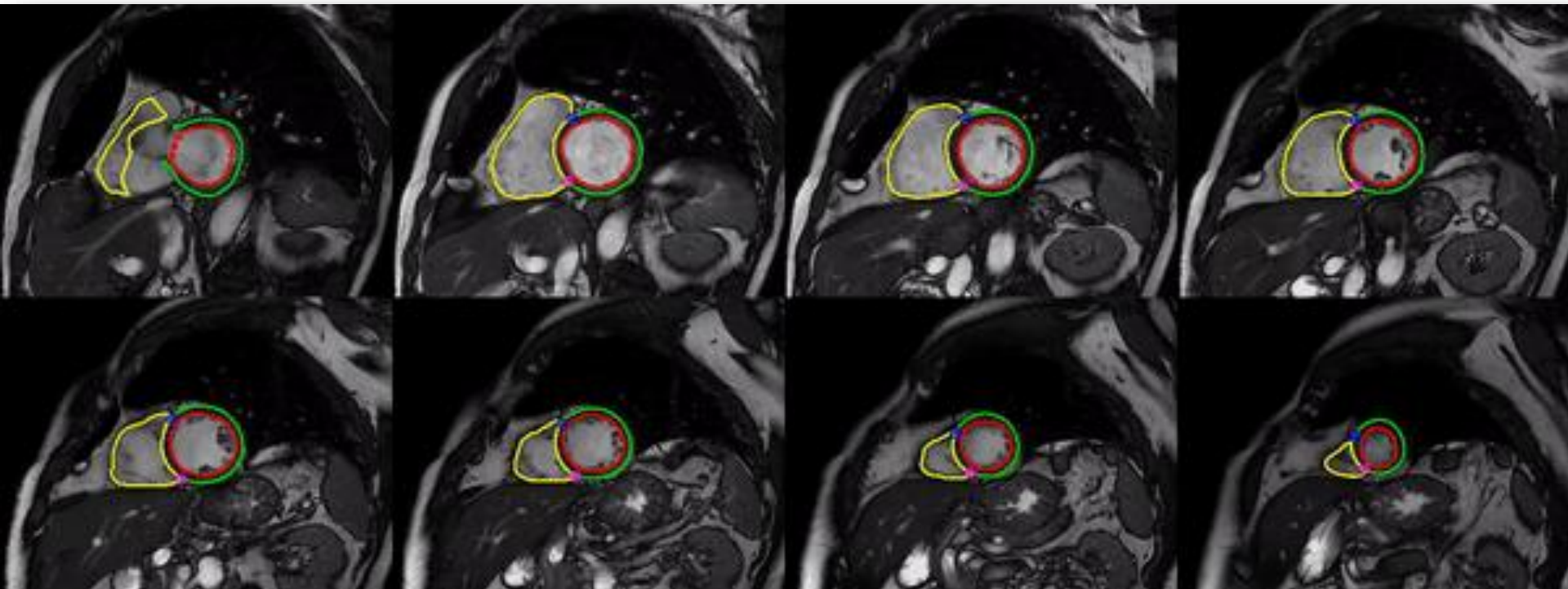
Table 3 Basic and advanced sequences of CMR in HCM.

Basic sequences	
Sequences	Objective
Cine SSFP sequences (4- 2- and 3-chamber views)	Structural assessment, motility evaluation
Cine SSFP short axis stack	Volume and functional evaluation
Cine SSFP sequences with orthogonal LVOT view	Rule out LVOT obstruction and SAM evaluation
Flow sequences LVOT (in-plane/through-plane)	LVOT obstruction presence and location. Peak velocity quantification (infraestimation as compared to echo)
Inversion-recovery fast gradient-echo (LGE assessment)	Presence and extension of fibrosis. Percentage of involvement in relation to the total myocardial mass.
Advanced/optional sequences	
Sequences	Objective
T1 mapping sequences pre- and post-contrast	Diffuse fibrosis and extracellular volume evaluation
Tagging sequences /Feature tracking	Dynamic myocardial deformation. Strain assessment
Perfusion sequences (rest/stress)	Detection of myocardial ischemia

Brenes et al., Global Cardiology Science and Practice, 2018

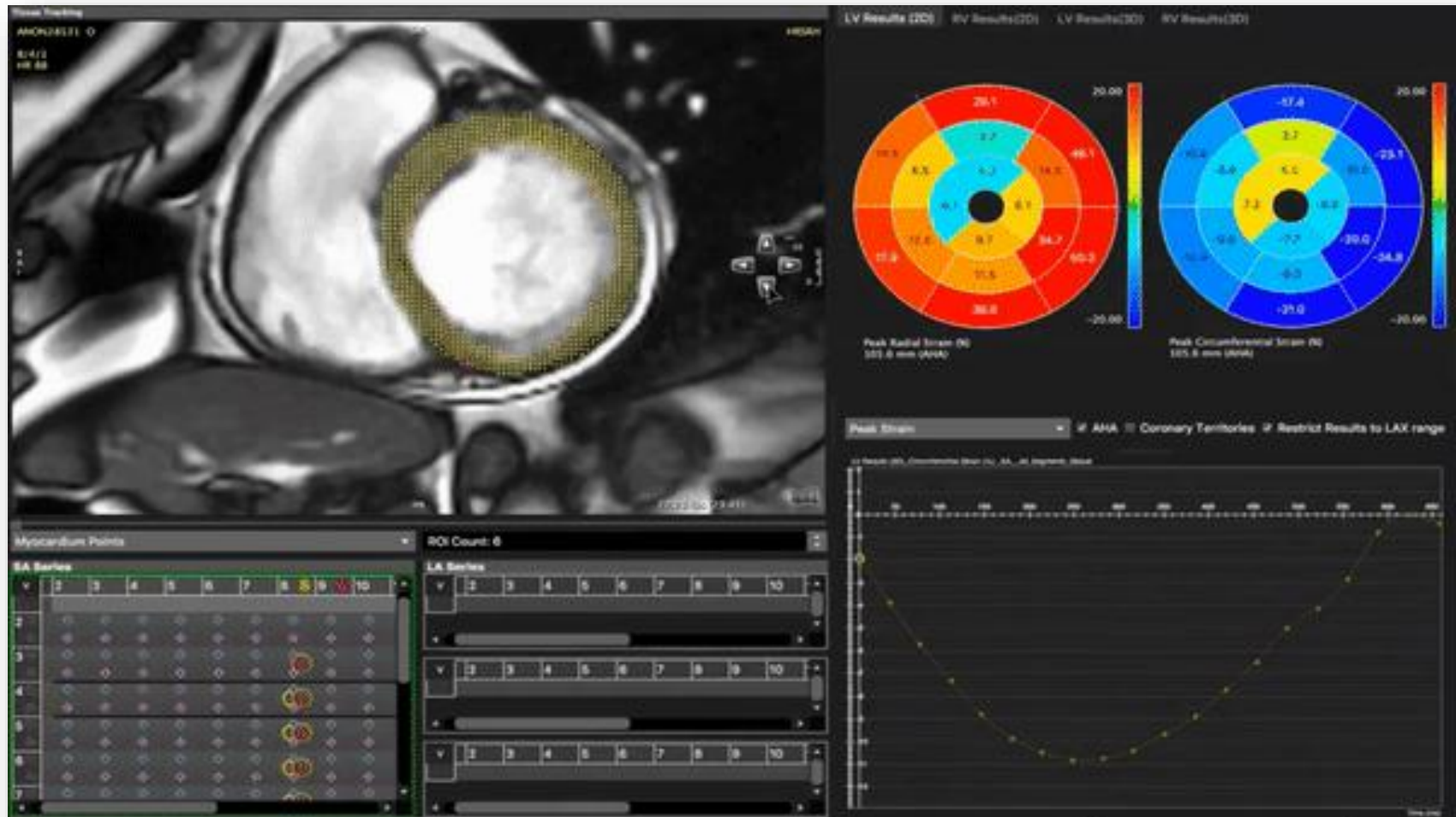
Cardiac Magnetic Resonance (CMR) – Diagnostic Tools

- Quantitative volumetric analysis of left and right ventricle



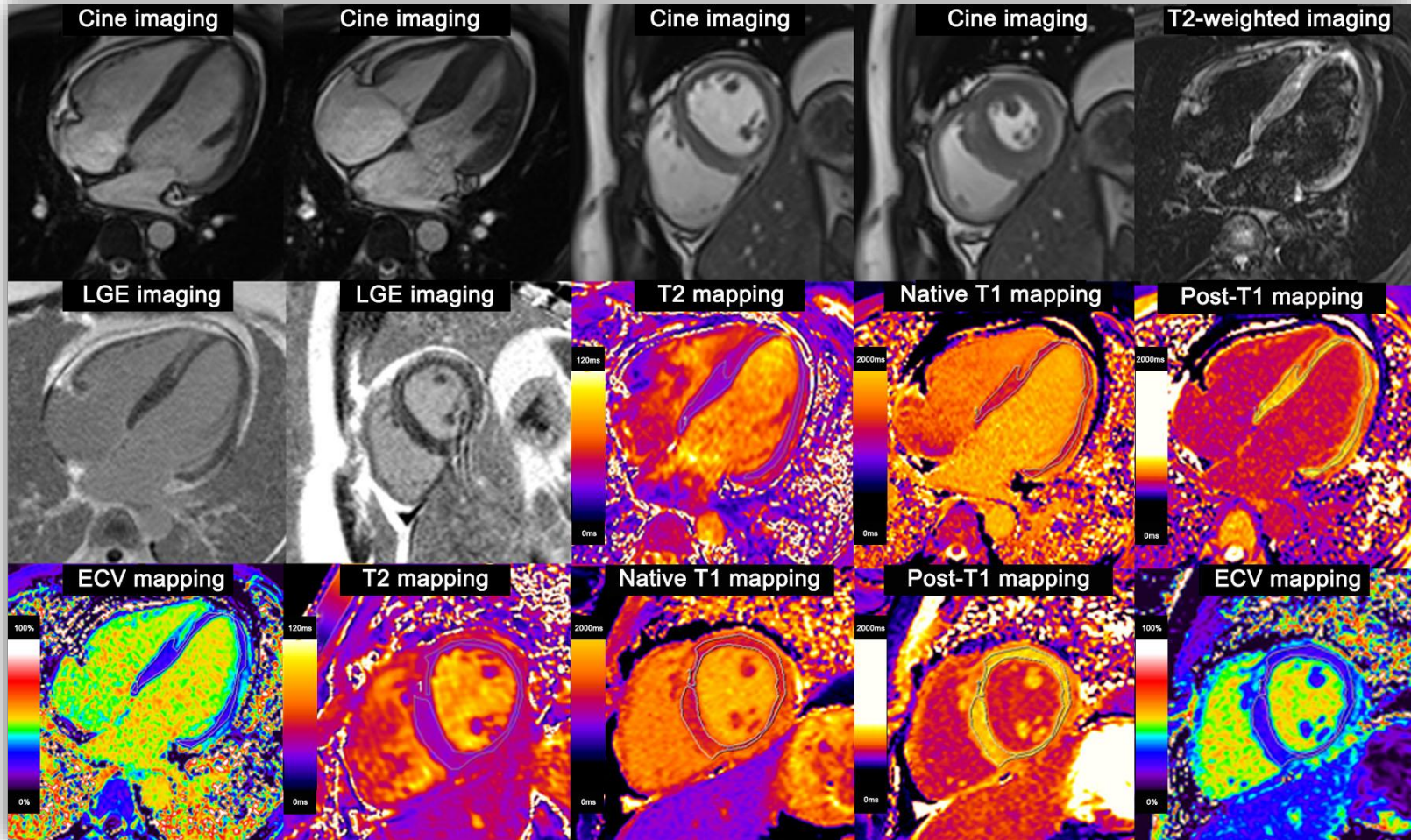
Cardiac Magnetic Resonance (CMR) – Diagnostic Tools

- Left ventricular **strain** measurement assessed by feature tracking



Cardiac Magnetic Resonance (CMR) – Diagnostic Tools

- Myocardial tissue characterization

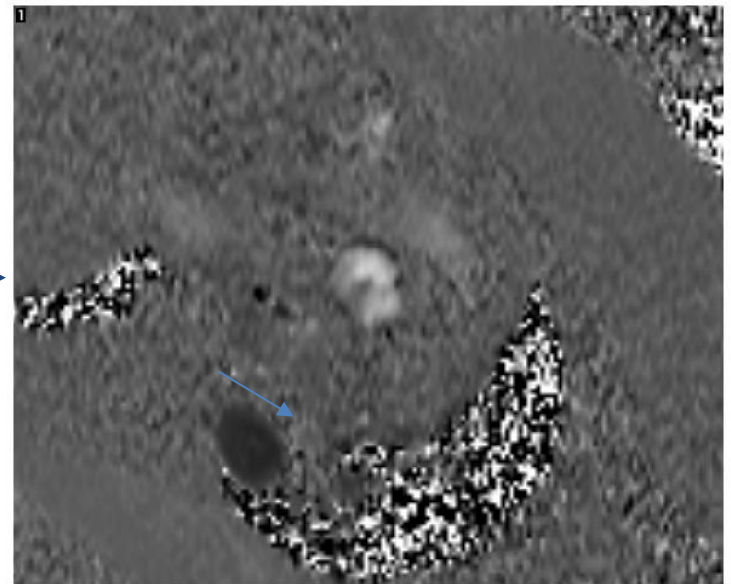


HCM: Cine Imaging

- The key questions to address are: -
 1. Presence, distribution, and severity of LVH and RVH. LV/RV mass and wall thickness
 2. Extent of septal involvement
 3. Distribution of hypertrophy in the variant forms of hypertrophic cardiomyopathy

HCM: LVOTO Assessment

- In-plane followed by through plane breath-hold flow mapping is performed to look at the peak velocity at the outflow tract (red-bar) and at the level of the aortic valve.



Assessment of Fibrosis

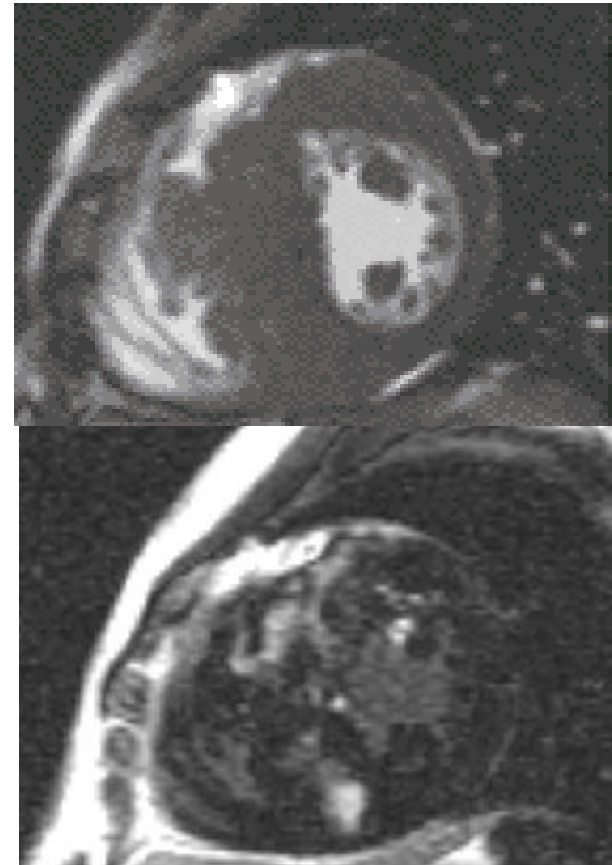
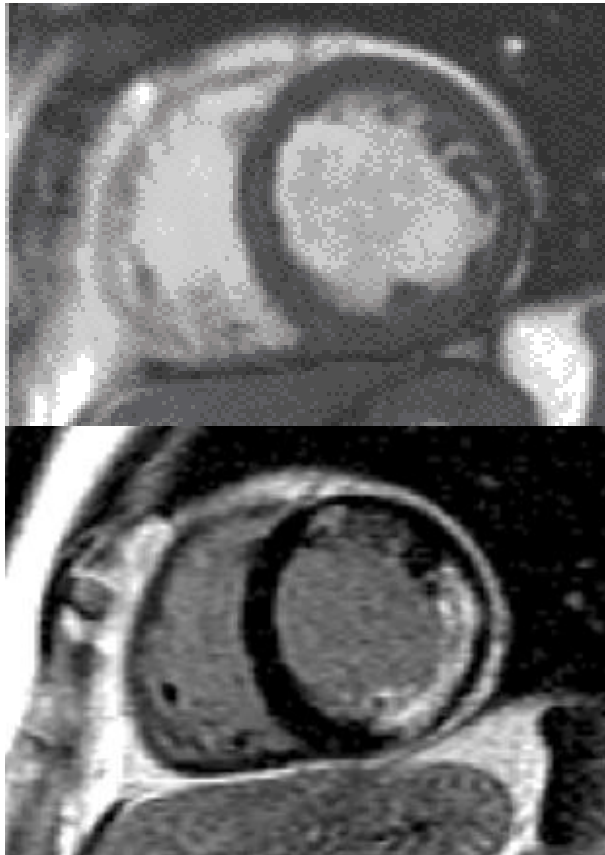
- The presence of replacement fibrosis can be detected using the inversion recovery late enhancement technique following gadolinium-DTPA administration.
- *Fibrosis is the main component of chronic MI which is visible with the late enhancement technique*

Fibrosis imaging in HCM

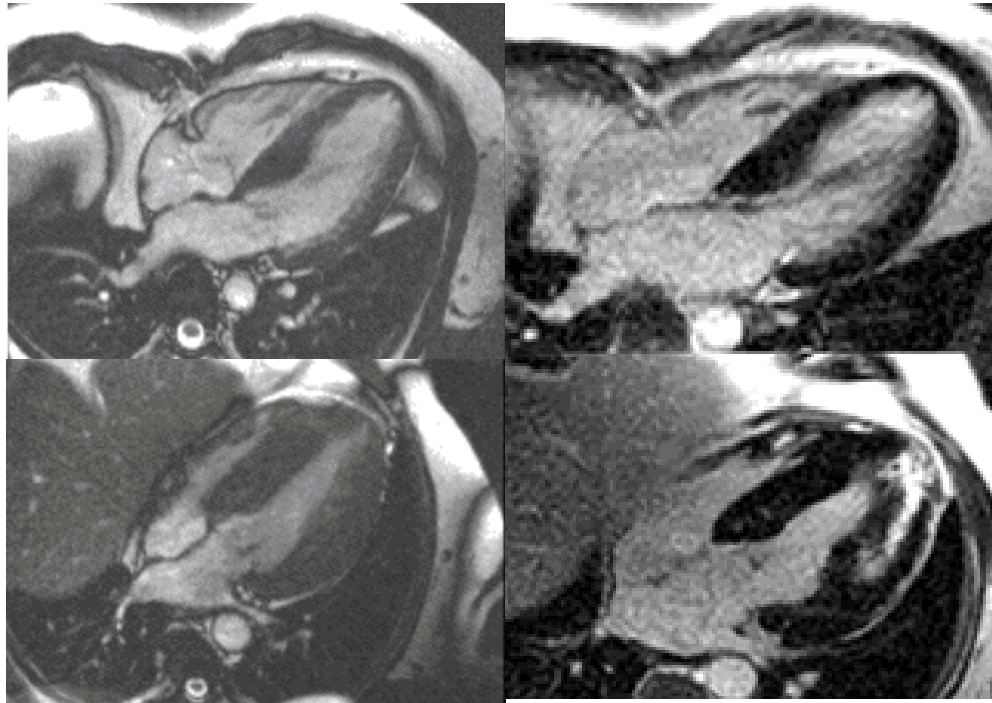
Gd infarct imaging



HCM fibrosis imaging?

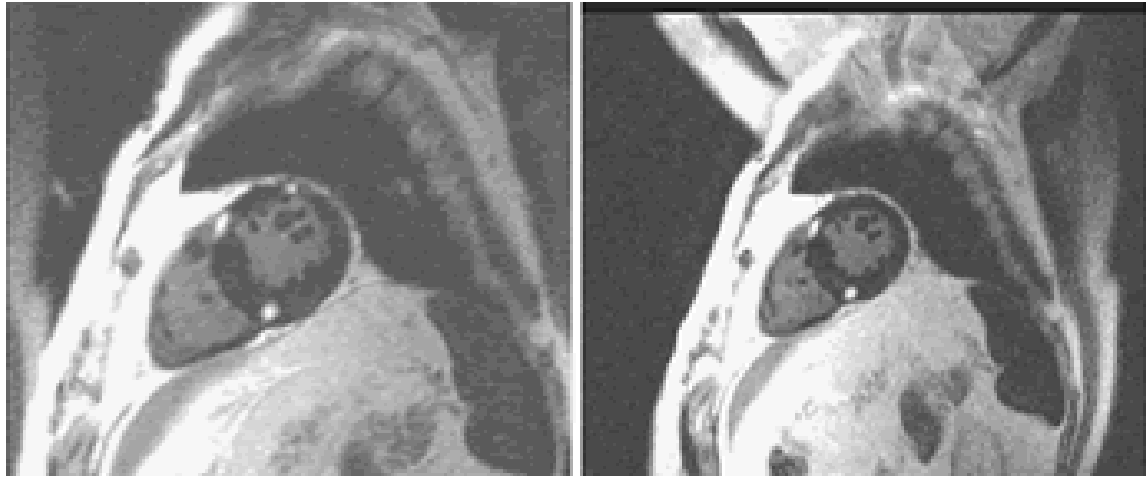


HCM – a wide variety of scar



2 patients. For the lower patient, scar is present and invisible without Gd-DTPA. Many patients have no *detectable* scar

RV insertion point enhancement

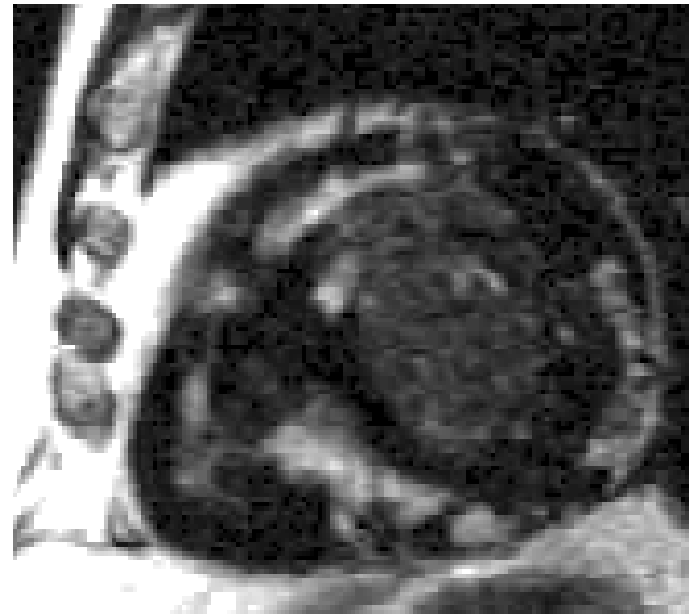
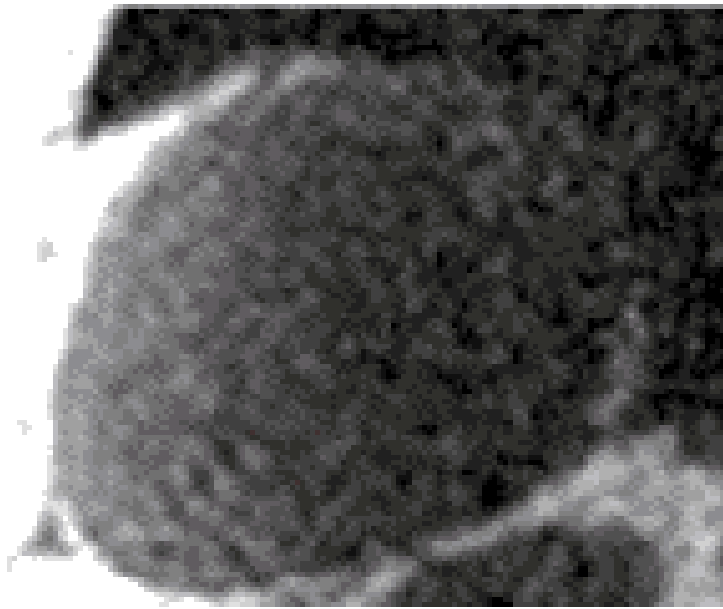


2 spots of enhancement at RV insertion points

■ The 3rd point is artefact

- Present AP phase encoding, disappears head-foot.
This is artefact ghosting across the image.

Perfusion defect



Perfusion defects in HCM – uncertain significance;
here matching enhancement

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

Risk Assessment of Sudden Cardiac Death (SCD) in HCM



At initial evaluation and every 1-2 years (Class I)



Assess the following (Class I):

- ✓ Personal history of cardiac arrest, sustained ventricular arrhythmia, OR unexplained syncope suspected to be arrhythmic
- ✓ Family history of premature SCD in a close relative
- ✓ Maximal LV wall thickness, EF $\leq$ 50%, apical aneurysm
- ✓ NSVT episodes on continuous ambulatory electrocardiographic monitoring; In select adult patients without major SCD risk factors, ICD may be considered in NSVT present on ambulatory monitoring (Class IIb).

IF none of the above:



CMR to help decision regarding ICD (Class I)



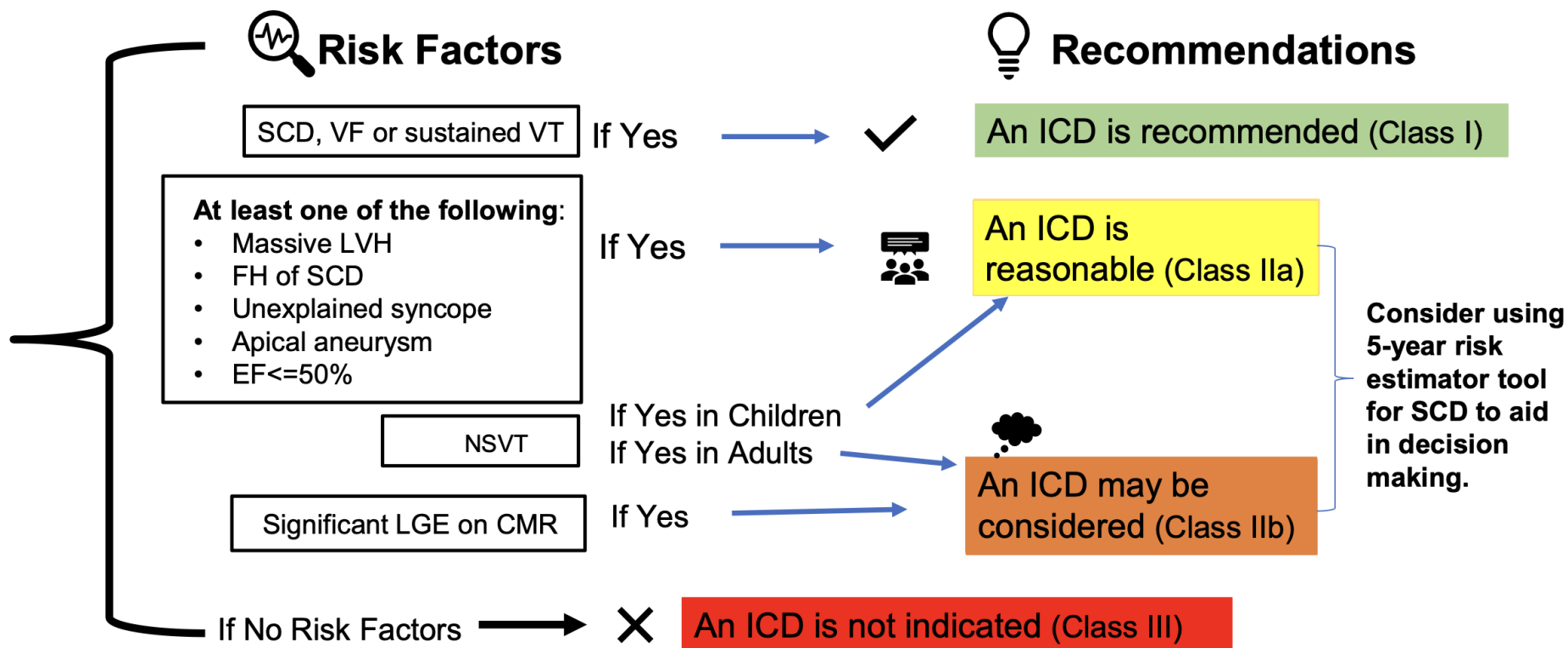
Reasonable to obtain echocardiographic LA diameter and LVOT gradient (Class IIa)

Abbreviations: EF indicates ejection fraction; NSVT, non-sustained ventricular tachycardia; CMR, cardiovascular magnetic resonance; ICD, implantable cardioverter defibrillator; LA, left atrium; LVOT, left ventricular outflow tract.

Ommen, SR et al. 2020 ACC/AHA Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. *Circulation*. XXX:XX-XX.

ΥΠΕΡΤΡΟΦΙΚΗ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΑ

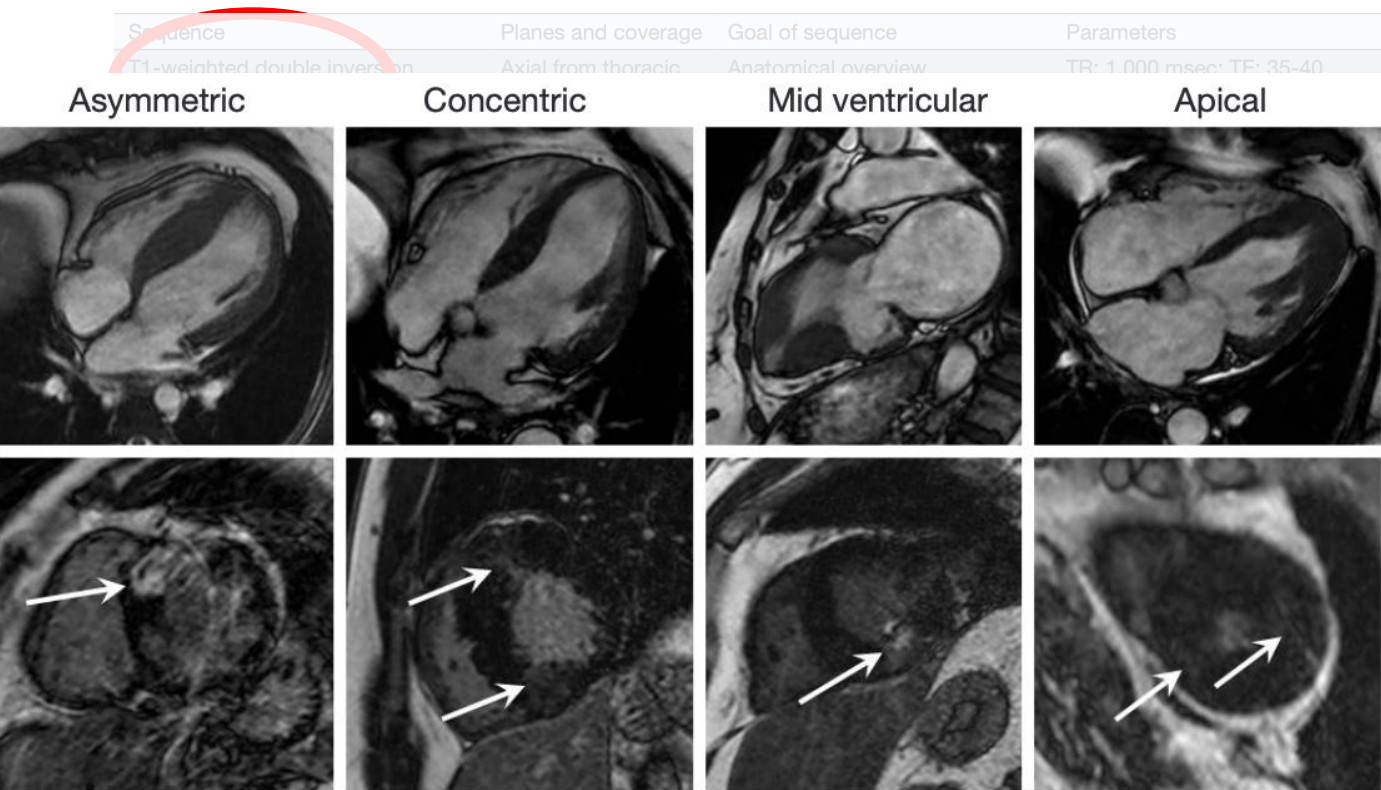
Indications for ICD in HCM Patients



Abbreviations: ICD indicates implantable cardioverter defibrillator; SCD, sudden cardiac death; VF, ventricular fibrillation; VT, ventricular tachycardia; LVH, left ventricular hypertrophy; FH, family history; EF, ejection fraction; NSVT, non-sustained ventricular tachycardia; LGE, late gadolinium enhancement; CMR, cardiac magnetic resonance imaging.

Ommen, SR et al. 2020 ACC/AHA Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. *Circulation*. XXX:XX-XX.



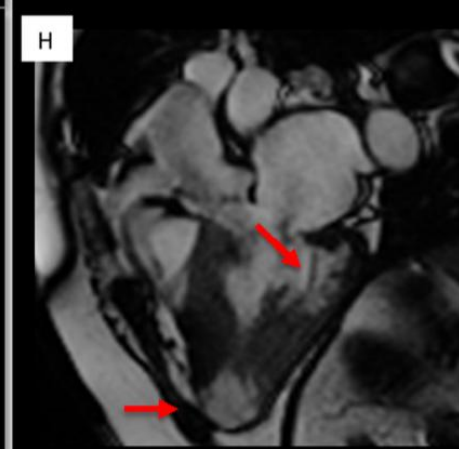
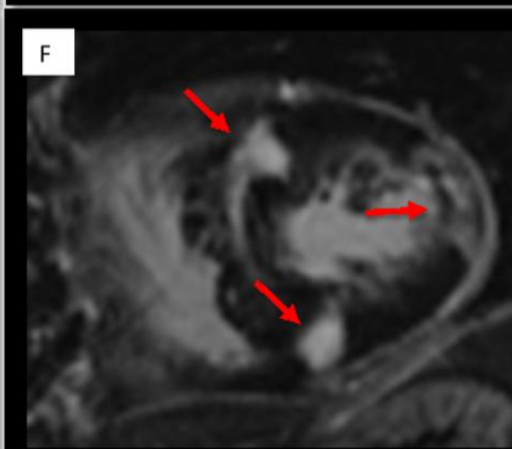
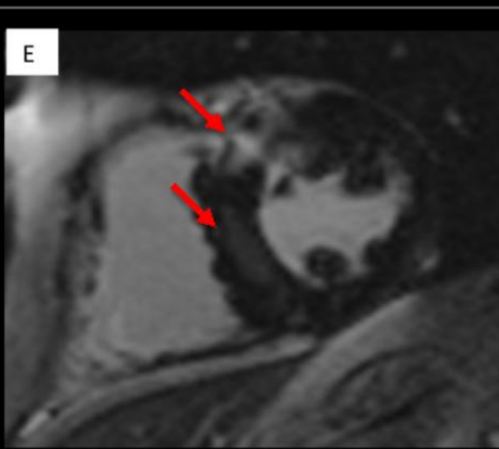
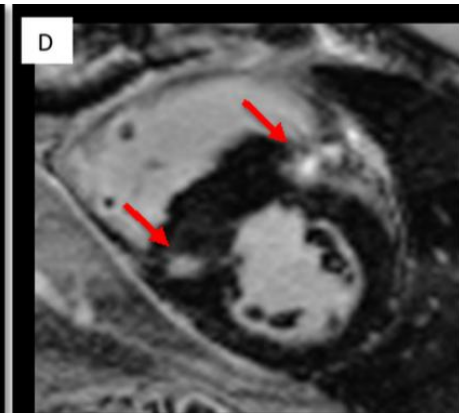
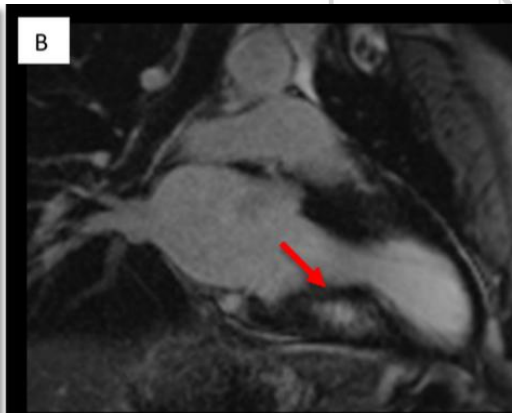
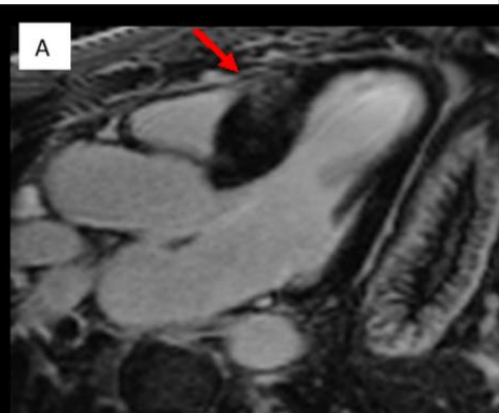


Πρωτόκολλο CMR

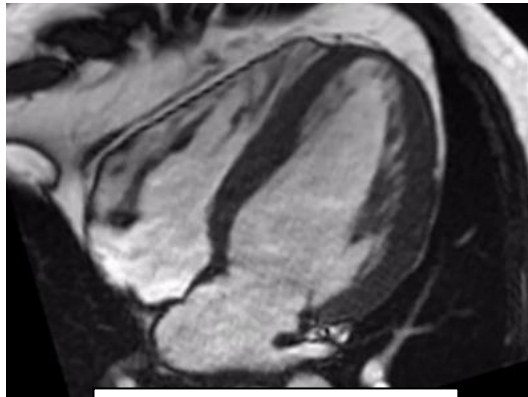
MRI, magnetic resonance imaging; HCM, hypertrophic cardiomyopathy; LVH, left ventricular hypertrophy.

Hoey et al., Quant Imaging Med Surg, 2014

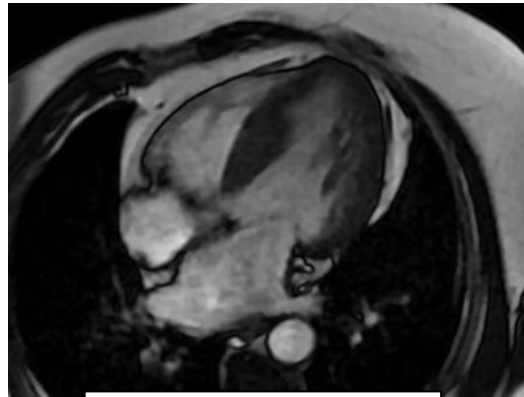
HYPERENHANCEMENT PATTERNS



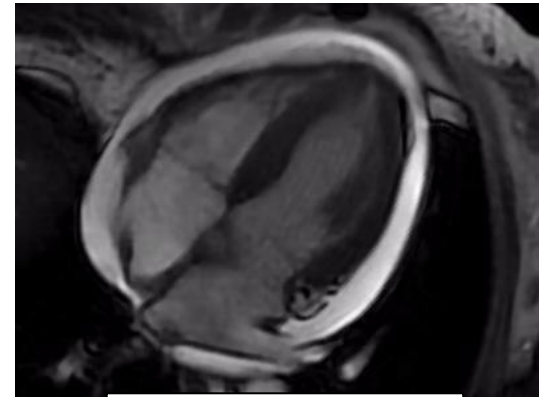
• Amyloidosis, Systemic Sclerosis, Post cardiac Bienes et al., Global Cardiology Science and Practice, 2018



Υπερτασική
Μυοκαρδιοπάθεια

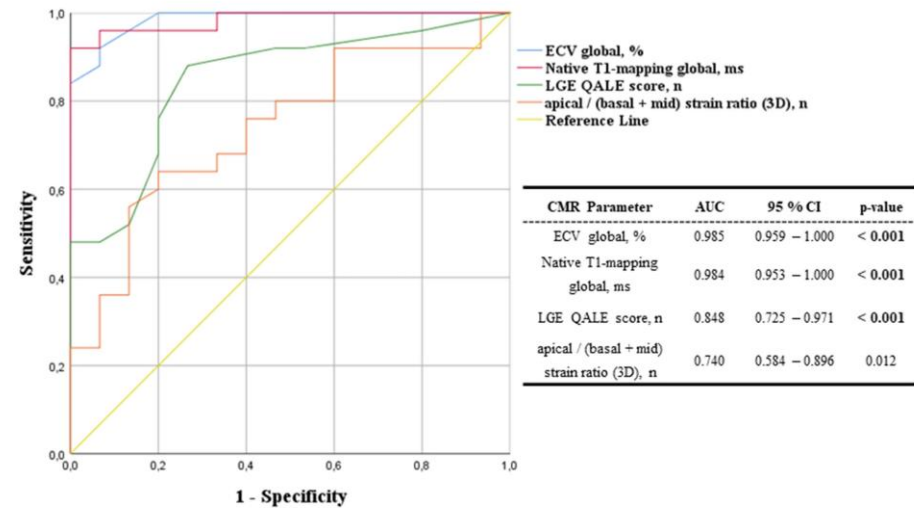
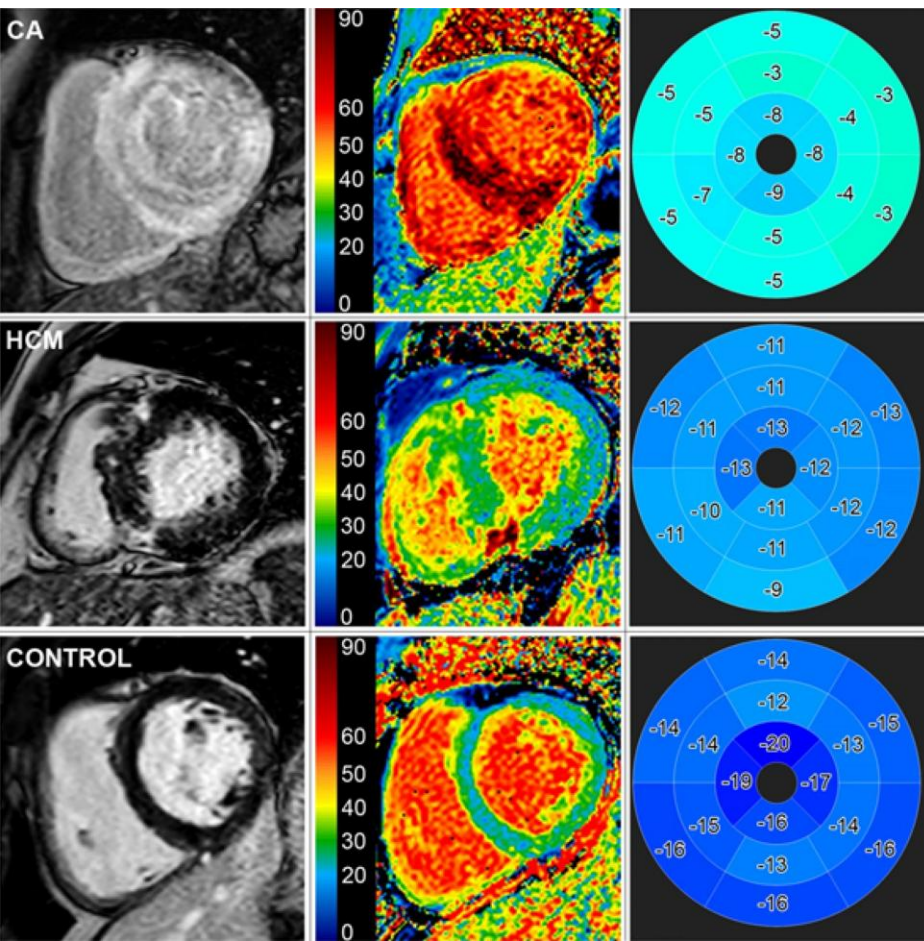


Υπερτροφική
Μυοκαρδιοπάθεια



Καρδιακή
Αμυλοείδωση

T1-/T2-
χαρτογράφη
ση
-
T1-/T2-
mapping

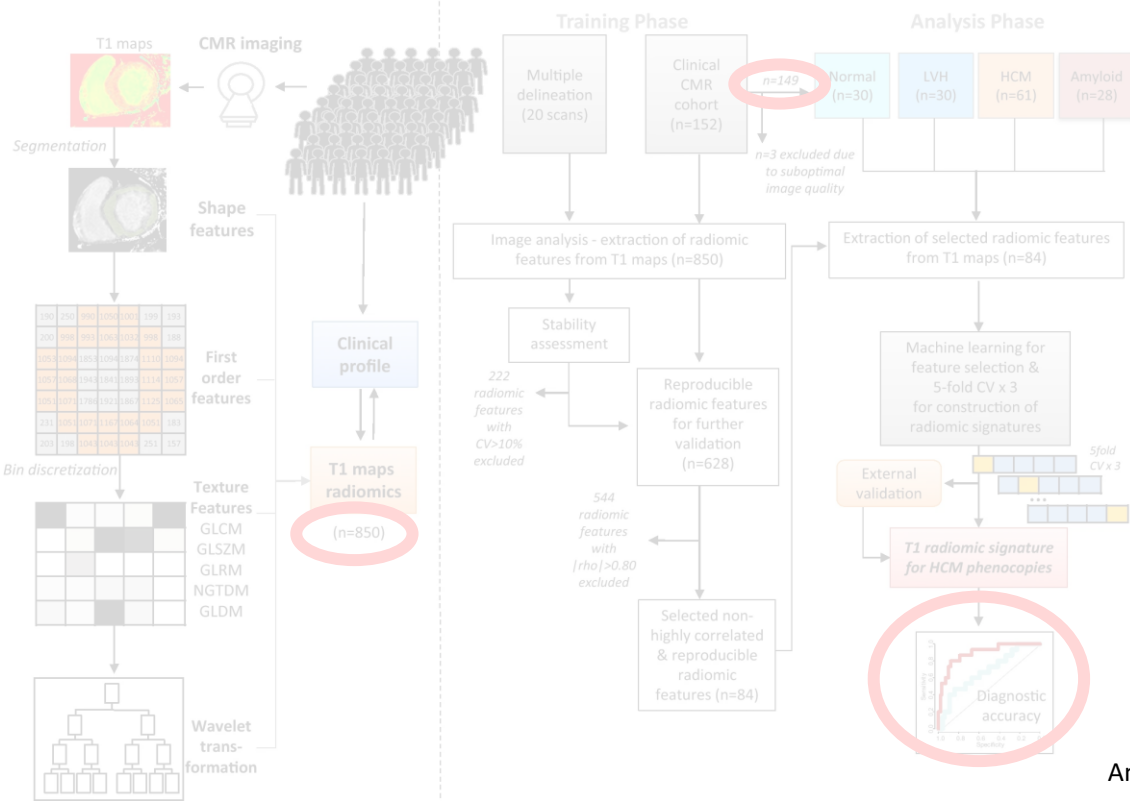


Korthals, Chatzantonis et al. Nature Scientific Reports, 2021

Workflow on radiomic feature extraction

Construction of a radiomic signature for classification of HCM phenocopies

Figure 1 | Workflow on radiomic feature extraction



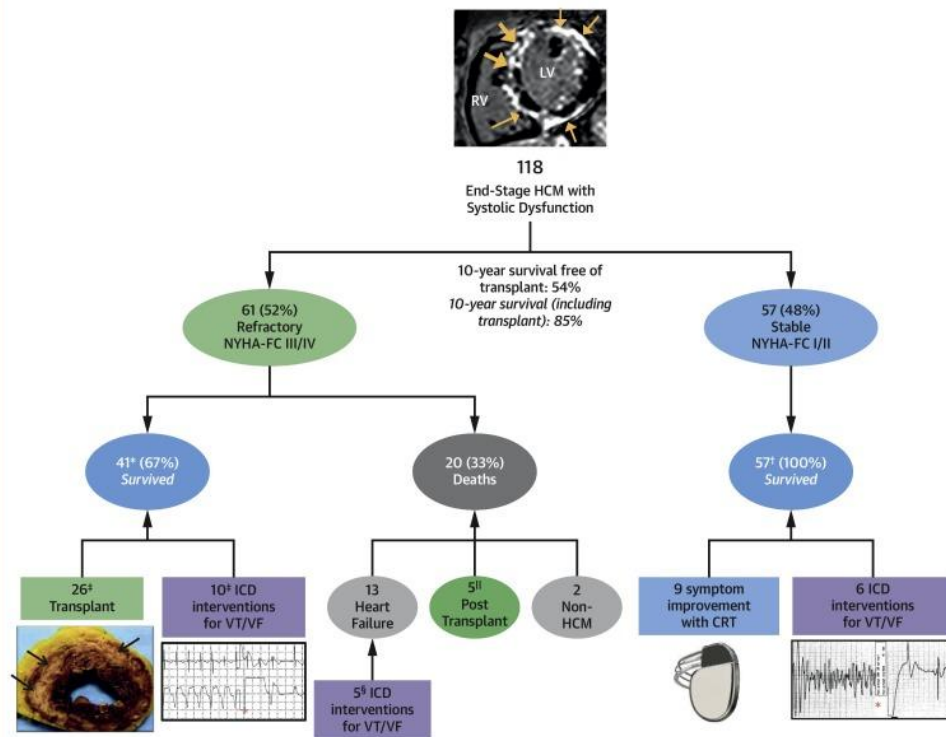
Antonopoulos, Boutsikou et al. Nature Scientific Reports, 2021

Διαγνωστική Αξία



Προγνωστική Αξία

CENTRAL ILLUSTRATION: Clinical Course and Outcome in End-Stage Hypertrophic Cardiomyopathy

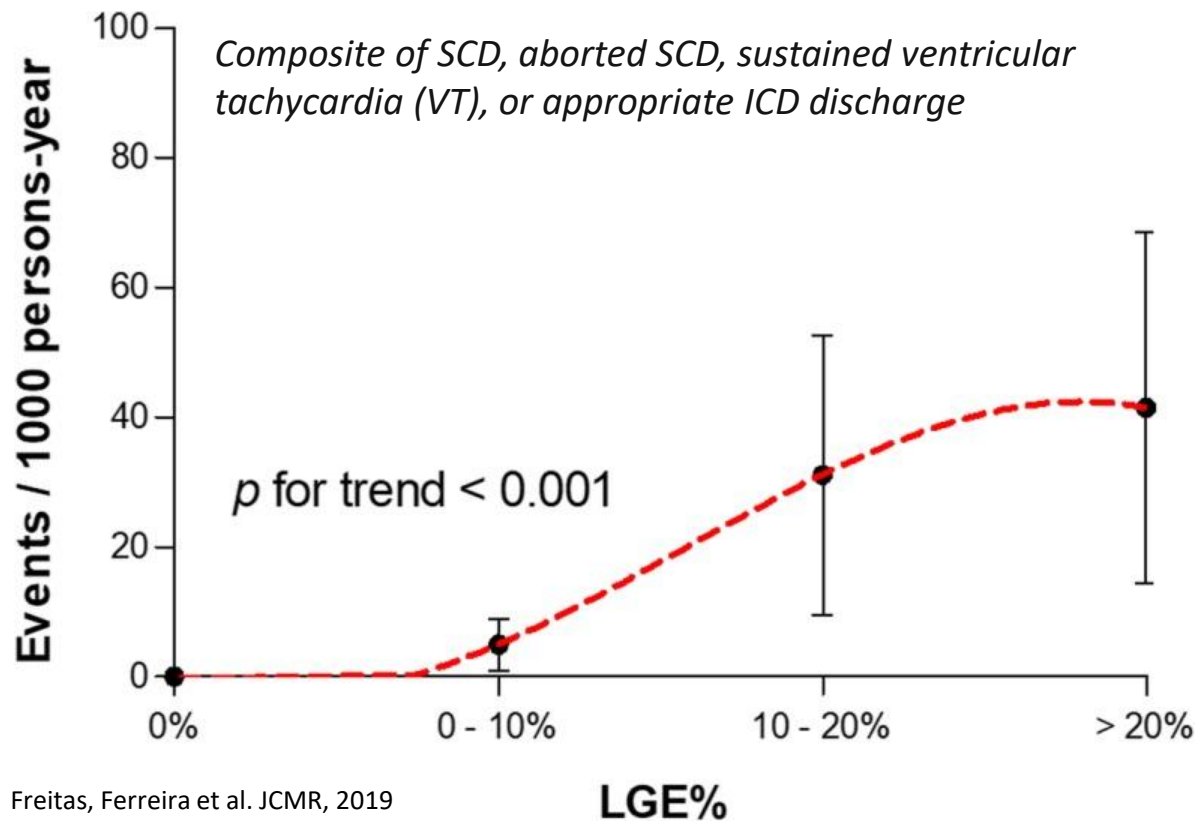


Rowin, E.J. et al. J Am Coll Cardiol. 2020;75(24):3033-43.

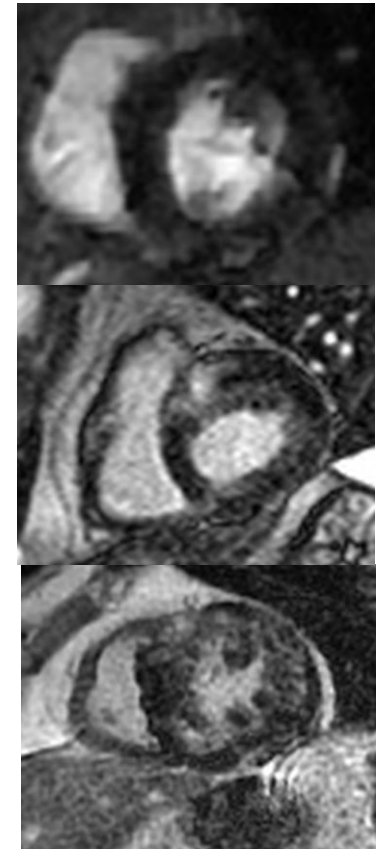
TABLE 3 Variables Associated With Development of End-Stage HCM in Multivariate Analysis

	Hazard Ratio (95% CI)	p Value
Age, yrs	0.98 (0.97-1.00)	0.13
NYHA functional class	1.78 (1.21-2.63)	0.004
Family history of end-stage HCM	1.87 (0.59-5.94)	0.29
Family history of HCM	1.45 (0.70-2.99)	0.32
History of appropriate ICD shock	2.26 (0.51-10.0)	0.29
Left atrial dimension, mm	0.99 (0.94-1.04)	0.71
Ejection fraction, %	0.89 (0.86-0.93)	<0.001
Maximum wall thickness, mm	1.06 (1.00-1.13)	0.06
LV end-diastolic dimension, mm	1.04 (0.99-1.09)	0.14
LV end-systolic dimension, mm	1.02 (0.96-1.08)	0.58
Extent of LGE, %	1.10 (1.04-1.17)	0.001

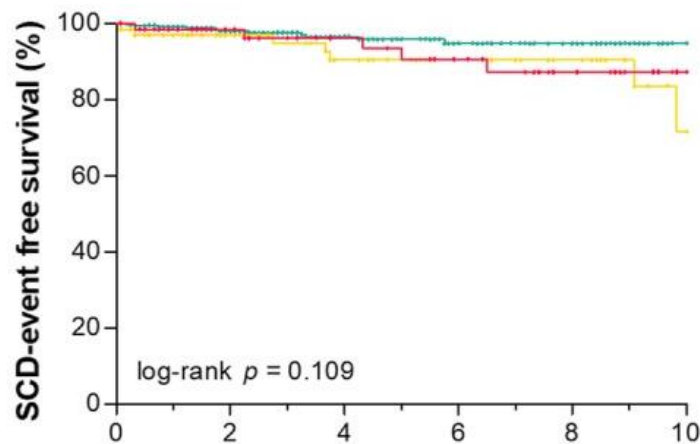
Bold p values indicate statistical significance.



Freitas, Ferreira et al. JCMR, 2019



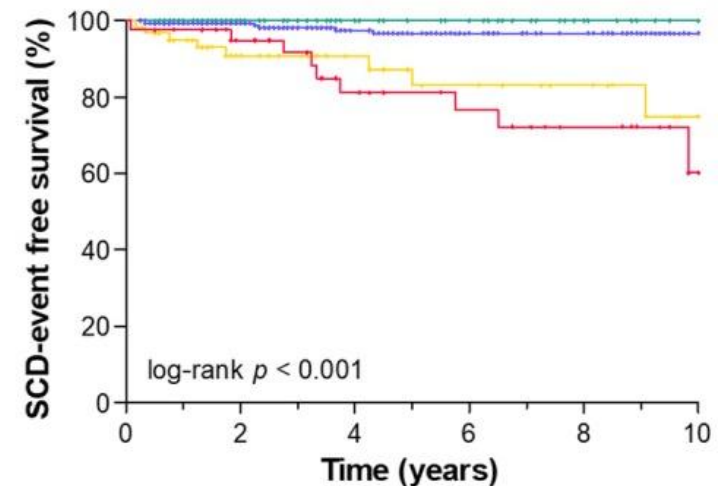
HCM Risk-SCD



N° at risk

Time (years)	0	2	4	6	8	10
Low risk	362	231	145	92	61	12
Intermediate risk	66	51	40	28	21	6
High risk	65	46	36	30	21	6

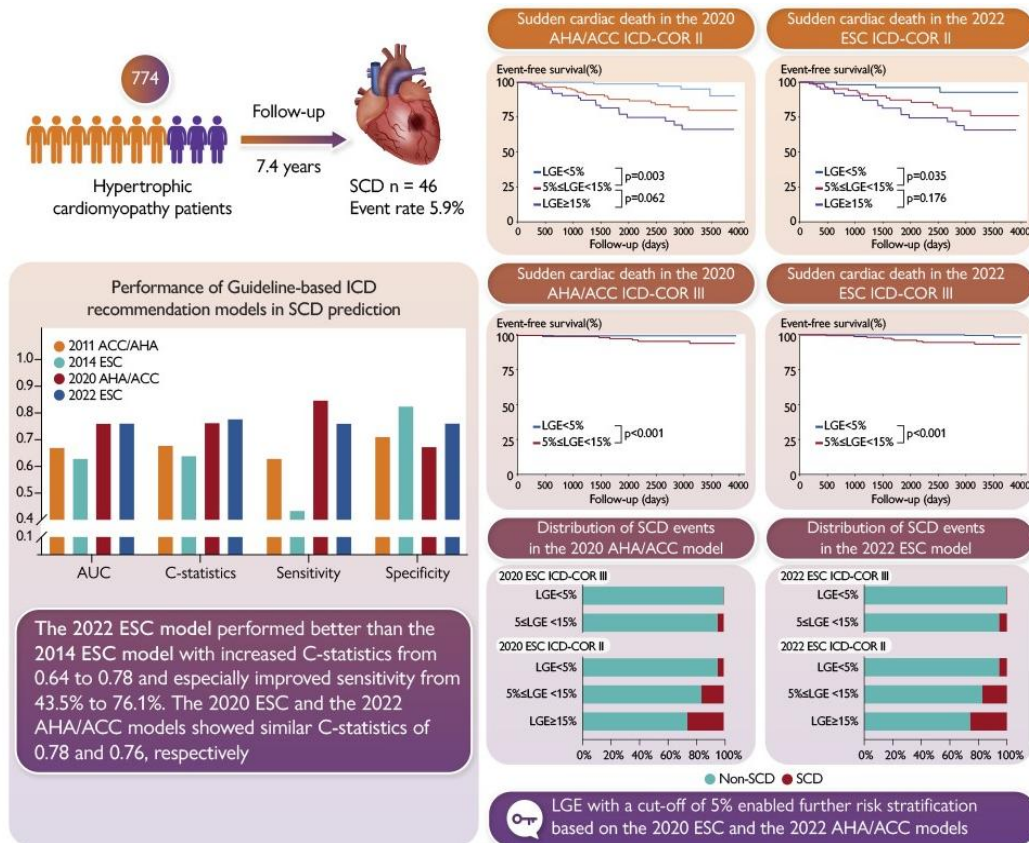
LGE



N° at risk

Time (years)	0	2	4	6	8	10
LGE 0%	102	65	42	31	16	6
LGE 0.1 - 10%	285	193	132	81	59	11
LGE 10.1 - 19.9%	63	36	27	20	16	4
LGE ≥ 20%	43	33	23	18	12	3

Freitas, Ferreira et al. JCMR, 2019



- Το μοντέλο πρόβλεψης αρρυθμικών συμβαμάτων της ESC (2022) είχε καλύτερη απόδοση από το μοντέλο της ESC (2014) με ιδιαίτερα βελτιωμένη την ευαισθησία
- Η LGE επέτρεψε περαιτέρω διαστρωμάτωση κινδύνου με βάση τις τρέχουσες κατευθυντήριες γραμμές

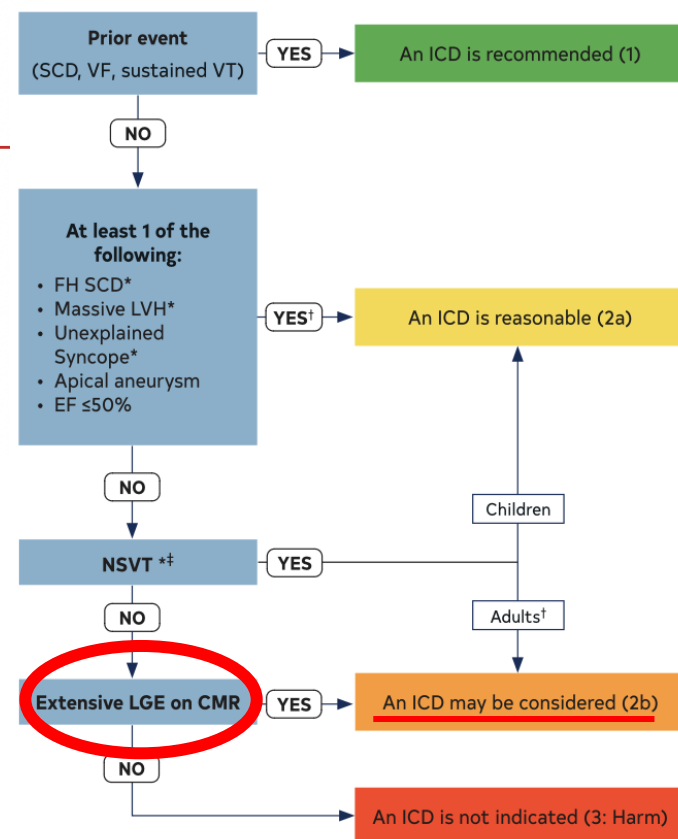
Wang J et al, Eur Heart J, 2023

Circulation

AHA/ACC CLINICAL PRACTICE GUIDELINE

2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy

A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines



2020 AHA/ACC
Guideline for the
Diagnosis and
Treatment of
Patients With
Hypertrophic
Cardiomyopathy

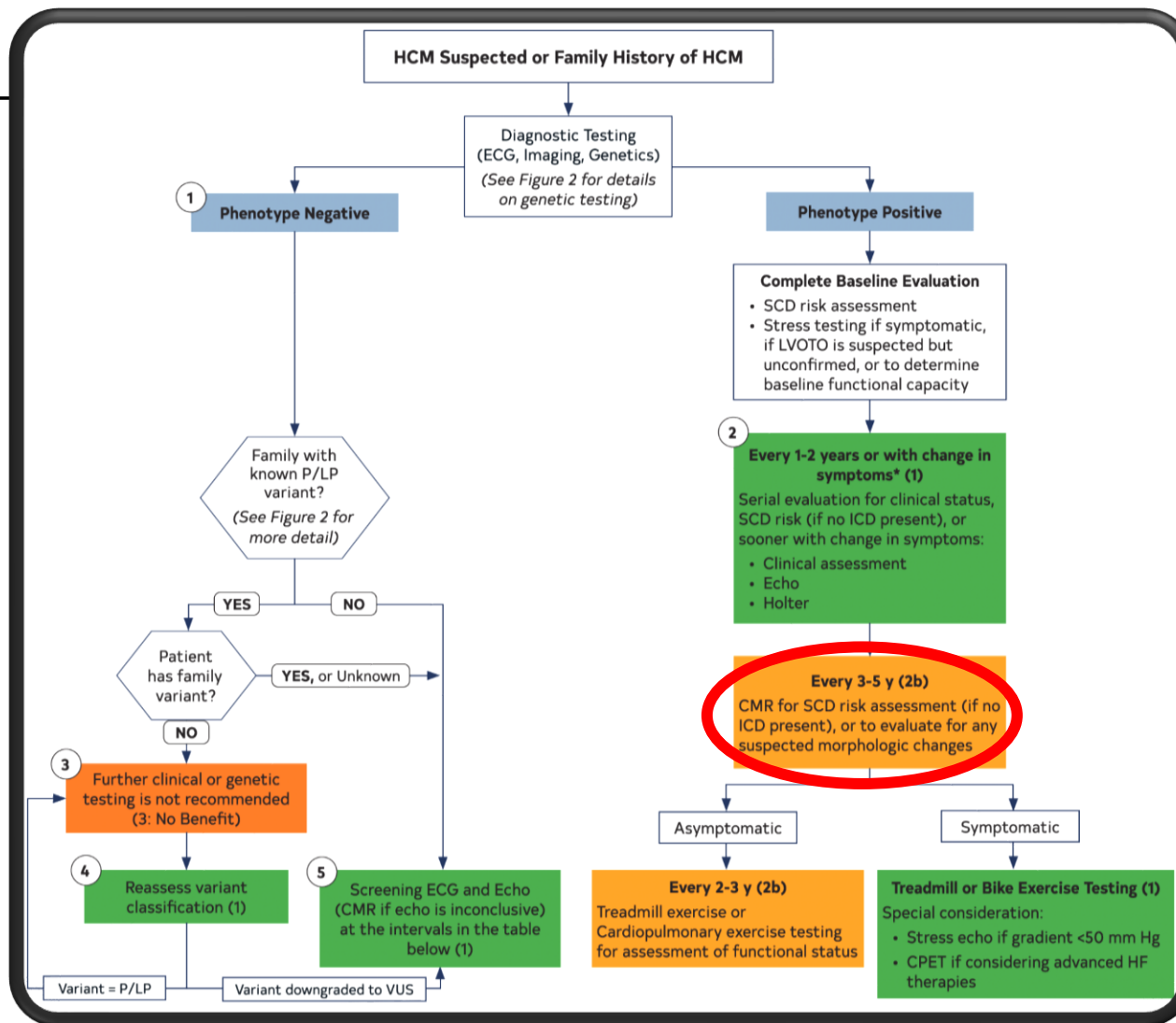


Table 7. Established Clinical Risk Factors for HCM Sudden Death Risk Stratification

Family history of sudden death from HCM	Sudden death judged definitively or likely attributable to HCM in ≥ 1 first-degree or close relatives who are ≤ 50 y of age. Close relatives would generally be second-degree relatives; however, multiple SCDs in tertiary relatives should also be considered relevant.
Massive LVH	Wall thickness ≥ 30 mm in any segment within the chamber by echocardiography or CMR imaging; consideration for this morphologic marker is also given to borderline values of ≥ 28 mm in individual patients at the discretion of the treating cardiologist. For pediatric patients with HCM, an absolute or z-score threshold for wall thickness has not been established; however, a maximal wall that corresponds to a z-score ≥ 20 (and >10 in conjunction with other risk factors) appears reasonable.
Unexplained syncope	≥ 1 Unexplained episodes involving acute transient loss of consciousness, judged by history unlikely to be of neurocardiogenic (vasovagal) etiology, nor attributable to LVOTO, and especially when occurring within 6 mo of evaluation (events beyond 5 y in the past do not appear to have relevance).
HCM with LV systolic dysfunction	Systolic dysfunction with EF $<50\%$ by echocardiography or CMR imaging.
LV apical aneurysm	Apical aneurysm defined as a discrete thin-walled dyskinetic or akinetic segment of the most distal portion of the LV chamber; independent of size.
Extensive LGE on CMR imaging	Diffuse and extensive LGE, representing fibrosis, either quantified or estimated by visual inspection, <u>comprising $\geq 15\%$ of LV mass</u> (extent of LGE conferring risk has not been established in children).
NSVT on ambulatory monitor	It would seem most appropriate to place greater weight on NSVT as a risk marker when runs are frequent (≥ 3), longer (≥ 10 beats), and faster (≥ 200 bpm) occurring usually over 24 to 48 h of monitoring. For pediatric patients, a VT rate that exceeds the baseline sinus rate by $>20\%$ is considered significant.

CMR indicates cardiovascular magnetic resonance; ICD, implantable cardioverter-defibrillator; LGE, late gadolinium enhancement; LV, left ventricular; LVH, left ventricular hypertrophy; LVOTO, left ventricular outflow tract obstruction; NSVT, nonsustained ventricular tachycardia; and SCD, sudden cardiac death.

2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy

2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

HCM

CMR with LGE is recommended in HCM patients for diagnostic work-up.

I

ICD implantation should be considered in HCM patients aged 16 years or more with an intermediate 5-year risk of SCD (≥ 4 to $< 6\%$)^f, and with (a) significant LGE at CMR (usually $> 15\%$ of LV mass); or (b) LVEF $< 50\%$; or (c) abnormal blood pressure response during exercise test^g; or (d) LV apical aneurysm; or (e) presence of sarcomeric pathogenic mutation.

IIa



ESC

European Society
of Cardiology

European Heart Journal (2023) 44, 3503–3626

<https://doi.org/10.1093/eurheartj/ehad194>

ESC GUIDELINES

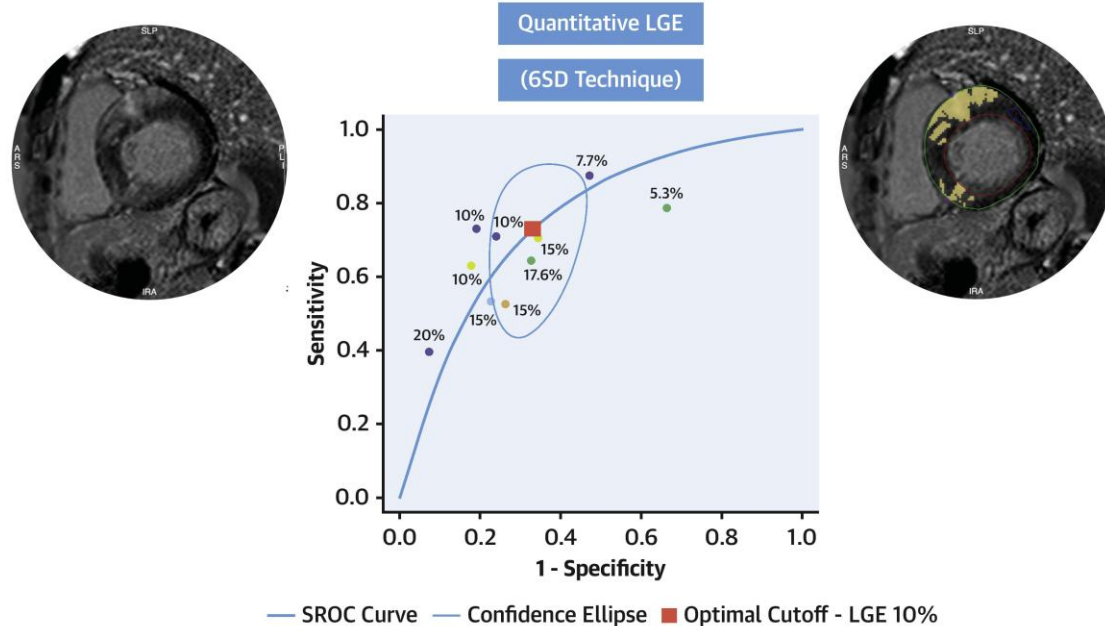
2023 ESC Guidelines for the management of cardiomyopathies

For patients who are in the low-risk category ($<4\%$ estimated 5-year risk of SCD), the presence of extensive LGE ($\geq 15\%$) on CMR may be considered in shared decision-making with patients about prophylactic ICD implantation, acknowledging the lack of robust data on the impact of scar quantification on the personalized risk estimates generated by HCM Risk-SCD or a validated paediatric model (e.g. HCM Risk-Kids).^{141,796,797,834–841}

IIb

B

CENTRAL ILLUSTRATION: Prognostic Value of LGE% in Predicting SCD in HCM

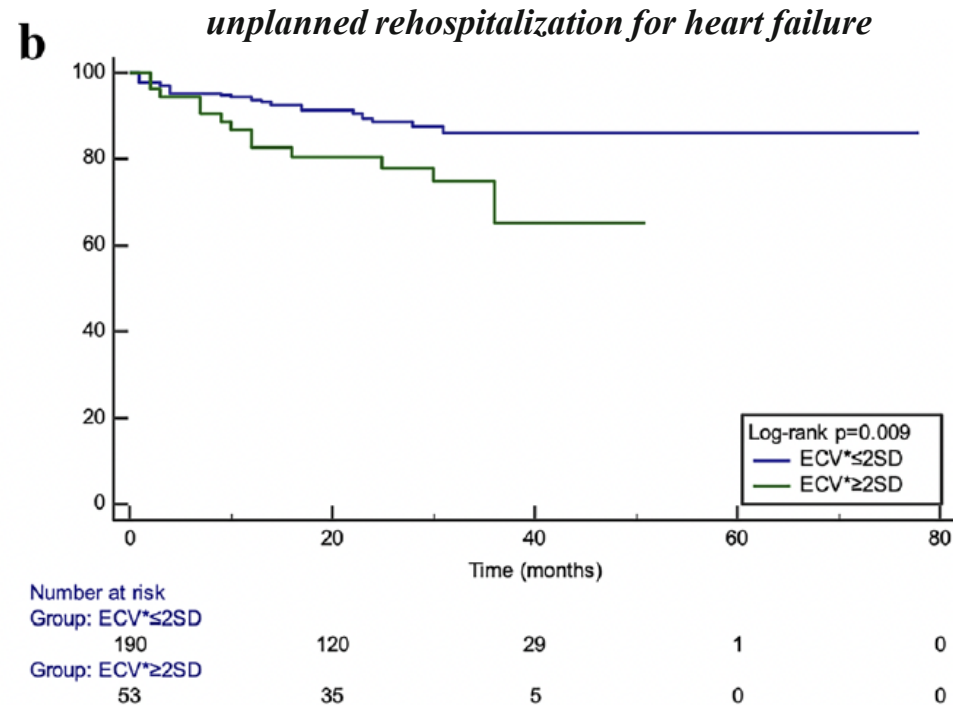
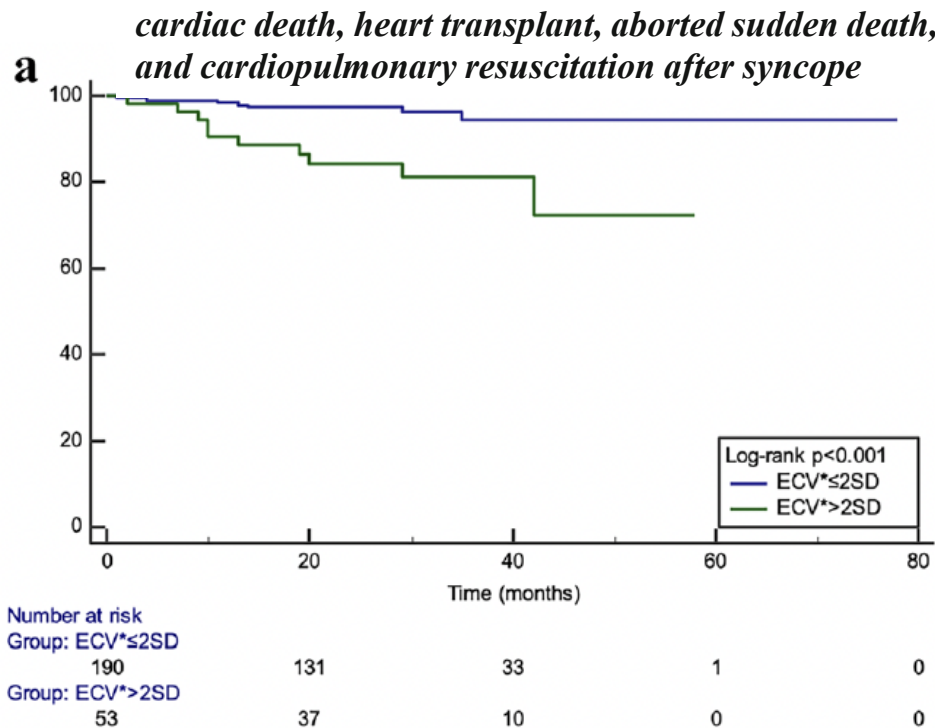


Kiaos A, et al. J Am Coll Cardiol Img. 2023;■(■):■-■.

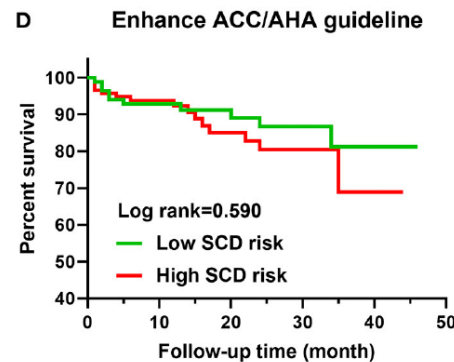
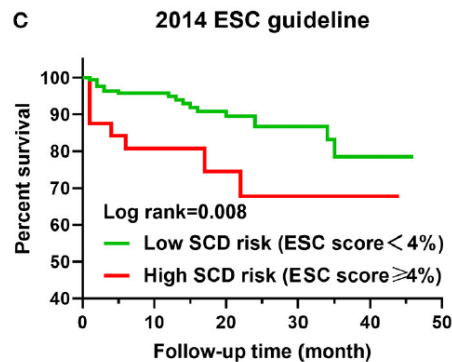
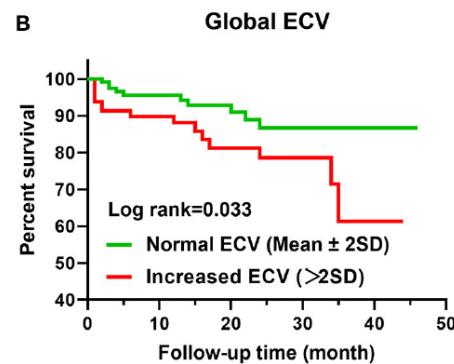
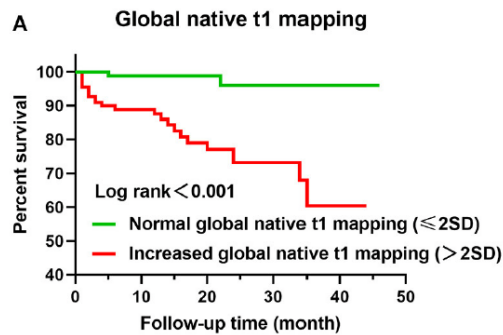
Πρέπει να πληρούνται συγκεκριμένες προϋποθέσεις:

- LGE > 6 SD από φυσιολογικό μυοκάρδιο
- Τυποποιημένο πρωτόκολλο LGE

Kiaos et al. Jacc Cardiovasc Imaging, 2023



Yuancheng Li et al. European Radiology, 2020

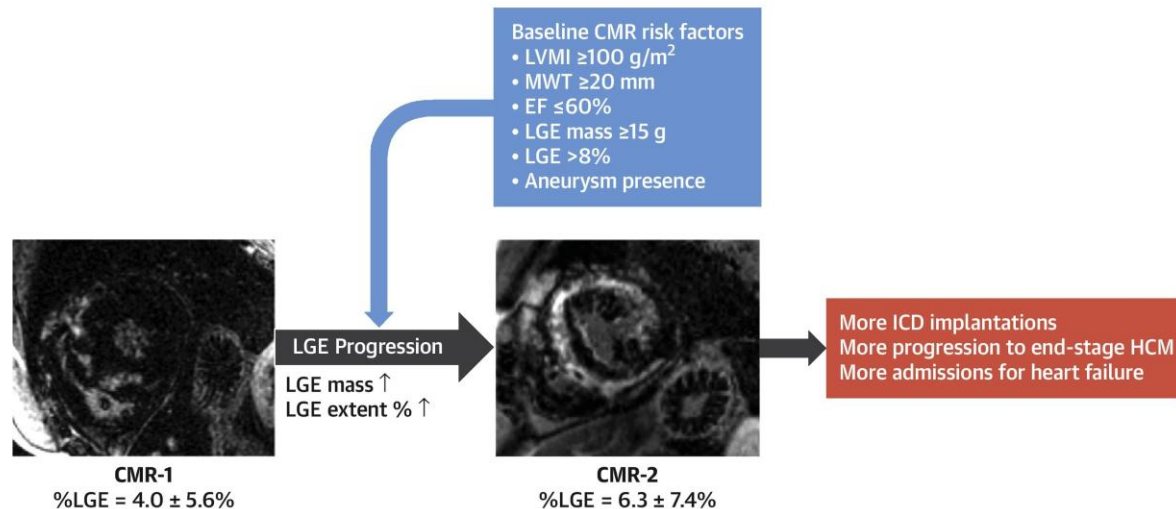


Incremental Values of T1 Mapping in the Prediction of Sudden Cardiac Death Risk in Hypertrophic Cardiomyopathy: A Comparison With Two Guidelines

Le Qin¹, Jiehua Min¹, Chihua Chen¹, Lan Zhu¹, Shengjia Gu¹, Mi Zhou², Wenjie Yang¹ and Fuhua Yan^{1*}

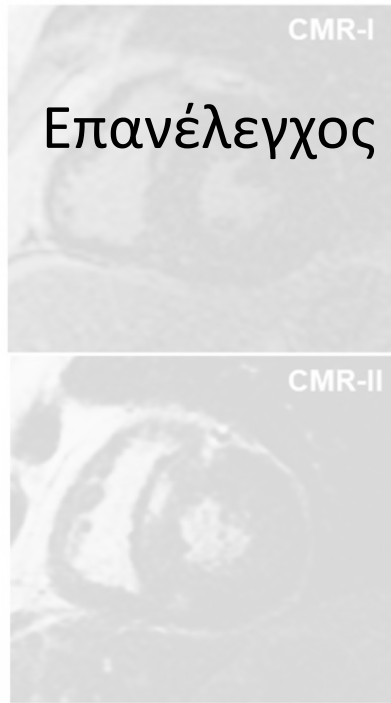
Επανελέγχος CMR (follow-up)

CENTRAL ILLUSTRATION: Risk Factors and Outcomes Associated With Progression of LGE in HCM Patients

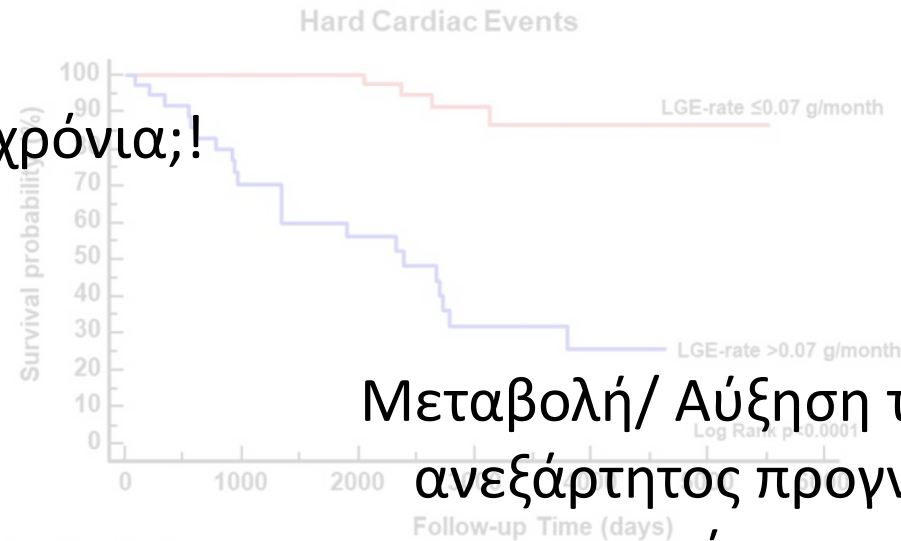


Habib, M. et al. J Am Coll Cardiol Img. 2021;14(5):947-58.

Επανάλεγχος CMR (follow-up)



Επανάλεγχος κάθε 2 χρόνια;!



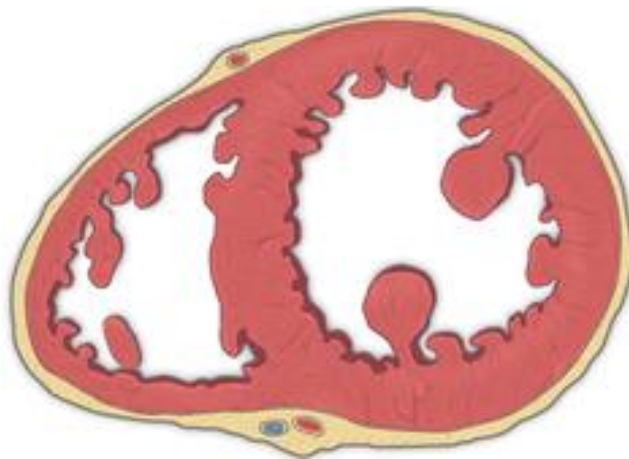
Μεταβολή/ Αύξηση του LGE ως
ανεξάρτητος προγνωστικός
παράγοντας;!

	Number at risk					
LGE-rate ≤ 0.0768	62	42	22	6	1	0
LGE-rate > 0.0737	22	16	7	2	0	0

Aquaro GD et al, Am J Card, 2024

Infiltrative Heart Diseases

- **Heterogeneous** group of rare myocardial disorders



Infiltrative Heart Diseases

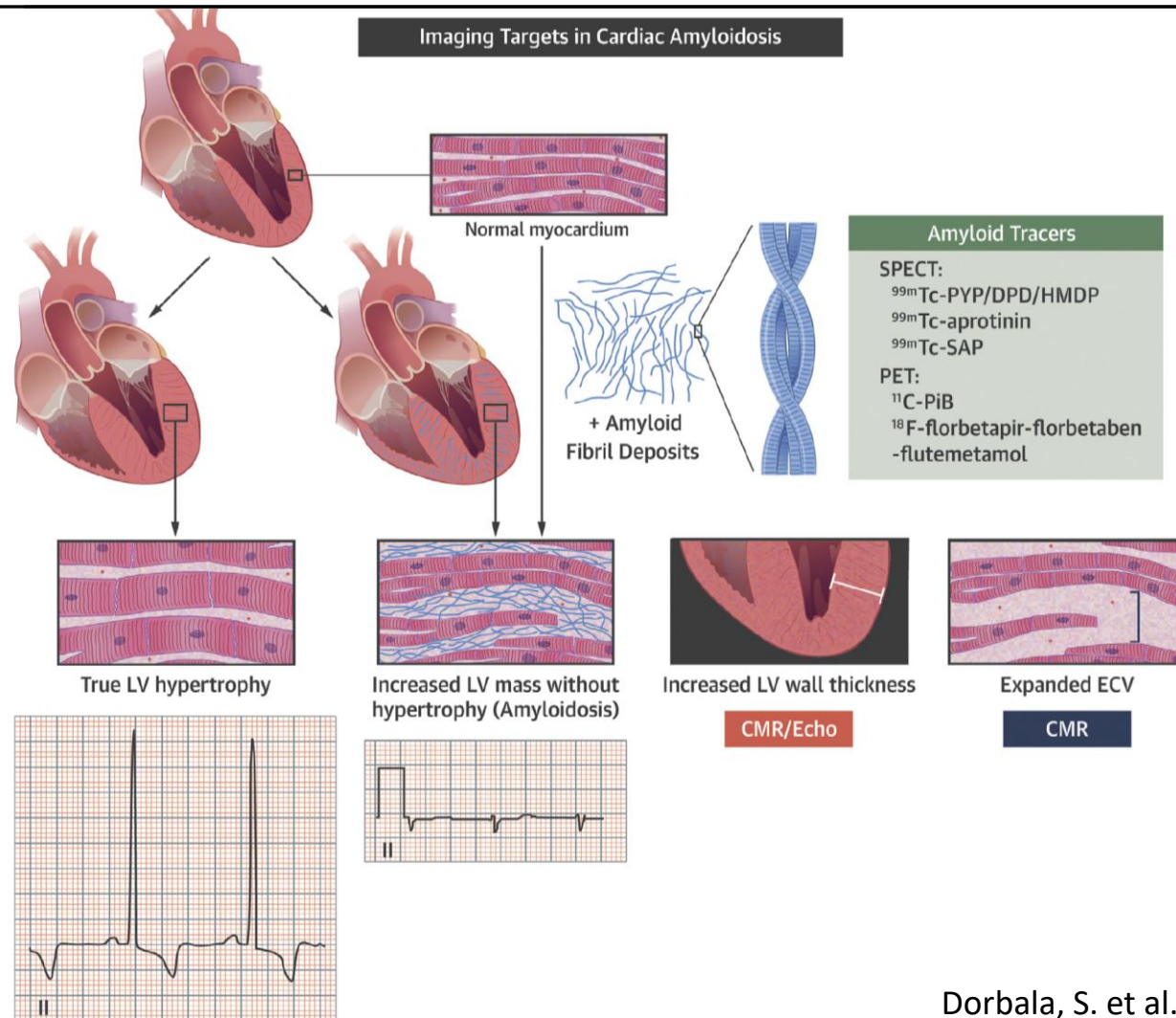
- Divided into **2** different main categories:
 - Cardiac Amyloidosis
 - Anderson-Fabry Disease
 - Glycogen Storage Cardiomyopathies
 - Neuromuscular Disorders (NMD)
 - Cardiac Sarcoidosis
 - Eosinophilic Myocarditis (Löffler Endocarditis)
 - Iron-Overload Cardiomyopathy
 - Granulomatosis with Polyangiitis (Wegener)

Cardiac Amyloidosis

- **Misfolded insoluble protein** deposition in the **extracellular** space of the heart



Cardiac Amyloidosis – Imaging Targets



- **Low** QRS voltage on the electrocardiogram
- Myocardial **hypertrophy**, **valvular thickening**, **pericardial effusion**, and **diastolic dysfunction** with **biatrial dilatation**
- Myocardial **bone-avid** radiotracer **uptake** in scintigraphy

Dorbala, S. et al. J Am Coll Cardiol Img. 2020;13(6):1368-83.

Cardiac Amyloidosis – CMR

Seung-Pyo, L. et al. J Cardiovasc Imaging. 2019 Jan;27(1):1-10 – (edited)



Cardiac Amyloidosis – CMR

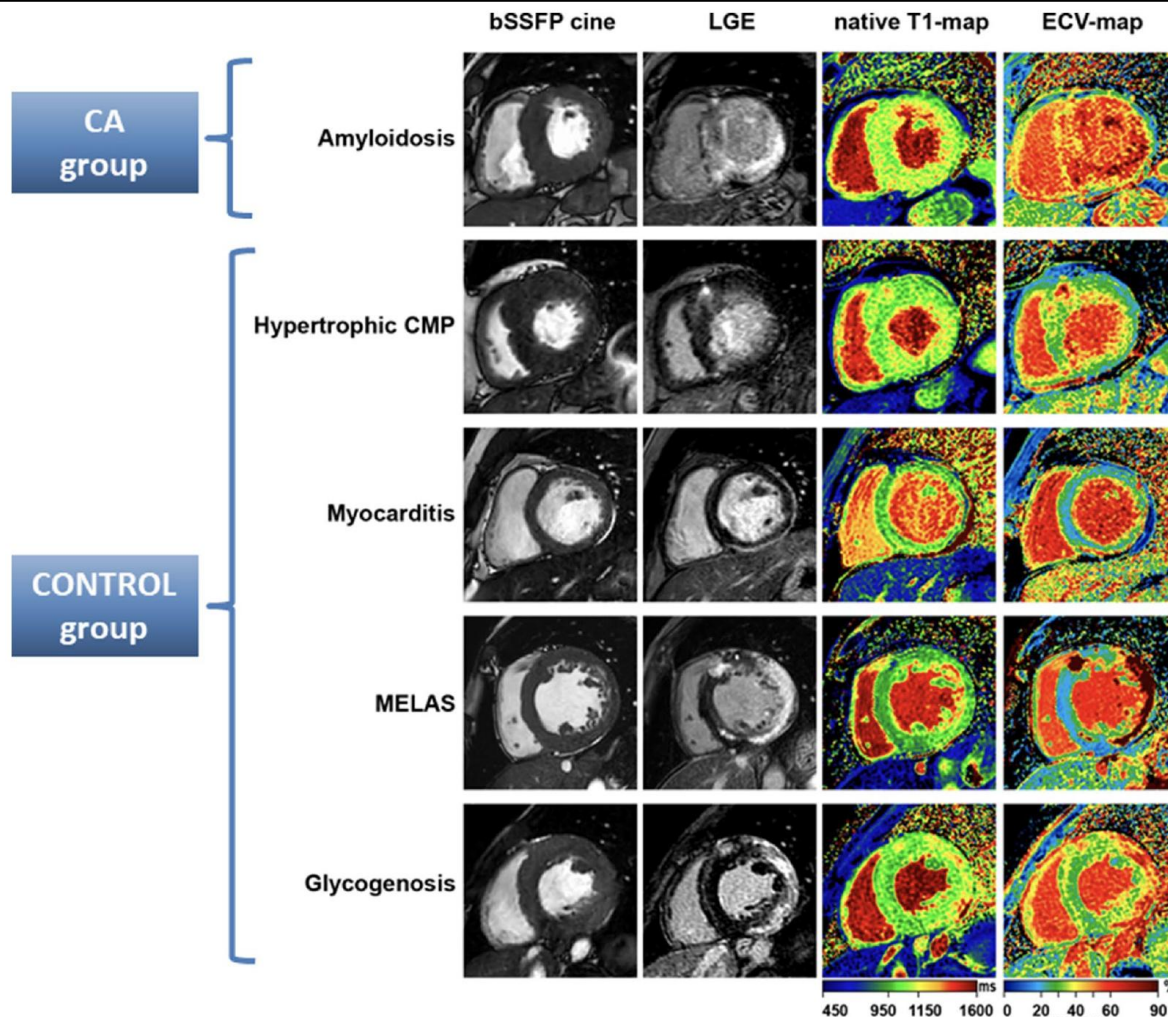
- **Diffuse**, circumferential, **subendocardial** Late Gadolinium Enhancement (LGE) and finally transmural LGE

Cardiac Amyloidosis – CMR

- Non-invasive CMR shows an **excellent diagnostic accuracy** and yield regarding Cardiac Amyloidosis

Chatzantonis, G. et al. Clin Res Cardiol. 2021; 110(4): 555–568.

Cardiac Amyloidosis – CMR



- N = **160** patients characterised by symptoms of **heart failure** and presence of left ventricular (LV) **hypertrophy** of unknown origin
- Diagnostic workup by both **CMR** and Endomyocardial Biopsy (**EMB**)

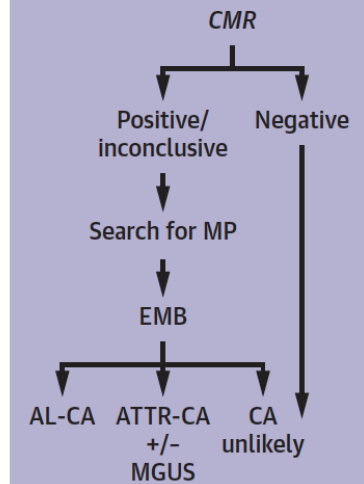
Chatzantonis, G. et al. Clin Res Cardiol. 2021; 110(4): 555–568.

Cardiac Amyloidosis – CMR

Suspicion of CA

- Clinical findings
- ECG
- Echocardiography

CMR Pathway

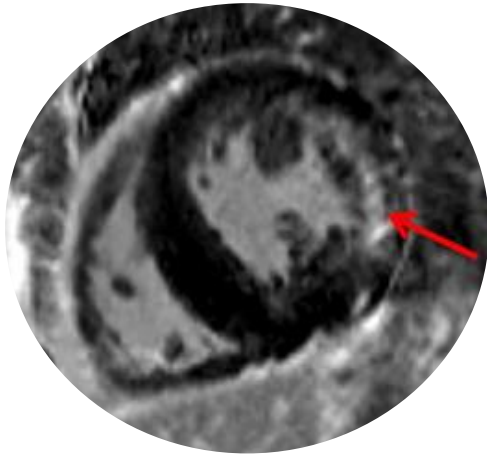


*DGK recommendations
(alternative to the MP/
scintigraphy pathways)*

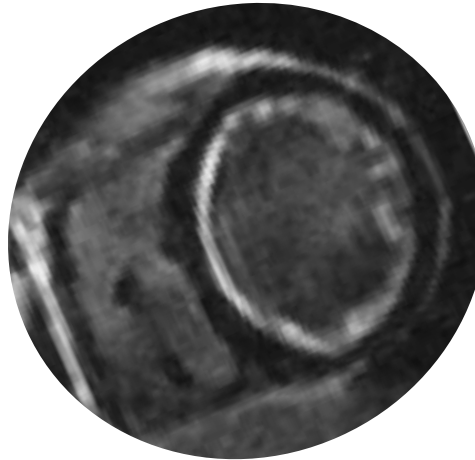
Rapezzi C et al. J Am Coll Cardiol. 2022 Apr 5;79(13):1288-1303.

Infiltrative Heart Diseases – CMR

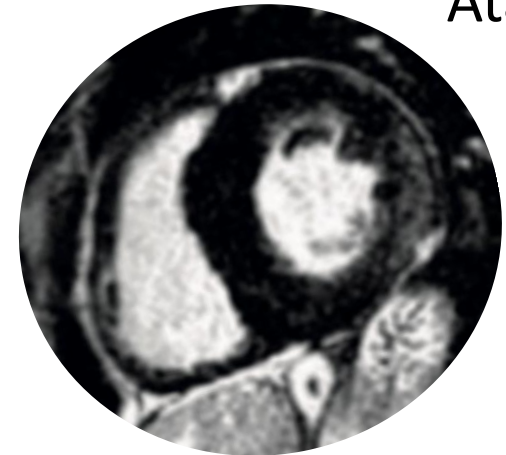
- Anderson-Fabry Disease



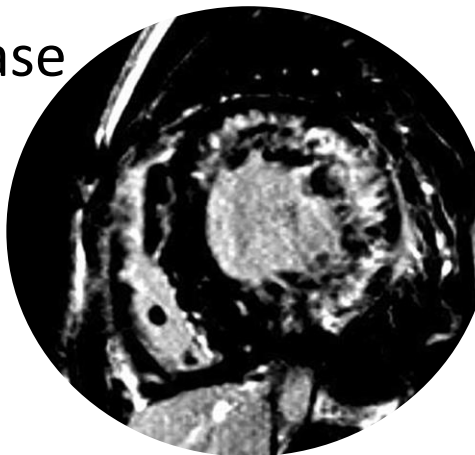
- Löffler Endocarditis



- Friedreich's Ataxia



- Danon Disease



- Wegener's granulomatosis

