Understanding HCM and recent guidelines

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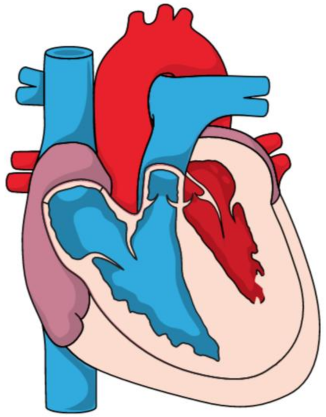
Disclosures

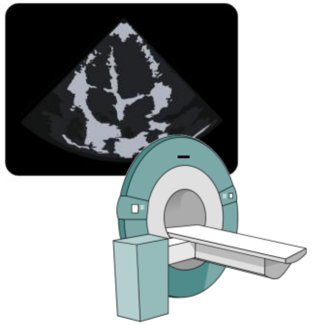
- **Speaking:** Biosense Webster, Medtronic, Bristol-Myers-Squibb
- **Consulting:** Boston Scientific

Hypertrophic Cardiomyopathy: definition



- Characterized by left ventricular hypertrophy
  Asymmetric septal hypertrophy is most characteristic
- No other cardiac, systemic or metabolic disease capable of producing the magnitude of increased LV wall thickness present
- Disease-causing variant in a sarcomere gene identified or genetic etiology unresolved

Diagnostic Criteria in Adults



2D echocardiography or cardiac MRI

Maximal end-diastolic LV wall thickness **>15 mm**

or

Maximal end-diastolic LV wall thickness **>13 mm** if there is a **family history of HCM** or a **sarcomere gene pathogenic variant** is present

Diagnostic Criteria in Children

2D echocardiography or cardiac MRI

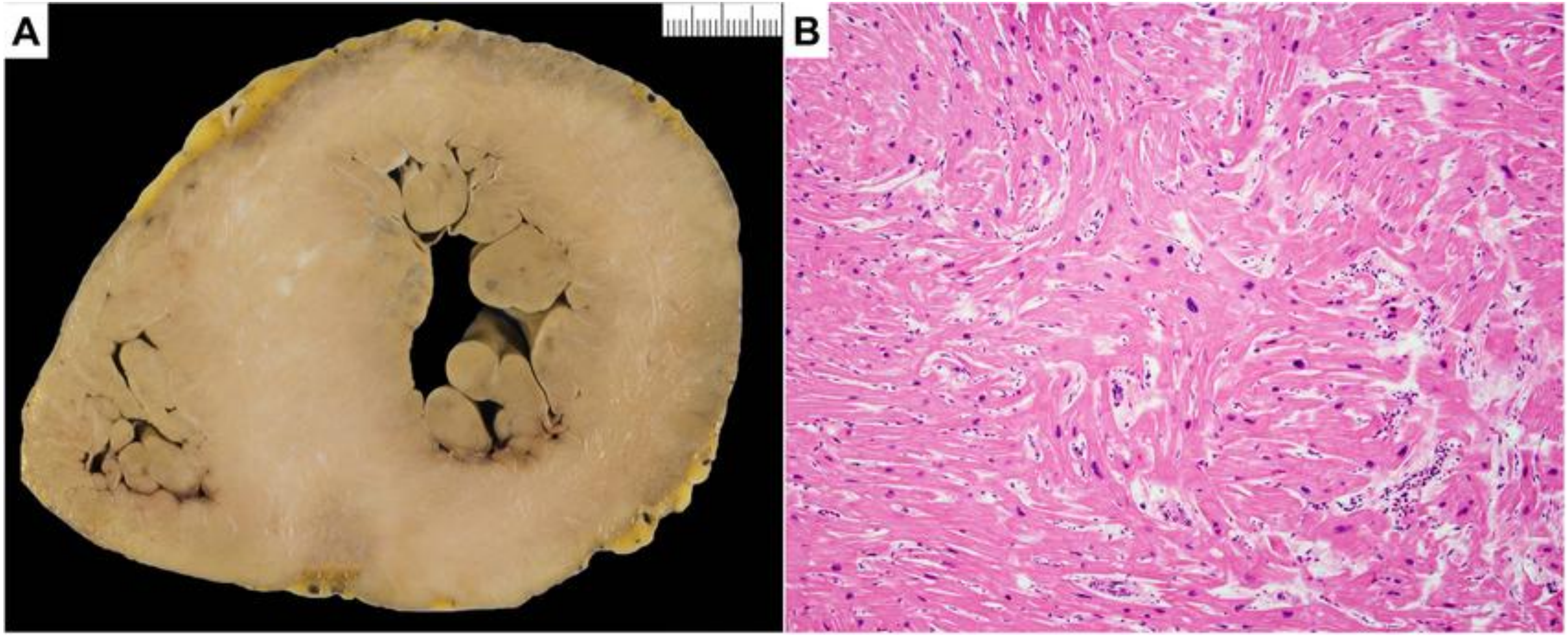
Maximal LV wall thickness **z-score >2 (ESC) or >2.5 (ACC/AHA)**

or

Maximal LV wall thickness **z-score >2 (ACC/AHA)** if there is a family history of HCM or a pathogenic sarcomere gene is present

Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

Ommen SR et al. J Am Coll Cardiol 2024;83(23):2324–2405

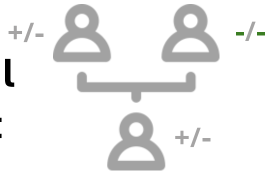


Sheppard MN et al. Virchows Arch 2023;482(4):653-669.

Hypertrophic Cardiomyopathy: prevalence, characteristics and outcomes

Inheritance pattern

Autosomal dominant



Sex distribution

Women are diagnosed less often and later

Prevalence

Estimated 1:500

Clinical suspicion

Symptoms
Cardiac murmur
Abnormal ECG/echo
Cardiac event
Family history

Sudden cardiac death

Progressive functional limitation

Atrial fibrillation

Heart failure

Thromboembolism

Although some patients with HCM have a normal life expectancy without limiting symptoms, many will have important consequences

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

Developed by the task force on the management of cardiomyopathies of the European Society of Cardiology (ESC)

Authors/Task Force Members: Elena Arbelo *†, (Chairperson) (Spain), Alexandros Protonotarios ‡, (Task Force Co-ordinator) (United Kingdom), Juan R. Gimeno ‡, (Task Force Co-ordinator) (Spain), Eloisa Arbustini (Italy),

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CLINICAL PRACTICE GUIDELINE

2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy

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

Developed in Collaboration With and Endorsed by the American Medical Society for Sports Medicine, the Heart Rhythm Society, Pediatric & Congenital Electrophysiology Society, and the Society for Cardiovascular Magnetic Resonance

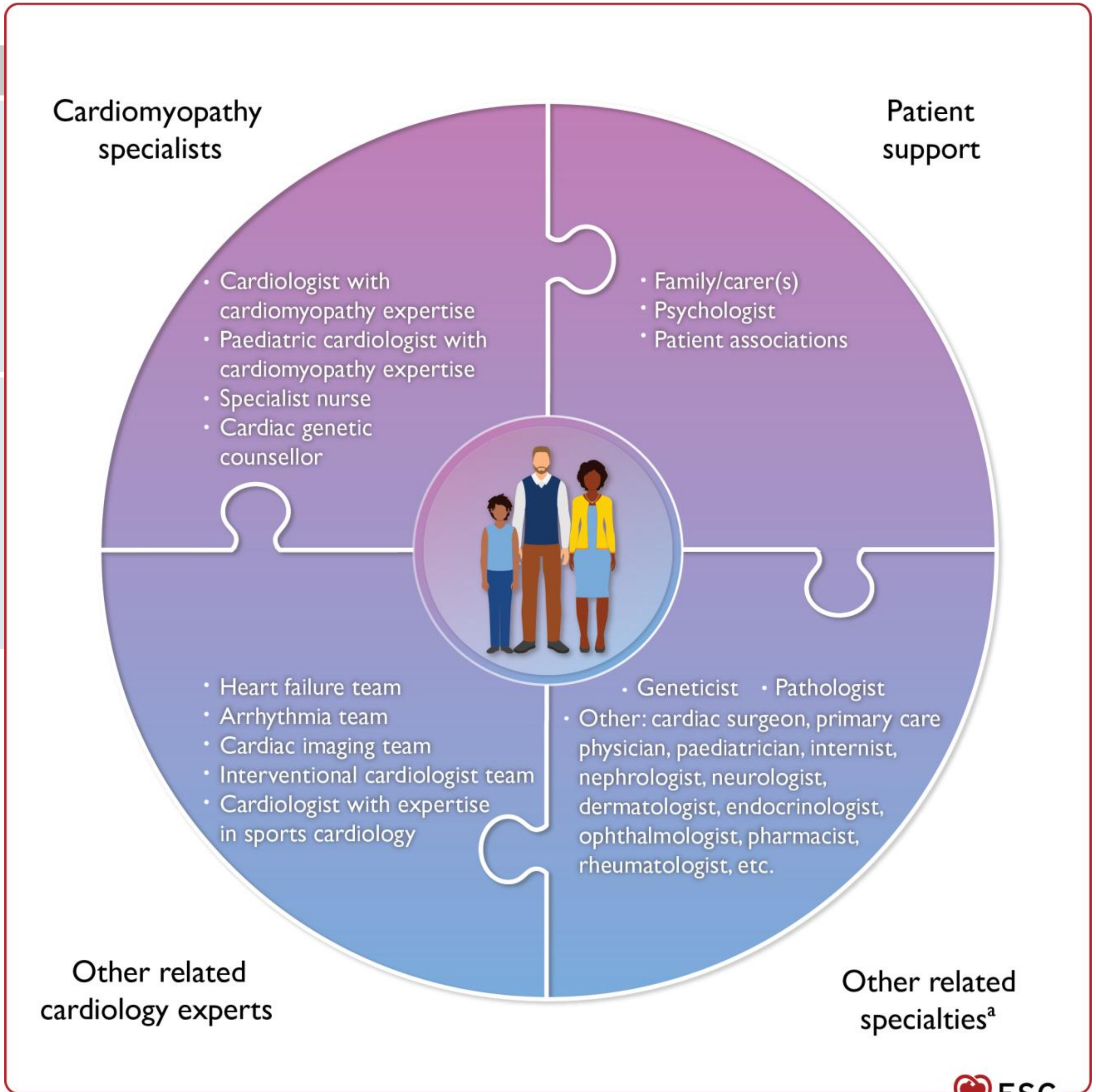
Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

Ommen SR et al. J Am Coll Cardiol 2024;83(23):2324–2405.

Multidisciplinary care of cardiomyopathies

Recommendations	Class
It is recommended that all patients with cardiomyopathy and their relatives have access to **multidisciplinary teams** with expertise in the diagnosis and management of cardiomyopathies.	I
Timely and adequate preparation for **transition of care from paediatric to adult services**, including joint consultations, is recommended in all adolescents with cardiomyopathy.	I

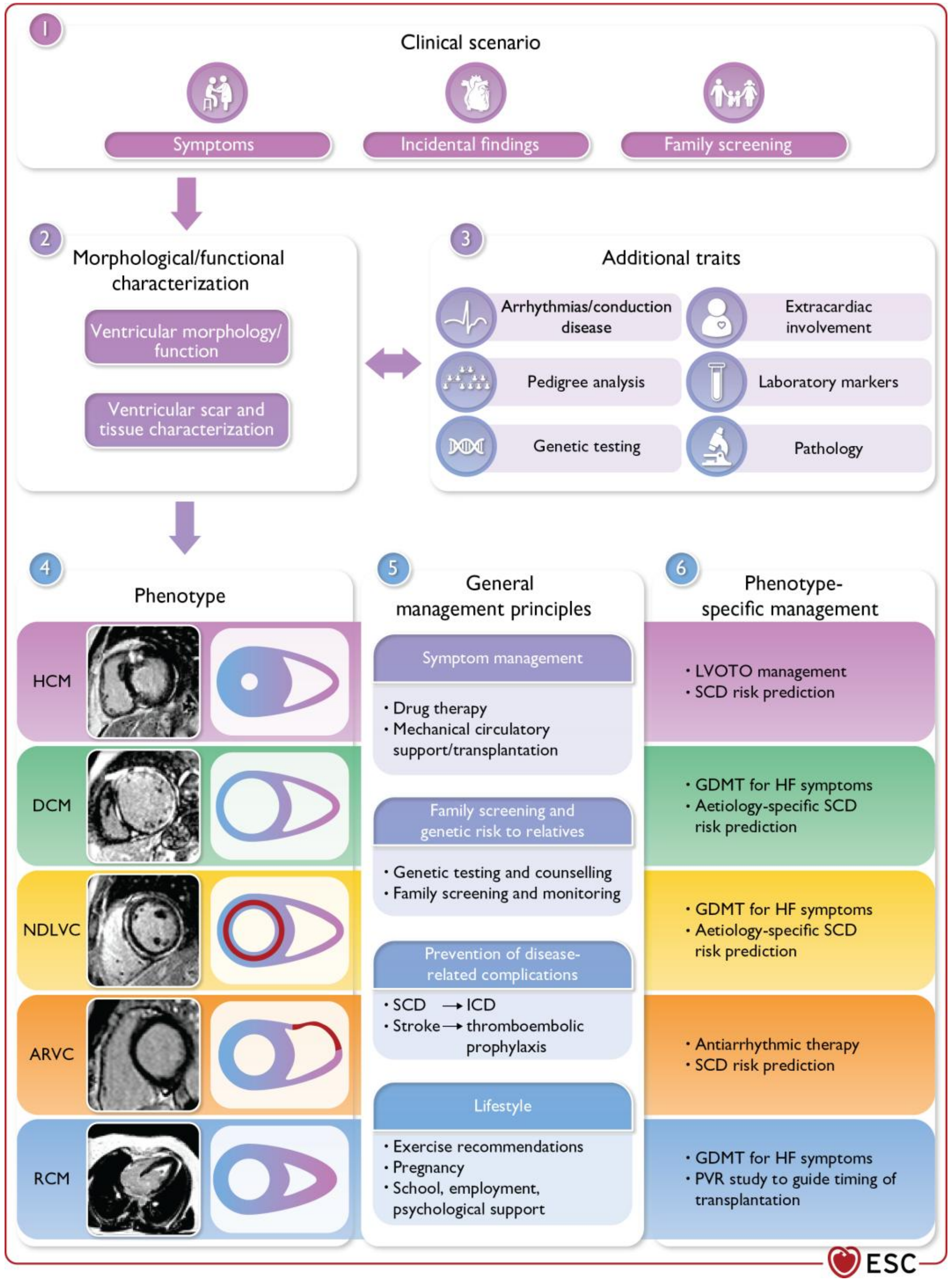
A shared and coordinated care approach between cardiomyopathy specialists and general adult and paediatric cardiology centres is strongly recommended



Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

The patient pathway

'Cardiomyopathy mindset'



Multidisciplinary

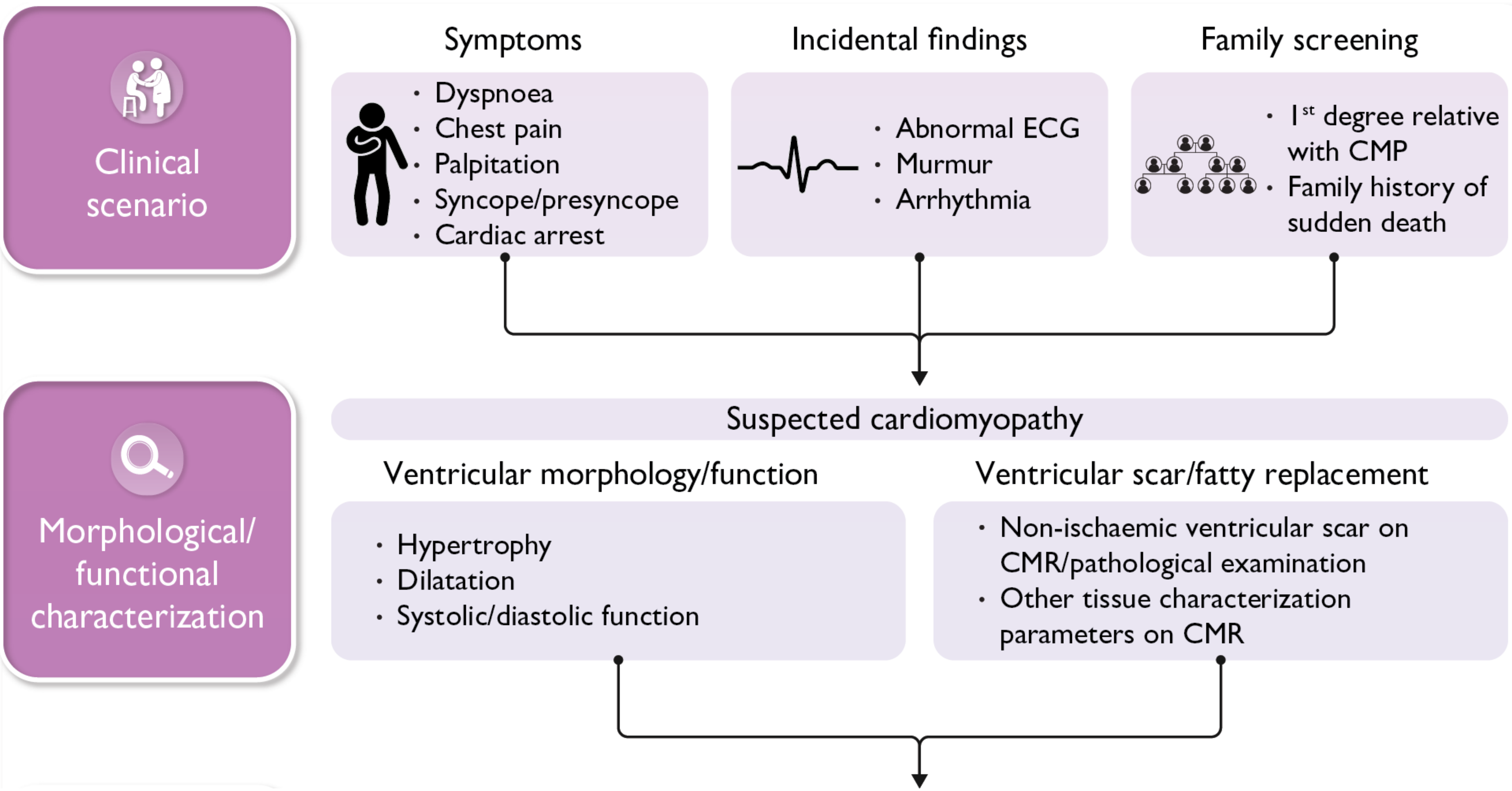
Coordinated

Patient-centred

Family-centred

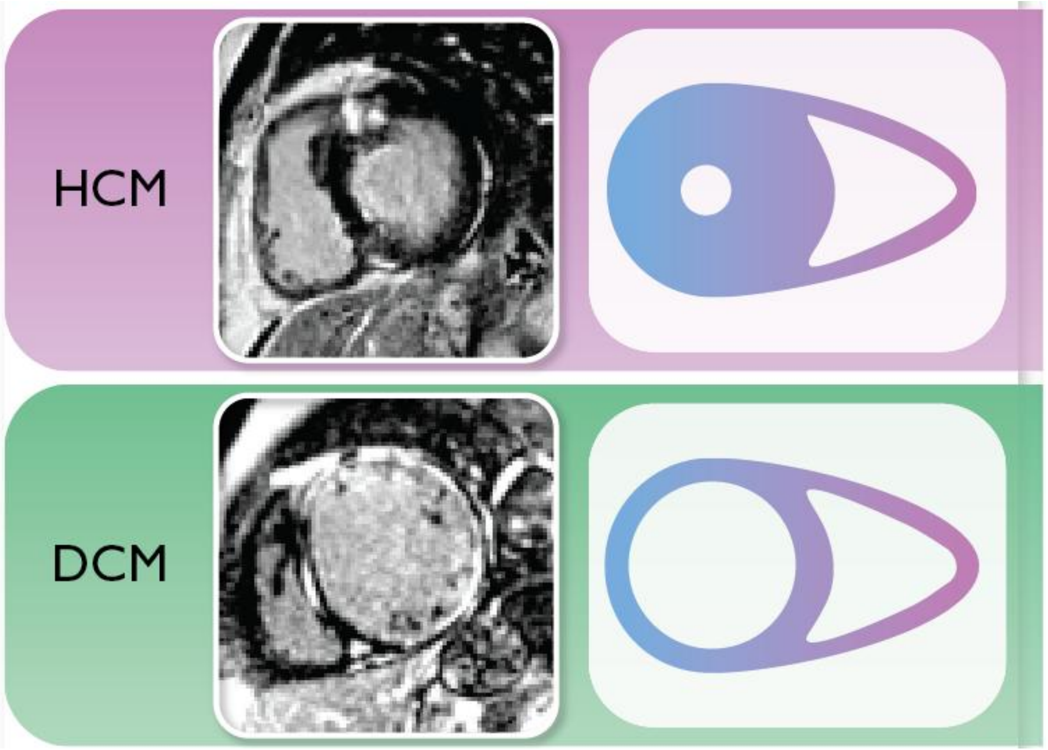
Key aspects in the evaluation and management of cardiomyopathies

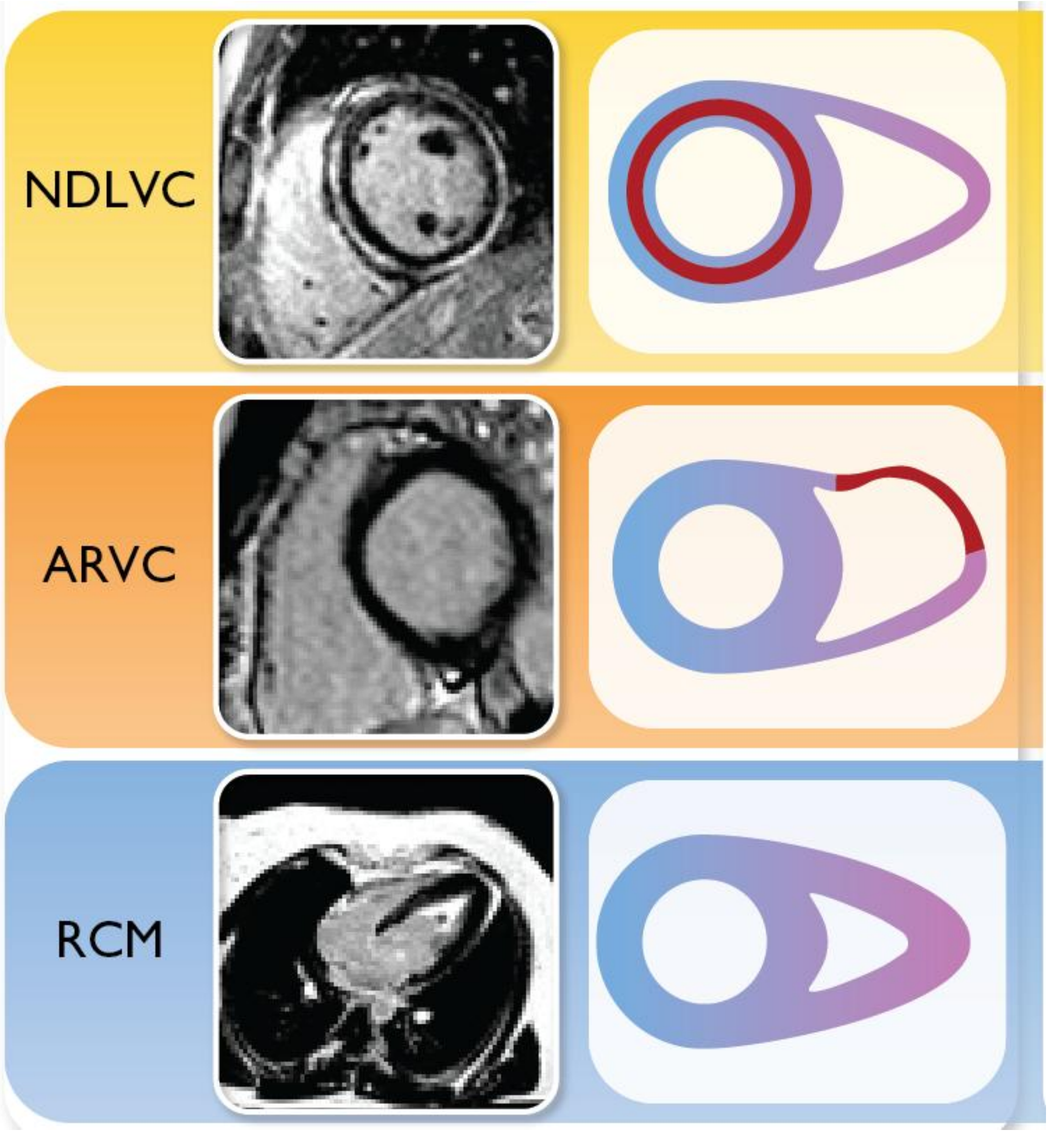
Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.



Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

Cardiomyopathy phenotypes

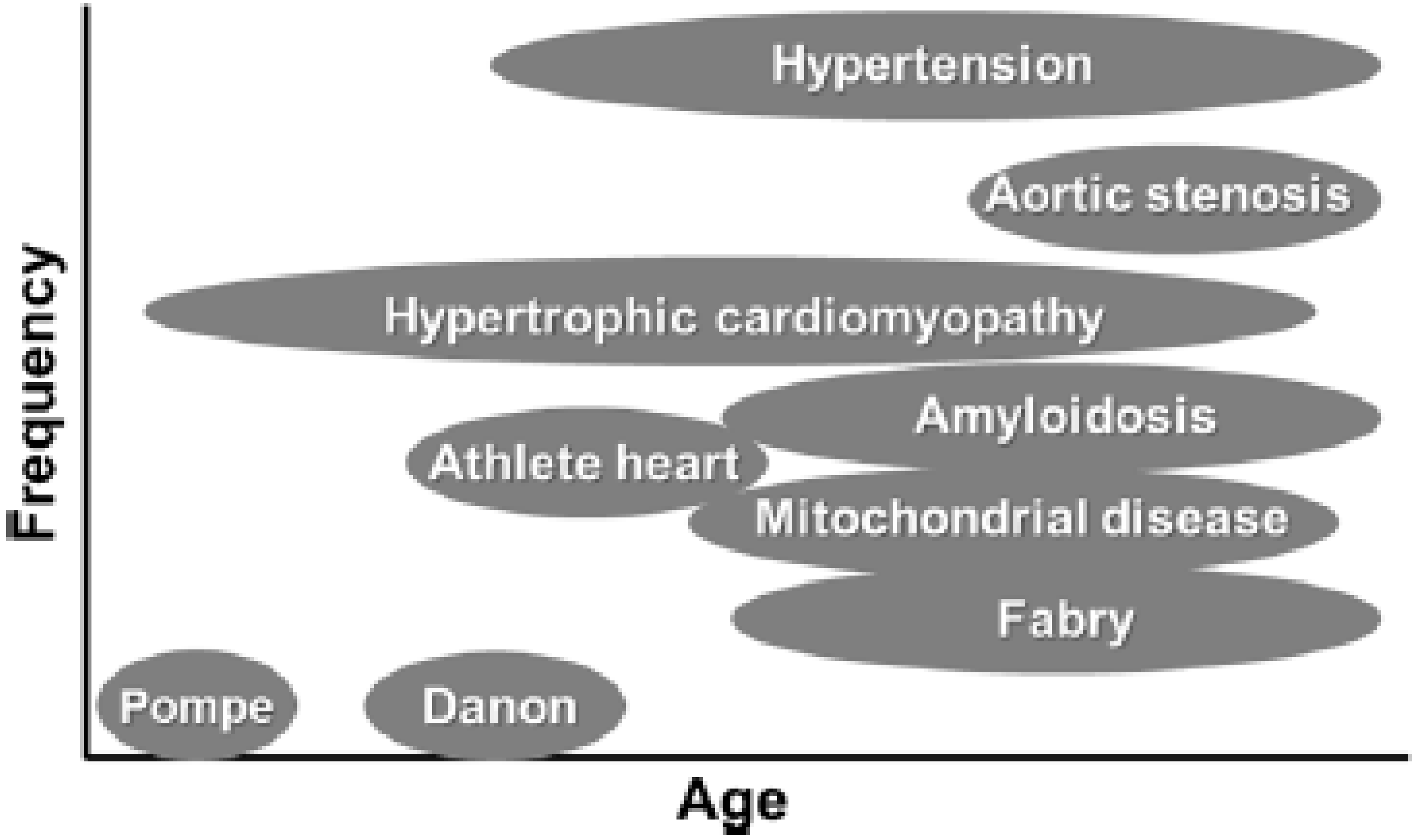




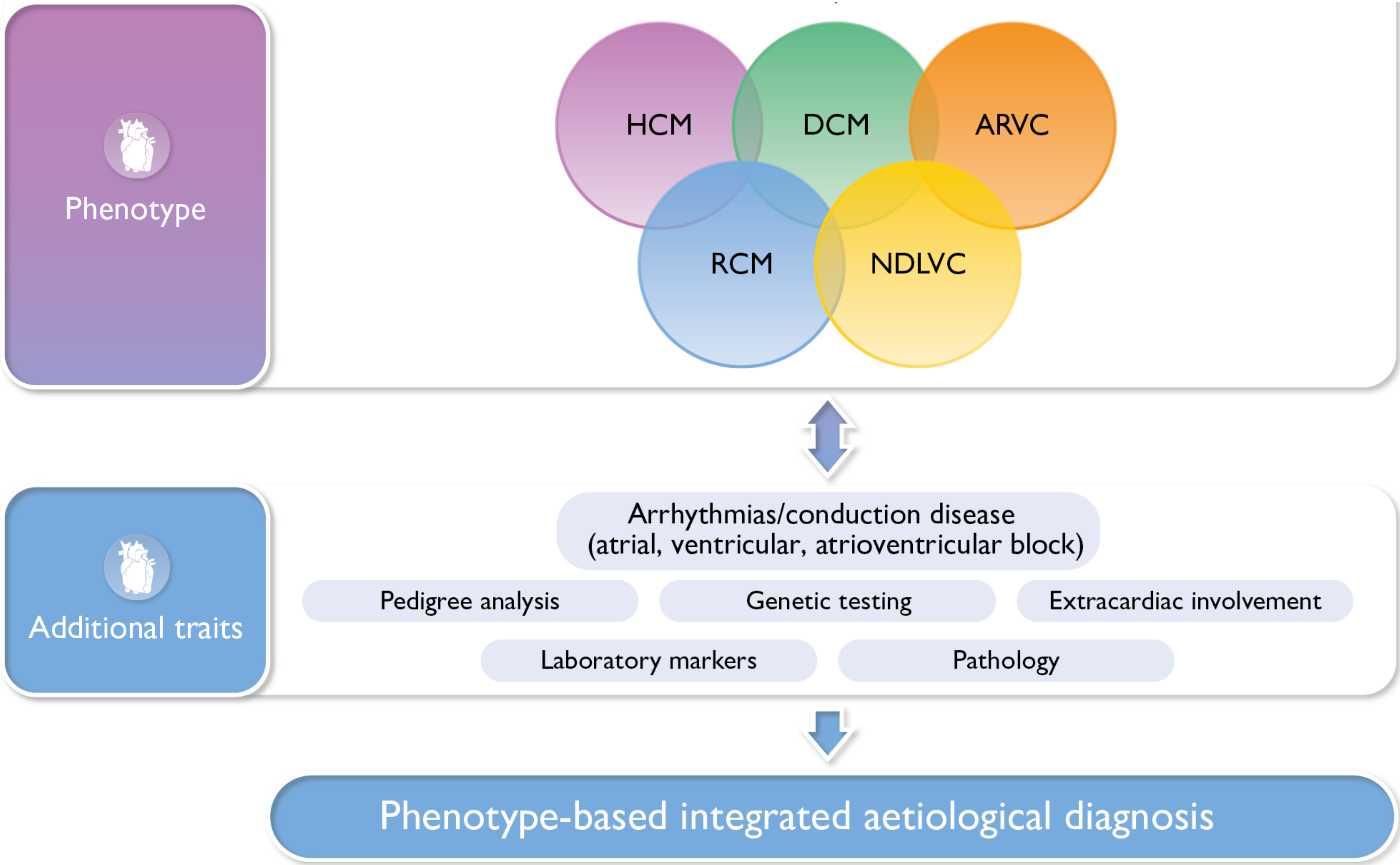
Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

HCM is not a diagnosis!

Differential diagnosis of LVH



Kubo et al. Curr Cardiol Rep. 2017;19(8):65.



Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

Family history & inheritance pattern → Age → Extracardiac signs and symptoms → Baseline ECG → Laboratory tests

Cardiomyopathy phenotype		AD	A	ilineal
HCM	Sarcomeric	X		
	Anderson–Fabry			
	Danon			
	TTR amyloidosis	X		
	RASopathy	X		
	Friedreich ataxia			
	Mitochondrial			
	Mitochondrial DNA			
	Nuclear DNA	X		

	HCM
Learning difficulties, developmental	Mitochondrial
	diseases
	Glycogenoses
	FHL1 variants
Palpebral ptosis	Mitochondrial diseases
Lentigines	NSML
Angiokeratomata	Anderson–Fabry disease

Cardiomyopathy phenotype	Finding
HCM	Short PR interval/pre-excitatio
	AV block
	Extreme LVH
	Low QRS voltage[a]
	Superior QRS axis ('northwes
	Q waves/pseudoinfarction pat

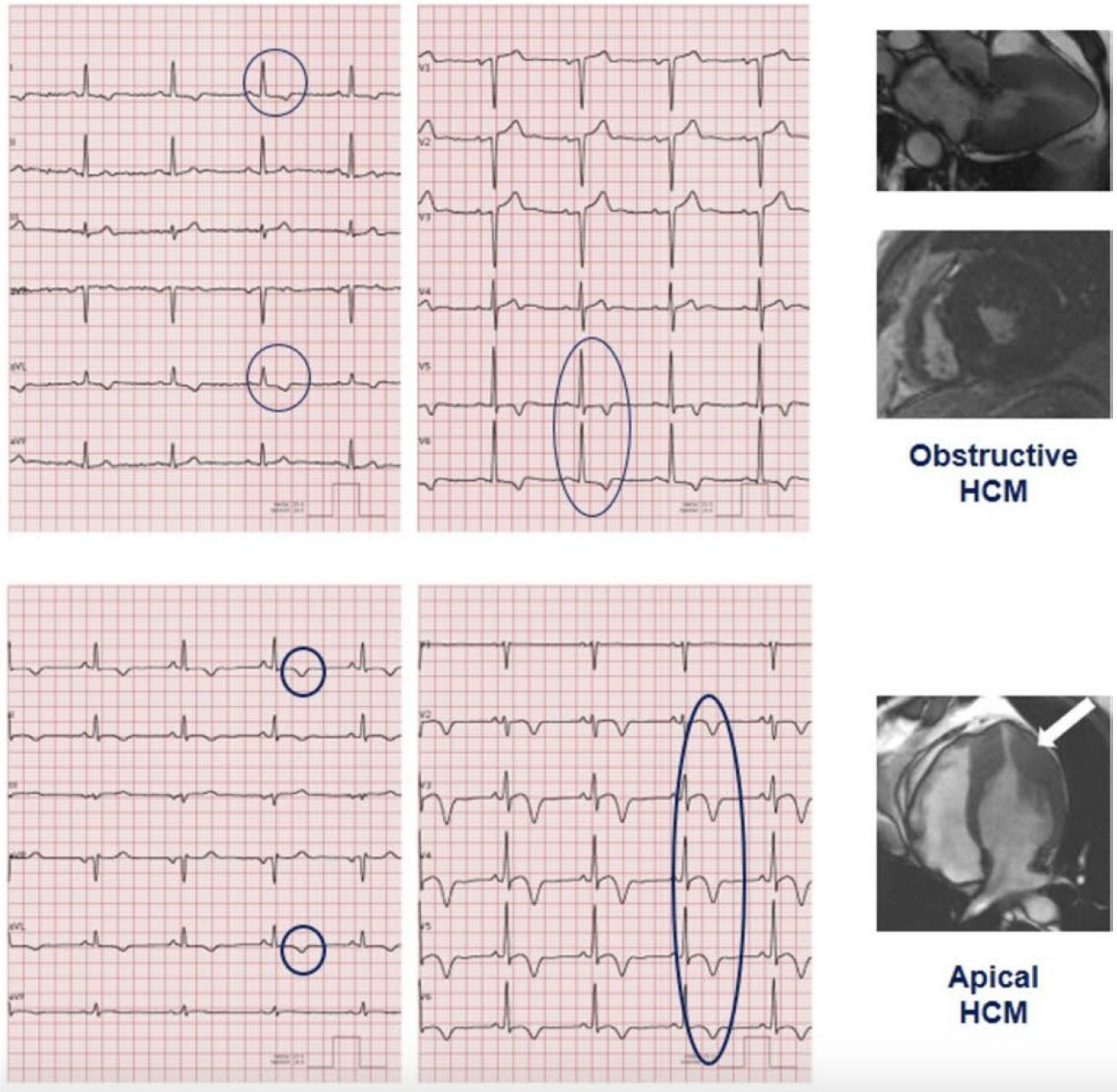
Finding	Main cardiac phenotype
	HCM
↑ Creatine kinase	Mitochondrial diseases Glycogenosis Danon disease
Proteinuria with/without ↓ glomerular filtration rate	Anderson–Fabry disease Amyloidosis
↑ Transaminase	Mitochondrial diseases Glycogenosis Danon disease
High transferrin saturation/ hyperferritinaemia	
Lactic acidosis	Mitochondrial diseases
Myoglobinuria	Mitochondrial diseases
Leucocytopenia	Mitochondrial diseases (*TAZ* gene/Barth Syndrome)

Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

Rapezzi M, et al. Eur Heart J 2013;34(19):1448-1458.

Value of ECG:

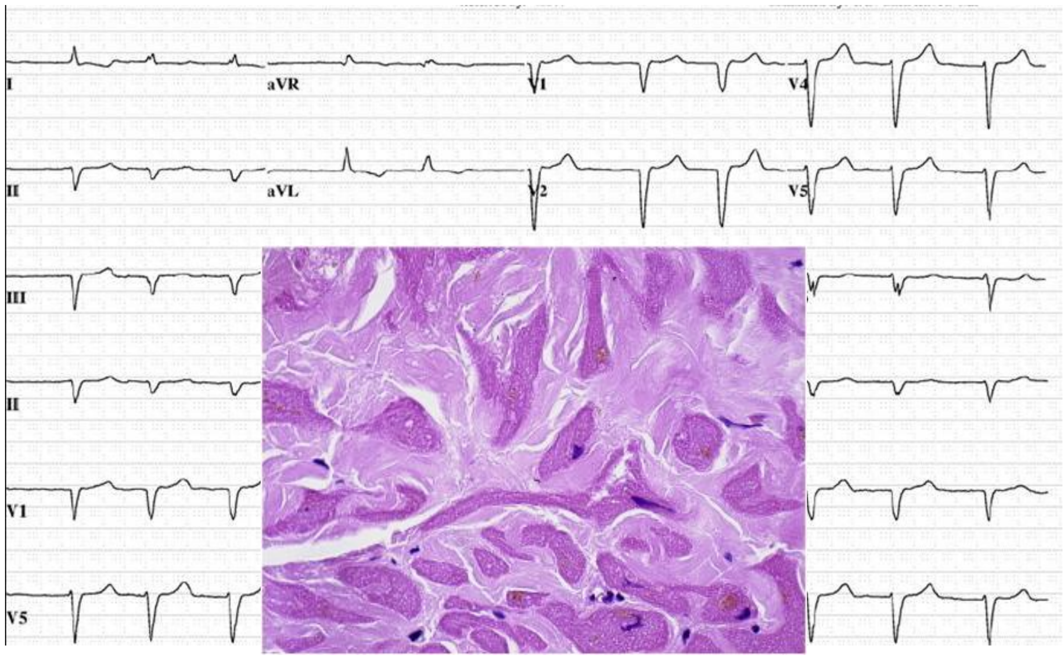
- Distribution of hypertrophy
- Myocardial fibrosis
- Early diagnosis in relatives
- Diagnostic red flags



Aimo A, et al. Heart Failure Reviews (2024) 29:151–164.

CARDIAC AMYLOIDOSIS

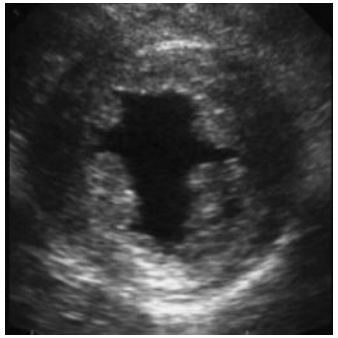
- Atrial fibril
- Low QRS voltages (disproportion)
- Pseudonecrosis

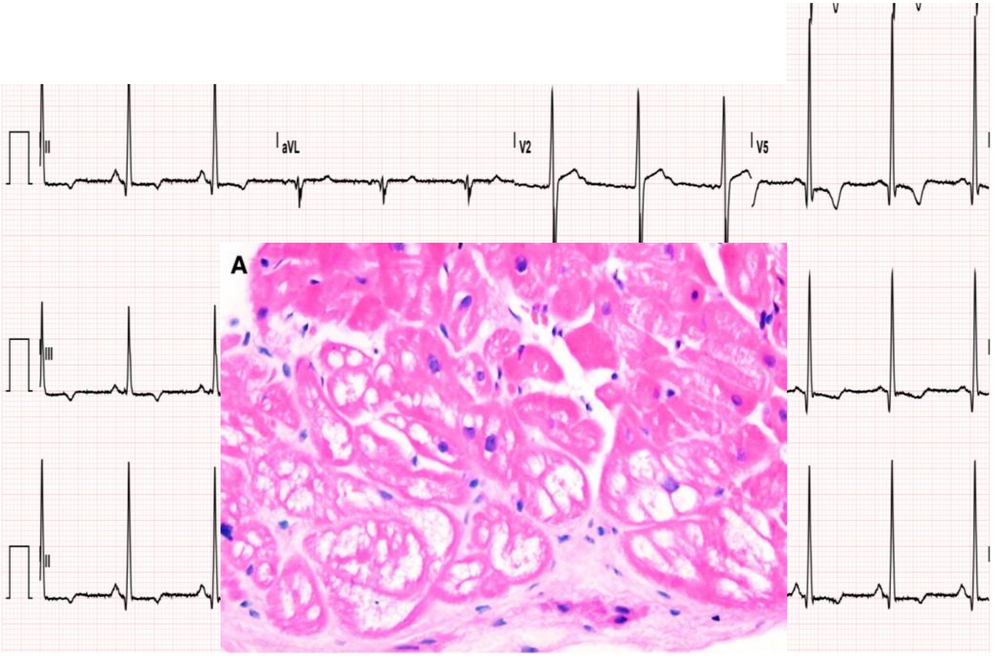


Myocardial infiltration

ANDERSON-FABRY DISEASE

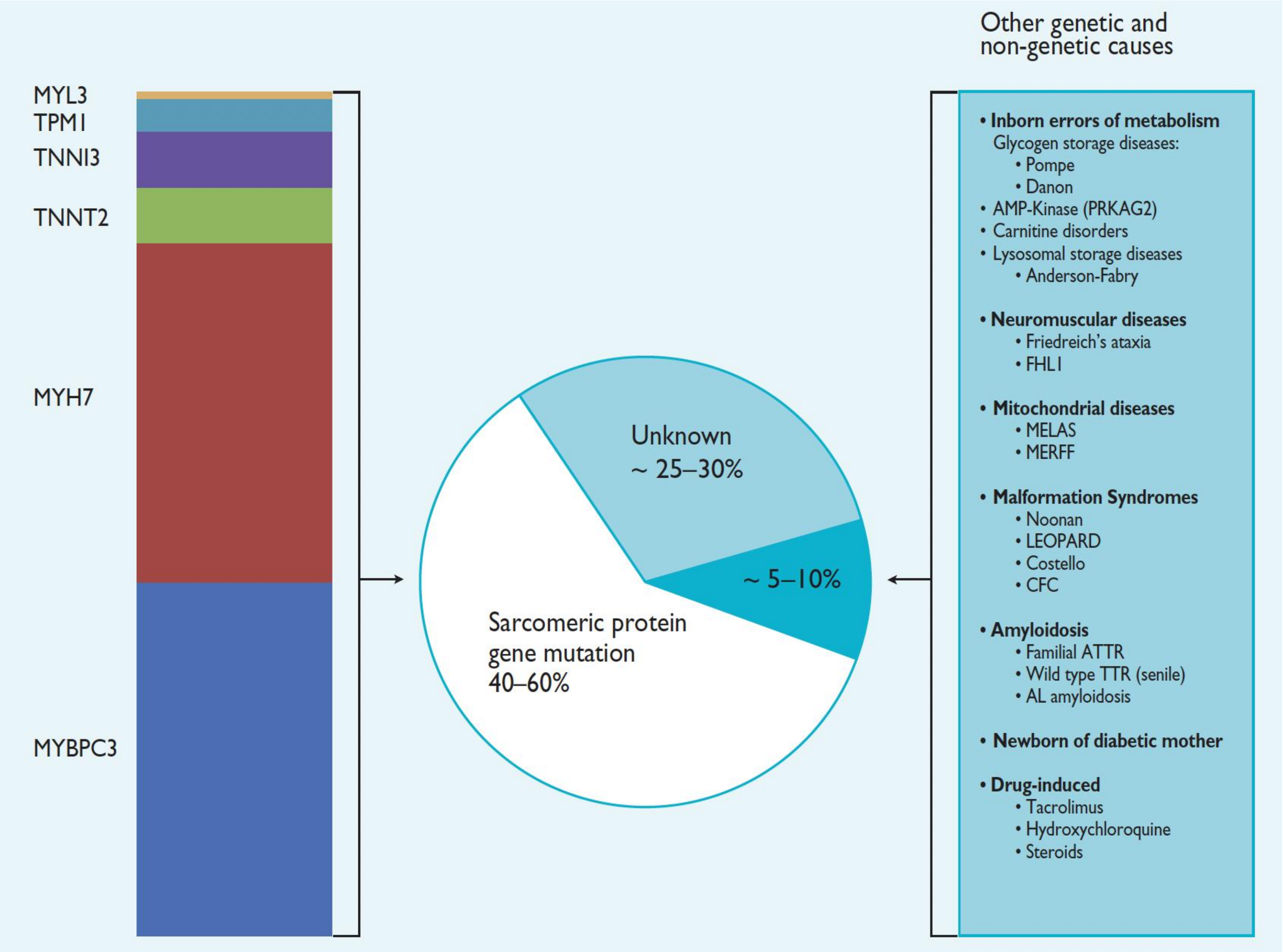
- Short PR
- High QRS voltages
- Repolarization abnormalities





Myocardial storage

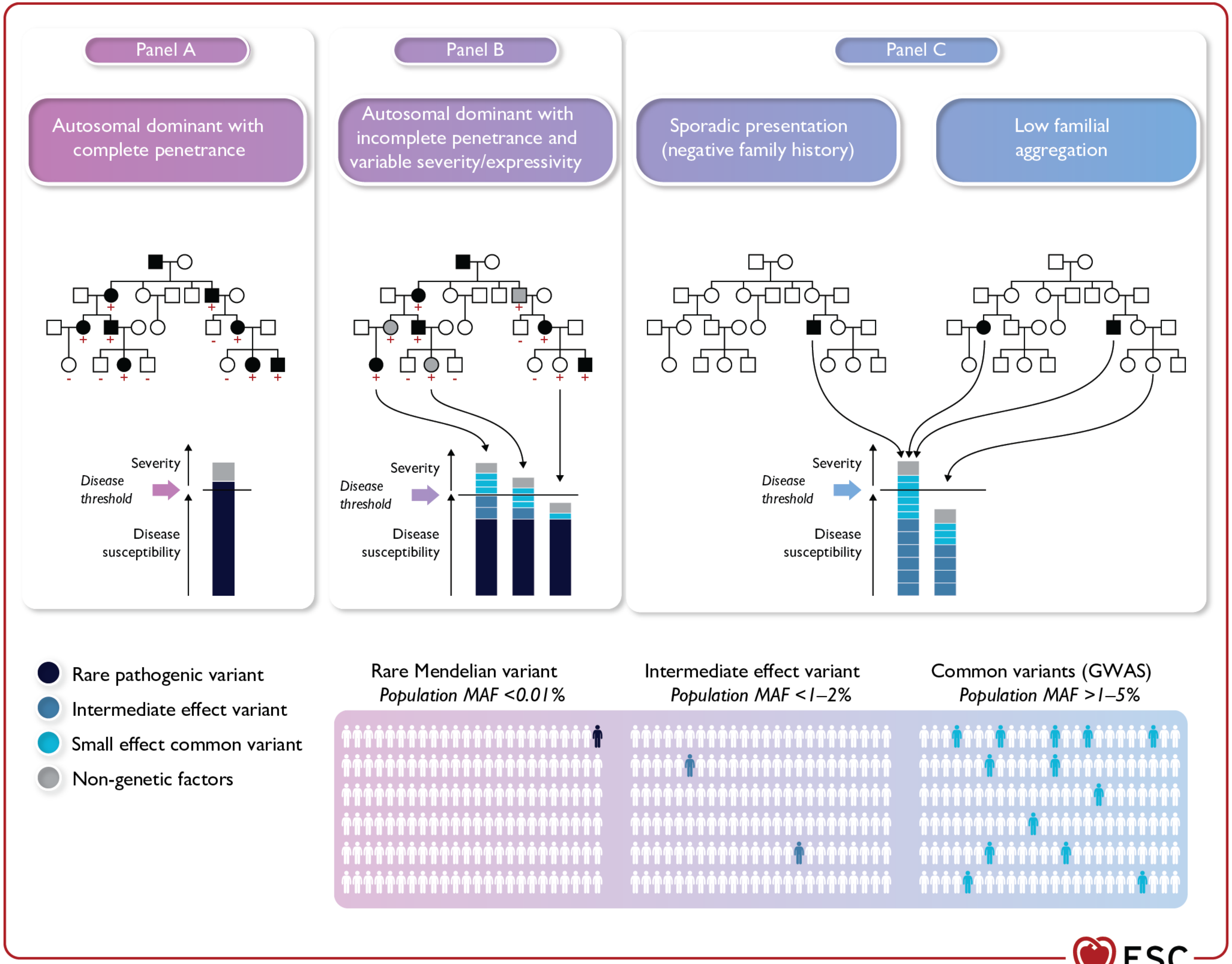
Presence of sarcomeric variants



Elliott PM et al. 2014 ESC HCM guidelines European Heart Journal 2014;35:2733–2779

Genetic architecture of cardiomyopathies

Monogenic forms
- dominant
- genetic heterogeneity
- incomplete penetrance
- variable expressivity



Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

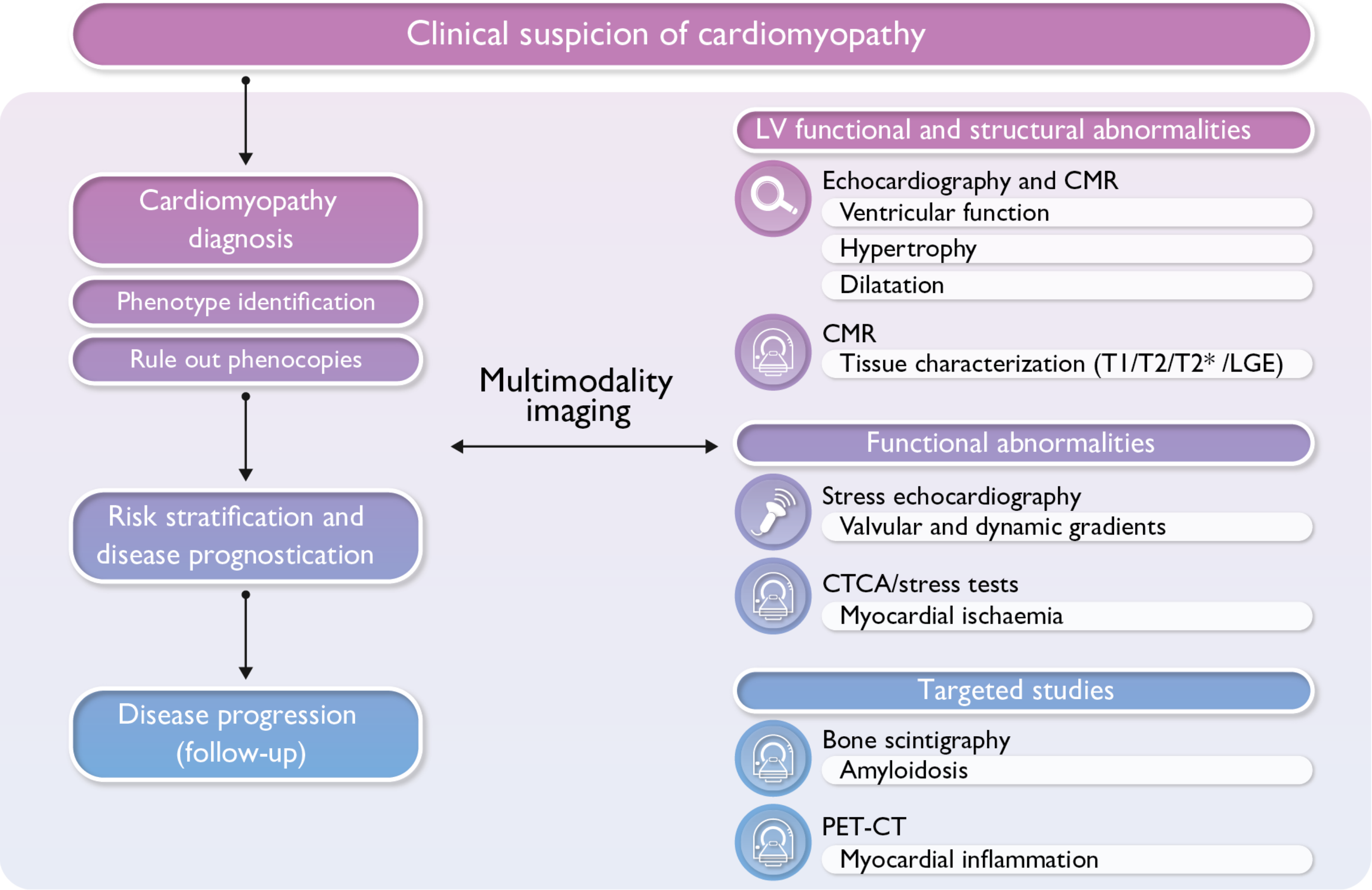
Genetic Testing

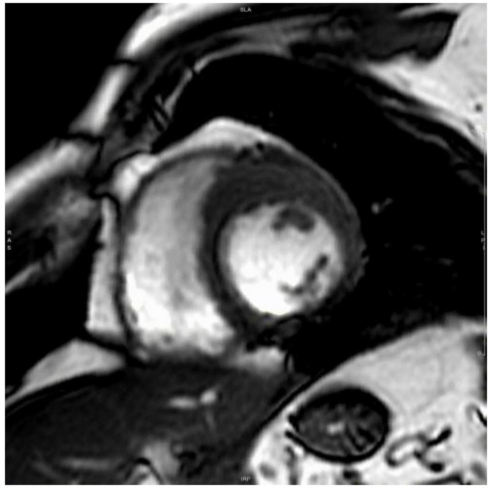
For the patient	For relatives
Diagnosis	An **individual who does not carry the genetic variant** proved to be responsible for disease in their family can be confidently reassured and discharged without surveillance, while an **individual who carries a disease-causing variant** can be followed closely, and potentially treated early
Prognosis	
Therapy	
Reproductive advice	

Recommendations	Class	Level
Index patients		
Genetic testing is recommended in **patients fulfilling diagnostic criteria for cardiomyopathy** in cases where it enables diagnosis, prognostication, therapeutic stratification, or reproductive management of the patient, or where it enables cascade genetic evaluation of their relatives who would otherwise be enrolled into long-term surveillance.	I	B

Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

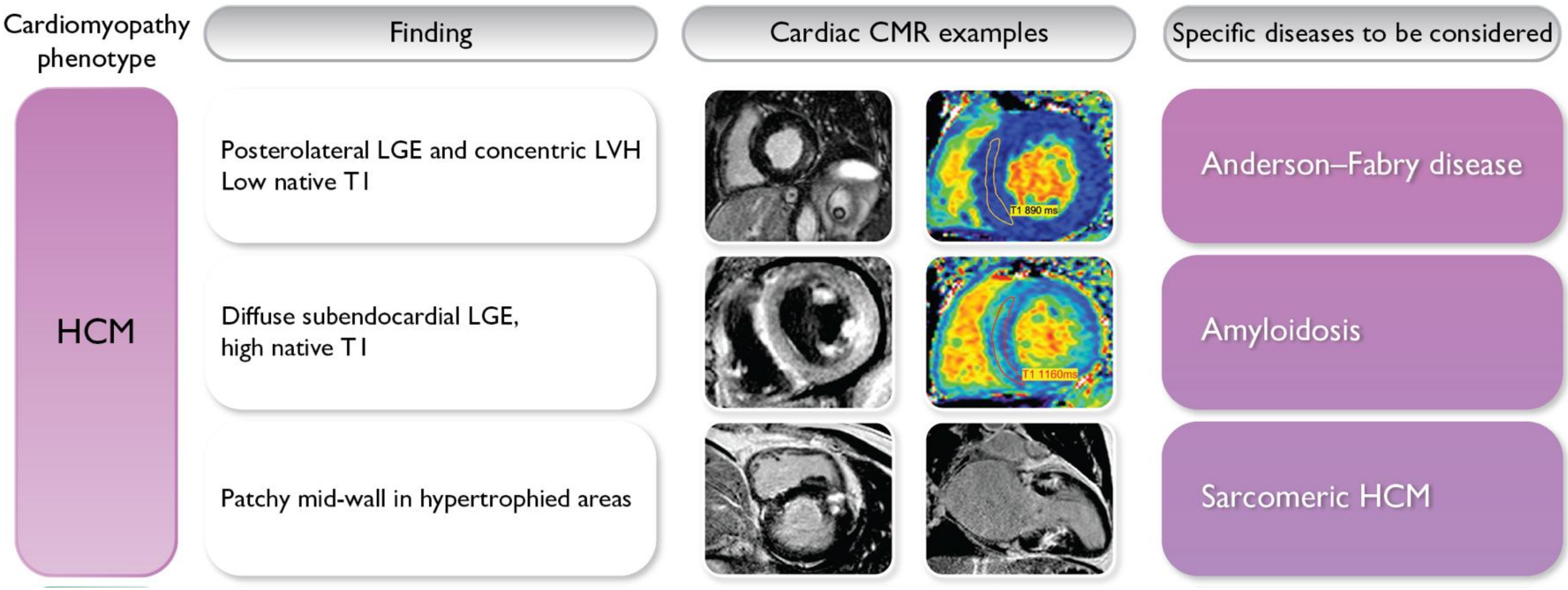
Multimodality imaging





Recommendation	Class	Level
A **comprehensive evaluation of cardiac dimensions and LV and RV systolic (global and regional) and LV diastolic function** is recommended in all patients with cardiomyopathy at initial evaluation, and during follow-up, to monitor disease progression and aid risk stratification and management.	I	B

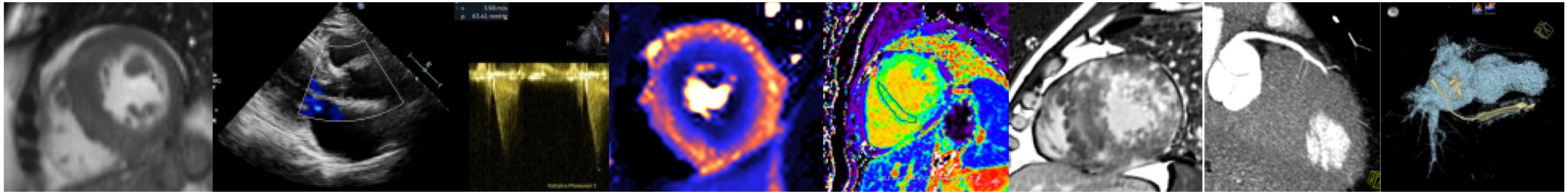
Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.



Recommendations	Class
Contrast-enhanced CMR is recommended in patients with cardiomyopathy at **initial evaluation.**	I
Contrast-enhanced CMR should be considered in **patients with cardiomyopathy** during **follow-up** to monitor *disease progression and aid risk stratification and management*.	IIa
Contrast-enhanced CMR should be considered for the serial **follow-up and assessment of *therapeutic response*** in patients with cardiac **amyloidosis, Anderson–Fabry disease, sarcoidosis, inflammatory cardiomyopathies, and haemochromatosis** with cardiac involvement.	IIa

Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

Role of imaging in HCM



Diagnosis

- Health vs. disease
- Phenotyping for aetiology
- Explain symptoms
- Family screening
- Guiding genetic testing

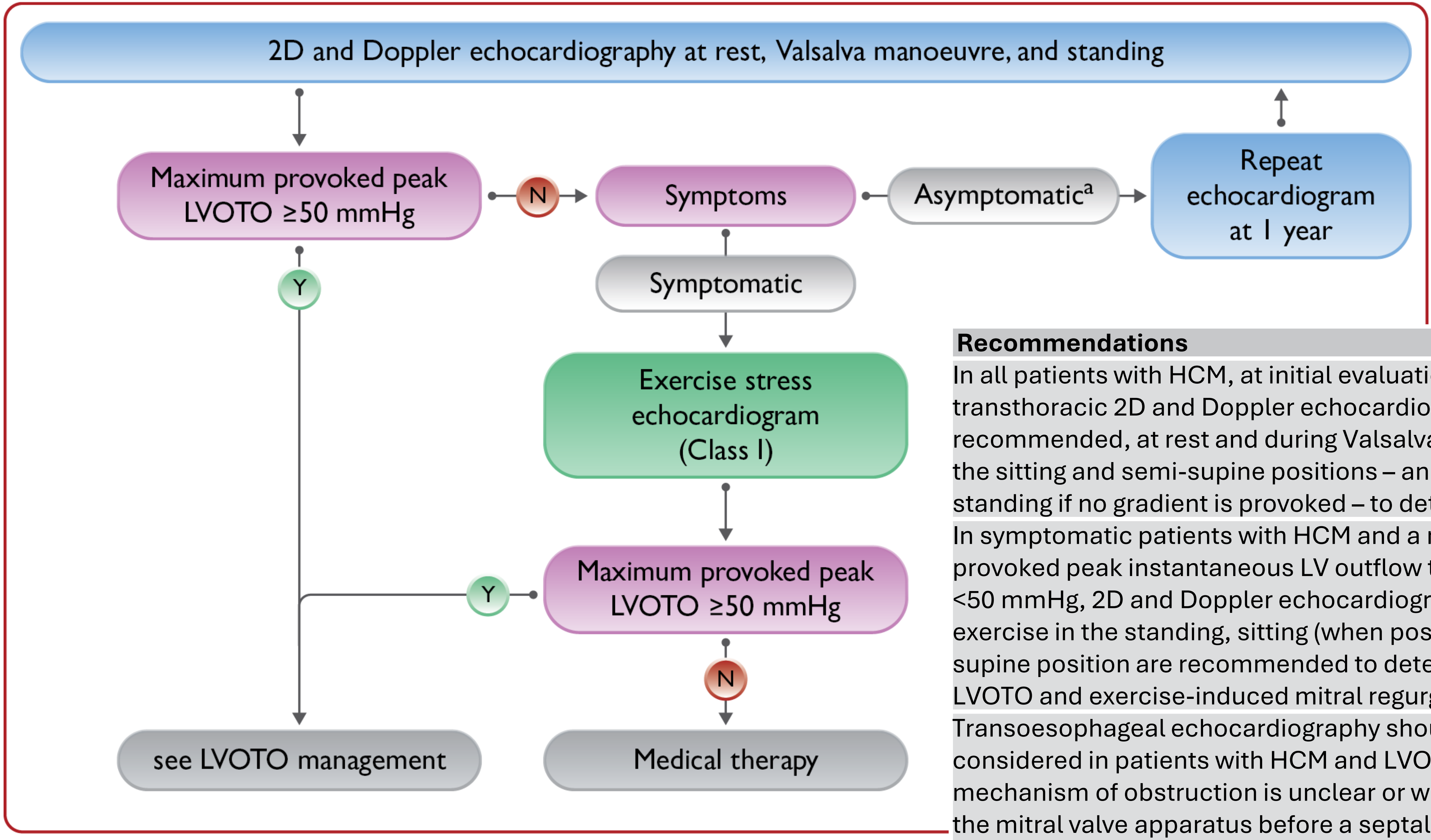
Guiding treatment

- Heart failure
- LVOT obstruction: cardiac myosin inhibitors, septal myectomy/ablation
- Treat other causes

Prognosis and surveillance

- SCD risk prediction
- Surveillance: treatment response, disease progression

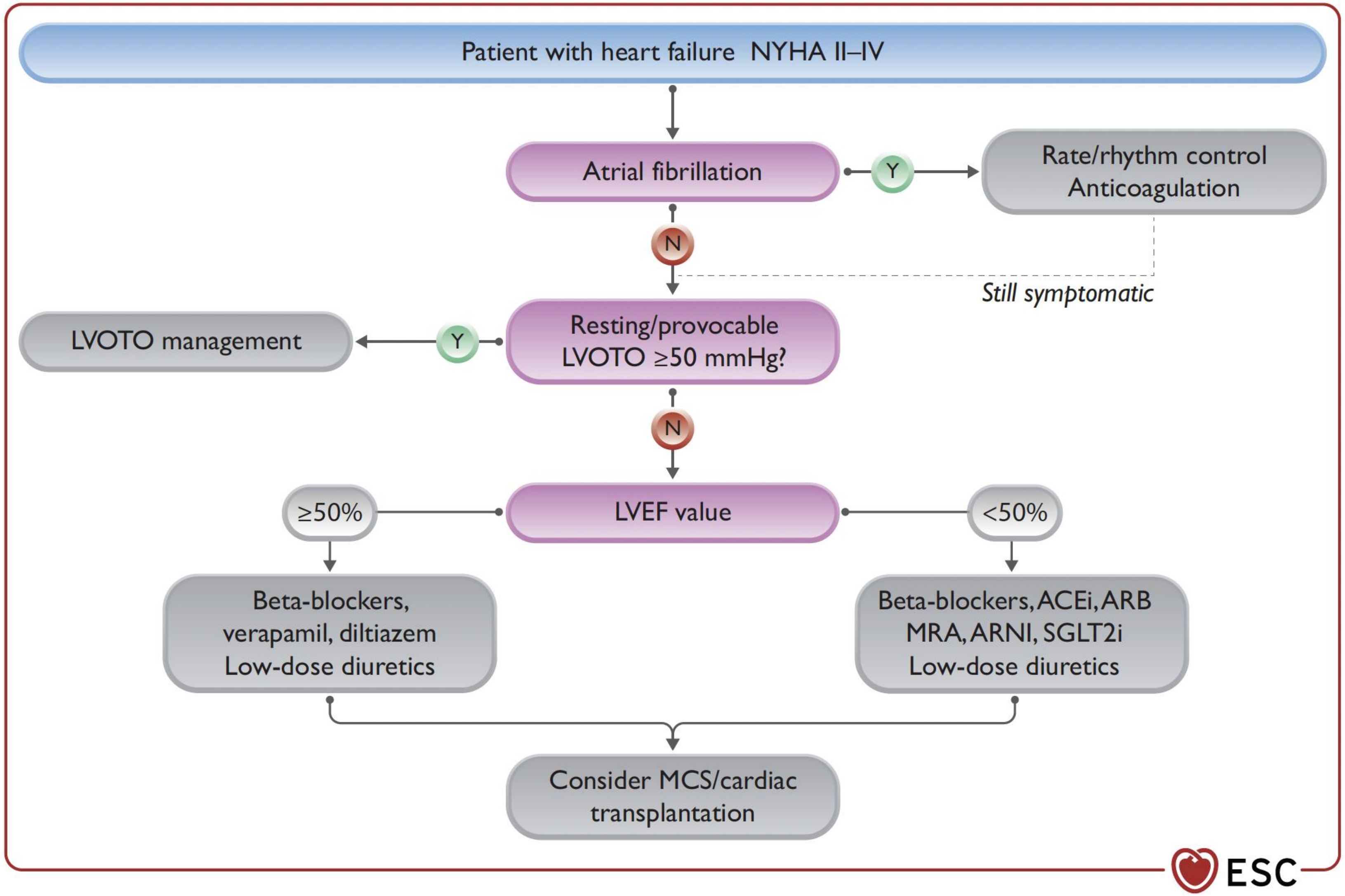
Echocardiography: LV obstruction assessment



Recommendations	Class	Level
In all patients with HCM, at initial evaluation, transthoracic 2D 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 – to detect LVOTO.	I	B
In symptomatic patients with HCM and a resting or provoked peak instantaneous LV outflow tract gradient <50 mmHg, 2D and Doppler echocardiography during exercise in the standing, sitting (when possible), or semi-supine position are recommended to detect provocable LVOTO and exercise-induced mitral regurgitation.	I	B
Transoesophageal echocardiography should be considered in patients with HCM and LVOTO if the mechanism of obstruction 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

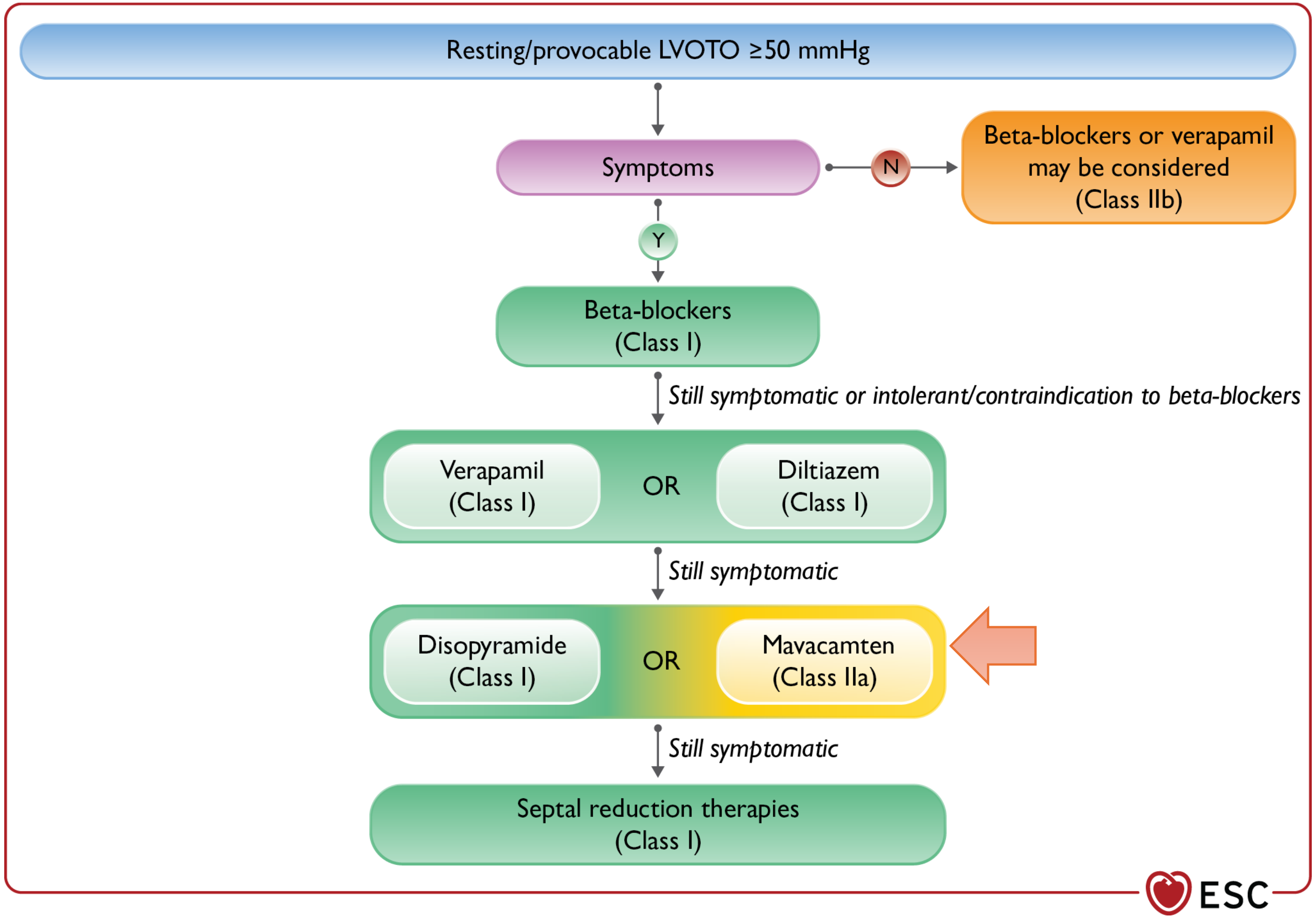
Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

Treatment of heart failure in hypertrophic cardiomyopathy



Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

Recommendations for medical treatment of LVOTO



Recommendations	Class[a]	Level[b]
Cardiac myosin ATPase inhibitor (mavacamten), titrated to maximum tolerated dose with echocardiographic surveillance of LVEF, should be considered in addition to a beta-blocker (or, if this is not possible, with verapamil or diltiazem) to improve symptoms in adult patients with resting or provoked[c] LVOTO.[622,642–646]	IIa	A
Cardiac myosin ATPase inhibitor (mavacamten), titrated to maximum tolerated dose with echocardiographic surveillance of LVEF, should be considered as monotherapy in symptomatic adult patients with resting or provoked[c] LVOTO (exercise or Valsalva manoeuvre) who are intolerant or have contraindications to beta-blockers, verapamil/diltiazem, or disopyramide.[622,644–646]	IIa	B

Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

Recommendations for septal reduction therapy

Recommendations	Class	Level
It is recommended that SRT be performed by experienced operators working as part of a multidisciplinary team expert in the management of HCM.	**I**	**C**
SRT to improve symptoms is recommended in patients with a resting or maximum provoked LVOT gradient of ≥50 mmHg who are in NYHA/Ross functional class III–IV, despite maximum tolerated medical therapy.	**I**	**B**
Septal myectomy, rather than ASA, is recommended in children with an indication for SRT, as well as in adult patients with an indication for SRT and other lesions requiring surgical intervention (e.g. mitral valve abnormalities).	**I**	**C**
SRT should be considered in patients with recurrent exertional syncope caused by a resting or maximum provoked LVOTO gradient ≥50 mmHg despite optimal medical therapy.	**IIa**	**C**
Mitral valve repair or replacement should be considered in symptomatic patients with a resting or maximum provoked LVOTO gradient ≥50 mmHg and moderate-to-severe mitral regurgitation that cannot be corrected by SRT alone.	**IIa**	**C**

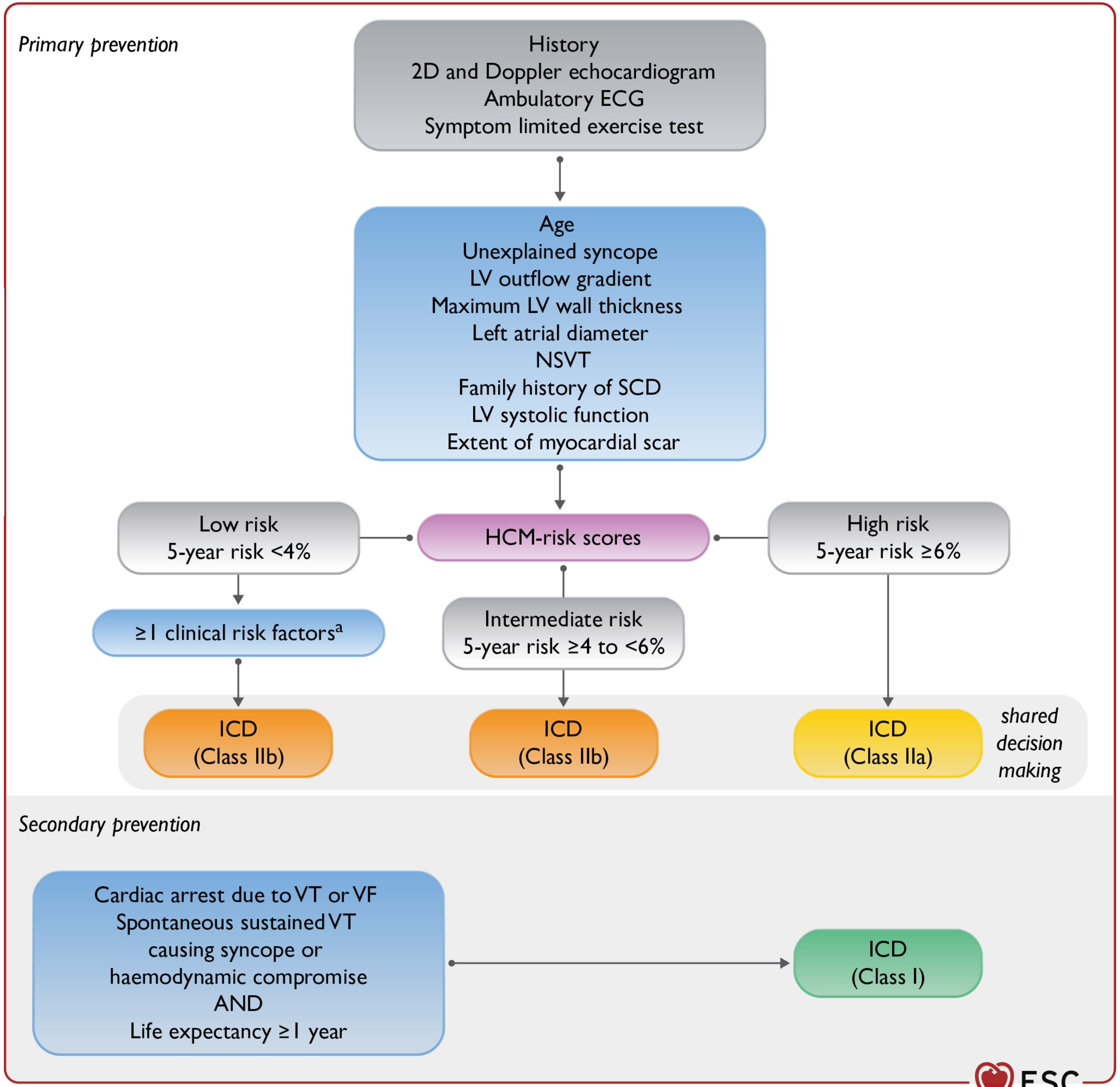
Recommendations	Class	Level
Mitral valve repair should be considered in patients with a resting or maximum provoked LVOTO gradient ≥50 mmHg when there is moderate-to-severe mitral regurgitation following isolated myectomy.	**IIa**	**C**
SRT may be considered in expert centres with demonstrable low procedural complication rates in patients with mild symptoms (NYHA class II) refractory to medical therapy who have a resting or maximum provoked gradient of ≥50 mmHg (exercise or Valsalva) and: • moderate-to-severe SAM-related mitral regurgitation; or • AF; or • moderate-to-severe left atrial dilatation.	**IIb**	**C**
Mitral valve replacement may be considered in patients with a resting or maximum provoked LVOTO gradient ≥50 mmHg when there is moderate-to-severe mitral regurgitation following isolated myectomy.	**IIb**	**C**
Surgical AF ablation and/or left atrial appendage occlusion procedures during septal myectomy may be considered in patients with HCM and symptomatic AF.	**IIb**	**C**

Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

ICD implantation in HCM

Recommendation Table 23 — Additional recommendations for prevention of sudden cardiac death in patients with hypertrophic cardiomyopathy

Recommendations	Class[a]	Level[b]
Primary prevention		
The HCM Risk-SCD calculator is recommended as a method of estimating risk of sudden death at 5 years in patients aged ≥16 years for primary prevention.[525,821–824]	I	B
Validated paediatric-specific risk prediction models (e.g. HCM Risk-Kids) are recommended as a method of estimating risk of sudden death at 5 years in patients aged <16 years for primary prevention.[81,833]	I	B

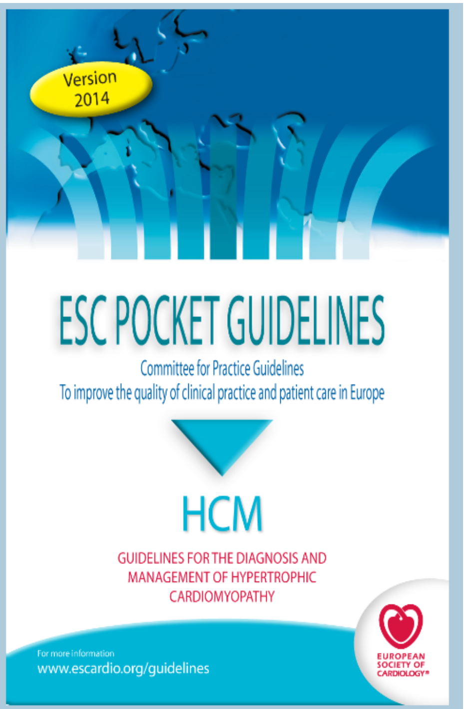


Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

EUROPEAN SOCIETY OF CARDIOLOGY®

HCM Risk-SCD Calculator

Field	Input	Unit	Description
Age		Years	*Age at evaluation*
Maximum LV wall thickness		mm	*Transthoracic Echocardiographic measurement*
Left atrial size		mm	*Left atrial diameter determined by M-Mode or 2D echocardiography in the parasternal long axis plane at time of evaluation*
Max LVOT gradient		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 Bernouilli equation: Gradient= $4V^2$, 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 (%):	
ESC recommendation:	

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.

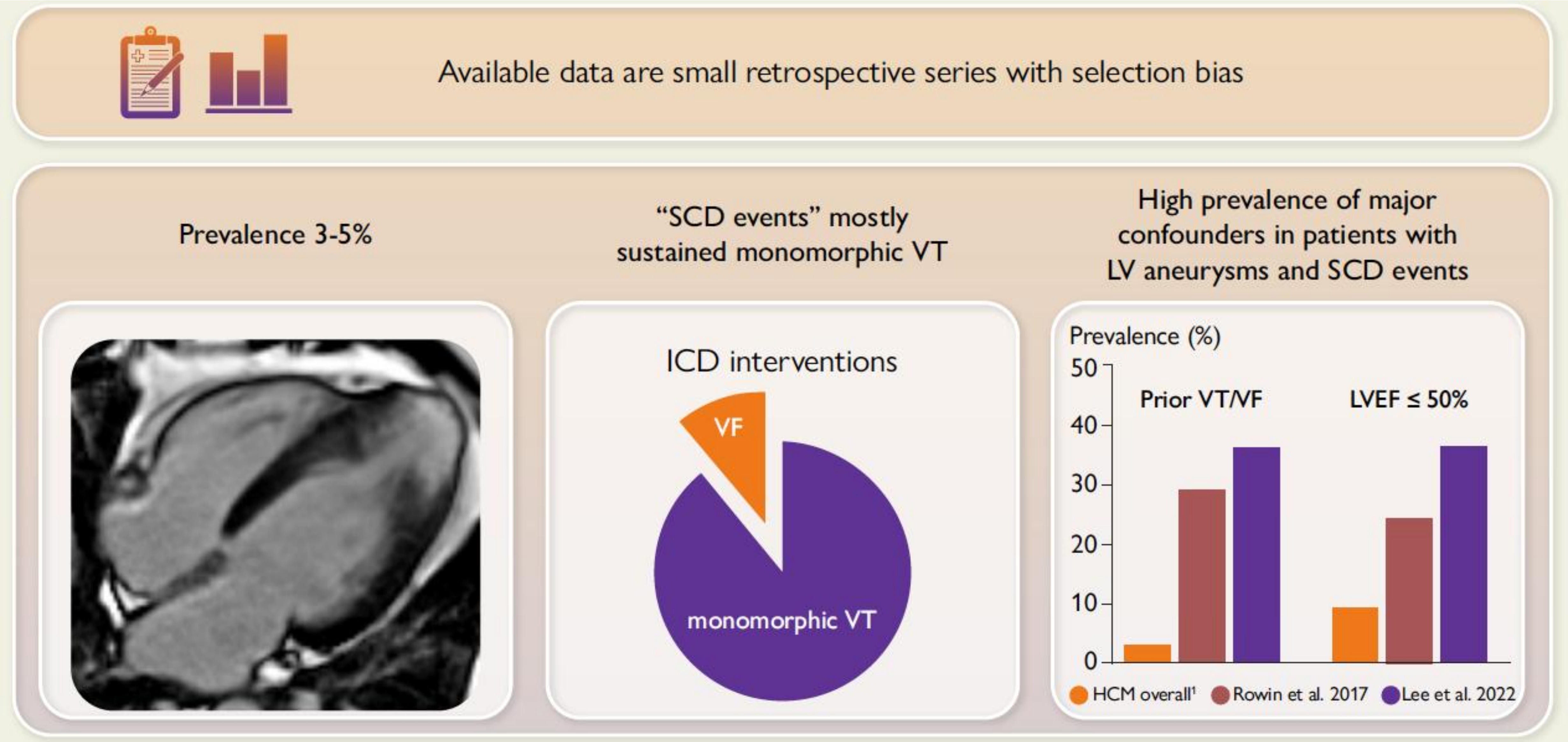
Pending further studies, HCM-RISK should be used cautiously in patients with a maximum left ventricular wall thickness ≥35 mm.

Additional recommendations for prevention of sudden cardiac death in patients with hypertrophic cardiomyopathy

Recommendations	**Class**	**Level**
Primary prevention		
Implantation of an ICD should be considered in patients with an estimated 5-year risk of sudden death of ≥6%, following detailed clinical assessment that considers: (i) the lifelong risk of complications; (ii) competing mortality risk from the disease and comorbidities; AND (i) the impact of an ICD on lifestyle, socio-economic status, and psychological health.	**IIa**	**B**
In patients with **LV apical aneurysms**, decisions about primary prevention ICD **based on an assessment of risk** using the HCM Risk-SCD or a validated paediatric risk prediction (e.g. HCM Risk-Kids) tool and **not solely** on the presence of the **aneurysm** should be considered.	**IIa**	**B**

Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

Apical Aneurysms



Lorenzini and Elliott. Eur Heart J 2023; 44(17):1519-1521.

Additional recommendations for prevention of sudden cardiac death in patients with hypertrophic cardiomyopathy

Recommendations	Class	Level
Primary prevention (continued)		
Implantation of an ICD may be considered in individual patients with an estimated 5-year risk of SCD of between ≥4% and <6%, following detailed clinical assessment that takes into account the lifelong risk of complications and the impact of an ICD on lifestyle, socio-economic status, and psychological health.	**IIb**	**B**
For patients who are in the **low-risk category** (<4% estimated 5-year risk of SCD), the presence of **extensive LGE (≥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).	**IIb**	**B**

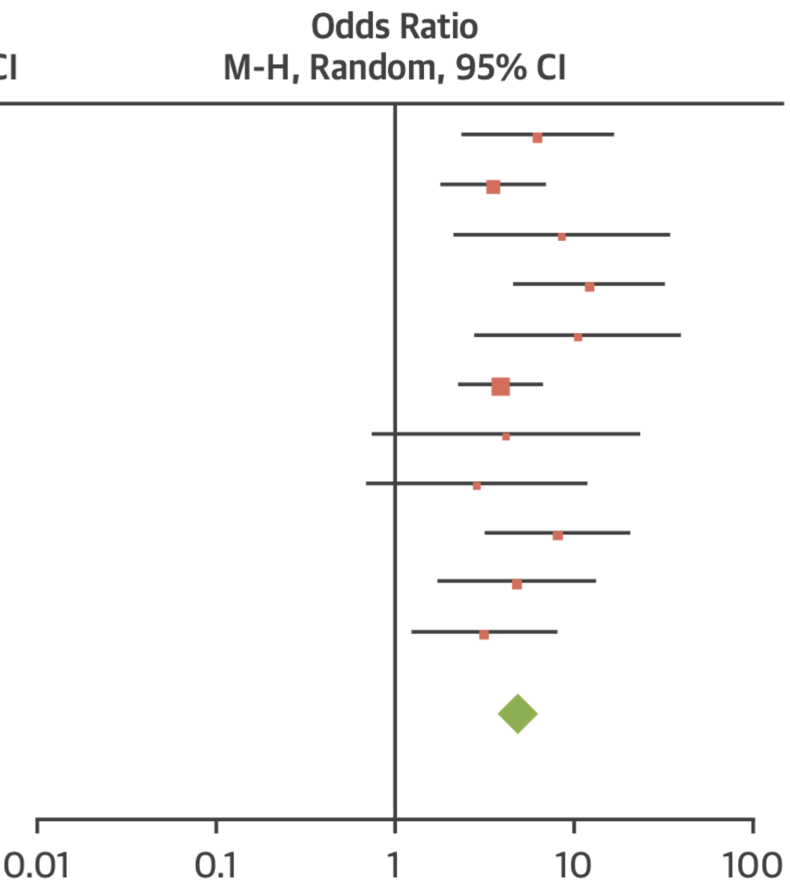
Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

Late-gadolinium enhancement for risk stratification

11 Studies
5,500 patients
Mean follow-up 4.5 years
SCD event rate 4.4%
LGE in 61% of patients

FIGURE 2 **LGE Extent as a Predictor of SCD in HCM**

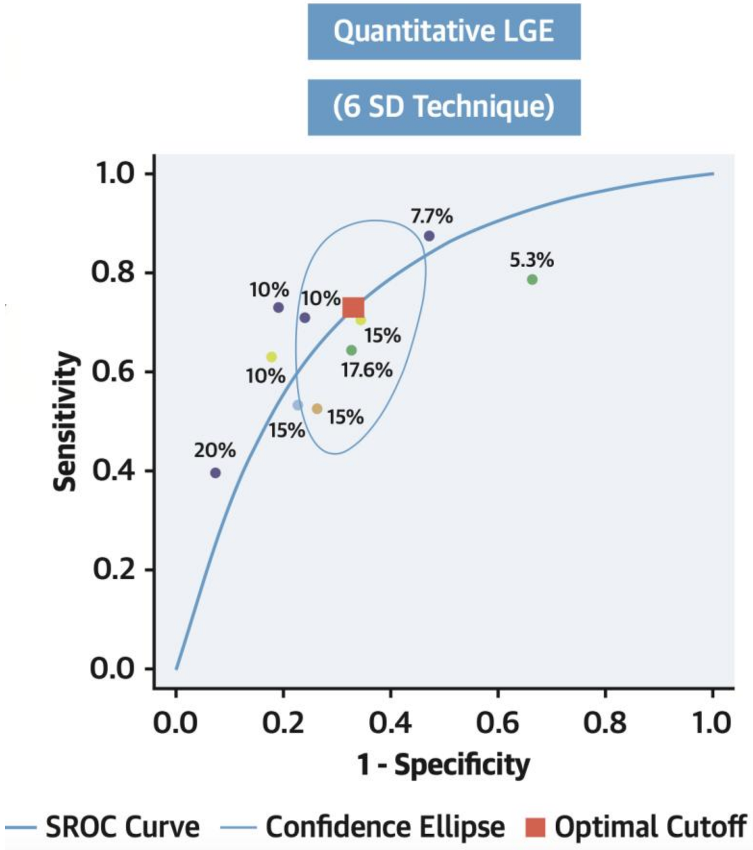
Study or Subgroup	Extensive LGE Events	Extensive LGE Total	Non-Extensive LGE Events	Non-Extensive LGE Total	Weight	Odds Ratio M-H, Random, 95% CI
Aquaro 2020	10	29	12	154	8.0%	6.23 [2.37, 16.37]
Chan 2014	18	285	19	1,008	17.1%	3.51 [1.82, 6.78]
Chen 2022	8	49	3	134	3.9%	8.52 [2.16, 33.61]
Freitas 2019	17	106	6	387	8.1%	12.13 [4.65, 31.64]
Greulich 2021	11	60	3	143	4.3%	10.48 [2.81, 39.12]
Mentias 2018	32	342	28	1,081	27.2%	3.88 [2.30, 6.55]
Park 2020	4	103	2	207	2.5%	4.14 [0.75, 23.00]
Rubinshtein 2010	4	112	4	312	3.8%	2.85 [0.70, 11.60]
Todiere 2019	14	73	8	281	8.9%	8.10 [3.25, 20.18]
Weissler-Snir 2020	15	72	6	115	7.4%	4.78 [1.76, 12.99]
Yang 2023	10	135	9	362	8.7%	3.14 [1.25, 7.90]
Total (95% CI)		**1,366**		**4,184**	**100.0%**	**4.93 [3.75, 6.47]**
Total events	143		100			



Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 9.99$, df = 10 ($P = 0.44$); $I^2 = 0\%$
Test for overall effect: Z = 11.46 ($P < 0.00001$)

Kiaos A, et al. J Am Coll Cardiol Img. 2024;17(5):489-497.

Late-gadolinium enhancement for risk stratification



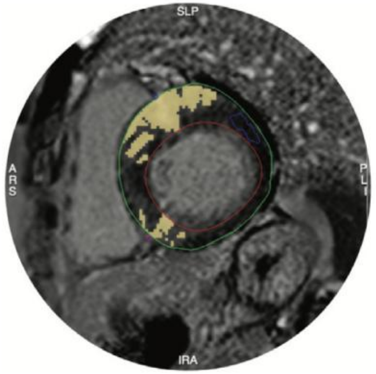


TABLE 4 Accuracy of LGE Extent[a] in Predicting SCD in HCM Patients Across Different Thresholds

Threshold (% of LV Mass)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio	Negative Likelihood Ratio
5%	0.89 (0.63-0.98)	0.43 (0.33-0.54)	1.56	0.26
10%	0.73 (0.49-0.88)	0.67 (0.57-0.76)	2.21	0.40
15%	0.58 (0.34-0.78)	0.79 (0.69-0.86)	2.76	0.53
20%	0.46 (0.22-0.73)	0.85 (0.76-0.91)	3.07	0.64

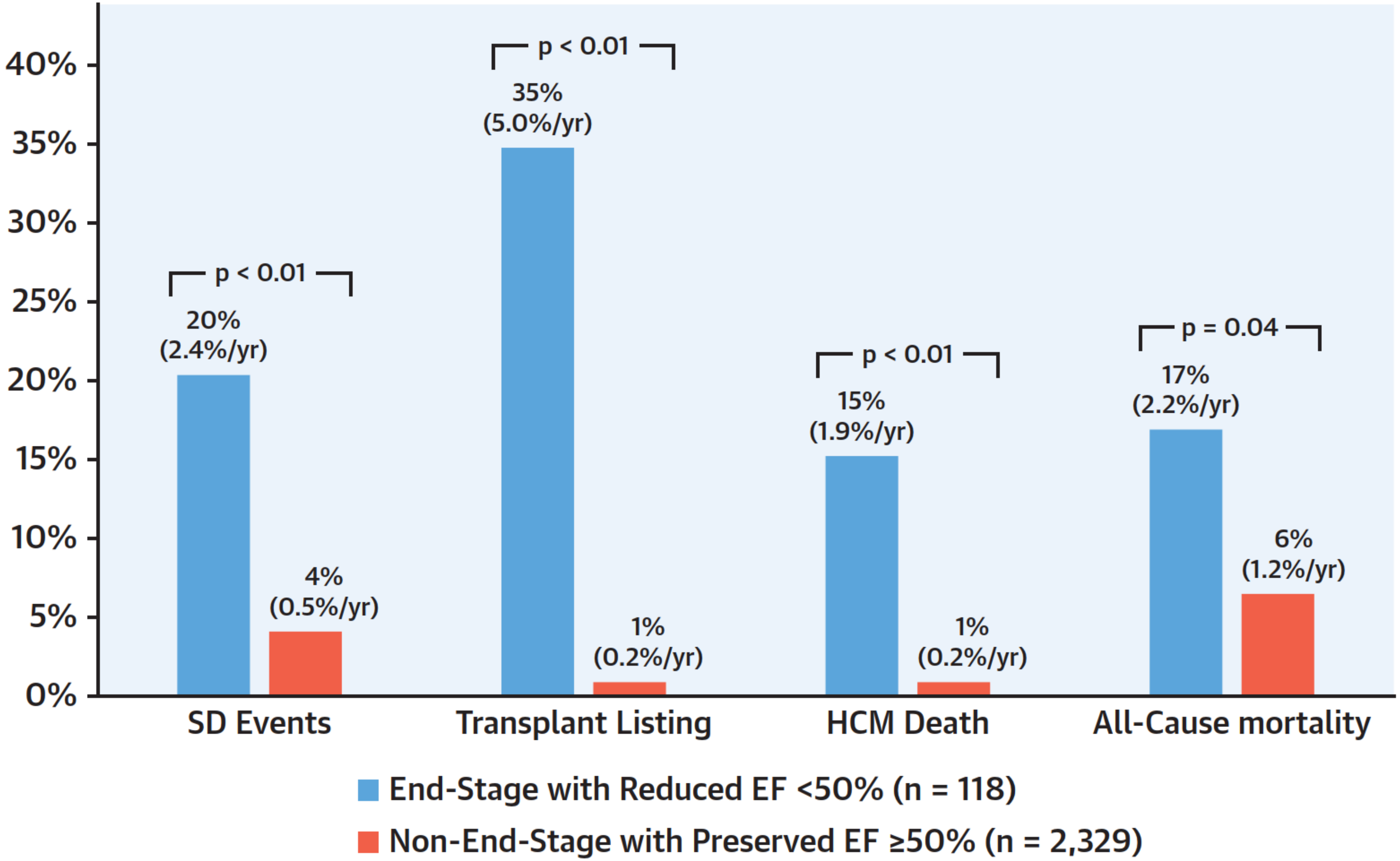
Kiaos A, et al. J Am Coll Cardiol Img. 2024;17(5):489-497.

Additional recommendations for prevention of sudden cardiac death in patients with hypertrophic cardiomyopathy

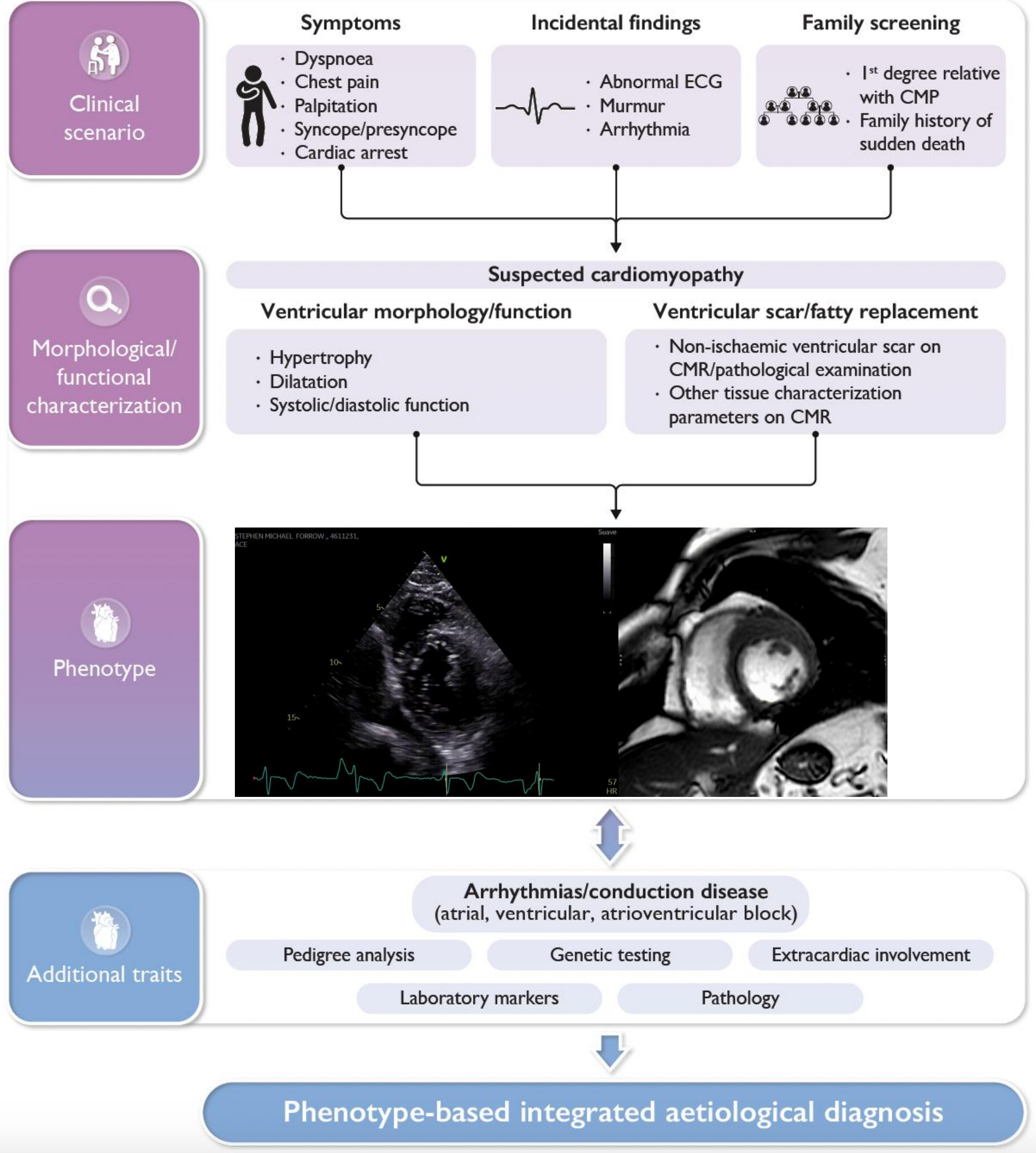
Recommendations	Class	Level
Primary prevention (continued)		
For patients who are in the **low-risk category** (<4% estimated 5-year risk of SCD), the presence of **LVEF <50%** may be considered in shared decision-making with patients about prophylactic ICD implantation, acknowledging the lack of robust data on the impact of systolic dysfunction on the personalized risk estimates generated by HCM Risk-SCD or a validated paediatric model (e.g. HCM Risk-Kids).	**IIb**	**B**

Arbelo E et al. Eur Heart J 2023;44(37):3503–3626.

LV systolic dysfunction



Rowin et al. J Am Coll Cardiol 2020;75(24):3033-3043.



Key messages

Multidisciplinary

Patient-centred

Family-centred

Multiparametric:

- Family history
- Signs and symptoms (extracardiac)
- Baseline ECG
- Lab tests
- Multimodality imaging (echo/CMR)
- Genetic testing
- Holter