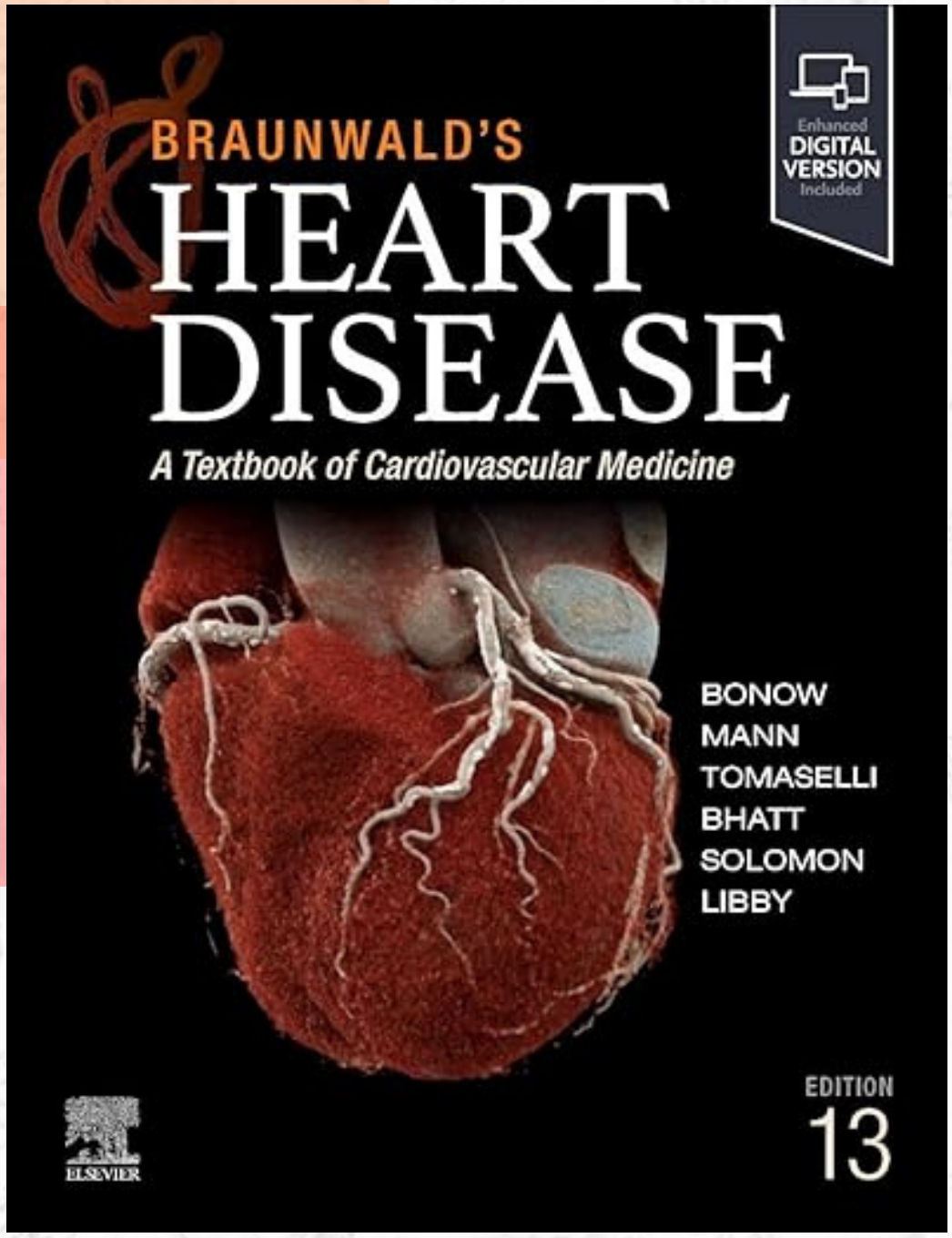
STEM-S

Last Minute Revision

LMR NOTES



INI-SS DM CARDIOLOGY

PRESENTED BY
Stem-S

- **ACC/AHA Recommendations for Percutaneous Coronary Intervention (PCI) to Improve Symptoms in Patients with Significant Anatomic or Physiologic Coronary Artery Stenosis**

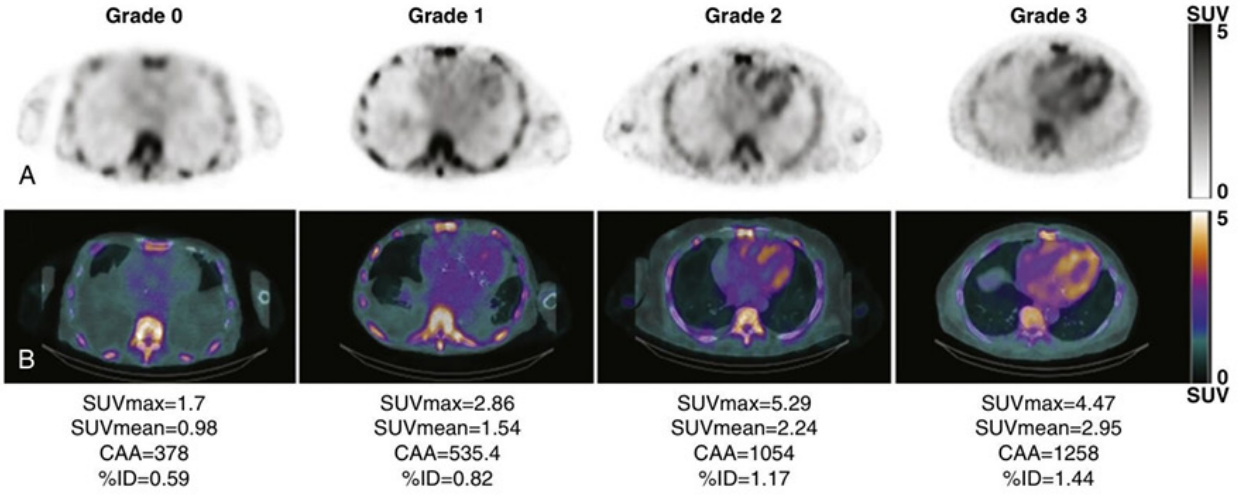
Anatomic Setting	COR	Recommendation	LOE
≥1 significant stenosis and unacceptable angina despite GDMT	I	PCI or CABG	A
≥1 significant stenosis and unacceptable angina in patients in whom GDMT cannot be implemented	IIa	PCI or CABG	C
Previous CABG with ≥1 significant stenosis associated with ischemia and unacceptable angina despite GDMT	IIa	PCI	C
Complex three-vessel CAD (e.g., SYNTAX score >22) and a good candidate for CABG	IIa	CABG preferred over PCI	B

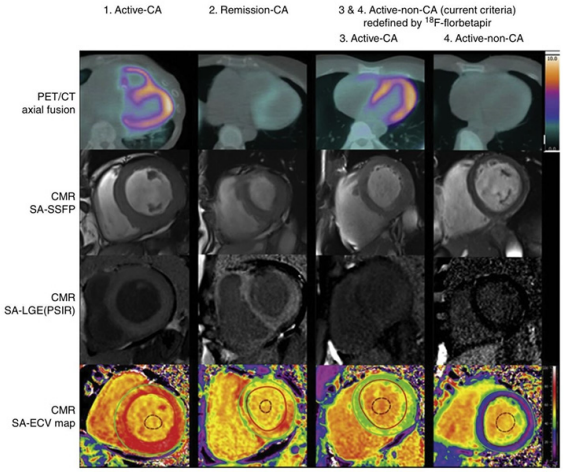
- **Appropriateness of Coronary Artery Bypass Grafting (CABG) and Percutaneous Coronary Intervention (PCI)**

Anatomic Setting	CABG	PCI
Two-vessel CAD with proximal LAD stenosis	A	A
Three-vessel CAD with low CAD burden (i.e., three focal stenoses, low SYNTAX score)	A	A
Three-vessel CAD with intermediate to high CAD burden (i.e., multiple diffuse lesions, presence of CTO, or high SYNTAX score)	A	U
Isolated left main stenosis	A	U
Left main stenosis and additional CAD with low CAD burden (i.e., additional involvement of one or two vessels or low SYNTAX score)	A	U
Left main stenosis and additional CAD with intermediate to high CAD burden (i.e., three-vessel involvement, presence of CTO, or high SYNTAX score)	A	I

- **Features of Cardiac Amyloidosis Based on Amyloid Type**

TYPE OF AMYLOIDOSIS	PRECURSOR PROTEIN	USUAL AGE AT ONSET	MAIN ORGANS INVOLVED	AVERAGE SURVIVAL TIME IN UNTREATED PATIENTS	SPECIFIC TREATMENT
AL (primary)	Abnormal light chains	50+	All except central nervous system; heart involved in 50% of cases	Noncardiac disease, 24 months; disease with heart failure, < 9 months	Chemotherapy aimed at plasma cells
Familial (ATTR)	Mutant TTR	20–70+ (partially dependent on mutation)	Peripheral and autonomic neuropathy; heart	7 to 10 years for neuropathy	Liver transplantation. Investigational agents to stabilize TTR (tafamidis) or suppress its production
Senile systemic amyloidosis (SSA)	Wild-type TTR	70+	Heart	5 to 7 years	Investigational agents to stabilize TTR (tafamidis) or suppress its production
Isolated atrial amyloidosis (IAA)	Atrial natriuretic peptide	Unknown	Cardiac atria (particularly in already diseased hearts)	No effect on survival	None needed
AA (secondary amyloidosis)	Serum amyloid A (SAA), an inflammatory protein	Teens upward, dependent on underlying inflammatory condition	Liver, kidney; heart rarely	10+ years	Treatment of underlying inflammatory condition



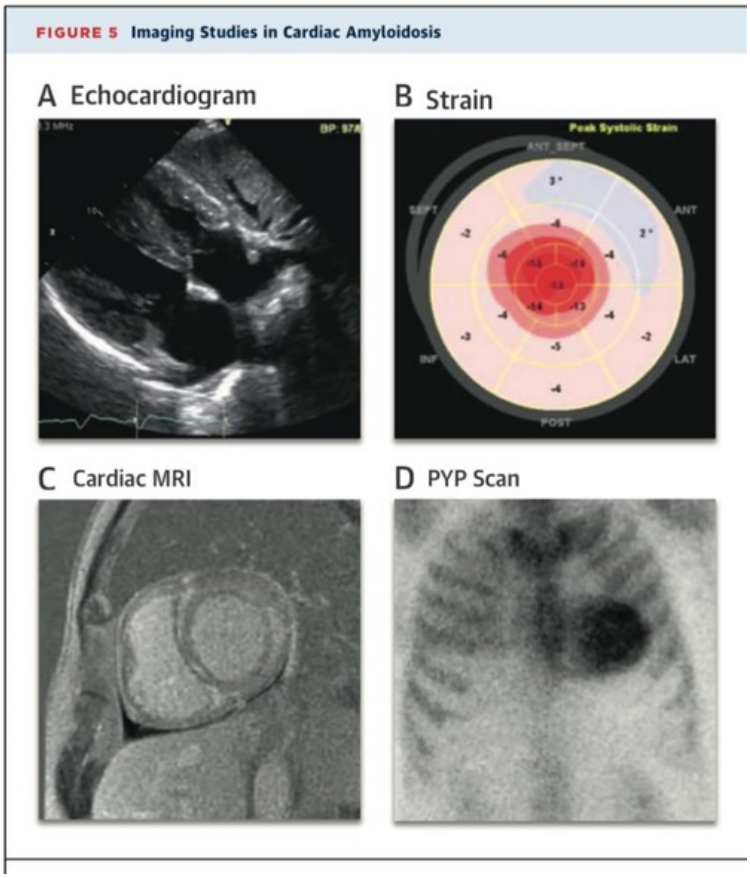


- **Comparison of Diagnostic Imaging Modalities in Cardiac Amyloidosis**

FEATURE	ECHOCARDIOGRAPHY	MRI	BONE SCINTIGRAPHY
Clinical clues	Pericardial or pleural effusions, thick right ventricle, small LV cavity, intra-atrial septal thickening, and impaired global longitudinal strain characteristically with sparing of the apex	Elevated native T1, increased extracellular volume fraction, late gadolinium enhancement in any pattern, abnormal gadolinium kinetics	Diagnostic for transthyretin amyloid cardiomyopathy (ATTR-CM) if normal light chain assays and grade 2/3 cardiac uptake with confirmation of myocardial retention by SPECT. False positives due to AL cardiac amyloidosis, previous myocardial infarction, diffuse myocardial scarring, overlying previous rib fracture, blood pool, hydroxychloroquine toxicity, and unusual forms of cardiac amyloidosis (ApoA1)
Relative cost	$	$$	$
Specialized expertise required for interpretation	No	Yes	No
Exposure to ionizing radiation	No	No	Yes
Cardiac devices affect image quality	No	Yes	No
Can identify nonamyloid causes of LV thickening	Yes (valvular disease, HCM, diastolic function) though amyloid CM may also be present	Yes (infiltrative disease, HCM)	No
Distinguish AL and ATTR	No	No	Yes*
Markers of worse prognosis	Lower stroke volume, greater regional variation in global longitudinal strain, worse global longitudinal strain, lower MCF, low EF (late phase)	Late gadolinium enhancement, higher extracellular volume fraction, higher native T1	H/CL ratio ≥1.6 at 1 hr

- **Common Types of Amyloid With Cardiac Involvement**

Type of Amyloid Pre-Cursor Protein (Source)	Clinical Features	PYP Scan Tissue Biopsy	Treatment
AL Immunoglobulin Light chain (bone marrow)	Heart failure; Weight loss; Nephrotic syndrome; Peripheral/autonomic neuropathy	Negative or mild uptake; Tissue biopsy mandatory	Chemotherapy; Autologous stem cell transplant; Monoclonal antibody
ATTR-m Transthyretin with mutation (liver)	Heart failure; Peripheral/autonomic neuropathy	Positive*; Diagnosis without tissue biopsy	Liver transplantation; Diflunisal†; Doxycycline and TUDCA‡; RNA-interfering therapy
ATTR-wt Transthyretin without mutation (liver)	Heart failure; Atrial fibrillation; Conduction disease; 90% male	Positive*; Diagnosis without tissue biopsy	Diflunisal†; Doxycycline† and TUDCA; RNA-interfering therapy

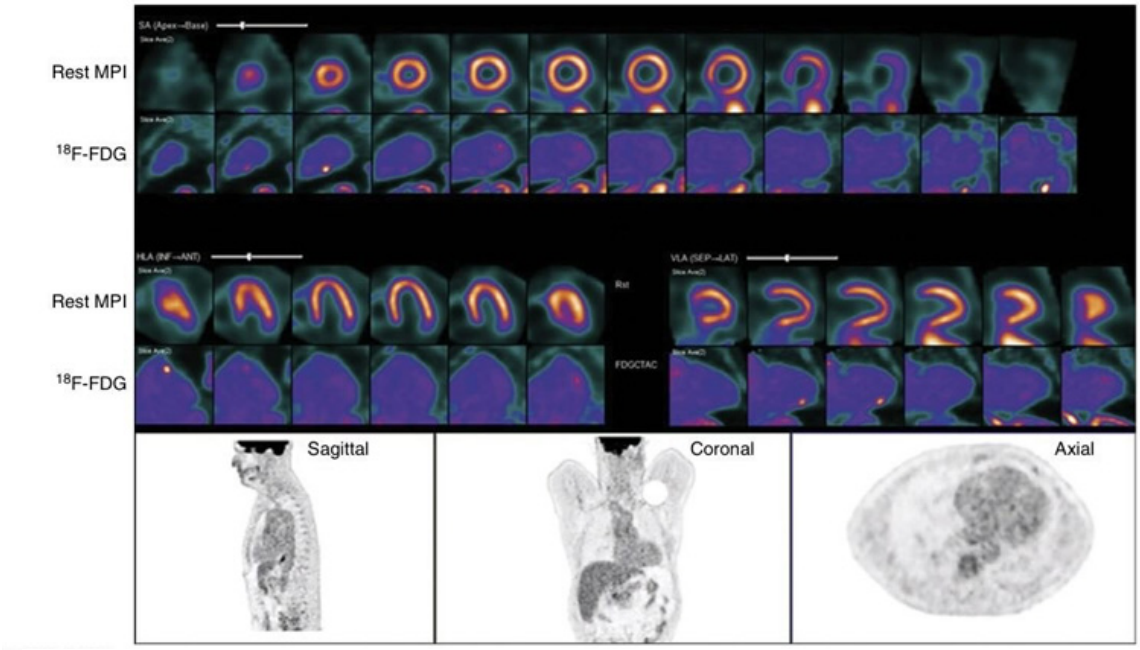


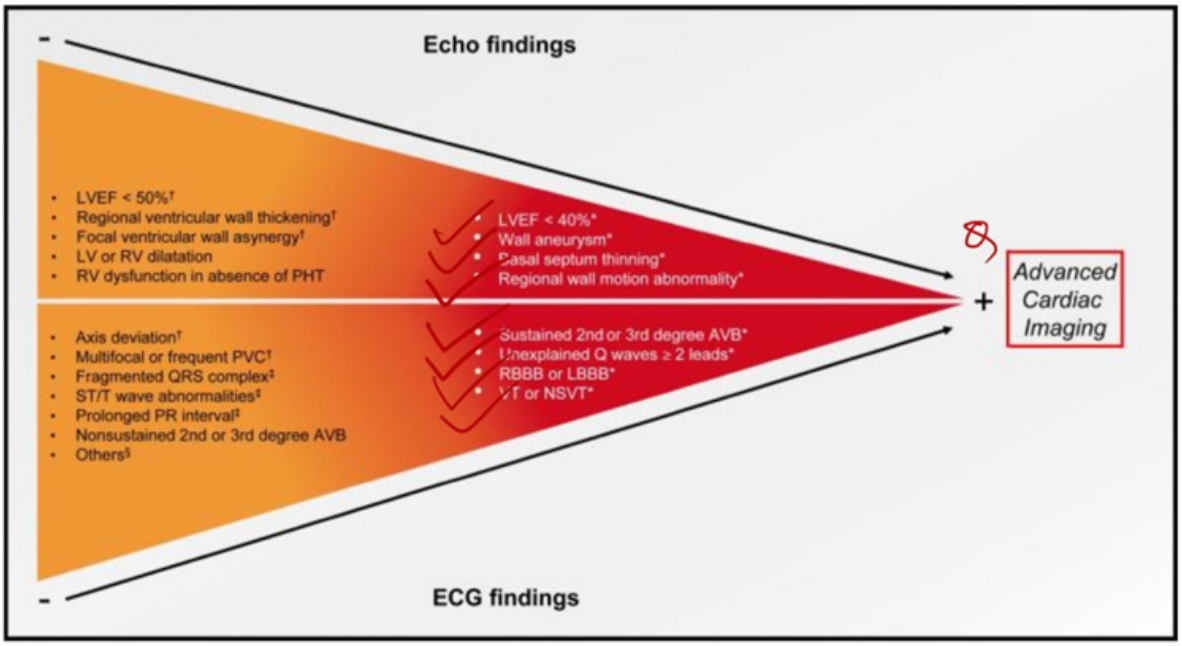
(A) Echocardiogram (subcostal view) demonstrating biventricular myocardial thickening and biatrial enlargement.

(B) Strain imaging with markedly reduced global averaged peak longitudinal systolic strain with apical preservation (“bullseye”) pattern, typical of cardiac amyloidosis.

(C) Cardiac magnetic resonance imaging short-axis image with global subendocardial late gadolinium enhancement.

(D) PYP scan shows severely increased myocardial uptake (grade 3, greater than bone) consistent with ATTR cardiac amyloidosis.





HRS Recommendations (Cardiac Sarcoidosis Arrhythmia)

- **Diagnosis & Screening**

Recommendation	Class
Ask biopsy-proven extracardiac sarcoidosis patients about **unexplained syncope/presyncope/palpitations**	I
Screen with **12-lead ECG**	I
Echocardiogram useful	IIa
CMR / FDG-PET if symptoms/ECG/echo abnormal	IIa
Screen (<60 yrs) with **unexplained Mobitz II / 3° AV block**	IIa
Advanced imaging **NOT recommended if initial screening normal**	III

- **Major Genes Associated with Hypertrophic Cardiomyopathy and Genocopies**

CORE SARCOMERIC GENES	PROTEIN ENCODED	% HCM ATTRIBUTABLE
MYBPC3	Cardiac myosin-binding protein C	~50%
MYH7	Cardiac β myosin heavy chain	30%–35%
TNNI3	Cardiac troponin I	~5%
TNNT2	Cardiac troponin T	~5%
TPM1	α-tropomyosin	<3%
MYL2	Myosin regulatory light chain	<3%
MYL3	Myosin essential light chain	<3%
ACTC1	α-cardiac actin	~1%

- **Other HCM-Associated Genes**

GENE	PROTEIN ENCODED	%
CSRP3	Muscle LIM protein	<1%
TNNC1	Cardiac troponin C	<1%
ACTN2	α-actinin	<1%
JPH2	Junctophilin-2	Rare

Genocopies

- **Storage Diseases**

GENE	DISEASE	PROTEIN
LAMP2	Danon disease	Lysosome-associated membrane protein 2 (X chromosome)
PRKAG2	Glycogen storage disease	Protein kinase AMP-activated non-catalytic subunit gamma 2
GLA	Fabry disease	α-galactosidase (X chromosome)

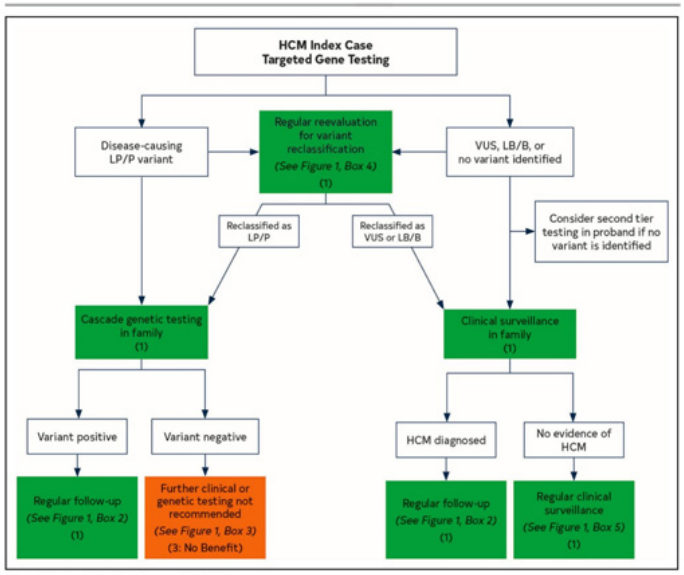


Figure 2. Genetic Testing Process in HCM.
Colors correspond to Table 3. HCM indicates hypertrophic cardiomyopathy; LB/B, likely benign/benign; LP/P, likely pathogenic or pathogenic; and VUS, variant of unknown significance.

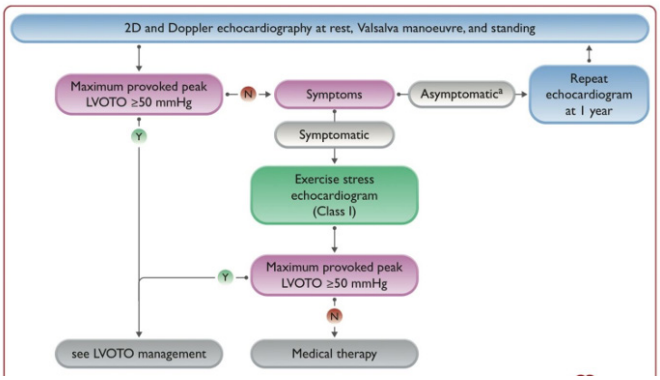
- **Pathophysiological Changes vs Clinical Symptoms/Signs**

Pathophysiological Changes	Clinical Symptoms/Signs
Hypercontractile left ventricle	Sharp upstroke carotid
Outflow obstruction	Normal or low amplitude pulse
Increased systolic tension with slow fall in tension	Sustained LV apex
Decreased LV compliance	Atrial kick, S4
Dynamic nature of obstruction (anterior leaflet MV and septum) (LV size; systemic resistance—aortic pressure; contractility)	Ejection murmur varying loudness
Increased LV filling pressure	Murmur louder on standing
LA pressure	Murmur softer on squatting
Increased O_2 demand	Dyspnea
Decreased sub-endocardial flow	Paroxysmal nocturnal dyspnea / orthopnea
Increased LA pressure	Angina
Decreased compliance	S3
Fixed output	Exertional syncope / presyncope
Mitral regurgitation	Atrial fibrillation
Myocardial disease	Palpitation, Ventricular arrhythmias

- **Echocardiographic features that suggest specific aetiologies in hypertrophic cardiomyopathy**

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/myopericarditis
Ground-glass appearance of ventricular myocardium on 2D echocardiography	Amyloidosis
Concentric LVH	Glycogen storage disease, Anderson–Fabry disease, PRKAG2 variants, Friedreich ataxia
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 variants, Danon disease, myocarditis, advanced sarcomeric HCM, Anderson–Fabry disease, Friedreich ataxia
RVOTO	Noonan syndrome and associated disorders
Apical sparing pattern on longitudinal strain imaging	Amyloidosis

- **Symptom/Sign vs Diagnosis**



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)

- **Symptom/Sign vs Diagnosis**

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

- **Distinguishing Hypertrophic Cardiomyopathy from Athlete's Heart (Gray Zone LVH)**

Feature	Pathologic LV Hypertrophy (HCM)	Physiologic LV Hypertrophy (Athlete's Heart)
Focal pattern of LV hypertrophy	+	0
LV cavity < 45 mm	+	0
LV cavity > 55 mm	0	+
Left atrium enlargement	+	0
Bizarre ECG patterns	+	+
Abnormal LV filling pattern	+	0
Family history of HCM	+	0
Decreased LV thickness with deconditioning	0	+
VO_2 increase > 110%	0	+
Late gadolinium enhancement	+	0
Pathogenic sarcomere mutation	+	0

- **Management of Drug-Refractory Obstructive Hypertrophic Cardiomyopathy**

Surgical Myectomy Management	Alcohol Septal Ablation Management
Pros:	**Pros:**
High clinical efficacy	More widely available
High success rate at experienced centers (>90%)	Less invasive; associated with a short hospital stay
Low operative risk in selected patients	Successful in ~80% of cases
Demonstrated long-term survival	Favorable long-term survival in some studies
Cons:	**Cons:**
High surgical mortality at inexperienced centers	Risk of pacemaker dependency
	Risk of potential scar in vulnerable patients
	Higher rates of residual/recurrent symptoms and need for possible repeat intervention