REVIEW ARTICLE

The role of echocardiography for diagnosis and prognostic stratification in hypertrophic cardiomyopathy

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Abstract

Hypertrophic cardiomyopathy (HCM) is the most frequent cardiac disease with genetic substrate, affecting about 0.2–0.5% of the population. While most of the patients with HCM have a relatively good prognosis, some are at increased risk of adverse events. Identifying such patients at risk is important for optimal treatment and follow-up. While clinical and electrocardiographic information plays an important role, echocardiography remains the cornerstone in assessing patients with HCM. In this review, we discuss the role of echocardiography in diagnosing HCM, the key features that differentiate HCM from other diseases and the use of echocardiography for risk stratification in this setting (risk of sudden cardiac death, heart failure, atrial fibrillation and stroke). The use of modern echocardiographic techniques (deformation imaging, 3D echocardiography) refines the diagnosis and prognostic assessment of patients with HCM. The echocardiographic data need to be integrated with clinical data and other information, including cardiac magnetic resonance, especially in challenging cases or when there is incomplete information, for the optimal management of these patients.

Keywords Hypertrophic cardiomyopathy · Echocardiography · Diagnosis · Prognosis

Introduction

Hypertrophic cardiomyopathy (HCM) is the most frequent disease with genetic substrate that involves the myocardium. The phenotype is usually heterogeneous as a result of both variability in the genetic mutations and incomplete penetrance in the affected population [1].

The current estimation of HCM prevalence (1 in 500 persons) is based on studies performed more than 20 years ago, notably the CARDIA cohort study [2–4]. Since the publication of those results, significant progress has been made in understanding the disease from both clinical and genetic perspectives, while the diagnostic tools have become

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more refined [5]. Thus, the true prevalence of HCM may be actually higher (up to 1 in 200 persons) [5–7]. While patients who are genotype positive–phenotype negative are not included in the prevalence estimates for HCM, they are nevertheless at increased risk of developing the disease, although the evolution to clinically significant disease is currently unpredictable [8–10].

Earlier diagnosis and proper prognostic stratification will allow reduction in disease-related morbidity/mortality by promoting timely treatment [11]. When first described, HCM was regarded as a rare disease affecting mostly the young, with a poor outcome, mainly related to the risk of sudden cardiac death (SCD) [12, 13]. Nowadays, it is recognized that HCM can affect patients of all ages and that the general prognosis of a patient with HCM is usually good, almost two-thirds having a normal life span with relatively low morbidity and with a general HCM-related mortality of about 0.7%/year [14–16]. However, some patients are at increased risk of SCD or of developing heart failure (HF)/atrial fibrillation (AF). Therefore, the identification of these patients is an important goal [1, 17]. Echocardiography is the cornerstone in screening, diagnosis, prognostic stratification and follow-up of HCM patients [1, 17, 18]. Echocardiographic measurements are included in current SCD

risk calculators endorsed by the ESC and the AHA, respectively [1, 17]. Advanced echocardiographic techniques (tissue Doppler, two-dimensional speckle tracking) can help differentiate HCM from other causes of hypertrophy and identify patients at risk of SCD or of developing HF. Three-dimensional echocardiography offers more information regarding the distribution of hypertrophy, the LV mass, and the mechanism of dynamic LV obstruction [18].

HCM diagnosis by echocardiography

Standard 2D echocardiography is the first-line imaging modality for the identification of LV hypertrophy (LVH) (Table 1). The current diagnostic criteria for HCM are an increase in LV wall thickness ≥ 15 mm in at least one myocardial segment or ≥ 13 mm for patients with a first-degree

relative with confirmed HCM, in the absence of abnormal loading conditions/other causes of LVH (e.g., hypertension, valvular heart disease) [1, 17]. The measurement of LV wall thickness in parasternal short-axis views at end-diastole is the most accurate.

While asymmetric hypertrophy (a septal-to-posterior wall thickness ratio ≥ 1.3 in normotensive patients or ≥ 1.5 in hypertensive patients) may be suggestive of HCM, it is not a specific finding (Fig. 1). Thus, about 10% of patients with hypertension (HTN) have asymmetric hypertrophy, and right ventricular (RV) hypertrophy can also lead to septal thickening [19]. Moreover, misalignment of the transducer beam can lead to oblique sections with wall thickness (WT) overestimation, while inclusion of RV structures (e.g., moderator band, trabeculations) when measuring the septum can also lead to a wrong HCM diagnosis [19]. The interventricular septum (IVS) morphology can also offer information about

Table 1 Key echocardiographic features specific/suggestive for HCM [17–19, 25–27, 33–37]

	Echocardiographic parameter	Cutoff values suggesting HCM
Hypertrophy	Wall thickness / IVS to PW ratio	> 15 mm[a], > 1.3[b]
	Distribution of hypertrophy	Asymmetric hypertrophy RV free wall hypertrophy ≥ 7 mm[c] Reverse hypertrophic IVS
Mitral valve apparatus	Anterior leaflet elongation	AML > 30 mm (17 mm/m^2)
	Posterior leaflet elongation	Absolute height of PL > 15 mm
	Papillary muscle abnormalities	Anterior displacement of AL PM
	Aorto-mitral angle	< 120°
	Mitral chordae	Elongation/thickening/buckling
	SAM	> 30% systolic contact with IVS
Systolic function	Systolic longitudinal dysfunction	Lateral S (TDI) < 4 cm/s Worse GLS (> − 10.6%)[d] Paradoxical apical strain (apical HCM)
	Normal/supranormal radial strain	
Diastolic function[e]	Impaired relaxation	Lateral e' < 4 cm/s
	Elevated filling pressures	Increase of A wave velocity during Valsalva maneuver[e] LAVI > 34 mL/m^2 [f] Ar-A ≥ 30 ms E/e' ratio > 10[g] PAPs > 35 mmHg
Intraventricular obstruction	LVOT gradient /Midventricular obstruction	> 30 mmHg "Dagger shaped"/"Lobster claw" Doppler envelope

HCM hypertrophic cardiomyopathy, *IVS* interventricular septum, *PW* posterior wall, *RV* right ventricle, *AML* anterior mitral leaflet length, *PL* posterior leaflet, *AL PM* anterolateral papillary muscle, *SAM* systolic anterior motion, *TDI* tissue Doppler imaging, *Ar* duration of atrial reverse wave of the pulmonary venous flow, *A* duration of transmitral A wave, *PAPs* systolic pulmonary artery pressure

[a]Absence of abnormal loading conditions. 13 mm cutoff for HCM relatives

[b]1.5 for hypertensive patients

[c]Absence of abnormal loading conditions for the RV

[d]Reduction in longitudinal strain is greater for hypertrophied segments

[e]Diastolic dysfunction is the hallmark of the disease; filling pressures are elevated, even in the presence of an impaired relaxation pattern of the transmitral flow

[f]Absence of atrial fibrillation/significant mitral regurgitation

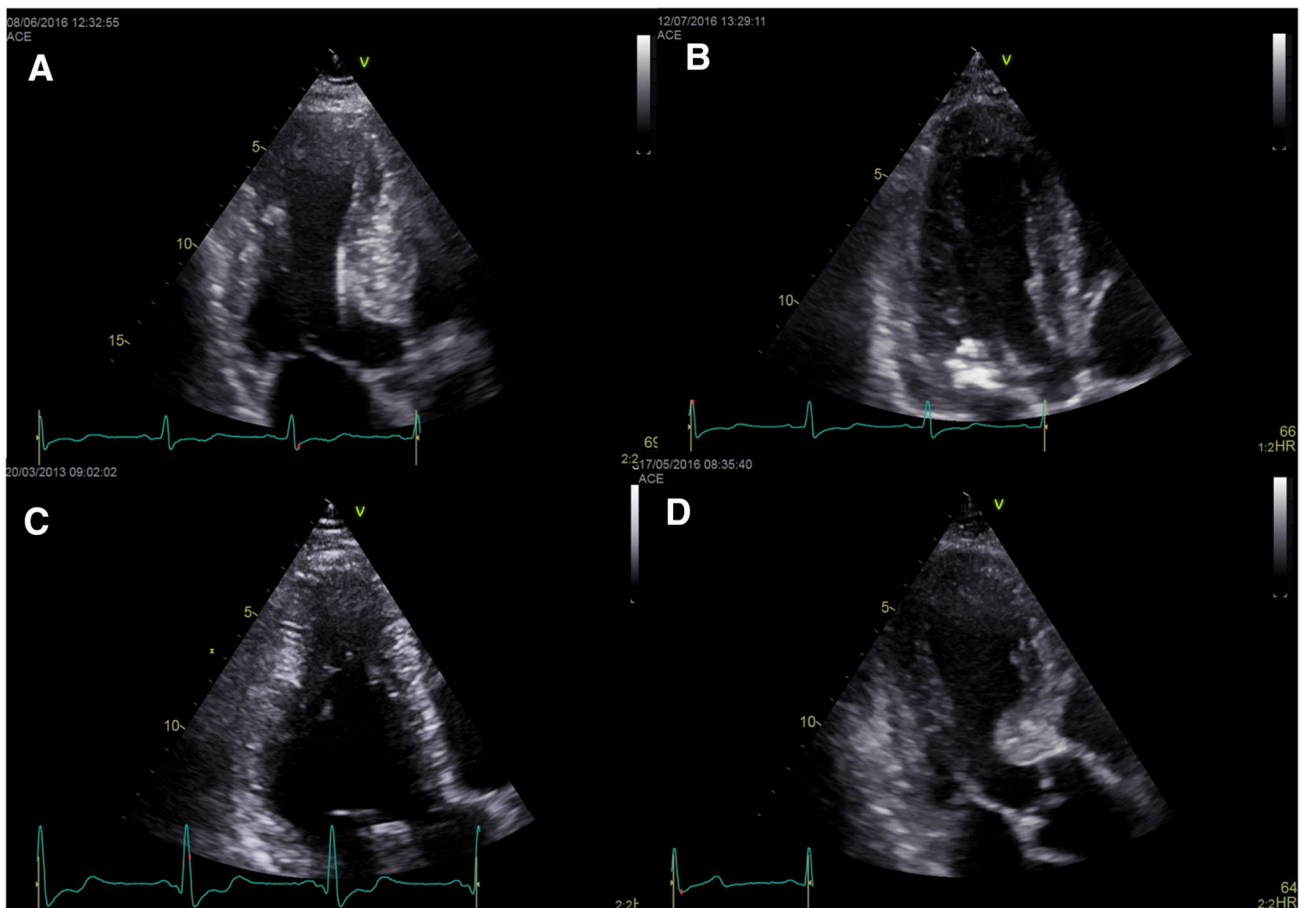[g]Less specific in HCM as a surrogate for elevated filling pressures

Fig. 1 Various patterns of left ventricular hypertrophy that can be found in HCM patients. **a** Predominant asymmetric septal hypertrophy. **b** Concentric, symmetric hypertrophy. **c** Apical hypertrophy. **d** Isolated basal septal hypertrophy. *HCM* hypertrophic cardiomyopathy

the presence of sarcomeric gene mutations. A reverse IVS curvature is associated with a high probability of disease-associated allele, while patients with a sigmoid IVS are much less likely to have a positive genetic test [20].

When native echocardiographic images are suboptimal, transpulmonary contrast echocardiography can improve visualization, especially when suspecting apical hypertrophy or an apical aneurysm [19].

The role of three-dimensional (3D) echocardiography is currently under discussion. It could improve the assessment of LV and LVOT geometry, and of LV mass.

Right ventricular hypertrophy is common, being found in more than 50% of the HCM patients, and it carries a worse prognosis. In the absence of secondary causes, it can act as an additional argument for HCM diagnosis. Caution should be taken not to include epicardial fat when measuring the RV free wall thickness [17, 19, 21].

Nevertheless, it should be noted that hypertrophy is a dynamic, noncontinuous and noncontiguous process in HCM, often affecting different, nonadjacent myocardial segments. It can be absent in childhood, appearing in

adolescence/young adulthood and usually "stabilizing" with age. Wall thickness can also increase sharply later in life if there are additional causes for LVH (e.g., HTN, valvular heart disease), while patients with phenocopies or severe disease can have significant LVH from an early age [19, 22]. Some sarcomeric mutations (e.g., cardiac myosin binding protein C) lead to mild LVH, while carrying an increased risk for SCD [18].

Other echocardiographic findings supporting the diagnosis of HCM

Mitral valve apparatus abnormalities

While initially thought to be a disease limited to the myocardium, it is now well known that up to 59% of patients diagnosed with HCM have at least one abnormality of the mitral valve apparatus (MVA) as a direct effect of genetic mutations [23]. More commonly, leaflet elongation and excessive leaflet tissue are present in about 50%
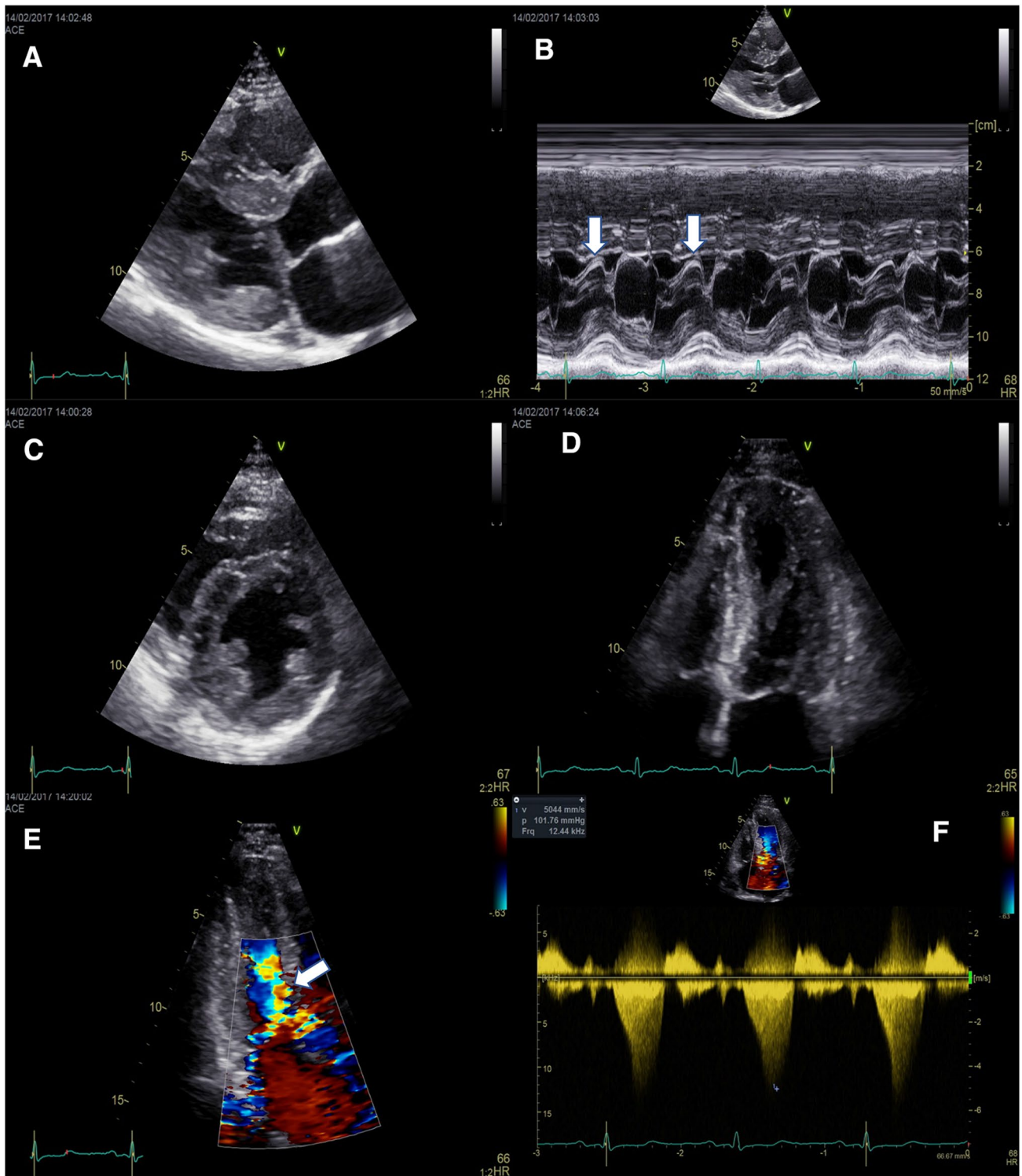
Fig. 2 Complex mechanisms leading to dynamic obstruction in a patient with HCM. Concentric hypertrophy involving mainly the basal septum (diastolic IVS thickness of 15 mm), and elongated mitral leaflets with systolic anterior motion (**a**); M-mode echocardiography shows the systolic contact of the mitral valve with the IVS (arrows) (**b**); anterior displacement of the hypertrophied papillary muscles (**c**, **d**); moderate eccentric (posteriorly oriented) mitral regurgitation secondary to SAM (**e**); and significant resting LVOT obstruction by CW Doppler (peak resting gradient of 102 mmHg) (**f**). Of note, there is severe LVOT obstruction without severe septal hypertrophy, explained by the significant abnormalities of the mitral valve apparatus. *HCM* hypertrophic cardiomyopathy, *IVS* interventricular septum, *LVOT* left ventricular outflow tract

of patients, while other anomalies like chordal elongation, prolapse and direct insertion of the papillary muscle into the anterior leaflet are present in about 25% of cases [19]. The abnormalities also extend to the papillary muscles (PM) and may be related to their relative position (apical/anterior displacement), insertion (directly on the mitral valve) and number (duplication, bifidity)/hypertrophy [19].

Systolic anterior motion (SAM) of the mitral valve/chordae was once thought to be a very specific finding in HCM, being present in about 30–60% of the cases [24]. This theory is currently disproven, since other causes can also lead to SAM. These need to be taken into account when assessing the patient (e.g., severe HTN with small LV cavity treated aggressively, mitral valve surgical repair, severe hypovolemia, inotrope use) [18, 19].

Mitral regurgitation (MR) can be a result of MVA abnormalities, SAM (usually eccentric, posterior MR jet) and/or coexistence of mitral valve degenerative disease (usually central MR jet) [18, 19, 25].

Left ventricular systolic function

Left ventricular ejection fraction (LVEF) is typically normal/supranormal in patients with HCM, and it only decreases in the late-stage "burnt-out" HCM in a small subset of patients (less than 15%) [17].

LVEF can remain normal in HCM because of the complex remodeling of LV structure and function. Thus, LVEF remains normal despite significant reduction in longitudinal and circumferential deformation, because of increased radial deformation in patients with increased WT and a small LV cavity [26]. Therefore, assessing myocardial deformation will better reflect LV systolic function in patients with HCM. Tissue Doppler imaging (TDI) can be used to assess mitral annular velocities and can detect subtle alteration in longitudinal function, even in segments without significant hypertrophy [27, 28]. While using TDI to assess strain and strain rate has Doppler-specific limitations (e.g., angle dependence), 2D-derived speckle tracking echocardiography (2D-STE) can provide more reproducible measurements of LV strain [29]. Typically, patients with HCM have a significant reduction in longitudinal strain (hypertrophied segments/segments with fibrosis being the most affected), even in early phases (subclinical systolic dysfunction), and a reduced LV untwisting [19, 29]. Moreover, paradoxical apical strain (systolic lengthening of apical segments) could be used to improve the diagnostic yield of echocardiography in apical HCM [30].

Left ventricular diastolic function

One of the main mechanisms of HF in patients with HCM is LV diastolic dysfunction which occurs early in the disease evolution and is due to increased LV mass and stiffness [18, 19]. Transmitral flow is usually abnormal, and early diastolic myocardial velocity (e') is frequently decreased, even in segments not affected by hypertrophy [31]. An increase in left atrium indexed volume (LAVI), especially if there is no significant MR/history of atrial fibrillation (AF), is a good surrogate for increased LV filling pressures [32]. It should be noted that transmitral flow E/A ratio and E/e' ratio have poor/modest correlations with LV filing pressures in patients with HCM [33]. The Valsalva maneuver can be used in patients with an impaired relaxation pattern to unmask elevated LV filling pressures, proven by an increase in A wave velocity during the maneuver [34]. Table 1 summarizes the main echocardiographic parameters that can be used for assessing LV filling pressures [35]. In the presence of normal LAVI/LV filling pressures, the diagnosis of HCM is less likely, especially in elderly patients [18].

Intraventricular obstruction in HCM

While usually located in the LVOT, the site of obstruction can also be midventricular. A peak gradient > 30 mmHg at rest or after provocative maneuvers (Valsalva/standing/exercise) is defined as intraventricular obstruction [17]. More than two-thirds of HCM patients have significant obstruction, but in half of them, this becomes apparent only after provocation [36]. Moreover, the intraventricular gradient has a significant variability, related to changes in loading conditions and in contractility [37]. In HCM, the main cause of LVOT obstruction is MVA abnormalities associated with a steeper LV to aortic root angle, leading to SAM, while the IVS thickness plays a lesser role by narrowing the LVOT (Fig. 2) [38]. Color flow mapping and pulse-wave (PW) Doppler can be used to identify the anatomic site of obstruction, and a careful assessment of the whole LV (apex/midventricular/LVOT) should be routinely made in all patients [18, 19]. Continuous-wave (CW) Doppler is useful in measuring the peak gradient. The Doppler envelope is typically "dagger shaped" (with an end-systolic peak), or like a "lobster claw" in cases of more severe obstruction (with a midsystolic temporary drop in pressure). Care should be taken not to measure the MR jet (which is "bell-shaped"), since this will overestimate obstruction severity [19]. Resting provocative maneuvers (e.g., Valsalva, standing) are mandatory in all patients [19].

Midventricular obstruction usually occurs in patients with significant midventricular hypertrophy and small LV cavity ("hourglass shaped ventricle"), more so if PM anomalies are present. It increases the risk of apical aneurysms that

Table 2 Echocardiographic features useful for differential diagnosis in HCM [18, 19, 49–52, 61–63]

Condition	Specific features (vs. HCM)
Athlete's heart	Normal/slightly increased LV volumes
	Normal/mildly dilated LA
	Normal/supranormal annular systolic and diastolic velocities by TDI
	Normal GLS
	Reversible hypertrophy
Hypertensive heart disease	Symmetric hypertrophy[a]
	End-systolic SAM
	Mild to moderate systolic longitudinal dysfunction: better GLS ($< -10.6\%$)
	Reduced systolic radial strain
Cardiac amyloidosis	Concentric, biventricular hypertrophy
	Thickening of the interatrial septum/cardiac valves
	Hyperechoic walls ("speckled" appearance)
	Pericardial effusion
	Significantly decreased longitudinal strain/strain rate, with "apical sparing"
Fabry disease	Concentric, biventricular hypertrophy
	Thickening of the PM/cardiac valves
	Lateral LV wall is most often affected (reduced longitudinal strain)
	Circumferential strain is normal
Valvular/subvalvular obstruction	Concentric LV hypertrophy
	Valve calcifications/restricted leaflet mobility (valvular obstruction)
	Fibrous membrane/ring, discrete ridges or diffuse LVOT narrowing (sub-valvular obstruction)
	Fixed LVOT obstruction with no SAM

HCM hypertrophic cardiomyopathy, *LV* left ventricle, *LA* left atrium, *TDI* tissue Doppler imaging, *GLS* global longitudinal strain, *PM* papillary muscles, *LVOT* left ventricular outflow tract, *SAM* systolic anterior motion of the mitral valve

[a]Asymmetric hypertrophy is uncommon (less than 10%)—when present, interventricular-to-posterior wall thickness ratio is < 1.3

in turn predispose to ventricular arrhythmias and systemic embolism (in cases of apical thrombi) [18, 19].

Exercise echocardiography (EE, by treadmill/bicycle) is recommended in all symptomatic patients with resting intraventricular gradients < 50 mmHg or in asymptomatic patients when it is relevant for their medical treatment and for further risk stratification. Exercise echocardiography is a safe and feasible investigation [1]. Beside gradient provocation, exercise echocardiography is very useful for assessing exercise tolerance/symptoms, response to therapy, MR severity, blood pressure response, myocardial ischemia and exercise-induced arrhythmias [19, 39].

Subclinical hypertrophic cardiomyopathy

Carriers of HCM gene mutations or subjects with ambiguous/negative genetic testing (30–40% of patients) who are asymptomatic and have some characteristics of HCM phenotype but do not fulfill the diagnostic criteria are considered to have subclinical HCM [40]. Even if the additional risk for SCD is very low in these patients, they should be carefully

monitored with frequent echocardiograms, as opposed to HCM relatives with no abnormalities [41].

Echocardiographic findings include normal WT/borderline hypertrophy (12–14 mm), mitral valve leaflet elongation, myocardial crypts and myocardial apical trabeculations (the latter are better seen at cardiac magnetic resonance, CMR), while the LA is usually normal or only mildly dilated [19, 40]. TDI-derived myocardial velocities and 2D strain analysis can be useful since even patients with normal WT can have reduced myocardial velocities and mild segmental longitudinal dysfunction [42]. Moreover, exercise echocardiography can be performed to look for exercise-induced intraventricular gradients due to SAM, an additional finding suggestive of HCM [39].

Advanced echocardiographic techniques

Three-dimensional echocardiography (3DE) has some advantages over standard 2D echocardiography. It can provide better information regarding the mechanism of intraventricular obstruction, distribution of hypertrophy, LV mass and systolic function. 3DE derived LV volumes, mass

Table 3 Echocardiographic parameters with prognostic value in HCM [14, 17, 34, 40, 56–63]

Echocardiographic parameter	Value	Prognostic implication
Maximal WT	≥ 30 mm	$3 \times$ higher risk for VAs
LVOT obstruction	≥ 30 mmHg at rest, ≥ 50 mmHg (provoked)	Increased risk of SCD (1.5% vs. 0.9% per year)
		Increased risk of HF/HF progression[a]
		Increased risk of stroke
LA diameter	> 45 mm	Increased risk of SCD
		Increased risk of AF/AF recurrence
		Increased risk of stroke
LA volume[b]	≥ 37 mL/m^2	Increased risk of AF
LA systolic strain[b]	$\leq 23.4\%$	Increased risk of AF
		HF symptoms
Apical aneurysm	[≥ 4 cm][c]	Increased risk of SCD (due to VAs and thrombus embolization)
RV hypertrophy	≥ 7 mm	Increased risk of VAs (NSVT)
		Increased risk of HF symptoms
Abnormal GLS	$\geq -16\%$	Increased risk of VAs
		Increased risk of HF/HF hospitalization/cardiac death
Systolic annular lateral wall velocity (S)	< 4 cm/s	Increased risk of HF/HF hospitalization
		Increased risk of cardiac death
Elevated filling pressures	E/e′ > 10, Ar-A ≥ 30 ms	Increased risk of HF/HF worsening
Mechanical dispersion	$\geq 64 \pm 22$ ms	Increased risk of NSVT
		Correlates with fibrosis (LGE) at CMR

WT wall thickness, *VA* ventricular arrhythmias, *LVOT* left ventricular outflow tract, *SCD* sudden cardiac death, *HF* heart failure, *LA* left atrium, *AF* atrial fibrillation, *NSVT* nonsustained ventricular tachycardia, *GLS* global longitudinal strain, *LGE* late gadolinium enhancement, *CMR* cardiac magnetic resonance

[a]Patients with obstruction at rest have a higher risk than patients with provoked gradients (specific maneuvers/exercise echocardiography)

[b]Additional predictive value in patients considered at low risk for developing atrial fibrillation

[c]Significant increase in risk if apical aneurysm is larger than 4 cm

and ejection fraction have a better correlation with those obtained using CMR [19]. Moreover, 3DE can be useful for the differential diagnosis with other causes of LV hypertrophy. A novel index based on the standard deviation of the segmental mass volumes called the mass dispersion index (MDI) was proven to be significantly higher in patients with HCM, irrespective of the localization of hypertrophy [43, 44].

Dyssynchronous contraction in the absence of intra/interventricular conduction defects on the ECG is common in patients with HCM, especially if they have significant LVOT obstruction or septal hypertrophy [44, 45].

Key echocardiographic features for differentiating HCM from other diseases leading to LV hypertrophy are presented in Table 2.

Prognostic stratification in patients with HCM

Echocardiography plays a central role in identifying markers associated with poor prognosis in patients with HCM (Table 3).

Assessing the risk of sudden cardiac death

While in the community, most patients with HCM have a relatively good prognosis, with an estimated SCD risk of about 1% annually (compared to 0.2% in the general population), the risk can be significantly higher (over 6%/5 years) in patients presenting with more risk factors. Therefore, risk stratification is paramount to assess the need for an implantable cardioverter–defibrillator, which is the only effective treatment in reducing the SCD risk [1, 17].
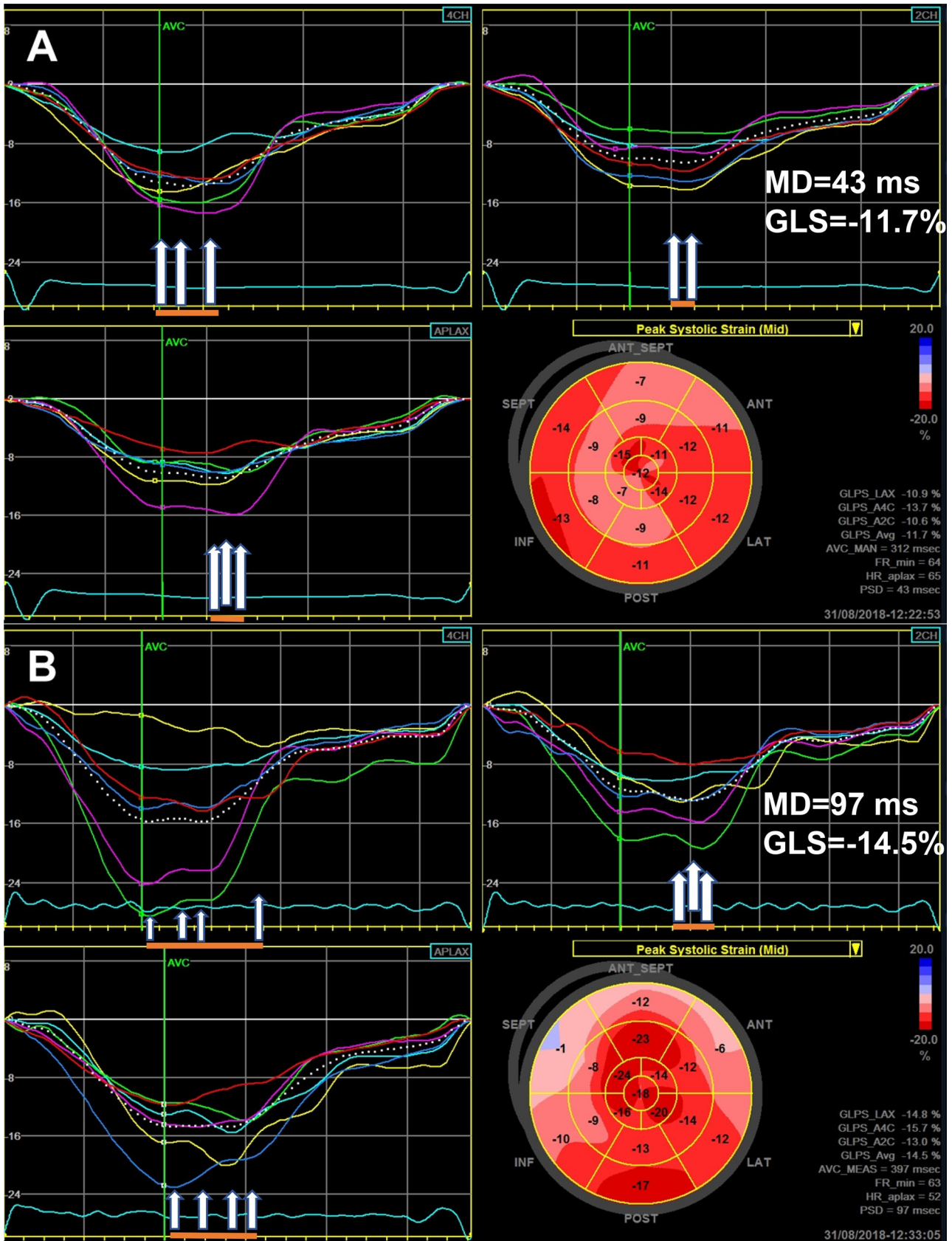
◄**Fig. 3** Global longitudinal strain (GLS) and myocardial dispersion (MD) in two patients with HCM. MD is calculated as standard deviation of the time from the beginning of ventricular systole to peak longitudinal shortening for each of the myocardial segments. The arrows mark the points of peak longitudinal shortening. A larger distance between arrows (orange line) means an increased MD. **a** Patient with HCM without history of VAs. **b** Patient with HCM and history of VAs (NSVTs) has a significantly higher MD. Moreover, patient B had significantly more fibrosis as assessed by CMR compared with patient A. Note that increased MD in patient B is independent of global longitudinal strain (which is better than for patient A), reflecting different functional information. *VA* ventricular arrhythmias, *HCM* hypertrophic cardiomyopathy, *NSVT* nonsustained ventricular arrhythmia, *CMR* cardiac magnetic resonance

Currently, there are two widely used multiparametric approaches for risk stratification, endorsed by ESC and AHA/ACC respectively, where all predictors are independently correlated with SCD. The risk model proposed by AHA/ACC is based on an international registry of 506 patients, has a very good sensitivity (SCD risk after applying the algorithm is less than 0.5%/year) and includes novel risk factors such as late gadolinium enhancement at CMR and the presence of LV apical aneurysms, beside maximal wall thickness > 30 mm, the presence of unexplained syncope, NSVT, family history of SCD and abnormal BP response to stress [17]. The main limitations are the fact that the model uses binary variables and does not include some risk modifiers [17]. The HCM SCD risk calculator proposed by the ESC is based on a multicenter cohort study of 3675 patients and provides individualized 5-year risk estimates using seven variables (age, maximum LV wall thickness, left atrial size, LVOT gradient at rest, family history of SCD, NSVT and unexplained syncope). Half of the parameters used in both models are derived from echocardiography [1].

The severity of hypertrophy assessed by maximal wall thickness (MWT) has been linked to VA, especially in younger patients. Patients with severe hypertrophy (MWT > 30 mm) have a threefold higher risk for VA. There are no data regarding the importance of ventricular mass/hypertrophy distribution and risk of VA [14, 45].

LVOT obstruction at rest increases the absolute risk of SCD from 0.9% to 1.5%. Unfortunately, the relation between severity of obstruction and SCD risk is less clear and there is low additive value in the absence of other risk factors. Moreover, LVOT gradients are highly variable [46].

LA remodeling is related to LV remodeling; therefore, an increase in LA diameter is a marker of disease severity. Currently, the relation between atrial fibrillation and SCD is still unclear. While the LA anteroposterior diameter is easy to measure, it is not ideal, since LA dilatation is not uniform, and LA diameter may underestimate the true LA size. Thus, LA volume may be a superior measure of LA size for risk stratification of patients with HCM [32]. However, more studies are needed to prove this hypothesis.

The presence of apical aneurysm increases the risk of SCD (40% patients have NSVT), with a significant prognostic value for aneurysms larger than 4 cm, and a mortality of 3.4%/year [47].

Beside well-established echocardiographic risk factors, there are novel echo parameters derived from 2D STE analysis that may provide additional insight in SCD risk stratification. In a study on more than 3000 HCM patients, abnormal GLS was associated with VA [48]. Mechanical dispersion (i.e., the standard deviation of the time from the onset of systole to maximum contraction for each of the myocardial segments, an expression of heterogeneous contraction and electrical activation) relates to the extent of fibrosis (assessed by CMR) and is an independent predictor of VA (Fig. 3) [49].

Assessing the risk of heart failure

The pathophysiology of HF in HCM is multifactorial—from diastolic dysfunction due to delayed LV relaxation, decreased chamber compliance, loss of LV suction and abnormal calcium homeostasis to LVOT obstruction and myocardial ischemia secondary to the reduction in myocardial blood supply, abnormal vasomotor response and vascular remodeling. Echocardiography plays an important role both in diagnosing cardiac remodeling and LVOT obstruction and in predicting progression to HF [19]. The finding of elevated LV filling pressure has a negative prognostic impact in HCM patients [50]. Right ventricular involvement, a common finding in about 50% of the patients, increases the risk for developing HF symptoms and VA (NSVT), with a direct correlation between RV wall thickness and heart failure symptoms [21].

Intraventricular obstruction increases the myocardial load and reduces the blood supply and cardiac output. The coexistence of significant MR can also worsen the HF symptoms. In symptomatic patients, in the absence of significant obstruction at rest (< 30 mmHg), gradient provocation (by specific maneuvers or by exercise echocardiography) should be pursued. LVOT obstruction is a predictor of HF symptoms (38% patients with resting obstruction have HF symptoms, compared with 20% of patients with provocable obstruction and 10% of patients without obstruction) and HF progression irrespective of its severity, with a greater magnitude in older patients (> 60 years) [51]. Exercise tolerance, lack of contractile reserve and the presence of inducible ischemia at exercise echocardiography have independent prognostic value [52].

Myocardial deformation can bring additional prognostic information. A marked reduction in LV systolic velocity by TDI (S < 4 cm/s at the lateral site) is an independent predictor of death or hospitalization for worsening HF [50]. Moreover, abnormal LV-GLS was associated with adverse composite cardiac outcomes [48]. Significant LA
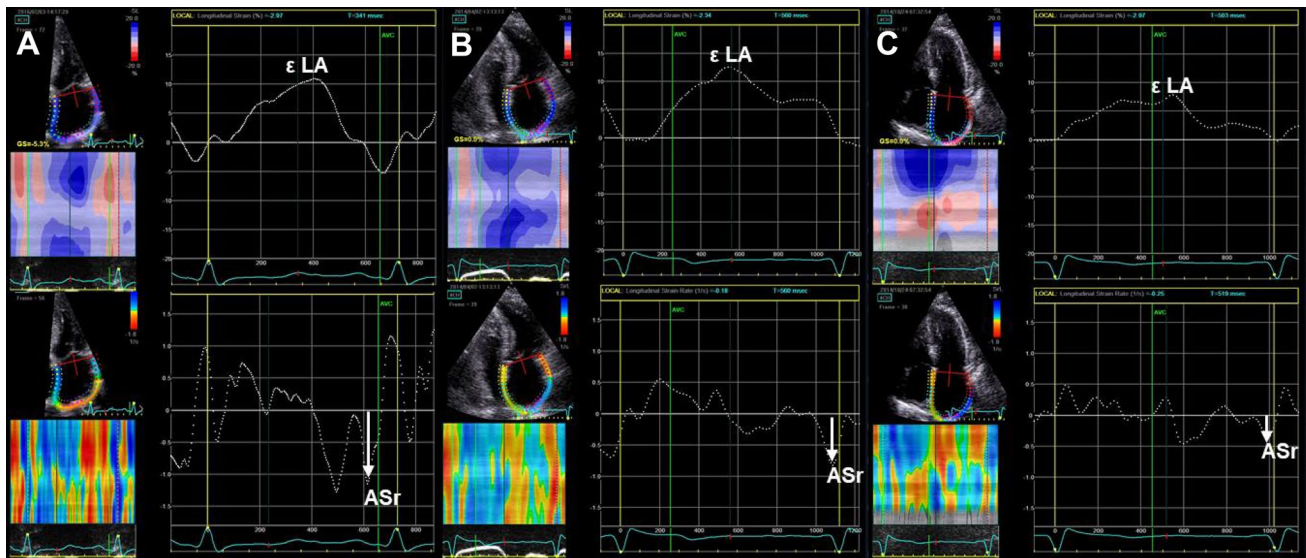
Fig. 4 The assessment of LA function (reservoir function—ƐLA, and booster pump function—ASr) by speckle tracking echocardiography in three patients with HCM: **a** A patient with HCM, with anterior–posterior LA diameter < 45 mm, and without history of AF. **b** A patient with HCM, with anterior–posterior LA diameter < 45 mm, and with paroxysmal AF. **c** A patient with HCM, with anterior–pos-

terior LA diameter > 45 mm, and with paroxysmal AF. Note that LA booster pump function is reduced in HCM patients in the presence of paroxysmal AF, furthermore if there is significant LA dilation (> 45 mm). ƐLA global longitudinal LA strain, ASr peak late diastolic strain rate, LA left atrium, AF atrial fibrillation, HCM hypertrophic cardiomyopathy, DAS anteroposterior LA diameter

dysfunction (assessed by STE) has also been shown to correlate independently with HF symptoms [53].

Assessing the risk for atrial fibrillation and the thromboembolic risk

The prevalence of AF in HCM is about 20–30%, compared to 1% in the general population [54]. The occurrence of AF increases morbidity and mortality leading to HF and thromboembolic events. Diagnosing AF can be difficult, since most paroxysmal AF episodes are asymptomatic. LA dimensions and age are independently associated with AF, but current tools to predict AF and thromboembolism lack in sensitivity and specificity [1, 17]. The ESC guidelines recommend screening for AF with ambulatory 48 h ECG monitoring for patients with an anteroposterior LA diameter > 45 mm [1]. Unfortunately, LA diameter lacks sensitivity. Among so-called low-risk patients (with an anteroposterior LA diameter < 45 mm), the incidence of AF is between 20 and 50% [54]. LA volume and strain can further refine risk stratification for AF in these patients, being more sensitive in detecting atrial remodeling, the main substrate of AF (Fig. 4). An indexed LA volume ≥ 37 mL/m^2 and LA strain ≤ 23.4% were predictive for new-onset AF, with good accuracy (AUC = 0.83, and AUC = 0.78, respectively) [54]. Predictors for stroke include the presence of HF (NYHA class III/IV), age > 60 years, LVOT obstruction and AF/LA size > 45 mm (the most accurate predictors) [55].

Limitations of echocardiography in HCM

While echocardiography is generally good in providing anatomical and functional details, it lacks the ability for tissue characterization. Cardiac magnetic resonance is very useful and may improve both the diagnosis and prognostic stratification in HCM, especially in patients with suboptimal echo images, borderline/conflicting echo findings or when suspecting phenocopies. It provides excellent morphological and functional data and information regarding the presence and distribution of myocardial fibrosis and extracellular volume [19].

Conclusions

Echocardiography is an essential tool in patients with proven or suspected HCM. It provides important diagnostic information and allows detailed evaluation of LV systolic and diastolic function, presence and mechanism of LVOT obstruction, LA size and function. It also provides useful information for risk stratification (e.g., for SCD, heart failure, AF and stroke) to guide therapy. The echocardiographic data need to always be integrated with clinical data and other information, notably from CMR, especially in challenging cases, when there is conflicting information about the diagnosis or risk assessment.

Compliance with ethical standards

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