GUIDELINES AND RECOMMENDATIONS

Transthoracic echocardiography of hypertrophic cardiomyopathy in adults: a practical guideline from the British Society of Echocardiography

Lauren Turvey[1], Daniel X Augustine[2,3], Shaun Robinson[4], David Oxborough[5], Martin Stout[6], Nicola Smith[1], Allan Harkness[7], Lynne Williams[8], Richard P Steeds[1] and William Bradlow[1]

[1]Department of Cardiology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK
[2]Royal United Hospitals Bath NHS Foundation Trust, Bath, UK
[3]Department for Health, University of Bath, Bath, UK
[4]Department of Cardiology, North West Anglia NHS Foundation Trust, Peterborough, Cambridgeshire, UK
[5]Research Institute for Sports and Exercise Physiology, Liverpool John Moores University, Liverpool, Merseyside, UK
[6]North West Heart Centre, Wythenshawe Hospital, Manchester University NHS Foundation Trust, Manchester, UK
[7]Department of Cardiology, Colchester Hospital NHS Trust, Colchester, UK
[8]Department of Cardiology, Papworth Hospital, Papworth Everard, Cambridge, UK

Correspondence should be addressed to W Bradlow: william.bradlow@uhb.nhs.uk

Abstract

Hypertrophic cardiomyopathy (HCM) is common, inherited and characterised by unexplained thickening of the myocardium. The British Society of Echocardiography (BSE) has recently published a minimum dataset for transthoracic echocardiography detailing the core views needed for a standard echocardiogram. For patients with confirmed or suspected HCM, additional views and measurements are necessary. This guideline, therefore, supplements the minimum dataset and describes a tailored, stepwise approach to the echocardiographic examination, and echocardiography's position in the diagnostic pathway, before advising on the imaging of disease complications and invasive treatments.

Key Words

- hypertrophic cardiomyopathy
- hypertrophic obstructive cardiomyopathy
- guidelines
- echocardiography

Intent behind update

These guidelines on hypertrophic cardiomyopathy (HCM) represent a six-year update (1). They contain a description of pertinent disease features and the critical echo parameters needed to evaluate the condition, alongside a recommended protocol. A specific HCM minimum data set, for use as an aide memoir when reporting, is provided.

The guideline also presents information on the use of echo measurements for sudden death risk stratification. This guideline aims to enhance baseline knowledge and to allow echocardiographers to develop a systematic approach to the image acquisition and echocardiographic reporting of patients with proven or suspected HCM. The guideline-writing committee anticipates that readers armed with this knowledge will approach these examinations with confidence, extract as much information about each patient's condition as possible and produce unambiguous, standardised reports. These actions will enhance clinical care by limiting the number of patients who are either under or over-diagnosed and highlight the sub-cohorts of patients who need additional investigations and treatments. The guidelines end with short sections covering the use of echo guidance for

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

transseptal alcohol ablation and surgical myectomy as well as strain, stress and three-dimensional echocardiography in patients with HCM.

Hypertrophic cardiomyopathy

HCM in adults is defined '*by a wall thickness ≥15 mm in one or more left ventricular (LV) myocardial segments that is not explained solely by loading conditions*' (2), for example, hypertension. In a smaller number of cases, described in the next section, HCM may be associated with an abnormal wall thickness which measures less than 15mm. This dimension-based diagnosis covers a diverse group of diseases, both inherited and acquired, which differ in their pathophysiology and management.

Due to the challenges in certain aspects of diagnosis and management of this patient group, referral to specialist centres focused on inherited cardiac conditions and cardiomyopathies is recommended for patients with suspected or confirmed disease (2). Where possible, echocardiographers should obtain dedicated training in the scanning and interpretation of this patient group.

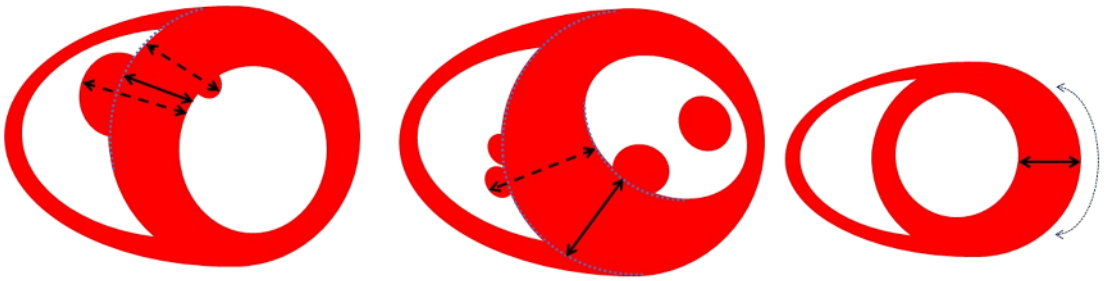
The condition affects between 0.2% (3) and 1.4% of individuals (4). Disease complications are reasonably common; in a multi-centre longitudinal study of patients with HCM, atrial fibrillation occurred in 20%, sudden cardiac death or resuscitated cardiac arrest in 4% (5) and left ventricular systolic dysfunction (ejection fraction <50%) in 8% (6).

The pattern of inheritance is autosomal dominant. A clinically meaningful gene change (found predominantly in MYBPC3 and MYH7) occurs in a fifth of patients where the family history is negative, and a half where it is positive (7). Finding a disease-causing gene change allows testing of family members using pre-symptomatic screening.

Echocardiography's position in the diagnostic pathway – wall thickness

Accurate measurement of wall thickness is fundamental to decision-making. Because of this, the echocardiographic examination is a key component of the diagnosis pathway. Ancillary features such as left ventricular outflow tract obstruction (LVOTO) do not contribute.

Measurements should be made in short-axis views orthogonal to the circumference of the endocardium and epicardium, wherever maximal wall thickness occurs. Elements attached to but not incorporated in the septum should be excluded (Fig. 1), as this will overestimate wall thickness and run the risk of misdiagnosis of HCM.



SEGMENT	BASAL	MID-VENTRICULAR	APICAL
PITFALLS (depicted by dashed lines)	Erroneously including septomarginal trabeculation and aberrant LV papillary muscles in measurement	Underestimating hypertrophy at the confluence of the mid inferior and inferoseptal wall. Overestimating wall thickness by including RV trabeculation papillary muscles	Missing apical hypertrophy, especially lateral wall (dotted line with arrows)
APPROACH (depicted by solid lines)	Exclude these components at their attachments using continuation of endo- and epicardial curve (dotted lines)	Carefully visualise this area. Exclude these components at their attachments using continuation of endo- and epicardial curve (dotted lines)	Clue in often abnormal ECG. Look for 'akinetic' apex. Use contrast to confirm

Figure 1
The challenges to accurate wall thickness measurement vary at each left ventricular chamber level. Dashed lines represent erroneous measurements and solid lines accurate measurements.

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

The report should state if the study failed to visualise any part of the LV (often the basal anterior and anterolateral walls) and recommend alternative imaging modalities, specifically cardiovascular magnetic resonance.

The dimensional threshold for HCM depends on the location of hypertrophy as well as the clinical context. In apical HCM, where normal tapering of both cavity and epicardium is lost, the apical wall thickness may be less than 15 mm (8). One criterion defines apical HCM when the ratio between apical and basal wall thickness exceeds 1.3:1 (9). Visualisation of this area can be difficult and may require the use of myocardial contrast (Fig. 2). By ensuring the apical four, two and three-chamber view section the apex, the echocardiographer will avoid giving the impression of apical hypertrophy by foreshortening views. Apical wall thickness should be measured in the short-axis view, ensuring the cut is not oblique to the long axes of the LV.

In first-degree relatives – who have a 50% risk of inheriting the causative gene – the wall thickness threshold for diagnosis of HCM is ≥13 mm (2). The yield of positive screening examinations in first degree relatives vary based on the population tested; in one report, 5% of first-degree relative children were diagnosed with HCM (10), rising to 30% of a mainly adult cohort in another, where many had a disease-causing gene (11). A feature of HCM is age-related penetrance, where the percentage of individuals carrying the disease-causing gene who express the condition increases with age. The yield of clinical screening is higher in families where the disease onset has been in childhood (10, 11).

HCM featuring the so-called dilated-hypokinetic or 'burnt-out' phase (6), or due to specific gene mutations (12, 13, 14), can be associated with only mild increases in wall thickness.

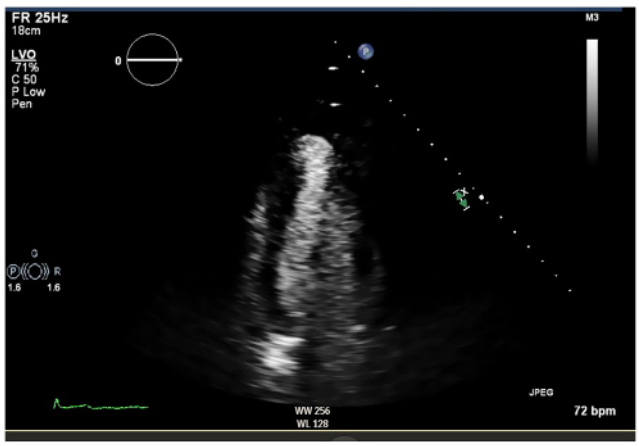


Figure 2
An apical four-chamber acquisition enhanced with contrast to show apical hypertrophic cardiomyopathy complicated by aneurysm formation.

Grey cases

Ethnicity, hypertension, renal disease, significant aortic stenosis, increased body mass index and athletic remodelling all influence left ventricular hypertrophy. Increased LV wall thickness secondary to these processes may fall into a 'grey zone', overlapping with the degree of LV hypertrophy (LVH) seen in HCM (Fig. 3). For example, a wall thickness of 15-20 mm can occur in hypertensive heart disease in individuals of African/Afro-Caribbean ethnicity, whereas the same degree of hypertrophy in a Caucasian hypertensive patient would suggest HCM (2). LVH in hypertensive heart disease and athletic remodelling tends to be uniform and symmetrical.

In athletes, gender, in addition to ethnicity, is relevant. Wall thickness is lower in female athletes than their male counterparts and does not exceed 13 mm in Caucasian athletes or 15 mm in athletes of African/Afro-Caribbean ethnicity (15). In a study of athletes with HCM compared with athletes without HCM (16), the diagnosis was definite in most individuals as maximal wall thickness was >16 mm, and often the LVH was distributed non-uniformly. The scenario in which there was uncertainty – where LVH was 13–16 mm and concentric (defined by a relative wall thickness of >0.42 (see BSE guidelines on normal reference intervals for cardiac dimensions and function for more information (17)) – cropped up in only 14% of athletes with HCM. Measures like left ventricular cavity size (previously reported to be a useful differentiator between HCM and athletic heart; being larger in the latter (18)) showed modest performance in picking out athletes with HCM. Additional tests were required to distinguish these individuals from athletes with physiological remodelling.

Recommended language in echocardiography report

Echocardiography's pivotal role means that a study's interpretation can strongly influence the clinical team's diagnostic decision. Because of this, we encourage the use of standardised language when reporting. In instances where there is uncertainty, *'raises the possibility of HCM'* is recommended. In individuals undergoing screening, where there is no evidence of left ventricular hypertrophy, the conclusion should contain the following suggested

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

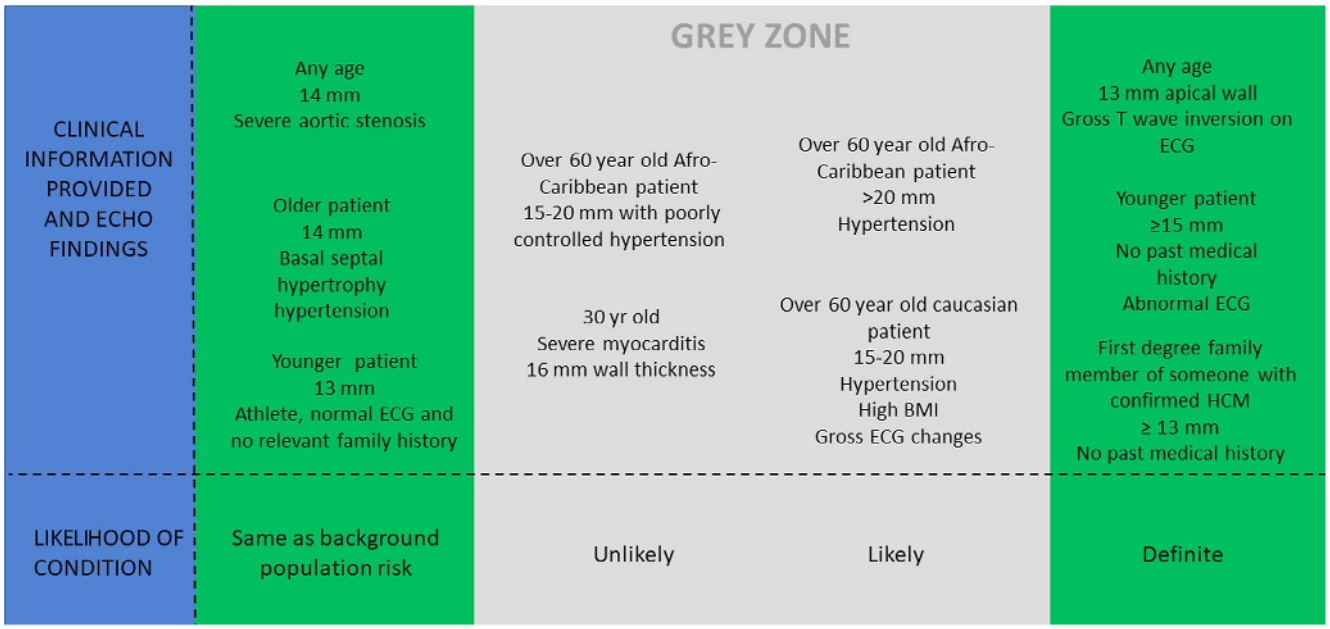


Figure 3
This schematic demonstrates various scenarios and the corresponding likelihood of the condition. Once investigations are complete, and a full clinical picture is available, this information is weighed by clinicians to reach a final diagnosis. Between cases where the likelihood of the condition is the same as the background population (left-hand side, green shading) and definite disease (right-hand side, green shading), lies the diagnostic grey zone (grey shading).

phrase: *'wall thickness is normal'*. The proposed language provides an objective statement about the echocardiogram findings, rather than a definitive clinical assertion. Hence *'wall thickness is normal'* is not the same as *'does not have HCM'*. Echocardiographers should exercise their judgement, but when the echocardiographic images show unequivocal evidence of HCM in an appropriate clinical context (clear-cut apical HCM, gross hypertrophy in a young patient and definite LVH in a screening echocardiogram), the phrase *'consistent with HCM'* should be used.

Post-echocardiography work-up

In patients with suspected HCM, the clinical team will contextualise the echocardiography report with information regarding past medical and family history, blood tests and ECG results, and often cardiovascular magnetic resonance. In grey cases, clinicians judge whether the degree of hypertrophy matches the severity of the comorbidity (Fig. 3). Clarification of the diagnosis in these instances is possible after assessing the response of wall thickness and LV mass to a sustained period of reduced afterload, for example, improved blood pressure control in the hypertensive patient, weight loss in the obese individual, aortic valve replacement in the patient with severe aortic stenosis or cessation of training in the athlete (19). In exceptional cases where there is non-apical hypertrophy measuring less than 15 mm, and an ECG highly suggestive of underlying cardiomyopathy, the clinical team might screen first-degree family members to look for clear-cut evidence of HCM. Given the likelihood of finding a negative result on gene testing of confirmed cases, it is rarely used as a diagnostic tool when there is ambiguity about the diagnosis.

Phenocopies

It is possible to find within the population of patients with hypertrophic cardiomyopathy rarer conditions, called phenocopies or 'mimics' (20). In general, these will come to light during clinical evaluation of the patient's medical history, family history, physical examination and the results of blood tests, including genetics, and other imaging modalities. However, there are particular features, termed 'red flags', which should alert the echocardiographer to the possibility of a phenocopy (Table 1). Of these, cardiac amyloidosis is the most obvious due to its classical signs: increased biventricular wall thickness, poor long axis function, relative sparing of

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

Table 1 Echocardiographic clues to the presence of phenocopies.

Condition	Echocardiographic 'Red Flags' which raise the possibility of a phenocopy*
Cardiac amyloidosis	Thickened intreratrial septum, mitral and tricuspid valves and right ventricular free wall, mild to moderate pericardial effusion; ground-glass appearance of the myocardium; global hypokinesia (with and without LV dilatation) in TTR amyloidosis; markedly reduced longitudinal function, relative sparing of apical longitudinal contraction/global longitudinal strain, a mismatch between LVH on echo and low amplitude voltages on ECG
Fabry disease	Thickened mitral and tricuspid valves and right ventricular free wall, concentric LVH; global hypokinesia (with and without LV dilatation)
Myocarditis	Thickened right ventricular free wall, mild to moderate pericardial effusion, global hypokinesia (with and without LV dilatation)
Danon disease	Extreme concentric LVH, global hypokinesia (with and without LV dilatation)
Pompe disease	Extreme concentric LVH
PRKAG2 mutations	Global hypokinesia (with and without LV dilatation)
Glycogenosis	Concentric LVH
Mitochondrial disease	Global hypokinesia (with and without LV dilatation)
Noonan syndrome and associated disorders	Right ventricular outflow tract obstruction

*Data from Rapezzi *et al*. (20) and Elliott *et al*. (2).

apical longitudinal contraction and global longitudinal strain (although not pathognomonic of amyloid), interatrial and valvar thickening, pericardial effusion, and mismatch between the degree of LVH seen on echo and low amplitude voltages on ECG. Diagnosing HCM should be avoided immediately after an acute cardiac injury such as myocarditis as the myocardium becomes oedematous and thickened; these changes resolve with time.

Defining the pattern of hypertrophy in HCM

The echocardiographic report should detail the distribution of LVH using the schema described in Fig. 4 as this informs the clinical team of the likelihood of finding a disease-causing gene change; being highest in patients with a reverse curvature pattern and lowest in those with a sigmoid septal pattern (21). Right ventricular hypertrophy is present in around 20% of patients with HCM. The echocardiographer should report this as it occurs in disease mimics; however, it does not add to the likelihood of finding a disease-causing mutation.

Hypertrophy can also extend to the papillary muscles, which can contribute to mid-cavity obstruction. Additional morphological abnormalities of papillary muscles in HCM which can cause LVOT obstruction include antero-apical displacement, double bifid (22) and anomalous papillary muscles which insert directly into the mitral valve leaflets (23, 24). Bands running between the apex and basal anteroseptal wall are seen in HCM (25).

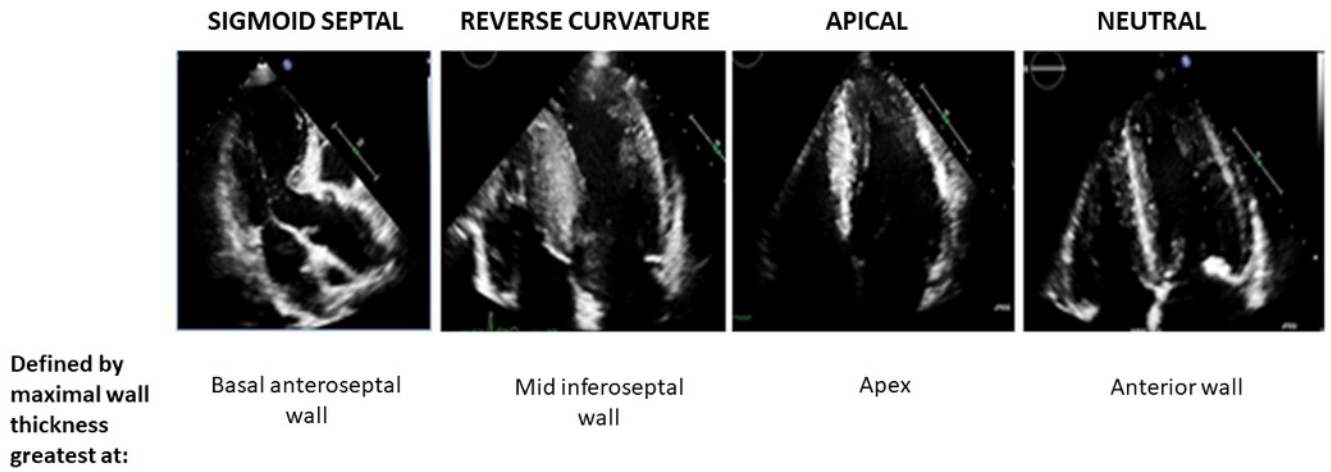


Figure 4
Echocardiographic images are displayed for the four main patterns of hypertrophy, accompanied by the criteria for each pattern.

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

Echo assessment in risk stratification and disease complications

Risk stratification of sudden death is the process clinicians follow to decide which patients should receive an implantable cardioverter-defibrillator. Using the European Society of Cardiology (ESC) calculator (2), it is possible to generate an estimate of the five-year risk of sudden death and categorise patients into low, intermediate, and high-risk groups. Echocardiography provides three of the seven parameters required in the online tool (maximal wall thickness, LVOT gradient and 2D parasternal long axis left atrial size). To allow this critical information to be accessed rapidly by the referring clinician, the conclusion for every report in a patient with suspected or confirmed HCM should contain these parameters. Although not included in the ESC risk calculator, the presence of left ventricular impairment (6) and an apical aneurysm (26) is also essential to include in the study conclusion as they modify risk of sudden cardiac death.

The importance of reporting cardiac rhythm in every echocardiogram report is particularly relevant in HCM as a significant proportion of patients will develop atrial fibrillation. The finding of new atrial fibrillation should be directly communicated to the referring team as anticoagulation is essential to prevent stroke or other embolic complications.

Heart failure can occur due to systolic impairment, diastolic dysfunction and LVOT obstruction. As a measure of systolic function, ejection fraction (EF) can be misleading in HCM being normal even when markers of systolic dysfunction such as abnormal regional wall motion and global longitudinal strain (27) (see the 'Strain imaging in HCM' section below) are present. Nonetheless, the absolute value helps clinical teams to identify patients in whom systolic dysfunction is likely to develop (50–60%) and those in whom it is overt (<50%) (6). Accurately determining EF using Simpson's biplane, and three-dimensional quantification where possible, and highlighting instances when this measurement is discordant with the systolic function will aid clinical management. Longitudinal systolic function should be assessed using tissue doppler imaging and in select cases strain (see the 'Strain imaging in HCM' section below), while radial systolic function should be assessed visually. Outcomes are generally adverse once the EF falls below 50% (6). Below this level, clinical teams should consider medications (2), heart transplant (2) and device therapy (28).

Diastolic dysfunction is common in HCM and results in elevated filling pressures and dilatation of the left atrium, whose diameter in the parasternal long axis is a predictor of sudden death in the ESC risk calculator (29), and of stroke and other thromboembolic events (30). Accurate classification of diastolic function grade is challenging in HCM due to the concomitant presence of left ventricular outflow tract obstruction and mitral regurgitation in many patients. Many independent echo variables have weak correlations with filling pressures. As such integration of several parameters is necessary to quantify diastolic function accurately.

It is essential to identify patients with preserved left ventricular ejection fraction but a restrictive diastolic filling pattern, which is often accompanied by pulmonary hypertension (31). These patients have adverse outcomes (32) and should be observed closely for evidence of deterioration as heart transplant is an option when symptoms related to heart failure are resistant to medical treatment (31).

Left ventricular outflow tract obstruction occurs as a result of a reduced cross-sectional area of the outflow tract due to hypertrophy, abnormalities of the mitral valve apparatus, and in most patients supranormal ejection, which drags the anterior mitral valve leaflet anteriorly towards the basal septum. The mitral valve coaptation is disrupted, with the resultant jet of mitral regurgitation in the majority of patients being directed posteriorly in mid-to-late systole (65% based on a recent study of patients undergoing myectomy with systolic anterior motion-related mitral regurgitation (33)). The same study found that posteriorly directed mitral regurgitation occurred in approximately a third of patients with intrinsic mitral valve disease.

There is a spectrum of LVOTO defined according to the severity and whether it is present at rest or with provocation (Table 2). Echocardiographers should try to provoke LVOT obstruction in every patient at the bedside by re-imaging while the patient is performing a Valsalva manoeuvre and in a seated and standing position. Obstruction in the mid and apical LV and right ventricle can also occur due to narrowing of the cavity as neighbouring myocardial walls contract towards each other. Accurate identification of the site of obstruction is relevant to guiding treatment strategies.

In patients who fail to respond to medical therapy directed at relief of LVOT obstruction, invasive septal reduction therapies (surgical myectomy and alcohol septal ablation) are considered. Given the potential complications of invasive therapies, it is important

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

Table 2 Definition of LVOT obstruction.

LVOT gradient at rest and with physiological provocation	Definition
Gradient ≥30mmHg at rest	Basal or resting obstruction
Gradient <30mmHg at rest and <30mmHg after provocation	Non-obstructive
Gradient <30mmHg at rest but ≥30mmHg with physiological provocation	Labile, provocable or dynamic obstruction

Data from Gersh *et al*. (42).

that patients fulfil the necessary clinical, anatomical, and hemodynamic criteria to determine suitability for a procedure, and this decision is based heavily on the echocardiographic assessment.

Although a complete discussion of the work-up for these procedures is outside this guideline's remit, pertinent echocardiographic features are summarised in Table 3. A clear description of the nature of LVH, mitral valve abnormalities, additional areas of obstruction, and aortic valve disease supports decision-making. The focus is on identifying those elements that point to the need for surgical intervention and not alcohol septal ablation. Surgery can address features aligned with the latter, but the converse is not true for *alcohol septal ablation*.

Alcohol septal ablation is performed through an angiographic percutaneous approach and provides a suitable alternative for patients of advanced age or with significant comorbidities that would lead to an increased surgical risk. Injection of alcohol via a septal perforator branch of the LAD is performed into the target myocardium. This site is the hypertrophied basal septum adjacent to the point of anterior mitral valve leaflet-basal septal (systolic anterior motion-septal) contact, creating an acute infarction and progressive thinning of the myocardium with scar formation over a 6–12-month period. Selective intracoronary injection of contrast is essential to guide the selection of the appropriate septal perforator vessel, ensuring that the selected branch supplies only the targeted area of the myocardium, with no enhancement of remote areas such as the papillary muscles, inferior wall of the LV, or right ventricular free wall. A decrease in resting and provocable LVOT gradients is seen immediately because of myocardial stunning, with a progressive reduction in resting and dynamic LVOT gradients over 3–6 months.

Finally, the examination should include careful evaluation for aneurysm formation and associated thrombi in patients with apical HCM using contrast when necessary (Fig. 2). Table 4 describes the relevance of various parameters captured by the echocardiography examination and Table 5 the minimum data set. A protocol for the transthoracic echo study in HCM is described in Table 6.

Stress imaging in HCM

By imaging the heart during controlled exercise, stress echocardiography can unmask latent obstruction in symptomatic patients whose baseline transthoracic echocardiography – despite the previously described physiological manoeuvres – has not shown LVOT gradients ≥50 mmHg. Symptom-limited exercise is safe using an exercise bike or treadmill. There is some evidence to suggest that treadmill exercise can provoke higher LVOT gradients compared to semi-supine bicycle exercise (34). Dobutamine is not employed in HCM since this infusion can induce LVOTO in normal subjects. When the patient has reached peak exercise, images are obtained within 60–90 seconds to detect obstruction which can be present before or after the patient's heart rate reaches 85% of age-predicted maximum heart rate. The protocol in Table 7 suggests an optimal scanning order to utilise peak heart

Table 3 Use of echocardiography when determining optimal invasive septal reduction approach.

Favours surgical myectomy	Aligned with alcohol ablation strategy	Unfavourable for either
Septal thickness >25mm	Focal basal septal hypertrophy or sigmoid septal morphology	Apical hypertrophy
Central or anteriorly-directed mitral regurgitation due to intrinsic valve disease	Posteriorly-directed mitral regurgitation secondary to systolic anterior motion	
Abnormal mitral subvalvar apparatus contributing to obstruction		Mid-cavity obstruction
Concomitant aortic valve disease or coronary artery disease necessitating CABG		

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

Table 4 Rationale for key echo parameters in hypertrophic cardiomyopathy.

Feature	Prognostic Relevance	Role in ESC HCM Guidelines (1)
Left atrial diameter	Sudden cardiac death (29), with >48 mm predicting all-cause mortality (43); risk of thromboembolism increases exponentially (30)	In risk calculator; if LA >45mm, for six to twelve monthly ambulatory monitoring
Indexed left atrial volume	>34 mL/m^2 predicts all-cause mortality, heart transplantation, sudden cardiac death, and appropriate implantable cardioverter-defibrillator therapy (27)	
Mitral valve filling pattern	Restrictive filling pattern in HCM patients with heart failure with preserved ejection fraction carry adverse prognosis HCM (32)	
Left ventricular wall thickness	Sudden cardiac death (29)	In risk calculator
Left ventricular outflow tract obstruction	>30 mmHg predictor of sudden cardiac death and heart failure (29, 44)	In risk calculator; if the patient has symptoms and ≥50 mmHg LVOTO resistant to medical therapy, invasive septal reduction indicated
Left ventricular function	Ejection fraction <50% associated with unfavourable outcome (45)	When ejection fraction <50% in patients with NYHA III-IV despite optimal medical therapy, heart transplant indicated

rate with minimal changes to the acoustic window. Table 8 illustrates the data acquired in each step of the protocol. In specific scenarios, the echocardiographer can employ additional measures to provoke LVOT obstruction. For patients with postprandial symptoms, exercise after eating is useful (35) while for those who cannot exercise, administering GTN spray can unmask obstruction (36).

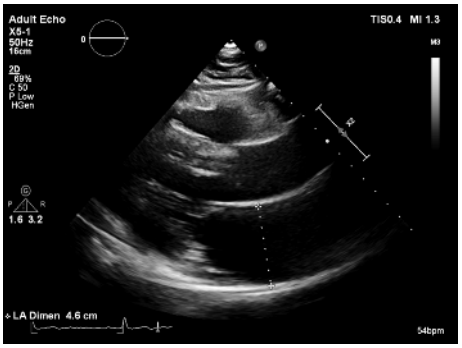
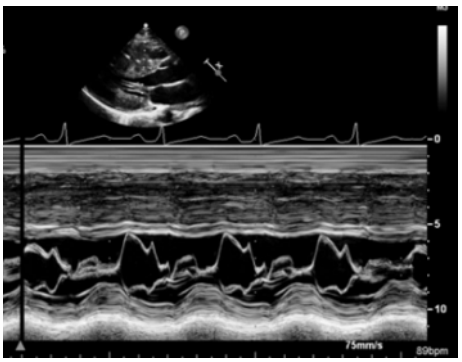
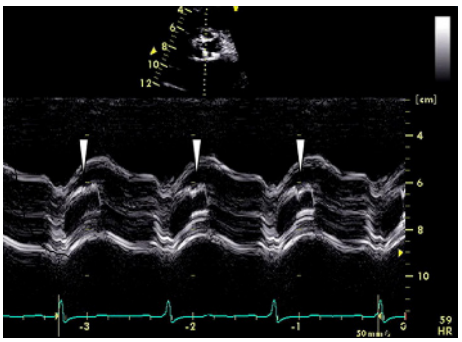
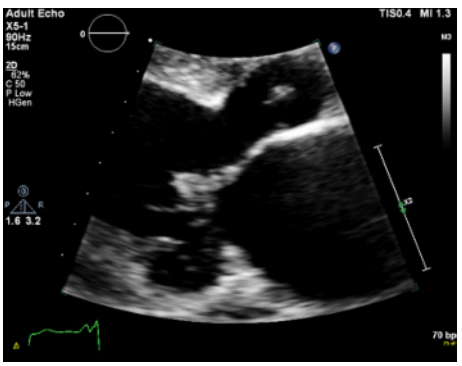
Table 5 Minimum dataset.

Structure and Function	Measurement			
Left atrium size	Diameter (mm)		Indexed biplane volume (mL/m^2)	
Mitral valve inflow Doppler	E wave (m/s)	A wave (m/s)	A wave duration (ms)	Deceleration time (ms)
Pulmonary venous Doppler	Systolic wave (m/s)	Diastolic wave (m/s)	Ar wave (m/s)	Ar duration (ms)
Mitral regurgitation	Severity	Mechanism	Direction of jet	
Systolic anterior motion	Yes/No	Valvular or chordal	Contact plaque	
Left ventricle wall thickness in short axis view	Septum at basal level, mid-ventricular level and apical level (mm)	Anterior wall at basal level, mid-ventricular level and apical level (mm)	Lateral wall at basal level, mid-ventricular level and apical level (mm)	Inferior wall at basal level, mid-ventricular level and apical level (mm)
LV dimensions	End diastolic dimension (cm)	End systolic dimension (cm)		
LV volumes	End-diastolic volume (mL), indexed to body surface area (mL/m^2)	End-systolic volume (mL), indexed to body surface area (mL/m^2)	Stroke volume (mL)	
LV systolic function	Ejection fraction by Simpson's Biplane (%)	Ejection fraction by visual assessment when Simpson's Biplane cannot be calculated (%)	Global longitudinal strain in selected cases (%)	
Tissue Doppler Imaging	Anterolateral annulus (Sm, E', A') (cm/s)	Inferoseptal annulus (Sm, E', A') (cm/s)	Anterior annulus* (Sm, E', A') (cm/s)	Inferior annulus* (Sm, E', A') (cm/s)
LVOT or intra-cavity obstruction (defining which)	Resting (mmHg)	Valsalva (mmHg)	Sitting (mmHg)	Standing (mmHg)
Right ventricle (RV)	Size and function	RV hypertrophy (mm)	RV outflow tract obstruction (mmHg)	
Tricuspid regurgitation and inferior vena cava	Severity	Probability of pulmonary hypertension (46)	Inferior vena cava size and collapse response	

*In individuals being screened for HCM.

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

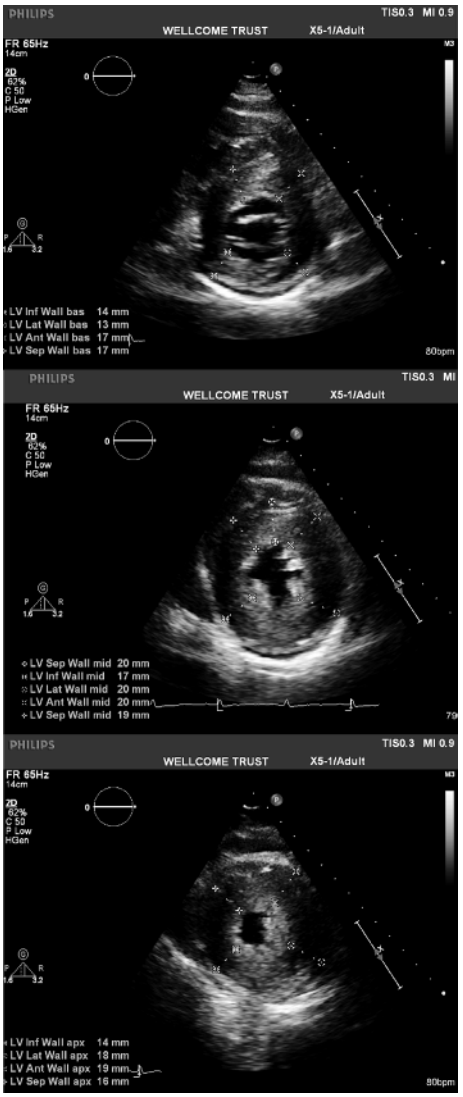
Table 6 Transthoracic HCM protocol.

Measurement	View	Modality	Explanation	Image
LA diameter	PLAX	2D Unit: mm	Measure LA dimension at end-systole just after the aortic valve closes using 2D acquisition as per BSE normal reference intervals guidelines (17). LA diameter is one of the criteria used in ESC risk calculator of SCD. Record in report conclusion.	
SAM	PLAX	M-mode	Place M-mode cursor through the MV leaflet tips, ensuring image is on-axis. Involves MV leaflets and/or chordae.	
Feature of LVOT obstruction	PLAX	M-mode 2D	Mid-systolic notching and coarse systolic fluttering of the aortic valve are ancillary echocardiographic features in LVOTO.	
Contact plaque	PLAX, A3C	2D	Increased echogeneticity occurs in the basal anteroseptal wall due to fibrosis where leaflet contact occurs due to SAM.	

(*Continued*)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

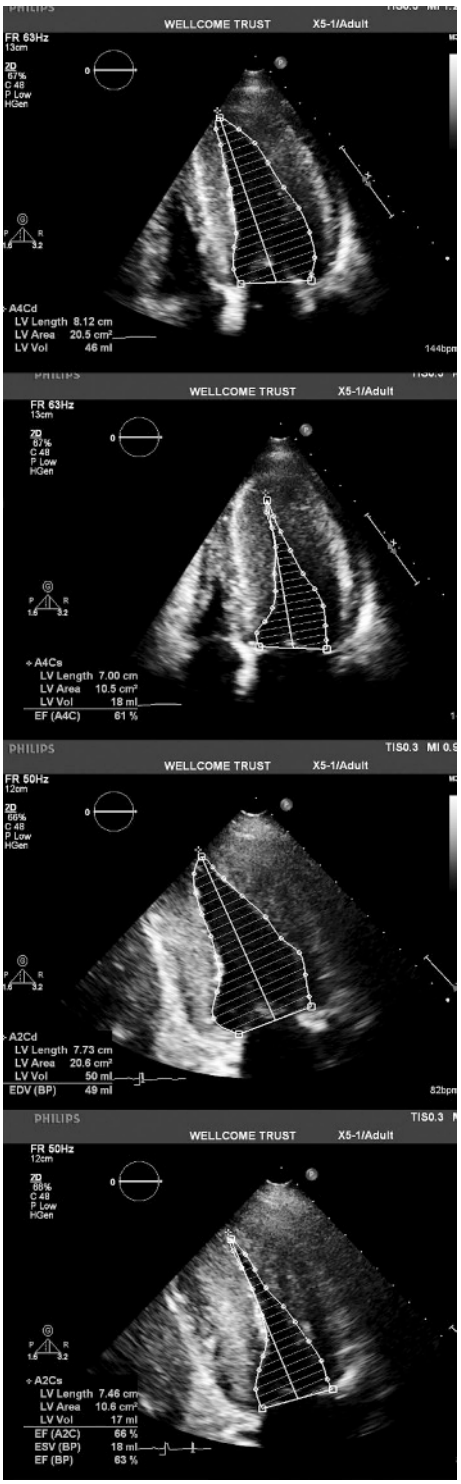
Table 6 Continued.

Measurement	View	Modality	Explanation	Image
LV wall thickness measurements	SAX MV level Mid-ventricular level Apical level	2D Units: mm	Freeze 2D image at end-diastole. Calliper diameter of maximal wall thickness – wherever it occurs – in the anterior, septum, inferior and lateral walls at the basal, mid-ventricular and apical levels (47). Be careful not to include right ventricular (RV) wall, papillary muscles, trabeculations or moderator band. The thickest segment may not be in the septum. Maximal wall thickness is one of the criteria used in ESC risk calculator of SCD. Record in report conclusion.	

(*Continued*)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

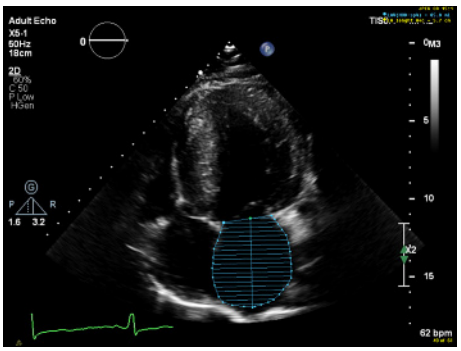
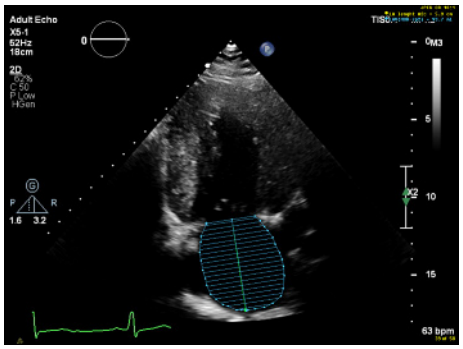
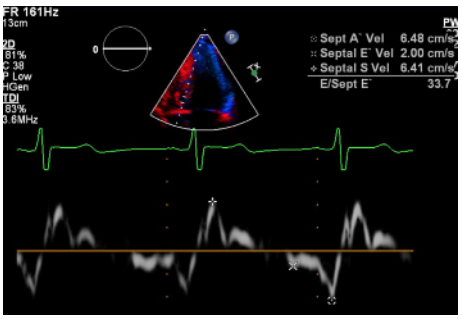
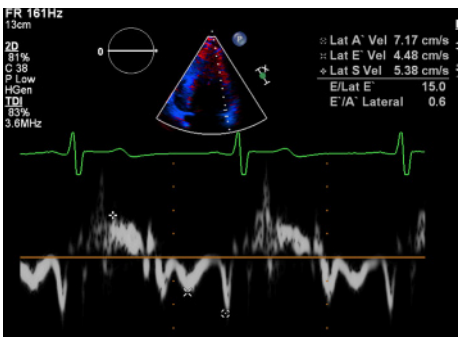
Table 6 Continued.

Measurement	View	Modality	Explanation	Image
LV Simpson's Biplane volumes and ejection fraction	A4C, A2C	2D Units: mL/m^2 and %	LV volumes should be obtained using 2D imaging from A4C and A2C, and wherever possible 3D imaging. Trace the endocardial border. LV length is defined as the distance between the midpoint of the mitral valve level line and the most distal point of the LV apex. Take care to ensure the LV is not foreshortened. Papillary muscles and trabeculations are excluded from the volumes and considered part of the chamber. Measure at end-diastole (onset of QRS complex) and end-systole (the frame before MV opens, where AV just closes) (17). Volumes are indexed to body surface area.	

(*Continued*)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

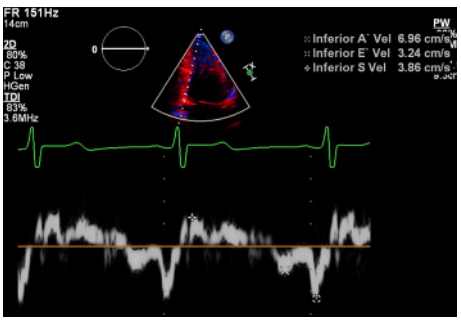
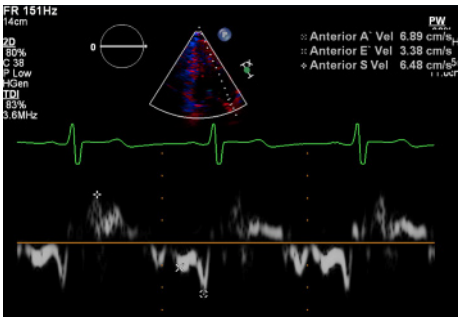
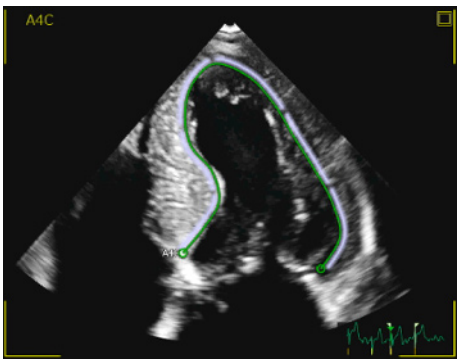
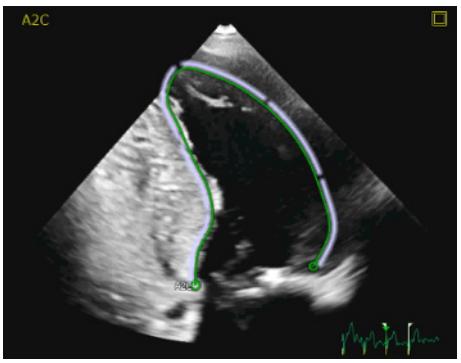
Table 6 Continued.

Measurement	View	Modality	Explanation	Image
LA biplane volume	A4C,A2C	2D biplane volume using independent A4C and A2C views Units: mL/m^2	LA volume should be obtained from apical 4- and 2-chamber windows (separated by 60° of rotation), optimised for LA assessment, using the biplane Simpson's method. Maximal LA volume should be obtained from the frame immediately prior to mitral valve opening. Values should be reported after indexing for BSA (17). Trace the inner aspect of the left atrial wall. At the mitral valve level, the contour is closed by a straight line between along the plane of the mitral valve annulus. Exclude left atrial appendage and pulmonary veins.	 
TDI velocities in all four walls	A4C, A2C	PW TDI Units: cm/s	Systolic (Sm), early (E') and atrial (A') relaxation velocities at anterolateral and inferoseptal walls. In screening studies, there is an argument for averaging E′ across anterolateral, inferoseptal, inferior and anterior LV annulus as a value <13.5 cm/s can be useful in identifying genotype positive phenotype negative individuals (48).	 

(*Continued*)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

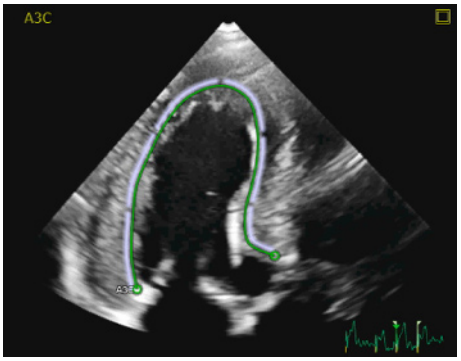
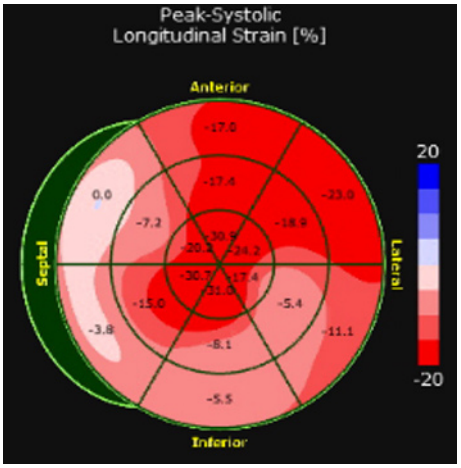
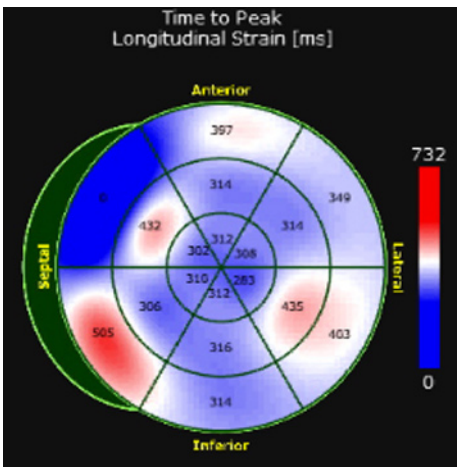
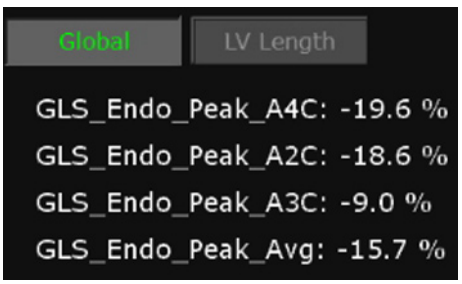
Table 6 Continued.

Measurement	View	Modality	Explanation	Image
				 
Global longitudinal strain (GLS)	A4C, A2C, A3C	2D Units: -%	This is recommended when cardiac amyloidosis or athletic remodelling are being considered. Average global longitudinal strain (GLS) is calculated using the apical long axis (A3C), four chamber A4C and two chamber A2C standard views. High quality image acquisition, maintaining a frame rate of 40 to 90 frames/second at a stable heart rate is key. Clear endocardial and epicardial definition (seen throughout the cardiac cycle) is required to ensure adequate segmental tracking during systole and diastole. Markers are placed in each of the respective basal and apical regions, utilising automated tracking where possible to maintain reproducible results. ROI should be manipulated as required to fit the myocardium. Automated tracking should also be combined with a visual assessment of tracking in each view across the whole region of interest including the endocardial and epicardial border. If more than two segments in any one view are not adequately tracked, the calculation of GLS should be avoided.	 

(*Continued*)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

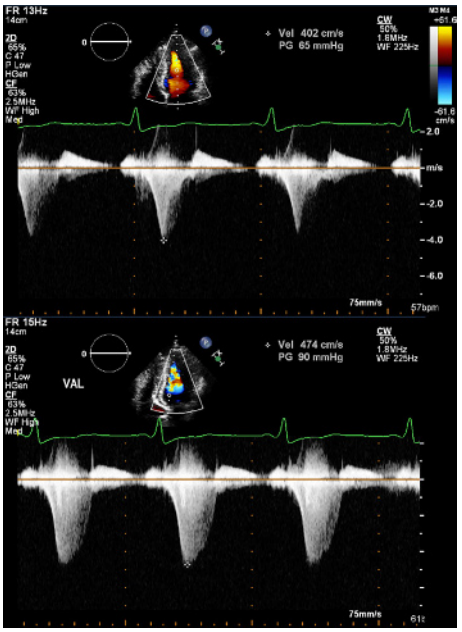
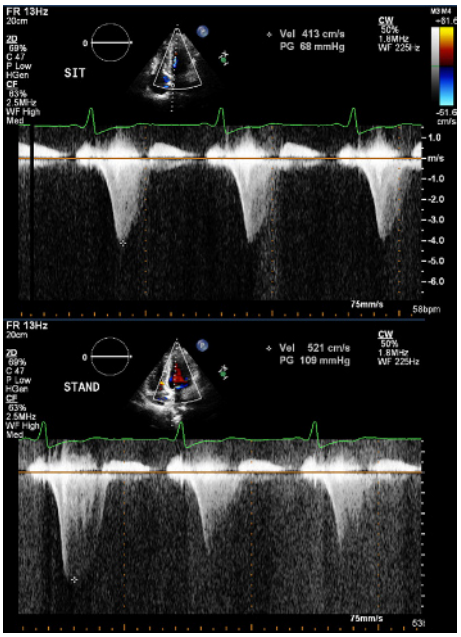
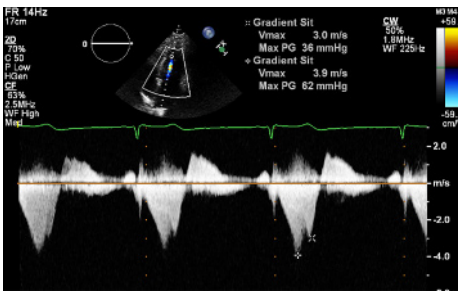
Table 6 Continued.

Measurement	View	Modality	Explanation	Image
				   

(*Continued*)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

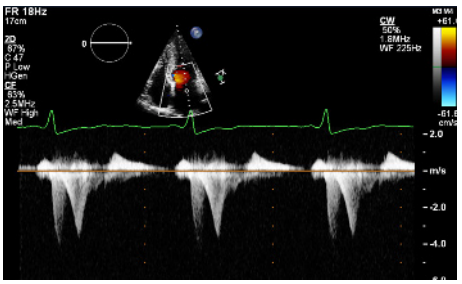
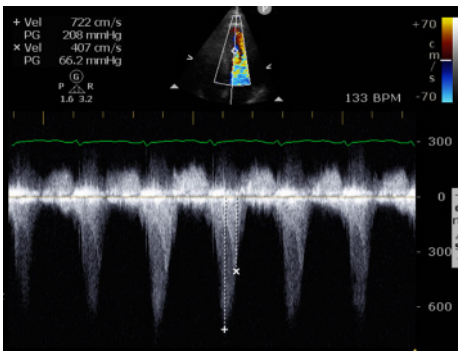
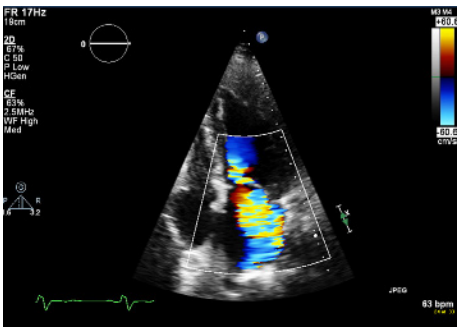
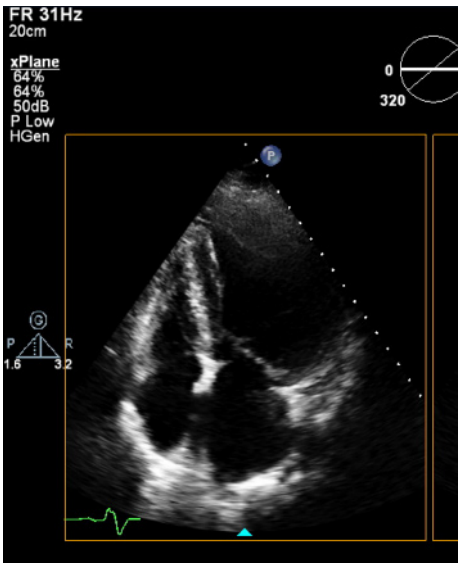
Table 6 Continued.

Measurement	View	Modality	Explanation	Image
LVOT or intra-cavity obstruction gradients	A4C, A5C	CW Doppler (or PW with HPRF as a significant gradient will alias on PW Doppler). Sampling PW Doppler throughout the LV cavity is a useful tool to pinpoint the exact location of obstruction if unclear on colour. Units: mmHg	Assess obstruction gradients at rest, with Valsalva manoeuvre and in sitting and standing positions. Align CW Doppler through entire turbulent colour flow for peak obstruction velocity. Peak LVOT obstruction gradient is one of the criteria used in ESC risk calculator of SCD. Record in report conclusion.	 
Multiple LV gradients	A4C, A5C	CW Doppler Colour flow mapping Units: mmHg	Intra-cavity obstruction at the apex produces an additional Doppler signal to the LVOTO signal.	

(*Continued*)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

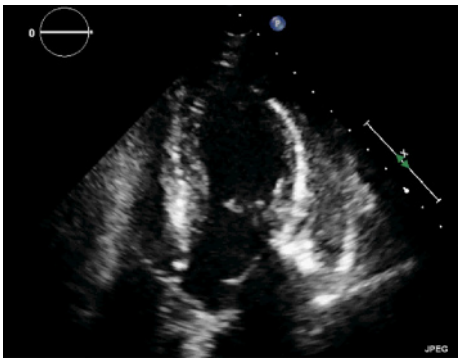
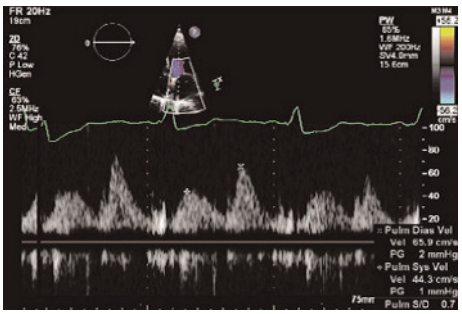
Table 6 Continued.

Measurement	View	Modality	Explanation	Image
MR versus LVOT obstruction	A4C, A5C	CW Doppler Colour flow mapping Units: mmHg	When mitral regurgitation occurs in the context of SAM or prolapse, its onset is later in mid to late systole. Otherwise, its onset in early systole helps distinguish it from the LVOT signal which begins later in systole (see right hand image). LVOT obstruction is dagger-shaped due to the progressive decrease in LVOT orifice size as systoles progresses, but of lower maximal velocity compared to mitral regurgitation. The lower image shows superimposed CW envelopes in a patient with mitral regurgitation and LVOTO. In this case mitral regurgitation starts later in systole, so timing of onset is a less useful discriminator. However, the velocity for the mitral regurgitation signal is far higher than for LVOTO.	 
Mitral regurgitation secondary to SAM	PLAX, A4C, A5C	Colour flow mapping CW	Mitral regurgitation quantification may be limited as the PISA dome may merge with turbulent LVOT flow. Mitral regurgitation secondary to SAM is mainly posteriorly directed. When quantitative assessment of MR is precluded by LVOTO, other indicators of MR severity should be considered. For example, an E velocity of <1.3 m/s and an E/A ratio <1 are strongly suggestive of non-severe MR.	 

(*Continued*)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

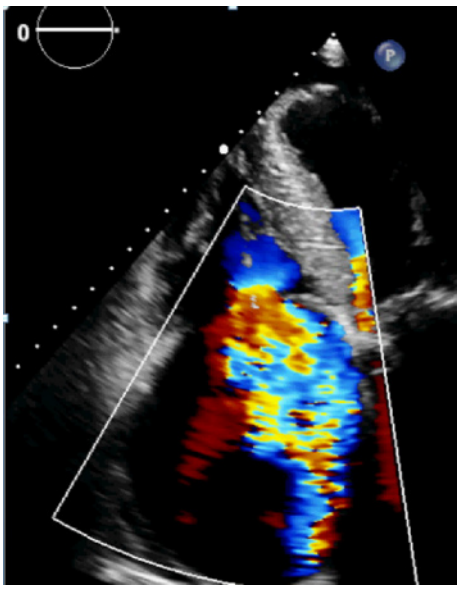
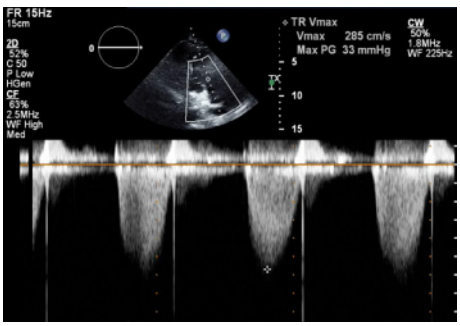
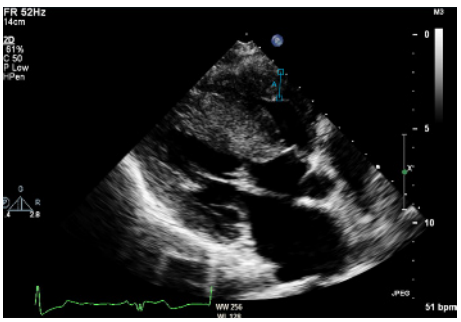
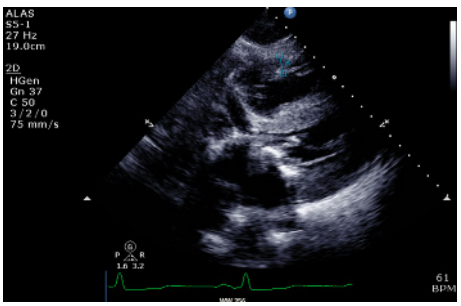
Table 6 Continued.

Measurement	View	Modality	Explanation	Image
Abnormal MV anatomy (elongated AMVL)	PLAX, A4C, A3C	2D	Describe MV anatomy; elongation of both leaflets, presence of SAM (and which leaflet(s) it involves), aberrant chordae running from anterior mitral valve leaflet to LVOT, anomalous papillary muscles running directly into the mitral valve leaflets and displacement of the papillary muscles antero- apically. If the anterior mitral valve leaflet is elongated (>16 mm), this increases the likelihood of LVOT obstruction (49).	
Pulmonary venous Doppler	A4C	PW Units: cm/s	Measure peak systolic (S) velocity, peak diastolic (D) velocity, the S/D ratio, peak atrial reversal (Ar) velocity in late diastole and the duration of the Ar velocity. In the apical 4-chamber view, superior angulation of the transducer and use of colour flow will help locate the pulmonary veins. This angle often brings the aorta into the visualised plane. The right upper pulmonary vein is usually easiest to see and is next to the atrial septum. If the signal is weak, ask the patient to adopt a more supine position. Place the PW Doppler sample volume (1–3 mm) 1–2 cm into the right upper vein. Wall filter settings should be lowered (100–200 MHz). Aim to include clear visualisation of the atrial reversal velocity waveform. Measurements should be averaged over 3 cardiac cycles, at end expiration. Additional parameters for diastolic function should include A wave duration on transmitral inflow. For the measurement of the mitral valve A wave duration, the PW Doppler sample should be placed at the level of the annulus rather than at the leaflet tips. This provides a cleaner signal for the start and end of the wave.	

(*Continued*)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

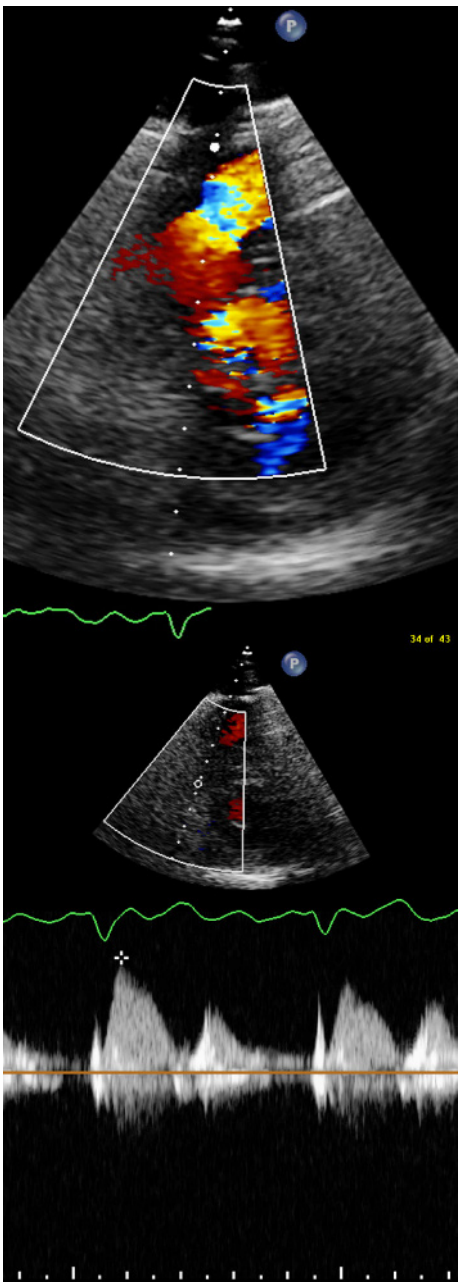
Table 6 Continued.

Measurement	View	Modality	Explanation	Image
TR jet velocity and probability of pulmonary hypertension	RV inflow, PSAX, A4C	CW Colour flow mapping Units: Vmax m/s, peak gradient mmHg	See BSE PHTN guidelines for risk of pulmonary hypertension (46).	 
RV hypertrophy	Subcostal view, PLAX	2D Units: mm	Freeze the PLAX or subcostal view of the RV free wall, scroll to end diastole and calliper the RV wall thickness.	 

(*Continued*)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

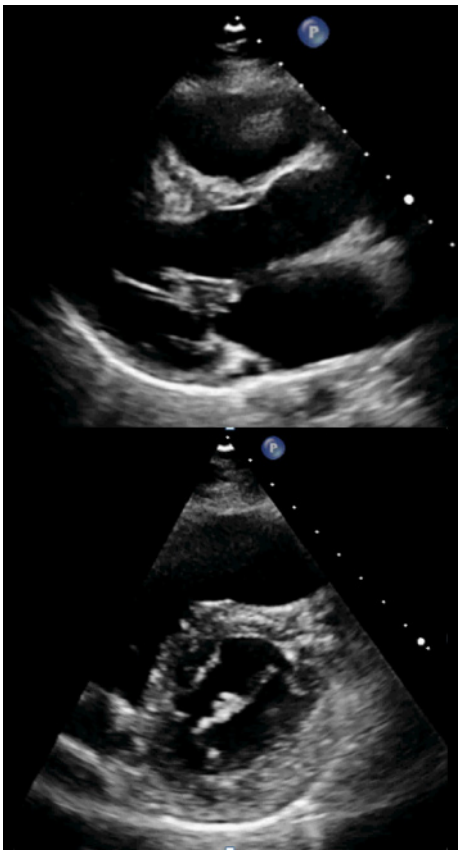
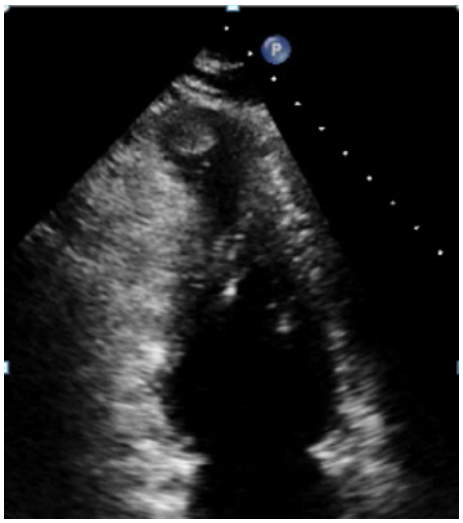
Table 6 Continued.

Measurement	View	Modality	Explanation	Image
RVOT obstruction	PSAX view	2D Colour flow mapping CW Doppler. Units: mmHg	Modify both the RV inflow and outflow to assess for RV hypertrophy and RV outflow tract obstruction. Use colour box as a guide for highest RVOT velocity.	

(*Continued*)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

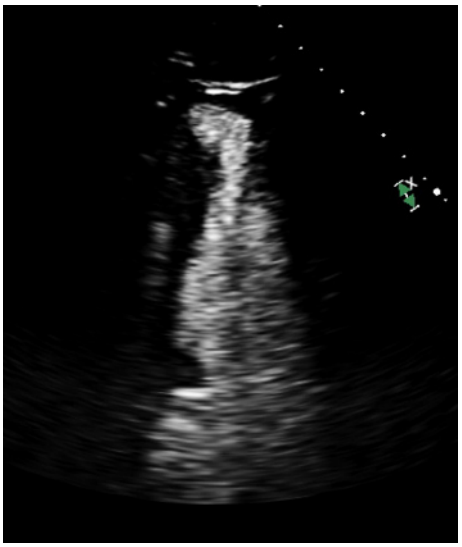
Table 6 Continued.

Measurement	View	Modality	Explanation	Image
Septal myectomy and septal ablation	PLAX, PSAX MV level, A4C, A3C, subcostal views.	2D	Basal septum has scalloped appearance and is hypokinetic/ akinetic. Colour flow Doppler should be applied to the area of myectomy to assess for iatrogenic VSD (systolic flow), and a denuded septal perforator vessel (diastolic flow). The pre-procedure HCM morphology cannot be determined in patients who have undergone a septal myectomy or septal ablation.	
Aneurysmal apex	A4C, A2C, A3C, PSAX apex level. +/– ultrasound enhanced echo with contrast	2D Colour flow mapping Contrast	Apical HCM can be accompanied by an apical aneurysm which encourages thrombus formation (see non-contrast image on right). Have a low threshold for giving contrast (bottom image) if endocardial definition is poor at the apex.	

(*Continued*)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

Table 6 Continued.

Measurement	View	Modality	Explanation	Image
HCM phenotypes	A4C, A2C, A3C, PLAX, PSAX.	2D	Four distinct phenotypes describe the distribution of left ventricular hypertrophy. Comment on morphology in the report conclusion.	

Strain imaging in HCM

Measurement of global longitudinal strain (GLS) by two-dimensional speckle tracking echocardiography is becoming more widely used in current practice. Strain is a measure of myocardial deformation in multiple directions throughout the cardiac cycle. Most commonly, analysis based on the Lagrangian method (derived from speckle tracking techniques) expresses strain as a fractional change in length. Shortening of the myocardium becomes a negative value and lengthening of the myocardium a positive value (37). In HCM, reduced overall left ventricular GLS occurred in individuals with preserved ejection fraction (38). A recent systematic review has shown an association between abnormal GLS and adverse outcomes (39).

However, the author group feel that several practical considerations limit routine use in every HCM patient. These include the expertise and experience needed to ensure the strain curves generated are accurate and the potential difficulties in tracking where there is gross hypertrophy, apical hypertrophy or apical insertion of the papillary muscles. Consequently, inter-observer variability may well be higher in HCM than for dilated cardiomyopathies. Finally, strain-based measures are yet to be adopted into clinical HCM guidelines and so will not routinely alter patient management.

For this reason, we recommend that GLS is used to help distinguish HCM from cardiac amyloidosis, and athletic remodelling. This position will be re-evaluated in the next update of the guideline as more evidence emerges and the technology evolves.

Three-dimensional echocardiography

Besides enabling accurate quantification of left and right ventricular volumes and ejection fraction, three-dimensional echocardiography also allows echocardiographers to describe mitral valve and LVOT morphology. Three-dimensional technology is also valuable in transoesophageal echocardiography to detail SAM's features and underlying causes (40, 41). We recommend that patients undergo transoesophageal echocardiography when the transthoracic study suggests significant abnormalities of the mitral valve apparatus,

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

Table 7 Stress echocardiography protocol in HCM.

	View	Modality	Explanation
LVOT or intra-cavity obstruction	A5C/A3C (view which obtained the highest gradient at rest)	CW Doppler (or PW with HPRF as a significant gradient will alias on PW Doppler) Sampling PW Doppler throughout the left ventricular cavity is a useful tool to pinpoint the exact location of obstruction if unclear on colour Units: mmHg	Increase in stroke volume with exercise Use colour box as a guide to aim CW Doppler beam through area of turbulence obtaining the highest gradient Assessment of LVOT obstruction assessment is performed prior to LV assessment it can be a short-lived phenomenon
MR	A4C, A3C	Colour mapping CW doppler	Be careful to differentiate mitral regurgitation from LVOT obstruction
MV	A4C	PW Doppler Units: m/s	Peak exercise and intermediate stage (100–120bpm) Pulse at MV leaflet tips to obtain inflow Doppler Description of MV morphology and SAM at intermediate and peak
TR	A4C (alternative views are RV inflow or PSAX, however time consuming as requires a different window)	CW Doppler Units: mmHg (m/s)	To exclude exercise induced pulmonary hypertension
LV size and systolic function	A4C, A2C, A3C, SAX	2D imaging Systolic TDI velocities in anterolateral and inferoseptal walls Units: cm/s	A4C and A2C for LV volumes and Simpson's Biplane EF Small LV cavity may make measuring volumes difficult at intermediate and peak stress
LV diastolic function	A4C, A2C	Diastolic TDI parameters in anterolateral and inferoseptal walls MV inflow flow Doppler E/e' average Units: cm/s	Peak exercise and intermediate stage (100–120bpm) E/A fusion will occur at high heart rates Intermediate imaging with supine bicycle only

and to evaluate both the mitral valve and the LVOT when planning for invasive septal reduction.

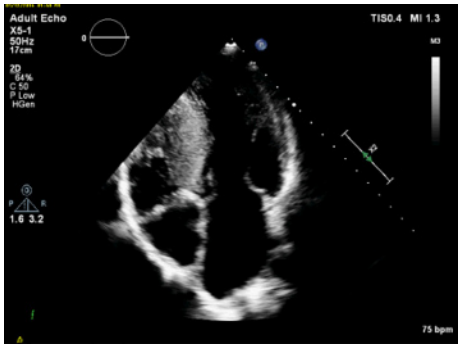
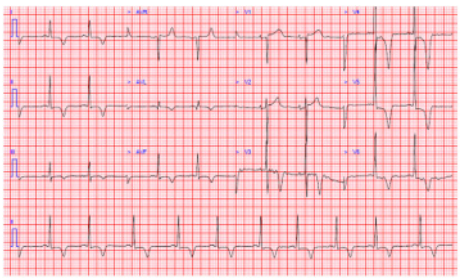
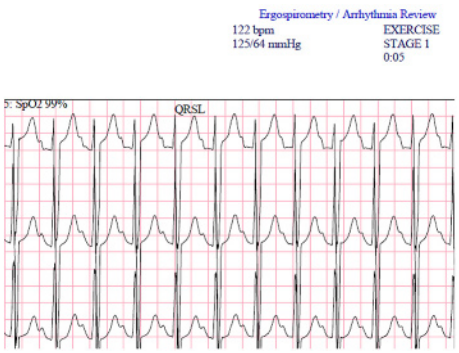
Recommendations

The echocardiogram report conclusion should include:

1. The following suggested phrases: when there is uncertainty: *raises the possibility of HCM;* when there is unequivocal evidence of HCM: *consistent with HCM;* for screening scans with no LVH: *wall thickness is normal*.
2. The presence of red flags pointing to a phenocopy.
3. The pattern of LVH: sigmoid septal, reverse curvature, apical or neutral.
4. The values for maximal wall thickness, LVOT gradient and LA size.
5. The presence or absence of disease complications:
   a. Left ventricular cavity size.
   b. Systolic dysfunction with EF 50–60%, EF <50%.
   c. Diastolic dysfunction, specifically the presence of a restrictive filling pattern with preserved ejection fraction.
   d. Systolic anterior motion, mitral regurgitation, LVOT obstruction and other forms of obstruction; at rest and with provocation. Evidence of intrinsic mitral valve disease.
   e. Aneurysm formation.
6. Image quality, completeness of LV visualisation and need for contrast and transoesophageal echocardiography, and cardiovascular magnetic resonance.

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

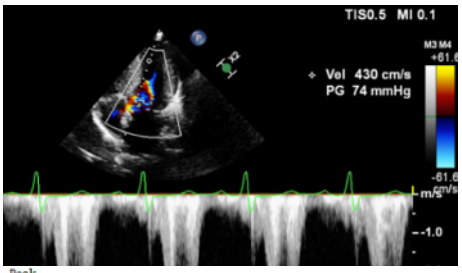
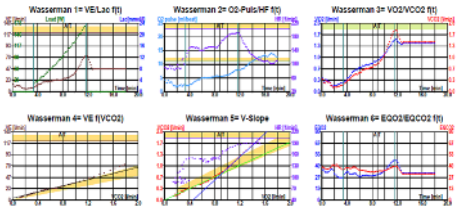
Table 8 Illustrated guide to stress echocardiography in HCM.

	HCM stress echo protocol – Quick guide	
1. Echo data – rest		• Resting BSE HCM guidelines 2021 • Exclude contraindications to exercise test
2. Resting haemodynamics		• Perform a resting ECG • Obtain resting blood pressure and standing blood pressure
3. Resting spriometry		• Obtain resting spirometry tests if performing combined cardiopulmonary test • Cardiopulmonary test data is used to establish exercise capacity and true exercise limitations
4. Exercise modality		• Bicycle or treadmill method of exercise • Treadmill – resting echo images obtained on echo bed • Bicycle – resting echo images obtained whilst patient on bike to ensure comparable echo windows
5. Exercise haemodynamic data		• Continuous monitoring of ECG and blood pressure throughout study • Pay particular attention to arrhythmias, ST segment changes and potential blood pressure drop at peak exercise

(*Continued*)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

Table 8 Continued.

	HCM stress echo protocol – Quick guide	
6. Transition from treadmill to bed		• Treadmill – stopped immediately at peak exercise, patient is carefully guided back onto the echo bed • Bicycle – peak images are obtained whilst patient is still on bicycle
7. Echo data – peak	 Peak Obstruction (mmHg) MR TR MV E A DT A dur: LV volumes EDV ESV SV EF TDIs S E' A' Septal Lateral Anterior Inferior	• Peak exercise images are obtained within 60–90s • This is before preload decreases and before the patient's heart rate recovers below 85% of age-predicted maximum heart rate • See table (below left) for echo parameters collected at peak exercise • Echo measurements are calculated post acquisition to utilise time at peak HR
8. Report		• Cardiopulmonary test, echo and haemodynamic data are combined to produce a clinical report

Conclusion

Transthoracic echocardiography plays an essential role in the assessment of patients with proven or suspected HCM, and their first-degree family members. The guideline writing committee hopes that this document equips readers with the knowledge and tools needed to perform and report these studies to a uniformly high level.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this guideline.

Funding
This work did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

References

1 Smith N, Steeds R, Masani N, Sandoval J, Wharton G, Allen J, Chambers J, Jones R, Lloyd G, Rana B, *et al*. A systematic approach to echocardiography in hypertrophic cardiomyopathy: a guideline protocol from the British Society of Echocardiography. *Echo Research and Practice* 2015 **2** G1–G7. (https://doi.org/10.1530/ERP-14-0115)
2 Authors/Task Force members, Elliott PM, Anastasakis A, Borger MA, Borggrefe M, Cecchi F, Charron P, Hagege AA, Lafont A, Limongelli G, *et al*. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the task force for the

Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). *European Heart Journal* 2014 **35** 2733–2779. (https://doi.org/10.1093/eurheartj/ehu284)

3 Maron BJ, Gardin JM, Flack JM, Gidding SS, Kurosaki TT & Bild DE. Prevalence of hypertrophic cardiomyopathy in a general population of young adults: echocardiographic analysis of 4111 subjects in the CARDIA study. *Circulation* 1995 **92** 785–789. (https://doi.org/10.1161/01.cir.92.4.785)

4 Massera D, McClelland RL, Ambale-Venkatesh B, Gomes AS, Hundley WG, Kawel-Boehm N, Yoneyama K, Owens DS, Garcia MJ, Sherrid MV, *et al*. Prevalence of unexplained left ventricular hypertrophy by cardiac magnetic resonance imaging in MESA. *Journal of the American Heart Association* 2019 **8** e012250. (https://doi.org/10.1161/JAHA.119.012250)

5 Ho CY, Day SM, Ashley EA, Michels M, Pereira AC, Jacoby D, Cirino AL, Fox JC, Lakdawala NK, Ware JS, *et al*. Genotype and lifetime burden of disease in hypertrophic cardiomyopathy: insights from the Sarcomeric Human Cardiomyopathy Registry (SHaRe). *Circulation* 2018 **138** 1387–1398. (https://doi.org/10.1161/CIRCULATIONAHA.117.033200)

6 Marstrand P, Han L, Day SM, Olivotto I, Ashley EA, Michels M, Pereira AC, Wittekind SG, Helms A, Saberi S, *et al*. Hypertrophic cardiomyopathy with left ventricular systolic dysfunction: insights from the SHaRe Registry. *Circulation* 2020 **141** 1371–1383. (https://doi.org/10.1161/CIRCULATIONAHA.119.044366)

7 Alfares AA, Kelly MA, McDermott G, Funke BH, Lebo MS, Baxter SB, Shen J, McLaughlin HM, Clark EH, Babb LJ, *et al*. Results of clinical genetic testing of 2912 probands with hypertrophic cardiomyopathy: expanded panels offer limited additional sensitivity. *Genetics in Medicine* 2015 **17** 880–888. (https://doi.org/10.1038/gim.2014.205)

8 Flett AS, Maestrini V, Milliken D, Fontana M, Treibel TA, Harb R, Sado DM, Quarta G, Herrey A, Sneddon J, *et al*. Diagnosis of apical hypertrophic cardiomyopathy: T-wave inversion and relative but not absolute apical left ventricular hypertrophy. *International Journal of Cardiology* 2015 **183** 143–148. (https://doi.org/10.1016/j.ijcard.2015.01.054)

9 Suzuki J, Shimamoto R, Nishikawa J, Yamazaki T, Tsuji T, Nakamura F, Shin WS, Nakajima T, Toyo-Oka T & Ohotomo K. Morphological onset and early diagnosis in apical hypertrophic cardiomyopathy: a long term analysis with nuclear magnetic resonance imaging. *Journal of the American College of Cardiology* 1999 **33** 146–151. (https://doi.org/10.1016/s0735-1097(98)00527-0)

10 Norrish G, Jager J, Field E, Quinn E, Fell H, Lord E, Cicerchia MN, Ochoa JP, Cervi E, Elliott PM, *et al*. Yield of clinical screening for hypertrophic cardiomyopathy in child first-degree relatives. *Circulation* 2019 **140** 184–192. (https://doi.org/10.1161/CIRCULATIONAHA.118.038846)

11 van Velzen HG, Schinkel AFL, Baart SJ, Oldenburg RA, Frohn-Mulder IME, van Slegtenhorst MA & Michels M. Outcomes of contemporary family screening in hypertrophic cardiomyopathy. *Circulation: Genomic and Precision Medicine* 2018 **11** e001896. (https://doi.org/10.1161/CIRCGEN.117.001896)

12 Coppini R, Ho CY, Ashley E, Day S, Ferrantini C, Girolami F, Tomberli B, Bardi S, Torricelli F, Cecchi F, *et al*. Clinical phenotype and outcome of hypertrophic cardiomyopathy associated With thin-filament gene mutations. *Journal of the American College of Cardiology* 2014 **64** 2589–2600. (https://doi.org/10.1016/j.jacc.2014.09.059)

13 van Velzen HG, Schinkel AFL, Oldenburg RA, van Slegtenhorst MA, Frohn-Mulder IME, van der Velden J & Michels M. Clinical characteristics and long-term outcome of hypertrophic cardiomyopathy in individuals with a MYBPC3 (myosin-binding protein C) founder mutation. *Circulation: Cardiovascular Genetics* 2017 **10** [epub]. (https://doi.org/10.1161/CIRCGENETICS.116.001660)

14 Page SP, Kounas S, Syrris P, Christiansen M, Frank-Hansen R, Andersen PS, Elliott PM & McKenna WJ. Cardiac myosin binding protein-C mutations in families with hypertrophic cardiomyopathy: disease expression in relation to age, gender, and long term outcome. *Circulation: Cardiovascular Genetics* 2012 **5** 156–166. (https://doi.org/10.1161/CIRCGENETICS.111.960831)

15 Sheikh N, Papadakis M, Carre F, Kervio G, Panoulas VF, Ghani S, Zaidi A, Gati S, Rawlins J, Wilson MG, *et al*. Cardiac adaptation to exercise in adolescent athletes of African ethnicity: an emergent elite athletic population. *British Journal of Sports Medicine* 2013 **47** 585–592. (https://doi.org/10.1136/bjsports-2012-091874)

16 Sheikh N, Papadakis M, Schnell F, Panoulas V, Malhotra A, Wilson M, Carré F & Sharma S. Clinical profile of athletes with hypertrophic cardiomyopathy. *Circulation: Cardiovascular Imaging* 2015 **8** e003454. (https://doi.org/10.1161/CIRCIMAGING.114.003454)

17 Harkness A, Ring L, Augustine DX, Oxborough D, Robinson S, Sharma V & Education Committee of the British Society of Echocardiography. Normal reference intervals for cardiac dimensions and function for use in echocardiographic practice: a guideline from the British Society of Echocardiography. *Echo Research and Practice* 2020 **7** G1–G18.

18 Caselli S, Maron MS, Urbano-Moral JA, Pandian NG, Maron BJ & Pelliccia A. Differentiating left ventricular hypertrophy in athletes from that in patients with hypertrophic cardiomyopathy. *American Journal of Cardiology* 2014 **114** 1383–1389. (https://doi.org/10.1016/j.amjcard.2014.07.070)

19 Pelliccia A, Maron BJ, De Luca R, Di Paolo FM, Spataro A & Culasso F. Remodeling of left ventricular hypertrophy in elite athletes after long-term deconditioning. *Circulation* 2002 **105** 944–949. (https://doi.org/10.1161/hc0802.104534)

20 Rapezzi C, Arbustini E, Caforio ALP, Charron P, Gimeno-Blanes J, Heliö T, Linhart A, Mogensen J, Pinto Y, Ristic A, *et al*. Diagnostic work-up in cardiomyopathies: bridging the gap between clinical phenotypes and final diagnosis. A position statement from the ESC Working Group on Myocardial and Pericardial Diseases. *European Heart Journal* 2013 **34** 1448–1458. (https://doi.org/10.1093/eurheartj/ehs397)

21 Binder J, Ommen SR, Gersh BJ, Van Driest SL, Tajik AJ, Nishimura RA & Ackerman MJ. Echocardiography-guided genetic testing in hypertrophic cardiomyopathy: septal morphological features predict the presence of myofilament mutations. *Mayo Clinic Proceedings* 2006 **81** 459–467. (https://doi.org/10.4065/81.4.459)

22 Kwon DH, Setser RM, Thamilarasan M, Popovic ZV, Smedira NG, Schoenhagen P, Garcia MJ, Lever HM & Desai MY. Abnormal papillary muscle morphology is independently associated with increased left ventricular outflow tract obstruction in hypertrophic cardiomyopathy. *Heart* 2008 **94** 1295–1301. (https://doi.org/10.1136/hrt.2007.118018)

23 Klues HG, Roberts WC & Maron BJ. Anomalous insertion of papillary muscle directly into anterior mitral leaflet in hypertrophic cardiomyopathy. Significance in producing left ventricular outflow obstruction. *Circulation* 1991 **84** 1188–1197. (https://doi.org/10.1161/01.cir.84.3.1188)

24 Lentz Carvalho J, Schaff HV, Morris CS, Nishimura RA, Ommen SR, Maleszewski JJ & Dearani JA. Anomalous papillary muscles-Implications in the surgical treatment of hypertrophic obstructive cardiomyopathy. *Journal of Thoracic and Cardiovascular Surgery* 2020 [epub]. (https://doi.org/10.1016/j.jtcvs.2020.04.007)

25 Gruner C, Chan RH, Crean A, Rakowski H, Rowin EJ, Care M, Deva D, Williams L, Appelbaum E, Gibson CM, *et al*. Significance of left ventricular apical–basal muscle bundle identified by cardiovascular magnetic resonance imaging in patients with hypertrophic cardiomyopathy. *European Heart Journal* 2014 **35** 2706–2713. (https://doi.org/10.1093/eurheartj/ehu154)

26 Rowin EJ, Maron BJ, Haas TS, Garberich RF, Wang W, Link MS & Maron MS. Hypertrophic cardiomyopathy with left ventricular apical aneurysm: implications for risk stratification and management. *Journal of the American College of Cardiology* 2017 **69** 761–773. (https://doi.org/10.1016/j.jacc.2016.11.063)

https://erp.bioscientifica.com
https://doi.org/10.1530/ERP-20-0042

27 Hiemstra YL, Debonnaire P, Bootsma M, van Zwet EW, Delgado V, Schalij MJ, Atsma DE, Bax JJ & Marsan NA. Global longitudinal strain and left atrial volume index provide incremental prognostic value in patients with hypertrophic cardiomyopathy. *Circulation: Cardiovascular Imaging* 2017 **10** e005706. (https://doi.org/10.1161/CIRCIMAGING.116.005706)

28 Maron MS, Rowin EJ, Wessler BS, Mooney PJ, Fatima A, Patel P, Koethe BC, Romashko M, Link MS & Maron BJ. Enhanced American College of Cardiology/American Heart Association strategy for prevention of sudden cardiac death in high-risk patients with hypertrophic cardiomyopathy. *JAMA Cardiology* 2019 **4** 644–657. (https://doi.org/10.1001/jamacardio.2019.1391)

29 O'Mahony C, Jichi F, Pavlou M, Monserrat L, Anastasakis A, Rapezzi C, Biagini E, Gimeno JR, Limongelli G, McKenna WJ, *et al*. A novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCM risk-SCD). *European Heart Journal* 2014 **35** 2010–2020. (https://doi.org/10.1093/eurheartj/eht439)

30 Guttmann OP, Pavlou M, O'Mahony C, Monserrat L, Anastasakis A, Rapezzi C, Biagini E, Gimeno JR, Limongelli G, Garcia-Pavia P, *et al*. Prediction of thrombo-embolic risk in patients with hypertrophic cardiomyopathy (HCM Risk-CVA). *European Journal of Heart Failure* 2015 **17** 837–845. (https://doi.org/10.1002/ejhf.316)

31 Rowin EJ, Maron BJ, Kiernan MS, Casey SA, Feldman DS, Hryniewicz KM, Chan RH, Harris KM, Udelson JE, DeNofrio D, *et al*. Advanced heart failure with preserved systolic function in nonobstructive hypertrophic cardiomyopathy: under-recognized subset of candidates for heart transplant. *Circulation: Heart Failure* 2014 **7** 967–975. (https://doi.org/10.1161/CIRCHEARTFAILURE.114.001435)

32 Biagini E, Spirito P, Rocchi G, Ferlito M, Rosmini S, Lai F, Lorenzini M, Terzi F, Bacchi-Reggiani L, Boriani G, *et al*. Prognostic implications of the Doppler restrictive filling pattern in hypertrophic cardiomyopathy. *American Journal of Cardiology* 2009 **104** 1727–1731. (https://doi.org/10.1016/j.amjcard.2009.07.057)

33 Hang D, Schaff HV, Nishimura RA, Lahr BD, Abel MD, Dearani JA & Ommen SR. Accuracy of jet direction on Doppler echocardiography in identifying the etiology of mitral regurgitation in obstructive hypertrophic cardiomyopathy. *Journal of the American Society of Echocardiography* 2019 **32** 333–340. (https://doi.org/10.1016/j.echo.2018.10.011)

34 Reant P, Dufour M, Peyrou J, Reynaud A, Rooryck C, Dijos M, Vincent C, Cornolle C, Roudaut R & Lafitte S. Upright treadmill vs. semi-supine bicycle exercise echocardiography to provoke obstruction in symptomatic hypertrophic cardiomyopathy: a pilot study. *European Heart Journal Cardiovascular Imaging* 2018 **19** 31–38. (https://doi.org/10.1093/ehjci/jew313)

35 Feiner E, Arabadjian M, Winson G, Kim B, Chaudhry F & Sherrid MV. Post-prandial upright exercise echocardiography in hypertrophic cardiomyopathy. *Journal of the American College of Cardiology* 2013 **61** 2487–2488. (https://doi.org/10.1016/j.jacc.2013.02.079)

36 Zemánek D, Tomašov P, Homolová S, Linhartová K & Veselka J. Sublingual isosorbide dinitrate for the detection of obstruction in hypertrophic cardiomyopathy. *European Journal of Echocardiography* 2011 **12** 684–687. (https://doi.org/10.1093/ejechocard/jer115)

37 Hoit BD. Strain and strain rate echocardiography and coronary artery disease. *Circulation: Cardiovascular Imaging* 2011 **4** 179–190. (https://doi.org/10.1161/CIRCIMAGING.110.959817)

38 Haland TF, Almaas VM, Hasselberg NE, Saberniak J, Leren IS, Hopp E, Edvardsen T & Haugaa KH. Strain echocardiography is related to fibrosis and ventricular arrhythmias in hypertrophic cardiomyopathy. *European Heart Journal Cardiovascular Imaging* 2016 **17** 613–621. (https://doi.org/10.1093/ehjci/jew005)

39 Tower-Rader A, Mohananey D, To A, Lever HM, Popovic ZB & Desai MY. Prognostic value of global longitudinal strain in hypertrophic cardiomyopathy: a systematic review of existing literature. *JACC: Cardiovascular Imaging* 2019 **12** 1930–1942. (https://doi.org/10.1016/j.jcmg.2018.07.016)

40 Nampiaparampil RG, Swistel DG, Schlame M, Saric M & Sherrid MV. Intraoperative two- and three-dimensional transesophageal echocardiography in combined myectomy-mitral operations for hypertrophic cardiomyopathy. *Journal of the American Society of Echocardiography* 2018 **31** 275–288. (https://doi.org/10.1016/j.echo.2017.11.016)

41 Vainrib A, Massera D, Sherrid MV, Swistel DG, Bamira D, Ibrahim H, Staniloae C, Williams MR & Saric M. Three-dimensional imaging and dynamic modeling of systolic anterior motion of the mitral valve. *Journal of the American Society of Echocardiography* 2021 **34** 89–96. (https://doi.org/10.1016/j.echo.2020.08.019)

42 Gersh BJ, Maron BJ, Bonow RO, Dearani JA, Fifer MA, Link MS, Naidu SS, Nishimura RA, Ommen SR, Rakowski H, *et al*. ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy. *Circulation* 2011 **124** e783–e831. (https://doi.org/10.1161/CIR.0b013e318223e2bd)

43 Nistri S, Olivotto I, Betocchi S, Losi MA, Valsecchi G, Pinamonti B, Conte MR, Casazza F, Galderisi M, Maron BJ, *et al*. Prognostic significance of left atrial size in patients with hypertrophic cardiomyopathy (from the Italian Registry for Hypertrophic Cardiomyopathy). *American Journal of Cardiology* 2006 **98** 960–965. (https://doi.org/10.1016/j.amjcard.2006.05.013)

44 Maron MS, Olivotto I, Betocchi S, Casey SA, Lesser JR, Losi MA, Cecchi F & Maron BJ. Effect of left ventricular outflow tract obstruction on clinical outcome in hypertrophic cardiomyopathy. *New England Journal of Medicine* 2003 **348** 295–303. (https://doi.org/10.1056/NEJMoa021332)

45 Harris KM, Spirito P, Maron MS, Zenovich AG, Formisano F, Lesser JR, Mackey-Bojack S, Manning WJ, Udelson JE & Maron BJ. Prevalence, clinical profile, and significance of left ventricular remodeling in the end-stage phase of hypertrophic cardiomyopathy. *Circulation* 2006 **114** 216–225. (https://doi.org/10.1161/CIRCULATIONAHA.105.583500)

46 Augustine DX, Coates-Bradshaw LD, Willis J, Harkness A, Ring L, Grapsa J, Coghlan G, Kaye N, Oxborough D, Robinson S, *et al*. Echocardiographic assessment of pulmonary hypertension: a guideline protocol from the British Society of Echocardiography. *Echo Research and Practice* 2018 **5** G11–G24. (https://doi.org/10.1530/ERP-17-0071)

47 Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, Pennell DJ, Rumberger JA, Ryan T, Verani MS, *et al*. American Heart Association Writing Group on myocardial segmentation and registration for cardiac imaging. *Circulation* 2002 **105** 539–542. (https://doi.org/10.1161/hc0402.102975)

48 Ho CY, Sweitzer NK, McDonough B, Maron BJ, Casey SA, Seidman JG, Seidman CE & Solomon SD. Assessment of diastolic function with Doppler tissue imaging to predict genotype in preclinical hypertrophic cardiomyopathy. *Circulation* 2002 **105** 2992–2997. (https://doi.org/10.1161/01.cir.0000019070.70491.6d)

49 Patel P, Dhillon A, Popovic ZB, Smedira NG, Rizzo J, Thamilarasan M, Agler D, Lytle BW, Lever HM & Desai MY. Left ventricular outflow tract obstruction in hypertrophic cardiomyopathy patients Without severe septal hypertrophy: implications of mitral valve and papillary muscle abnormalities assessed using cardiac magnetic resonance and echocardiography. *Circulation: Cardiovascular Imaging* 2015 **8** e003132. (https://doi.org/10.1161/CIRCIMAGING.115.003132)

Received in final form 30 December 2020
Accepted 25 February 2021
Accepted Manuscript published online 5 March 2021