



## LJMU Research Online

**Turvey, L, Augustine, DX, Robinson, S, Oxborough, D, Stout, M, Smith, N, Harkness, A, Williams, L, Steeds, RP and Bradlow, W**

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

<http://researchonline.ljmu.ac.uk/id/eprint/14624/>

### Article

**Citation** (please note it is advisable to refer to the publisher's version if you intend to cite from this work)

**Turvey, L, Augustine, DX, Robinson, S, Oxborough, D, Stout, M, Smith, N, Harkness, A, Williams, L, Steeds, RP and Bradlow, W (2021) Transthoracic echocardiography of hypertrophic cardiomyopathy in adults: a practical guideline from the British Society of Echocardiography. Echo Research and**

LJMU has developed [LJMU Research Online](#) for users to access the research output of the University more effectively. Copyright © and Moral Rights for the papers on this site are retained by the individual authors and/or other copyright owners. Users may download and/or print one copy of any article(s) in LJMU Research Online to facilitate their private study or for non-commercial research. You may not engage in further distribution of the material or use it for any profit-making activities or any commercial gain.

The version presented here may differ from the published version or from the version of the record. Please see the repository URL above for details on accessing the published version and note that access may require a subscription.

For more information please contact [researchonline@ljmu.ac.uk](mailto:researchonline@ljmu.ac.uk)

<http://researchonline.ljmu.ac.uk/>

1 **Title:** Transthoracic Echocardiographic of Hypertrophic Cardiomyopathy in Adults: A Practical  
2 Guideline from the British Society of Echocardiography

3 **Authors:** Lauren Turvey<sup>1</sup>, Daniel Augustine<sup>2</sup>, Shaun Robinson<sup>3</sup>, David Oxborough<sup>4</sup>, Martin Stout<sup>5</sup>,  
4 Nicola Smith<sup>1</sup>, Allan Harkness<sup>6</sup>, Lynne Williams<sup>7</sup>, Richard Steeds<sup>1</sup> and William Bradlow<sup>1</sup>

5 **Corresponding author's postal and email address**

6 Dr W. Bradlow. Department of Cardiology, University Hospitals Birmingham NHS Foundation Trust,  
7 Mindelsohn Way, Edgbaston, Birmingham, B15 2TH.

8 william.bradlow@uhb.nhs.uk

9 **Authors Institutions:**

- 10 1. Department of Cardiology, University Hospitals Birmingham NHS Foundation Trust,  
11 Birmingham  
12 2. Department of Cardiology, Royal United Hospital Bath, Bath. Department for Health,  
13 University of Bath, Bath, UK.  
14 3. Department of Cardiology, North West Anglia NHS Foundation Trust, Peterborough  
15 4. Research Institute for Sports and Exercise Physiology, Liverpool John Moores University,  
16 Liverpool  
17 5. North West Heart Centre, Wythenshawe Hospital, Manchester University NHS Foundation  
18 Trust, Manchester  
19 6. Department of Cardiology, Colchester Hospital NHS Trust, Colchester  
20 7. Department of Cardiology, Papworth Hospital, Papworth Everard, Cambridge

21 **Short Title:** BSE HCM Guideline

22 **Keywords:** Hypertrophic cardiomyopathy, hypertrophic obstructive cardiomyopathy, guidelines,  
23 echocardiography

24 **Word count:** 8394 (including tables and references)

25

26

1 **Abstract**

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

9

## 1 Intent behind update

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

6 The guideline also proposes an echocardiographic approach to diagnosis as well as information on the  
7 use of echo measurements for sudden death risk stratification. This guideline aims to enhance  
8 baseline knowledge and to allow echocardiographers to develop a systematic approach to the image  
9 acquisition and echocardiographic reporting of patients with proven or suspected HCM. The guideline-  
10 writing committee anticipates that readers armed with this knowledge will approach these  
11 examinations with confidence, extract as much information about each patient's condition as possible  
12 and produce unambiguous, standardised reports. These actions will enhance clinical care by limiting  
13 the number of patients who are either under or over-diagnosed and highlight the sub-cohorts of  
14 patients who need additional investigations and treatments. The guidelines end with short sections  
15 covering the use of echo guidance for transseptal alcohol ablation and surgical myectomy as well as  
16 strain, stress and three-dimensional echocardiography in patients with HCM.

## 17 Hypertrophic Cardiomyopathy

18 HCM in adults is defined '*by a wall thickness  $\geq 15$  mm in one or more left ventricular (LV) myocardial*  
19 *segments that is not explained solely by loading conditions'*(1), for example, hypertension. In a smaller  
20 number of cases, described in the next section, HCM may be associated with an abnormal wall  
21 thickness which measures less than 15mm. This dimension-based diagnosis covers a diverse group of  
22 diseases, both inherited and acquired, which differ in their pathophysiology and management.

23 Due to the challenges in certain aspects of diagnosis and management of this patient group, referral  
24 to specialist centres focused on inherited cardiac conditions and cardiomyopathies is recommended

1 for patients with suspected or confirmed disease(1). Where possible, echocardiographers should  
2 obtain dedicated training in the scanning and interpretation of this patient group.

3 The condition affects between 0.2%(2) and 1.4% of individuals(3). Disease complications are  
4 reasonably common; in a multi-centre longitudinal study of patients with HCM, atrial fibrillation  
5 occurred in 20%, sudden cardiac death or resuscitated cardiac arrest in 4%(4) and left ventricular  
6 systolic dysfunction (ejection fraction <50%) in 8%(5).

7 The pattern of inheritance is autosomal dominant. A clinically meaningful gene change (found  
8 predominantly in MYBPC3 and MYH7) occurs in a fifth of patients where the family history is negative,  
9 and a half where it is positive(6). Finding a disease-causing gene change allows testing of family  
10 members using pre-symptomatic screening.

#### 11 Echocardiography's Position in the Diagnostic Pathway – Wall thickness

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

15 Measurements should be made in short-axis views orthogonal to the circumference of the  
16 endocardium and epicardium, wherever maximal wall thickness occurs. Elements attached to but not  
17 incorporated in the septum should be excluded (Figure 1), as this will overestimate wall thickness and  
18 run the risk of misdiagnosis of HCM. The report should state if the study failed to visualise any part of  
19 the LV (often the basal anterior and anterolateral walls) and recommend alternative imaging  
20 modalities, specifically cardiovascular magnetic resonance.

21 The dimensional threshold for HCM depends on the location of hypertrophy as well as the clinical  
22 context. In apical HCM, where normal tapering of both cavity and epicardium is lost, the apical wall  
23 thickness may be less than 15 mm(7). One criterion defines apical HCM when the ratio between apical  
24 and basal wall thickness exceeds 1.3: 1(8). Visualisation of this area can be difficult and may require

1 the use of myocardial contrast (Figure 2). By ensuring the apical four, two and three-chamber view  
2 section the apex, the echocardiographer will avoid giving the impression of apical hypertrophy by  
3 foreshortening views. Apical wall thickness should be measured in the short-axis view, ensuring the  
4 cut is not oblique to the long axes of the LV.

5 In first-degree relatives - who have a 50% risk of inheriting the causative gene - the wall thickness  
6 threshold for diagnosis of HCM is  $\geq 13$  mm (1). The yield of positive screening examinations in first  
7 degree relatives vary based on the population tested; in one report, 5% of first-degree relative children  
8 were diagnosed with HCM(9), rising to 30 % of a mainly adult cohort in another, where many had a  
9 disease-causing gene(10). A feature of HCM is age-related penetrance, where the percentage of  
10 individuals carrying the disease-causing gene who express the condition increases with age. The yield  
11 of clinical screening is higher in families where the disease onset has been in childhood(9,10).

12 HCM featuring the so-called dilated-hypokinetic or 'burnt-out' phase (5), or due to specific gene  
13 mutations(11–13), can be associated with only mild increases in wall thickness.

#### 14 Grey Cases

15 Ethnicity, hypertension, renal disease, significant aortic stenosis, increased body mass index and  
16 athletic remodelling all influence left ventricular hypertrophy. Increased LV wall thickness secondary  
17 to these processes may fall into a 'grey zone', overlapping with the degree of LV hypertrophy (LVH)  
18 seen in HCM (Figure 3). For example, a wall thickness of 15 -20 mm can occur in hypertensive heart  
19 disease in individuals of African/Afro-Caribbean ethnicity, whereas the same degree of hypertrophy  
20 in a Caucasian hypertensive patient would suggest HCM(1). LVH in hypertensive heart disease and  
21 athletic remodelling tends to be uniform and symmetrical.

22 In athletes, gender, in addition to ethnicity, is relevant. Wall thickness is lower in female athletes than  
23 their male counterparts and does not exceed 13 mm in Caucasian athletes or 15 mm in athletes of  
24 African/Afro-Caribbean ethnicity(14). In a study of athletes with HCM compared with athletes without

1 HCM(15), the diagnosis was definite in most individuals as maximal wall thickness was >16 mm, and  
2 often the LVH was distributed non-uniformly. The scenario in which there was uncertainty – where  
3 LVH was 13-16 mm and concentric (defined by a relative wall thickness of >0.42 (see BSE guidelines  
4 on normal reference intervals for cardiac dimensions and function for more information (16)) –  
5 cropped up in only 14% of athletes with HCM. Measures like left ventricular cavity size (previously  
6 reported to be a useful differentiator between HCM and athletic heart; being larger in the latter (17))  
7 showed modest performance in picking out athletes with HCM. Additional tests were required to  
8 distinguish these individuals from athletes with physiological remodelling.

### 9 Recommended Language in Echocardiography Report

10 Echocardiography's pivotal role means that a study's interpretation can strongly influence the clinical  
11 team's diagnostic decision. Because of this, we encourage the use of standardised language when  
12 reporting. In instances where there is uncertainty, '*raises the possibility of HCM*' is recommended. In  
13 individuals undergoing screening, where there is no evidence of left ventricular hypertrophy, the  
14 conclusion should contain the following suggested phrase: '*wall thickness is normal*'. The proposed  
15 language provides an objective statement about the echocardiogram findings, rather than a definitive  
16 clinical assertion. Hence '*wall thickness is normal*' is not the same as '*does not have HCM*'.  
17 Echocardiographers should exercise their judgement, but when the echocardiographic images show  
18 unequivocal evidence of HCM in an appropriate clinical context (clear-cut apical HCM, gross  
19 hypertrophy in a young patient and definite LVH in a screening echocardiogram), the phrase  
20 '*consistent with HCM*' should be used.

### 21 Post-echocardiography Work-Up

22 In patients with suspected HCM, the clinical team will contextualise the echocardiography report with  
23 information regarding past medical and family history, blood tests and ECG results, and often  
24 cardiovascular magnetic resonance. In grey cases, clinicians judge whether the degree of hypertrophy  
25 matches the severity of the comorbidity (Figure 3). Clarification of the diagnosis in these instances is

1 possible after assessing the response of wall thickness and LV mass to a sustained period of reduced  
2 afterload, for example, improved blood pressure control in the hypertensive patient, weight loss in  
3 the obese individual, aortic valve replacement in the patient with severe aortic stenosis or cessation  
4 of training in the athlete(18). In exceptional cases where there is non-apical hypertrophy measuring  
5 less than 15 mm, and an ECG highly suggestive of underlying cardiomyopathy, the clinical team might  
6 screen first-degree family members to look for clear-cut evidence of HCM. Given the likelihood of  
7 finding a negative result on gene testing of confirmed cases, it is rarely used as a diagnostic tool when  
8 there is ambiguity about the diagnosis.

### 9 Phenocopies

10 It is possible to find within the population of patients with hypertrophic cardiomyopathy rarer  
11 conditions, called phenocopies or 'mimics'(19). In general, these will come to light during clinical  
12 evaluation of the patient's medical history, family history, physical examination and the results of  
13 blood tests, including genetics, and other imaging modalities. However, there are particular features,  
14 termed 'red flags', which should alert the echocardiographer to the possibility of a phenocopy (Table  
15 1). Of these, cardiac amyloidosis is the most obvious due to its classical signs: increased biventricular  
16 wall thickness, poor long axis function, relative sparing of apical longitudinal contraction and global  
17 longitudinal strain (although not pathognomonic of amyloid), interatrial and valvar thickening,  
18 pericardial effusion, and mismatch between the degree of LVH seen on echo and low amplitude  
19 voltages on ECG. Diagnosing HCM should be avoided immediately after an acute cardiac injury such  
20 as myocarditis as the myocardium becomes oedematous and thickened; these changes resolve with  
21 time.

### 22 Defining the pattern of hypertrophy in HCM

23 The echocardiographic report should detail the distribution of LVH using the schema described in  
24 Figure 4 as this informs the clinical team of the likelihood of finding a disease-causing gene change;  
25 being highest in patients with a reverse curvature pattern and lowest in those with a sigmoid septal



1 pattern(20). Right ventricular hypertrophy is present in around 20% of patients with HCM. The  
2 echocardiographer should report this as it occurs in disease mimics; however, it does not add to the  
3 likelihood of finding a disease-causing mutation.

4 Hypertrophy can also extend to the papillary muscles, which can contribute to mid-cavity obstruction.  
5 Additional morphological abnormalities of papillary muscles in HCM which can cause LVOT obstruction  
6 include antero-apical displacement, double bifid(21) and anomalous papillary muscles which insert  
7 directly into the mitral valve leaflets(22,23). Bands running between the apex and basal anteroseptal  
8 wall are seen in HCM(24).

### 9 Echo assessment in risk stratification and disease complications

10 Risk stratification of sudden death is the process clinicians follow to decide which patients should  
11 receive an implantable cardioverter-defibrillator. Using the European Society of Cardiology (ESC)  
12 calculator(1), it is possible to generate an estimate of the five-year risk of sudden death and categorise  
13 patients into low, intermediate, and high-risk groups. Echocardiography provides three of the seven  
14 parameters required in the online tool (maximal wall thickness, LVOT gradient and 2D parasternal long  
15 axis left atrial size). To allow this critical information to be accessed rapidly by the referring clinician,  
16 the conclusion for every report in a patient with suspected or confirmed HCM should contain these  
17 parameters. Although not in the ESC risk calculator, the presence of left ventricular impairment(5) and  
18 an apical aneurysm(25) is also essential to include in the study conclusion as they modify risk of sudden  
19 cardiac death.

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

1 Heart failure can occur due to systolic impairment, diastolic dysfunction and LVOT obstruction. As a  
2 measure of systolic function, ejection fraction (EF) can be misleading in HCM being normal even when  
3 markers of systolic dysfunction such as abnormal regional wall motion and global longitudinal  
4 strain(26) (see the section below) are present. Nonetheless, the absolute value helps clinical teams to  
5 identify patients in whom systolic dysfunction is likely to develop (50-60%) and those in whom it is  
6 overt (<50%)(5). Accurately determining EF using Simpson's biplane, and three-dimensional  
7 quantification where possible, and highlighting instances when this measurement is discordant with  
8 the systolic function will aid clinical management. Longitudinal systolic function should be assessed  
9 using tissue doppler imaging and in select cases strain (see section below), while radial systolic  
10 function should be assessed visually. Outcomes are generally adverse once the EF falls below 50% (5).  
11 Below this level, clinical teams should consider medications(1), heart transplant(1) and device therapy  
12 (27).

13 Diastolic dysfunction is common in HCM and results in elevated filling pressures and dilatation of the  
14 left atrium, whose diameter in the parasternal long axis is a predictor of sudden death in the ESC risk  
15 calculator (28), and of stroke and other thromboembolic events (29). Accurate classification of  
16 diastolic function grade is challenging in HCM due to the concomitant presence of left ventricular  
17 outflow tract obstruction and mitral regurgitation in many patients. Many independent echo variables  
18 have weak correlations with filling pressures. As such integration of several parameters is necessary  
19 to quantify diastolic function accurately. Diastolic function assessment should include Doppler tissue  
20 imaging and pulmonary vein Ar timings as per BSE guidelines(30).

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

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

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

15 In patients who fail to respond to medical therapy directed at relief of LVOT obstruction, invasive  
16 septal reduction therapies (surgical myectomy and alcohol septal ablation) are considered. Given the  
17 potential complications of invasive therapies, it is important that patients fulfil the necessary clinical,  
18 anatomical, and hemodynamic criteria to determine suitability for a procedure, and this decision is  
19 based heavily on the echocardiographic assessment.

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

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

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

### 17 Stress Imaging in HCM

18 By imaging the heart during controlled exercise, stress echocardiography can unmask latent  
19 obstruction in symptomatic patients whose baseline transthoracic echocardiography – despite the  
20 previously described physiological manoeuvres – has not shown LVOT gradients  $\geq 50$  mmHg.  
21 Symptom-limited exercise is safe using an exercise bike or treadmill. There is some evidence to suggest  
22 that treadmill exercise can provoke higher LVOT gradients compared to semi-supine bicycle  
23 exercise(34). Dobutamine is not employed in HCM since this infusion can induce LVOTO in normal  
24 subjects. When the patient has reached peak exercise, images are obtained within 60-90 seconds to  
25 detect obstruction which can be present before or after the patient's heart rate reaches 85% of target

1 heart rate. The protocol in Table 7 suggests an optimal scanning order to utilise peak heart rate with  
2 minimal changes to the acoustic window. Table 8 illustrates the data acquired in each step of the  
3 protocol. In specific scenarios, the echocardiographer can employ additional measures to provoke  
4 LVOT obstruction. For patients with postprandial symptoms, exercise after eating is useful(35) while  
5 for those who cannot exercise, administering GTN spray can unmask obstruction(36).

6

### 7 Strain Imaging in HCM

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

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

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

## 1 Three-dimensional echocardiography

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

## 9 Recommendations

10 The echocardiogram report conclusion should include:

- 11 1. The following suggested phrases: when there is uncertainty: *raises the possibility of HCM*;  
12 when there is unequivocal evidence of HCM: *consistent with HCM*; for screening scans with  
13 no LVH: *wall thickness is normal*.
- 14 2. The presence of red flags pointing to a phenocopy.
- 15 3. The pattern of LVH: sigmoid septal, reverse curvature, apical or neutral.
- 16 4. The values for maximal wall thickness, LVOT gradient and LA size.
- 17 5. The presence or absence of disease complications.
  - 18 a. Left ventricular cavity size
  - 19 b. Systolic dysfunction with EF 50-60%, EF<50%.
  - 20 c. Diastolic dysfunction, specifically the presence of a restrictive filling pattern with  
21 preserved ejection fraction.
  - 22 d. Systolic anterior motion, mitral regurgitation, LVOT obstruction and other forms of  
23 obstruction; at rest and with provocation. Evidence of intrinsic mitral valve disease.
  - 24 e. Aneurysm formation.

1        6. Image quality, completeness of LV visualisation and need for contrast and transoesophageal  
2            echocardiography, and cardiovascular magnetic resonance.

3    Conclusion

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

8

## 1 **Declaration of Interest**

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

## 4 **Funding**

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

7

## 8 **Figure Titles**

9 Figure 1. Measurement of Wall Thickness by Echocardiography

10 Figure 2. Use of Contrast in Apical Hypertrophic Cardiomyopathy

11 Figure 3. Thinking Underlying Clinical Decision-Making in HCM

12 Figure 4. Different Phenotypes of Left Ventricular Hypertrophy in Hypertrophic Cardiomyopathy

## 13 **Figure Legends**

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

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

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

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



1

2

## 1 References

- 2 1. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: The Task  
3 Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European  
4 Society of Cardiology (ESC). *Eur Heart J*. 2014 Oct 14;35(39):2733–79.
- 5 2. Maron BJ, Gardin JM, Flack JM, Gidding SS, Kurosaki TT, Bild DE. Prevalence of Hypertrophic  
6 Cardiomyopathy in a General Population of Young Adults: Echocardiographic Analysis of 4111  
7 Subjects in the CARDIA Study. *Circulation*. 1995 Aug 15;92(4):785–9.
- 8 3. Massera D, McClelland RL, Ambale-Venkatesh B, Gomes AS, Hundley WG, Kawel-Boehm N, et  
9 al. Prevalence of Unexplained Left Ventricular Hypertrophy by Cardiac Magnetic Resonance  
10 Imaging in MESA. *J Am Heart Assoc*. 2019 Apr 6;8(8).
- 11 4. Ho CY, Day SM, Ashley EA, Michels M, Pereira AC, Jacoby D, et al. Genotype and Lifetime  
12 Burden of Disease in Hypertrophic Cardiomyopathy. *Circulation*. 2018 Oct 2;138(14):1387–98.
- 13 5. Marstrand P, Han L, Day SM, Olivotto I, Ashley EA, Michels M, et al. Hypertrophic  
14 Cardiomyopathy With Left Ventricular Systolic Dysfunction: Insights From the SHaRe Registry.  
15 *Circulation*. 2020 Apr 28;141(17):1371–83.
- 16 6. Alfares AA, Kelly MA, McDermott G, Funke BH, Lebo MS, Baxter SB, et al. Results of clinical  
17 genetic testing of 2,912 probands with hypertrophic cardiomyopathy: expanded panels offer  
18 limited additional sensitivity. *Genet Med*. 2015 Nov;17(11):880–8.
- 19 7. Flett AS, Maestrini V, Milliken D, Fontana M, Treibel TA, Harb R, et al. Diagnosis of apical  
20 hypertrophic cardiomyopathy: T-wave inversion and relative but not absolute apical left  
21 ventricular hypertrophy. *International Journal of Cardiology*. 2015 Mar;183:143–8.
- 22 8. Suzuki J, Shimamoto R, Nishikawa J, Yamazaki T, Tsuji T, Nakamura F, et al. Morphological  
23 onset and early diagnosis in apical hypertrophic cardiomyopathy: a long term analysis with  
24 nuclear magnetic resonance imaging. *J Am Coll Cardiol*. 1999 Jan;33(1):146–51.
- 25 9. Norrish G, Jager J, Field E, Quinn E, Fell H, Lord E, et al. Yield of Clinical Screening for  
26 Hypertrophic Cardiomyopathy in Child First-Degree Relatives. *Circulation*. 2019 Jul  
27 16;140(3):184–92.
- 28 10. van Velzen H, Schinkel A, Baart S, Oldenburg R, Frohn-Mulder I, van Slegtenhorst M, et al.  
29 Outcomes of Contemporary Family Screening in Hypertrophic Cardiomyopathy. *Circulation:  
30 Genomic and Precision Medicine*. 2018 Apr 1;11(4):e001896.
- 31 11. Coppini R, Ho CY, Ashley E, Day S, Ferrantini C, Girolami F, et al. Clinical Phenotype and  
32 Outcome of Hypertrophic Cardiomyopathy Associated With Thin-Filament Gene Mutations. *J  
33 Am Coll Cardiol*. 2014 Dec 23;64(24):2589–600.
- 34 12. van Velzen HG, Schinkel AFL, Oldenburg RA, van Slegtenhorst MA, Frohn-Mulder IME, van der  
35 Velden J, et al. Clinical Characteristics and Long-Term Outcome of Hypertrophic  
36 Cardiomyopathy in Individuals With a MYBPC3 (Myosin-Binding Protein C) Founder Mutation.  
37 *Circ Cardiovasc Genet* [Internet]. 2017 Aug [cited 2020 Nov 15];10(4). Available from:  
38 <https://www.ahajournals.org/doi/10.1161/CIRCGENETICS.116.001660>

- 1 13. Page SP, Kounas S, Syrris P, Christiansen M, Frank-Hansen R, Andersen PS, et al. Cardiac myosin  
2 binding protein-C mutations in families with hypertrophic cardiomyopathy: disease expression  
3 in relation to age, gender, and long term outcome. *Circ Cardiovasc Genet*. 2012 Apr  
4 1;5(2):156–66.
- 5 14. Sheikh N, Papadakis M, Carre F, Kervio G, Panoulas VF, Ghani S, et al. Cardiac adaptation to  
6 exercise in adolescent athletes of African ethnicity: an emergent elite athletic population. *Br J*  
7 *Sports Med*. 2013 Jun;47(9):585–92.
- 8 15. Sheikh N, Papadakis M, Schnell F, Panoulas V, Malhotra A, Wilson M, et al. Clinical Profile of  
9 Athletes With Hypertrophic Cardiomyopathy. *Circ Cardiovasc Imaging*. 2015 Jul;8(7):e003454.
- 10 16. Harkness A, Ring L, Augustine DX, Oxborough D, Robinson S, Sharma V. Normal reference  
11 intervals for cardiac dimensions and function for use in echocardiographic practice: a guideline  
12 from the British Society of Echocardiography. *Echo Research and Practice*. 2020 Mar 1;7(1):G1–  
13 18.
- 14 17. Caselli S, Maron MS, Urbano-Moral JA, Pandian NG, Maron BJ, Pelliccia A. Differentiating Left  
15 Ventricular Hypertrophy in Athletes from That in Patients With Hypertrophic Cardiomyopathy.  
16 *The American Journal of Cardiology*. 2014 Nov;114(9):1383–9.
- 17 18. Pelliccia A, Maron BJ, De Luca R, Di Paolo FM, Spataro A, Culasso F. Remodeling of Left  
18 Ventricular Hypertrophy in Elite Athletes After Long-Term Deconditioning. *Circulation*. 2002  
19 Feb 26;105(8):944–9.
- 20 19. Rapezzi C, Arbustini E, Caforio ALP, Charron P, Gimeno-Blanes J, Heliö T, et al. Diagnostic work-  
21 up in cardiomyopathies: bridging the gap between clinical phenotypes and final diagnosis. A  
22 position statement from the ESC Working Group on Myocardial and Pericardial Diseases. *Eur*  
23 *Heart J*. 2013 May 14;34(19):1448–58.
- 24 20. Binder J, Ommen SR, Gersh BJ, Van Driest SL, Tajik AJ, Nishimura RA, et al. Echocardiography-  
25 guided genetic testing in hypertrophic cardiomyopathy: septal morphological features predict  
26 the presence of myofilament mutations. *Mayo Clin Proc*. 2006 Apr;81(4):459–67.
- 27 21. Kwon DH, Setser RM, Thamilarasan M, Popovic ZV, Smedira NG, Schoenhagen P, et al.  
28 Abnormal papillary muscle morphology is independently associated with increased left  
29 ventricular outflow tract obstruction in hypertrophic cardiomyopathy. *Heart*. 2008 Oct  
30 1;94(10):1295–301.
- 31 22. Klues HG, Roberts WC, Maron BJ. Anomalous insertion of papillary muscle directly into anterior  
32 mitral leaflet in hypertrophic cardiomyopathy. Significance in producing left ventricular outflow  
33 obstruction. *Circulation*. 1991 Sep;84(3):1188–97.
- 34 23. Lentz Carvalho J, Schaff HV, Morris CS, Nishimura RA, Ommen SR, Maleszewski JJ, et al.  
35 Anomalous papillary muscles-Implications in the surgical treatment of hypertrophic obstructive  
36 cardiomyopathy. *J Thorac Cardiovasc Surg*. 2020 Apr 15;
- 37 24. Gruner C, Chan RH, Crean A, Rakowski H, Rowin EJ, Care M, et al. Significance of left ventricular  
38 apical–basal muscle bundle identified by cardiovascular magnetic resonance imaging in  
39 patients with hypertrophic cardiomyopathy. *Eur Heart J*. 2014 Oct 14;35(39):2706–13.

- 1 25. Rowin E, Maron B, Haas T, Garberich R, Wang W, Link M, et al. Hypertrophic Cardiomyopathy  
2 With Left Ventricular Apical Aneurysm: Implications for Risk Stratification and Management. *J*  
3 *Am Coll Cardiol*. 2017 21;69(7):761–73.
- 4 26. Hiemstra Y, Debonnaire P, Bootsma M, van Zwet E, Delgado V, Schalij M, et al. Global  
5 Longitudinal Strain and Left Atrial Volume Index Provide Incremental Prognostic Value in  
6 Patients With Hypertrophic Cardiomyopathy. *Circulation: Cardiovascular Imaging*. 2017 Jul  
7 1;10(7):e005706.
- 8 27. Maron MS, Rowin EJ, Wessler BS, Mooney PJ, Fatima A, Patel P, et al. Enhanced American  
9 College of Cardiology/American Heart Association Strategy for Prevention of Sudden Cardiac  
10 Death in High-Risk Patients With Hypertrophic Cardiomyopathy. *JAMA Cardiol*. 2019 Jul  
11 1;4(7):644.
- 12 28. O'Mahony C, Jichi F, Pavlou M, Monserrat L, Anastasakis A, Rapezzi C, et al. A novel clinical risk  
13 prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCM risk-SCD).  
14 *Eur Heart J*. 2014 Aug 7;35(30):2010–20.
- 15 29. Guttmann OP, Pavlou M, O'Mahony C, Monserrat L, Anastasakis A, Rapezzi C, et al. Prediction  
16 of thrombo-embolic risk in patients with hypertrophic cardiomyopathy (HCM Risk-CVA). *Eur J*  
17 *Heart Fail*. 2015 Aug;17(8):837–45.
- 18 30. BSE Guidelines for Diastolic Function - in press.
- 19 31. Rowin E, Maron B, Kiernan M, Casey S, Feldman D, Hryniewicz K, et al. Advanced Heart Failure  
20 With Preserved Systolic Function in Nonobstructive Hypertrophic Cardiomyopathy. *Circulation:*  
21 *Heart Failure*. 2014 Nov 1;7(6):967–75.
- 22 32. Biagini E, Spirito P, Rocchi G, Ferlito M, Rosmini S, Lai F, et al. Prognostic Implications of the  
23 Doppler Restrictive Filling Pattern in Hypertrophic Cardiomyopathy. *The American Journal of*  
24 *Cardiology*. 2009 Dec 15;104(12):1727–31.
- 25 33. Hang D, Schaff HV, Nishimura RA, Lahr BD, Abel MD, Dearani JA, et al. Accuracy of Jet Direction  
26 on Doppler Echocardiography in Identifying the Etiology of Mitral Regurgitation in Obstructive  
27 Hypertrophic Cardiomyopathy. *Journal of the American Society of Echocardiography*. 2019 Mar  
28 1;32(3):333–40.
- 29 34. Reant P, Dufour M, Peyrou J, Reynaud A, Rooryck C, Dijos M, et al. Upright treadmill vs. semi-  
30 supine bicycle exercise echocardiography to provoke obstruction in symptomatic hypertrophic  
31 cardiomyopathy: a pilot study. *European Heart Journal - Cardiovascular Imaging*. 2018 Jan  
32 1;19(1):31–8.
- 33 35. Feiner E, Arabadjian M, Winson G, Kim B, Chaudhry F, Sherrid MV. Post-Prandial Upright  
34 Exercise Echocardiography in Hypertrophic Cardiomyopathy. *Journal of the American College*  
35 *of Cardiology*. 2013 Jun;61(24):2487–8.
- 36 36. Zemánek D, Tomašov P, Homolová S, Linhartová K, Veselka J. Sublingual isosorbide dinitrate for  
37 the detection of obstruction in hypertrophic cardiomyopathy. *Eur J Echocardiogr*. 2011 Sep  
38 1;12(9):684–7.
- 39 37. Hoit BD. Strain and Strain Rate Echocardiography and Coronary Artery Disease. *Circ Cardiovasc*  
40 *Imaging*. 2011 Mar;4(2):179–90.

- 1 38. Haland TF, Almaas VM, Hasselberg NE, Saberniak J, Leren IS, Hopp E, et al. Strain  
2 echocardiography is related to fibrosis and ventricular arrhythmias in hypertrophic  
3 cardiomyopathy. *Eur Heart J Cardiovasc Imaging*. 2016 Jun;17(6):613–21.
- 4 39. Tower-Rader A, Mohananeey D, To A, Lever HM, Popovic ZB, Desai MY. Prognostic Value of  
5 Global Longitudinal Strain in Hypertrophic Cardiomyopathy: A Systematic Review of Existing  
6 Literature. *JACC: Cardiovascular Imaging*. 2019 Oct 1;12(10):1930–42.
- 7 40. Nampiaparampil RG, Swistel DG, Schlame M, Saric M, Sherrid MV. Intraoperative Two- and  
8 Three-Dimensional Transesophageal Echocardiography in Combined Myectomy-Mitral  
9 Operations for Hypertrophic Cardiomyopathy. *Journal of the American Society of  
10 Echocardiography*. 2018 Mar 1;31(3):275–88.
- 11 41. Vainrib A, Massera D, Sherrid MV, Swistel DG, Bamira D, Ibrahim H, et al. Three-Dimensional  
12 Imaging and Dynamic Modeling of Systolic Anterior Motion of the Mitral Valve. *J Am Soc  
13 Echocardiogr*. 2020 Oct 12;
- 14 42. Gersh B, Maron B, Bonow R, Dearani J, Fifer M, Link M, et al. 2011 ACCF/AHA Guideline for the  
15 Diagnosis and Treatment of Hypertrophic Cardiomyopathy. *Circulation*. 2011 Dec  
16 13;124(24):e783–831.
- 17 43. Nistri S, Olivotto I, Betocchi S, Losi MA, Valsecchi G, Pinamonti B, et al. Prognostic significance  
18 of left atrial size in patients with hypertrophic cardiomyopathy (from the Italian Registry for  
19 Hypertrophic Cardiomyopathy). *Am J Cardiol*. 2006 Oct 1;98(7):960–5.
- 20 44. Maron MS, Olivotto I, Betocchi S, Casey SA, Lesser JR, Losi MA, et al. Effect of Left Ventricular  
21 Outflow Tract Obstruction on Clinical Outcome in Hypertrophic Cardiomyopathy. *New England  
22 Journal of Medicine*. 2003 Jan 23;348(4):295–303.
- 23 45. Harris K, Spirito P, Maron M, Zenovich A, Formisano F, Lesser J, et al. Prevalence, Clinical  
24 Profile, and Significance of Left Ventricular Remodeling in the End-Stage Phase of Hypertrophic  
25 Cardiomyopathy. *Circulation*. 2006 Jul 18;114(3):216–25.
- 26 46. Augustine DX, Coates-Bradshaw LD, Willis J, Harkness A, Ring L, Grapsa J, et al.  
27 Echocardiographic assessment of pulmonary hypertension: a guideline protocol from the  
28 British Society of Echocardiography. *Echo Res Pract*. 2018 May 11;5(3):G11–24.
- 29 47. American Heart Association Writing Group on Myocardial Segmentation and Registration for  
30 Cardiac Imaging; Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, et al.  
31 Standardized Myocardial Segmentation and Nomenclature for Tomographic Imaging of the  
32 Heart: A Statement for Healthcare Professionals From the Cardiac Imaging Committee of the  
33 Council on Clinical Cardiology of the American Heart Association. *Circulation*. 2002 Jan  
34 29;105(4):539–42.
- 35 48. Ho C, Sweitzer N, McDonough B, Maron B, Casey S, Seidman J, et al. Assessment of diastolic  
36 function with Doppler tissue imaging to predict genotype in preclinical hypertrophic  
37 cardiomyopathy. *Circulation*. 2002 Jun 25;105(25):2992–7.
- 38 49. Patel P, Dhillon A, Popovic ZB, Smedira NG, Rizzo J, Thamilarsan M, et al. Left Ventricular  
39 Outflow Tract Obstruction in Hypertrophic Cardiomyopathy Patients Without Severe Septal  
40 Hypertrophy: Implications of Mitral Valve and Papillary Muscle Abnormalities Assessed Using  
41 Cardiac Magnetic Resonance and Echocardiography. *Circ Cardiovasc Imaging*. 2015  
42 Jul;8(7):e003132.

1

1 **Tables**2 **Table 1. Echocardiographic Clues to the Presence of Phenocopies**

<b>Condition</b>	<b>Echocardiographic 'Red Flags' which raise the possibility of a phenocopy *</b>
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

3 \*Adapted from Rapezzi et al(19) and Elliott et al(1).

4

5

1 **Table 2. Definition of LVOT obstruction.**

<b>LVOT gradient at rest and with physiological provocation</b>	<b>Definition</b>
Gradient $\geq 30$ mmHg at rest	Basal or resting obstruction
Gradient $\leq 30$ mmHg at rest and $\leq 30$ mmHg after provocation	Non-obstructive
Gradient $\leq 30$ mmHg at rest but $> 30$ mmHg with physiological provocation	Labile, provokable or dynamic obstruction

2 Adapted from Gersh et al. (42)

3 **Table 3. Use of Echocardiography When Determining Optimal Invasive Septal Reduction Approach**

<b>Favours surgical myectomy</b>	<b>Aligned with alcohol ablation strategy</b>	<b>Unfavourable for either</b>
Septal thickness $> 25$ mm	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		

4

5

6

7

8

9

10

11



1

2 **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 (28), with >48 mm predicting all-cause mortality(43). Risk of thromboembolism increases exponentially (29)	In risk calculator. If LA >45mm, for six to twelve monthly ambulatory monitoring
Indexed Left atrial volume	>34 mL/m <sup>2</sup> predicts all-cause mortality, heart transplantation, sudden cardiac death, and appropriate implantable cardioverter-defibrillator therapy (26)	
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(28)	In risk calculator
Left ventricular outflow tract obstruction	>30 mmHg predictor of sudden cardiac death and heart failure(28,44)	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

3

4 **Table 5. Minimum Dataset**

Structure and Function	Measurement			
	Left atrium size	Diameter (mm)		Indexed biplane volume (mL/m <sup>2</sup> )
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	Septum at basal	Anterior wall at	Lateral wall at basal	Inferior wall at basal

3

thickness in short axis view	level, papillary muscle level and apex level (mm)	basal level, papillary muscle level and apex level (mm)	level, papillary muscle level and apex level (mm)	level, papillary muscle level and apex 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 <sup>2</sup> )	End-systolic Volume (ml), indexed to body surface area (ml/m <sup>2</sup> )	Systolic 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	


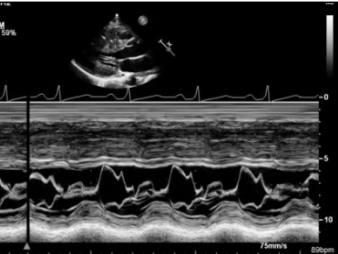

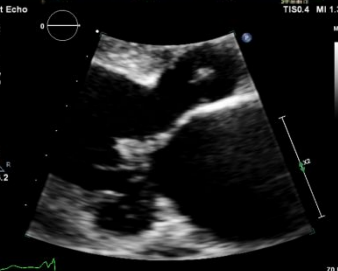
- 1
  - In individuals being screened for HCM

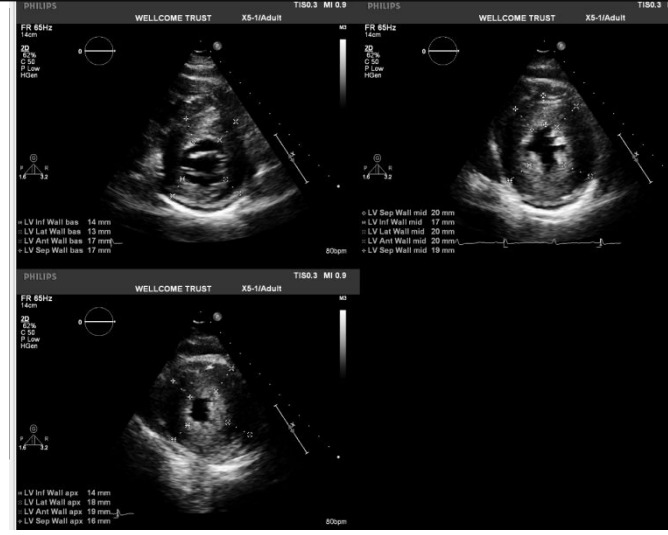
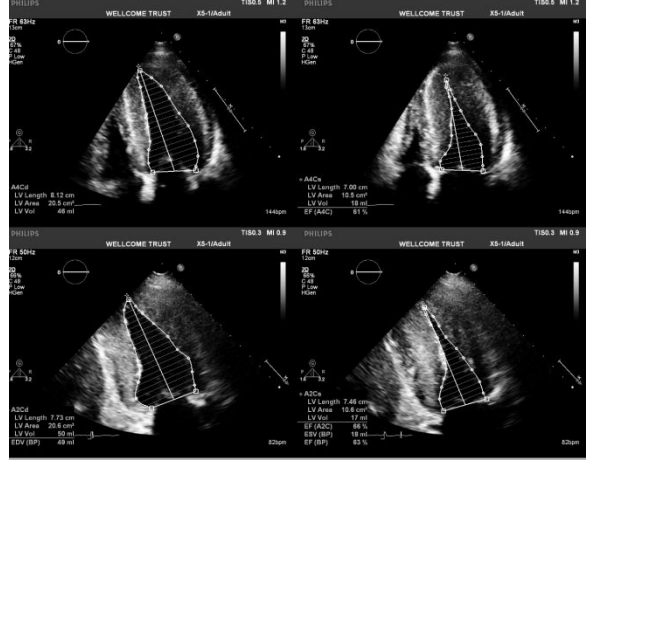
- 2

- 3

1 **Table 6. Transthoracic HCM protocol**

2

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 (16). 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 echogenicity occurs in the basal anteroseptal wall due to fibrosis where leaflet contact occurs due to SAM.	

<p>LV wall thickness measurement</p>	<p>SAX MV level Papillary level Apex level</p>	<p>2D Units: mm</p>	<p>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.</p>	
<p>LV Simpson's Biplane volumes and ejection fraction</p>	<p>A4C, A2C</p>	<p>2D Units: mL/m<sup>2</sup> and %</p>	<p>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)(16). Volumes are indexed to</p>	

			BSA.	
LA biplane volume	A4C,A2C	<p>2D biplane volume using independent A4C and A2C views.</p> <p>Units: ml/m<sup>2</sup></p>	<p>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(16,30).</p> <p>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.</p>	

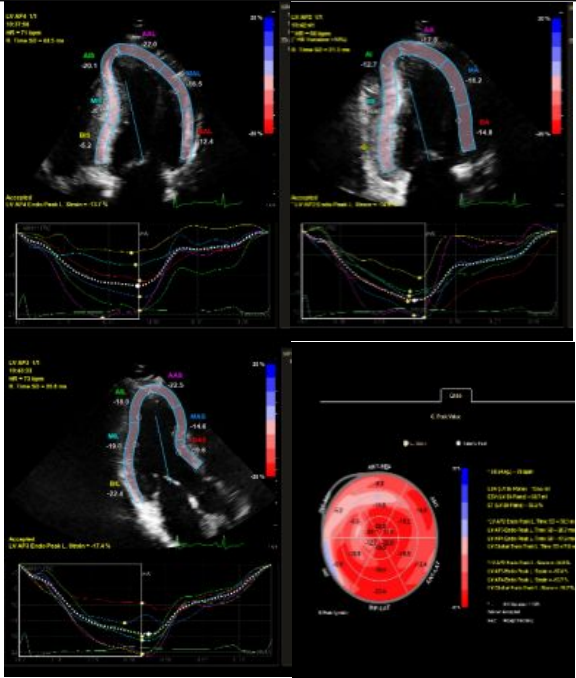
<p>TDI velocities in all four walls</p>	<p>A4C, A2C</p>	<p>PW TDI Units: cm/s</p>	<p>Systolic (Sm), early (E') and atrial (A') relaxation velocities at anterolateral and inferoseptal walls(30).</p> <p>In screening studies, there is an argument for averaging E' across anterolateral, inferoseptal, inferior and anterior LV annulus as a value &lt;13.5 cm/s can be useful in identifying genotype positive phenotype negative individuals(48).</p>	
---	-----------------	-------------------------------	---	--

Global longitudinal strain (GLS)

A4C, A2C, A3C

2D  
Units: -%

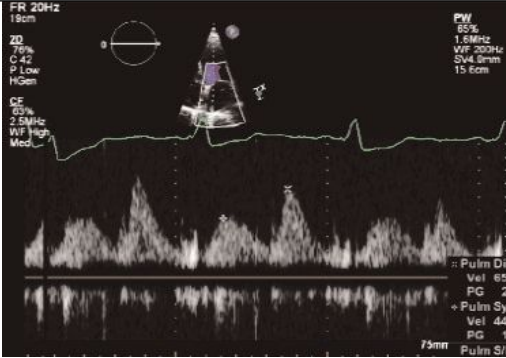
This is recommended when cardiac amyloidosis or athletic remodelling are being considered. Average global longitudinal strain (GLS) is calculated using the apical long axis (A3C), four chamber A4C and two chamber A2C standard views. High quality image acquisition, maintaining a frame rate of 40 to 90 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.

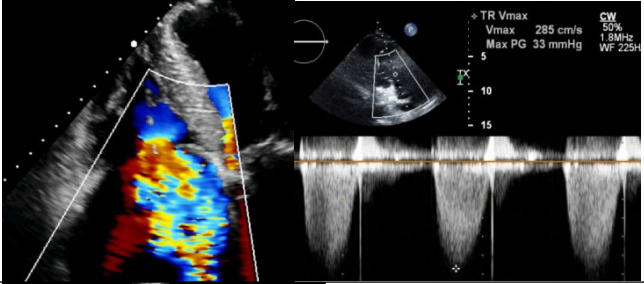
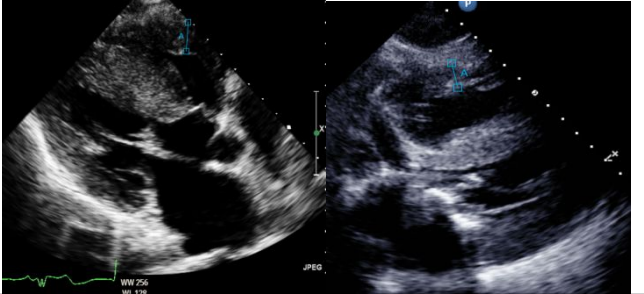
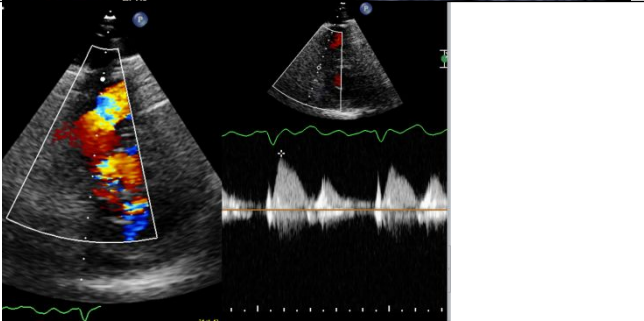


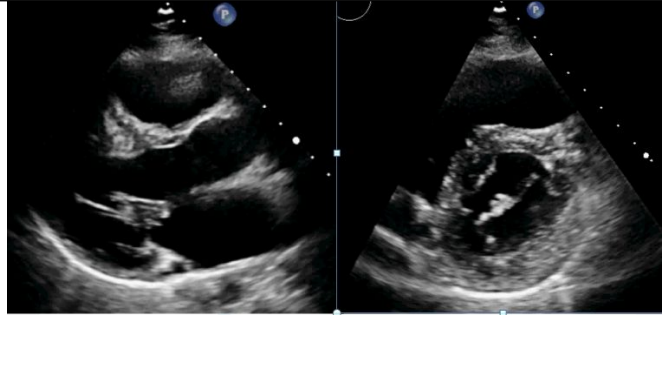



LVOT or intra-cavity obstruction gradients	A4C, A5C	<p>CW Doppler (or PW with HPRF as a significant gradient will alias on PW Doppler). Sampling PW Doppler throughout the LV cavity is a useful tool to pinpoint the exact location of obstruction if unclear on colour.</p> <p>Units: mmHg</p>	<p>Assess obstruction 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.</p>	
Multiple LV gradients	A4C, A5C	<p>CW Doppler Colour flow mapping</p> <p>Units: mmHg</p>	<p>Intra-cavity obstruction at the apex produces an additional Doppler signal to the LVOTO signal.</p>	
MR versus LVOT obstruction	A4C, A5C	<p>CW Doppler Colour flow mapping</p> <p>Units: mmHg</p>	<p>When mitral regurgitation occurs in the context of SAM or prolapse, its onset is later in mid to late systole. Otherwise, its onset is in early systole helps distinguish it from the LVOT signal which begins later in systole (see right hand image).</p> <p>LVOT obstruction is dagger-shaped due to the progressive decrease in LVOT orifice size as systoles progresses but of</p>	

			<p>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.</p>	
<p>Mitral regurgitation secondary to SAM</p>	<p>PLAX, A4C, A5C</p>	<p>Colour flow mapping CW</p>	<p>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 &lt; 1.3 m/s and an E/A ratio &lt;1 are strongly suggestive of non-severe MR.</p>	
<p>Abnormal MV anatomy (elongated AMVL)</p>	<p>PLAX, A4C, A3C</p>	<p>2D</p>	<p>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 (&gt;16 mm), this increases the likelihood of LVOT</p>	

			obstruction(49).	
Pulmonary venous Doppler	A4C	PW  Units: cm/s	<p>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.</p> <p>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 is usually easiest 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.</p> <p>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</p>	

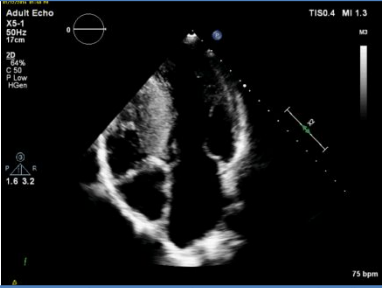
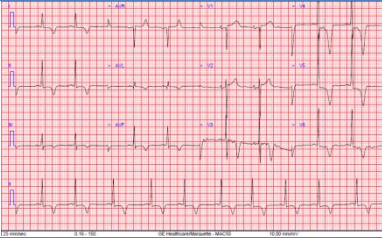
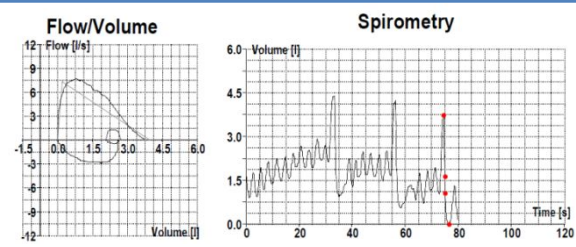

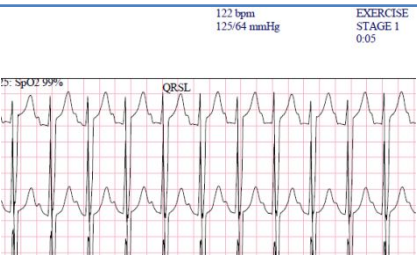

			annulus rather than at the leaflet tips. This provides a cleaner signal for the start and end of the wave. See BSE guidelines for diastolic function(30).	
TR jet velocity and probability of pulmonary hypertension	RV inflow, PSAX, A4C	CW Colour flow mapping  Units: Vmax m/s, peak gradient mmHg	See BSE 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.	
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.	

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 (far right image) if endocardial definition is poor at the apex.	
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.	

**Table 7. Stress Echocardiography protocol in HCM**

	<b>View</b>	<b>Modality</b>	<b>Explanation</b>
<b>LVOT or intra-cavity obstruction</b>	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
<b>MR</b>	A4C, A3C	Colour mapping CW doppler	Be careful to differentiate mitral regurgitation from LVOT obstruction.
<b>MV</b>	A4C	PW Doppler  Units: cm/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.
<b>TR</b>	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.
<b>LV size and systolic function</b>	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.
<b>LV diastolic function</b>	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.

Table 8. Illustrated Guide to Stress Echocardiography in HCM

Table 2 HCM stress echo protocol – Quick guide	
<p><b>COLUMN C</b> <b>ROW 1</b> <b>(C1)</b></p> <p>1. Echo data – rest</p> <p><b>COLUMN C</b> <b>ROW 2</b> <b>(C2)</b></p>	 <ul style="list-style-type: none"> <li>Resting BSE HCM guidelines 2020.</li> <li>Exclude contraindications to exercise test.</li> </ul>
<p>2. Resting haemodynamics</p> <p><b>COLUMN C</b> <b>ROW 3</b> <b>(C3)</b></p>	 <ul style="list-style-type: none"> <li>Perform a resting ECG.</li> <li>Obtain resting BP and standing BP.</li> </ul>
<p>3. Resting spirometry</p> <p><b>COLUMN C</b> <b>ROW 4</b> <b>(C4)</b></p>	 <ul style="list-style-type: none"> <li>Obtain resting spirometry tests if performing combined CPEX.</li> <li>CPEX data is used to establish exercise capacity and true exercise limitations.</li> </ul>
<p>4. Exercise modality</p> <p><b>COLUMN C</b> <b>ROW 5</b> <b>(C5)</b> Image 1 Image 2</p>	 <ul style="list-style-type: none"> <li>Bicycle or treadmill method of exercise</li> <li>Treadmill – resting echo images obtained on echo bed.</li> <li>Bicycle – resting echo images obtained whilst patient on bike to ensure comparable echo windows.</li> </ul>
<p>5. Exercise haemodynamic data</p> <p><b>COLUMN C</b> <b>ROW 6</b> <b>(C6)</b></p>	 <ul style="list-style-type: none"> <li>Continuous monitoring of ECG and BP throughout study.</li> <li>Pay particular attention to arrhythmias, ST changes and potential BP drop at peak exercise.</li> </ul>
<p>6. Transition from treadmill to bed</p> <p><b>COLUMN C</b> <b>ROW 7</b> <b>(C7)</b></p>	 <ul style="list-style-type: none"> <li>Treadmill – stopped immediately at peak exercise, patient is carefully guided back onto the echo bed.</li> <li>Bicycle – peak images are obtained whilst patient is still on bicycle.</li> </ul>

**7. Echo data – peak**

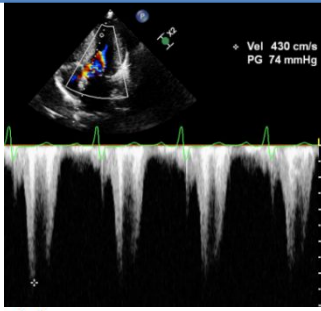
**COLUMN C**

**ROW 8**

**(C8)**

**Image 1**

**Image 2**



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			

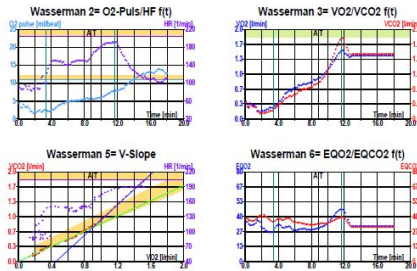
- Peak exercise images are obtained within 60-90s.
- This is before preload decreases and before the patient's heart rate recovers below 85% of THR.
- See table 1 for echo parameters collected at peak exercise.
- Echo measurements are calculated post acquisition to utilise time at peak HR.

**8. Report**

**COLUMN C**

**ROW 9**

**(C9)**



- CPEX, echo and haemodynamic data are combined to produce a clinical report.



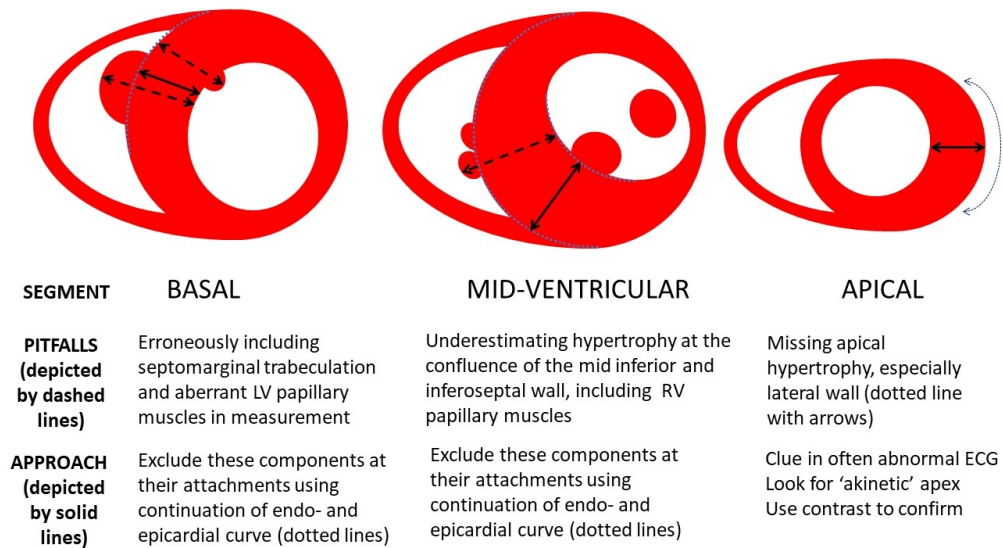


Figure 1.

338x190mm (96 x 96 DPI)

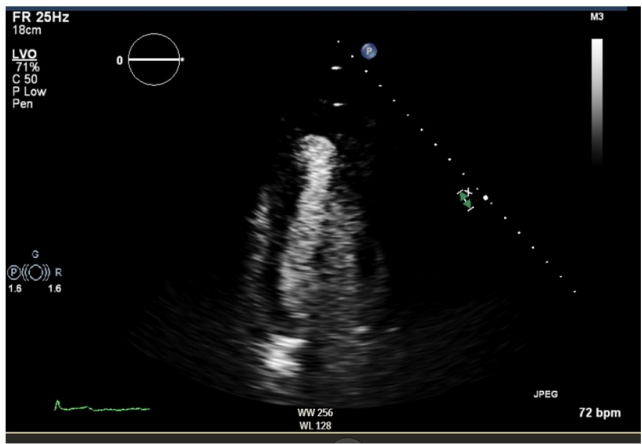


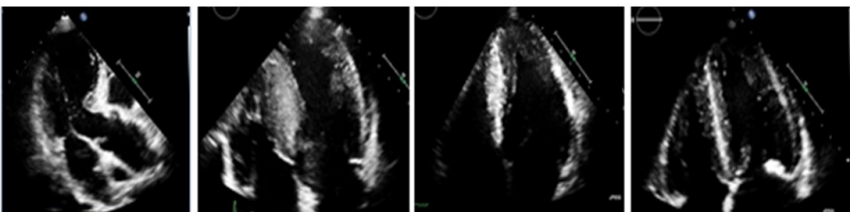
Figure 2

338x190mm (96 x 96 DPI)

CLINICAL INFORMATION PROVIDED AND ECHO FINDINGS	<p>Any age 14 mm Severe aortic stenosis</p> <p>Older patient 14 mm Basal septal hypertrophy hypertension</p> <p>Younger patient 13 mm Athlete, normal ECG and no relevant family history</p>	GREY ZONE		<p>Any age 13 mm apical wall Gross T wave inversion on ECG</p> <p>Younger patient ≥15 mm No past medical history Abnormal ECG</p> <p>First degree family member of someone with confirmed HCM ≥ 13 mm No past medical history</p>
		<p>Over 60 year old Afro-Caribbean patient 15-20 mm with poorly controlled hypertension</p> <p>30 yr old Severe myocarditis 16 mm wall thickness</p>	<p>Over 60 year old Afro-Caribbean patient &gt;20 mm Hypertension</p> <p>Over 60 year old caucasian patient 15-20 mm Hypertension High BMI Gross ECG changes</p>	
LIKELIHOOD OF CONDITION	Same as background population risk	Unlikely	Likely	Definite

338x190mm (96 x 96 DPI)

SIGMOID SEPTAL      REVERSE CURVATURE      APICAL      NEUTRAL



Defined by maximal wall thickness greatest at:

Basal anteroseptal wall      Mid inferoseptal wall      Apex      Anterior wall

338x190mm (96 x 96 DPI)