1   **Title:** Transthoracic Echocardiographic of Hypertrophic Cardiomyopathy in Adults: A Practical

2   Guideline from the British Society of Echocardiography

3   **Authors:** Lauren Turvey[1], Daniel Augustine[2], Shaun Robinson[3], David Oxborough[4], Martin Stout[5],

4   Nicola Smith[1], Allan Harkness[6], Lynne Williams[7], Richard Steeds[1] and William Bradlow[1]

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   <u>Intent behind update</u>

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   <u>Hypertrophic Cardiomyopathy</u>

18   HCM in adults is defined '*by a wall thickness ≥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

3

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   <u>Echocardiography's Position in the Diagnostic Pathway – Wall thickness</u>

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

4

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 ≥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   <u>Recommended Language in Echocardiography Report</u>

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 <u>Post-echocardiography Work-Up</u>

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

6

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   <u>Phenocopies</u>

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   <u>Defining the pattern of hypertrophy in HCM</u>

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

7

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 <u>Echo assessment in risk stratification and disease complications</u>

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).

9

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.

10

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 provocable 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   <u>Stress Imaging in HCM</u>

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 ≥ 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

11

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   <u>Strain Imaging in HCM</u>

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.

12

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   <u>Recommendations</u>

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   <u>Conclusion</u>

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

14

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.

15

1

2

16

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

17

13. Page SP, Kounas S, Syrris P, Christiansen M, Frank-Hansen R, Andersen PS, et al. Cardiac myosin binding protein-C mutations in families with hypertrophic cardiomyopathy: disease expression in relation to age, gender, and long term outcome. Circ Cardiovasc Genet. 2012 Apr 1;5(2):156–66.

14. Sheikh N, Papadakis M, Carre F, Kervio G, Panoulas VF, Ghani S, et al. Cardiac adaptation to exercise in adolescent athletes of African ethnicity: an emergent elite athletic population. Br J Sports Med. 2013 Jun;47(9):585–92.

15. Sheikh N, Papadakis M, Schnell F, Panoulas V, Malhotra A, Wilson M, et al. Clinical Profile of Athletes With Hypertrophic Cardiomyopathy. Circ Cardiovasc Imaging. 2015 Jul;8(7):e003454.

16. Harkness A, Ring L, Augustine DX, Oxborough D, Robinson S, Sharma V. 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 Mar 1;7(1):G1–18.

17. 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. The American Journal of Cardiology. 2014 Nov;114(9):1383–9.

18. 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 Feb 26;105(8):944–9.

19. Rapezzi C, Arbustini E, Caforio ALP, Charron P, Gimeno-Blanes J, Heliö T, 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. Eur Heart J. 2013 May 14;34(19):1448–58.

20. Binder J, Ommen SR, Gersh BJ, Van Driest SL, Tajik AJ, Nishimura RA, et al. Echocardiography-guided genetic testing in hypertrophic cardiomyopathy: septal morphological features predict the presence of myofilament mutations. Mayo Clin Proc. 2006 Apr;81(4):459–67.

21. Kwon DH, Setser RM, Thamilarasan M, Popovic ZV, Smedira NG, Schoenhagen P, et al. Abnormal papillary muscle morphology is independently associated with increased left ventricular outflow tract obstruction in hypertrophic cardiomyopathy. Heart. 2008 Oct 1;94(10):1295–301.

22. 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 Sep;84(3):1188–97.

23. Lentz Carvalho J, Schaff HV, Morris CS, Nishimura RA, Ommen SR, Maleszewski JJ, et al. Anomalous papillary muscles-Implications in the surgical treatment of hypertrophic obstructive cardiomyopathy. J Thorac Cardiovasc Surg. 2020 Apr 15;

24. Gruner C, Chan RH, Crean A, Rakowski H, Rowin EJ, Care M, et al. Significance of left ventricular apical–basal muscle bundle identified by cardiovascular magnetic resonance imaging in 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.

19

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, Mohananey 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, Thamilarasan 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.

20

1

1   **Tables**

2   **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

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

4

5

1

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

LVOT gradient at rest and with physiological provocation	Definition
Gradient ≥30mHg 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

2   Adapted from Gersh et al. (42)

3   **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		

4

5

6

7

8

9

10

11

2

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/m² 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/m²)	
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/m²)	End-systolic Volume (ml), indexed to body surface area (ml/m²)	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	
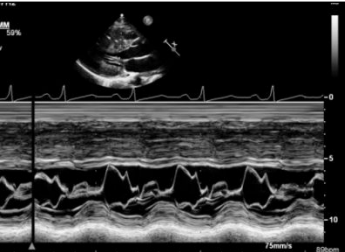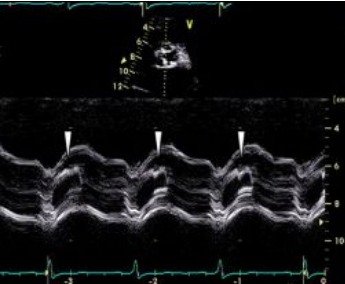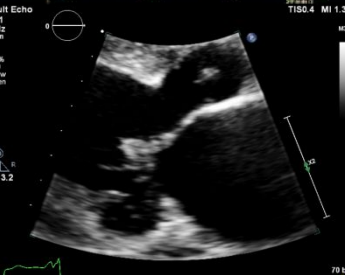
1   • In individuals being screened for HCM

2

3

4
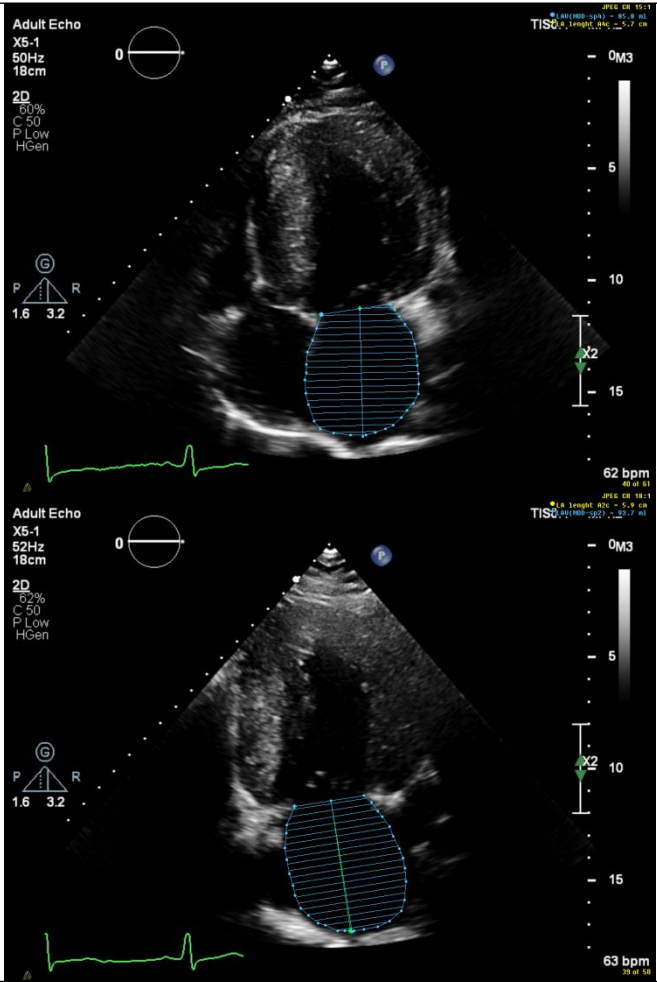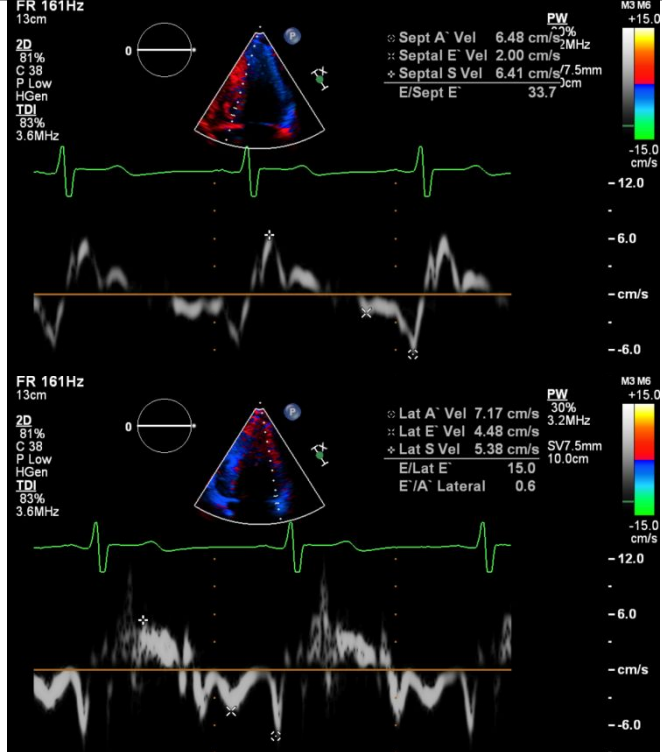
1   **Table 6. Transthoracic HCM protocol**

2

5

Copyright © 2019 the authors
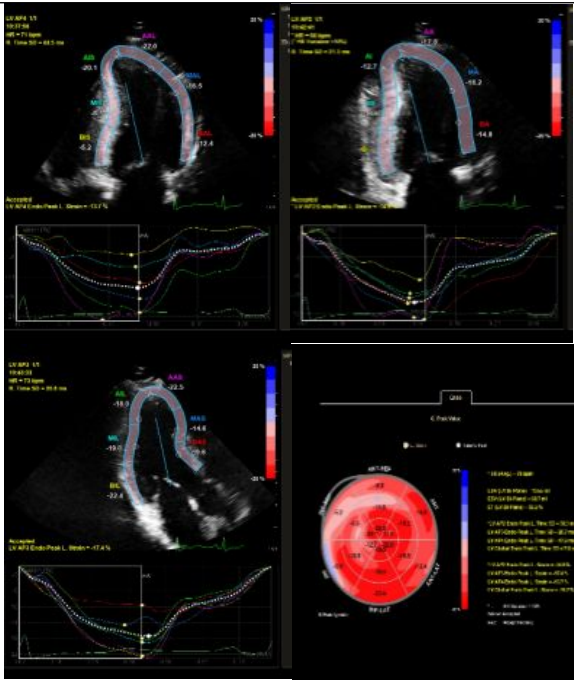
Measurement	View	Modality	Explanation	Image
LA diameter	PLAX	2D Unit: mm	Measure LA dimension at end-systole just after the aortic valve closes using 2D acquisition as per BSE normal reference intervals guidelines (16). LA diameter is one of the criteria used in ESC risk calculator of SCD. Record in 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 echogeneticity occurs in the basal anteroseptal wall due to fibrosis where leaflet contact occurs due to SAM.	

6
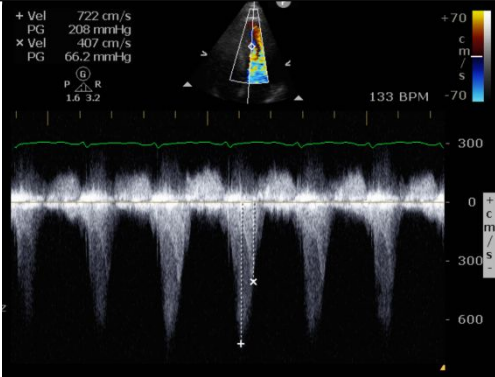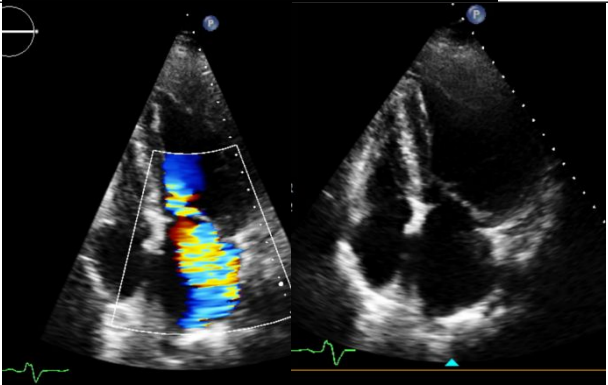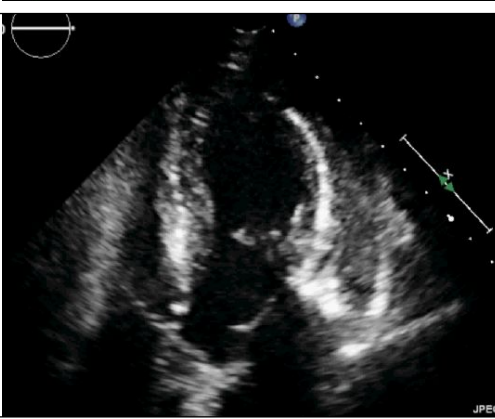
| LV wall thickness measurembents | SAX

MV level
Papillary level
Apex 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. | |
|---|---|---|---|---|
| LV Simpson's Biplane volumes and ejection fraction | A4C, A2C | 2D Units: mL/m² 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)(16). Volumes are indexed to | |
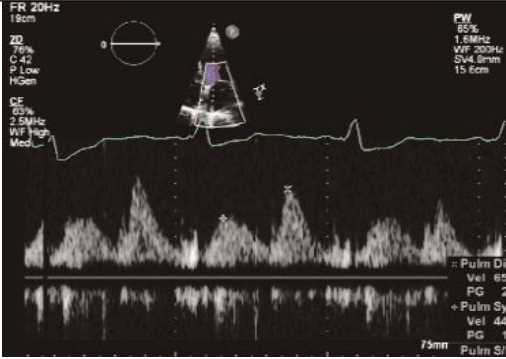
			BSA.	
LA biplane volume	A4C,A2C	2D biplane volume using independent A4C and A2C views. Units: ml/m²	LA volume should be obtained from apical 4- and 2-chamber windows (separated by 60° of rotation), optimised for LA assessment, using the biplane Simpson's method. Maximal LA volume should be obtained from the frame immediately prior to mitral valve opening. Values should be reported after indexing for BSA(16,30). 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.	

8
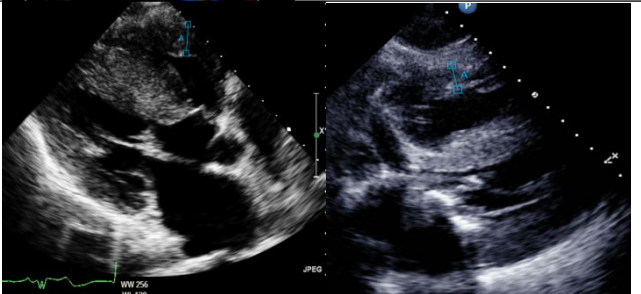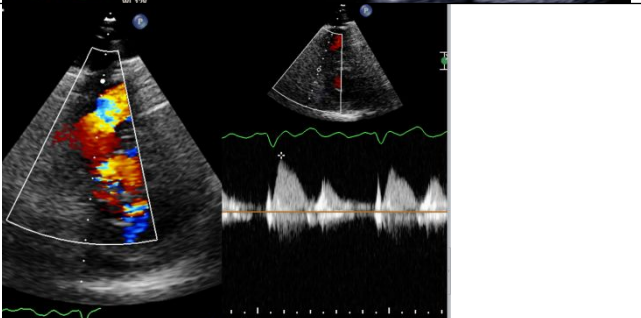
| TDI velocities in all four walls | A4C, A2C | PW TDI

Units: cm/s | Systolic (Sm), early (E') and atrial (A') relaxation velocities at anterolateral and inferoseptal walls(30).

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). | |

| 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. | |

10

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.	
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 is 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	

11

			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.	
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	

12

			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 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. 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	

13

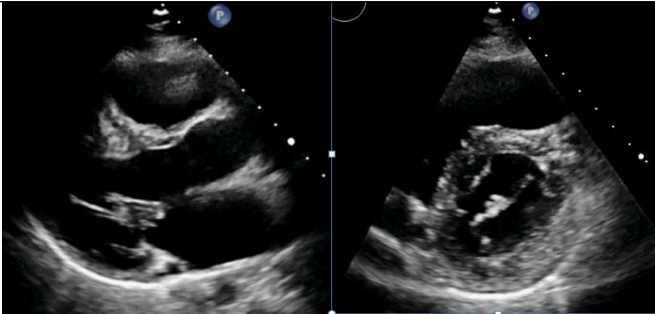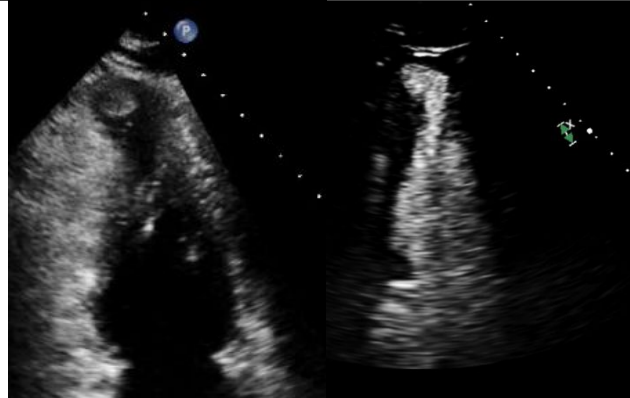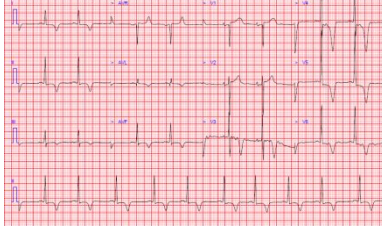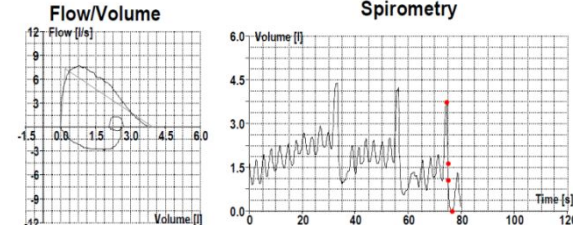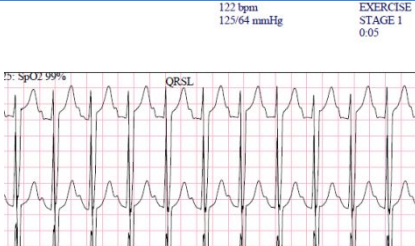|			annulus rather than at the leaflet tips. This provides a cleaner signal for the start and end of the wave. See BSE guidelines for diastolic function(30).	
TR jet velocity and probability of pulmonary hypertension	RV inflow, PSAX, A4C	CW Colour flow mapping Units: Vmax m/s, peak gradient mmHg	See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

14

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.	

15

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: 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.
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.

Table 8. Illustrated Guide to Stress Echocardiography in HCM

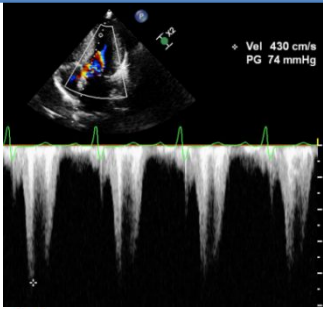| Table 2 COLUMN C ROW 1 (C1)	HCM stress echo protocol – Quick guide	
1. **Echo data – rest** COLUMN C ROW 2 (C2)		• Resting BSE HCM guidelines 2020. • Exclude contraindications to exercise test.
2. **Resting haemodynamics** COLUMN C ROW 3 (C3)		• Perform a resting ECG. • Obtain resting BP and standing BP.
3. **Resting spriometry** COLUMN C ROW 4 (C4)		• Obtain resting spirometry tests if performing combined CPEX. • CPEX data is used to establish exercise capacity and true exercise limitations.
4. **Exercise modality** COLUMN C ROW 5 (C5) Image 1 Image 2		• 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** COLUMN C ROW 6 (C6)		• Continuous monitoring of ECG and BP throughout study. • Pay particular attention to arrhythmias, ST changes and potential BP drop at peak exercise.
6. **Transition from treadmill to bed** COLUMN C ROW 7 (C7)		• 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.

Copyright © 2019 the authors

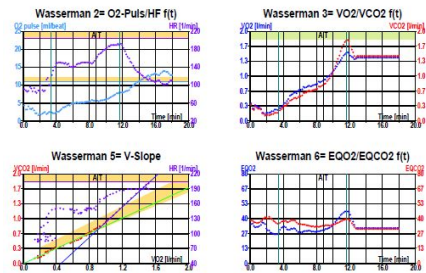|		
7. Echo data – peak **COLUMN C** **ROW 8** **(C8)** **Image 1** **Image 2**	 Peak | Obstruction (mmHg)	
MR	
TR		 	MV	E	A	DT	A dur:
LV volumes	EDV	ESV	SV	EF | | TDIs	S	E'	A'
Septal			
Lateral			
Anterior			
Inferior					• Peak exercise images are obtained within 60-90s. • This is before preload decreases 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.

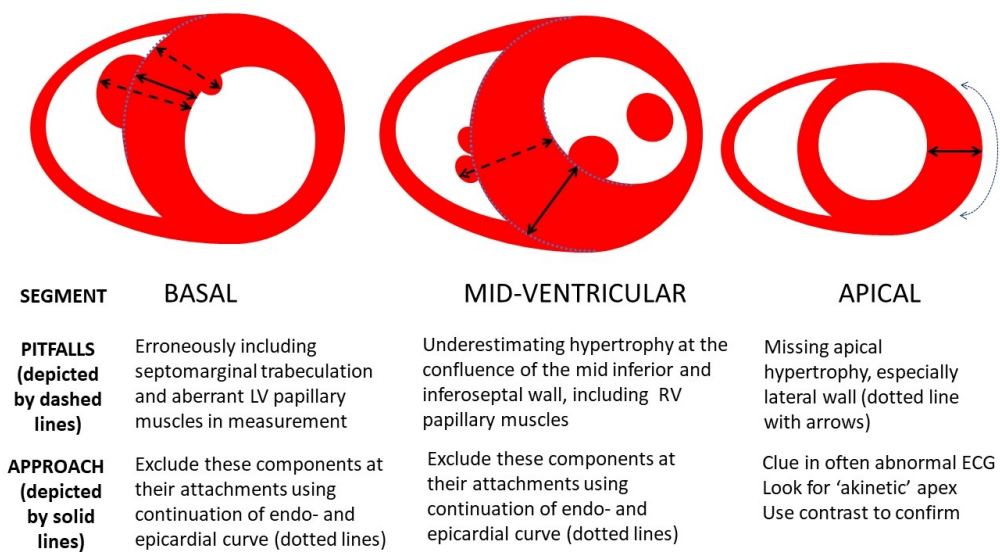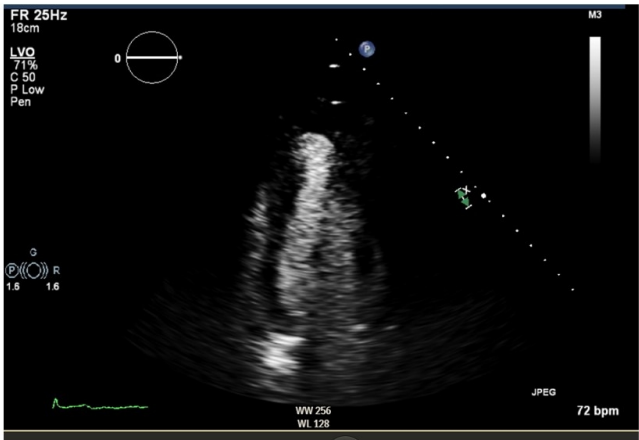| SEGMENT	BASAL	MID-VENTRICULAR	APICAL
PITFALLS (depicted by dashed lines)	Erroneously including septomarginal trabeculation and aberrant LV papillary muscles in measurement	Underestimating hypertrophy at the confluence of the mid inferior and inferoseptal wall, including RV papillary muscles	Missing 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)	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.

338x190mm (96 x 96 DPI)
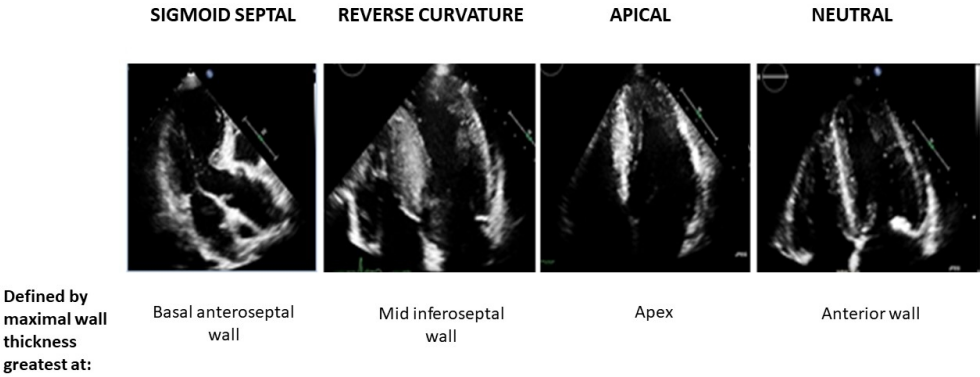
Figure 2

338x190mm (96 x 96 DPI)

CLINICAL INFORMATION PROVIDED AND ECHO FINDINGS	Any age 14 mm Severe aortic stenosis Older patient 14 mm Basal septal hypertrophy hypertension Younger patient 13 mm Athlete, normal ECG and no relevant family history	GREY ZONE		Any age 13 mm apical wall Gross T wave inversion on ECG Younger patient ≥15 mm No past medical history Abnormal ECG First degree family member of someone with confirmed HCM ≥ 13 mm No past medical history
		Over 60 year old Afro-Caribbean patient 15-20 mm with poorly controlled hypertension 30 yr old Severe myocarditis 16 mm wall thickness	Over 60 year old Afro-Caribbean patient >20 mm Hypertension Over 60 year old caucasian patient 15-20 mm Hypertension High BMI Gross ECG changes	
LIKLEHOOD 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)

Copyright © 2019 the authors