

# American Society of Echocardiography Clinical Recommendations for Multimodality Cardiovascular Imaging of Patients with Hypertrophic Cardiomyopathy

Endorsed by the American Society of Nuclear Cardiology, Society for Cardiovascular Magnetic Resonance, and Society of Cardiovascular Computed Tomography

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(J Am Soc Echocardiogr 2011;24:473-98.)

**Keywords:** Hypertrophic cardiomyopathy, Echocardiography, Nuclear imaging, Cardiovascular magnetic resonance, Cardiac computed tomography

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The following authors reported no actual or potential conflicts of interest in relation to this document: Sherif F. Nagueh, MD, FASE, S. Michelle Bierig, RDCS, FASE, Matthew J. Budoff, MD, Milind Desai, MD, Vasken Dilsizian, MD, Benjamin Eidem, MD, FASE, Steven A. Goldstein, MD, Judy Hung, MD, FASE, Steve R. Ommen, MD, and Anna Woo, MD. The following author reported a relationship with one or more commercial interests: Martin S. Maron, MD, serves as a consultant for PGx Health.

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0894-7317/\$36.00

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doi:10.1016/j.echo.2011.03.006

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**Abbreviations****ASE** = American Society of Echocardiography**CAD** = Coronary artery disease**CMR** = Cardiovascular magnetic resonance**CT** = Computed tomography**EF** = Ejection fraction**HCM** = Hypertrophic cardiomyopathy**ICD** = Implantable cardioverter-defibrillator**LA** = Left atrial**LGE** = Late gadolinium enhancement**LV** = Left ventricular**LVOT** = Left ventricular outflow tract**MCE** = Myocardial contrast echocardiography**RV** = Right ventricular**SAM** = Systolic anterior motion**STE** = Speckle-tracking echocardiography**SPECT** = Single photon-emission computed tomography**TEE** = Transesophageal echocardiography**3D** = Three-dimensional**TTE** = Transthoracic echocardiography**2D** = Two-dimensional

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The purpose of this document is to review the strengths and applications of the current imaging modalities and provide recommendation guidelines for using these techniques to optimize the management of patients with HCM. The recommendations are based on observational studies, sometimes obtained in a small number of patients, and from the clinical experience of the writing group members, given the scarcity of multimodality imaging comparative effectiveness studies. Notwithstanding these recommendations, the writing group believes that the selection of a given imaging modality must be individualized.

**1. INTRODUCTION**


HCM is the most common genetic cardiomyopathy. Across multiple geographies and ethnicities, the prevalence is approximately 0.2%.<sup>1</sup> HCM is transmitted in an autosomal dominant inheritance pattern. The natural history is benign in the majority of patients, with a near normal life span. However, adverse outcomes, including sudden cardiac death, lifestyle-limiting symptoms secondary to dynamic left ventricular (LV) outflow tract (LVOT) obstruction and/or diastolic filling abnormalities, atrial fibrillation, and LV systolic dysfunction, occur in some patients.<sup>1</sup>

The clinical diagnosis of HCM is based on the demonstration of LV hypertrophy in the absence of another disease process that can reasonably account for the magnitude of hypertrophy present.<sup>1</sup> Many patients are diagnosed serendipitously when a cardiac murmur or electrocardiographic abnormality prompts echocardiographic evaluation. Others present with dyspnea, chest pain, and/or presyncope. Sudden cardiac death occurs in approximately 1% of patients with HCM each year, and detecting patients at risk for sudden cardiac death is one of the most challenging clinical dilemmas. At the current time, a set of clinical risk factors<sup>1</sup> and imaging results are considered in the context of each patient's specific circumstances to help each patient decide whether an implantable cardioverter-defibrillator (ICD) represents an appropriate choice for that patient.<sup>1</sup>

The management of HCM is based on a thorough understanding of the underlying anatomy and pathophysiology. In addition, careful assessment for concomitant structural heart disease is crucial to allow appropriate patient selection for advanced therapies.

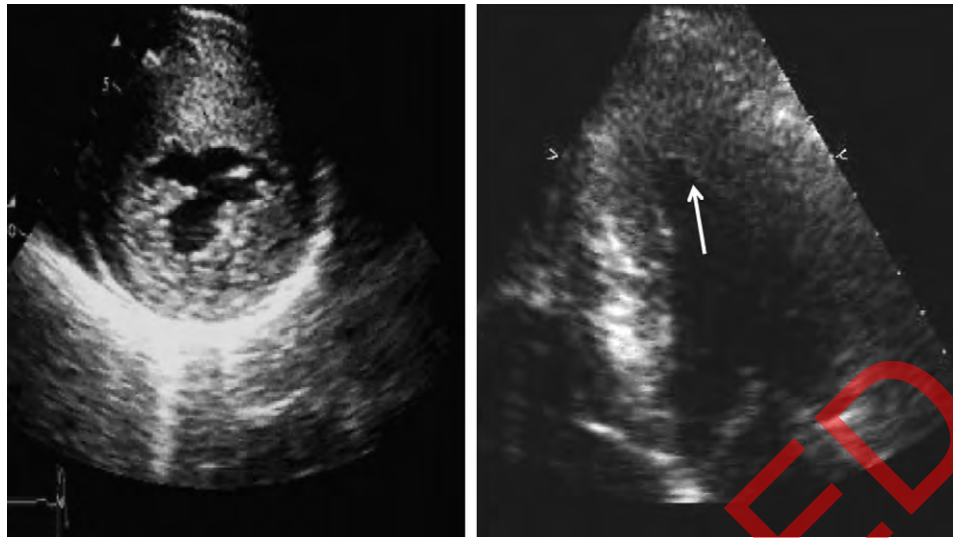
Various imaging modalities can be used to assess cardiac structure and function, the presence and severity of dynamic obstruction, the presence of mitral valve abnormalities, and the severity of mitral regurgitation, as well as myocardial ischemia, fibrosis, and metabolism. In addition, imaging can be used to guide treatment, screening and preclinical diagnosis and to detect phenocopies.

**2. ECHOCARDIOGRAPHY****A. Cardiac Structure**

LV volumes and the pattern of hypertrophy can be well defined by echocardiography (Figure 1, Video 1  view video clip online, Table 1). Ventricular volumes in HCM are usually normal or slightly reduced. Traditionally, the biplane Simpson's method has been applied to the measurement of LV volumes and ejection fraction (EF).<sup>2</sup> Recently, real-time three-dimensional (3D) echocardiography has been shown to provide more accurate means of quantification,<sup>3</sup> though there is a paucity of data on its accuracy in HCM. All imaging windows should be used to accurately define the areas of increased wall thickness. Hypertrophied segments often have slightly increased

**ORGANIZATION OF THE WRITING GROUP AND EVIDENCE REVIEW**

The writing group was composed of acknowledged experts in hypertrophic cardiomyopathy (HCM) and its imaging representing the ASE, the American Society of Nuclear Cardiology, the Society for Cardiovascular Magnetic Resonance, and the Society of Cardiovascular Computed Tomography. The document was reviewed by the ASE Guidelines and Standards Committee and four official reviewers nominated by the American Society of Nuclear Cardiology, Society for Cardiovascular Magnetic Resonance, Society of Cardiovascular Computed Tomography, and the American College of Cardiology Foundation.



**Figure 1** (Left) Parasternal short-axis view from a patient with severe asymmetric HCM involving the anterior septal and anterior lateral walls. (Right) Apical four-chamber view from a patient with apical HCM. The arrow points to the hypertrophy in the distal lateral wall.

**Table 1** Echocardiographic evaluation of patients with HCM

|  |
|--|
| 1. Presence of hypertrophy and its distribution; report should include measurements of LV dimensions and wall thickness (septal, posterior, and maximum)   |
| 2. LV EF   |
| 3. RV hypertrophy and whether RV dynamic obstruction is present  |
| 4. LA volume indexed to body surface area  |
| 5. LV diastolic function (comments on LV relaxation and filling pressures)   |
| 6. Pulmonary artery systolic pressure  |
| 7. Dynamic obstruction at rest and with Valsalva maneuver; report should identify the site of obstruction and the gradient   |
| 8. Mitral valve and papillary muscle evaluation, including the direction, mechanism, and severity of mitral regurgitation; if needed, TEE should be performed to satisfactorily answer these questions |
| 9. TEE is recommended to guide surgical myectomy, and TTE or TEE for alcohol septal ablation   |
| 10. Screening  |

brightness in comparison with segments having normal end-diastolic wall thickness.

LV hypertrophy, although usually asymmetric, can also be concentric. The distribution of hypertrophy can be in any pattern and at any location, including the right ventricle. Although septal predominance is more common, hypertrophy can be isolated to the LV free wall or apex (Figure 1). The presence of hypertrophy localized to the anterolateral wall can be missed, and careful imaging and extra care during interpretation are needed. When the extent of hypertrophy is difficult to visualize, having a high index of suspicion and meticulous imaging of the LV apex and/or the use of LV cavity opacification by intravenous contrast aids in the accurate diagnosis<sup>4</sup> (Videos 2 and 3 [▶] view video clips online). In particular, apical HCM and apical aneurysms can be missed without contrast. Transthoracic echocardiography (TTE) combined with the intravenous injection of an echocardiographic contrast agent should be performed in patients with HCM with suspected apical hypertrophy, to define the extent of

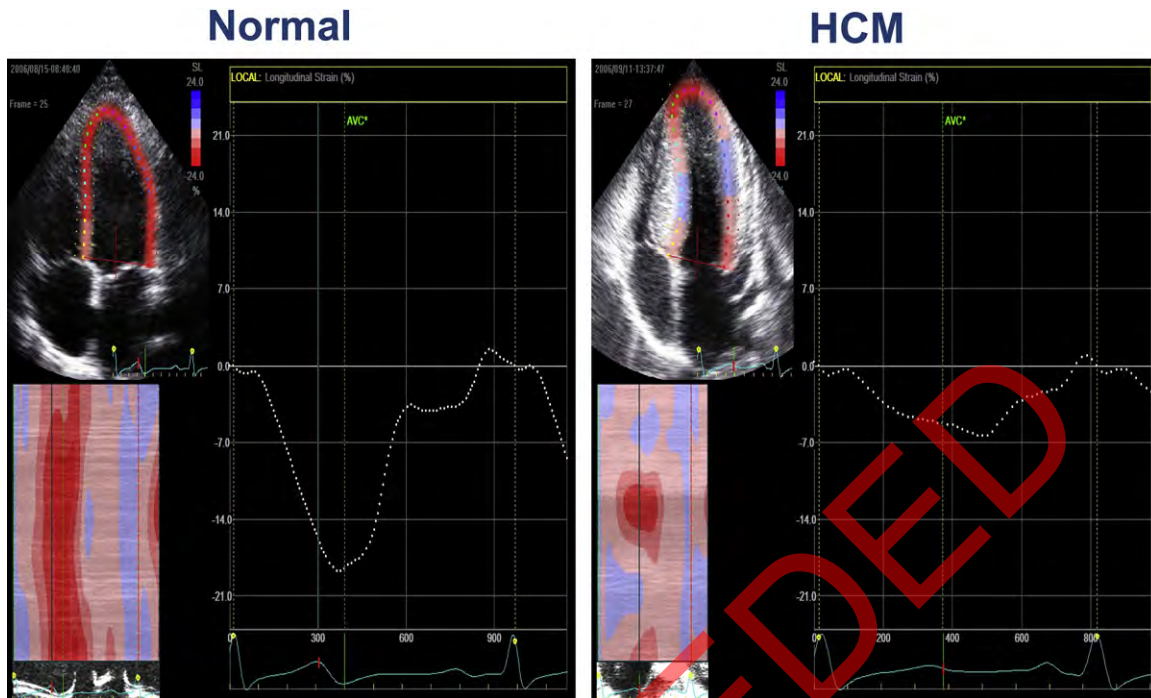
hypertrophy and to diagnose apical aneurysms and clots.<sup>4-8</sup> It is possible to express the severity of hypertrophy using semiquantitative scores,<sup>5,6</sup> which are based on wall thickness measurements by two-dimensional (2D) imaging in parasternal short-axis views at end-diastole. In the presence of adequate-quality images and expertise, 3D echocardiography provides the most accurate echocardiographic approach for quantifying LV mass.

#### B. Assessment of LV Systolic Function

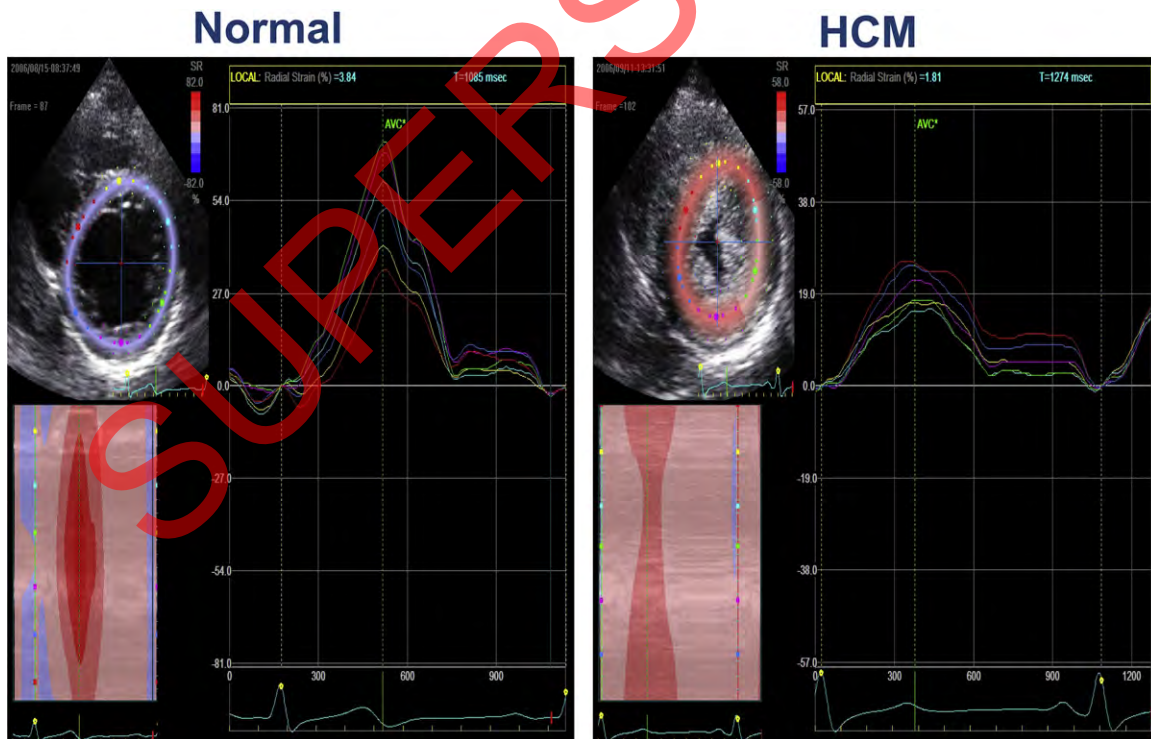
LV EF is usually normal or increased in patients with HCM and should be assessed in all imaging studies. Of note, patients with HCM with significant hypertrophy can have small LV end-diastolic volumes and therefore reduced stroke volumes despite having normal EFs. Overt LV systolic dysfunction, termed the “dilated or progressive phase of HCM,” “end-stage HCM,” or “burnt-out HCM,” is usually defined as an LV EF < 50% and occurs in a minority (2%–5%) of patients. Prognosis is markedly worse in the presence of LV systolic dysfunction.<sup>7</sup> Likewise, the development of an apical aneurysm is an uncommon but important complication that can be readily recognized with contrast echocardiography.<sup>8</sup>

In addition to 2D and 3D imaging, Doppler methods have been used to assess for the presence of subclinical LV systolic dysfunction. Doppler tissue imaging measures the velocity of myocardial motion in systole and in diastole. Reduced systolic (Sa) and reduced early diastolic (Ea or e') velocities can occur before the onset of overt hypertrophy.<sup>9,10</sup> Doppler tissue imaging can also be used to measure myocardial strain and strain rate, which unlike tissue Doppler velocities are not affected by translation and tethering. Strain rate imaging has been shown to be useful in differentiating nonobstructive HCM from hypertensive LV hypertrophy.<sup>11</sup> However, tissue Doppler–derived strain imaging has technical limitations due to its angle dependence. Speckle-tracking echocardiography (STE) directly assesses myocardial motion from B-mode (2D) images and is independent of angulation between the ultrasound beam and the plane of motion. Several studies have shown reductions in strain (Figures 2 and 3) in patients with HCM compared with controls.<sup>12,13</sup> In terms of rotational motion, STE allows for quantification of the





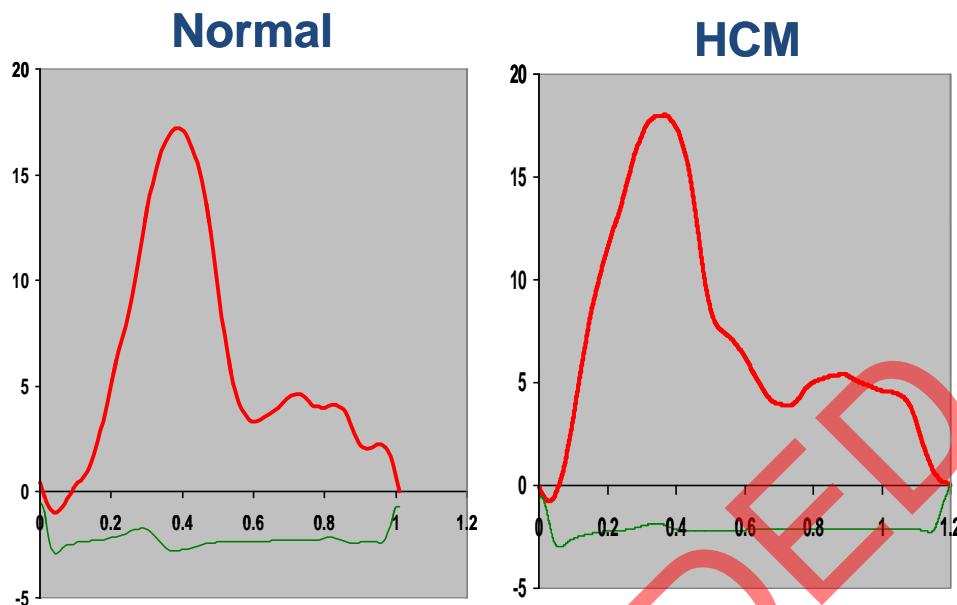
**Figure 2** LV global longitudinal strain by STE in a control subject (*left*) and a patient with HCM and hyperdynamic left ventricle (*right*). LV global strain is markedly reduced at 7% in the patient with HCM. AVC, Aortic valve closure.



**Figure 3** (*Left*) Radial strain in the LV short-axis view from six myocardial segments by STE in a control subject. (*Right*) Strain from a patient with HCM and hyperdynamic left ventricle. Radial strain is markedly reduced in all six segments in the patient with HCM. AVC, Aortic valve closure.

twisting (or wringing) motion of the heart. Observing LV torsion in normal subjects from an apical perspective, the base rotates clockwise while the apex rotates counterclockwise, creating a coordinated “wringing” motion of the left ventricle. Rotation

velocities of twisting and untwisting are usually similar in patients with HCM as a group and in control subjects (Figure 4), although individual variations exist. Although the extent of rotation is usually normal, there can be differences in the direction of rotation. For example,



**Figure 4** Twist by STE in a control subject (*left*) and a patient with HCM (*right*). Both exhibit an initial clockwise rotation followed by a counterclockwise rotation of 17°.

mid-LV rotation in patients with HCM occurs in a clockwise direction, opposite to the direction seen in normal subjects.<sup>13</sup>

Although STE is a promising method to evaluate myocardial function, there are significant differences between strain values across the 17 LV segments in normal individuals. Therefore, the variation of regional strain across the left ventricle necessitates the use of site-specific normal ranges, and the routine use of STE is not recommended at the present time.

### C. Assessment of LV Diastolic Function

LV and left atrial (LA) filling abnormalities have been reported in patients with HCM irrespective of the presence and extent of LV hypertrophy. The assessment of LV diastolic function in HCM can be limited by the relatively weak correlations between the mitral inflow and pulmonary venous flow velocities and invasive parameters of LV diastolic function.<sup>14,15</sup> However, the atrial reversal velocity and its duration (Figure 5) recorded from the pulmonary veins have a significant correlation with LV end-diastolic pressure.<sup>15</sup>

Previous studies have noted reasonable correlations between E/e' ratio and LV filling pressures.<sup>15</sup> This was found across a wide range of annular velocities, including in patients in whom lateral annular e' velocity was >8 cm/sec (Figures 5 and 6). A recent study noted modest correlations in patients with HCM with severely impaired LV relaxation and markedly reduced annular velocities.<sup>16</sup> The E/e' ratio has also been correlated with exercise tolerance in adults<sup>17</sup> and children<sup>18</sup> with HCM. In addition, septal e' velocity appears to be an independent predictor of death and ventricular dysrhythmia in children with HCM.<sup>18</sup>

A comprehensive approach is recommended when predicting LV filling pressures in patients with HCM,<sup>19</sup> taking into consideration the above velocities and ratios, as well as pulmonary artery pressures and LA volume, particularly in the absence of significant mitral regurgitation and atrial fibrillation, as the latter two conditions lead to LA enlargement in the presence of a normal LA pressure.

LA size provides important prognostic information in HCM.<sup>20-22</sup> LA enlargement in HCM is multifactorial in origin, with important

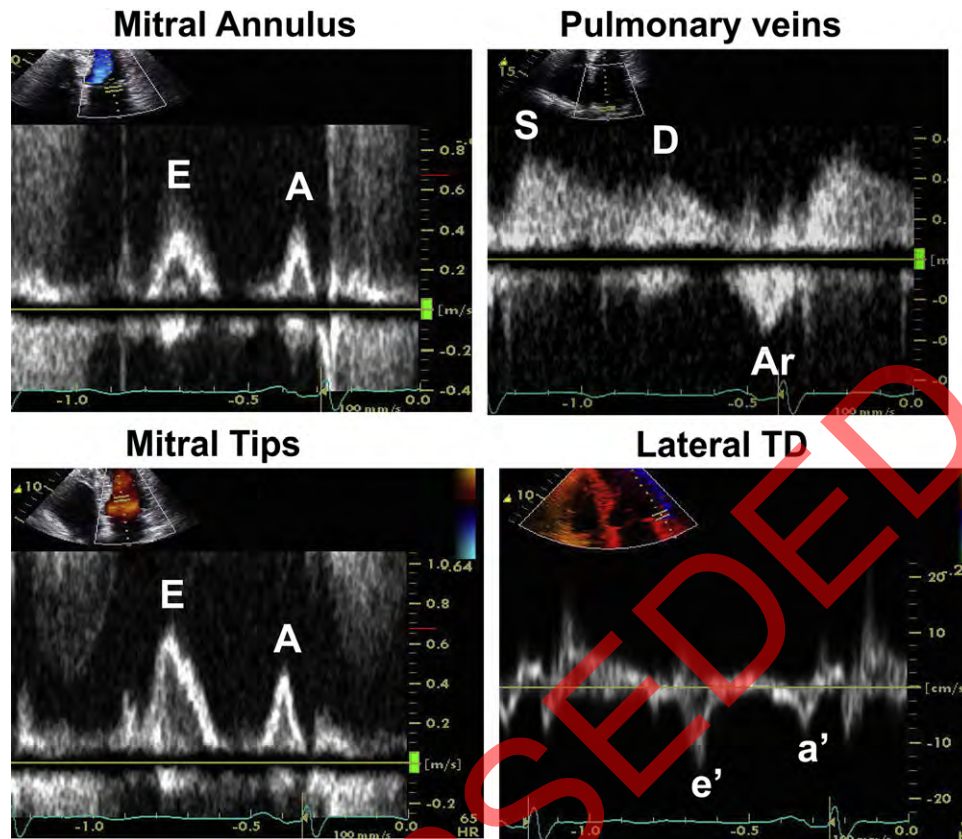
contributions from the severity of mitral regurgitation, the presence of diastolic dysfunction, and possibly atrial myopathy,<sup>1</sup> because LA volume has been shown to be the more accurate index of LA size, LA volume indexed to body surface area should be assessed in accordance with ASE guidelines.<sup>2</sup>

There are three main mechanical functions of the left atrium: (1) reservoir function (during ventricular systole and isovolumic relaxation), (2) conduit function (during early diastole), and (3) contractile (booster pump) function (during atrial systole). The assessment of LA function via Doppler echocardiographic techniques has been performed by indirect methods using pulmonary venous inflow signals and LA volumes by 2D and 3D echocardiography during the different atrial phases.<sup>19</sup> Other indirect measurements of LA function have included the calculation of LA ejection force and kinetic energy, which are increased in patients with obstructive HCM and are reduced (though not normalized) after relief of obstruction.<sup>23</sup>

Strain imaging of the left atrium allows for more direct assessment of LA function. Longitudinal strain of the LA by tissue Doppler and 2D strain during all three atrial phases was assessed in HCM.<sup>24</sup> LA strain values were reduced in all three atrial phases and were significantly lower in patients with HCM compared with those with secondary LV hypertrophy. In general, 2D atrial strain is more reproducible and less time-consuming than tissue Doppler strain, but it is not recommended at the present time for routine clinical application.

### D. Dynamic Obstruction and Mitral Valve Abnormalities

Primary structural abnormalities of the mitral valve apparatus in HCM include hypertrophy of the papillary muscles, resulting in anterior displacement of the papillary muscles, and intrinsic increase in mitral leaflet area and elongation.<sup>25,26</sup> In addition, abnormalities of the mitral valve apparatus predispose the leaflets to be swept into the LVOT by drag forces created by a hyperdynamic EF.<sup>27</sup> This results in systolic anterior motion (SAM) of the mitral valve or chordate,



**Figure 5** Assessment of LV diastolic function in a patient with HCM with elevated LV end-diastolic pressure but normal LA pressure. Mitral inflow shows a short mitral A duration at the level of the mitral annulus, whereas the Ar velocity in pulmonary venous flow is increased in amplitude and duration. Lateral annular  $e'$  velocity is normal, and the ratio of peak E velocity (at the level of mitral tips) to  $e'$  velocity is  $<8$ , consistent with normal LA pressure. (Right) Tissue Doppler (TD) velocities. A, Peak mitral late diastolic velocity;  $a'$ , late diastolic TD velocity; Ar, atrial reversal signal in pulmonary veins; E, peak mitral early diastolic velocity;  $e'$ , early diastolic TD velocity; D, diastolic velocity in pulmonary veins; S, systolic velocity in pulmonary veins.

which is the mitral valve abnormality that is characteristic of obstructive HCM. Of note, significant obstruction is caused by valvular rather than chordal SAM. SAM is defined as systolic motion of the mitral leaflets into the LVOT (Figure 7) resulting in turbulent flow, appreciated as a mosaic pattern by color flow Doppler. SAM also results in distortion of mitral leaflet coaptation, resulting in mitral regurgitation (Figure 7). The maximal instantaneous gradient, reflecting the severity of LVOT obstruction, is determined by measuring the peak LVOT velocity. This is measured by continuous-wave Doppler. Care should be taken to avoid contamination of the LVOT signal with the mitral regurgitation jet (Figure 8).

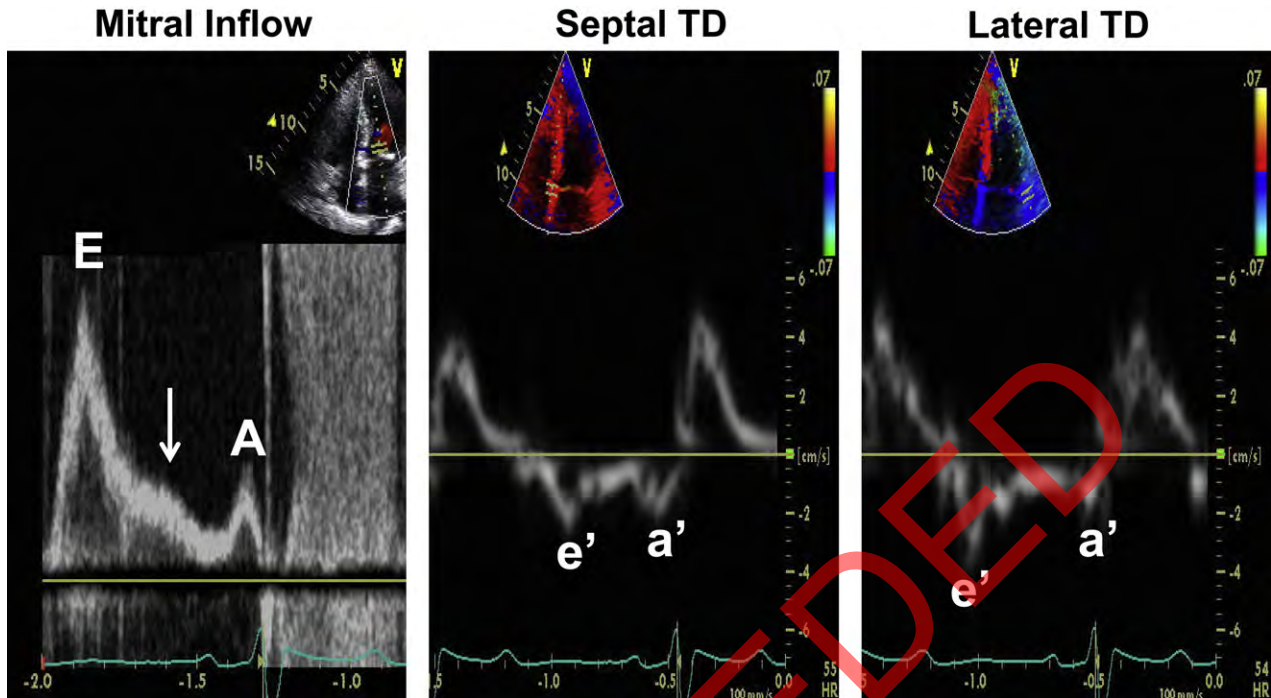
Distinguishing a dynamic LVOT gradient from fixed LVOT obstruction by a subvalvular membrane is important. In addition, concomitant aortic valve stenosis should be excluded by examination of the aortic valve anatomy, including transesophageal echocardiography (TEE) if necessary, and the use of pulsed-wave Doppler at the aortic annular level, paying particular attention to early systole, as the aortic valve may demonstrate premature leaflet closure or fluttering due to the LVOT obstruction. Examination of the LVOT for diseases causing fixed obstruction, such as a membrane, is another important reason to consider TEE. These patients should be identified, as they are surgical candidates. Helpful clues for the presence of fixed subvalvular stenosis on TTE include an early peaking LVOT signal by continuous-wave Doppler similar to that of aortic stenosis, as well as aortic regurgitation,

which is uncommon in patients with HCM who have not had surgical myectomy.

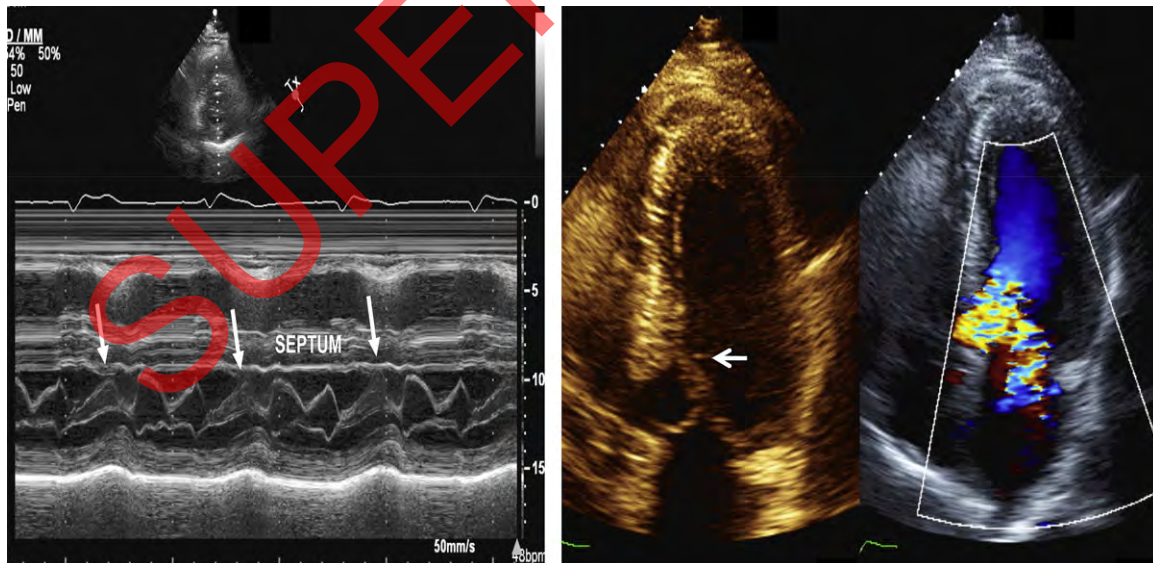
Midcavitary obstruction can occur with and without LVOT obstruction in ventricles with hyperdynamic function and/or concentric hypertrophy. This is frequently observed in elderly patients with a sigmoid septum. The site of obstruction is determined by pulsed-wave and color Doppler showing high velocities at the site of obstruction (velocity aliasing by pulsed-wave Doppler). LVOT obstruction contributes to dynamic systolic dysfunction in obstructive HCM, as manifested by the midsystolic drop in LV ejection velocities at the entrance of the LVOT and the reduced longitudinal strain, both of which improve with treatment of obstruction.<sup>27</sup>

A number of abnormalities contribute to SAM. These include the anterior displacement of the papillary muscles and the reduced posterior leaflet restraint. These mechanisms were highlighted in both in vitro and in vivo studies of mitral valve models that mimicked the anteriorly displaced papillary muscles in obstructive HCM.<sup>28</sup> Anterior displacement of the papillary muscles shifts the mitral leaflets anteriorly toward the LVOT and leads to chordal and leaflet laxity. As drag forces generated by the left ventricle pull the anteriorly displaced and elongated leaflets into the outflow tract in early systole, the distal one half to one third of the leaflets form an angle anteriorly into the LVOT, creating a "funnel" composed of both leaflets (Figure 7). The coaptation point between the anterior and posterior leaflets is





**Figure 6** Assessment of LV diastolic function in a patient with HCM with elevated LA pressure. Mitral inflow shows a restrictive inflow pattern (E velocity, 140 cm/sec). The *arrow* points to an L velocity in mid-diastole, which is observed in the presence of impaired relaxation and increased filling pressures. Lateral annular and septal annular tissue Doppler (TD) velocities (both *e'* and *a'*) are markedly reduced consistent with severely impaired LV relaxation. The markedly increased E/*e'* ratio is consistent with increased LA pressure > 20 mm Hg. The reduced mitral A velocity with its short deceleration time and the severely reduced *a'* velocity are consistent with increased LV end-diastolic pressure. A, Peak mitral late diastolic velocity; *a'*, late diastolic TD velocity; E, peak mitral early diastolic velocity; *e'*, early diastolic TD velocity.

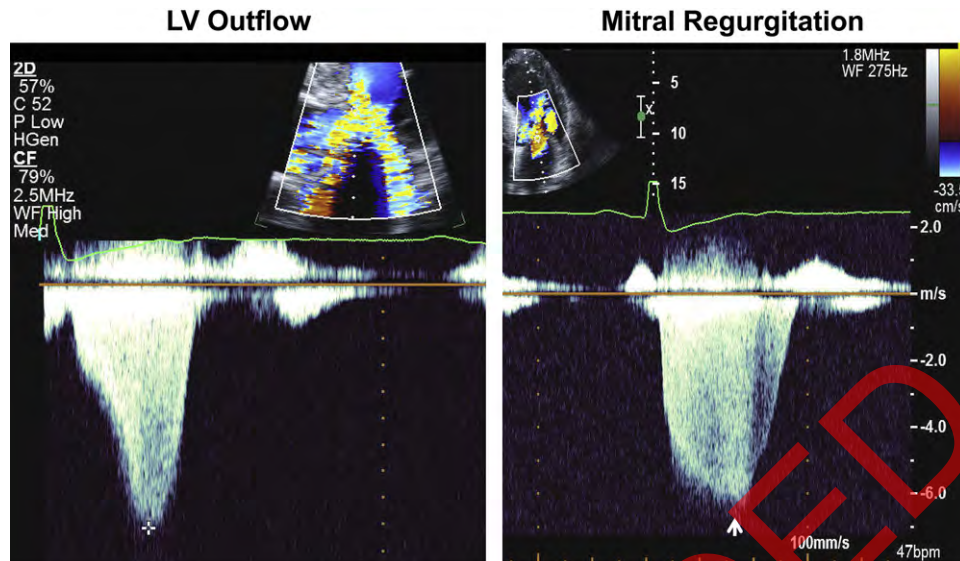


**Figure 7** (Left) M-mode recording of SAM and mitral leaflet septal contact (*arrows*). (Right) SAM on 2D echocardiography (*arrow*). In the same panel, color Doppler shows the high velocities across the LVOT in mosaic color and the eccentric mitral regurgitation jet that is directed posterolaterally.

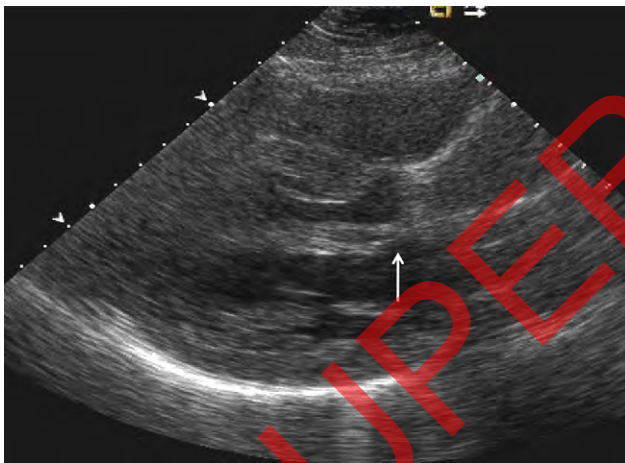
typically eccentric because of the greater anterior leaflet motion relative to the posterior leaflet.

The drag forces that create SAM play an important role in the generation of an LVOT gradient. The extent of septal hypertrophy and

resultant narrowing of the LVOT also contribute to the LVOT gradient. In addition to the role of drag forces on the mitral valve leaflets created by LV contraction, Venturi forces created as flow enters the narrowed LVOT may contribute to obstruction. But SAM often begins



**Figure 8** Continuous-wave (CW) Doppler recordings of peak velocity across the LVOT (cross: 4.5 m/sec) (left) and peak velocity of mitral regurgitation signal (arrow: 6.3 m/sec) (right). The concave-to-the-left contour of the Doppler CW jet causes a decrease in the LVOT orifice size as systole progresses and as the mitral valve is pushed further into the septum. Identification of this contour can be useful to differentiate high CW jets of dynamic LVOT obstruction from mitral regurgitation and from valvular aortic stenosis.



**Figure 9** Anomalous insertion of the papillary muscle, which inserts directly into the anterior mitral leaflet (arrow).

before the aortic valve opens, at a time when LVOT velocities are low.<sup>27</sup> Moreover, the velocity of LVOT Doppler flow at SAM onset does not differ from velocities observed in the outflow tract of normal subjects. This indicates that though Venturi forces are present in the outflow tract, they are not a major contributor to SAM. Recognition by echocardiography of the importance of drag forces as the dominant cause of SAM led to a modification of myectomy, which is now extended past the tips of the mitral valve and in some cases to the base of the papillary muscles.

Anomalous insertion of the papillary muscles in which one or both heads of the papillary muscles insert directly (with absent chordae tendineae) into the ventricular aspect of the mitral leaflets can occur in up to 13% of patients with HCM and can contribute to LVOT obstruction (Figure 9, Video 4 [▶] view video clip online). The recognition of these abnormalities can be facilitated using off-axis views and consideration of TEE if valvular pathology cannot be discerned. The

echocardiographic report should contain a clear statement about the papillary muscle size (if hypertrophy is present) and if there is direct insertion into the mitral leaflets contributing to LVOT obstruction.

#### E. Mitral Regurgitation in HCM

Because the anterior leaflet motion is greater than that of the posterior leaflet during SAM, an interleaflet gap occurs, resulting in a posteriorly directed jet of mitral regurgitation, which can be significant (moderate or greater depending on the extent of the gap). The gap is created between the leaflets because of the failure of the posterior leaflet to move toward the outflow tract as much as the anterior leaflet. This is because the anterior leaflet has the greater surface area and hence greater redundancy and mobility.<sup>25</sup> The degree of mitral regurgitation relates to the extent of mismatch of anterior to posterior leaflet length and the decreased mobility of the posterior leaflet to move anteriorly.<sup>29</sup> The mismatch can be quantified by measuring the coaptation length between the two leaflets, which is shorter with the above-described posterior leaflet abnormalities. Dynamic obstruction also affects the severity of mitral regurgitation,<sup>30</sup> such that mitral regurgitation is dynamic in HCM and is affected by the same factors that influence the severity of obstruction.

Not all mitral regurgitation associated with HCM is related to SAM. Patients with HCM can have intrinsic valvular abnormalities, such as mitral valve prolapse, leaflet thickening secondary to injury from repetitive septal contact or turbulent regurgitation jet, chordal rupture, chordal elongation or thickening, and infectious etiologies.<sup>30</sup> Importantly, the presence of a central or an anteriorly directed jet should prompt careful evaluation of the mitral valve apparatus by TEE to identify intrinsic valvular abnormalities.

There are specialized situations, such as in the operating room or intensive care unit, in which the pathophysiologic settings can mimic obstructive HCM. An example of this is the postoperative repair of a myxomatous mitral valve in a patient with basal septal hypertrophy or sigmoid septum, in which the left ventricle is underfilled coming off bypass. In this situation, a number of factors converge and produce



SAM along with LVOT obstruction. These include elongated mitral leaflets, a narrow LVOT, a small LV cavity, and hyperdynamic EF. In general, these can be reversed with volume loading, afterload increase, and stopping inotropic agents. Similarly, SAM with dynamic obstruction can be seen in patients on inotropic drugs, who are volume depleted, and in the elderly with basal septal hypertrophy or as part of the clinical presentation of stress-induced cardiomyopathy.

#### F. Myocardial Ischemia, Fibrosis, and Metabolism

In general, there is a limited role for echocardiography in diagnosing myocardial ischemia in HCM. Large areas of regional fibrosis can lead to segmental dysfunction manifested by reduced strain. However, a reduction in strain also occurs in segments without replacement fibrosis and has a reduced specificity for this diagnosis.

Measurement of coronary flow reserve in the left anterior descending coronary artery is feasible with transthoracic imaging. Abnormal flow reserve can be due to macrovascular and microvascular coronary artery disease (CAD). The technique requires experience, and an abnormal flow reserve has low positive predictive value in identifying patients with epicardial CAD. It is not yet feasible to use echocardiography for studying myocardial metabolism.

#### G. Echocardiography for Guidance of Septal Reduction Procedures

**i. Surgical Myectomy.** Direct cardiac visualization during myectomy is hampered by both the transaortic approach and the empty heart, potentially leading to imprecision in the extent of the myectomy. These limitations may result in either an inadequate resection, resulting in persistent LVOT obstruction, or too large a resection, which may inflict ventricular septal defect, complete heart block, or both. Therefore, intraoperative TEE has become an essential accompaniment to surgical myectomy, as it contributes to surgical planning, aids in determining the adequacy of repair, and detects complications.

Both the safety and efficacy of septal myectomy are improved with intraoperative TEE, which provides a road map of septal anatomy and geometry to the surgeon.<sup>25,30,31</sup> Important information obtained from TEE includes the maximum thickness of the septum (Figure 10), the distance of maximum thickness from the aortic annulus, the location of the endocardial fibrous plaque (friction or impact lesion), and the apical extent of the septal bulge. Moreover, functional and intrinsic mitral valve abnormalities are well characterized by TEE. Importantly, TEE can identify mitral valve abnormalities and guide the necessary repairs or replacement.<sup>32</sup> In particular, TEE can more clearly identify the direct insertion of papillary muscles into the middle or base of the anterior mitral leaflet. Surgical techniques have been developed to address this pathology and avoid postoperative residual obstruction, including the release and selective resection of anomalous papillary muscle connections. Also, selected patients coming to surgery have very long redundant mitral valve leaflets. In these selected patients, anterior mitral leaflet plication has been successfully used to limit SAM. Horizontal anterior leaflet plication has emerged as a safe and useful technique when used in selected patients who are identified preoperatively by echocardiography and in the operating room by direct inspection. It decreases leaflet length and slack and stiffens the leaflet against deformation. Immediately after cardiopulmonary bypass, TEE is repeated to assess evidence of residual obstruction, or more than mild mitral regurgitation, so that further resection or repair can be performed.

Uncommon complications, including iatrogenic ventricular septal defects, may occur, and immediate recognition by TEE can lead to successful repair. Although the exact mechanism is unknown, aortic regurgitation (usually of mild severity) can occur, perhaps due to direct injury to the leaflets or destabilization of the annulus by beginning the myectomy too close to the right coronary cusp.<sup>32</sup>

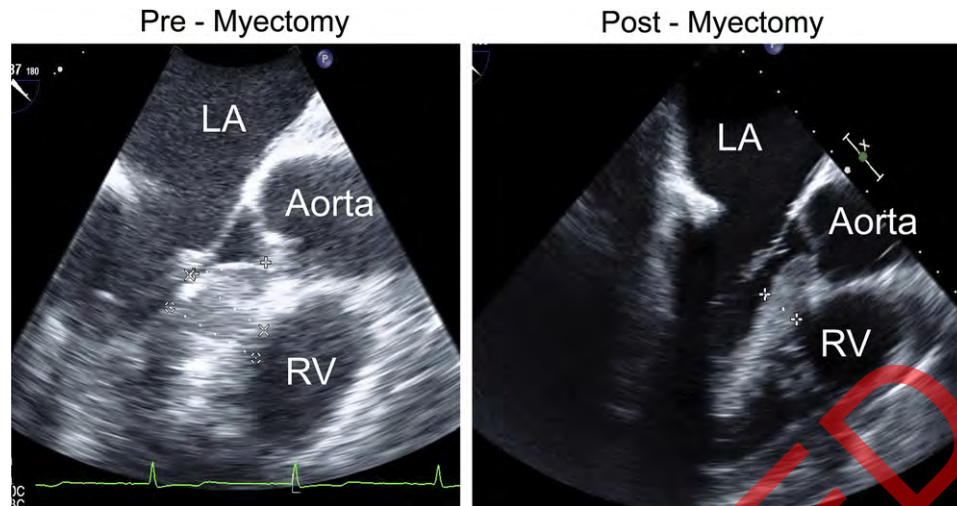
**ii. Alcohol Septal Ablation.** Alcohol septal ablation is an alternative to surgery when medical therapy has failed or is not tolerated. This technique involves the injection of alcohol into a proximal septal perforator branch of the left anterior descending coronary artery to produce a localized myocardial infarction of the thickened proximal ventricular septum involved in causing dynamic obstruction (Figure 11). The use of myocardial contrast echocardiography (MCE) with the injection of echocardiographic contrast agent into the proposed target septal arteries to delineate the vascular distribution of the individual perforator branches is one of the important modifications to septal ablation and is key to the success of the procedure, as defined by at least a 50% reduction in LVOT gradient (Figure 12, Table 2).

Because there is considerable individual variation in the number, size, and vascular territory of the septal perforators, it is important to determine the vessel or vessels that should receive the alcohol injection. The initial method to identify the target septal perforator was to evaluate the gradient decrease during probatory balloon inflation. This has now been replaced at most centers by intraprocedural MCE under transthoracic or transesophageal echocardiographic guidance.<sup>33,34</sup>

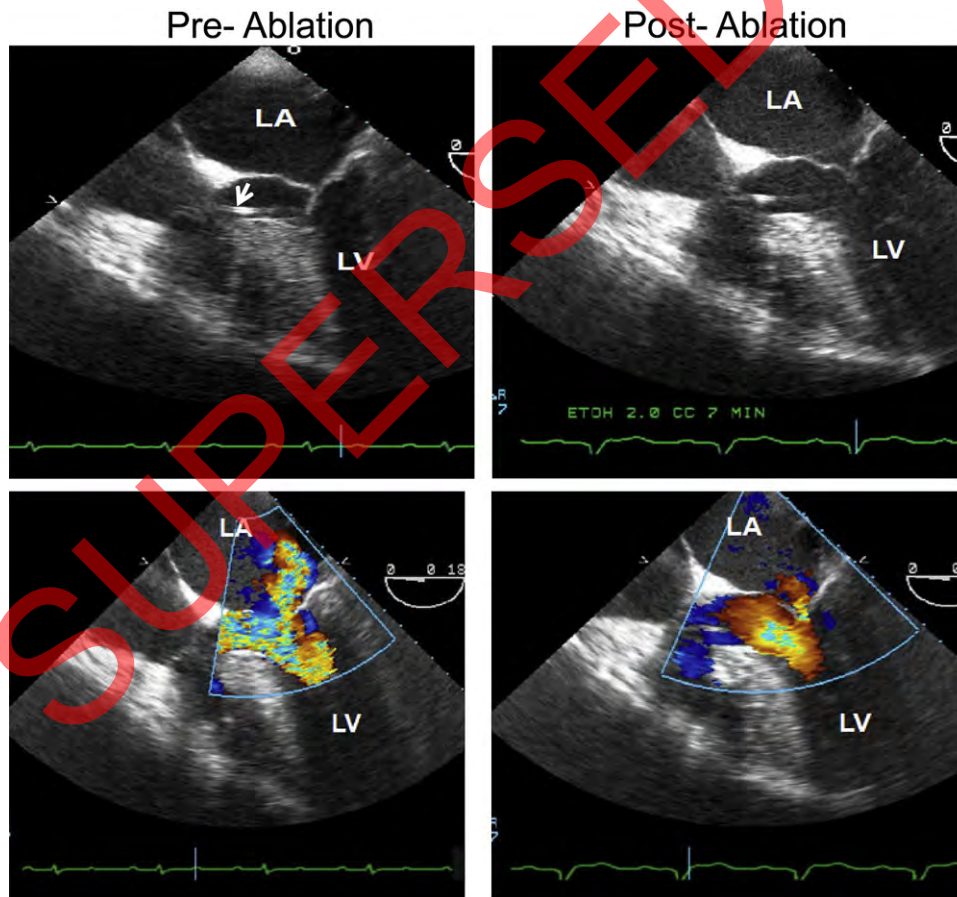
After the target septal perforator is identified and cannulated, a balloon catheter is advanced into the vessel and inflated to prevent backflow. Subsequently, 1 to 2 cm<sup>3</sup> of a diluted echocardiographic contrast agent (e.g., Definity, Lantheus Medical Imaging, North Billerica, MA; Optison, GE Healthcare, Milwaukee, WI; Levovist, Berlex Laboratories, Montville, NJ) is injected through the balloon catheter followed by a 1-mL to 2-mL saline flush during continuous imaging. The contrast agent should be diluted with normal saline to optimize myocardial opacification and minimize attenuation.<sup>8</sup> Details of the dilution vary with the contrast agent used. Agitated radiographic contrast can be used instead of an ultrasound contrast agent.<sup>8</sup> The optimal target territory of the basal septum should also include the color Doppler region of maximal flow acceleration in the area of mitral leaflet and septal contact. Typically, MCE produces a demarcated area with increased echo density in the basal septum and an acoustic shadowing effect. In addition, it is important to document the absence of perfusion of myocardial segments remote from the targeted areas for ablation, including the LV anterior wall, right ventricular (RV) free wall, and papillary muscles.

In patients treated before the introduction of intraprocedural MCE, the main reason for unsatisfactory gradient reduction was suboptimal scar location. Intraprocedural guidance using MCE can lead to changes in the perforator vessel selected for ethanol injection<sup>35</sup> and even cancellation of the procedure, and some of these patients may be referred for surgery. This may be the case when the target septal perforator also supplies papillary muscles or in settings when it is not possible to cannulate the target septal vessel.

At most centers, TTE is used for intraprocedural guidance. Multiple views, including apical four-chamber and three-chamber views and parasternal short-axis and long-axis views, are recommended to delineate opacification of both target and nontarget regions. Limitations of TTE include the difficulty of continuous monitoring during the procedure and suboptimal images in the supine position on the



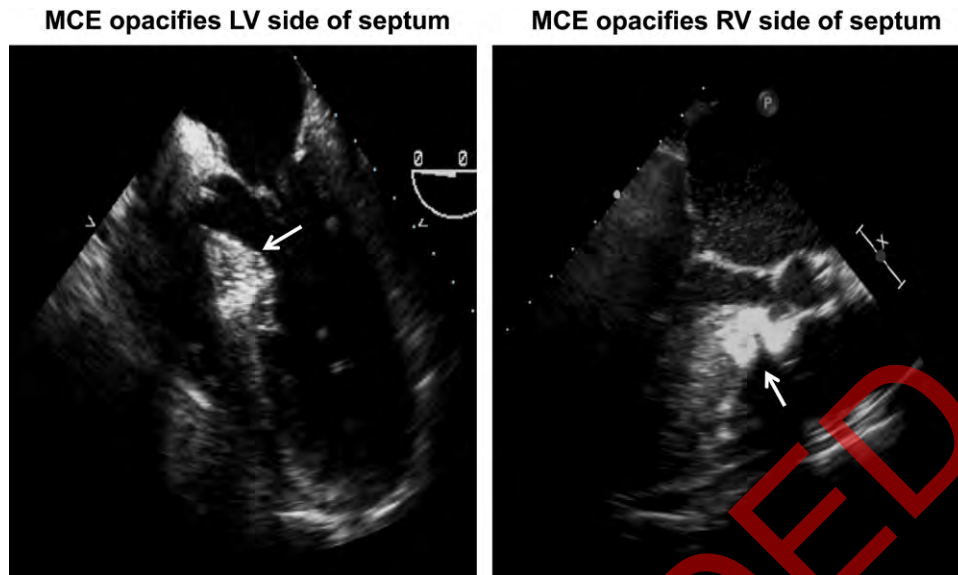
**Figure 10** TEE of septal measurements before myectomy (*left*) (thickness, 2.9 cm) and after myectomy (*right*) (thickness, 1.5 cm). LA, Left atrium; RV, right ventricle.



**Figure 11** Transesophageal echocardiographic images from a patient who underwent alcohol septal ablation. Before ablation, 2D image shows narrowed LVOT with SAM (*top left*). (*Top right*) Two-dimensional images after ablation. Color Doppler before ablation shows high-velocity signals in mosaic color with eccentric mitral regurgitation directed posterolaterally (*bottom left*). After ablation, velocities are much lower across the LVOT, and mitral regurgitation appears trivial (*bottom right*). The *arrow* points to the catheter across the LVOT, which is used to measure LV pressure during the procedure. LA, Left atrium; LV, left ventricle.

catheterization table. Some groups prefer TEE because it generally provides higher quality images. TEE usually requires general anesthesia, which can alter loading conditions and therefore LVOT gradients.

If TEE is used, the apical four-chamber view (deep gastric at 0°) and longitudinal view (midesophageal, aortic valve level, 120°–130°) should be used. These views may be supplemented by the transgastric



**Figure 12** Myocardial contrast echocardiographic (MCE) images from two patients with HCM undergoing alcohol septal ablation. (Left) Opacification of the LV side of the basal septum (arrow), which is involved in the contact with the anterior mitral leaflet and the desired location to induce infarction. (Right) Opacification of the RV side of the septum (arrow), which is not the location that affects dynamic obstruction.

**Table 2** Advantages of MCE during alcohol septal ablation

- |                                    |
|------------------------------------|
| 1. Shorter intervention time       |
| 2. Shorter fluoroscopy time        |
| 3. Fewer occluded vessels          |
| 4. Smaller amount of ethanol used  |
| 5. Smaller infarct size            |
| 6. Lower likelihood of heart block |
| 7. Higher likelihood of success    |

short-axis view to assess for possible perfusion of the papillary muscles or the right ventricle.<sup>36</sup> The deep transgastric view is useful for measuring the intracavitary gradient with TEE, though it is usually more challenging than with TTE. There are preliminary data on intracardiac imaging during septal ablation.<sup>37</sup> Intracardiac imaging provides high-quality near-field imaging and can be performed by interventional cardiologists. Because of the complex nature of the LVOT anatomy, 3D echocardiography can provide additional information. However, the added benefit of 3D TEE during alcohol ablation has not yet been defined.

Intraprocedural echocardiography is also useful for evaluating the results of the procedure.<sup>36,38</sup> The region of the basal septum, which is infarcted by the alcohol infusion, is typically intensely echo dense. This region of the septum should also have reduced thickening and excursion. There is usually a reduction or elimination of mitral regurgitation when it is due to SAM.<sup>38</sup> Most important, there should be elimination or reduction of dynamic obstruction.<sup>38</sup>

**iii. Permanent Pacing.** Although pacing is no longer considered a primary treatment for most patients with obstructive HCM, it may be useful in select patients and is essential in a subset who develops high-grade atrioventricular block after septal reduction therapy. There is seldom need for echocardiographic guidance of pacemaker implantation. However, if there are doubts about whether the RV lead is positioned in the RV apex or there are concerns about

perforation, TTE should be performed.<sup>39</sup> Echocardiography is important for the evaluation and follow-up of response to this intervention and selection of the most optimal atrioventricular delay.<sup>39</sup>

#### H. Screening and Preclinical Diagnosis

At the present time, echocardiography is the most practical technique for HCM screening. Although it is felt that the most active phase of hypertrophy development occurs during adolescence, it is appreciated that late-onset hypertrophy (into the fifth or sixth decade of life) can also occur. Therefore, periodic screening is recommended at intervals of every 12 months during adolescence and every 5 years in adults,<sup>40</sup> as well as at the onset of symptoms suggestive of HCM. All myocardial segments, not only the septum, should be carefully examined for evidence of hypertrophy on these screening examinations. Cardiovascular magnetic resonance (CMR) should be considered in patients with technically challenging echocardiograms, and in patients in whom electrocardiographic results is or have become abnormal, with still normal results on echocardiography.

Studies in transgenic animal models have noted the presence of abnormal myocardial function before the development of hypertrophy.<sup>41</sup> These observations have led to the investigation of Doppler tissue imaging in the preclinical diagnosis of HCM in individuals carrying sarcomeric protein mutations encoding HCM. Some studies have shown annular  $e'$  velocity to be promising,<sup>9,10,42</sup> whereas one study noted that  $a'$  velocity is abnormally reduced in preclinical HCM.<sup>43</sup> Limitations to this approach include the lower specificity in older individuals or those with coexisting disease. Furthermore, it is difficult to interpret Doppler data and provide counsel to subjects who carry the mutation but who still have normal velocity values. Given the variable penetrance, these subjects may never develop HCM including abnormal myocardial function. Alternatively, it is possible that the abnormality in cardiac function is present but at a mild degree that is not amenable to diagnosis by myocardial imaging. Therefore, abnormal Doppler velocities do not establish the diagnosis



**Table 3** Nuclear imaging of patients with HCM

|  |
|--|
| 1. Myocardial perfusion  |
| 2. LV volumes and EF by radionuclide angiography and gated SPECT   |
| 3. Monitoring medical and nonmedical therapy for dynamic obstruction, when echocardiography and CMR are not available (changes in LV volumes, EF, and filling rates with medical and invasive therapy for dynamic obstruction) |
| 4. Coronary flow reserve by PET  |
| 5. Cardiac metabolism by PET (research application)  |
| 6. Myocardial receptors and neurotransmission by SPECT or PET (research application)   |

of HCM but can help identify gene carriers who may benefit from closer follow-up.

### 3. NUCLEAR IMAGING

#### A. Cardiac Structure

Gated blood-pool radionuclide angiography can provide measurements of LV volumes and EF and RV volumes and EF. Thickened myocardium without a definable cause, usually in an asymmetric pattern with predominant septal involvement, can easily be identified by radionuclide angiography. Gated single photon-emission computed tomography (SPECT) can also provide similar data (Table 3). However, echocardiography and CMR have higher spatial resolution and provide accurate measurements. Accordingly, the use of nuclear imaging for the sole purpose of assessment of cardiac structure is no longer recommended.

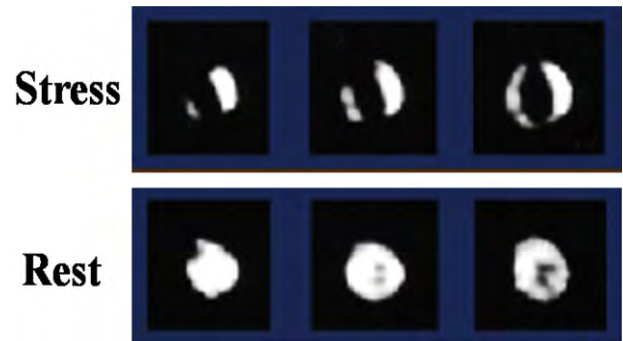
#### B. Radionuclide Angiography for LV Systolic Function

Gated blood-pool radionuclide angiography provides reliable and reproducible measurements of LV EF in patients with HCM. In most patients, radionuclide angiographic findings suggestive of HCM include normal or supranormal EF, disproportionate septal thickening, and systolic ventricular cavity obliteration. A small subset of patients develop LV systolic dysfunction late in the course of disease; in such patients, EF falls below normal and can be easily detected by radionuclide angiography. However, the routine application of radionuclide angiography for the sole purpose of EF assessment is often not needed given the availability of echocardiography and CMR.

#### C. Radionuclide Angiography for LV Diastolic Function

Quantitative parameters of LV filling are derived from the time-activity curve, which closely approximates the changes in LV volume during diastole. High-temporal resolution methods are preferred to avoid underestimation of LV filling. Peak filling rate is the most widely used radionuclide angiographic parameter of diastolic function and represents the maximum value of the first derivative of the time-activity curve. Improvement in LV filling and reduction in symptoms have been observed after therapy with calcium channel blockers, such as verapamil,<sup>44,45</sup> though these drugs can lead to aggravation of diastolic dysfunction in some patients with increased LV early diastolic filling parameters due to increased LV filling pressures.<sup>46</sup>

Echocardiography, which allows beat-to-beat measurement of diastolic filling patterns as well as the less load dependent indices of LV relaxation, is the technique of choice for assessing diastolic function in HCM.



**Figure 13** Three consecutive short-axis thallium tomograms from apex to base are displayed for stress (*top*) and rest reinjection (*bottom*) in a patient with HCM but not CAD. There are multiple exercise-induced thallium perfusion defects in the anterior, septal, and inferior regions that normalize on reinjection images (reversible defects), consistent with myocardial ischemia. In addition, there is apparent exercise-induced LV cavity dilatation with extensive hypertrophy.

#### D. Dynamic Obstruction and Mitral Valve Abnormalities

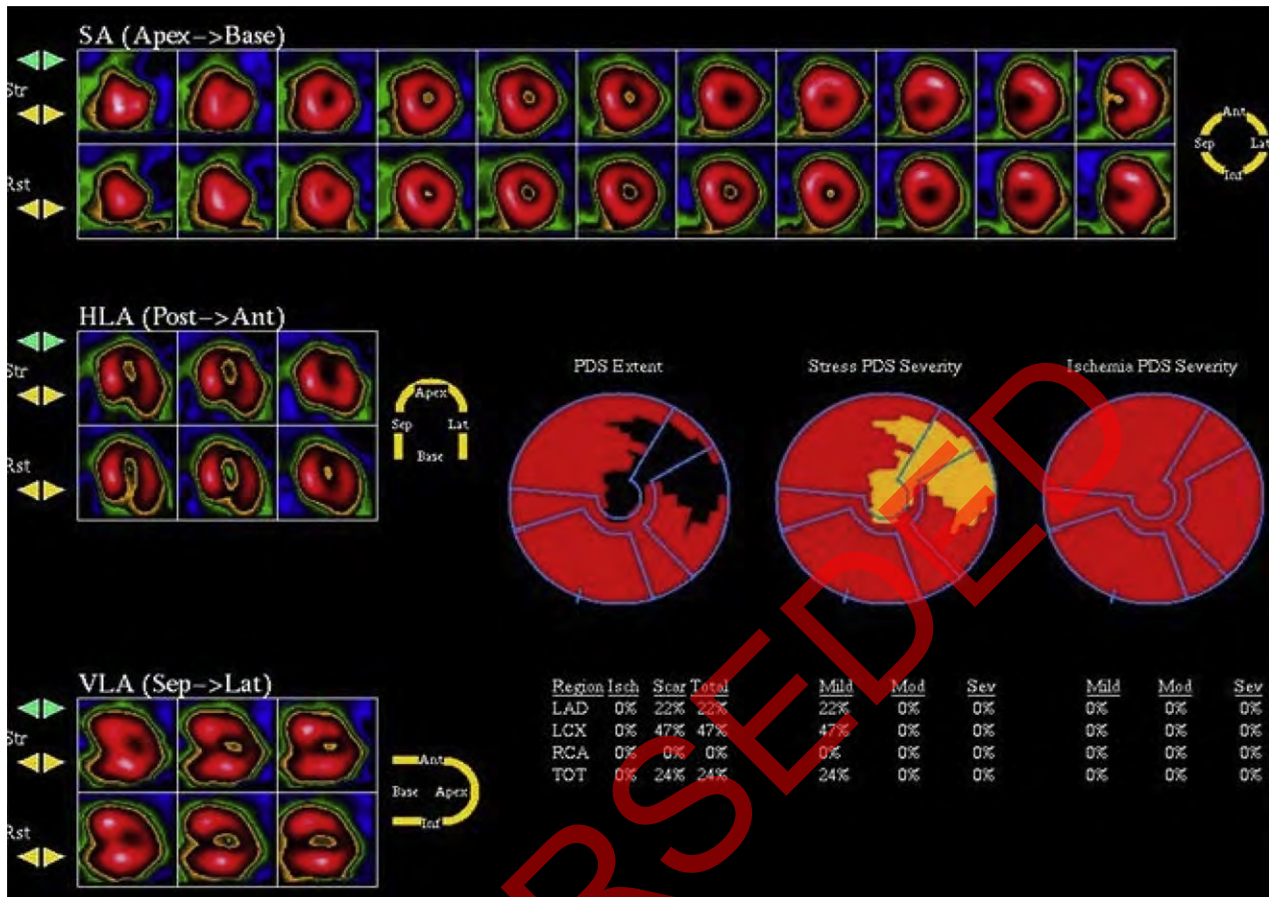
Nuclear techniques cannot show the presence of SAM or assess the severity and location of dynamic obstruction. However, the scan can show the presence of a hyperdynamic left ventricle with cavity obliteration.

#### E. Mitral Regurgitation in HCM

It is not possible to visualize the mechanisms behind mitral regurgitation using nuclear imaging. However, it is possible to quantify the severity of mitral regurgitation in patients with isolated lesions (i.e., no concomitant significant valvular regurgitation aside from mitral regurgitation) as the difference between LV and RV stroke volumes. Echocardiography is the recommended and preferred modality for that objective, given the limitations of the other techniques.

#### F. Myocardial Ischemia, Fibrosis, and Metabolism

**i. SPECT.** Ischemia in patients with HCM, in the absence of epicardial coronary artery stenosis, may be due to intramural small-vessel abnormalities, abnormal myocellular architecture, massive hypertrophy, and abnormalities of the intramural microcirculation leading to inadequate myocardial blood flow, particularly during increased myocardial oxygen demand with exertion. Myocardial oxygen demand is also increased by LV hypertrophy and outflow tract obstruction in many patients. Myocardial ischemia can be induced by exercise, vasodilators such as adenosine, and dobutamine. However, because of concerns of inducing and possibly aggravating the severity of dynamic obstruction with untoward hemodynamic effects, dobutamine is not preferred in conjunction with perfusion imaging in patients with HCM. The presence and severity of ischemia can be assessed by reversible abnormalities in regional thallium uptake (Figure 13) and is a well-established pathophysiologic feature of HCM in adults.<sup>47-49</sup> It has been associated with potentially lethal arrhythmias, adverse LV remodeling, and systolic dysfunction, even in the absence of epicardial disease.<sup>49,50</sup> In addition to the above mechanisms, impaired LV relaxation and increased LV end-diastolic pressure can compress the coronary microcirculation and further restrict coronary



**Figure 14** Single photon-emission computed tomographic perfusion imaging from a patient with HCM. Septal (Sep) thickness is increased, as is the count activity (*hot spot*) in the septum relative to lateral (Lat) wall. The computer analysis software registered a fixed perfusion defect (*scar*) (PDS) in the lateral and apical regions upon normalization to the septum. Ant, anterior; HLA, horizontal long-axis; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; TOT, total; VLA, vertical long-axis. Reproduced with permission from *J Am Coll Cardiol*.<sup>39</sup>

artery blood flow.<sup>50-55</sup> Recurrent myocardial ischemia can cause myocardial injury and scarring (characterized as fixed defects), which can potentially reduce the threshold for ventricular arrhythmias. In particular, fixed defects have been associated with syncope, larger LV cavity dimensions, and reduced exercise capacity.<sup>56</sup>

In a selected group of young patients with HCM, sudden cardiac arrest or syncope was shown to be frequently related to myocardial ischemia.<sup>49</sup> However, the relation between ischemia and clinical events was not observed in all studies.<sup>56</sup> In addition, SPECT can have reduced specificity for diagnosing epicardial coronary lesions. False-positive results (Figure 14) without actual ischemia can occur because of increased radioactive isotope uptake in regions with hypertrophy (such as the septum) and the apparent lower counts in other segments compared with regions with segmental hypertrophy.<sup>39</sup> While routine performance of stress perfusion imaging in conjunction with SPECT is not recommended, on the other hand, in HCM patients with chest pain and low probability of CAD, stress SPECT imaging can be considered.

**ii. Positron Emission Tomography (PET).** Although SPECT cameras are more widely available for clinical studies in HCM

patients, the assessment of regional myocardial perfusion defects with SPECT is limited to assessing the distribution of the radiotracer in the myocardium in relative terms, rather than quantifying myocardial blood flow in absolute terms, in milliliters per minute per gram. Although the quantification of regional myocardial blood flow with PET has become an indispensable tool in cardiovascular research, it is used less frequently in clinical practice. The main drawbacks are the cost and accessibility of PET cameras as well as the radiotracers, which require either a cyclotron or an expensive generator for isotope production.

In patients with HCM with normal coronary arteries, myocardial perfusion positron emission tomographic studies have shown that although resting myocardial blood flow, in milliliters per gram per minute, may be similar to normal control subjects, the augmentation of blood flow with vasodilation (e.g., dipyridamole) may be significantly blunted. In addition, such abnormal myocardial blood flow reserve with vasodilation was shown to be more pronounced in the sub-endocardial regions, consistent with so called “apparent” transient ischemic cavity dilatation.<sup>52,55</sup> Such quantifiable abnormalities in myocardial blood flow reserve, in the absence of epicardial CAD, could be attributed to myocardial ischemia from microvascular dysfunction and have prognostic importance.<sup>50</sup> Overall cumulative

survival free from unfavorable outcomes in these patients with HCM was associated with the level of hyperemic myocardial blood flow achieved during pharmacologic vasodilatation. Patients with HCM with the greatest attenuated myocardial blood flow responses to dipyridamole were more likely to subsequently develop LV remodeling, decreased LV EFs, and severe heart failure symptoms. In conclusion, routine positron emission tomographic screening of HCM patients for underlying myocardial ischemia cannot be advocated on the basis of the current literature but may be considered in selected patients with angina or heart failure, irrespective of LV EF.

**iii. Imaging Metabolism.** In the future, radiotracers that assess myocardial metabolism,<sup>57</sup> sympathetic innervations,<sup>58-60</sup> and  $\beta$ -adrenergic receptor density<sup>61</sup> may further elucidate the pathophysiology of HCM and its role in the progression of LV dysfunction and remodeling, the development of heart failure, and sudden cardiac death. However, the clinical utility of these radiotracers in HCM is currently preliminary and observational.

### G. Guidance of Septal Reduction Procedures

Nuclear imaging is not needed for case selection for septal reduction therapy given its limitations with respect to imaging the mitral valve and the evaluation of dynamic obstruction, as discussed above. However, the technique has provided important insight into LV function and perfusion after these procedures.<sup>62,63</sup> Among symptomatic patients with HCM who underwent myocardial perfusion SPECT before and after septal myectomy or mitral valve replacement, 85% had thallium perfusion defects before surgery, of whom 65% exhibited complete normalization or improvement in the magnitude and distribution of perfusion defects.<sup>52</sup> This was associated with an improvement in lung uptake and transient cavity dilatation after the surgery.

When alcohol ablation was used for septal reduction, there was a decrease in LVOT gradient immediately after alcohol ablation, with the subsequent development of fixed septal perfusion defects in 97% of patients 6 weeks after treatment, without affecting LV EF.<sup>62</sup> When the effect of alcohol septal ablation on septal perfusion defects and LV EF was examined 8 months after ablation, the basal septal perfusion defect decreased from 9.4% of the LV myocardium from early after alcohol ablation to 5.2%, without causing an increase in LV outflow obstruction or recurrence of symptoms.<sup>63</sup> The routine performance of nuclear imaging for the assessment of cardiac function post invasive therapy is not recommended unless there are technical limitations with echocardiography and CMR studies.

### H. Screening and Preclinical Diagnosis

There is no role at the present time for nuclear imaging in the screening of patients for HCM and preclinical diagnosis.

## 3. CARDIOVASCULAR MAGNETIC RESONANCE

### A. Cardiac Structure

CMR has emerged as an important 3D tomographic imaging technique, which provides images of the heart at high spatial and temporal resolution, in any plane and without ionizing radiation.<sup>64-91</sup> Current cine CMR imaging sequences are breath-hold and retrospectively or prospectively electrocardiographically gated acquisitions acquired in nearly identical imaging planes as that of 2D echocardiography.<sup>66</sup>

**Table 4** CMR imaging of patients with HCM

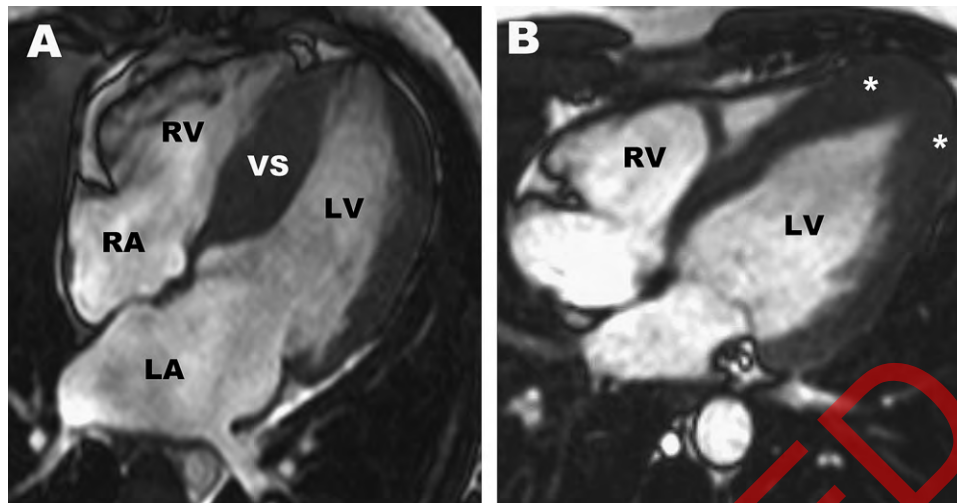
|  |
|--|
| 1. LV morphology including extent and distribution of hypertrophy  |
| 2. RV morphology   |
| 3. Mitral valve apparatus and papillary muscles  |
| 4. Global and regional LV function   |
| 5. Evaluation of LVOT obstruction (limited role in presence of echocardiography) and mitral regurgitation mechanism and severity |
| 6. Myocardial ischemia evaluation with stress perfusion imaging  |
| 7. Contrast-enhanced CMR for focal fibrosis and differentiation of phenocopies   |
| 8. Monitoring of invasive therapy (myectomy and alcohol septal ablation)   |
| 9. Screening   |
| 10. Vascular-ventricular interactions  |

Furthermore, LV short-axis stacks are thin myocardial slices (typically 7 mm) providing complete tomographic coverage of the entire myocardium. Cine imaging sequences (without contrast injection) produce sharp contrast between the bright blood pool and the dark myocardium and therefore can provide detailed characterization of the HCM phenotype, including accurate wall thickness measurements<sup>67-69</sup> and highly reproducible measurements of ventricular volumes and mass (Table 4).

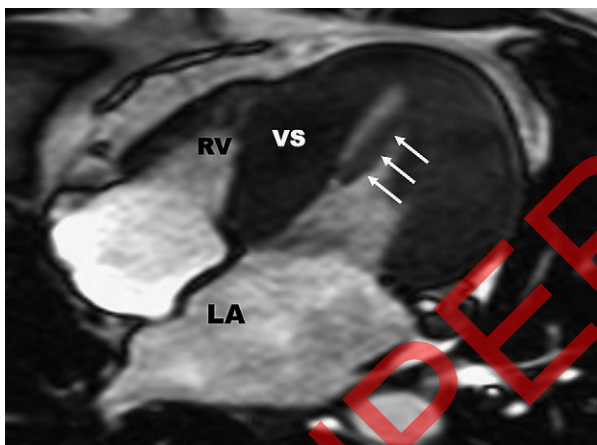
CMR is particularly useful for characterizing the presence, location, and extent of LV hypertrophy in HCM (Figure 15), which can be limited to one or two LV segments in approximately 10% of the HCM population.<sup>67</sup> Although maximal LV wall thickness measurements are often similar between echocardiography and CMR, focal regions of increased wall thickness may not be well visualized by 2D echocardiography but can be detected by CMR in a subset of patients with HCM. The basal anterolateral free wall is one location in the left ventricle where hypertrophy may not be well seen by echocardiography, because the lateral epicardial border in this region is difficult to differentiate (because of the loss of spatial resolution) from the adjacent thoracic parenchyma in the short-axis orientation.<sup>69</sup> The LV apex is another region of the myocardium where CMR may provide an advantage over echocardiography in identifying hypertrophy.<sup>68</sup> Likewise, CMR can identify the presence of apical aneurysms in patients with HCM, which can have management implications.<sup>75</sup> CMR can also provide accurate characterization of the extent of LV hypertrophy. A recent study noted diffuse hypertrophy involving >50% of the left ventricle and eight or more segments in 54% of patients with HCM.<sup>67</sup> The technique is very helpful in the identification of segments with massive hypertrophy (>30 mm), which carries implications for ICD implantation. Therefore, CMR imaging should be considered in the evaluation of patients with HCM in whom the LV myocardium is not well visualized.

CMR in HCM has demonstrated that up to one third of patients have increased RV wall thickness and mass,<sup>76</sup> and if the septomarginal area is involved, RV outflow tract obstruction may be observed. Papillary muscle number and mass are also increased in patients with HCM.<sup>77</sup> Furthermore, there appears to be a small subset of patients with HCM in whom LV hypertrophy is focal and limited (with normal LV mass) but who demonstrate substantially hypertrophied papillary muscles. CMR assessment of papillary muscles has provided insight into the mechanism of outflow obstruction by demonstrating that the presence of an apically displaced anterolateral or double bifid





**Figure 15** (A) Four-chamber end-diastolic CMR image of a 27-year-old asymptomatic patient with HCM with predominately ventricular septal hypertrophy (maximal wall thickness, 24 mm). (B) Four-chamber end-diastolic CMR image in a 16-year-old patient demonstrates increased left ventricular wall thickness confined to the apex (asterisks), consistent with a diagnosis of apical HCM. LV, Left ventricle; RA, right atrium; RV, right ventricle; VS, interventricular septum.



**Figure 16** Apically displaced papillary muscle in HCM. Four-chamber midsystolic cine CMR image in a 44-year-old man with a resting LVOT gradient of 85 mm Hg and an apically displaced papillary muscle (arrows), which contributes to the mechanism of outflow obstruction by positioning the plane of the mitral valve closer to the ventricular septum. LA, Left atrium; RV, right ventricle; VS, interventricular septum.

papillary muscle is associated with a significantly higher likelihood of having a resting LVOT gradient<sup>78</sup> (Figure 16).

#### B. Assessment of LV Systolic Function

CMR measurements of ventricular volumes and EF are accurate and reproducible. In addition, quantitative measurements of regional systolic and diastolic function can be obtained using myocardial tagging methods.<sup>79,80</sup> A limited number of studies using this technique in patients with HCM have confirmed that regional differences in myocardial function are present.<sup>79</sup> However, the clinical utility of myocardial tagging in discriminating HCM from forms of secondary hypertrophy (i.e., hypertensive cardiomyopathy or athlete's heart) or whether abnormalities identified by tagging are present before the development of LV hypertrophy has not been well established.

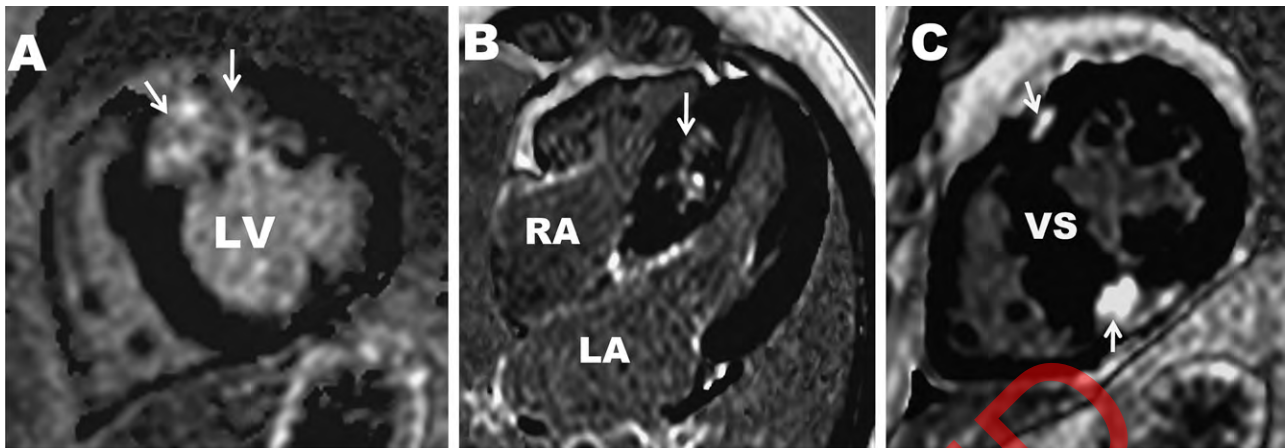
#### C. Assessment of LV Diastolic Function

It is possible to measure mitral inflow, pulmonary vein, and mitral annular velocities by CMR. Likewise, LV filling rates can be computed. However, the specific applications of these velocities by CMR in patients with HCM have not been evaluated, and this indication is not recommended at the present time.

With the increasing use of CMR, we are gaining further insights into the complex ventricular-vascular interactions in HCM. It was recently demonstrated that the LVOT and aortic root are oriented at a steeper angle to the left ventricle in patients with HCM compared with controls<sup>81</sup> and that the angle was independently associated with the LVOT gradient. Recently, pulsed-wave velocity using phase-contrast CMR demonstrated increased aortic stiffness in patients with HCM in comparison with controls and that aortic stiffness was higher in patients with HCM with replacement fibrosis than in those without late gadolinium enhancement (LGE).<sup>82</sup> Further work has demonstrated that increased aortic stiffness adversely affects exercise capacity, independent of LV morphology, diastolic function, and LVOT gradient.<sup>83</sup>

#### D. Dynamic Obstruction and Mitral Valve Abnormalities

Cine CMR can accurately identify the presence of mitral-septal contact in both long-axis and basal short-axis images. Furthermore, a systolic signal void jet can often be observed in the region of mitral-septal contact, a result of high-velocity flow, supporting the presence of subaortic obstruction (Video 5 [▶] view video clip online). To characterize the magnitude of subaortic obstruction in HCM, phase velocity flow-mapping sequences can be applied to determine peak velocity through the LVOT. However, only a small number of studies have assessed the accuracy of CMR-derived LVOT velocities compared with continuous-wave Doppler-derived pressure gradients.<sup>84</sup> Therefore, it is uncertain how well CMR-derived outflow tract velocities correspond to those obtained by Doppler echocardiography.<sup>85</sup> In addition, a number of technical limitations related to the phase velocity flow-mapping sequence make it difficult to apply it reliably in clinical scenarios. At the present time, CMR-derived velocities can be assessed only under basal conditions, which represents a major limitation,



**Figure 17** Contrast-enhanced CMR with LGE in HCM. **(A)** Asymptomatic 58-year-old woman with a large transmurular area of LGE in the basal anterior septum and anterior wall. **(B)** Diffuse and patchy area of LGE in the midmyocardial area of the ventricular septum in a 21-year-old man. **(C)** LGE confined to the area of RV free wall insertion into the anterior and posterior ventricular septum. *LA*, Left atrium; *LV*, left ventricle; *RA*, right atrium; *VS*, interventricular septum.

because one third of patients with HCM have outflow obstruction only during provocation. For these reasons, management decisions related to outflow obstruction should be predicated on pressure gradients derived from Doppler echocardiography.

#### E. Mitral Regurgitation in HCM

It is possible to visualize the mitral valve apparatus and assess the severity and mechanism of mitral regurgitation by CMR (Video 5), although formal quantification of the severity of mitral regurgitation is more commonly performed by echocardiography. CMR also can provide important information on the size and location of papillary muscles, as described above. These findings can be of potential value in planning surgery for the treatment of dynamic obstruction. Therefore, CMR should be considered in patients with HCM with suboptimal visualization of the mitral valve or papillary muscles by echocardiography, if patients decline TEE, or when the latter procedure is contraindicated.

#### F. Myocardial Ischemia, Fibrosis, and Metabolism

**i. Ischemia.** With the use of gadolinium-based contrast agents, myocardial blood flow under resting and stress conditions can be assessed using CMR.<sup>70</sup> Advances in CMR perfusion sequences now permit accurate qualitative and quantitative assessment of myocardial blood flow at rest and during pharmacologic stress (typically using adenosine). Stress CMR has demonstrated blunted myocardial blood flow in response to vasodilator stress in patients with HCM, which appears greater in the subendocardial layer in comparison with the subepicardial layer and is present in both hypertrophied and nonhypertrophied segments. There are currently no data relating CMR-derived measures of myocardial ischemia to clinical outcomes. Routine vasodilator stress CMR is not clinically recommended at this time.

**ii. Fibrosis.** Contrast-enhanced CMR with LGE sequences can detect areas of focally abnormal myocardial substrate in patients with HCM.<sup>72,74,86-88</sup> Areas of LGE can be planimeted and the amount quantified and expressed as a percentage of total LV mass. Selected reports in native hearts after transplantation of patients with end-stage HCM have demonstrated concordance between *in vivo* LGE CMR images and gross and histopathologic evidence of fibrosis.<sup>87</sup>

However, it still remains uncertain whether all LGE in patients with HCM with normal or hyperdynamic EF represents myocardial fibrosis. Similarly, the LGE technique misses background diffuse myocardial fibrosis changes, although new CMR techniques show promise in the quantification of diffuse myocardial fibrosis.

The prevalence of LGE in HCM is approximately 50% to 80% and when present occupies on average 10% of the overall LV myocardial volume.<sup>72,74,86,88</sup> There is no specific pattern of LGE characteristic for HCM, although predominately the distribution of LGE in HCM does not correspond to a coronary vascular distribution, as in patients who have had myocardial infarctions. LGE is most often located in the ventricular septum but not uncommonly can be confined to only the LV free wall or insertion points of the RV free wall and ventricular septum (Figure 17).<sup>74</sup> LGE is more common in segments with hypertrophy and in patients with HCM with larger LV mass indices.<sup>72,74,86</sup>

A number of studies have demonstrated a relationship between the extent of LGE and adverse LV remodeling associated with systolic dysfunction. The magnitude of LGE is greatest in patients with HCM in the end-stage phase of the disease (EF < 50%) and is less prevalent in patients with hyperdynamic EFs.<sup>72,74,86,88</sup> However, it is still unclear if the extent of LGE can be used to prospectively identify patients with HCM at risk for progressing toward systolic dysfunction. Likewise, a number of cross-sectional studies have demonstrated a significant association between the presence of LGE and ventricular tachyarrhythmias (including rapid ventricular tachycardia) on ambulatory 24-hour Holter electrocardiography.<sup>71,73</sup> However, it is not clear whether the extent of LGE provides greater predictive value in identifying patients with HCM at risk for sudden death compared with only the presence of LGE. Prognostic data with regard to LGE and cardiovascular outcome have now been evaluated in recent prospective short-term studies.<sup>86,88</sup> In one of these studies, a statistically nonsignificant trend toward an increased adverse cardiovascular event rate was observed in patients with HCM with LGE.<sup>86</sup> A significant relationship was observed between LGE and either sudden death or appropriate ICD discharge<sup>88</sup> in a more recent study. However, given the small number of adverse events, it is necessary to obtain longer follow-up in larger study cohorts to have the statistical robustness necessary to determine if LGE is indeed an independent predictor of adverse events in HCM.

Therefore it is not recommended for routine clinical decision making at this time.

**iii. Imaging Metabolism.** Nuclear magnetic resonance has been used to evaluate myocardial metabolism in few patients with HCM.<sup>89,90</sup> However, additional studies are needed to elucidate the pathophysiology of HCM and the development of progressive remodeling and heart failure as they relate to myocardial metabolism. Therefore, the clinical application of nuclear magnetic resonance in HCM is not recommended at the present time.

### G. Guidance of Septal Reduction Procedures

CMR can identify accessory papillary muscles, which are thought to contribute to the obstruction and which require resection for optimal relief of outflow gradients. Therefore, CMR can be a useful guide for preoperative surgical planning. CMR short-axis and long-axis cine imaging can demonstrate the myectomy trough in the area corresponding to the site of resection.

Contrast-enhanced CMR can accurately quantify the amount of tissue necrosis after septal ablation as well as provide important information regarding the relationship between the location of scarring and LVOT morphology. On average, the amount of myocardial infarct produced is 10% of the total LV mass.<sup>91</sup> CMR can determine the mechanism of suboptimal results after alcohol septal ablation, because in few patients, tissue necrosis involves predominately the RV side of the septum at the midventricular level, with septal thinning occurring distal to the area of mitral-septal contact, and resulting in the persistence of dynamic obstruction. CMR has demonstrated that LVOT gradient reduction after alcohol septal ablation results in LV remodeling associated with a reduction in mass of the ventricular septum and regions of myocardium remote from the area of infarction.<sup>92</sup> The routine performance of CMR after septal reduction therapy is not recommended, but it can be of value in selected patients when questions arise about LV function and remodeling after the procedure that could not be satisfactorily answered by echocardiography, or when gradients recur late after the procedure.

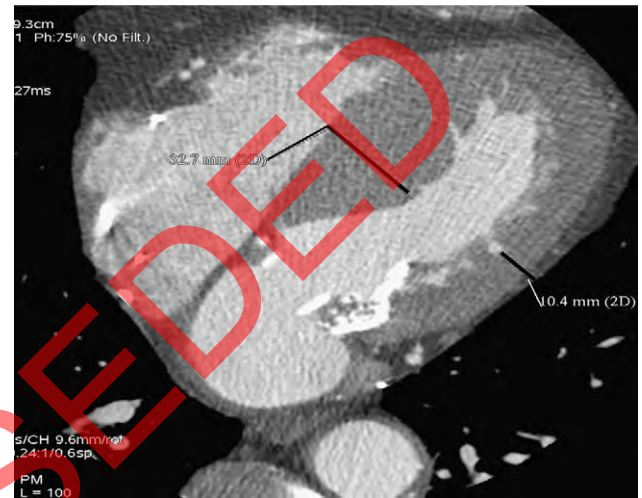
### H. Screening and Preclinical Diagnosis

A variety of potential morphologic abnormalities identified by CMR may be present in preclinical (genotype [+]/phenotype [–]) patients with HCM. Specifically, crypt formations localized predominately in the inferior septum have been demonstrated by CMR in preclinical patients, although the etiology of these structural abnormalities remains uncertain.<sup>93</sup> However, additional investigations are necessary to further clarify the prevalence and clinical significance of these CMR-derived morphologic abnormalities among preclinical patients with HCM, as some of these findings may be present in normal individuals.

At present, there are no systematic data evaluating the efficacy of CMR compared with echocardiography with regard to family screening for the detection of HCM. Given that CMR can identify LV hypertrophy not seen by echocardiography, CMR could still be considered in the evaluation of at risk family members, if there are suboptimal echocardiographic images, when all LV regions are not well visualized, when abnormal results of additional testing such as electrocardiography raise the suspicion of a diagnosis of HCM despite normal results on echocardiography, or in particularly high-risk family pedigrees in which a diagnosis of HCM remains equivocal but would have direct and immediate implications on treatment strategies such as implanta-

**Table 5** Cardiac CT in patients with HCM

1. LV morphology in patients with suboptimal echocardiographic studies and who cannot undergo CMR (eg, because of ICD or pacemaker)
2. Computed tomographic angiography for CAD evaluation
3. Can provide information on coronary anatomy and mitral annulus if needed before and after septal ablation (usually not needed in the presence of echocardiography and CMR)



**Figure 18** High contrast resolution on gated cardiac CT allows clear delineation of the myocardium, with sharp separation of contrast (white) and the myocardium (gray) and therefore can provide detailed characterization of the HCM phenotype. This patient with asymmetric septal hypertrophy had undergone pacemaker implantation, so CMR imaging was not possible. The lines and measurements refer to septal wall and lateral wall thickness.

tion of ICD for primary prevention of sudden death or exclusion from organized competitive sports.

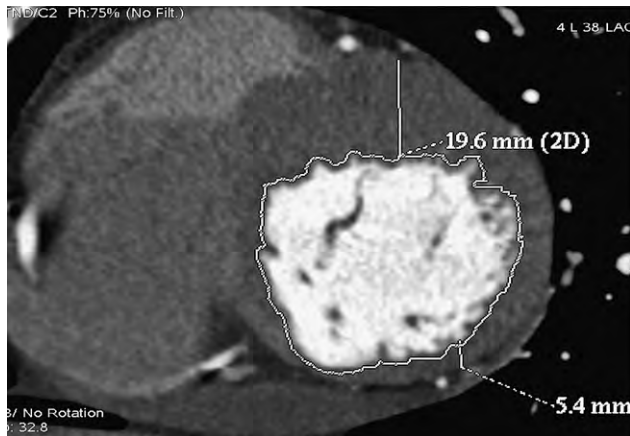
## 4. CARDIAC COMPUTED TOMOGRAPHY

### A. Cardiac Structure

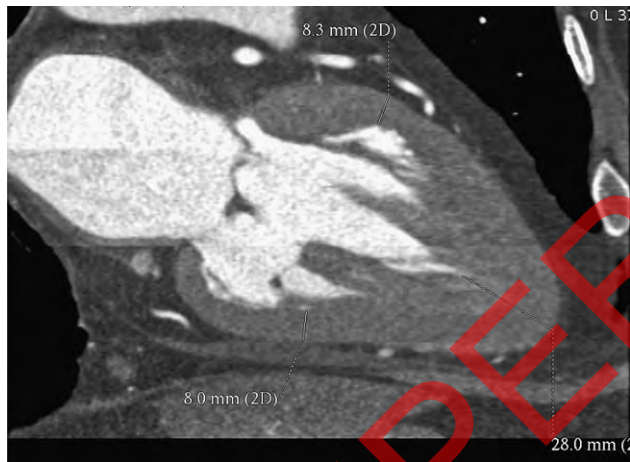
Cardiac computed tomography (CT) is a 3D tomographic imaging technique that provides images of the heart with good spatial and temporal resolution.<sup>94</sup> Because of isotropic imaging, LV short-axis and long-axis views can be created in 0.4-mm thin slices, providing complete tomographic coverage of the entire myocardium (Table 5).

High contrast resolution allows clear delineation of the myocardium, with sharp separation of contrast (white) and the myocardium (gray), and therefore can provide detailed characterization of the HCM phenotype (Figure 18), including accurate wall thickness measurements and highly reproducible measurements of ventricular volumes, EF, and mass.<sup>95,96</sup> The performance of 64-channel coronary computed tomographic angiography in patients with cardiomyopathy of uncertain etiology has been studied and compared with both CMR and invasive angiography,<sup>97</sup> but no studies systematically evaluating patients with HCM have been reported.





**Figure 19** Short-axis cardiac computed tomographic image demonstrating asymmetric myocardial hypertrophy. The measurements shown are those of the anterior septum (19.6 mm) and inferolateral wall (5.4 mm).



**Figure 20** All cardiac structures including papillary muscles are well visualized in this contrast computed tomographic reconstruction, which demonstrates apical hypertrophy. The anterior and inferior walls have normal end-diastolic wall thickness (8.3 and 8 mm, respectively), while the apex shows severe hypertrophy (28 mm) on cardiac CT.

Cardiovascular CT permits the simultaneous imaging of the coronary arteries, the presence of myocardial bridging, RV and LV volumes and mass, and both global and regional function.<sup>98,99</sup> All cardiac structures including papillary muscles are well visualized (Figure 19). Apical (Figure 20), septal, and papillary muscle hypertrophy can be readily delineated. CT provides accurate characterization of the extent of LV hypertrophy, including the identification of patients with marked hypertrophy (maximum wall thickness > 30 mm), which can be helpful for selection of patients for ICD therapy.

In summary, there are some advantages to cardiac CT in selected patients. Specifically, although poor acoustic windows may limit echocardiography, cardiac CT can reliably identify all LV segments and provide accurate measurements of wall thickness. Because of the higher spatial resolution of CT over CMR and echocardiography, it is at least equivalent or more likely superior with respect to volume

and mass measurements. However, CMR has superior tissue characterization capabilities.

At present, there are no systematic data evaluating the efficacy of cardiac CT compared with echocardiography or CMR with regard to evaluation or detection of HCM, so cardiac CT is generally not clinically recommended. Nevertheless, cardiac CT can be a useful modality in selected scenarios, including suboptimal echocardiographic images and when CMR is contraindicated (e.g., pacemaker or ICD implantation, when claustrophobia prohibits CMR, or when patients cannot hold their breath for long periods). In these scenarios, cardiac CT can be used, though the concern remains with higher radiation exposure with retrospective electrocardiographic gating, so prospective triggering should be used whenever possible.<sup>100</sup>

#### B. Assessment of LV Systolic Function

Cardiac CT provides an accurate assessment of LV volumes and EF. However, there are no data on its specific application in HCM.

#### C. Assessment of LV Diastolic Function

Cardiac CT is not indicated at this time for the assessment of LV diastolic function, because of its limited temporal resolution.

#### D. Dynamic Obstruction and Mitral Valve Abnormalities

Cardiac CT has been used to evaluate the 3D shape, size, and motion of the mitral annulus<sup>101</sup> and can delineate the presence of SAM of the anterior mitral valve leaflet in the multiphase images as well as the presence and extent of annular calcification.

Cardiac CT is not indicated at the present time for the evaluation of dynamic obstruction in patients with HCM, because of the ability to acquire such data by echocardiography and CMR without exposure to radiation.

#### E. Mitral Regurgitation in HCM

Papillary muscle abnormalities that affect mitral valve function can be assessed by CT. These abnormalities include the position and extent of hypertrophy of papillary muscles. However, the application of the technique for the assessment of mitral regurgitation in patients with HCM has not been evaluated.

#### F. Myocardial Ischemia, Fibrosis, and Metabolism

CT can readily image the coronary arteries, identify the presence, location, and extent of stenotic lesions, and identify the presence of myocardial bridging. It should be considered in the diagnostic workup of patients with HCM with chest pain who have intermediate to high probability of epicardial CAD. CT has no role at the present time for the evaluation of myocardial fibrosis and metabolism.

#### G. Guidance of Septal Reduction Procedures

CT can simultaneously image the length of the coronary arteries and the LV myocardium, allowing for the clear depiction of the relationship of the coronary arteries to the LV myocardium. This information can be useful for surgical myectomy and the planning and evaluation of alcohol septal ablation in HCM.<sup>102</sup> Although this is a promising role, routine cardiac CT is not indicated at the present time for this objective.

## H. Screening and Preclinical Diagnosis

There is no role at the present time for CT in the screening of patients for HCM and preclinical diagnosis.

## 5. HYPERTROPHIC CARDIOMYOPATHY IMAGING IN THE PEDIATRIC POPULATION

Two-dimensional echocardiography is the major diagnostic modality used in the noninvasive evaluation of HCM in the pediatric population.<sup>103,104</sup> Anatomic and physiologic features of HCM that are the hallmarks of this disease in adults are also characteristically prominent in children, including asymmetric thickening of the ventricular myocardium, dynamic LVOT obstruction, systolic and diastolic ventricular dysfunction, SAM of the mitral valve and chordal apparatus, and variable degrees of mitral regurgitation. In both children and adults, the anatomic pattern of hypertrophy (the “septal curvature”) has been shown to correlate with the presence of genetic mutation.<sup>105</sup>

Echocardiography also plays a pivotal role in excluding other causes of hypertrophy. Children with congenital heart disease, including coarctation of the aorta and valvular or subvalvular aortic stenosis, often present with significant LV hypertrophy due to increased afterload. Systemic diseases in the pediatric population can elicit marked hypertrophy, including systemic hypertension, renal arterial stenosis, pheochromocytoma, and metabolic or storage diseases. Syndromes including Noonan syndrome, LEOPARD syndrome, and Friedreich’s ataxia can also present with asymmetric or concentric forms of hypertrophy, mimicking sarcomeric HCM.

Recent studies have shown that LA volume has a similar association to disease severity in children with HCM, and is significantly related to the grade of diastolic dysfunction, clinical symptoms, and decreased exercise capacity.<sup>106</sup> After surgical myectomy in children with significant LVOT obstruction, LA volume has been shown to correlate with improved exercise performance and long-term outcomes.<sup>107</sup>

Doppler echocardiography plays a major role in the evaluation of children with HCM. Routine pulsed-wave mitral inflow and pulmonary venous inflow Doppler reflects impaired myocardial relaxation. Reduced early transmitral filling, prolonged isovolumic relaxation time, and prolonged atrial reversal in pulmonary venous flow are all characteristic of abnormal diastolic function in pediatric patients with HCM. The presence of a mid-diastolic transmitral filling wave may also be present in patients with HCM with markedly impaired relaxation.<sup>108</sup> In children with HCM, annular systolic and early diastolic tissue Doppler velocities at the septal and lateral mitral annulus are significantly decreased.<sup>18</sup> The septal E/e’ ratio has been shown to be a clinical predictor of increased risk for death, cardiac arrest, or ventricular tachycardia in children with HCM. It correlated closely with clinical symptoms and was inversely related to peak oxygen consumption.<sup>18</sup>

Novel echocardiographic methods that evaluate myocardial deformation have been reported in healthy children<sup>109,110</sup> and in young patients with HCM.<sup>111,112</sup> Children with HCM demonstrate decreased systolic deformation, with the most marked abnormalities of strain and strain rate noted in the most hypertrophied myocardial segments. However, even myocardial segments without evidence of hypertrophy have impaired deformation compared with healthy controls. Similar analyses of myocardial deformation in children with varying etiologies of LV

hypertrophy demonstrate decreased systolic deformation regardless of the underlying etiology, suggesting that hypertrophy has more influence on myocardial deformation than the cause of the hypertrophy.

## 6. ROLE OF IMAGING IN THE DIFFERENTIAL DIAGNOSIS OF HYPERTROPHIC CARDIOMYOPATHY

The diagnosis of HCM is based on the presence of LV hypertrophy in the absence of another disease process that is capable of producing a similar magnitude of hypertrophy. Cardiac amyloidosis, glycogen-storage diseases, Anderson-Fabry disease, and Friedreich’s ataxia can all cause hypertrophy but usually have concomitant noncardiac signs and symptoms that help steer the clinician toward the systemic disease process, including abnormally elevated creatine kinase, preexcitation pattern on electrocardiography, skeletal myopathy, skin involvement, or cerebral, cerebellar, or retinal disease or sensory-neural deficits. Cardiac morphology can also be helpful, because most of these other conditions produce concentric hypertrophy, while HCM produces asymmetric hypertrophy in most cases. LVOT obstruction is less common in these other conditions. CMR with gadolinium enhancement can facilitate identification of some of these systemic diseases. For example, adult patients with Anderson-Fabry disease have LGE confined largely to the basal inferolateral wall, which is unusual for sarcomeric HCM.<sup>113</sup> Furthermore, CMR may also help clarify the diagnosis of LV noncompaction in patients initially diagnosed with (or presumed to have) apical HCM. CMR can demonstrate the presence of prominent trabeculations consistent with the diagnosis of LV noncompaction.<sup>114</sup>

It can be difficult to determine whether hypertrophy is due to hypertension or caused by HCM. However, hypertension usually results in concentric rather than asymmetric hypertrophy. It is also rare for hypertension to produce wall thickness in excess of 18 to 19 mm, whereas it is quite common for HCM patients to have wall thicknesses > 20 mm.

In some elderly subjects, discrete hypertrophy may be localized to the upper septum, with or without a sigmoid septal morphology. The latter is identified by a generally ovoid LV cavity and a concave septum toward the left ventricle, with a pronounced basal septal bulge. Sometimes, the sigmoid septum occurs in the presence of normal septal thickness. Although these patients can have dynamic obstruction, they are much less likely to have sarcomeric protein mutations.

A relatively common concern has to do with the differentiation of possible HCM from the physiologic myocardial hypertrophy that develops in response to intense athletic training.<sup>115</sup> Because HCM is the most common cause of sudden death among athletes in North America, patients with HCM are counseled against participation in competitive athletics.<sup>1,116</sup> However, the large body sizes of many advanced athletes and the potential for physiologic hypertrophy can result in a picture similar to HCM. Therefore, the implications of distinguishing these two situations are important. Studies of elite-level athletes have shown that it is quite rare (<1.5%) for even the most advanced athletes to demonstrate LV wall thicknesses > 12 mm.<sup>117-119</sup> Another common morphologic feature of athlete’s heart is chamber dilation, such that the end-diastolic dimensions are at or exceed the usual normal range,<sup>119</sup> whereas patients with HCM have small LV cavity dimensions. The pattern of hypertrophy is usually concentric or eccentric in athletes.

**Table 6** Summary of clinical applications

|   | Echocardiography                          | Nuclear imaging  | CMR  | Cardiac CT   |
|---|---|--|--|--|
| 1. LV dimensions, wall thickness            | Recommended as initial test               | Not recommended  | Recommended with inadequate echocardiography | Rarely needed if echocardiography and CMR are not feasible |
| 2. LV EF and regional function              | Recommended as initial test               | Not needed if echocardiography and CMR are available       | Recommended with inadequate echocardiography | Not needed if echocardiography and CMR are available       |
| 3. LV filling pressures                     | Recommended                               | Not recommended as it provides only indirect evidence      | Not recommended                              | Cannot be used for this purpose                            |
| 4. Pulmonary artery pressure                | Recommended                               | Cannot be used for this purpose                            | Cannot be used for this purpose              | Cannot be used for this purpose                            |
| 5. LA volume and function                   | Recommended                               | Cannot be used for this purpose                            | Recommended with inadequate echocardiography | Rarely needed if echocardiography and CMR are not feasible |
| 6. Dynamic obstruction                      | Recommended                               | Cannot be used for this purpose                            | Recommended with inadequate echocardiography | Cannot be used for this purpose                            |
| 7. Mitral regurgitation                     | Recommended                               | Not recommended  | Recommended with inadequate echocardiography | Not recommended  |
| 8. Ischemia/CAD (if clinically indicated)   | Considered if nuclear and CT not feasible | Recommended  | Research application                         | Recommended if epicardial CAD in question                  |
| 9. Cardiac metabolism and neurotransmission | Cannot be used for this purpose           | Research application                                       | Research application                         | Cannot be used for this purpose                            |
| 10. Monitoring of invasive therapy          | Recommended                               | Rarely needed if echocardiography and CMR are not feasible | Recommended with inadequate echocardiography | Rarely needed if echocardiography and CMR are not feasible |
| 11. Image replacement fibrosis              | Research application                      | Not recommended  | Recommended test                             | Cannot be used for this purpose                            |
| 12. Screening                               | Recommended                               | Not recommended  | Recommended with inadequate echocardiography | Not recommended  |

Because HCM is a pathologic process, whereas athletic training results in physiologic adaptation, the goal of cardiac imaging is to look for other evidence of pathology that would favor the diagnosis of HCM. To this end, extreme LA enlargement and myocardial dysfunction (systolic and diastolic) do not occur in athlete's heart but are common features of HCM. Doppler tissue imaging,<sup>120</sup> coronary flow reserve,<sup>121</sup> and gadolinium imaging have all been reported to allow distinction of athlete's heart from HCM. Ultimately, cessation of training can result in regression of hypertrophy in athletes, with no impact on wall thickness in patients with HCM.

The evaluation of aortic valve disease in patients with HCM with coexisting dynamic obstruction and aortic stenosis can be challenging with TTE. High-resolution transesophageal echocardiographic images can be used to measure the aortic valve area by planimetry.

## 7. RECOMMENDATIONS FOR CLINICAL APPLICATIONS

### A. Assessment of Morphology

A comprehensive echocardiographic examination is the appropriate imaging modality to consider in patients with HCM (Table 6). The report should specifically include LV dimensions, wall thickness

(including end-diastolic thickness of the septum, inferolateral wall, and maximum thickness in any segment), pattern (asymmetric, concentric), and distribution of LV hypertrophy (segments involved and whether apical hypertrophy is present). Not infrequently, RV hypertrophy occurs as well, and RV wall thickness should be measured in subcostal or the parasternal images.<sup>2</sup> Contrast echocardiography, if needed, should be used as described above in the "Echocardiography" section. In most patients, this basic assessment can be readily obtained by echocardiography.

In patients with suboptimal images, CMR should be performed. In addition, CMR may be considered in the initial evaluation of patients when any segment of the LV myocardium is not well visualized by echocardiography. CMR is currently not a diagnostic option in patients with ICDs or pacemakers (but newer pacemakers may permit CMR evaluation). In these cases, cardiac CT can be used for morphologic characterization.

Repeat echocardiographic evaluation is usually considered with any change in clinical status. because a small subset of patients can develop progressive LV dilatation along with decreases in EF, serial assessment may be considered every 1 to 2 years, even in asymptomatic patients. In addition, it is useful to assess changes in septal thickness and LV dimensions and volumes after septal reduction therapy, particularly in patients with residual symptoms.



### Key Points.

1. **Echocardiography is the initial imaging modality of choice for the evaluation of cardiac morphology.**
2. **CMR is recommended with suboptimal echocardiographic images and in patients with incomplete and/or unsatisfactory assessment of individual segmental wall thickness by echocardiography. CMR may be considered in selected patients with high index of suspicion for HCM.**
3. **Cardiac CT is recommended when echocardiographic images are inadequate and when CMR is contraindicated, as in patients with ICDs or pacemakers.**
4. **The imaging report should include measurement results of LV dimensions, wall thickness (including maximum wall thickness), and pattern of hypertrophy and its severity and distribution.**

### B. Assessment of LV Systolic and Diastolic Function

Echocardiographic assessment of LV EF is feasible in most patients. CMR should be considered in patients with suboptimal images. In the presence of suboptimal echocardiographic images and a contraindication to CMR, radionuclide angiography or cardiac CT may be considered. Measurement of myocardial deformation and torsion is feasible with tissue Doppler and speckle tracking by echocardiography, as well as CMR. At the present time, routine measurement of strain and torsion is not recommended. However, it remains a useful research tool for understanding the pathophysiology of HCM and the effects of treatment on myocardial function.

The vast majority of patients with HCM have diastolic dysfunction, and echocardiography is the recommended imaging modality because of its versatility and high temporal resolution. A comprehensive assessment as recommended in the recent ASE guidelines<sup>19</sup> is feasible in most patients. Conclusions should be included in the report as to the status of LV relaxation, filling pressures, LA volume, and pulmonary artery pressures. Filling rates, whether by CMR or radionuclide angiography, although feasible, have limitations in this population, as discussed above.

### Key Points.

1. **Echocardiography is the initial imaging modality of choice for the evaluation of LV EF, which should be included in the report.**
2. **CMR is recommended with suboptimal echocardiographic images.**
3. **Cardiac CT or radionuclide angiography can be considered for EF assessment when echocardiographic images are inadequate and CMR is contraindicated.**
4. **Echocardiography is the only modality recommended for the evaluation of LV diastolic function, and a comprehensive approach should be followed per the recent ASE and European Association of Echocardiography guidelines.<sup>19</sup>**

### C. Assessment of LVOT Obstruction

In approximately 70% of patients, dynamic LVOT obstruction due to the combination of hypertrophy, abnormal blood flow vectors, and SAM of the mitral valve is an important feature. Obstruction is highly load dependent and is augmented in states of reduced preload (as in hypovolemia), reduced afterload, or increased contractility. The day-to-day variability of LVOT gradient can exceed 30 mm Hg.

Echocardiography is the imaging modality of choice to assess the hemodynamics of dynamic obstruction. LVOT obstruction should be assessed by pulsed-wave Doppler to localize the site of obstruction

and continuous-wave Doppler to estimate the peak gradient, taking care to avoid the mitral regurgitation jet. Of note, dynamic obstruction can also occur at the midcavity level and at the ventricular apex. For patients with gradients < 30 mm Hg, it is important to perform provocative maneuvers. A significant increase in LVOT velocity can be recorded during the strain phase of the Valsalva maneuver (due to decreased preload) or with amyl nitrite, which decreases afterload in many patients. It is important to proceed to stress echocardiography on symptomatic patients without significant dynamic obstruction at rest, because exercise-induced gradients are often much higher than those provoked by the Valsalva maneuver.

For patients who can exercise, the more physiologic treadmill stress test should be performed, because it provides data not only on dynamic obstruction but also on exercise tolerance and the changes in blood pressure with exercise.<sup>122</sup> Stress testing using supine bicycle protocols can be considered in selected patients who are unable to perform upright exercise and can facilitate the measurement of LV filling pressures and pulmonary artery systolic pressure at rest and during exercise.<sup>19</sup> However, given the increased venous return in a supine position, LVOT gradients can be lower during supine bicycle protocols. Although low-dose dobutamine echocardiography (up to 20  $\mu\text{g}/\text{kg}/\text{min}$ ) can be used as a method of provocation for patients unable to exercise but with symptoms (in the absence of a gradient at rest), such patients are best assessed at more experienced centers. This method of provocation is similar to using isoproterenol in the catheterization laboratory to provoke dynamic obstruction. Pharmacologic provocation needs to be done with careful imaging to ensure that the observed Doppler signal is due not to cavity obliteration but to SAM. Importantly, identifying and treating provokable obstruction results in an improvement in qualitative and quantitative measurements of exercise tolerance and hemodynamic status.<sup>123</sup>

Because of the technical limitations of CMR and limited experience, LVOT gradients by Doppler echocardiography are recommended for clinical decisions, but CMR may be considered in more challenging clinical scenarios, as in patients with suspected subvalvular pathology or those with previous intervention.

### Key Points.

1. **Echocardiography is the recommended test. Pulsed-wave Doppler is used to localize site of obstruction, and continuous-wave Doppler is needed to determine peak gradient.**
2. **In symptomatic patients with LVOT gradients < 30 mm Hg at rest, gradients can be provoked by the Valsalva maneuver, amyl nitrite (when available), and if possible with exercise (preferably treadmill exercise).**
3. **CMR may be considered in more challenging clinical scenarios, as in patients with suspected subvalvular pathology or those with previous intervention.**

### D. Evaluation of Patients Undergoing Invasive Therapy

In symptomatic patients, the goal of imaging is to characterize the interplay among the three entities resulting in SAM and LVOT obstruction: septal thickness and excursion and mitral valve and papillary muscle geometry.<sup>124</sup> Although 2D TTE is sufficient in many cases, 3D echocardiography and CMR are rapidly emerging as useful adjuncts, especially for the assessment of mitral valve and papillary muscle morphology. Once the decision has been made to proceed with surgery, intraoperative TEE is important for operative planning, including an estimate of the amount of myocardium that needs to be removed and the length of the anterior mitral leaflet. It is also

**Table 7** Risk factors for sudden cardiac death

| Risk factor                           | Imaging modality  |
|---------------------------------------|---|
| 1. Maximum wall thickness $\geq 3$ cm | Echocardiography, CMR, cardiac CT                           |
| 2. End-stage HCM (EF < 50%)           | Echocardiography, radionuclide angiography, CMR, cardiac CT |
| 3. Apical aneurysms                   | Contrast echocardiography, CMR, and cardiac CT              |
| 4. LVOT gradient $\geq 30$ mm Hg      | Doppler echocardiography                                    |
| 5. Perfusion defects                  | SPECT (though no association in some studies)               |
| 6. Reduced coronary flow reserve      | PET (observations limited to very few patients)             |
| 7. LGE (presence and extent)          | CMR (evidence not conclusive)                               |

important after surgery to determine if residual SAM, dynamic obstruction (either spontaneously or using isoproterenol), and mitral regurgitation are present, which may necessitate further intervention.

For patients undergoing alcohol septal ablation, contrast echocardiography is essential to help identify the culprit septal segments and avoid inducing infarction in remote sites. Follow-up echocardiography after either procedure can be considered to assess the effects of either procedure on LV hypertrophy, EF, diastolic function, and mitral regurgitation. Both SPECT and LGE CMR can be used to determine the presence, distribution, and extent of scar after septal ablation. CMR has the advantage of better spatial resolution while avoiding radioactive isotopes. However, the routine performance of SPECT and CMR is not recommended. CMR can be considered in the presence of suboptimal echocardiographic images or in patients with residual obstruction.

#### Key Points.

- 1. Echocardiography is recommended before septal reduction therapy to assess septal thickness and mitral valve and papillary muscle pathology.**
- 2. In patients undergoing surgical myectomy, intraoperative TEE is needed to guide surgery. In the operating room after myectomy, TEE is recommended to determine the presence of SAM, residual obstruction, mitral regurgitation, and ventricular septal defects.**
- 3. Intracoronary contrast echocardiography is essential before alcohol septal ablation to help identify the culprit septal segments and avoid inducing infarction in other sites.**

#### E. Diagnosis of CAD in Patients With HCM

Although stress echocardiography can be used to evaluate for regional dysfunction with exercise, there are few studies that have examined its accuracy in this population. There are also concerns about its lower sensitivity in patients with LV hypertrophy and potentially lower wall stress. The use of vasodilator stress testing in conjunction with SPECT does not have the same limitations of echocardiography. However, false-positive results can occur because of increased counts from the septum due to asymmetric hypertrophy and the approach of normalizing counts to this site. Furthermore, true perfusion defects can occur because of microvascular and not epicardial CAD. The presence of normal wall motion on gated studies in areas with spuriously low counts can help avoid erroneous conclusions. CMR stress testing with vasodilators has been applied in other populations, but there remains little information about the validity of this approach in HCM. Computed tomographic angiography provides a direct assessment of the coronary arteries and can identify changes in the coronary circulation after septal ablation.

#### Key Points.

- 1. In patients with HCM with chest pain and low probability of CAD, stress SPECT can be considered.**
- 2. Coronary angiography, including computed tomographic angiography, is recommended in patients with chest pain and intermediate pretest probability of CAD.**

#### F. Screening

##### Key Points.

- 1. Echocardiography is recommended as the initial screening modality in first-degree relatives.**
- 2. Echocardiography should be performed at yearly intervals during adolescence and every 5 years in adults.**
- 3. CMR is indicated with technically challenging echocardiographic studies or when a complete satisfactory evaluation of all myocardial segments by echocardiography is not feasible.**

#### G. Role of Imaging in Identifying Patients at High Risk for Sudden Cardiac Death

Massive LV hypertrophy is among the currently recognized risk factors that can be identified by imaging. A maximum wall thickness  $\geq 3$  cm is one of the major risk factors and can be reliably obtained by echocardiography, CMR, and cardiac CT. These imaging modalities can also identify additional subgroups of patients with HCM who remain at high risk for events, including those with "end-stage" HCM and patients with apical aneurysms (Table 7).

The presence of an LVOT gradient  $\geq 30$  mm Hg on echocardiography has been associated with a higher likelihood of mortality.<sup>125</sup> However, the load-dependent labile nature of the gradient limits its utility in clinical practice. It is uncertain whether LGE on CMR predicts sudden cardiac death, though it has been associated with clinical risk factors and ventricular arrhythmias. Of note, none of the four short-term follow-up studies<sup>8,6,88,126,127</sup> of LGE in HCM demonstrated that LGE is an independent predictor of sudden death. These studies used composite end points made up of a number of clinical events that were grouped. Furthermore, it is unclear whether the presence or a threshold amount of LGE is enough. It is our belief that the current data do not support routine LGE for risk stratification to make decisions about ICD therapy for primary prevention. However, LGE may be of potential value in selected patients when risk stratification for sudden cardiac death is not conclusive.

Perfusion defects on SPECT and reduced coronary flow reserve on PET are additional findings, though only a few studies in a small

number of patients have reported on these findings. Accordingly, the writing group recommends using echocardiography to determine maximum wall thickness, LV EF, the presence of apical aneurysm, and the severity of dynamic obstruction. CMR is recommended in patients with suboptimal images and when myocardial segments are not adequately visualized by echocardiography.

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