CME

Screening for hypertrophic cardiomyopathy

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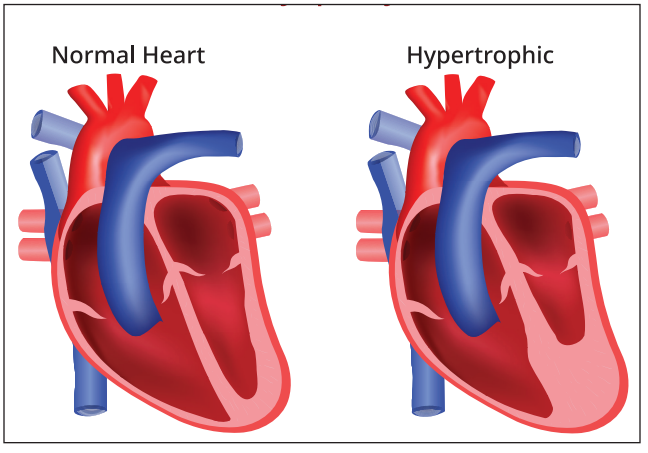
ABSTRACT

Hypertrophic cardiomyopathy (HCM) is the most common inherited cardiomyopathy and causes changes in the cardiac muscle affecting ventricular, valvular, and cellular functions. Because HCM is an inherited disorder, all age groups are affected; however, it commonly presents in adolescents, especially athletes. Many patients are asymptomatic and undiagnosed, putting them at risk for sudden cardiac death. This article describes screening and management of patients with HCM.

Keywords: hypertrophic cardiomyopathy, inherited, cardiac disease, left ventricular hypertrophy, sudden cardiac death, screening

Learning objectives

- Describe the clinical presentation of HCM.
- Identify diagnostic tools for diagnosing HCM.
- Outline the typical treatment for HCM.



Hypertrophic cardiomyopathy (HCM) is an autosomal dominant inherited cardiac disease that results in left ventricular (LV) hypertrophy and disproportionate septal hypertrophy. In undiagnosed patients, HCM can be a silent killer because complications can lead to further cardiac dysfunction and death.[1] HCM is one of the most common causes of sudden cardiac death, especially in competitive young athletes who may exhibit no symptoms despite the presence of disease.[2]

Screening children for HCM is important because they may not exhibit symptoms if they do not play sports or participate in activities that cause physical exertion.[1] Screening for symptoms and assessing ECG findings may help with early diagnosis and reduce complications.[3]

PATHOPHYSIOLOGY

MYH7, *MYBPC3*, *TNNT2*, and *TNNI3* are the most common genes responsible for HCM and encode for the sarcomere proteins that are found in the myocardium.[4] The incidence rate of HCM is 1 in 500 in the United States; however, the incidence is projected to be higher (1 in 200) because of the high number of asymptomatic patients.[5] HCM is more common in males than females.[5]

HCM may occur at different anatomical regions of the heart, including the septum, apex, and ventricular walls.[1] Patients may experience symptoms including dyspnea on exertion, angina, atypical chest pain, fatigue, syncope, and palpitations. HCM may progress to dilated cardiomyopathy because dilation of the ventricles leads to diastolic and/or systolic dysfunction. Although most patients with HCM are diagnosed as preadolescents, clinicians should consider screening older children and adults based on the patient's symptoms and medical and family history.

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Key points

- Screen patients for HCM early, especially those with a strong family history, to prevent sudden cardiac death or progression to heart failure.
- Screening sensitivity and specificity increases with using multiple diagnostic tools such as the AHA 14-point evaluation, ECG, and echocardiogram.
- Lifestyle modification is the initial treatment for patients with HCM; heart transplant is definitive.

PHYSICAL EXAMINATION FINDINGS

A patient history of syncope, chest pain and dyspnea with exertion, palpitations, or family history of sudden cardiac death are associated with HCM.[4] Physical examination may reveal a harsh crescendo-decrescendo systolic murmur best heard at the apex with radiation to the axilla upon auscultation of the heart. This mitral regurgitation murmur is caused by the LV outflow tract obstruction and increases with Valsalva maneuvers. Other physical examination findings include an S_4 heart sound and/or a left ventricular lift on palpation of the chest. Some patients may be asymptomatic; they would need to be screened to assess for abnormal myocardial thickening to aid in the diagnosis of HCM.[6]

ECG An ECG may be indicated based on patient symptoms, family history, or positive physical findings. Routine screening with an ECG is not recommended.[3] Abnormal findings usually are associated with septal wall thickness and worsening of symptoms.

ECG findings may include P-wave changes due to left atrial enlargement, septal Q waves in inferior and lateral leads, left axis deviation, inverted T waves in leads V_2-V_4, and LV hypertrophy. ECG is the most sensitive, routine diagnostic test for HCM; however, a normal ECG result should prompt further evaluation if the patient has documented physical examination findings such as a harsh crescendo-decrescendo systolic murmur.[7] Although signs of HCM may be present on physical examination, ECG findings associated with HCM may not appear until the disease progresses.

The sensitivity and specificity of diagnosing HCM can be increased by using ECG along with the American Heart Association (AHA) 14-point screening tool (**Table 1**).

Williams and colleagues recommend using AHA's 14-point evaluation in all routine medical visits for students under age 19 years, and referring patients for further cardiac evaluation if more than one item is positive.[3] Williams and colleagues evaluated the performance of the AHA 14-point evaluation compared with an ECG and found that the AHA evaluation had a sensitivity of 18.8% and a specificity of 75.1% compared with ECG, which had a sensitivity of 87.5.% and a specificity of 97.5%.[3] History, physical examination findings, and ECG are important steps to diagnosing HCM, although ECG should not be used as the sole screening method.[3]

TABLE 1. AHA 14-point evaluation for competitive athletes

Personal history
- Exertional chest pain or discomfort
- Unexplained syncope or near-syncope
- Excessive and unexplained dyspnea, fatigue, or palpitations associated with exercise
- Previous recognition of a heart murmur
- Elevated systemic BP
- Previous restriction from participating in sports
- Previous cardiac testing ordered by a physician

Family history
- Premature death (sudden and unexpected, or otherwise) before age 50 years due to heart disease in one or more relatives
- Disability from heart disease in a close relative under age 50 years
- Specific knowledge of genetic cardiac conditions in family members: hypertrophic or dilated cardiomyopathy, long QT syndrome or other ion channelopathy, Marfan syndrome, or clinically important dysrhythmias

Physical examination
- Heart murmur judged likely to be organic and unlikely to be innocent; auscultate with the patient in supine and standing positions or with Valsalva maneuver, specifically to identify murmurs of dynamic LV outflow tract obstruction
- Femoral pulses to exclude aortic coarctation
- Physical stigmata of Marfan syndrome
- Brachial artery BP (sitting position, preferably taken in both arms)

Reprinted with permission from Maron BJ, Friedman RA, Kligfield P, et al. Assessment of the 12-lead ECG as a screening test for detection of cardiovascular disease in healthy general populations of young people (12-25 years of age). *Circulation.* 2014;130(15):1303-1334.

24-hour ambulatory ECG Further testing may be warranted, such as 24-hour ambulatory ECG monitoring for patients for continuous evaluation of symptoms and possible dysrhythmias (such as ventricular tachycardia) that could lead to sudden cardiac death.[8] The 24-hour ambulatory ECG could be used in patients who have displayed symptoms in the past or are showing symptoms.[8] This test also could be used in a patient who has a positive family history of dysrhythmias or sudden cardiac death.

Genetic testing Although genetic testing can be used to diagnose HCM, use is low because it is very costly, averaging $3,000 to $3,500 for initial testing.[9] HCM is an autosomal dominant transmitted disorder that results from a mutation in one of nine sarcomere proteins' genetic makeup but can also occur due to *de novo* mutations. Multigene panels can diagnose HCM by looking at several genes associated with HCM.[10] The genomic deoxyribonucleic acid is isolated from the patient's sample and tested for particular sequences in the coding exons and adjacent

nucleotides through polymerase chain reaction and sequencing.[11] The identified genes make up 80% of the known genetic causes of HCM. In addition, two-thirds of pediatric cases of HCM have been linked to a genetic cause.[12] Consider genetic counseling and testing in patients who have a family history of cardiomyopathies and unexplained causes of sudden death, history of unexplained syncope, and any other symptoms as discussed earlier.

Echocardiogram HCM often can be diagnosed and monitored via echocardiogram. According to one study, HCM is diagnosed when the patient has unexplained myocardial thickening of greater than 15 mm, or a septal-to-posterior-wall thickness ratio greater than 1.3 in patients who do not have a history of hypertension. A posterior wall thickness ratio greater than 1.5 in patients with history of hypertension confirms the diagnosis of HCM.[13] Because an increase in septal thickness is associated with increase in risk of cardiac death, patients with a diagnosis of HCM should have an echocardiogram to further assess wall thickness. The echocardiogram also can let clinicians see any LV hypertrophy, assess for LV outflow tract obstruction, see systolic anterior motion, measure the left atrial size, and assess systolic and diastolic LV function.[14]

Cardiac MRI Myocardial edema can be visualized on cardiac MRI. Cardiac MRI has many benefits; compared with echocardiography, it can better identify patterns of hypertrophy and assess LV mass and diastolic wall thickness.[15] Cardiac MRI also could be used to assess fibrotic changes in the heart if beta-blocker treatments become less effective. Assessing myocardial fibrosis is important because fibrosis can influence the prognosis of patients with HCM as increased fibrosis in turn causes the heart to work harder leading to the development of symptoms and strain placed on the heart.[15] Although cardiac MRI is beneficial in patients with HCM, it is expensive, time-consuming, can make patients feel claustrophobic, and is contraindicated in patients with implanted cardioverter-defibrillators (ICDs).[15]

In conclusion, several diagnostic studies can be used to diagnose HCM. **Figure 1** maps out which studies should be ordered based on the patient's initial history and physical examination findings if further testing is warranted.

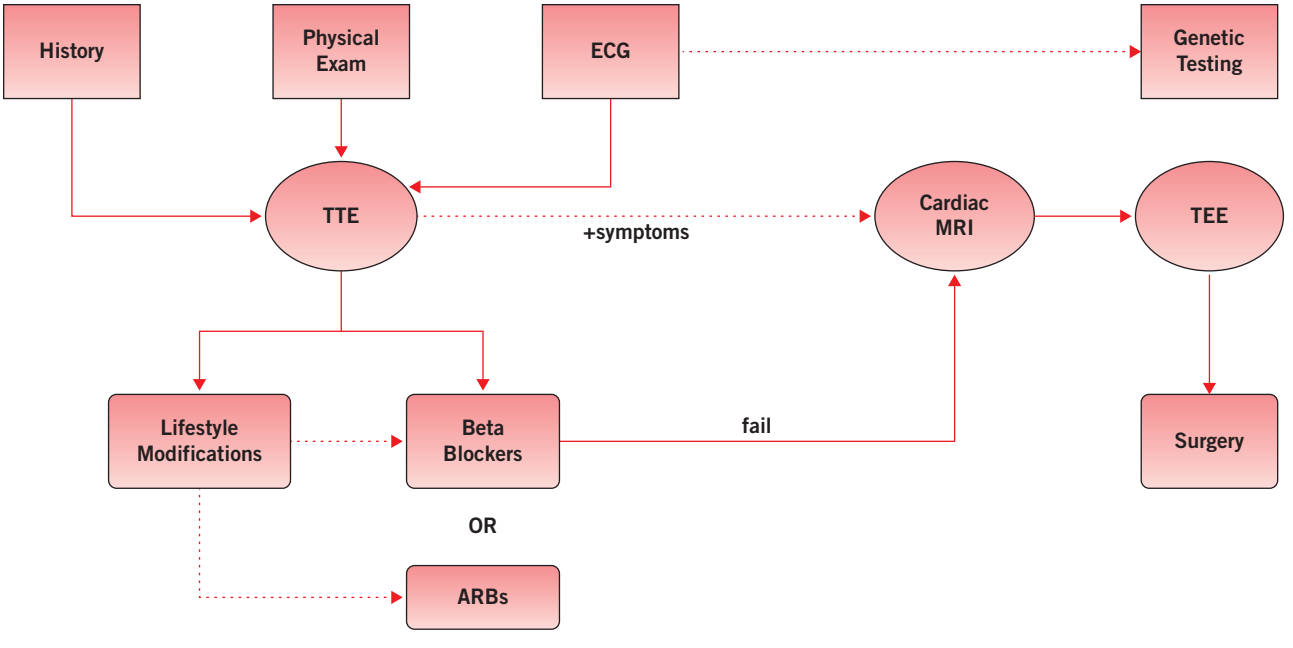
RECOMMENDATIONS

The AHA recommends its 2011 14-point evaluation for screening healthy patients ages 12 to 25 years for HCM; if one item is positive, the patient should be evaluated further (**Table 1**).[16] The guidelines also recommend against universal screening with a 12-lead ECG because of the cost burden on the healthcare system.[17] Patients diagnosed with HCM who participate in strenuous physical activity may need additional routine follow-up with their cardiologist to assess for development of new symptoms.

First-degree relatives of patients with HCM should be screened clinically with or without genetic testing.[18] Patients with HCM should undergo genetic counseling and evaluation of familial inheritance. However, the usefulness of genetic testing in assessing patient risk of sudden cardiac death is not known.[19]

Based on the 2011 ACCF/AHA guidelines, a transthoracic echocardiogram (TTE) is recommended for initial evaluation of HCM, which is in line with the recommendations made by Fox and colleagues while using point-of-care ultrasound.[8,19] Additionally, first-degree relatives should be evaluated via TTE.[20] Transesophageal echocardiogram

FIGURE 1. Diagnostic algorithm for HCM



(TEE) is recommended for patients who are candidates for a surgical myectomy due to an obstructive pattern. Pressure tracings during a left cardiac catheterization may reveal LV outflow tract obstruction based on LV peaking systolic pressure of greater than 200 mm Hg and a gradient of 95 mm Hg between the LV and aorta.[21]

The 2011 ACCF/AHA guidelines recommend using cardiac MRI for patients with suspected HCM when echocardiography is inconclusive for the diagnosis.[8] Patients with HCM also should undergo cardiac MRI if the imaging may affect management, especially in regard to invasive management.[22] If echocardiography cannot define apical hypertrophy, cardiac MRI is reasonable. Finally, consider cardiac MRI with assessment of late gadolinium enhancement for patients with known HCM with inconclusive risk stratification for sudden cardiac death, or patients with LV hypertrophy with a raised suspicion of HCM.[23]

TREATMENT

Treatment options for HCM start with patient education about lifestyle modifications. To prevent sudden cardiac death in athletes, patients must stay well hydrated and work with their healthcare provider to make an individualized exercise plan.[24] Patients should continue with 30 minutes of moderate exercise three times a week, such as aerobic walking or running, to promote general wellbeing, reduce the risk of obesity, and improve diastolic functioning capacity.[25]

Diet is an important component of lifestyle changes. Patients with HCM should eat a low-sodium, low-carbohydrate diet to promote heart health.[26] Patients should have yearly lipid profiles to check their LDL levels.[27] LDL levels should be below 100 mg/dL to reduce the risk of coronary artery disease and myocardial infarction.[27] Weight management is critical to reduce the effects of comorbidities; increased afterload can markedly reduce LV function.[28]

Close follow-up with the healthcare team is encouraged for patients with HCM, to prevent further complications. Patients should see their dentist every 6 months to reduce the possibility of dental or oral infections that can lead to endocarditis.[29] Patients also should follow up with their primary care provider or cardiologist every 6 to 12 months depending on disease severity.[30] Keeping BP below 130/80 mm Hg can help patients reduce the risk of developing LV hypertrophy secondary to increased afterload.[31] Lastly, educate patients on avoiding smoking and illicit drugs.[32,33]

Medication management is the next step in treatment, because LV hypertrophy can lead to hypertension, aortic stenosis, and increased afterload.[28] Patients who have exercise-induced symptoms such as chest pain and syncope are candidates for pharmacologic treatment.[34] The primary goal of medication management is to reduce symptoms and control hypertension.[8,35] Medications that have been used in the past include beta-blockers (atenolol, metoprolol, and propranolol), calcium channel blockers (verapamil and diltiazem), HMG-CoA reductase inhibitors (atorvastatin), angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers, and antiarrhythmics (disopyramide and amiodarone).[35] Beta-blockers inhibit sympathetic stimuli, reducing heart rate and myocardial workload.[36]

Patients may be candidates for an ICD if their risk of sudden cardiac death is high. A sudden-death risk score may be used; however, the sensitivity for predicting sudden cardiac death is low.[37] Thus, ICD placement should be considered for patients with known HCM because the structural cardiac changes put them at greater risk for dysrhythmias.[38,39] Patients must be aware of the risks associated with ICD placement, including inappropriate shocks and device malfunction such as lead fracture.

Surgical intervention is an option for patients with HCM, especially if they meet New York Heart Association class III and IV categories and are symptomatic. A septal myectomy is considered the preferred treatment option for these patients.[39] Patients with concomitant valvular disease and coronary artery disease are candidates for a surgical myectomy of the interventricular septum, especially if they are not responding to medication management.[34] A surgical procedure such as a septal myectomy will help improve the rate of blood flow.[21] Ultimately, the most definitive treatment for HCM is a heart transplant.

COMPLICATIONS

Undiagnosed HCM may lead to sudden cardiac death, especially in young athletes. Nonsustained ventricular tachycardia and ventricular premature beats are common dysrhythmias in patients with HCM.[35] Additionally, supraventricular dysrhythmias also may be present in patients with HCM. Patients with LV outflow obstruction may have complications such as elevated ventricular pressure from mitral valve regurgitation leading up to heart failure.

CONCLUSION

Although the prevalence of HCM is low compared with other cardiac conditions such as hypertension and myocardial infarction, limited screening and testing mean that many patients are undiagnosed, putting them at increased risk for morbidity and mortality. Based on the AHA recommendations, the 14-point history questionnaire is one key component to diagnose HCM.[40] Clinicians should evaluate patients for clinical signs and symptoms and evaluate diagnostic test results to diagnose patients with HCM for proper disease management. This will help reduce complications and prevent sudden cardiac death, especially among athletes. **JAAPA**

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