Hypertrophic Cardiomyopathy

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Abstract

Hypertrophic cardiomyopathy is a common, genetically transmitted cardiovascular disease affecting 1 in 500 persons. Patients with hypertrophic cardiomyopathy can be asymptomatic. Often the first presenting symptom is sudden cardiac death. The nurse practitioner must be aware of the diagnostic impact of hypertrophic cardiomyopathy on the patient and family, the importance of early diagnosis, and current management and treatment options. The purpose of this article is to review hypertrophic cardiomyopathy and increase awareness of this disease among nurse practitioners.

CLINICAL DESCRIPTION

Hypertrophic cardiomyopathy (HCM) is a familial, genetic, cardiovascular disorder affecting 1 in 500 persons (1). Dr. Robert Donald Teare was one of the first physicians to recognize HCM. Over 50 years ago, he observed characteristic asymmetrical thickening of the ventricular septum and sudden cardiac death in a group of patients from the same family (1). As asymmetric ventricular hypertrophy involving the septum is only one feature of HCM, healthcare professionals now know that other features include atrial enlargement, myocyte disarray, and interstitial fibrosis (1). HCM causes stiffening and delayed relaxation of the ventricles, thus requiring higher pressure to expand with the inflow of blood (1). As a consequence diastolic heart failure develops and may progress to a dilated or systolic heart failure.

HCM can be non-obstructive or obstructive to blood flow. Non-obstructive HCM is the more common form and is characterized by ventricular muscle thickening without impedance of blood flow out of the left ventricle. Left ventricular outflow obstruction is seen in 25% of patients with HCM and is often referred to as hypertrophic obstructive cardiomyopathy (HOCM) (2). In the past, HOCM was known as idiopathic hypertrophic subaortic stenosis (IHSS). Obstruction of blood flow out of the left ventricular outflow tract generates rapid ejection of blood, resulting in the pulling the anterior leaflet of the mitral valve toward the thickened septum. The pulling motion is called systolic anterior motion (SAM), and constant pulling of the mitral valve leaflet leads to mitral regurgitation. The blood flow obstruction seen in HOCM can be transient or persistent (3, 4). HCM varies widely among patients in both the severity of the disease and the complications that may occur.

Most patients with HCM are asymptomatic or have very few symptoms. Clinical progression of the disease is slow, and medications help. HCM takes one of four different paths (5). The first path is sudden cardiac death from ventricular arrhythmias that occur due to the myocte disarray of the cardiac cells which causes disturbances in the normal conduction of the electrical activity of the heart. The second path presents progressive symptoms of dyspnea on exertion, chest pain, pre-syncope, dizziness, and syncope. The third path is the progression of the HCM to heart failure followed by a dilated form of cardiomyopathy which occurs in 10 to 15% of patients (2). The fourth path is comprised of complications related to the development of atrial fibrillation secondary to HCM (5). Atrial fibrillation and the loss of atrial kick associated with atrial fibrillation decreases cardiac output and presents symptoms in patients who were originally asymptomatic. The fact that many patients with HCM are asymptomatic suggests that the incidence and prevalence of HCM may be under estimated (6).

INCIDENCE/PREVALENCE

Although HCM is the most common inherited cardiac disorder, no differences in incidence exist between genders (7). HCM is also a common cause of exercise-related sudden cardiac death in athletes less than 35 years old, and the most common cause of death in athletic events (2). For adults, the peak incidence of HCM is in the second decade of life, while the peak distribution is in the fourth through the sixth

decades of life (7).

The prevalence of HCM in the general population is 0.2% (12). The annual rate of sudden cardiac death secondary to HCM ranges from 0.5% to 1.5% (3). Four-percent of patients with HCM die each year (7). Although most deaths occur from sudden cardiac death secondary to arrhythmias, heart failure is less likely to be the cause of death. A recent study of 2155 patients with HCM in Japan found that patients with a low ventricular ejection fraction, a left bundle branch block on the electrocardiogram, or a high cardiothoracic ratio on a chest x-ray had poorer prognoses (8).

GENETICS

HCM has an autosomal-dominant mode of inheritance, where autosomal refers to a mutation on one of the numbered chromosomes (9). When a mutation is passed on in a dominant way, only one mutation is sufficient to cause the condition, and a person with one dominant mutation of HCM will develop HCM (9). A child of a person with HCM has a 50% chance of getting the mutation. Despite the identification of genetic mutations leading to HCM, this disorder remains genetically diverse with more than 450 known mutations in 13 genes (10). In the past HCM was considered idiopathic, but is now recognized as a disorder resulting from dominant mutations in genes encoding the proteins of the contractile apparatus (8). HCM can be caused by mutations in genes encoding cardiac myosin heavy chain BMHC, MyBPC, cardiac troponin T, cardiac troponin I, essential light chains, regulatory light chains, and cardiac actin (11).

The variability in clinical course may be explained by the different roles that mutant proteins play in the sarcomere (10). Mutations in the gene-encoding cardiac myosin heavy chain were the first to be identified as a cause of familial HCM. The genes of HCM may present early in life, and is believed to cause severe hypertrophy, increase the risk of outflow obstruction, and increase the risk of sudden death. The cardiac myosin-binding protein C (MyBPC) mutations often cause late onset HCM and have a favorable prognosis (8). The variability in HCM is also affected by the co-existence of hypertension or ischemic heart disease. Tsoutsman and colleagues found Tnl-203/MHC-403 double mutant mice developed a severe cardiac phenotype characterized by heart failure and early death (10). The authors concluded that the presence of two disease-causing mutations predisposes individuals to a greater risk of developing severe heart failure than human HCM caused by a single gene mutation.

Genetic testing for HCM has been limited by costs (1). Mutation analysis for eight sarcomeric genes is now commercially available for clinical testing (9). However, the test costs over $4000, and many insurance companies do not pay for testing. Due to the heterogeneity of HCM, false negative test results may occur, although a negative test does not exclude the possibility that the individual's HCM is caused by a mutation that was not tested (9). The lack of specific genetic testing does not prevent testing with standard diagnostics, such as echocardiography and electrocardiogram.

The traditional recommended screening interval/follow-up for patients and families with HCM is every 12 to 18 months (2). Screening involves performing both echocardiogram and electrocardiogram (7). Testing of family members should begin at age 12, and, if no evidence of hypertrophy throughout the years develops, testing may conclude at age 21 (7). However, the guideline is controversial. As substantial molecular diversity and heterogeneity of HCM, some believe testing should continue into mid-life (6).

DIAGNOSIS

Early identification and evaluation of the subtle symptoms related to HCM by the NP may avoid the initial presentation of sudden cardiac death. A comprehensive physical examination and review of symptoms by the nurse practitioner may lead to a diagnosis of HCM. The most common symptoms of HCM are dyspnea, chest pain, fatigue, palpitations, dizziness, and syncope. Syncope can result from inadequate cardiac output secondary to left ventricular outflow obstruction or from ventricular arrhythmias and may be provoked by exertion or exercise. Ventricular arrhythmias occur in 75% of HCM patients undergoing ambulatory monitoring (2). Chest pain and heart failure symptoms also develop from diastolic dysfunction and from outflow obstruction, which causes mitral regurgitation and fluid backs up into the left atrium and lungs. Significant shortness of breath occurs if the mitral regurgitation and or outflow obstruction worsens. A careful patient and family history by the NP also may reveal clues to HCM. However, a physical exam and history may not provide any signs of HCM. A diagnosis of HCM may be suspected if the patient has a history of syncope or a family history of sudden death. Patients with HCM often have a harsh, systolic crescendo-decrescendo murmur at the left

sternal border (7). The murmur must be carefully assessed, as the systolic murmur of HCM may be misinterpreted to be the systolic murmur of aortic stenosis. Typically, the intensity of the systolic murmur diminishes with squatting and increases with standing (5). Radiating, systolic murmurs along the carotid arteries are most likely to be the systolic murmur of aortic stenosis.

NPs must provide a comprehensive work-up and thorough history and physical with attention to the review of symptoms in the attempt to identify those patients at risk for HCM. As a result, providing early interventions may prevent the sequela of complications associated with HCM. The awareness of the NP of how HCM is diagnosed and knowledge of the risk factors for sudden death are key in helping to prevent complications of HCM. All patients with HCM should be assessed for risk of sudden cardiac death according to the American College of Cardiology/European Society of Cardiology guidelines (Table 1) (2).

Figure 1

Table 1: Risk Factors for Sudden Cardiac Death in Patients with HCM

History of Cardiac Arrest
Family History of Sudden Cardiac Death
Left Ventricular Thickness > 30 mm
Non-Sustained Ventricular Tachycardia on Holter
Syncope
Decrease Blood Pressure with Exercise
Intense Exercise
Left Ventricular Outflow Obstruction
Myocardial Ischemia
Atrial Fibrillation

An echocardiogram is gold standard and used to confirm the diagnosis of HCM (6). More specifically, a left ventricular wall thickness greater than 15 mm establishes HCM (2). The echocardiogram also identifies outflow obstruction. The electrocardiogram may be normal in patients with HCM, but typically shows ST-segment and T-wave abnormalities, and giant negative T-waves in the precordial leads may be seen (2). Holter monitoring is also used to detect any arrhythmias.

Differential diagnoses for HCM include disorders that cause hypertrophy of the left ventricle. These disorders include the athlete's heart syndrome, left ventricular hypertrophy secondary to hypertension, and cardiac amyloidosis (11). Whereas the hypertrophy seen in HCM is asymmetrical, the hypertrophy seen in hypertension, cardiac amyloidosis, and athlete's heart syndrome is concentric. Once the diagnosis of HCM is made or suspected, the NP must individualize the patient's treatment plan.

MANAGEMENT/TREATMENT

Medical management is directed towards reducing symptoms and preventing complications. The treatment and management is often difficult because of the heterogeneous nature of the disorder and the lack of randomized controlled trials. Recent guidelines on HCM published by the American College of Cardiology and the European Society of Cardiology help clinicians in decision making. Currently, no specific algorithm is available to guide treatment and assess prognosis so treatment plans must be individualized. Management and treatments include beta blocker therapy, calcium channel blocker therapy, antiarrhythmic therapy, internal cardiac defibrillator (ICD) placement, alcohol ablation of the intraventricular septum, septal myectomy surgery, and surveillance.

The most common medications used are beta blockers which slow the heart rate, enhance diastolic filling, and decrease myocardial oxygen demand (3). The use of beta blockers helps the heart to contract and relax. Calcium channel blockers also help to relax the stiff left ventricle and increase filling of the ventricles. An antiarrhythmic drug, such as amiodarone, is commonly used in patients found to have ventricular arrhythmias on holter monitoring. Medications that decrease afterload of the heart should be avoided as these agents cause a further reduction in the filling pressures, a fall in blood pressure and syncope.

The prophylactic treatment of asymptomatic HCM patients with ICDs is controversial. An ICD can be life saving to the patient with HCM and ventricular arrhythmias as sudden cardiac death is most commonly caused by ventricular arrhythmias. Rapid defibrillation is critical to the patient's survival. ICD placement is indicated in high risk HCM patients, such as those that have a decreased blood pressure with exercise, history of cardiac arrest or ventricular tachycardia, family history of cardiac arrest, history of unexplained syncope, and or severe muscle thickening. Takagi, Yamakado, and Nakano studied both completely asymptomatic and symptomatic patients with HCM and found that patients who were completely asymptomatic have a significantly lower mortality rate than those with symptoms (0.9 % vs. 1.9 % respectively, $p<0.05$) (12). ICD insertion in young patients may be lifesaving, yet invoke many psychosocial issues.

Maron and colleagues examined the clinical risk profile of sudden cardiac death from ventricular arrhythmias and the

use of ICDs (7). These authors studied 506 patients with HCM who underwent ICD placement for primary or secondary prevention of sudden cardiac death. The mean age of the participants was 42 years, and all patients were followed for four years. The authors found that the ICD successfully terminated ventricular arrhythmias in 20% of the patients. The researchers also discovered that patients who received an internal cardiac defibrillator for only one risk factor had a similar incidence of internal cardiac defibrillator firings. The authors looked at four risk factors, which included a family history of sudden death due to HCM, massive left ventricular hypertrophy, non-sustained ventricular tachycardia on holter monitoring, and prior unexplained syncope (7). The conclusion was that a single risk factor for sudden cardiac death in HCM may be enough to justify implantation of an internal cardiac defibrillator as primary prevention.

Approximately 20 to 40 % of patients with HOCM who develop heart failure symptoms will be refractory to medical therapy. Alcohol septal ablation (ASA) of the intraventricular septum can be performed via alcohol infused into the septal coronary artery that supplies blood to the septum. The alcohol causes death of that area of the septum and reduces the hypertrophy. The reduction in the septal hypertrophy decreases the left ventricular outflow obstruction. A systematic review of 42 ASA studies by Alam, Dokainish, and Lakkis found that ASA offers good outcomes to patients with HCOM (13). Patients who had ASA performed had an increase in exercise tolerance and decrease in the diameter of the basal septum. The mortality within 30 days of the procedure was 1.5% and the mortality after 30 days was 0.5%. Although ASA is a percutaneous procedure and much less invasive than surgery, complete heart block during and after the procedure may require permanent pacemaker insertion.

Another treatment option for HCM patients who are refractory to medical treatment is surgical septal myectomy which involves re-sectioning a small amount of the ventricular septum (6). Surgery may also involve repair of the mitral valve. Surgery is much more invasive than ASA.

Education regarding activity, medications and follow-up is critical. Patients must be instructed to avoid hypovolemia which may reduce the filling pressures of the heart and increase the risk of syncope. Patients with HCM should avoid strenuous activities and competitive sports. The NP is in a unique position to educate the patient and family members about HCM. Education regarding all aspects of HCM is critical, including the risk of sudden cardiac death. The diagnosis of HCM impacts not only the patient, but the family. Family members, as well as patients with HCM, may feel anxiety about the possible development of HCM. The patient with HCM may live in fear of sudden cardiac death. The NP can provide support for the patients and family and help to relieve their anxieties. Education regarding a home automated external defibrillator and cardiopulmonary resuscitation should be included.

CONCLUSION

HCM is a common inherited cardiovascular disorder, yet is often under-recognized. Nurse practitioners must be aware of HCM and how the condition is diagnosed. The NP can play a major role in identifying patients with HCM. The importance of assessing risk and relaying treatments options to patients is an important role. The NP also plays a critical part in the symptom management, family evaluation and prevention of sudden cardiac death in patients with HCM. Patients with HCM can be identified through a complete history and physical examination. Individualized care can then be developed for each patient with HCM, as HCM varies in the severity of symptoms and complications. The nurse practitioner is in a key position to provide education on activity, risk factors for sudden cardiac death, genetic testing, and follow-up for the patient and family. In the future, genetic testing and identification of genes will continue to help clarify the treatment and management of patients with HCM.

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