in symptoms and cardiac function, but in others, the disease is progressive and associated with a high mortality rate.

Hypertrophic Cardiomyopathy

Definition and Epidemiology

Hypertrophic cardiomyopathy (HCM) is a disease state characterized by unexplained left ventricular hypertrophy with nondilated ventricular chambers in the absence of an apparent cause for hypertrophy (e.g., hypertensive disease, aortic stenosis). This is a relatively common genetic disease (1 case in 500 people in the general population) with autosomal dominant inheritance, although spontaneous mutations have been described. More than 1400 mutations identified among at least eight genes encoding proteins of the cardiac sarcomere have been described, with mutations of the β-myosin heavy chain being the most common.

Pathology

The main pathophysiologic abnormalities seen in HCM are left ventricular outflow obstruction, diastolic dysfunction, mitral regurgitation, and arrhythmias. Obstruction of left ventricular outflow occurs in roughly one half of the patients. During systole, the hypertrophied septum bulges into the left ventricular outflow tract, creating a gradient between the lower part of the left ventricular cavity and the left ventricular outflow. This causes high-velocity turbulent flow through the narrowed path, which results in a suction force (i.e., Venturi effect) that pulls the anterior leaflet of the mitral valve into the outflow tract. This worsens the obstruction and causes mitral regurgitation. Diastolic dysfunction from impaired relaxation properties of the abnormal myocardium causes marked elevation of left ventricular filling and pulmonary venous pressures, pulmonary congestion, and limitation in cardiac output. Patients with HCM are also predisposed to supraventricular and ventricular arrhythmias.

Clinical Presentation

HCM is a heterogeneous cardiac disease with a diverse course and clinical manifestations. Most patients probably do not suffer sequelae from this disease during their lifetimes. When the disease does result in complications, there are three relatively discrete but not mutually exclusive clinical manifestations: sudden cardiac death due to unpredictable ventricular tachyarrhythmia, most commonly in young asymptomatic patients (<35 years of age); heart failure characterized by exertional dyspnea (with or without chest pain) that may progress despite preserved systolic function and sinus rhythm; and atrial fibrillation that associates with various degrees of heart failure.

Heart failure symptoms result from the dynamic obstruction to left ventricular outflow and diastolic dysfunction. The most frequent symptom is dyspnea on exertion, followed by ischemic chest pain due to the increased oxygen demand by the hypertrophied ventricle and elevated wall tension that reduces blood flow to the subendocardium. Abnormalities of the structure of small myocardial arteries in HCM can contribute to myocardial ischemia. Presyncope or syncope can result from outflow tract obstruction and an inability to increase cardiac output during exertion or from arrhythmias that can be triggered by exertion. In some, sudden death caused by ventricular arrhythmia is the initial manifestation of the disease.

Physical examination findings include pulsus bisferiens, a brisk initial upstroke in pulse followed by a mid-systolic dip corresponding to the development of left ventricular outflow tract obstruction, followed by another rise in late systole. Cardiac examination may shows a forceful and sustained apical impulse, an audible S_4 gallop, and a harsh crescendo-decrescendo systolic murmur best heard along the left sternal border with radiation to the base of the heart.

Patients may also have an apical holosystolic murmur of mitral regurgitation. The intensity of the murmur of HCM varies with changing degrees of obstruction. This can be observed with physiologic or pharmacologic maneuvers that change preload (i.e., left ventricular filling) or contractility. The intensity of the murmur increases with a Valsalva maneuver, with assuming a standing position, and after administration of nitroglycerin or inotropic drugs. The intensity of the murmur decreases with squatting, volume loading, and administration of β-blockers.

Diagnosis

Clinical diagnosis is made most commonly with echocardiography and increasingly with cardiac MRI. The diagnosis is based on a maximal left ventricular wall thickness of 15 mm or more; a wall thickness of 13 to 14 mm is considered borderline. The diagnosis can be made in the setting of other compelling information (e.g., family history of HCM). Genetic testing is available to confirm the diagnosis and to screen family members.

Treatment

The ACC/AHA hypertrophic cardiomyopathy guideline recommends tailored therapy based on the individual patient. For asymptomatic patients, the usefulness of β-blockade and verapamil is a class IIb recommendation. For patients symptomatic with dyspnea or angina, β-blockers and verapamil are recommended (level of evidence B). If patients remain symptomatic, it is reasonable to add disopyramide to a β-blocker or verapamil (level of evidence B).

Nonpharmacologic therapies should be considered in patients with considerable symptoms despite medical management. Septal reduction therapy is recommended only for patients with severe drug-refractory symptoms and left ventricular outflow tract obstruction (level of evidence C) (Fig. 10-3). Use of ICD therapy is guided by the perceived risk for ventricular arrhythmias in individual patients; it can prevent sudden death in these patients (level of evidence C). Some of the characteristics that have been associated with this risk are prior cardiac arrest or sustained ventricular tachycardia; great (>30 mm) ventricular wall thickness; syncope, especially if exertional or recurrent; and a first-degree relative with sudden cardiac death. Certain genotypes appear to convey an increased risk of sudden cardiac death. Patients with HCM should be excluded from most competitive sports and should avoid strenuous exercise.

Prognosis

The clinical course of HCM varies. Sudden cardiac death is the leading cause of mortality. Heart failure symptoms may gradually progress, and some patients who are unresponsive to conventional therapy may require heart transplantation.