Hypertrophic Cardiomyopathy
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Clinical diagnosis of HCM is usually established with two-dimensional echocardiography by demonstrating left ventricular (LV) hypertrophy, typically asymmetric in distribution, and associated with a nondilated chamber in the absence of another cardiac or systemic disease capable of producing the magnitude of hypertrophy evident.2,4 This definition of HCM is independent of whether LV outflow obstruction or cardiac symptoms are present.

During the past few decades, numerous investigations have led to an evolution in our understanding of the clinical, genetic, and pathologic spectrum of HCM.1 In the process, the disease has acquired a myriad of names largely related to its substantial clinical, functional, and morphologic diversity. Hypertrophic cardiomyopathy is the preferred name because it describes the overall disease extent without introducing the misleading inference that outflow tract obstruction is an invariable feature.1,2,4

Epidemiologic studies with a variety of study designs have shown similar estimates for the prevalence of phenotypically expressed HCM in the adult general population of approximately 0.2% (1:500).3 Therefore, HCM is not rare and, in fact, is the most common genetic cardiovascular disease transmitted as an autosomal dominant trait.5 It is now apparent, based on discrepancies between the prevalence of HCM in the general population compared with cardiology practice, that most patients affected by this disease are unrecognized clinically, including many at high-risk for SCD.1–3 Furthermore, because more than 30 million patients undergo a surgical procedure each year in North America, it may be expected that a substantial number of HCM patients will receive perioperative and anesthetic care at least one time during their lives.

It is possible to regard most of the HCM clinical spectrum as a single, unified disease entity and a primary disorder of the sarcomere. Mutations in the β-myosin heavy chain and myosin-binding protein C genes comprise almost one half of the genotyped patients to date, whereas six other sarcomere genes each account for a small number of cases, i.e., cardiac troponin T, cardiac troponin I, α-tropomyosin, cardiac α-actin myosin regulatory light chain, myosin essential light chain.2 This genetic diversity is compounded by intragenic heterogeneity, with more than 400 mutations now identified.5 These are most commonly missense mutations with a single amino acid residue substituted for another but also include insertions, deletions, and splice (split site) mutations encoding truncated sarcomeric proteins.

Most recently, mutations in two nonsarcomeric genes have been recognized as causing diseases with LV hyper-

HYPERTROPHIC cardiomyopathy (HCM) is a genetic cardiac disorder caused by mutations in one of at least 12 sarcomeric or nonsarcomeric genes and is recognized as the most common cause of sudden cardiac death (SCD) in the young and an important substrate for disability at any age.1,2 The broad phenotypic expression and disease complexity have consistently generated uncertainty regarding this disorder. Technological developments coupled with advanced understanding of epidemiology, clinical course, and molecular defects responsible for HCM have promoted new diagnostic management strategies.2 Anesthesia providers caring for patients with this heterogeneous disease should be aware of its potential life-threatening nature and should be familiar with new clinical insights to afford optimal treatment during the perioperative period. Conversely, anesthesiologists may be confronted with clinically unrecognized HCM and should be prepared to anticipate the hemodynamic changes and cardiovascular instability that such patients may impose.

Nomenclature, Etiology, and Prevalence

Hypertrophic cardiomyopathy is unique among cardiovascular diseases by virtue of its potential for clinical presentation during any phase of life, from infancy to older than 90 yr.3 Although adverse clinical consequences of the disease, particularly sudden cardiac death, are well documented, a more balanced perspective regarding prognosis has recently evolved in which normal longevity is recognized in a substantial proportion of patients.5

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trophy (often associated with Wolff-Parkinson-White pattern on electrocardiogram) that mimic HCM but are due to glycogen storage in the myocardium, i.e., the gene encoding the \( \gamma_2 \)-regulatory subunit of the adenosine monophosphate–activated protein kinase (PRKAG2) and a mutant gene for Danon disease involving the lysosome-associated membrane protein 2-\( \alpha \)-galactosidase or acid \( \alpha_1,4 \)-glucosidase, usually with massive degrees of hypertrophy.\(^6\) The phenotypic expression of HCM is believed to be the product not only of a disease-causing mutation, but also of modifier genes and environmental factors. Therefore, a large number of genes and mutations (including many not yet identified) may influence the expression of the HCM phenotype.

Recent studies have recognized the role of genetics in the genesis of electrophysiologic abnormalities associated with HCM. For example, increased risk of atrial fibrillation in HCM has been linked to a particular misexpression of the HCM phenotype.\(^6\) The phenotypic expression of HCM is believed to be the product not only of a disease-causing mutation, but also of modifier genes and environmental factors. Therefore, a large number of genes and mutations (including many not yet identified) may influence the expression of the HCM phenotype.

Recent studies have recognized the role of genetics in the genesis of electrophysiologic abnormalities associated with HCM. For example, increased risk of atrial fibrillation in HCM has been linked to a particular missense mutation in the \( \beta \)-myosin heavy chain gene. However, many adolescents (and some adults) harboring a genetic defect for HCM do not necessarily express typical clinical and phenotypic features, although electrocardiographic abnormalities or evidence of diastolic dysfunction by tissue Doppler imaging may precede appearance of LV hypertrophy on echocardiogram.\(^7\)

Although laboratory DNA analysis for mutant genes is the most definitive method for establishing the HCM diagnosis, important obstacles remain for translating such research-based genetic technology into practical clinical strategies on a widespread and routine basis. These factors include the aforementioned genetic heterogeneity of HCM, as well as the methodologic difficulties associated with identifying a single disease-causing mutation among a total of at least 12 possible HCM genes. However, when a HCM mutation is identified in a proband, definition of genetic status can be achieved in all family members efficiently and inexpensively. Diagnostic molecular laboratories\(^8\) have recently begun to address these challenges by offering rapid, direct DNA sequencing for a subset of HCM disease genes.\(^9\) Nonetheless, a significant potential remains for false-negative results (i.e., in which HCM diagnosis cannot be ruled out).

**Morphologic Characteristics**

**Anatomical Features**

Virtually all possible patterns of LV wall thickening occur in the HCM patient population, and none can be regarded as classic or typical of the disease, although anterior ventricular septum is usually the predominant region of hypertrophy.\(^1,4\) Distribution of LV hypertrophy is almost always asymmetric, although a small proportion (approximately 1%) show a concentric or symmetric form.\(^1,4\) A large proportion of affected patients show diffuse involvement of the septum and LV free wall, but that is not invariably, and approximately 30% of patients have only localized (usually mild) thickening confined to a single segment of the wall, including unusual areas such as the LV apex, anterolateral free wall, or posterior portion of the septum\(^4\) (fig. 1).
**Histologic Features**

Many cardiac muscle cells in both the ventricular septum and the LV free wall show increased transverse diameter and bizarre shapes, as well as disorganized architectural patterns with adjacent cells arranged at oblique and perpendicular angles. Cardiac muscle cell disarray is present in 95% of patients who die of HCM and usually occupies substantial portions of the LV (average area, approximately 33%). These histopathologic findings are not confined to the hypertrophied regions of LV but are also present in areas of normal wall thickness. In addition, there is substantial collagen distribution within the LV wall as part of an expanded interstitial (matrix) compartment.

Abnormal intramural coronary arterioles with thickened walls and narrow lumen may account for bursts of myocardial ischemia. The degree to which there is a mismatch between myocytes and arterioles depends largely on the magnitude of LV mass. Therefore, disorganized myocardial architecture and myocardial replacement scarring as a repair process after ischemia due to small vessel disease (and consequently cell death), as well as the large collagen matrix compartment, probably serve as the electrically unstable arrhythmogenic substrate predisposing some susceptible patients to life-threatening reentrant ventricular tachyarrhythmias (fig. 1).

**Mitrail Valve Abnormalities**

Primary malformations of the mitral valve apparatus, responsible for dynamic LV outflow tract obstruction, are present in at least two thirds of patients in an HCM population. These abnormalities include enlargement and elongation of the mitral leaflets in a variety of patterns with increased mitral valve tissue area (ranging up to twice normal), as well as anomalous papillary muscle insertion directly into the anterior mitral leaflet, producing muscular midcavity obstruction. These structural malformations of the mitral apparatus expand the morphologic definition of HCM by demonstrating that the disease process is not confined to cardiac muscle alone (fig. 2).

**Age-related Morphologic Changes**

It is generally believed (in the absence of genetic testing) that when both LV hypertrophy on echocardiogram and electrocardiographic abnormalities are not present in HCM family members by the time full growth has been achieved at the age of approximately 18 yr, it is unlikely that the disease phenotype will develop. Such clinical judgments have generally proved reasonable because, in the majority of affected individuals, virtually complete penetrance of the phenotype is evident by the end of the adolescent growth period. However, recent genotype-phenotype investigations have shown, in fact, that de novo LV remodeling and development of the HCM phenotype may extend into midlife or even beyond, particularly in patients with myosin-binding protein C gene mutations.

Paradoxically, a subtle decrease in LV wall thickness seems to be associated with aging in the adult HCM population, particularly in women. Extreme reduction in wall thickness associated with systolic dysfunction and chamber enlargement represents evolution into the end-stage phase (for which heart transplantation is the only treatment option).

**Athlete’s Heart and HCM**

Hypertrophic cardiomyopathy is the most common cause of SCD in young competitive athletes. Relevant to this consideration is the clinical dilemma frequently encountered in distinguishing HCM from physiologic (and benign) LV hypertrophy due to athletic training.
Increased LV wall thickness (in the “gray zone” of 13–15 mm) in trained athletes may trigger the differential diagnosis between a mild morphologic form of HCM and an extreme expression of “athlete’s heart.” This important distinction can be resolved clinically by documenting HCM in a relative or by noninvasive testing of other clinical variables. 

### Diagnostic Modalities

Clinical identification of HCM continues to be customarily based on transthoracic two-dimensional echocardiographic recognition of the disease phenotype with LV hypertrophy (wall thickness ≥ 15 mm), unassociated with ventricular cavity enlargement. However, genotype–phenotype correlations in family members have demonstrated that virtually any LV wall thickness (including normal) is compatible with the presence of a mutant HCM gene. Maximum LV wall thicknesses show a particularly wide range, extending up to 60 mm and the most substantial in any cardiac disease. Mean LV wall thickness in a population of HCM patients is 21–22 mm, far exceeding on average that observed in systemic hypertension or aortic valve stenosis.

The degree of LV outflow tract obstruction is assessed by continuous-wave Doppler echocardiography, at rest or with physiologic provocation under exercise conditions, by virtue of the characteristic midsystolic peaking waveform. Mitral regurgitation, usually mild to moderate in degree, accompanies outflow obstruction with the regurgitant jet typically directed posteriorly. Flow duration, maximum velocity, and Doppler spectral configuration differentiate the mitral regurgitation jet from that of LV outflow. Markedly impaired myocardial relaxation due to hypertrophied myocardium is characteristic. Isovolumic relaxation time is prolonged, peak velocity of early filling is reduced, and deceleration time prolonged. Generally, transesophageal echocardiography has only a limited clinical role in HCM but is useful in the operating room for monitoring outflow obstruction and hemodynamic changes associated with fluid management and drug administration, as well as operative strategy and assessment of the results during septal myectomy.

The 12-lead electrocardiogram is abnormal in 75–90% of patients with HCM, showing a variety of abnormal patterns, none of which is pathognomonic or highly specific for this disease. Most common are tall voltages consistent with LV hypertrophy, ST-segment alterations and T-wave inversion, left atrial enlargement, abnormal Q waves, and diminished or absent R waves in the left precordial leads. Furthermore, there is little correlation between electrocardiographic voltages and magnitude of LV hypertrophy assessed by echocardiography; the heterogeneous patterns observed on electrocardiogram have little predictive value for clinical outcome. Nevertheless, abnormal electrocardiograms may have diagnostic value by raising suspicion of HCM in young family members who do not yet show LV hypertrophy on echocardiogram.

Contemporary cardiac magnetic resonance imaging provides high-resolution, tomographic images of the entire LV and represents an additional diagnostic modality in HCM. Magnetic resonance is particularly valuable in patients with technically suboptimal echocardiographic studies or occasionally when hypertrophy is confined to unusual locations within the LV wall (e.g., anterolateral free wall or apex). Therefore, magnetic resonance has an evolving role as a supplemental clinical imaging test and may be superior to echocardiography in selected HCM patients.

### Pathophysiology

The pathophysiologic determinants of clinical course and disease progression in HCM include (1) dynamic obstruction to LV outflow due to mitral valve systolic anterior motion and ventricular septal contact; (2) diastolic dysfunction, associated with increased filling pressures resulting from impaired LV relaxation and filling of a hypertrophied and noncompliant LV; (3) impaired coronary vasodilator reserve and myocardial ischemia; and (4) supraventricular and ventricular tachyarrhythmias (e.g., atrial fibrillation [AF] and ventricular tachycardia/fibrillation) (fig. 3).

**Left Ventricular Outflow Tract Obstruction**

Although previously subject to periodic controversy, there is now widespread acceptance that the subaortic gradient and associated increases in intracavity LV pressure reflect true mechanical impedance to outflow and there-

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**Fig. 3.** Pathophysiologic and hemodynamic interrelations among left ventricular (LV) hypertrophy, subaortic obstruction, diastolic dysfunction, and myocardial ischemia in hypertrophic cardiomyopathy. BP = blood pressure; LVFP = left ventricular filling pressure; LVSP = left ventricular systolic pressure.
fore are of prognostic importance to HCM patients. A recent multicenter study showed LV outflow obstruction to be an independent long-term determinant of heart failure progression, and heart failure and stroke death, although weakly associated with sudden death. Furthermore, a large proportion of HCM patients are susceptible to physiologically provocative LV outflow tract gradients with stress, including many without systolic anterior motion or obstruction under resting (basal) conditions. Outflow obstruction in HCM is determined by a number of structural abnormalities, including small LV outflow tract area, degree of septal bulge into the outflow tract and elongated, and anteriorly displaced mitral leaflets in association with hyperdynamic LV ejection, pulling (and/or pushing) the mitral valve toward the septum.

Obstruction is characteristically dynamic, i.e., most patients do not demonstrate obstruction under resting (basal) conditions, although many have development of subaortic gradients of varying magnitude with a variety of provocative maneuvers that include exercise or Valsalva, but also by nonphysiologic pharmacologic interventions, such as intravenous administration of inotropic agents or isoproterenol. The outflow gradient in HCM may also be spontaneously labile and may even vary considerably with hydration or consumption of a heavy meal or modest amounts of alcohol. Outflow gradients are responsible for systolic ejection murmurs at the left lower sternal border and apex, which may be present in the supine position or provoked with standing (or Valsalva) and are diminished with squatting. Systolic anterior motion is responsible not only for subaortic obstruction, but also for concomitant mitral regurgitation due to incomplete leaflet apposition. Disease consequences related to chronic outflow gradients, such as progressive heart failure, are likely mediated by increased LV wall stress, myocardial ischemia, and eventually myocyte death and replacement fibrosis. Particularly relevant to the operating room and perioperative care, outflow obstruction in HCM can be dynamic and occur acutely and unexpectedly, provoked or accentuated by conditions that increase myocardial contractility (e.g., tachycardia and stress) or decrease preload and ventricular volume (e.g., vasodilators, hypovolemia, and hypotension). Mitral regurgitation in HCM responds to pharmacologic intervention in a paradoxical fashion to that observed in intrinsic valvular disease. Therefore, in HCM, vasodilators augment subaortic gradient with a resultant increase in MR, whereas vasoconstrictors decrease obstruction and regurgitant volume.

### Diastolic Dysfunction

Abnormalities in relaxation and filling are present in approximately 80% of HCM patients and represent an important determinant of clinical course, particularly in the absence of LV outflow obstruction. The isovolumic relaxation phase of diastole is significantly prolonged and therefore results in a decreased rate and volume of filling. Consequently, there is a compensatory increase in the contribution of atrial systole to overall ventricular filling. The increased LV end-diastolic pressure for any LV end-diastolic volume negatively affects the diastolic coronary perfusion pressure gradient. Paradoxically, the severity of limiting heart failure symptoms due to diastolic dysfunction (or outflow tract obstruction) are not directly related to the magnitude of LV hypertrophy. Progressive symptoms are no more frequent in patients with massive LV hypertrophy than in patients with lesser degrees of hypertrophy.

### Myocardial Ischemia

Microvascular dysfunction and myocardial ischemia are common features of HCM and reflect the interplay of a variety of pathophysiologic mechanisms, including reduced arteriolar density relative to magnitude of LV hypertrophy, myocardial fibrosis, myocyte disarray, and diastolic dysfunction. Failure of myocardial blood flow to increase appropriately on demand predisposes HCM patients to myocardial ischemia, which has been implicated in the pathogenesis of syncope, abnormal blood pressure response to exercise, LV systolic and diastolic dysfunction, and SCD. A recent positron-emission tomography study showed that the degree of microvascular dysfunction in patients with HCM is an independent predictor of heart failure symptoms and death and may precede clinical deterioration by many years.

### Atrial Fibrillation

Atrial fibrillation is the most common sustained arrhythmia in HCM and usually justifies aggressive therapeutic strategies. Paroxysmal episodes or chronic AF ultimately occur in 20–25% of HCM patients, are linked to marked left atrial enlargement, and show increasing incidence with age. AF is reasonably well tolerated by approximately one third of patients and is not an independent determinant of sudden death. Nevertheless, AF is independently associated with heart failure–related death, occurrence of fatal and nonfatal stroke, and long-term disease progression. Paroxysmal episodes of AF may also be responsible for acute clinical deterioration, with syncope or heart failure resulting from reduced diastolic filling and cardiac output, as a consequence of increased ventricular rate and with loss of atrial contribution in a hypertrophied and noncompliant LV. Electrical or pharmacologic cardioversion are indicated in those patients presenting within 48 h of onset, assuming that the presence of atrial thrombi can be excluded. Amiodarone is generally regarded as the most effective antiarrhythmic agent for preventing long-term recurrences of AF. An aggressive strategy for maintaining sinus rhythm is warranted in HCM because of the association...
of AF with the aforementioned disease complications. In chronic AF, β blockers and verapamil (and digoxin) have proved effective in controlling heart rate, although atrioventricular node ablation and permanent ventricular pacing may be necessary in selected patients.

Natural History

The clinical course of HCM is typically variable, and patients may remain stable over long periods of time, with a significant proportion achieving normal longevity. Although adverse clinical consequences, including premature death, are well documented, a more balanced perspective regarding prognosis has recently evolved. The risks of HCM have been previously overestimated by dependence on reports from tertiary referral centers (mortality rates up to 6% annually). More recent studies during the past 10 yr from less selected regional or community-based HCM patient cohorts cite much lower overall annual mortality rates of approximately 1%, not dissimilar to that expected in the general adult U.S. population. Therefore, HCM may be associated with important symptoms and premature death, but often with no or relatively mild disability and without the necessity for major therapeutic interventions.

Patients who experience symptoms as a consequence of HCM have a clinical course that evolves along one or more pathways: progressive heart failure with exertional dyspnea; fatigue and chest pain; occasional evolution to end-stage phase; AF; and sudden death (some high-risk subsets associated with annual mortality of ≥ 5%). Sudden death frequently occurs as the initial disease presentation, often in asymptomatic or mildly symptomatic young patients, and remains the most common mode of demise and most devastating and unpredictable complication of HCM. Although high-risk patients constitute only a minority of the overall disease spectrum, historically, a major investigative focus has been clinical identification of this important patient subset by acknowledged risk factors (fig. 4). Although considerable data are available on stratification of risk and a large measure of understanding has been achieved, criteria for precise identification of all high-risk patients by clinical risk markers are not complete. A substantial minority of those HCM patients who die suddenly are with no or only one risk factor.

Management

Medical Treatment

Negative inotropic drugs such as β blockers and verapamil have been used extensively to control heart failure–related symptoms of exertional dyspnea and anginal (or atypical) chest pain in patients with HCM. Beneficial effects of β blockers on exercise tolerance are due largely to decrease in heart rate with prolongation of the diastolic passive filling period. Patients who do not experience improvement of symptoms with either β blockers or verapamil may subsequently benefit from the other strategies, but combined administration of these drugs is not recommended. Caution should be exercised regarding administration of verapamil to some patients with severe LV outflow obstruction and heart failure with increased filling pressures. There are few data available regarding use of other calcium channel blockers such as diltiazem.

The negative inotropic and type I-A antiarrhythmic drug disopyramide (in combination with a β blocker) has been introduced into the treatment regimen of patients with obstructive HCM who are refractory to β blockers and verapamil, and has been shown to reduce heart failure symptoms and outflow gradient without excessive proarrrhythmia. Angiotensin-converting enzymes inhibitors are generally avoided in HCM due to their potential for provoking or accentuating dynamic LV outflow obstruction.

Surgical Treatment

Throughout the past 40 yr, based on the experience of many centers worldwide, the ventricular septal myectomy operation (Morrow procedure) has been established as the primary therapeutic option for adults and children with obstructive HCM (gradient ≥ 50 mmHg at rest or with physiologic [exercise] provocation) and severe drug-refractory symptoms. These patients represent a small (i.e., 5%) although important subset of the overall HCM population.

Surgical myectomy is performed through an aortotomy and involves resection of a small amount of muscle from the proximal ventricular septum, extending from near the base of the aortic valve to beyond the distal margins.
of mitral leaflets and the point of obstruction due to mitral–septal contact. With surgery, the LV outflow tract is enlarged, and the mechanical impedance to LV ejection and mitral regurgitation is usually abolished. Surgical normalization of LV pressures leads to relief of heart failure symptoms and functional limitation in the majority of patients and therefore represents a reversible form of heart failure, also capable of extending longevity. Operative mortality is now low (≤ 1%) in most major centers.

Emerging Alternatives to Surgery

During the past 10 yr, alternative treatment options for patients with severe drug-refractory symptoms and outflow obstruction have evolved. Early observational data suggested that dual-chamber pacing, using the optimal atrioventricular interval, decreased outflow gradient and symptoms in many HCM patients. However, subsequent randomized trials reported that the clinical effects of pacing in HCM were most consistent with a placebo response. Mechanisms by which pacing reduces gradient are not well understood, although preexcitation of the right ventricle seems to play a major role by altering the synergy of ventricular contraction. Dual-chamber pacing has now been largely abandoned as an alternative to surgery, given the recent enthusiasm for percutaneous alcohol septal ablation.

Catheter-based alcohol ablation has emerged in the past 5–6 yr as a potential alternative to surgical septal myectomy in selected patients. This technique involves introduction of 1–3 ml absolute alcohol into a target septal perforator branch of the left anterior descending coronary artery to produce a transmural myocardial infarction within the proximal ventricular septum. Septal ablation mimics myectomy by reducing septal thickness and excision and also enlarging the LV outflow tract, thereby lessening systolic anterior motion and mitral regurgitation. A major unresolved concern raised with respect to alcohol ablation is the potential long-term risk for arrhythmia-related events (including sudden death) directly attributable to the septal infarct. In contrast to septal myectomy, which usually produces left bundle branch block but not an intramycocardial scar, alcohol ablation commonly results in right bundle branch block and a large scar.

Prevention of Sudden Death

Historically, treatment strategies to protect high-risk HCM patients against SCD due to ventricular tachyarhythmias have been predicated on administration of drugs such as β-adrenergic blockers, verapamil, or type I-A antiarrhythmic agents (e.g., quinidine, procainamide, and more recently amiodarone). However, there is no evidence suggesting that prophylactic administration of such drugs to asymptomatic HCM patients is efficacious in mitigating the likelihood for SCD. Therefore, contemporary practice dictates that when risk level is judged to be unacceptably high, the implantable cardioverter–defibrillator is the most effective treatment option, with the potential for altering the natural history of HCM in some patients. The implantable cardioverter–defibrillator is strongly warranted for secondary prevention of SCD in patients with previous cardiac arrest or sustained ventricular tachycardia (appropriate interventions 11% per year) and for primary prevention in patients with high-risk status defined by noninvasive markers (appropriate interventions 5% per year).
formed every year in the United States, it may be expected that a not inconsequential subset of HCM patients will present for surgery and anesthesia without an established diagnosis. This issue constitutes a challenge for the anesthesiologist charged with the clinical responsibility for HCM patients who are often young, otherwise healthy, and usually undergoing relatively minor operative procedures.

Standard preoperative personal and family history (i.e., targeting cardiac symptoms of exertional dyspnea, fatigue, angina, syncope, or family history of HCM) and the physical examination (i.e., systolic ejection murmur, particularly if increased with standing and decreased with squatting) may raise the clinical suspicion of HCM, thereby triggering a full cardiovascular evaluation, with the diagnosis ultimately confirmed by echocardiography before anesthesia is administered. The nonobstructive form of HCM may be challenging to identify, given the absence of a loud heart murmur.16

Invasive monitoring for blood pressure and LV filling pressures are important in HCM patients undergoing noncardiac surgery. An arterial line should be placed before induction to recognize hypotensive events, allowing therapeutic interventions to be instituted in a timely fashion. Pulmonary capillary wedge pressure may overestimate true volume status as a result of reduced diastolic compliance. Transthoracic echocardiography with Doppler color-flow imaging allows observations regarding the morphology of LV outflow tract as well as mitral valve and chamber geometry and may guide intraoperative management by providing information on development of dynamic obstruction to the LV outflow, mitral regurgitation, and diastolic dysfunction as well as evidence of myocardial ischemia (by virtue of abnormal LV wall motion). These alterations may be important to recognize early, considering that mechanical changes often precede electrical abnormalities evidenced by electrocardiogram.

In patients with known HCM, clinical evaluation should similarly focus on anticipating the potential for dynamic LV obstruction, malignant arrhythmias, and myocardial ischemia to which these patients may be particularly sensitive in the perioperative period and under the influence of anesthesia. Proper hydration and drugs that mildly depress myocardial contractility and reduce oxygen demand while maintaining intravascular fluid volume and systemic vascular resistance are the mainstay in avoiding provocation of LV outflow tract obstruction. Either increased or decreased intraventricular volume potentially threatens the patient with HCM, and overly aggressive fluid therapy in an attempt to sustain preload may have negative consequences by promoting heart failure.

Patients without signs of LV outflow obstruction at rest preoperatively should not be regarded as free from the possibility of developing dynamic obstruction with the administration of anesthetic agents. Although there is no evidence that the magnitude of LV wall thickness is directly related to risk of a perioperative event, a massive degree of LV hypertrophy (wall thickness \( \geq 30 \) mm) is an independent risk factor for arrhythmic sudden death,27 and therefore, it is a reasonable assumption that such HCM patients could be susceptible to potentially lethal tachyarrhythmias in the operating room.

Anxiolytics (benzodiazepines) are indicated to blunt sympathetic activation, although administration of anti-cholinergics such as atropine or glycopyrrolate should be avoided because of a potential for tachycardia. Scopolamine is preferred, owing to a lesser effect on heart rate and when used in conjunction with other central nervous system depressant drugs. The possibility of drug-induced hypotension or increased sympathetic activation upon initiating anesthesia should be considered when choosing an induction agent, and slow titration of these drugs should be used. Sufficient depression of the sympathetic system should be achieved before attempting intubation, while at the same time maintaining adequate afterload. When muscle relaxants are used, consideration should be given to the consequences of histamine release, vagolytic and muscarinic activity, and prevention of catecholamine reuptake that these drugs produce. In this regard, vecuronium seems to be an acceptable agent.

Because myocardial depression is generally desirable during the maintenance of anesthesia, volatile anesthetics are indicated in patients with HCM, although vigilance for sudden hemodynamic changes or junctional rhythm is important. Isoflurane has the tendency to increase heart rate secondary to decreased systemic vascular resistance when administered rapidly. Moreover, in high concentrations, isoflurane seems to increase both heart rate and blood pressure much like desflurane. Nitrous oxide can occasionally cause sympathetic stimulation and increased pulmonary arterial pressures, whereas when administering desflurane, a sudden increase in concentration can lead to tachycardia and systemic arterial hypertension as well as unwanted catecholamine release. Sevoflurane is a mild myocardial depressant, and its administration results in a more modest decrease in systemic vascular resistance and blood pressure than encountered with isoflurane or desflurane, while at the same time causing only small or no increase in heart rate.

Negative inotropic agents (esmolol and metoprolol) are useful in perioperative management because an increase in inotropy is considered unfavorable in HCM. Reduction in venous return as occurs with high airway pressure induced by mechanical ventilation is poorly tolerated and may acutely provoke LV outflow obstruction. Small tidal volumes and higher respiratory rates should be used to maintain sufficient minute ventilation. Adequate hydration is particularly important before initiating these maneuvers.
Treatment of acute hypotension in the operating room requires prompt volume replacement and administration of \(\alpha\)-agonists (e.g., phenylephrine). Drugs with \(\beta\)-adrenergic agonist activity, such as dopamine, dobutamine, or ephedrine, are poor choices because increased inotropy and chronotropy associated with their use are likely to promote LV outflow tract obstruction and increase myocardial oxygen demand. Systemic hypertension should promote LV outflow tract obstruction and increase myocardial ischemia. Sepsis and hemorrhagic shock secondary to pain or hypothermia can lead to decreased inotropic and chronotropic state to mitigate response, remains a priority. Increased catecholamine release secondary to pain or hypothermia can lead to increased myocardial oxygen demand, promoting ischemia, dynamic LV outflow obstruction, and possibly malignant arrhythmias.

Cardiopulmonary resuscitation after cardiac arrest in HCM patients requires an awareness of the disease pathophysiology. Inotropic agents (epinephrine) are contraindicated in HCM because these patients require a decreased inotropic and chronotropic state to mitigate outflow tract obstruction, diastolic dysfunction, and myocardial ischemia. Sepsis and hemorrhagic shock severely decrease afterload and preload, respectively, and may predispose HCM patients to dynamic obstruction, with all its inherent deleterious consequences.

Pregnancy in HCM patients raises management issues because of the unique cardiovascular changes that may occur. In the late phases of parturition, aortocaval compression or major blood loss during labor and delivery may decrease preload measurably. Moreover, the pain and stress of delivery cause sympathetic stimulation, thereby increasing heart rate and contractility, which in turn can contribute to a deteriorating hemodynamic condition. Recent studies indicate that absolute maternal mortality with HCM is very low and seems to be confined to women who are at particularly high risk because of underlying HCM. Major progression of symptoms, AF, and syncpe occur only uncommonly and are largely related to the patient’s previous clinical condition. There is no evidence that regional anesthesia increases risk in women with HCM when used during standard vaginal delivery. Both general and regional anesthesia have been used successfully without complications for cesarean deliveries in parturients with HCM. Successful administration of epidural, combined spinal and epidural, and continuous spinal anesthesia have been documented in case reports.

Conclusions

During the past several decades, a vast and sometimes contradictory literature has accumulated regarding HCM, an autosomal dominant genetic cardiac disease caused largely by a variety of mutations in genes encoding sarcomeric proteins and characterized by an asymmetrically hypertrophied and nondilated LV with a broad and expanding clinical spectrum. Appreciation that HCM, although an important cause of sudden cardiac death and disability, does not invariably convey ominous prognosis (and is in fact compatible with normal longevity) dictates a large measure of reassurance for many patients. Nevertheless, when HCM patients are subjected to the stress of anesthesia and surgery, intraoperative and perioperative complications occur not uncommonly and include congestive heart failure, myocardial ischemia, diastolic dysfunction, hypotension, and arrhythmias.

Anesthesiologists should be aware of and recognize those relevant pathophysiologic mechanisms that may trigger or accentuate dynamic LV outflow obstruction and, in turn, develop strategies to respond acutely and reverse this and other potential complications resulting from the interaction of anesthesia with HCM. These considerations are relevant to anticipating and reacting to perioperative problems when administering anesthesia during noncardiac surgery to patients with undiagnosed (or known) HCM.

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