Cardiomyopathy, Hypertrophic

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Risk

- Relatively common inherited disorder; 0.2% or 1 in 500 Americans are affected. It is equally distributed between males and females and has no racial group predominance. The median age of clinical manifestation is 35 years, but it can manifest in any age.
- The clinical presentation is variable, reflecting a diverse genetic background. Pts may be totally asymptomatic or present with MI, CHF, arrhythmias, or even sudden death. HCM is not an infrequent cause of SCD in young athletes.
- Pts with the disorder may be asymptomatic (20–25%) or undiagnosed at the time of anesthetic. Anesthesia may "unmask" HCM.

Perioperative Risks

- Dynamic LV outflow obstruction (either at rest or provoked) is present in approx 60% of pts with HCM, which is a risk of hemodynamic instability.
- Risk for heart failure and pulm edema from impaired relaxation and diastolic dysfunction from a hypertrophic and noncompliant LV.
- Risk for myocardial ischemia and injury, even in the absence of obstructive CAD, due to increased myocardial O_2 demand (LVH, high intraventricular pressure) and limited supply (impaired coronary reserve, due to dysfunction of the coronary microvasculature).
- Supraventricular (atrial fibrillation) and ventricular dysrhythmias.

Worry About

- Factors that aggravate or trigger dynamic outflow obstruction can cause hemodynamic compromise, such as decreased preload and afterload, decreased end diastolic volume, increased sympathetic activation (from pain, surgical stimulation, medications), increased LV contractility, and tachycardia.
- Myocardial ischemia (even with "normal" coronary angiogram or radionuclide imaging).
- Diastolic dysfunction; heart failure difficult to control with traditional diuresis (caution with volume depletion).
- Arrhythmias: Supraventricular and ventricular dysrhythmias may cause hemodynamic instability, increase the risk of embolic stroke (AFIB), and cause shortness of breath or CHF (diastolic dysfunction).
- Pts with HCM who undergo noncardiac surgery bear a higher risk for periop MI, death (4.2%), and higher incidence of periop complications.

Etiology

- Genetic disease with autosomal dominant inheritance and extremely heterogeneous genotype. Over 1400 mutations have been identified in at least 11 genes. This is most likely the reason for the extremely variable genetic expression or phenotype. Mutations that encode for the myosin heavy chain (MYH7) and myosin-binding protein C3 account for 70%–80% of sarcomeric mutations. Genetic testing is recommended for pts and their first-degree relatives.

Overview

- Synonyms: HCM has replaced the following older terms: muscular subaortic stenosis, idiopathic hypertrophic subaortic stenosis, hypertrophic obstructive cardiomyopathy, and asymmetric septal hypertrophy.
- Definition: Hypertrophied and abnormally thickened LV, nondilated (except at end stage), often asymmetrical, in absence of other cardiac or systemic causes for LVH (e.g., AS or Htn), associated with myocardial disarray.
- Pathophysiology: The structural cardiac abnormalities in HCM are
  - Histopathologic picture consists of myocytes that are not aligned parallel but form a disorganized pattern (myocardial disarray).
  - Through the disease process, the myocardial microvasculature develops increased vessel wall to lumen ratio, which leads to dysfunction. Thus over time, affected myocardium with microvascular dysfunction can develop ischemia, injury, and chronic fibrosis.
  - Remodeling changes start and evolve before onset of symptoms.
- Clinical presentation: Clinical manifestations of HCM relate to
  - Diastolic heart failure (dyspnea, fatigue, exercise intolerance);
  - Ischemia (angina, MI, often in the absence of obstructive CAD);
  - Arrhythmias (dizziness, palpitations, syncope/sudden death);
  - LVOT obstruction (dizziness, hypotension, shortness of breath, syncope); or
  - Mitral regurgitation (SOB, CHF, pulm edema, pulm Htn).

  There is a wide clinical spectrum of presentations that varies from totally asymptomatic to severely symptomatic. Approximately one-third of pts with HCM do not have LVOT obstruction at rest or with provocative maneuvers (peak gradient <30 mm Hg); a third do not have LVOT obstruction at rest but will develop with provocative maneuvers (Valsalva, inhalation of amyl-nitrate a potent vasodilator or sympathetic stimulation, administration of catecholamines, exercise, tachycardia, hypovolemia, post PVC); and a third of HCM pts have LVOT obstruction at rest (peak gradient >30 mm Hg), which worsens with provocative maneuvers.
  - Morphologic characteristics, a mechanism of LVOT obstruction, include:
  - LV wall thickness—The majority of the patients have LVH with normal systolic function and LVEF in the 70% range, with almost obliteration of the LV cavity at end systole. Disproportionately thick intraventricular septum is seen in approximately 90% of cases (>13 mm, >15 mm in hypertensives), with septal wall thickness to posterior wall thickness ratio >1.3. The risk of sudden death is significantly elevated: 18/1000 person-years when wall thickness is >30 mm. Patients with mid septal thickening, which is the most prevalent type, are symptomatic at a younger age and have a larger LV mass, which is associated with a higher incidence of sudden death and worse symptoms (NYHA 3 or 4 symptoms and grade 3 or restrictive diastolic dysfunction by ECHO).
  - The mitral valve—The specific morphologic characteristics of the mitral valve apparatus in HCM plays an important role in the development of dynamic LVOT obstruction. More specifically, (1) the anteriorly positioned papillary muscles that support the leaflets of the mitral valve, (2) elongated or redundant mitral valve leaflets, (3) thickened intraventricular septum, and (4) normal or hyperdynamic LV systolic function contribute to narrowing of the LVOT and most likely predispose to abnormal systolic anterior motion of the anterior mitral valve leaflet (SAM) toward the intraventricular septum. SAM further narrows the LVOT, which results in generation of the dynamic systolic flow gradient across the LVOT. SAM is the main mechanism of MR in HCM, with LVOT obstruction in the absence of intrinsic mitral disease. A posteriorly and laterally directed MR jet is generated, which peaks in mid- to late systole. It is a dynamic jet that improves as the gradient across the LVOT decreases with appropriate management and worsens with provocative maneuvers.
  - Mechanism of LVOT obstruction: Recent studies have shown that the mechanism of SAM is not the venturi forces generated from the high-velocity flow through the LVOT as we used to believe. It is rather a flow-drag phenomenon: as the LV diastolic inflow (normally directed posteriorly) passes via the anteriorly displaced mitral valve, it forms an anteriorly directed jet that hits the intraventricular septum. Then, as blood flow is directed posteriorly, it forms the outflow jet, directed from the posterior wall toward the LVOT, and drags the mitral valve leaflets even more anteriorly toward the LVOT in a flow-drag phenomenon.

    Risk factors for SAM and LVOT obstruction are anteriorly placed mitral valve and papillary muscles, posterior mitral annular calcifications, mid septal hypertrophy, mitral leaflet c-sept <2.5 cm, anterior to posterior mitral valve leaflet ratio <1.3, and normal LV systolic function with small ventricular cavity.
  - In cases of severe HCM with small ventricular cavity, in the absence of LVOT obstruction or aortic stenosis, significant systolic intraventricular outflow gradient may be generated from the severely thickened myocardium.
  - In 10–20% of cases, significant intrinsic mitral valve disease coexists. In such cases, the mitral regurgitation does not improve, despite significant decrease of the LVOT gradient with appropriate management.
  - Approximately 10% of cases progress to terminal stages with advanced fibrosis, significant LV dilation, and decreased LVEF. This resembles dilated cardiomyopathy and has poor prognosis.
- Diagnostic modalities: Because the clinical presentation resembles that of fixed AS, or coronary artery disease, the following diagnostic modalities aid in the differential diagnosis:

  ECG: Indicates changes associated with LVH, not specific to HCM: SR or supraventricular arrhythmias like AFIB, pathologic Q waves, poor R wave progression in the precordial leads, S in V_1 >35 mm, R in V_5 >35 mm, intraventricular conduction delay with QRS duration >0.12 ms, left axis deviation, left anterior fascicular block, LBBB, characteristic deep T-wave pattern in more than 2 leads, ST depression.
  - ECHO: 2D, 3D, and Doppler ECHO, via TTE or TEE route, are extremely helpful in diagnosis and assessment of the severity, differential diagnosis and risk stratification of HCM. ECHO measurements are also used to tailor management in the chronic or perioperative setting (particularly identifying whether there is LVOT obstruction and the severity of), assess the effectiveness of intervention, identify additional pathology, or risk stratify and determine the prognosis. Typical findings are LVH, LVEF >60–70%, +/−LVOT gradient at rest or with provoking maneuvers, SAM, MR, or other mitral valve abnormalities.
  - Newer developing ECHO modalities, TDI and Strain, are more sensitive in identifying contractile dysfunction or impairment of the lusitropic ability of the myocardium while the LVEF is still normal and before changes appear on ECG. These techniques may be utilized to differentiate between LVH from chronic Htn and HCM. The presence of SAM is not pathognomonic for HCM. SAM has been noted to happen occasionally after mitral valve repair and has also been observed in elderly pts with chronic Htn, normal LVEF, sigmoid septum, and calcified mitral valve leaflets in the presence of provocative conditions such as hypovolemia and hypotension.

- Cardiac cath: Frequently performed to exclude CAD and confirm the diagnosis, or "localize" the gradient (differentiate from AS) when ECHO images are suboptimal.
- Cardiac MRI and CT scan: MRI and CT scan images provide great description of the anatomy helpful if surgery is planned but no information regarding the hemodynamics. MRI images with late gadolinium enhancement are indicative of myocardial fibrosis which is associated with higher incidence of cardiovascular events.
- Other tests such as Holter, exercise stress ECHO, and myocardial biopsy may be used on an individual basis to provide additional information.
- Treatment: The therapeutic goal is to alleviate symptoms with agents and techniques that improve the diastolic dysfunction and decrease the LVOT gradient and MR. Prophylactic AICD is placed in high-risk pts. Arrhythmia management with cardioversion, EP study/ablation, and antiarrhythmic medications are often needed. Pacemaker or resynchronization therapy helps improve symptoms in cases of branch block and needed in complete heart block.
  - Pharmacologic: Agents that decrease the heart rate and contractility, such as beta blockers and Ca^{2+}-channel blockers, as well as antiarrhythmics (disopyramide), are commonly used.
  - Surgical: Septal myomectomy is the gold standard for the correction of LVOT obstruction in pts with disproportionately thickened septum who are refractory to medical management. It may need to be combined with mitral valve repair or replacement. Complications include VSD (high risk if preop septal wall thickness is <20 mm), heart block, severed septal perforator coronary artery, and AI. Mortality rate is 1–2% in experienced high volume centers.
  - Percutaneous intervention: Septal ablation by alcohol injection is reserved for pts with intraventricular septum thicker than 16 mm, who are not surgical candidates and do not have mitral valve pathology. Complications include RBBB in 50% of cases, MI, ethanol injection in the wrong artery, ventricular septal rupture, heart block, and coronary dissection.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Myocardial ischemia	Angina	Worse with nitrates (avoid)	ECG, exercise tests, coronary angio (may be "normal"), cardiac MRI
	LVOT obstruction	Dyspnea, syncope, dizziness	Systolic murmur accentuated by Valsalva	ECHO
	Mitral regurgitation	Dyspnea	Holosystolic murmur	ECHO
	Dysrhythmias	Syncope, sudden death, palpitations	Rales, wheeze, edema	ECG, Holter
	Diastolic dysfunction	Dyspnea		ECHO, CXR
RESP	Pulm congestion Secondary pulm Htn	Dyspnea, orthopnea	Rales, wheeze	CXR Right heart cath
CNS	Syncope	Syncope, presyncope		Negative CNS work-up

Key References: Pollack LC, Barron ME, Maron BJ: Hypertrophic cardiomyopathy, *Anesthesiology* 104(1):183–192, 2006; Hensley N, Dietrich J, Nyhan D, et al.: Hypertrophic cardiomyopathy: a review, *Anesth Analg* 120(3):554–569, 2015.

Perioperative Implications

Preoperative Preparation

- Avoid physiologic changes that reduce LV cavity size (maintain preload and afterload; avoid tachycardia).
- Ensure adequate preload, and replace any preop volume depletion.
- Continue beta-blocker, Ca^{2+}-channel blocker, and antiarrhythmic.
- Also note disopyramide (used preop in severe HCM) has anticholinergic activities.
- Sedate adequately to prevent anxiety-induced sympathetic stimulation.
- SBE prophylaxis is not recommended for HCM pts with severe MR unless after surgery, septal myomectomy, or mitral valve repair or replacement.
- ICD/pacemaker interrogation

Monitoring

- Aside from the ASA standard monitors, the decision that additional monitors should be used depends on the surgical procedure, the severity of HCM, presence of CHF, and the pt's condition, in addition to other comorbidities. Invasive arterial pressure monitoring, CVP and/or PA cath, or even the noninvasive PPV could be used as needed for optimal pt management. Transesophageal ECHO is very useful, especially in the event of major blood loss, volume shifts, or sympathetic stimulation are anticipated.

General Anesthesia

- When choosing an induction agent, avoid drug-induced vasodilation or sympathetic activation; etomidate may be advantageous over ketamine or propofol. Ketamine in smaller dosages, as part of a balanced anesthetic, can provide hemodynamic stability in such pts. Ketamine should be avoided in larger doses because of sympathetic stimulation and tachycardia. Propofol should be used with caution; it can be used in incremental doses, but the provider should be ready to promptly correct the blood pressure with alpha agonist. Profound vasodilation caused by large bolus of propofol may be poorly tolerated.
- Phenylephrine infusion (alternatives: vasopressin, norepinephrine) should be immediately available, as worsening dynamic LVOT obstruction is anticipated with any anesthetic provoked decrease in BP and SVR or surgery provoked increase in sympathetic stimulation.
- Avoid prolonged laryngoscopy, as it may induce sympathetic stimulation.
- Insertion of CVP/PAC may be helpful to manage the pt particularly if significant blood loss is anticipated; invasive monitoring may induce atrial or ventricular dysrhythmias.

Maintenance

- Volatile agents that decrease LV contractility without severe vasodilation are desirable. Halothane is the classic example. Likewise, sevoflurane is preferable over isoflurane or desflurane.
- Avoid agents that decrease preload and afterload (e.g., nitroglycerin, nitroprusside) or increase contractility (inotropes), as well as agents associated with significant histamine release.
- Avoid agents that directly or indirectly increase HR and contractility (e.g., pancuronium, atropine, epinephrine, ephedrine).
- Promptly treat hypotension with volume expansion (avoid anemia; promptly replete blood loss) or pure alpha-adrenergic agonist (e.g., phenylephrine).
- Consider early electrical cardioversion for atrial fibrillation. Defibrillator available in OR.
- Consider beta-blockade or Ca^{2+}-channel blockade to prevent and treat tachycardia, LVOT obstruction, or ischemia.
- Although pulm edema from diastolic dysfunction and MR is difficult to treat (use diuretics very judiciously), patients with severe LVH and diastolic dysfunction are prone to develop CHF easily from volume overload. Careful fluid balance is necessary.
- Secondary PHT from HCM with MR worsens with "conventional" pulm vasodilators (increase LVOT obstruction). MR will improve with relief of LVOT obstruction.
- It is advisable to maintain minute ventilation by using higher rates and lower tidal volumes (higher tidal volumes with lower rates will decrease venous return).

Extubation

- Avoid sympathetic stimulation. Ensure adequate analgesia.
- Utilize beta-blockade or Ca^{2+}-channel blockade to abolish sympathetic response during emergence of anesthesia.

Neuraxial Anesthesia

- Although spinal and epidural anesthesia can be performed in pts with HCM, for the reasons mentioned previously, a slow controlled titration of medication via epidural is preferred.

Postoperative Period

- The goal should be aggressive postop pain management for avoidance of sympathetic stimulation from pain. Nerve blocks are preferred. Some pts without severe disease might tolerate epidural, as long as the anesthetic is titrated slowly. Epidural narcotic analgesia can be used when indicated.