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Anesthetic Considerations in the Patient With Valvular Heart Disease Undergoing Noncardiac Surgery

Alexander JC Mittnacht, MD, Michael Fanshawe, MD, and Steven Konstadt, MD, MBA, FACC

Valvular heart disease can be an important finding in patients presenting for noncardiac surgery. Valvular heart disease and resulting comorbidity, such as heart failure or atrial fibrillation, significantly increase the risk for perioperative adverse events. Appropriate preoperative assessment, adequate perioperative monitoring, and early intervention, should hemodynamic disturbances occur, may help prevent adverse events and improve patient outcome. This review article aims to guide the practitioner in the various aspects of anesthetic management in the perioperative care of patients with valvular heart disease. The pharmacological approach to optimization of patient outcome with drugs, such as β-blockers and lipid-lowering medications (statins), is an evolving field, and recent developments are discussed in this article.

Keywords: valvular disease; aortic stenosis; mitral stenosis; aortic insufficiency; mitral regurgitation; noncardiac surgery

Valvular heart disease is not an uncommon finding in many patients presenting for noncardiac surgery. In 2000, it was estimated that the prevalence of moderate or severe valvular heart disease in the United States is 2.5%, ranging from 0.7% in the 18- to 44-year-old age group to 13.3% in the individuals 75 years or older.[1] Valvular heart disease and resulting comorbidity, such as heart failure or atrial fibrillation, significantly increase the risk for perioperative adverse events in patients undergoing noncardiac surgery.[2-5] Despite a great deal of literature devoted to the prevention of perioperative myocardial ischemia in the patient at risk, there is a lack of literature about providing anesthesia in those patients with severe valvular heart disease undergoing noncardiac surgery.[6,7] Most anesthetic practice in these situations is based on dogma handed down through generations of anesthesiologists rather than evidence based. For example, there is a common belief amongst many anesthesiologists that aortic stenosis (AS) mandates a general anesthetic, and AS is considered a contraindication for neuraxial nerve block. This is despite the fact that there is increasing evidence that neuraxial techniques can be performed safely in the presence of AS.[8-10] The key is appropriate preoperative assessment, appropriate monitoring, and early treatment of expected side effects, such as hypotension. Similarly, many practitioners believe that lesions, such as AS, should always be surgically repaired before any elective noncardiac surgery is carried out. However, mortality in the cardiac surgery has to be considered when looking at the overall patient outcome, and will be discussed in more detail below.

This review article aims to guide the practitioner in the various aspects of anesthetic management in the perioperative care of patients with valvular heart disease.

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General Considerations

Risk Considerations

Surgical risk classification for patients undergoing noncardiac surgery is based upon the type of surgery and the hemodynamic changes associated with the procedure. Typically, surgery considered high risk (reported cardiac risk often more than 5%) are most vascular surgery cases including aortic and other major vascular and peripheral vascular surgery cases.[11] There is a general perception that general surgery poses less risk for adverse events compared with cardiac surgery. However, preoperative dehydration due to fasting and bowel preparation particularly in the older patients, hemodynamic changes associated with capnoperitoneum during laparoscopic procedures, trauma cases with large fluid losses, patient positioning, inadequate pain control following even minor procedures, are just a few examples of frequently encountered scenarios that may significantly compromise hemodynamic stability in the patient with compensated valvular heart disease. Additionally, unlike in cardiac surgery, valvular pathology persists after noncardiac surgery and is of particular concern in the postoperative period. Unlike patients scheduled for cardiac surgery, patients following low risk or intermediate risk noncardiac surgery frequently are not referred to an intensive care unit. Inadequate monitoring, shortage of nursing staff, personnel inexperienced in hemodynamic concerns of patients with valvular disease, all increase the risk of adverse events in patients with valvular disease following noncardiac surgery.

Antibiotic prophylaxis. There is little dispute that patients with underlying valvular disease have an increased lifetime risk of infectious endocarditis (IE).[12,13] On the basis of previous recommendations, antibiotic prophylaxis was recommended in these patients for certain dental, gastrointestinal, or genitourethral tract procedures.[14-16] However, recently, the American Heart Association (AHA) updated their guidelines for the prevention IE.[17] Most importantly, the AHA no longer recommends IE prophylaxis in patients with underlying cardiac conditions solely on an increased lifetime risk of acquisition of IE. One of the major changes regarding patients with valvular disease is that antibiotic prophylaxis is no longer recommended in patients with mitral valve (MV) prolapse or other valvular diseases. Prophylaxis is recommended, though, for patients with prosthetic cardiac valves, those with a previous episode of IE, certain types of congenital heart disease, and cardiac transplantation recipients who developed cardiac valvuloplasty. On the basis of these updated recommendations it can be concluded that much fewer patients with valvular disease will require antibiotic prophylaxis for the prevention of IE.

Anticoagulation. Patients with valvular heart disease often require anticoagulation for concomitant findings, such as atrial fibrillation. The preoperative management of oral anticoagulation regimens is not routinely performed by the anesthesia staff; however, patients may present to the operating room emergently, or for elective cases with residual effects of oral anticoagulation medications or intravenous substitutes. Therefore, the preoperative anesthesia assessment of patients with valvular disease should always include a history about bleeding and a blood coagulation screen. Intraoperative central neuraxial anesthesia (eg, spinal and epidural) and postoperative neuraxial analgesia are contraindicated in patients with significant anticoagulation or antiplatelet therapy, and anesthetic management has to be planned accordingly. The establishment of guidelines for the use of neuraxial anesthesia and analgesia in patients who have or will receive anticoagulants is an evolving process, and the reader is referred to the recommendations by the American Society of Regional Anesthesia for current updates on neuraxial procedures in these patients.[1,18]

β-*blockade.* The place of β-blockers in patients with valvular heart disease is still uncertain. Although initial trials suggested that all patients undergoing high-risk surgery would benefit, data from later trials has been less convincing and have created some controversy regarding the use of β-blockers in patients undergoing noncardiac surgery.[19,20] The revised cardiac risk index (RCRI) describes perioperative risk factors (high-risk surgery, history of ischemic heart disease, history of congestive heart failure (CHF), history of cerebrovascular disease, preoperative treatment with insulin, and preoperative serum creatinine >2.0 mg/dL) associated with major cardiac events in noncardiac surgery.[21] Unlike the original cardiac risk index, severe valvular disease is not listed as an independent risk factor, although it has to be considered a risk factor. Both ischemic disease and CHF are often found in patients with severe valvular disease. Additionally, the prevalence of severe AS was low in the study cohort used to

evaluate the RCRI. Current data suggest that those with a low cardiac risk based on the RCRI may actually be harmed by perioperative β-blockade. Those at intermediate risk may or may not benefit, and those with a high RCRI risk score seem to clearly benefit from perioperative β-blockade.[22] Regarding valvular disease and β-blocker use, no specific recommendations are made by The American College of Cardiology/American Heart Association (ACC/AHA) Task Force on Practice Guidelines on perioperative β-blocker use.[23] However, the ACC/AHA guidelines state that perioperative use of β-blockers is clearly recommended (class I indication, sufficient data from randomized trials that treatment is effective) in patients who received β-blockers prior to surgery and in patients undergoing vascular surgery at high cardiac risk based upon signs of myocardial ischemia on preoperative testing. A class IIA indication (benefit outweighs risk, additional studies needed) included patients in whom preoperative assessment for vascular surgery identifies high cardiac risk as defined by the presence of multiple risk factors. Major clinical predictors of increased perioperative cardiovascular risk included severe valvular disease (particularly severe AS and mitral stenosis (MS), decompensated heart failure, and significant arrhythmias.[24-30] Obviously, the use of β-blockers in patients with valvular disease has to be made on an individual basis and treatment of hemodynamic variables, such as heart rate (HR; eg, tachycardia in patients with severe AS), may be warranted in selected cases to treat ischemia or improve hemodynamics when β-blockade is not universally recommended.[31] Generally, once the indication has been determined, practitioners should titrate β-blocker medications to appropriate HRs, which may differ between the various valvular lesions as discussed below.

Statins. Lipid-lowering medications, also known as statins are 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase inhibitors, have been associated with improved patient outcome, including patients with CHF, acute coronary syndrome, and in patients undergoing high-risk surgery.[32-42] How exactly statins exert their beneficial effect is not completely understood, and the proposed mechanism include plaque stabilization, antiatherosclerotic, antithrombotic, vasodilatative, and anti-inflammatory properties.[43,44] Their potential benefit in the perioperative period has not been fully determined. Most data to date suggest that application is safe, and statin therapy is associated with improved outcome following high-risk surgery.[45-47] Statins have also been shown to improve outcome in patients with heart failure despite a normal ejection fraction (EF). This is important in the context of this article, as many patients with valvular disease fit into the category of heart failure despite a preserved EF. The suggested anti-inflammatory properties of statins were thought of slowing down the progression and possibly reversing the calcific AS. It was theorized that calcific AS was an inflammatory process as evidenced by increased tissue expression and serum levels of various endothelial cellular adhesion molecules. Unfortunately, several studies could not confirm that statin therapy helps slow or reverse the progression of calcific AS.[48-50] Furthermore, large randomized prospective studies are currently carried out to assess the exact role of statins in the perioperative period, including patients with valvular disease.[51,52] In summary, there is no conclusive data to date regarding statin administration in patients with valvular disease undergoing noncardiac surgery. Recently, published data suggest that discontinuation of statin therapy is associated with worsened cardiac outcome.[53,54] Consequently, a conservative approach would be to at least continue therapy in patients who received lipid-lowering medications preoperatively, until further data is available.

α-2 agonists. The α-2-agonists, such as clonidine and dexmedetomidine, have mostly been evaluated in patients at risk for perioperative ischemic cardiac events. They exhibit sympatholytic, sedative or anxiolytic, antiarrhythmic, and analgesic properties and have been demonstrated to reduce anesthetic requirements and improve hemodynamic stability during the intraoperative period. There is some evidence that prophylactic administration of these medications reduces the incidence of perioperative myocardial ischemia and possibly improves patient outcome.[55-58] However, evidence is less robust compared with other preventive pharmacological therapy, such as β-blockers, and based upon currently available data, no general recommendations can be made regarding their use in patients with valvular disease undergoing noncardiac surgery.[29]

Nesiritide. Nesiritide is a recombinant brain natriuretic peptide (BNP). It decreases pulmonary artery pressure and myocardial oxygen consumption, whereas increasing coronary blood flow and urine output. The synthesis and release of BNP are increased in heart failure patients, including those with valvular disease.

Levels of BNP correlate with severity of disease and have been shown to be an independent predictor of poor outcomes.[59,60] Several recent studies in patients with cardiac disease undergoing noncardiac surgery found preoperatively elevated BNP levels to be correlated with perioperative cardiac events including myocardial infarction, CHF, and death.[61-64] If further studies confirm these findings, BNP levels may be useful in the preoperative risk assessment of patients with cardiac disease scheduled for noncardiac surgery.

Administration of recombinant BNP (nesiritide) has been used to optimize patients with severe mitral regurgitation (MR) preoperatively.[65] However, despite some favorable reports demonstrating a possible short-term benefit, its use has been associated with worsening renal function and an increased mortality. Therefore, recombinant BNP should be used cautiously in the perioperative period in patients with valvular disease until further data is available.[66]

Specific Valvular Lesions

Aortic Stenosis

Introduction. Aortic stenosis derives its position as the most important valvular lesion in patients presenting for noncardiac surgery because of several reasons. It has a relatively high prevalence in the older generation, a significant potential for sudden death, and high perioperative morbidity, and because of the inability to obtain adequate systemic perfusion by external cardiac massage during a cardiac arrest. As such, AS in patients scheduled for noncardiac surgery has received particular attention.

Etiology. The main etiologies of AS are senile calcification, rheumatic heart disease, congenital abnormalities, and infective endocarditis. Senile calcification of a trileaflet aortic valve (AV) is common in patients over 70 years of age.[67] Using transthoracic Doppler echocardiography in a population sample of randomly selected men and women between 75 and 86 years of age, critical AS (valve area ≤0.8 cm^2) had a prevalence of 2.9%.[68] Women may be affected more frequently.[69] A bicuspid AV can be found in 1% to 2% of the general population (Figures 1 and 2).[70] A congenitally bicuspid or monocuspid AV usually becomes calcified and stenotic earlier in life compared with a tricuspid AV, with symptoms of aortic regurgitation (AR) developing as early as 20 to 40 years of age. Two-thirds of patients between 50 to 70 years of age referred for AV surgery had bicuspid AVs.[71] Tissue abnormalities are not only confined to the AV, and these patients are at increased risk of aortic dissection.[72] Rheumatic AS is almost always associated with some degree of rheumatic MV disease. This etiology is becoming less common in developed countries because of the widespread use of antibiotic therapy.

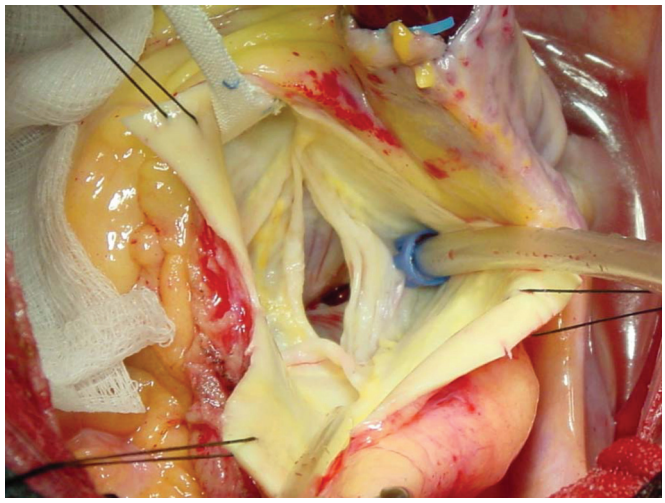

Figure 1. Bicuspid AV, intraoperative view from aortic side. AV indicates aortic valve.

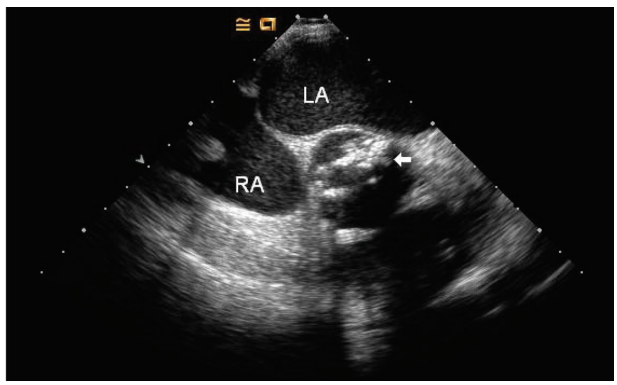

Figure 2. Midesophageal AV short-axis view. Arrow represents calcified bicuspid AV. AV indicates aortic valve; LA, left atrium; RA, right atrium.

Symptoms. Patients with mild to moderate AS are usually asymptomatic or have minimal symptoms as long as the hypertrophied left ventricle (LV) compensates for an increasing pressure gradient. The classic

symptoms in patients with severe AS (valve area <1 cm^2) are angina, CHF, and syncope. Angina is the initial symptom in 50% to 75% of patients, but only about 25% to 50% have CAD.[73,74] Syncope is the initial symptom in 15% to 30% of patients, and is usually caused by exercise-induced vasodilatation in the face of a fixed cardiac output (CO). There is no good correlation between symptoms and severity of disease; however, as soon as the compensatory mechanisms fail, long-term prognosis becomes worse. Life expectancy decreases significantly in untreated cases of AS when symptoms of angina or syncope develop, and survival without surgery may be less than 2 years after developing CHF. Pellikka et al,[75] followed 622 patients with asymptomatic AS (peak systolic velocity ≥4 m/s) over 5 years. Two-thirds of the patients became symptomatic within the study period, and sudden death occurred in 4.1% of the patients who were not referred for AV surgery.

Pathophysiology. The normal AV orifice measures 2 to 4 cm^2. There is no universally accepted definition of what constitutes severe AS; however, blood velocity of >4 m/s, a mean gradient of more than 50 mm Hg across the stenotic AV, an AV orifice <1 cm^2, and the relation of AV orifice area to left ventricular outflow tract (LVOT) area of <0.25, are generally indicative of severe AS.[76,77] As the valve orifice narrows, resistance to the flow develops and a pressure gradient across the valve occurs. The chronic pressure overload leads to compensatory concentric hypertrophy of the LV to normalize the wall stress. Greater intraventricular pressures may be generated with lower wall tension, which is the most inefficient way of performing cardiac work. However, the hypertrophied myocardium has an increased oxygen demand compared with the normal size ventricle. This increased oxygen demand becomes even more important in the setting of decreased oxygen delivery seen in patients with AS. The hypertrophied LV requires high filling pressures (left ventricular end-diastolic pressure [LVEDP]) to accommodate adequate preload and to sustain adequate CO. Low diastolic aortic pressures, especially when AR coexists, impairs coronary perfusion even further (coronary perfusion pressure [CPP] = diastolic aortic pressure – LVEDP). Additionally, the neovascularization of the pressure-overloaded, hypertrophied heart has been shown to be inadequate. The isovolumic phase of relaxation is inappropriately long, shortening diastole, and leaving less time for coronary perfusion. Therefore, patients with AS are at high risk of developing myocardial ischemia during anesthesia even with normal coronary arteries.

Initially, CO is maintained; however, when the compensatory mechanisms fail, and left ventricular filling pressures increase even further, the failing ventricle is unable to overcome the resistance of a severely narrowed AV orifice. The CO will decrease, and pressure gradients may no longer accurately reflect the severity of the disease. The relationship between valve area, CO, and pressure gradient has been described by the Gorlin formula.[78] The simplified version states that the valve area is proportional to the flow across the valve divided by the square root of the mean pressure gradient. Thus, knowing the pressure gradient in the absence of the CO (flow) is not a reliable indicator of the severity of aortic disease.

Even in the ventricle with preserved systolic function, signs of diastolic dysfunction, such as high left ventricular filling pressures, reduced diastolic relaxation, and compliance can be observed. With worsening diastolic function, and high left ventricular filling pressures, normal sinus rhythm (SR) becomes more important, and atrial systole may account for up to 40% of ventricular filling and thus CO. Often, the patient with AS cannot compensate for the loss of SR because marked increases in left atrial pressure would be required to maintain an adequate stroke volume.

Preoperative evaluation and risk assessment. Aortic stenosis in patients undergoing noncardiac surgery can be an incidental finding mainly in the asymptomatic patient during routine preoperative workup or part of the patient's known medical history. In a large study of 5201 patients, Stewart et al[67] found age, male sex, smoking, and arterial hypertension to be independent clinical risk factors of degenerative AV disease. Patients with known AS are usually followed up closely, with an estimated progressively decreasing valve orifice of 0.04 to 0.1 cm^2 per year.[79]

The incidence of sudden death in patients with severe AS is approximately 1% per year.[75] Although it is generally accepted that patients with symptomatic AS should undergo AV surgery, unfortunately, there are no good clinical predictors to identify asymptomatic patients who are at increased risk of sudden death.

In 1977, Goldman et al[80] described AS to be one of the independent factors associated with adverse cardiac events in patients undergoing noncardiac surgery. In a following study, Rohde et al[81] found an AV gradient of ≥40 mm Hg to be a significant risk factor of perioperative cardiac complications (relative risk = 6.8; 95% confidence interval [CI], 1.3-31). In the

2007 updated practice guidelines, the ACC/AHA refers to patient-related risk factors associated with adverse events in noncardiac surgery as active cardiac conditions.[11] Active cardiac conditions (formerly known as major clinical predictors) include severe or symptomatic valvular disease (particularly severe aortic and MS), decompensated heart failure, unstable coronary syndromes, and significant arrhythmias. Kertai et al[82] compared patients undergoing noncardiac surgery with known AS to a control group. The main outcome measure of the study was a composite of perioperative mortality and nonfatal myocardial infarction. There was a higher incidence of the composite end point in patients with a mean AV gradient >25 mm Hg (14% vs 2 %). Patients with severe AS (mean AV gradient >50 mm Hg) had more perioperative complications when compared with patients with moderate AS (31% vs 11%). After adjusting for cardiac risk factors, AS remained a strong predictor of the composite end point (odds ratio [OR] = 5.2; 95% CI, 1.6-17.0) However, in the lowest cardiac risk index group (low-risk surgery, no coronary artery disease, no history of heart failure, no history of cerebrovascular disease, no insulin diabetes mellitus, preoperative creatinine <2 mg/dL), there was no perioperative cardiac events in either group. Zahid et al,[83] in a multivariate analysis on 5149 patients with known AS undergoing noncardiac surgery, found AS to be independently associated with an increased risk of perioperative myocardial infarction (OR = 1.55); however, the presence of AS did not increase the overall mortality when compared with patients without AS. In a case series of 55 patients with a mean AV area of 0.9 cm^2 undergoing noncardiac surgery, there was no difference in the perioperative cardiac events when compared with a historic matched control group; however, patients with AS had more intensive perioperative management.[84] In another study, patients with severe AS (valve area <0.5 cm^2/m^2), that did not have AV replacement prior to noncardiac surgery, had acceptable outcome according to the authors (2 of 19 patients died in the postoperative period, 28 surgical procedures were performed) when careful anesthetic management was applied.[9] Previous studies suggested that the risk of perioperative cardiac events in patients with AS presenting for noncardiac surgery is dependent on the severity of AS, concomitant cardiac risk factors, such as CAD or CHF, and the risk of the planned noncardiac surgery (eg, expected hemodynamic disturbances, fluid shifts, etc).

The preoperative cardiac work up in patients with AS should address the optimization of the patient's cardiac risk profile. Possible interventions largely depend on the urgency of the planned procedure, patient's comorbidities, surgery-related risk, and hospital setting-related factors. The ACC/AHA guidelines list an algorithm for the preoperative evaluation of patients with suspected or known cardiovascular disease undergoing noncardiac surgery.[11] Severe valvular disease, such as severe AS, is listed under active cardiac conditions. In cases of symptomatic severe AS, elective surgery should be postponed. Patients with asymptomatic severe AS presenting for elective noncardiac surgery should have a cardiac evaluation for less than 1 year, including noninvasive or if indicated invasive testing to guide further management.

Information obtained from a preoperative cardiac work up in patients with AS should include information about the severity of AV disease and concomitant morbidities, such as CAD, that add to the overall risk of adverse events during noncardiac surgery. In general, a thorough medical history and physical exam is an important initial step in the preoperative assessment. In patients with AS, the electrocardiograph (ECG) typically shows signs of left ventricular hypertrophy. The ECG should be carefully interpreted for myocardial ischemia, which frequently coexists in patients with AS. A chest radiograph may show signs of left ventricular heart failure, such as pulmonary edema or pleural effusions. A reasonable approach in patients with a history of AS, a systolic murmur on auscultation, symptoms of CHF, syncope, or angina, would be to perform a noninvasive evaluation (eg, transthoracic 2-dimensional and Doppler echocardiography) of the valvular and the cardiac function regardless of the urgency of noncardiac surgery.[85] When the hospital setting does not allow for such testing in a timely manner, emergency procedures may have to be performed regardless of the availability of such preoperative evaluation. In patients with asymptomatic AS, exercise or dobutamine stress testing has been recommended to assess the severity of AS, ventricular function, and ischemic disease.[86-88] Exercise testing can also be used for risk stratification. Amato et al[89] showed that patients with asymptomatic AS and a positive stress test had a worse prognosis than those patients with negative stress test. However, exercise or dobutamine stress testing is contraindicated in patients with symptomatic AS. Even though, invasive testing, such as cardiac catheterization, has been

largely replaced by noninvasive methods to determine the severity of AS, cardiac catheterization is still frequently performed in patients with severe AS who are scheduled for high-risk noncardiac surgery, if risk factors for CAD coexist. Aside from coronary evaluation, further important measurements are obtained during catheterization, such as AV gradient, AV area, filling pressures (LVEDP), and assessment of cardiac function (EF).

Preoperative treatment options. The decision if patients with AS should be medically optimized preoperatively only, or if AV replacement (AVR), or alternative interventions, such as balloon valvuloplasty or percutaneous valve replacement be performed prior to the planned noncardiac procedure, should be discussed on an individual basis. Amongst other factors, the risk of adverse events related to cardiac surgery has to be weighed against the estimated risk of cardiac events in the perioperative period of the planned noncardiac procedure. The patient's comorbidities, age, and life expectancy should be considered in the decision making. It is now generally accepted that symptomatic patients with severe AS should have their AV replaced regardless of the necessity of noncardiac surgery.[77,90] However, in asymptomatic patients with moderate or severe AS, a watchful waiting policy may be indicated. These patients are usually followed up closely to assess the progression of the disease. The indication of AVR in this patient population should be reevaluated if the planned noncardiac surgery is expected to be of high risk for hemodynamic disturbances. If only low-risk surgery is planned, the risk of adverse events related to AVR alone may exceed the risk of adverse events during noncardiac surgery without prior AVR.

Pharmacological treatment options are limited and include treatment of coexisting ischemic disease and symptoms of heart failure. The perioperative use of β-blockers may be indicated in patients with AS and risk factors for CAD.[23] Aortic balloon valvuloplasty can be quickly accomplished in selective candidates if the practice setting allows for cardiac catheterization and cardiac interventions. The effect is usually only temporary, and there is a significant risk of causing AR, but in patients with severe AS scheduled for urgent noncardiac surgery, balloon valvuloplasty can be considered to temporarily optimize the patient who is not a candidate for AV replacement.[91-94] Another more recent development is percutaneous AVR. Though currently still in the investigational stages, this is a potentially promising option for nonsurgical candidates.[95]

Perioperative anesthesia care for the patient with as presenting for noncardiac surgery. Favorable outcome in patients with AS undergoing noncardiac surgery is related to the anesthesiologist's awareness of the severity of AV disease.[9] Therefore, a thorough preoperative anesthetic assessment is essential, followed by appropriate anesthetic management. Premedication in patients with AS is potentially problematic. Oversedation may lead to hypotension and decreased CPP, whereas undersedation may lead to an anxious, tachycardic patient who is prone to myocardial ischemia. All patients should receive oxygen via a nasal cannula in the holding area.

The main goals for the anesthesia management in patients with AS is to maintain adequate systemic vascular resistance (SVR; afterload), CO, relatively slow HR, and SR (Table 1). Tachycardia has to be avoided because it decreases diastolic filling time, shortens systolic ejection time and thus decreases CO, leading to a vicious cycle that may lead to sudden hemodynamic decompensation and cardiac arrest. Conversely, blood flow across the stenotic AV is relatively fixed, and severe bradycardia (HR <40) will result in low CO. The ideal HR is probably between 60 and 70 beats per minute. This allows for adequate diastolic filling, whereas providing sufficient CO. In mixed AV lesions (AS and AR), the stenotic lesion is more concerning. However, slightly higher HRs can be tolerated if severe AR coexists with AS. Arrhythmias are poorly tolerated and it is important to maintain SR. A defibrillator should be readily available in the operating room. In patients in whom the surgical access or the positioning of the patient does not allow for immediate application of the defibrillator paddles, defibrillator pads should be placed on the patient prior to positioning and sterile draping of the patient. In the unstable patient with supraventricular tachyarrhythmias, cardioversion should be considered as the first-line therapy. In the stable patient, a therapeutic diagnostic maneuver (vagal stimulation, adenosine) can be attempted. When the exact underlying rhythm is identified, treatment of supraventricular tachyarrhythmias usually consists of β-adrenergic blockers (eg, esmolol), amiodarone or cardioversion, depending upon the rhythm. In the patient with impaired cardiac function (EF <40%, CHF) or when ventricular tachycardia (VT) cannot be ruled out, amiodarone is the

Table 1. Hemodynamic Goals in Patients With Valvular Disease

	HR	Contractility	Preload	Afterload	Concerns	Drugs
AS	n/↓	n/↑	↑	↑	Maintain SR Spinal anesthesia relatively contraindicated Avoid too low HR (fixed CO) Immediate defibrillation if VT/VF (CPR ineffective)	Phenylephrine Norepinephrine
AI	↑	n/↑	↑	↓		Ephedrine Epinephrine
MS	↓	n	n/↑	↑	Maintain SR If other than SR control HR Avoid precipitators of PHT	Phenylephrine Norepinephrine Epinephrine
MR	↑	n/↑	↑	↓	Often underlying cardiac dysfunction (not apparent from EF)	Ephedrine Epinephrine Norepinephrine
HCM	↓	↓	↑	↑	Avoid increase in contractility Avoid β-agonists	β-blocker Phenylephrine Norepinephrine

NOTE: HR = heart rate; AS = aortic stenosis; SR = sinus rhythm; CO = cardiac output; VT = ventricular tachycardia; VF = ventricular fibrillation; CPR = cardiopulmonary resuscitation; AI = aortic insufficiency; MS = mitral stenosis; PHT = pulmonary hypertension; MR = mitral regurgitation; EF = ejection fraction; HCM = hypertrophic cardiomyopathy.

preferred drug. Bradyarrhythmias should be treated carefully to avoid tachycardia that may lead to sudden hemodynamic decompensation or ischemia. Anticholinergics, combined α- and β-adrenergic agonists, or atrioventricular sequential pacing should be considered. The intervention that results in the most predicable increase in HR should be chosen.

Patients with AS are critically sensitive to preload, and an appropriate intravascular volume status has to be assured prior to anesthesia induction. In most patients, some fluid replacement is indicated prior to induction. Systemic vascular resistance has to be maintained at all times. Thus, neuraxial anesthesia with the risk of sympatholysis should only be administered if there is frequent blood pressure monitoring and if vasoconstrictor therapy is available, in patients with AS. If a neuraxial technique is chosen, an epidural technique is preferred because it allows for incremental dosing and adjustment of analgesia level and thus a sudden drop in SVR can usually be avoided.[96] A combined spinal/epidural technique may offer advantages, and if high doses of intrathecal local anesthetic drug administration are avoided, stable hemodynamic parameters can be maintained.[97] Continuous spinal anesthesia techniques have been successfully administered in patients with AS, with good outcome.[98]

General anesthesia offers the advantage of good hemodynamic control, especially if adequate monitoring is established. Etomidate, opioids, and midazolam are reasonably good choices but should be titrated to effect. Vecuronium and cisatracurium are neuromuscular blockers with favorable hemodynamic profiles. Drugs, such as ketamine, pancuronium, and rocuronium, may increase HR that may be poorly tolerated in the patient with severe AS. Thiopental may cause decreased preload and contractility and should probably be avoided. Similarly, propofol is associated with reduced contractility and afterload reduction resulting in hypotension and thus is also relatively contraindicated with severe AS.

Anesthesia can be maintained with many different techniques so long as preload, afterload, HR, and contractility are monitored to avoid adverse hemodynamic responses. All anesthetic drugs should be titrated carefully with attention to maintaining SVR and CO. Hypotension should be treated immediately, and an α agonist, such as phenylephrine, is the agent of choice. The aim is to preserve CPP, so that the heart does not enter a vicious cycle of irreversible ischemia. In general, pure α-adrenergic receptor agonists are the preferred vasoconstrictor agents. They do not cause tachycardia, and thus the CPP is increased and

diastolic filling time is maintained, without causing an increase in oxygen demand. However, too aggressive treatment of hypotension leading to excessively high arterial pressures with significant increase in left ventricular wall tension, increases oxygen demand, decreases myocardial perfusion, and may cause ischemia in the hypertrophied LV of patients with AS.

Perioperative monitoring should be according to the recommendations of the American Society of Anesthesiologists (ASA). Because patients with AS are at increased risk for ischemia and arrhythmias, monitoring should include leads II and V_5. The sensitivity of this lead combination for detecting myocardial ischemia is approximately 80%. Aside from the standard anesthesia monitoring recommended by the ASA, beat-to-beat arterial blood pressure monitoring, typically via an indwelling arterial catheter, should be established prior to anesthesia induction. A central venous catheter may be useful in these patients. A pulmonary artery catheter (PAC) is routinely used to estimate left-sided filling pressures in some centers, but its use remain controversial. It must be recognized that the pulmonary capillary wedge pressure (PCWP) is a poor estimate of preload in patients with AS. Filling pressures tend to underestimate the true preload due to the decreased ventricular compliance of the hypertrophied LV. Furthermore, the insertion of a PAC may cause arrhythmias that may be poorly tolerated in patients with AS. However, many practitioners would opt to place a PAC in patients with severe AS undergoing high-risk surgery, and the correct interpretation of hemodynamic measurements can be used to guide treatment options. Nevertheless, there is no data from randomized controlled studies at this point that shows improved outcome of patients with AS undergoing noncardiac surgery managed with or without a PAC. Transesophageal echocardiography (TEE) can be useful to guide the practitioner in the differential diagnosis and in the treatment options should intraoperative hemodynamic disturbances occur. Using 2-dimensional echocardiography (end-diastolic area) to determine preload is more accurate compared with pressure-(PCWP) guided preload assessment. The 2003 updated ACC/AHA/American Society of Echocardiography (ASE) guidelines for the clinical application of echocardiography lists the intraoperative use of TEE as a class IIA indication (weight of evidence/opinion is in favor of usefulness/efficacy) for surgical procedures in patients at increased risk of myocardial ischemia, myocardial infarction, or hemodynamic disturbances.[99]

In summary, there is insufficient evidence that a single anesthesia technique offers better outcome. The anesthetic management in patients with AS should be tailored to the individual case. The severity of AS, comorbidities, the surgical procedure, and the experience of the practitioner should be taken into account.

Hypertrophic Obstructive Cardiomyopathy

Introduction. The ACC/European Society of Cardiology (ESC) clinical consensus document on hypertrophic cardiomyopathy (HCM) recommends the use of the term HCM to describe the heterogenic group of cardiomyopathies, that typically present with asymmetric thickening of the left ventricular wall, independent of left ventricular outflow obstruction.[100] One rationale for including this lesion in this review article is, that similar to AS, the obstructive form of HCM (hypertrophic obstructive cardiomyopathy [HOCM]) results in obstruction to LV ejection, can precipitate sudden death, and poses a significant risk for adverse events in patients undergoing noncardiac surgery.[101,102]

Etiology. A genetic etiology is thought to be present with an autosomal dominant trait and gene mutations that affect the protein components of the cardiac sarcomere.[103-105] The prevalence is relatively high with 1 of 500 young adults, women and men equally being affected.[106] The phenotypic expression of HCM is incomplete, may vary between individuals, and is influenced by factors, such as modifier genes or environmental factors.[107] The clinical presentation and onset of symptoms in patients with inherited gene mutations associated with HCM may thus vary, and is difficult to predict. In patients presenting for noncardiac surgery who report a family history of HCM or sudden cardiac death, preoperative noninvasive testing is, therefore, usually indicated. The presence or absence of LVOT obstruction is an important determination in the clinical care of patients with HCM. The LVOT obstruction (>30 mm Hg) is present in 37% of patients with HCM at rest and 70% with exercise.[108]

Symptoms. The clinical presentation of patients with HCM varies, and individuals may be completely asymptomatic and even be unaware of their condition or on the other extreme show signs of severe heart failure. Sudden, unexpected cardiac death may be the first manifestation of the disease.[109,110]

Other symptoms of HCM are chest pain, angina, exertional dyspnea, syncope, dizziness, heart failure, atrial fibrillation, and stroke. Mortality rates are reported to be about 1% annually, but adverse events may be more common in some subgroups of patients with HCM and patients with left ventricular outflow obstruction.[111,112]

Pathophysiology. The main anatomic feature of HCM is asymmetric hypertrophy of the ventricular muscle. In the obstructive form of HCM, this typically involves the base of the septum in the LVOT. Obstruction to LV outflow may or may not be present at baseline or precipitated by physiologic changes or alterations in loading conditions and contractility as can be seen during exercise, major surgery, and general anesthesia. Various mechanisms have been described to explain the incidence and the dynamic pattern of LVOT obstruction. Hypertrophy of the ventricular septum, in the form of a septal bulge, causes narrowing of the LVOT and increases the angle of the flow in the LVOT relative to the MV. The resultant anterior position of the left ventricular papillary muscles relative to the LVOT places the coaptation point of the MV in the path of flow across the LVOT. Systolic anterior motion (SAM) of the MV leaflets is the most common cause of LVOT obstruction (Figure 3).[113] The hemodynamic cause of SAM is debated, and the reader is referred to a review of its pathophysiology discussing drag (pushing) versus venturi (pulling) mechanisms that produce the anterior motion of both MV leaflets.[114,115] Although the anterior leaflet is usually enlarged or elongated, chordal slack is generally necessary for SAM to occur. Restricted MV leaflet motion will prevent typical SAM, but significant MR may occur when restriction of motion is limited only to the posterior leaflet.[116]

The SAM causes a dynamic subaortic pressure gradient and is typically associated with MR. The dynamic outflow tract obstruction increases the pressure load and results in hypertrophy of the LV. Subsequently, left ventricular compliance decreases, and high filling pressures are required to maintain adequate end-diastolic volumes and CO. Regular SR and the atrial contraction become increasingly important for left ventricular filling. Factors that influence LVOT distension and thus the severity of outflow obstruction are the loading conditions of the heart, contractility, and HR. Hypovolemia, tachycardia, systemic vasodilation, and increased contractility all exacerbate the obstruction.

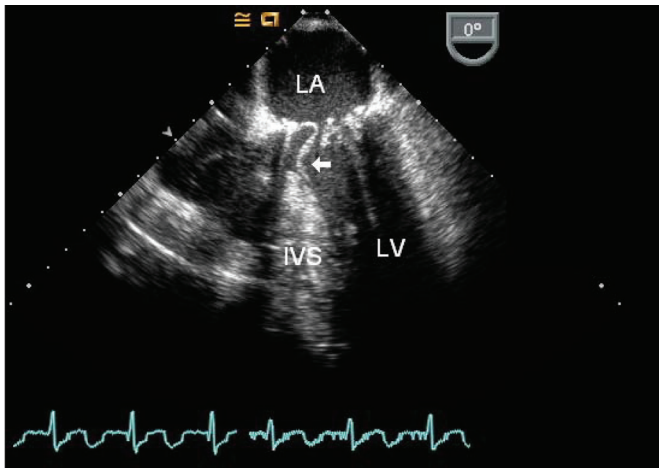

Figure 3. Midesophageal 4-chamber view. The SAM of the (anterior) MV leaflet causing left ventricular outflow obstruction (arrow). SAM indicates systolic anterior motion; MV, mitral valve; LA, left atrium; LV, left ventricle; IVS, interventricular septum.

Preoperative evaluation and risk assessment. The perioperative risk for adverse events in patients with HCM presenting for noncardiac surgery is significantly increased. In a recent retrospective database analysis, 227 patients with HCM undergoing noncardiac surgery were matched with 554 controls. Patients with HCM had an almost 3-fold increased risk of perioperative death or acute MI compared with the control group (OR = 2.82; 95% CI, 2.59-3.07).[117] In a retrospective chart review Haering et al,[118] identified 77 patients who underwent noncardiac surgery in whom a prior echocardiography exam had showed HCM. In all, 40% (31 of 77) of these patients had 1 or more adverse perioperative cardiac events; no perioperative death was reported. Adverse cardiac events that occurred were CHF (12 of 77), myocardial infarction (1 of 77), life-threatening dysrhythmias, myocardial ischemia, stable dysrhythmias, and transient hypotension. Factors that were significantly associated with adverse cardiac events were length of surgery, high-risk surgery, and intensity of monitoring. Length of surgery was the strongest predictor and together with the high incidence of CHF led the authors conclude that anesthetic management and aggressive fluid management in an attempt to maintain preload precipitated this outcome. More invasive monitoring was associated with worse outcome and may reflect selection bias. Surprisingly, in

distinction to the out-patient longitudinal studies, in intraoperative studies, factors, such as resting outflow gradient, SAM, prior MI, were not associated with adverse outcome. Neither was anesthetic technique significantly associated with adverse events.

In a different retrospective analysis, 60% of patients with HCM undergoing noncardiac surgery had perioperative cardiac events (CHF 3 of 30, myocardial ischemia 4 of 30 patients), no death were recorded.[119]

In a prospective observational study, Maron et al[120] assessed the effect of resting LVOT obstruction on morbidity and mortality in patients with HCM. Of 1101 patients who were followed up, 273 patients had a resting gradient greater than 30 mm Hg. Overall, a total of 127 patients died in the observation period (mean 6.3 ± 6.2 years), 20% of the remaining patients had symptoms of severe progressive heart failure. The resting LVOT gradient was a strong, independent predictor of death, and cardiac morbidity. Elliott et al,[121] observed 917 patients (median time 61 month) to evaluate the influence of LVOT gradient on sudden death, ventricular fibrillation, or automatic implantable cardioverter defibrillator (AICD) discharge in patients with HCM. A resting gradient >30 mm Hg was an independent risk factor for sudden cardiac death or AICD discharge, even though, the overall annual rate was low (0.37%, 95% CI, 0.05-1.35). However, symptomatic patients and patients with additional risk factors were at increased risk for sudden cardiac death or AICD discharge.

The preoperative evaluation in patients with HCM presenting for noncardiac surgery should rule out significant cardiac and noncardiac morbidity in the presence of known HCM. A thorough medical history should be taken, and a physical examination should be performed to assess for symptoms of heart failure, ischemia, significant dysrhythmias, residues of transient ischemic attacks (TIAs) or strokes. In patients with a resting gradient, a systolic ejection murmur may be heard at the left lower sternal border and apex. However, the LVOT obstruction is dynamic and auscultatory findings may be insignificant unless provocative maneuvers are performed. A 12-lead echocardiogram is abnormal in the majority of patients. Signs of LV hypertrophy, ST-segment alterations, and dysrhythmias, such as atrial fibrillation, are amongst the unspecific findings. A preoperative echocardiography examination should be performed at rest, and provocative maneuvers are used, such as a valsalva maneuver, to elicit LVOT obstruction. The type and severity of HCM, the resting gradient across the LVOT, the presence of SAM, and the severity of MR should be determined. Other significant echocardiography findings in patients with HCM are asymmetric left ventricular hypertrophy with sparing of the basal posterior wall and a late systolic peaking LVOT gradient. Magnetic resonance imaging (MRI) is an evolving imaging technique with excellent image quality and can be indicated in selected patients. Because HCM is a genetic cardiac disorder, a family history of HCM in a first-degree relative of a patient should alert the practitioner to the increased risk of HCM, and thus an echocardiogram before elective surgery can be indicated.

Preoperative treatment options. Long-term treatment in patients with HCM is directed at symptom relief and the prevention of sudden cardiac death.[122] The medical therapy is based on β-blockers, which depress contractility and slow the HR leading to improved diastolic filling and cardiac relaxation. Verapamil is used in patients who may not be candidates for β-blockers. Disopyramide, a type IA antiarrhythmic agent with negative inotropic and peripheral vasoconstrictive effects, has been used in patients whose symptoms are poorly controlled otherwise. Supraventricular and ventricular arrhythmias are treated with antiarrhythmics, such as amiodarone.[123] In patients with a high resting LVOT gradient (>30 mm Hg) or symptomatic patients, surgical interventions can be indicated. Surgical options in patients with significant LVOT obstruction are septal myectomy with or without MV valvuloplasty or MV replacement.[124,125] Percutaneous alcohol septal ablation is performed in the catheterization laboratory with good results.[126-128] Potential complications of surgical correction or septal ablation include complete heart block and late formation of a ventricular septal defect due to septal infarction. The implantation of a dual-chamber pacemaker had been suggested, but results were disappointing, and at this point, it is only recommended in selected patients.[129] The AICDs are frequently implanted to treat arrhythmias and to prevent sudden cardiac death.[130,131] Anticoagulation should be considered in patients at increased risk for embolic events. Extensive guidelines for the management of patients with HCM have been released by the ACC and the ESC.[100]

Perioperative anesthesia care for the patient with HCM presenting for noncardiac surgery. Premedication in patients with obstructive HCM prior to surgery is typically indicated to prevent tachycardia caused by anxiety.

Short-acting benzodiazepines are a good choice; they offer reliable anxiolysis and sedation without significant unwarranted hemodynamic effects, such as systemic vasodilation. Atropine or glycopyrrolate should be avoided because of their potential tachycardic effect. Preoperative β-adrenergic blockade or calcium-channel blocker therapy should be continued.

The main goals for the anesthesia management in patients with obstructive HCM are to maintain adequate preload and afterload, a relatively slow HR, and SR (Table 1). An increase in myocardial contractility typically provokes LVOT obstruction and thus is best avoided in patients with obstructive HCM.

Almost all anesthetic techniques have been performed successfully in patients with HCM. However, a sudden decrease in afterload typically seen secondary to sympathectomy following the administration of large doses intrathecally administered local anesthetics is poorly tolerated, and thus single-dose spinal anesthesia is often considered to be relatively contraindicated in patients with obstructive HCM. Continuous spinal, epidural, and combined spinal or epidural techniques can be titrated to effect and offer good hemodynamic stability. A regional anesthetic technique, if the surgical procedure allows, may be the anesthetic technique of choice. General anesthesia is chosen by many practitioners. Adequate anesthetic depth should be maintained at all times because sympathetic stimulation caused by tracheal intubation or surgical manipulation results in an increase in contractility and tachycardia, both of which may worsen LVOT obstruction.

Besides the standard anesthesia monitoring recommended by the ASA, beat-to-beat arterial blood pressure monitoring, typically via an indwelling arterial catheter, should be established prior to anesthesia induction. A central venous catheter may be useful in patients with significant outflow tract obstruction or patients undergoing more than minor procedures. A PAC can be indicated if large fluid shifts and hemodynamic disturbances are expected. However, there is no data at this point showing improved outcome with PAC monitoring, and patients with HCM can be especially sensitive to arrhythmias caused by catheter placement. The TEE provides useful data on ventricular performance, loading conditions, the dynamic mechanism of the LVOT obstruction, and the accompanying MR.

General anesthesia is typically induced intravenously. In children, an inhalational technique with halothane or sevoflurane may be chosen. Halothane decreases HR and myocardial contractility and has the least effect on SVR. However, halothane is no longer available in the market. Etomidate or thiopental are good choices for anesthesia induction. Etomidate has only minimal hemodynamic effects, and thiopental decreases contractility and maintains afterload, both of which is warranted in patients with HCM. Ketamine and pancuronium is best avoided because of their sympathomimetic effects. Propofol is used frequently, but aside from its negative inotropic effect also decreases afterload that may not be tolerated in patients with severe LVOT obstruction. Morphine and neuromuscular blocking agents that are known to release histamine, such as atracurium or mivacurium, are best avoided. All induction agents should be titrated to affect in order to avoid a sudden drop in blood pressure. Anesthesia can be maintained with inhalational agents only if preload and afterload are maintained. Alternatively, a high-dose opioid technique may be chosen. Isoflurane and desflurane cause pronounced peripheral vasodilation; sevoflurane decreases SVR to a lesser extent and thus may be preferable.

Blood loss and postural changes can decrease preload, and sympathetic stimulation caused by surgical manipulation results in an increase in contractility and tachycardia, all of which may worsen LVOT obstruction. The acute onset of atrial fibrillation may be poorly tolerated in patients with HCM who require high filling pressures and the atrial contribution during ventricular filling to maintain CO.

In patients who become hemodynamically instable, inotropes, β-adrenergic agonists and calcium are best given only after ruling out LVOT obstruction and SAM as the cause of the instability. Hypovolemia should be corrected immediately, and the α-1-agonist phenylephrine is the drug of choice to treat acute hypotension. Alternatively, norepinephrine can be chosen. Tachycardia is poorly tolerated in patients with HOCM because it decreases systolic ventricular volume thereby narrowing the outflow tract. Intravenous propanolol, metoprolol, esmolol, or verapamil may be administered intraoperatively to improve hemodynamic performance. Atrial fibrillation associated with VT should be treated promptly. Drugs that lower SVR, such as nitroglycerin, nitroprusside, or angiotensin-converting enzyme (ACE) inhibitors, should be avoided in the perioperative setting.

Anesthesia management for labor and delivery in the parturient with HOCM is not discussed in the content of this article.

Mitral Stenosis

Etiology. Similar to AS, MS may be congenital or acquired. The vast majority of acquired cases of MS are rheumatic in origin. Rheumatic fever is an inflammatory disease, a delayed complication in susceptible individuals following a group A streptococcal infection. In its chronic course, it can lead to valvular disease, typically MS. In a large retrospective analysis of over 24 000 echocardiograms, Movahed et al,[132] found MS to be more prevalent in women (1.6% vs 0.4%, $P < .001$). Even though the prevalence in the industrialized countries has declined drastically, it is still a major health problem in developing countries.[133] Due to its typical latency, with onset of symptoms including the childbearing age, MS is the most common valvular lesion in pregnancy.[134,135] Congenital MS is rare, and usually part of a more complex malformation, such as hypoplastic left heart syndrome or associated with additional left-sided obstructions. In its severe form, congenital MS is not compatible with life unless palliated or corrected at very early age.[136] Other causes of acquired MS are: IE, systemic lupus erythematosus, rheumatoid arthritis, atrial myxoma, malignant carcinoid, sarcoidosis, and iatrogenic MS after MV annuloplasty.[137-139]

Symptoms. Mitral stenosis is a narrowing of the MV orifice resulting in left atrial hypertension, limited filling of the LV, pulmonary congestion, and in moderate to severe cases pulmonary arterial hypertension (PHT), right ventricular pressure overload, and right ventricular failure. In a small percentage of patients with MS, left ventricular failure can be seen. Patients usually are not symptomatic before the valve area falls below 2.5 cm^2. Exertional dyspnea is the most common symptom as the valve area falls below 1.5 cm^2. The initial presentation is often due to an episode of atrial fibrillation or by an unrelated condition, such as pregnancy, thyrotoxicosis, anemia, or sepsis. Other common symptoms include fatigue, palpitations, or hemoptysis. In many patients, there is latency of 30 to 40 years or even more, between the episode of acute rheumatic fever that is seen typically in children between 5 to 15 years of age, and the onset of clinical symptoms of MS.[140]

Pathophysiology. In the normal adult, the MV orifice area measures 4 to 5 cm^2. The natural course of patients with MS is quite variable. In a follow-up echocardiographic study, the stenosis progressed at a rate of 0.09 ± 0.21 cm^2 per year; patients with a greater initial mean gradient had a more progressive course.[141] As the orifice narrows, to less than 2 cm^2, the pressure gradient between the left atrium (LA) and the LV must increase to maintain adequate flow across the stenotic MV. A MV area less than 1.0 cm^2 is considered severe MS (Figure 4).[15] The increase in left atrial pressure is necessary to maintain left ventricular filling and thus CO. High left atrial pressures that develop overtime cause pulmonary venous congestion and pulmonary edema. In more advanced stages of MS, PHT can be seen, and symptoms of right ventricular failure subsequently may develop.

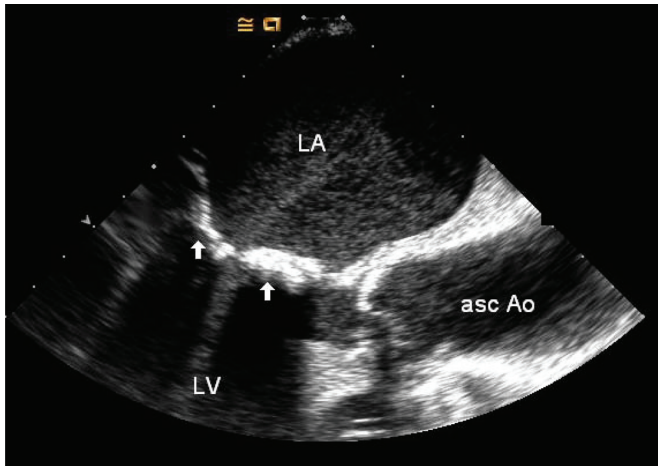

Figure 4. Midesophageal long-axis view of a patient with a history of rheumatic fever resulting in severe MS. Note the calcification of the MV (arrows), the enlargement of the LA with spontaneous echo contrast. MS indicates mitral stenosis; MV, mitral valve; LA, left atrium; LV, left ventricle; asc Ao, ascending aorta.

Tachycardia shortens diastole and diminishes the time available for flow across the MV. This, in turn, impairs left atrial emptying and left ventricular filling. The CO decreases, pulmonary congestion increases, and hemodynamic decompensation ensues.

According to the Gorlin's formula, an increased flow across the stenotic orifice will significantly increase the pressure gradient across the MV. Sudden increase in HR and physiologic changes during pregnancy, for example, an increase in CO, may lead to increased left atrial pressure. This increase in left atrial pressure will result in increased pulmonary vessel pressure and possibly increased lung water.

Passive filling of the LV during the early phase of diastole is impaired due to the narrowed MV orifice. Consequently, the atrial contribution becomes more important in maintaining adequate left ventricular filling, and an acute loss of SR may cause sudden hemodynamic decompensation. However, as the disease progresses, the LA dilates and many patients with MS present with chronic atrial fibrillation.[142] Control of HR becomes the main objective in these patients.

Thromboembolic events can be seen frequently in patients with MS, especially in the presence of paroxysmal atrial fibrillation, a large LA, and the presence of spontaneous echo contrast on echocardiography examination.[143,144]

Although the LV is protected from pressure or volume overload, left ventricular contractility may be impaired by rheumatic involvement of the papillary muscles and mitral annulus. Left ventricular function may also be impaired due to interdependency of the right ventricle (RV) and the LV. A shift of the interventricular septum toward the LV that can be seen with elevated right ventricular pressures, causing right and left ventricular dysfunction.[145,146]

Preoperative evaluation and risk assessment. The perioperative risk in patients with MS can be difficult to assess. Patients with MS are typically asymptomatic for many years until sudden onset of atrial fibrillation or the physiological stress during pregnancy lead to acute decompensation. Patients with mild MS and normal exercise tolerance will only experience a minimal increased risk of perioperative adverse cardiac events. However, patients with severe MS or patients with associated PHT have a significant risk of perioperative morbidity. Most of the data on perioperative risk in patients with MS is published on the parturient with rheumatic MV disease. Even though, this data cannot be extended to the nonpregnant patient scheduled for noncardiac surgery, it highlights some of the risk factors for adverse cardiac events in patients with MS. More than mild MS (valve area <1.5 cm^2), and the presence of cardiac events (eg, arrhythmias, pulmonary edema, stroke) before the pregnancy, were independently associated with adverse maternal cardiac complications.[135] The New York Heart Association (NYHA) functional class was strongly associated with maternal and fetal complications during pregnancy in patients with cardiac disease including patients with MS.[134] Parturients with severe PHT reach mortality rates up to 40% during pregnancy and after delivery, despite modern management.[147]

As an initial step in the preoperative assessment, patients with known MS should undergo a thorough physical examination. Atrial fibrillation, a weak pulse with a reduced pulse pressure, a diastolic murmur, neck vein distension, and auscultatory signs of pulmonary edema are some of the findings in patients with MS. Exercise tolerance should be carefully assessed. The ACC/AHA guidelines for perioperative cardiovascular evaluation for noncardiac surgery include the functional capacity in their assessment algorithm.[11] Even though this algorithm was not specifically developed for patients with MS, good exercise tolerance, such as being able to climb a flight of stairs, running a short distance, or even participate in moderate or strenuous sports, are good indicators for adequate functional capacity. These patients can usually undergo less than high-risk surgery without any further interventions as long as HR is well controlled in the perioperative period (β-blocker use). However, in cases of symptomatic severe MS, elective surgery should be postponed. Patients with asymptomatic severe MS presenting for elective noncardiac surgery should have a cardiac evaluation, including noninvasive or if indicated invasive testing to guide further management.[11,148] Echocardiography can evaluate left and right ventricular function, MV morphology, establish a gradient across the MV, estimate left atrial pressure, and assess left atrial enlargement. Additionally, other cardiac valves can be evaluated, right-sided pressures can be estimated, and LA thrombus formation can be detected. Exercise or dobutamine stress echocardiography may be warranted to assess the response to increased CO and HR and thus aide in the decision making of preoperative interventions.[149,150] In selected cases, cardiac catheterization may be indicated. During cardiac catheterization, the MV orifice area can be calculated using the Gorlin formula described above, CO and the degree of PHT can be assessed. The response to pulmonary vascular dilators, such as nitric oxide, can be tested to determine if PHT is reversible or reactive to vasodilators. A percutaneous balloon commissurotomy may be performed in the same session.

Preoperative treatment options. Medical treatment usually consists HR control and anticoagulation in patients with atrial fibrillation or in patients with spontaneous echo in the LA to prevent thromboembolic events. Thus, patients with MS are frequently on a combination of coumadin, β-blocker, digoxin, and calcium-channel blocker therapy.

The ACC/AHA guidelines for the management of patients with valvular heart disease recommend MV interventions, such as percutaneous balloon valvotomy or MV surgery, in symptomatic patients (NYHA class II, III, and IV) with a MV orifice area of ≤1.5 cm^2, or patients with MS and pulmonary hypertension. The presence of left atrial thrombi, moderate to severe MR, and severe MV calcification are all considered contraindications for balloon valvotomy.[15,151] Percutaneous balloon valvotomy is well tolerated especially in younger patients.[152,153] However, in patients older than 70 years of age, only 19% were in NYHA class I and II, and mortality reached 59%, 5 years after MV balloon valvuloplasty.[154] The MV surgery is usually reserved for symptomatic patients with contraindications for balloon valvotomy.

The patient with MS and severe PHT is at high risk for perioperative adverse events, and the necessity of elective surgery should be carefully evaluated, and the risk or benefit options is discussed with the patient. Preoperative medical optimization of PHT should be attempted prior to noncardiac surgery.

Perioperative anesthesia care for the patient with MS presenting for noncardiac surgery. The anesthetic goals for patients with MS are to control HR, if possible, preserve SR, and to prevent systemic vasodilation (Table 1). Preload and intravascular volume status has to be maintained carefully, without increasing LA pressure and pulmonary capillary pressure beyond the point where pulmonary edema ensues. Especially in the presence of right ventricular impairment, volume administration should be carefully monitored. Afterload (SVR) should be kept high to maintain perfusion pressure in the face of a relatively fixed CO. Heart rate should be kept slow to maximize diastolic filling of the LV. Contractility should not be diminished to maintain adequate CO that is already low in these patients. Hypotension is equally poorly tolerated. In patients with elevated pulmonary artery pressures, hypercarbia, acidosis, and hypothermia, all may exacerbate PHT, cause right ventricular failure, and thus should be avoided.

Because tachycardia is poorly tolerated, premedication before surgery to control anxiety while carefully monitoring systemic blood pressure is beneficial. Rate control drugs, such as calcium-channel blockers and β–blockers, should be continued until the time of surgery. Coumadin should be discontinued and heparin anticoagulation initiated accordingly. Potassium levels must be monitored carefully to prevent digitalis toxicity and arrhythmias. Supplemental oxygen is indicated in transit to the operating room. In patients with PHT, pulmonary vasodilators have to be continued throughout the perioperative period to prevent rebound PHT that can be seen when some of these medications are discontinued. A multidisciplinary approach is indicated to plan the perioperative management in patients with MS and severe PHT prior to noncardiac surgery.

The choice of anesthesia technique should be made on an individual basis. Patient-related factors, type of surgery, and practitioner experience should be considered. General anesthesia offers the advantage of good hemodynamic control, especially if adequate monitoring is established. Neuraxial anesthesia techniques are not contraindicated as long as sudden sympathectomy and hypotension can be avoided.[155,156]

Intraoperative monitoring also depends on the severity of MV disease, the presence of PHT, associated comorbidities, type of surgery, and practitioner-related factors. In more than minor risk surgery and moderate or severe MS, invasive arterial blood pressure monitoring is usually indicated. In these patients, an indwelling arterial catheter should always be placed before the induction of anesthesia. In symptomatic patients with MS and significant PHT, placing a PAC prior to anesthesia induction should be considered. The benefits of a PAC in these patients include the ability to gather information on left atrial filling pressure, pulmonary artery pressure, CO, and pulmonary and SVRs. Knowledge of pulmonary artery pressures is particularly important in the presence of RV dysfunction because successful therapy includes manipulation of RV afterload. Even though, as mentioned earlier, there is no good data from prospective randomized studies showing improved outcome with the use of PACs, PHT and RV dysfunction are considered by many practitioners an indication for PAC placement.[157] The TEE is particularly useful, as it provides the opportunity to observe biventricular function, loading conditions, left atrial dimensions, and valvular function. In patients with RV dysfunction, TEE allows for direct assessment of the RV response to volume loading and inotrope management. The ACC/AHA/ASE guidelines on the intraoperative use of TEE do not specifically refer to the management of patients with MS. Nevertheless, surgical procedures in patients at increased risk for hemodynamic disturbances are listed as a class IIA indication (weight of evidence/opinion is in favor of usefulness/efficacy) for TEE monitoring.[99]

A balanced anesthesia technique, using opioids, benzodiazepines, and etomidate is a reasonable choice for anesthetic induction in patients with MS. Opioids also have the advantage of increasing the vagal tone and slowing the HR, usually without associated hypotension. Short-acting barbiturates produce undesirable venodilation and myocardial depression. Ketamine is relatively contraindicated on the basis of its tachycardic effects. Volatile agents produce both myocardial depression and vasodilation and should be used cautiously in low concentrations. Theoretically, the most suitable neuromuscular blocking agents for MS are succinylcholine, vecuronium, rocuronium, and cisatracurium. Pancuronium is contraindicated because it produces tachycardia.

The management of hemodynamic disturbances should be based upon the underlying etiology and the coexistence of RV dysfunction or PHT. Hypotension is best treated with an α-adrenergic agonist, such as phenylephrine, which would increase arterial pressure and decrease HR via baroreceptor-mediated reflexes. Vasoconstriction is necessary to preserve vital organ perfusion in the face of a fixed low CO. The β-adrenergic agonists cause tachycardia and vasodilation, which are undesirable effects in patients with MS. Thus, ephedrine, dopamine, dobutamine, and epinephrine, are relatively contraindicated.

Aortic Regurgitation

Etiology. The etiology of AR may be congenital or acquired. The AR can be caused by changes affecting the valve leaflets itself or due to processes affecting the AV annulus and aortic root. At a younger age, a bicuspid AV or aortic root dilatation seen in connective tissue disease, such as Marfan syndrome (Figure 5), can be associated with AR. Rheumatic disease predominantly affects the MV; however, the AV may be involved also and may be the cause AR. Endocarditis causing lesions on the AV valve cusps, or vegetations preventing the AV to function properly, are other causes of AR. Acute AR can be seen in a type A aortic dissection, either traumatic or secondary to changes of the aortic tissue seen in connective tissue diseases. Senile aortic calcification not only causes AS but also some degree of AR coexists.

Symptoms. Acute AR is poorly tolerated and can be life threatening. Typical symptoms include acute chest pain, shortness of breath, and symptoms of cardiogenic shock. Patients with chronic AR are usually asymptomatic for many years. Finally, chronic left ventricular volume overload and slowly decreasing left ventricular function clinically manifests with exertional dyspnea or shortness of breath even at rest, tachycardia, angina, and palpitations caused by ventricular or supraventricular arrhythmias.

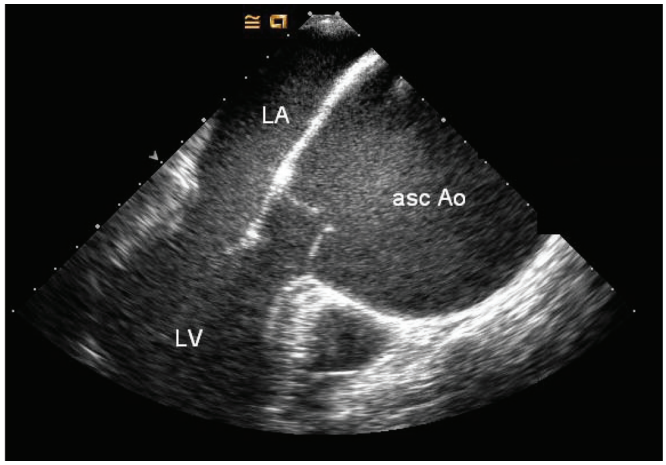

Figure 5. Midesophageal long-axis view of a patient with Marfan syndrome with aortic root dilatation. LA indicates left atrium; LV, left ventricle; asc Ao, ascending aorta.

Pathophysiology. AR, either acute or chronic, leads to volume overload of the LV.

In the acute form, the sudden increase in left ventricular wall tension acutely increases the work load of the LV. In severe AR, the regurgitant fraction is more than 60% of the total stroke volume, and CO can only be maintained by an increase in HR and work load on the LV. A steep rise in LVEDP impairs myocardial perfusion, which is even further diminished by the low diastolic aortic pressure seen with AR. Thus, myocardial oxygen demand is increased and oxygen supply decreased, and myocardial ischemia may occur. The CO is acutely decreased, and the acute volume load and high filling pressures can cause the MV to become insufficient, and acute pulmonary edema may ensue. Overall, the clinical picture of acute cardiogenic shock may develop, only partially compensated for by an increase in SVR.

Chronic left ventricular volume overload is much better tolerated, and typically, it leads to eccentric hypertrophy and massive dilatation of the LV. According to the law of Laplace, this dilatation leads to a decrease in wall tension, and myocardial oxygen balance is maintained for a long time. The

dilated LV is highly compliant, and even large increases in left ventricular end-diastolic volume only cause the LVEDP to be mildly elevated. Even though, patients can be asymptomatic, the underlying myocardial function is usually impaired.

Preoperative evaluation and risk assessment. Compared with stenotic valvular lesions, there is only limited data on the perioperative risk of patients with AR undergoing noncardiac surgery. Asymptomatic patients with mild AR probably only have a minimally increased risk of adverse cardiac events when undergoing noncardiac surgery. However, patients with severe AR, especially patients who are symptomatic (NYHA III-IV) have a significant increased morbidity and mortality when compared with the general population even without surgery.[158] According to the recently updated ACC/AHA guidelines, patients with severe AR should be considered for further evaluation before undergoing elective noncardiac surgery.[11]

Acute AR, either traumatic or in the setting of an acute dissection of the ascending aorta, usually presents as an emergency and poses a major risk for noncardiac surgery.

On physical examination, a characteristic high-pitched diastolic murmur can be heard on auscultation in patients with AR. Bounding pulses due to a widened pulse pressure are typically found with significant AR. In the ECG, signs of left ventricular hypertrophy can be seen, and a chest radiograph typically shows left ventricular enlargement. The patients functional status should be evaluated, and signs of volume overload and pulmonary edema should be assessed. The diagnosis and grading of the severity of AR is usually performed noninvasively via echocardiography examination. Radionuclide angiography, MRI, and computed tomography techniques can be indicated. Exercise stress testing is useful in patients with chronic AR to assess the functional capacity prior to noncardiac surgery. Some of the findings supporting the diagnosis of severe AR are a regurgitant fraction ≥0.6, a holo-diastolic flow reversal in the descending aorta, and a large regurgitant jet seen on echocardiography. Any preoperative evaluation of AR should rule out coexisting AS, which could be the leading lesion in terms of risk assessment in a patient presenting for noncardiac surgery.

Preoperative treatment options. In patients with chronic AR presenting for noncardiac surgery, medical therapy should be optimized. Especially in the patient with dilation of the ascending aorta, hypertensive medication and β-blockade should be continued preoperatively to prevent rebound hypertension seen with abrupt discontinuation of these medications. Hypotension and vasoplegic syndrome have been reported with the use ACE inhibitors and angiotensin II antagonists. However, there is controversy about recommendations to discontinue these medications prior to surgery.[159-162] The patients volume status should be assessed, and signs of preoperative CHF should be treated prior to noncardiac surgery. The AV replacement is recommended in patients with severe AR, patients with progressive left ventricular dysfunction, and patients with significant aortic root dilatation.[15,163] However, the perioperative risk of cardiac surgery should be considered in the decision making of AV replacement in the patient with significant AR scheduled for noncardiac surgery. Obviously, the type of noncardiac surgery is a major determinant in the risk assessment and preoperative treatment of patients with AR. Although minor surgery may not need any further interventions, major noncardiac surgery with large fluid shifts and the risk for perioperative hemodynamic instability warrants a more aggressive preoperative approach.

Perioperative anesthesia care for the patient with AR presenting for noncardiac surgery. Premedication as indicated usually does not pose a major hemodynamic risk for the patient with AR. The general anesthetic goal is to maintain the high HR and low afterload to promote forward flow (Table 1). This principal concept in regurgitant valvular lesions should be considered when choosing an anesthetic technique and anesthetic agents in patients with AR presenting for noncardiac surgery. There is no definite contraindication of any particular anesthetic technique, and regional, neuraxial, and general anesthesia can be applied safely. Hemodynamic monitoring should be according to the guidelines of the ASA. In more severe forms of AR, and particularly in patients with preoperative symptoms of CHF, continuous arterial blood pressure monitoring should be established prior to anesthesia induction. Central venous access is recommended especially in patients with poor peripheral venous access; it allows for central venous pressure monitoring, and more importantly vasodilators, such as nitroprusside, can be administered more safely. In cases of severe AR and patients with decompensated CHF, a PAC can be indicated to guide fluid administration and hemodynamic management. Again, outcome data about the use of

PAC is inconclusive at best, and pulmonary capillary occlusion pressure may underestimate preload in patients with significant AR due to the premature closure of the MV. Even in asymptomatic patients with AR, the underlying myocardial function can be impaired, and thus anesthetic agents with minimal negative inotropic effects should be chosen. Postoperatively, the patient with AR should be monitored for symptoms of CHF, especially if large intraoperative fluid shifts occurred.

Mitral Regurgitation

Etiology. Mitral regurgitation is one of the most common valvular lesions, with at least mild MR occurring in more than 1 in 5 adults.[164,165] The MV prolapse (with or without MR) can be found in 1% to 3% of the population.[165,166] Advancements in imaging technologies, such as echocardiography and MRI, and rapidly evolving surgical techniques for the correction of MR have led to a more thorough understanding of the complexity of MR. Mitral regurgitation can occur secondary to changes of the MV leaflets (organic MR) or due to changes in the complex interaction between the various structures composing the MV (functional MR) with normal MV leaflets. Additionally, the same etiology can either cause changes effecting the MV itself (eg, papillary muscle rupture in acute myocardial infarction) or cause chronic changes in the functional MV unit (eg, remodeling of the LV following myocardial infarction). Functional and degenerative MR are now recognized as the most common causes of chronic MR in the Western world. Ischemic heart disease is the leading cause of functional MR, whereas degenerative MR is often caused by myxomatous degeneration of the MV (Figure 6) leaflets, fibroelastic deficiency, and senile calcification of the valvular apparatus. Rheumatic MV disease is still frequently found in the developing countries and aside from MS, some degree of MR almost invariably coexists. Vegetations found in infective endocarditis can impair proper MV closure, and leaflet perforation or chordal rupture leading to MR can be found. Some of the rarer causes of MR are connective tissue disorders (eg, Marfan syndrome, Ehlers-Danlos syndrome, systemic lupus erythematosus), myocardial diseases (eg, cardiomyopathies, sarcoidosis, amyloidosis), trauma, cardiac tumors, and congenital MR (eg, cleft MV).

Symptoms. Patients with acute MR due to trauma or papillary muscle rupture present with symptoms of left ventricular failure, such as acute pulmonary edema, dyspnea, chest pain, and cardiogenic shock. Biventricular failure may ensue secondary to the acute volume overload and markedly elevated left atrial pressures.

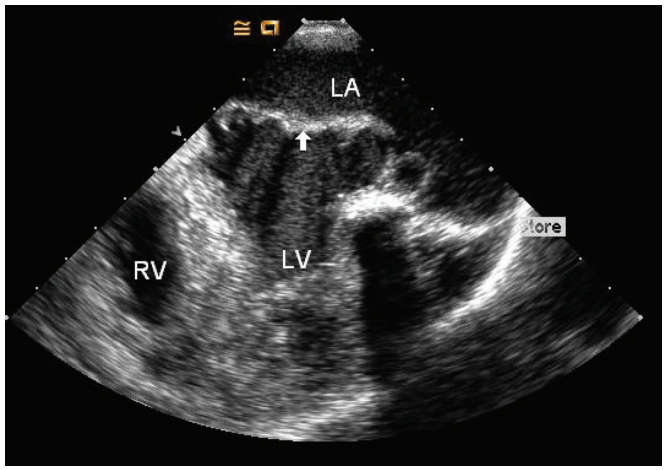

Figure 6. Midesophageal 4-chamber view showing significant bileaflet MVP (arrow). The echocardiographic findings shown are typical for degenerative MV disease (Barlow's type). MVP indicates mitral valve prolapse; LA, left atrium; LV, left ventricle; RV, right ventricle.

Chronic MR is usually well tolerated until the compensatory mechanisms fail, and patients present with symptoms of forward failure, such as fatigue, decreased exercise tolerance, and increasing shortness of breath. The symptoms may be triggered by new onset of atrial fibrillation that can be seen in many patients with chronic MR. Symptoms in MV prolapse can be related to MR; however, patients may be symptomatic even without MR due to an increased prevalence of autonomic dysfunction. Patients with MV prolapse syndrome experience palpitations, chest pain, dyspnea, fatigue, and orthostatic hypotension. Even though, patients with chronic MR may remain asymptomatic for a long period of time, MR is not a benign disease and several studies have shown a significantly increased morbidity and mortality in these patients. Ling et al[167] published data on the course of MR due to a flail leaflet. The majority of patients were in NYHA class I-II, and patients were treated medically only. The reported yearly mortality rate was 6.3%, with a high morbidity after 10 years (heart failure 63%, atrial fibrillation 30%).[167] The risk of sudden death is also increased in patients with MR.[168] In a recent prospective observational study on 456 asymptomatic patients with organic MR (43% had severe MR as per effective regurgitant orifice area), the estimated 5-year

rate of death from cardiac events was 33% (cardiac causes, heart failure, or new atrial fibrillation).[169] Independent determinants of survival were increasing age, diabetes mellitus, and severity of MR as estimated by effective regurgitant orifice size. Patients with functional MR are more often symptomatic as a consequence to their underlying pathology such as ischemic heart disease. Symptoms can be acute as in acute myocardial ischemic event, or evolve overtime as the underlying disease process progresses.

Pathophysiology. In MR, part of the total stroke volume is ejected backwards (regurgitant fraction), and the LA (systole) and the LV (diastole) are subject to an increased volume load.

In acute MR, no compensatory mechanisms and structural changes are present, and the regurgitant volume is imposed on a normal sized LA causing a steep rise in left atrial pressure. Increased left atrial pressure increases pulmonary venous pressure and pressure in the lung microvasculature, leading to transudation of fluid into the pulmonary interstitium and alveoli with the clinical picture of acute pulmonary edema. The high filling pressures on the left side of the heart can acutely increase right ventricular workload and biventricular failure may ensue.

In chronic MR, eccentric hypertrophy of the LV evolves, along with a markedly dilated LA. In the early stages of chronic MR, ventricular systolic and diastolic functions are still preserved. However, with more advanced MV disease, underlying systolic dysfunction is almost universally present and is typically masked by unloading into the highly compliant LA. Measures of ventricular function that are loading dependent, such as EF, will significantly underestimate the severity of myocardial dysfunction. Diastolic function is frequently impaired in advanced stages of MR as the LV becomes less compliant and filling pressures increase.

Chronic MR can cause pulmonary vascular changes, and many patients with longstanding severe MR also have some degree of pulmonary hypertension and right ventricular impairment. It is now recognized, that some of the etiologies leading to structural changes of the MP apparatus also affect the tricuspid valve. Thus, in patients with MV disease, often some degree of tricuspid regurgitation can be found.

Preoperative evaluation and risk assessment. A holosystolic murmur can be heard on auscultation. The pulse may be irregular and features of atrial fibrillation can be found frequently on the ECG in patients with chronic MR. Cardiomegaly can be diagnosed on a chest radiography. The severity and underlying mechanism of MR is usually determined noninvasively via echocardiography, but cardiac catheterization also allows for an estimation of the regurgitant fraction and grading of MR. The severity of MR is usually reported as mild, moderate, or severe, with mild-to moderate and moderate-to-severe in cases where overlap occurs.[170] Magnetic resonance imaging is a developing technique that provides insight into the mechanism of MR and a calculation of the regurgitant volume. As mentioned above, indices of left ventricular function that are load dependent, such as EF and fractional shortening, are not reliable markers of true myocardial inotropy, and severe underlying left ventricular dysfunction can be present even in patients with MR and a normal EF. Coexisting pulmonary hypertension can be diagnosed by direct pressure measurement and calculation of pulmonary vascular resistance during cardiac catheterization or estimated noninvasively via tricuspid regurgitant jet using Doppler echocardiography.

Patients with acute severe MR usually do not present for noncardiac surgery and elective surgery or interventions are contraindicated. Patients with chronic MR who are asymptomatic and have no signs of CHF usually tolerate noncardiac surgery well. More severe MR and particularly symptomatic patients scheduled for more than minor procedures should undergo further evaluation.[11] Risk evaluation in patients with functional MR undergoing noncardiac surgery is far more complex. Not only the severity of MR to be taken into consideration, more importantly, but also the underlying etiology of functional MR, such as severe coronary artery disease, acute myocardial ischemia, and ischemic cardiomyopathy, significantly increase the risk for perioperative adverse events.

Preoperative treatment options. Acute MR is a medical emergency, and patients are typically treated with afterload reduction, diuretics, and inotropic support prior to cardiac surgery.

Medical therapy should be optimized in all patients with chronic MR. However, asymptomatic patients with only mild or moderate chronic MR usually do not require further interventions prior to noncardiac surgery. In all symptomatic patients and in patients with new onset of symptoms, such as atrial fibrillation or dyspnea, a more detailed preoperative workup should be performed. Patients in atrial fibrillation who are at risk for systemic embolization are frequently on oral

anticoagulation, which has to be considered particularly if a neuraxial anesthetic technique is chosen. Coumadin should be discontinued, and heparin anticoagulation should be initiated accordingly. The β-blockers, calcium-channel blockers, digoxin, and amiodarone are given for rate control. Rate control drugs, such as β–blockers, should be continued. The ACE-inhibitors are frequently administered to patients with chronic MR and have been associated with perioperative hypotension.

There is a clear trend toward MV surgery earlier in the course of regurgitant MV disease; however, MV surgery is rarely indicated in the patient with organic MR prior to elective noncardiac surgery. However, patients with functional MR may warrant a different approach. If functional MR is secondary to severe ischemic heart disease, myocardial revascularization, and mitral annuloplasty may have to be considered prior to noncardiac surgery.[171]

Perioperative anesthesia care for the patient with MR presenting for noncardiac surgery. Premedication as needed usually does not pose a major hemodynamic risk for the patient with MR. The general anesthetic goals are similar to patients with AR. Heart rate should be kept high and afterload low in patients with MR to promote forward flow (Table 1). General or neuraxial anesthesia techniques are both well tolerated. Afterload is usually decreased under anesthesia, and thus the use of nitroprusside to promote forward flow is rarely needed. Hemodynamic monitoring should be according to the guidelines of the ASA. In patients with severe MR, and particularly in patients with preoperative symptoms of impaired myocardial function or CHF, continuous arterial blood pressure monitoring should be considered. Patients with only mild MR undergoing surgery with minimal risk do usually not require invasive hemodynamic monitoring. The placement of a PAC did not show improved patient outcome; however, in patients with signs of CHF and especially in patients with coexisting PHT it can be of use in guiding hemodynamic management, particularly in high-risk surgical cases. Inotropic agents with β-1 agonistic effects, such as ephedrine, dobutamine, or epinephrine, are preferred over predominantly α-1 agonists, such as phenylephrine, in cases of systemic hypotension.

Postoperatively, patients with MR should be monitored for symptoms of CHF, especially if large intraoperative fluid shifts occurred.

The Postoperative Period

Significant valvular disease is a risk factor for adverse events following noncardiac surgery.[4,5,172] In a retrospective analysis, 84 patients with moderate or severe MR undergoing low-risk or intermediate-risk noncardiac surgery (no patient was classified as having high-risk surgery), only experienced minor intraoperative complications, such as controllable hypotension and bradycardia; however, the postoperative period was complicated by serious complications, such as pulmonary edema and prolonged mechanical ventilation, with an overall morbidity and mortality of 27.4% and 11.9%, respectively.[173] Surgical risk (OR = 5.1; 95% CI, 1.3-20.4), left ventricular EF (OR = 0.9; 95% CI, 0.9-1.0), and atrial fibrillation (OR = 3.1; 95% CI, 1.0-9.1) were independently associated with postoperative morbidity, whereas atrial fibrillation predicted in-hospital death (OD = 11.6; 95% CI, 2.6-59.4). The overall high morbidity and mortality in the postoperative period in this series is surprising and emphasizes the importance of adequate hemodynamic monitoring and management beyond the intraoperative period. Pain, high catecholamine levels, hypercoagulability, hypovolemia, anemia, intravascular volume shifts, residual drug effects, and a lower level of monitoring all probably contribute to this phenomenon. Emergence from anesthesia is frequently accompanied by hypertension, tachycardia, incomplete analgesia, shivering, all of which may be poorly tolerated in patients with valvular disease. Oxygen consumption is typically increased and particularly patients with AS or coexisting CAD are at increased risk for adverse cardiac events, such as myocardial ischemia, malignant ventricular arrhythmia, and cardiac death. Mobilization of fluid or excessive iatrogenic fluid administration may cause pulmonary edema or CHF in patients with MV disease. Pulmonary hypertension may be precipitated by hypercarbia, hypoxia, acidosis, hypothermia, and pain, all of which are frequently encountered in the postoperative period. Hemodynamic goals for patients with the various valvular lesions, which were discussed in detail above, still should be followed in the postoperative period. Supplemental oxygen and adequate hemodynamic monitoring can be universally recommended in patients with valvular disease. In case of postoperative hypertension or tachycardia, prompt intervention, such as adequate analgesia and β-blockade, should be provided to patients at increased risk for adverse cardiac events, such as

myocardial ischemia and infarction.[24,174-175] New-onset atrial fibrillation should be treated accordingly. As discussed above, atrial contribution is essential to ventricular filling particularly in some of the valvular lesions, such as AS and MS, and sudden onset atrial fibrillation in the postoperative period may cause sudden hemodynamic compromise. The exact role of statin therapy and α-2-agonists is still under investigation and has been discussed at the beginning of this article.

Conclusions

Multiple studies clearly show an increased risk of adverse events for patients with valvular disease undergoing noncardiac surgery. Adequate monitoring and early intervention is crucial to prevent adverse events. It is important to recognize that the management of the patient with valvular disease is not confined to the intra-operative period and has to be extended into the postoperative period. Even though, basic principles in anesthesia care for patients with valvular disease remain unchanged, pharmacological advances particularly in preventing adverse events is an evolving field.

References

1. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart disease: a population-based study. *Lancet*. 2006;368: 1005-1011.
2. Davenport DL, Ferraris VA, Hosokawa P, Henderson WG, Khuri SF, Mentzer RM. Multivariable predictors of postoperative cardiac events after general and vascular surgery: results from the patient safety in surgery study. *J Am Coll Surg*. 2007;204:1199-1210.
3. Kumar R, McKinney WP, Raj G, et al. Adverse cardiac events after surgery: assessing risk in a veteran population. *J Gen Intern Med*. 2001;16:507-518.
4. Sprung J, Abdelmalak B, Gottlieb A, et al. Analysis of risk factors for myocardial infarction and cardiac mortality after major vascular surgery. *Anesthesiology.* 2000;93:129-140
5. Hernandez AF, Whellan DJ, Stroud S, Sun JL, O'Connor CM, Jollis JG. Outcomes in heart failure patients after major noncardiac surgery. *J Am Coll Cardiol*. 2004;44: 1446-1453.
6. Messika-Zeitoun D, Iung B, Philip I. Recommendations for noncardiac surgery in aortic stenosis. *Ann Cardiol Angeiol*. 2005;54:112-115.
7. Sista RR, Ernst KV, Ashley EA. Perioperative cardiac risk: pahophysiology, assessment and management. *Expert Rev Cardiovasc Ther*. 2006;4:731-743.
8. Bundgaard-Nielsen M, Foss NB, Kristensen BB. Use of epidural blockade in a patient with hip fracture and aortic stenosis. *Eur J Anesthesiol*. 2005;22:471-472.
9. Torsher LC, Shub C, Rettke SR, Brown DL. Risk of patients with severe aortic stenosis undergoing noncardiac surgery. *Am J Cardiol*. 1998;81:448-452.
10. Delvaux B, Collinet B. Echocardiography for management of low cardiac output state after axillary block in a dehydrated patient with aortic stenosis: case report. *Acta Anaesthesiol Belg*. 2005;56:303-305.
11. Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 Guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery. *J Am Coll Cardiol*. 2007;50:e159-e241.
12. Steckelberg JM, Wilson WR. Risk factors for infectious endocarditis. *Infect Dis Clin North Am*. 1993;7:9-19.
13. Mylonakis E, Calderwood SB. Infectious endocarditis in adults. *N Engl J Med*. 2001;345:1318-1330.
14. Dajani AS, Taubert KA, Wilson W, et al. Prevention of bacterial endocarditis: recommendations by the American Heart Association. *Clin Infect Dis*. 1997;25:1448-1458.
15. Bonow RO, Carabello BA, Chatterjee K, et al. ACC/AHA 2006 Practice guidelines for the management of patients with valvular heart disease: executive summary a report of the American College of Cardiology/American Heart a Association task force on practice guidelines (writing committee to revise the 1998 guidelines for the management of patients with valvular heart disease) developed in collaboration with the society of cardiovascular anesthesiologists endorsed by the society for cardiovascular angiography and interventions and the society of thoracic surgeons. *J Am Coll Cardiol*. 2006;48:598-675.
16. Bach DS, Eagle RA. Perioperative assessment and management of patients with valvular heart disease undergoing noncardiac surgery. *Minerva Cardioangiol*. 2004; 52:255-261.
17. Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis. Guidelines from the American Heart Association. a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation* 2007;116:1736-1754.
18. Horlocker TT, Wedel DJ, Benzon H, et al. Regional anesthesia in the anticoagulated patient: defining the risks (The second ASRA consensus conference on neuraxial anesthesia and anticoagulation). *Reg Anesth Pain Med*. 2003;28:172-197.
19. Schouten O, Bax JJ, Dunkelgrun M, Feringa HH, Poldermans D. Pro: Beta-blockers are indicated for patients at risk for cardiac complications undergoing noncardiac surgery. *Anesth Analg*. 2007;104:8-10.

20. London MJ. Con: Beta-blockers are indicated for all adults at increased risk undergoing noncardiac surgery. *Anesth Analg*. 2007;104:11-14.
21. Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation*. 1999;100:1043-1049.
22. Lindenauer PK, Pekow P, Wang K, Mamidi DK, Gutierrez B, Benjamin EM. Perioperative beta-blocker therapy and mortality after major non-cardiac surgery. *N Engl J Med*. 2005;353:349-361.
23. Fleisher LA, Beckman JA, Brown KA, et al.ACC/AHA 2006 guideline update on perioperative cardiovascular evaluation for noncardiac surgery: focused update on perioperative beta-blocker therapy: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to update the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery): developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society for Vascular Medicine and Biology. *Circulation*. 2006;113:2662-2674.
24. Mangano DT, Layug EL, Wallace A, Tateo I. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. *N Engl J Med*. 1996;335:1731-1720.
25. Poldermans D, Boersma E, Bax JJ, et al.The effecy of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. *N Engl J Med*. 1999;341:1789-1794.
26. Biccard BM, Sear JW, Foex P. Acute peri-operative beta blockade in intermediate risk patients. *Anaesthesia*. 2006;61:924-931.
27. Auerbach AD, Goldman L. Beta blockers and reduction of cardiac events in non-cardiac surgery: scientific review. *JAMA*. 2002;287:1435-1444.
28. Devereaux PJ, Beattie WS, Choi PT, et al. How strong is the evidence for the use of preoperative beta blockers in non-cardiac surgery? Systematic review and meta analysis of randomized clinical trials. *BMJ*. 2005;331:313-321.
29. Steven RD, Burri H, Tramer MR. Pharmacologic myocardial protection in patients undergoing noncardiac surgery: a quantitative systematic review. *Anesth Analg*. 2003;97:623-633.
30. Venkataraman R. Vascular surgery critical care: perioperative cardiac optimization to improve survival. *Crit Care Med*. 2006;34:S200-S207.
31. Nakagawa H, Nanba M, Okayama J. Landiolol prevented myocardial ischemia in a patient with severe aortic stenosis undergoing total gastrectomy. *Masui*. 2007;56:582-585.
32. Folkeringa RJ, Van Kraaij DJ, Nieman FH, Pinto YM, Crijns HJ. Statins associated with reduced mortality in patients admitted for congestive heart failure. *J Card Fail*. 2006;12:134-138.
33. Horwich TB, MacLellan WR, Fonarow GC. Statin therapy s associated with improved survival in ischemic and non-ischemic heart failure. *J Am Coll Cardiol*. 2004;43:642-648.
34. Fukuta H, Sane DC, Brucks S, Little WC. Statin therapy may be associated with lower mortality in patients with diastolic heart failure: a preliminary report. *Circulation*. 2005;112:357-363.
35. Fonarow GC, Wright RS, Spencer FA, et al. Effect of statin use within the first 24 hours of admission for acute myocardial infarction on early morbidity and mortality. *Am J Cardiol*. 2005;96:611-616.
36. Collard CD, Body SC, Shernan SK, Wang S, Mangano DT. Preoperative statin therapy is associated with reduced cardiac mortality after coronary artery bypass graft surgery. *J Thorac Cardiovasc Surg*. 2006;132:392-400.
37. Kinlay S, Ganz P. Early statin therapy in acute coronary syndromes. *Semin Vasc Med*. 2003;3:419-424.
38. Allen Maycock CA, Muhlestein JB, Horne BD, et al. Statin therapy is associated with reduced mortality across all age groups of individuals with significant coronary disease, including very elderly patients. *J Am Coll Cardiol*. 2002;40:1777-1785.
39. Lindenauer PK, Pekow P, Wang K, Gutierrez B, Benjamin EM. Lipid-lowering therapy and in-hospital mortality following major noncardiac surgery. *JAMA*. 2004;291:2092-2099.
40. Kertai MD, Boersma E, Westerhout CM, et al. A combination of statins and beta-blockers is independently associated with a reduction in the incidence of perioperative mortality and nonfatal myocardial infarction in patients undergoing abdominal aortic aneurysm surgery. *Eur J Vasc Endovasc Surg*. 2004;28:343-352.
41. Durazzo AE, Machado FS, Ikeoka DT, et al. Reduction in cardiovascular events after vascular surgery with atorvastatin: a randomized trial. *J Vasc Surg*. 2004;39:967-975.
42. O'Neil-CallahanK, Katsimaglis G, Tepper MR, et al. Statins decrease perioperative cardiac complications in patients undergoing noncardiac vascular surgery: the Statins for Risk Reduction in Surgery (StaRRS) study. *J Am Coll Cardiol*. 2005;45:336-342.
43. Dupuis J, Tardif JC, Cernacek P, Theroux P. Cholesterol reduction rapidly improves endothelial function after acute coronary syndromes. The RECIFE trial. *Circulation*. 1999;99:3227-3233.
44. Kinlay S, Schwartz GG, Olsson AG, et al. High-dose atorvastin enhances the decline in inflammatory markers in patients with acute coronary syndromes in the MIRACL study. *Circulation*. 2003;108:1560-1566.
45. Poldermans D, Bax JJ, Kertai MD, et al. Statins are associated with reduced incidence of perioperative mortality in patients undergoing major noncardiac vascular surgery. *Circulation*. 2003;107:1848-1851.

46. Hindler K, Shaw AD, Samuels J, et al. Improved postoperative outcomes associated with preoperative statin therapy. *Anesthesiology*. 2006;105:1260-1272.
47. Schouten O, Kertai MD, Bax JJ, et al. Safety of perioperative statin use in high-risk patients undergoing major vascular surgery. *Am J Cardiol*. 2005;95:658-660.
48. Pate GE, Tahir MN, Murphy RT, Foley JB. Anti-inflammatory effects of statins in patients with aortic stenosis. *J Cardiovasc Pharacol Ther*. 2003;8:201-206.
49. Cowell SJ, Newby DE, Prescott RJ, et al. A randomized trial of intensive lipid lowering therapy in calcific aortic stenosis. *N Engl J Med*. 2005;352:2389-2397.
50. Chua D, Kaib K. Statins and progression of calcified aortic stenosis. *Ann Pharmacother*. 2006;40:2195-2199.
51. Rossebo AB, Pedersen TR, Allen C, et al. Design and baseline characteristics of the Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) study. *Am J Cardiol*. 2007;99: 970-973.
52. Schouten O, Poldermans D, Visser L, et al. Fluvastatin and bisoprolol for the reduction of perioperative cardiac mortality and morbidity in high-risk patients undergoing noncardiac surgery: rationale and design of the DECREASE-IV study. *Am Heart J*. 2004;148:1047-1052.
53. Manach YL, Godet G, Coriat P, et al. The impact of postoperative discontinuation of chronic statin therapy on cardiac outcome after major vascular surgery. *Anesth Analg*. 2007;104:1326-1333.
54. Heeschen C, Hamm CW, Laufs U, Snappin S, Bohm M, White HD. Withdrawal of statins increases event rates in patients with acute coronary syndromes. *Circulation*. 2002;105:1446-1452.
55. Wallace AW, Galindez D, Salahieh A, et al. Effect of clonidine on cardiovascular morbidity and mortality after noncardiac surgery. *Anesthesiology*. 2004;101:284-293.
56. Oliver MF, Goldman L, Julian DG, Holme I. Effect of mivazerol on perioperative cardiac complications during non-cardiac surgery in patients with coronary heart disease: the European Mivazerol Trial (EMIT). *Anesthesiology*. 1999;91:951-961.
57. Wijeysundera DN, Naik JS, Beattie WS. Alpha-2 adrenergic agonists to prevent perioperative cardiovascular complications: a meta-analysis. *Am J Med*. 2003;114:742-752.
58. Yin YC, Chow LH, Tsao CM, et al. Oral clonidine reduces myocardial ischemia in patients with coronary disease undergoing noncardiac surgery. *Acta Anaesthesiol Sin*. 2002;40:197-203.
59. Lim P, Monin JL, Monchi M, et al. Predictors of outcome in patients with severe aortic stenosis and normal left ventricular function: role of B type natriuretic peptide. *Eur Heart J*. 2004;25:2048-2053.
60. Yusoff R, Clayton N, Keevil B, Morris J, Ray S. Utility of plasma N-terminal brain natriuretic peptide as a marker of functional capacity in patients with chronic severe mitral regurgitation. *Am J Cardiol*. 2006;97:1498-1501.
61. Leibowitz D, Planer D, Rott D, et al. Brain natriuretic peptide levels predict perioperative events in cardiac patients undergoing noncardiac surgery: A prospective study. *Cardiology*. 2007;110:266-270.
62. Gibson SC, Payne CJ, Byrne DS, et al. B-type natriuretic peptide predicts cardiac morbidity and mortality after major surgery. *Br J Surg*. 2007;94:903-909.
63. Cuthbertson BH, Amiri AR, Croal BL, et al. Utility of B-type natriuretic peptide in predicting perioperative cardiac events in patients undergoing major non-cardiac surgery. *Br J Anaesth*. 2007;99:170-176.
64. Feringa HH, Bax JJ, Elhendy A, et al. Association of plasma N-terminal pro-B-type natriuretic peptide with postoperative cardiac events in patients undergoing surgery for abdominal aortic aneurysm or leg bypass. *Am J Cardiol*. 2006;98:111-115.
65. Salzberg SP, Filsoufi F, Anyanwu A, et al. High risk mitral valve surgery: perioperative hemodynamic optimization with nesiritide (BNP). *Ann Thorac Surg*. 2005; 80:502-506.
66. Shah SJ, Teerlink JR. Nesiritide: a reappraisal of efficacy and safety. *Expert opin Pharmacother*. 2007;8:361-369.
67. Stewart BF, Siscovick D, Lind BK, et al. Clinical factors associated with calcific aortic valve disease. Cardiovascular Health Study. *J Am Coll Cardiol*. 1997;29:630-634.
68. Lindroos M, Kupari M, Heikkila J, Tilvis R. Prevalence of aortic valve abnormalities in the elderly: an echocardiographic study of a random population sample. *J Am Coll Cardiol*. 1993;21:1220-1225.
69. Iivanainen AM, Lindroos M, Tilvis R, Heikkila J, Kupari M. Natural history of aortic valve stenosis of varying severity in the elderly. *Am J Cardiol*. 1996;78:97-101.
70. Lewin MB, Otto CM. The bicuspid aortic valve: adverse outcomes from infancy to old age. *Circulation*. 2005; 111:832-834.
71. Roberts WC, Ko JM. Frequency by decades of unicuspid, bicuspid, and tricuspid aortic valves in adults having isolated aortic valve replacement for aortic stenosis, with or without associated aortic regurgitation. *Circulation*. 2005; 111:920-925.
72. Januzzi JL, Isselbacher EM, Fattori R, et al. Characterizing the young patient with aortic dissection: results from the International Registry of Aortic Dissection (IRAD). *J Am Coll Cardiol*. 2004;43:665-669.
73. Otto CM, Lind BK, Kitzman DW, Gersh BJ, Siscovick DS. Association of aortic-valve sclerosis with cardiovascular mortality and morbidity in the elderly. *N Engl J Med*. 1999;341:142-147.
74. Silaruks S, Clark D, Thinkhamrop B, Sia B, Buxton B, Tonkin A. Angina pectoris and coronary artery disease in severe isolated valvular aortic stenosis. *Heart Lung Circ*. 2001;10:14-23.
75. Pellikka PA, Sarano ME, Nishimura RA, et al. Outcome of 622 adults with asymptomatic, hemodynamically significant aortic stenosis during prolonged follow-up. *Circulation*. 2005;111:3290-3295.
76. Carabello BA. Clinical practice. Aortic stenosis. *N Engl J Med*. 2002;346:677-682.

77. Otto CM. Valvular aortic stenosis: disease severity and timing of intervention. *J Am Coll Cardiol*. 2006;47: 2141-2151
78. Gorlin R, Gorlin SG. Hydraulic formula of the area of stenotic mitral valve, other cardiac valves and central circulatory shunts. *Am Heart J*. 1951;41:1-29.
79. Bahler RC, Desser DR, Finkelhor RS, Brener SJ, Youssefi M. Factors leading to progression of valvular aortic stenosis. *Am J Cardiol*. 1999;84:1044-1048.
80. Goldman L, Caldera DL, Nussbaum SR, et al. Multifactorial index of cardiac risk in non-cardial surgical procedures. *N Engl J Med*. 1977;297:845-850.
81. Rohde LE, Polanczyk CA, Goldman L, Cook EF, Lee RT, LeeTH. Usefulness of transthoracic echocardiography as a tool for risk stratification of patients undergoing major noncardiac surgery. *Am J Cardiol*. 2001;87:505-509.
82. Kertai MD, Bountioukos M, Boersma E, et al. Aortic stenosis: an underestimated risk factor for perioperative complications in patients undergoing noncardiac surgery. *Am J Med*. 2004;116:8-13.
83. Zahid M, Sonel AF, Saba S, Good CB. Perioperative risk of noncardiac surgery associated with aortic stenosis. *Am J Cardiol*. 2005;96:436-438.
84. Raymer K, Yang H. Patients with aortic stenosis: cardiac complications in non-cardiac surgery. *Can J Anaesth*. 1998;45:855-859.
85. Christ M, Sharkova Y, Geldner G, Maisch B. Preoperative and perioperative care for patients with suspected or established aortic stenosis facing noncardiac surgery. *Chest*. 2005;128:2944-2953.
86. Lange RA, Hillis LD. Dobutamine stress echocardiography in patients with low-gradient aortic stenosis. *Circulation*. 2006;113:1718-1720.
87. Alborino D, Hoffmann JL, Fournet PC, Bloch A. Value of exercise testing to evaluate the indication for surgery in asymptomatic patients with valvular aortic stenosis. *J Heart Valve Dis*. 2002;11:204-209.
88. Lancellotti P, Lebois F, Simon M, Tombeux C, Chauvel C, Pierard LA. Prognostic importance of quantitative exercise doppler echocardiography in asymptomatic valvular aortic stenosis. *Circulation*. 2005;112(suppl 9):I377-382.
89. Amato MCM, Moffa PJ, Werner KE, Ramirez JAF. Treatment decision in asymptomatic aortic valve stenosis: role of exercise testing. *Heart*. 2001;86:381-386.
90. Aikawa K, Otto CM. Timing of aortic stenosis. *Prog Cardiovasc Dis*. 2001;43:477-493.
91. Levine MJ, Berman AD, Safian RD, Diver DJ, McKay RG. Palliation of valvular aortic stenosis by balloon valvuloplasty as preoperative preparation for noncardiac surgery. *Am J Cardiol*. 1988;62:1309-1310.
92. Roth RB, Palacios IF, Block PC. Percutaneous aortic balloon valvuloplasty: its role in the management of patients with aortic stenosis requiring major noncardiac surgery. *J Am Coll Cardiol*. 1989;13:1039-1041.
93. Hayes SN, Holmes DR, Nishimura RA, Reeder GS. Palliative percutaneous aortic balloon valvuloplasty before noncardiac operations and invasive diagnostic procedures. *Mayo Clin Proc*. 1989;64:753-757.
94. Klein A, Lee K, Gera A, Ports TA, Michaels AD. Long-term mortality, cause of death, and temporal trends in complications after percutaneous aortic balloon valvuloplasty for calcific aortic stenosis. *J Interv Cardiol*. 2006; 19:269-275.
95. Lutter G, Ardehali R, Cremer J, Bonhoeffer P. Percutaneous valve replacement: current state and future prospects. *Ann Thorac Surg*. 2004;78:2199-2206.
96. McDonald SB. Is neuraxial blockade contraindicated in the patient with aortic stenosis? *Reg Anesth Pain Med*. 2004;29:496-502.
97. VanHelder T, Smedstad KG. Combined spinal epidural anesthesia in a primigravida with valvular heart disease. *Can J Anaesth*. 1998;45:488-490.
98. Collard CD, Eappen S, Lynch EP, Concepcion M. Continuous spinal anesthesia with invasive hemodynamic monitoring for surgical repair of the hip in two patients with severe aortic stenosis. *Anesth Analg*. 1995;81:195-198.
99. Cheitlin M, Armstrong WF, Aurigemma GP, et al. ACC/AHA/ASE 2003 Guideline update for the clinical application of echocardiography: summary article. A report of the American College of Cardiology/American Heart Association task force on practice guidelines (ACC/AHA/ASE committee to update the 1997 guidelines for the clinical application of echocardiography). *J Am Soc Echocardiogr*. 2003;16:1091-1110.
100. Maron BJ, McKenna WJ, Danielson GK, et al.; Task Force on Clinical Expert Consensus Documents, American College of Cardiology; European Society of Cardiology Committee for Practice Guidelines. American College of Cardiology/European Society of Cardiology clinical expert consensus document on hypertrophic cardiomyopathy. A report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents and the European Society of Cardiology Committee for Practice Guidelines. *J Am Coll Cardiol*. 2003;42:1687-1713.
101. Poliac LC, Barron M, Maron BJ. Hypertrophic cardiomyopathy. *Anesthesiol*. 2006;104:183-192.
102. Kovacic JC, Muller D. Hypertrophic cardiomyopathy: state-of-the-art review, with focus on the management of outflow obstruction. *Intern Med J*. 2003;33:521.
103. Charron P, Komajda M. Molecular genetics in hypertrophic cardiomyopathy: towards individualized management of the disease. *Expert Rev Mol Diagn*. 2006; 6:65-78.
104. Arad M, Seidman JG, Seidman CE. Phenotypic diversity in hypertrophic cardiomyopathy. *Hum Mol Genet*. 2002;11:2499-2506.

105. Chung MW, Tsoutsman T, Semsarian C. Hypertrophic cardiomyopathy: from gene defect to clinical disease. *Cell Res*. 2003;13:9-20.
106. Maron BJ, Gardin JM, Flack JM, Gidding SS, Kurosaki TT, Bild DE. Prevalence of hypertrophic cardiomyopathy in a general population of young adults. Echocardiographic analysis of 4111 subjects in the CARDIA Study. Coronary Artery Risk Development in (Young) Adults. *Circulation*. 1995;92:785-789.
107. Brugada R, Kelsey W, Lechin M, et al. Role of candidate modifier genes on the phenotypic expression of hypertrophy in patients with hypertrophic cardiomyopathy. *J Investig Med*. 1997;45:542-551.
108. Maron MS, Olivotto I, Zenovich AG, et al. Hypertrohpic cardiomyopathy is predominantly a disease of left ventricular outflow tract obstruction. *Circulation*. 2006;114: 2232-2239.
109. Maron BJ, Olivotto I, Spirito P, et al. Epidemiology of hypertrophic cardiomyopathy-related death: revisited in a large non-referral-based patient population. *Circulation*. 2000;102:858-864.
110. Maron BJ. Sudden death in young athletes. *N Engl J Med*. 2003;349:1064-1075.
111. Elliott PM, Gimeno JR, Thaman R, et al. Historical trends in reported survival rates in patients with hypertrophic cardiomyopathy. *Heart*. 2006;92:785-791.
112. Maron BJ, Casey SA, Poliac LC, Gohman TE, Almquist AK, Aeppli DM. Clinical course of hypertrophic cardiomyopathy in a regional united states cohort. *JAMA*. 1999;281:650-655.
113. Sherrid MV, Chaudhry FA, Swistel DG. Obstructive hypertrophic cardiomyopathy: echocardiography, pathophysiology, and the continuing evolution of surgery for obstruction. *Ann Thorac Surg*. 2003;75:620.
114. Sherrid MV, Chu CK, Delia E, Mogtader A, Dwyer EM Jr. An echocardiographic study on the fluid mechanics of obstruction in hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 1993;22:816-825.
115. Sherrid MV. Pathophysiology and treatment of hypertrophic cardiomyopathy. *Prog Cardiovasc Dis*. 2006; 49:123-151.
116. Schwammenthal E, Nakatani S, He S, et al. Mechanism of mitral regurgitation in hypertrophic cardiomyopathy: mismatch of posterior to anterior leaflet length and mobility. *Circulation*. 1998;98:856-865.
117. Hreybe H, Zahid M, Sonel A, Good CB, Shaver J, Saba S. Noncardiac surgery and the risk of death and other cardiovascular events in patients with hypertrophic cardiomyopathy. *Clin Cardiol*. 2006;29:65-68.
118. Haering JM, Comunale ME, Parker RA, et al. Cardiac risk of non-cardiac surgery in patients with asymmetric septal hypertrophy. *Anesthesiol*. 1996;85:254-259.
119. Kuroiwa M, Arai M, Ueno T, Takenaka T, Okamoto H, Hoka S. Perioperative cardiovascular complications in patients with hypertrophic cardiomyopathy. *Masui*. 2003;52:733-739.
120. Maron MS, Olivotto I, Betocchi S, et al. Effect of left ventricular outflow tract obstruction on clinical outcome in hypertrophic cardiomyopathy. *N Engl J Med*. 2003;348:295-303.
121. Elliott PM, Gimeno JR, Tome MT, et al. Left ventricular outflow tract obstruction and sudden death risk in patients with hypertrophic cardiomyopathy. *Eur Heart J*. 2006;27:1933-1941.
122. Spirito P, Autore C. Management of hypertrophic cardiomyopathy. *BMJ*. 2006;332:1251-1255.
123. Sachdev B, Hamid MS, Elliott PM. The prevention of sudden death in hypertrophic cardiomyopathy. *Expert Opin Pharmacother*. 2002;3:499-504.
124. van der Lee C, Kofflard MJ, van Herwerden LA. Sustained improvement after combined anterior mitral leaflet extension and myectomy in hypertrophic obstructive cardiomyopathy. *Circulation*. 2003;108:2088-2092.
125. Ommen SR, Maron BJ, Olivotto I, et al. Long-term effects of surgical septal myectomy on survival in patients with obstructive hypertrophic cardiomyopathy. *J Am Coll cardiol*. 2005;46:470-476.
126. Alam M, Dokainish H, Lakkis N. Alcohol septal ablation for hypertrophic cardiomyopathy: a systematic review of published studies. *J Interv cardiol*. 2006, 19:319-327.
127. Knight CJ. Alcohol septal ablation for obstructive hypertrophic cardiomyopathy. *Heart*. 2006;92:1339-1344.
128. Gietzen FH, Leuner CJ, Raute-Kreinsen U, et al. Acute and long-term results after transcoronary ablation of septal hypertrophy (TASH). Catheter interventional treatment for hypertrophic obstructive cardiomyopathy. *Eur Heart J*. 1999;20:1342-1354.
129. Maron BJ, Nishimura RA, McKenna WJ, Rakowski H, Josephson ME, Kieval RS. Assessment of permanent dual-chamber pacing as a treatment for drug-refractory symptomatic patients with obstructive hypertrophic cardiomyopathy. A randomized, double-blind, crossover study (M-PATHY). *Circulation*. 1999;99:2927-2933.
130. Freedman RA. Use of implantable pacemakers and implantable defibrillators in hypertrophic cardiomyopathy. *Curr Opin Cardiol*. 2001;16:58.
131. Maron BJ, Shen WK, Link MS, Epstein AE. Efficacy of implantable cardioverter-defibrillators for the prevention of sudden death in patients with hypertrophic cardiomyopathy. *N Engl J Med*. 2000;342:365.
132. Movahed MR, Ahmadi-Kashani M, Kasravi B, Saito Y. Increased prevalence of mitral stenosis in women. *J Am Soc Echocardiogr*. 2006;19:911-913
133. Chockalingam A, Gnanavelu G, Elangovan S, Chockalingam V. Clinical spectrum of chronic rheumatic heart disease in India. *J Heart Valve Dis*. 2003;12:577-581.

134. Bhatla N, Lal S, Behera G, et al. Cardiac disease in pregnancy. *Int J Gynaecol Obstet*. 2003;82:153-159.
135. Silversides CK, Colman JM, Sermer M, Siu SC. Cardiac risk in pregnant women with rheumatic mitral stenosis. *Am J Cardiol*. 2003;91:1382-1385.
136. McElhinney DB, Sherwood MC, Keane JF, et al. Current management of severe congenital mitral stenosis. Outcomes of transcatheter and surgical therapy in 108 infants and children. *Circulation* 2005;112:707-714.
137. Nishida H, Takahara Y, Takeuchi S, Mogi K. Mitral stenosis after mitral valve repair using the duran flexible annuloplasty ring for degenerative mitral regurgitation. *J Heart Valve Dis*. 2005;14:563-564.
138. Horstkotte D, Niehues R, Strauer BE. Pathomorphological aspects, aetiology and natural history of acquired mitral valve stenosis. *Eur Heart J*. 1991;12 (suppl B): 55-60.
139. Parissis JT, Zezas S, Sfiras N, Kastellanos S. An atypical left atrial myxoma causing intracavitary pressure gradient and typical diastolic transmitral flow of severe mitral stenosis. *Int J Cardiol*. 2005;102:165-167.
140. Chakko S, Bisno AL. Acute rheumatic fever. In: Fuster V, Alexander RW, O'Rourke RA, eds. *Hurst's The Heart*. 11th ed. New York, NY: McGraw-Hill; 2004:1635-1642.
141. Gordon SP, Douglas PS, Come PC, Manning WJ. Two-dimensional and Doppler echocardiographic determinants of the natural history of mitral valve narrowing in patients with rheumatic mitral stenosis: implications for follow-up. *J Am Coll Cardiol*. 1992;19:968-973.
142. Diker E, Aydogdu S, Ozdemir M, et al. Prevalence and predictors of atrial fibrillation in rheumatic valvular heart disease. *Am J Cardiol*. 1997;77:96-98.
143. Kaymaz C, Ozdemir N, Kirma C, Sismanoglu M, Daglar B, Ozkan M. Location, size and morphological characteristics of left atrial thrombi as assessed by echocardiography in patients with rheumatic mitral valve disease. *Eur J Echocardiogr*. 2001;2:270-276.
144. Chiang CW, Lo SK, Ko YS, Cheng NJ, Lin PJ, Chang CH. Predictors of systemic embolism in patients with mitral stenosis. *Ann Intern Med*. 1998;128:885-889.
145. Popescu BA, Antonini-Canterin F, Temporelli PL, et al. Right ventricular functional recovery after acute myocardial infarction: relation with left ventricular function and interventricular septum motion. GISSI-3 echo substudy. *Heart*. 2005;91:484-488.
146. Saleh S, Liakopoulos OJ, Buckberg GD. The septal motor of biventricular function. *Eur J Cardiothorac Surg*. 2006;29 (suppl 1):S126-S138.
147. Bonnin M, Mercier FJ, Sitbon O, et al. Severe pulmonary hypertension during pregnancy: mode of delivery and anesthetic management of 15 consecutive cases. *Anesthesiology*. 2005;102:1133-1137.
148. Rahimtoola SH, Durairaj A, Mehra A, Nuno I. Current evaluation and management of patients with mitral stenosis. *Circulation*. 2002;106:1183-1188.
149. Reis G, Motta MS, Barbosa MM, Esteves WA, Souza SF, Bochi EA. Dobutamine stress echocardiography for non-invasive assessment and risk stratification of patients with rheumatic mitral stenosis. *J Am Coll Cardiol*. 2004;43:393-401.
150. Lev EI, Sagie A, Vaturi M, Sela N, Battler A, Shapira Y. Value of exercise echocardiography in rheumatic mitral stenosis with and without significant mitral regurgitation. *Am J Cardiol*. 2004;93:1060-1063.
151. Carabello BA. Modern management of mitral stenosis. *Circulation* 2005;112:432-437.
152. Guerios EE, Bueno R, Nercolini R, et al. Mitral stenosis and percutaneous mitral valvuloplasty (part 1). *J Invasive Cardiol*. 2005;17:382-386.
153. Guerios EE, Bueno R, Nercolini R, et al. Mitral stenosis and percutaneous mitral valvuloplasty (part 2). *J Invasive Cardiol*. 2005;17:440-444.
154. Shaw TRD, Sutaria N, Prendergast B. Clinical and hemodynamic profiles of young, middle aged, and elderly patients with mitral stenosis undergoing mitral balloon valvotomy. *Heart*. 2003;89:1430-1436.
155. Ngan Kee WD, Shen J, Chiu AT, Lok I, Khaw KS. Combined spinal-epidural analgesia in the management of labouring parturients with mitral stenosis. *Anaesth Intensive Care*. 1999;27:523-526.
156. Pan PHD, Angelo R. Anesthetic and analgesic management of mitral stenosis during pregnancy. *Reg Anesth Pain Med*. 2004;29:610-615.
157. Reich DL, Mittnacht A, London M, Kaplan JA. Monitoring of the heart and vascular system. In: Kaplan JA, Reich DL, Lake CL, Konstadt SL, eds. *Kaplan's Cardiac Anesthesia*. 5th ed. Philadelphia, PA: Saunders Elsevier. 2006:385-436.
158. Dujardin KS, Enriquez-Sarano M, Schaff HV, Bailey KR, Sewward JB, Tajik AJ. Mortality and morbidity of aortic regurgitation in clinical practice: a long-term follow up study. *Circulation*. 1999;99:1851-1857.
159. Groban L, Butterworth J. Perioperative management of chronic heart failure. *Anesth Analg*. 2006;103:557-575.
160. Comfere T, Sprung J, Kumar MM, et al. Angiotensin system inhibitors in a general surgical population. *Anesth Analg*. 2005;100:636-644.
161. Licker M, Schweizer A, Hohn L, Farinelli C, Morel DR. Cardiovascular responses to anesthetic induction in patients chronically treated with angiotensin-converting enzyme inhibitors. *Can J Anaesth*. 2000;47: 433-440.
162. Bertrand M, Godet G, Meersschaert K, Brun L, Salcedo E, Coriat P. Should the angiotensin II antagonists be discontinued before surgery? *Anesth Analg*. 2001;92:26-30.
163. Iung B, Gohlke-Baerwolf C, Tornos P,et al. Working group on valvular heart disease: Recommendations on the management of the asymptomatic patient with valvular heart disease. *Eur Heart J*. 2002;23:1253-1266.

164. Singh JP, Evans JC, Levy D, et al. Prevalence and clinical determinants of mitral, tricuspid, and aortic regurgitation (the Framingham Heart Study) *Am J Cardiol*. 1999;83:897-902.
165. Freed LA, Levy D, Levine RA, et al. Prevalence and clinical outcome of mitral-valve prolapse. *N Engl J Med* 1999;341:1-7.
166. Theal M, Sleik K, Anand S, Yi Q, Yususf S, Lonn E. Prevalence of mitral valve prolapse in ethnic groups. *Can J Cardiol*. 2004;20:511-515.
167. Ling LH, Enriquez-Sarano M, Seward JB, et al. Clinical outcome of mitral regurgitation due to flail leaflets. *N Engl J Med*. 1996;335:1417-1423.
168. Grigioni F, Enriquez-Sarano M, Ling L, et al. Sudden death in mitral regurgitation due to flail leaflet. *J Am Coll Cardiol*. 1999;34:2078-2085.
169. Enriquez-Sarano M, Avierinos JF, Messika-Zeitoun D, et al. Quantitative determinants of the outcome of asymptomatic mitral regurgitation. *N Engl J Med*. 2005;352:875-883.
170. Zoghbi WA, Enriquez-Sarano M, Foster E, et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr*. 2003;16:777-802.
171. Filsoufi F, Aklog L, Byrne JG, Cohn LH, Adams DH. Current results of combined coronary artery bypass grafting and mitral annuloplasty in patients with moderate ischemic mitral regurgitation. *J Heart Valve Dis*. 2004;13:747-753.
172. Mackey WC, Fleisher LA, Haider S, et al. Perioperative myocardial ischemic injury in high-risk vascular surgery patients: incidence and clinical significance in a prospective clinical trial. *J Vasc Surg*. 2006;43:533-538.
173. Lai HC, Lai HC, Lee WL, Wang KY, Ting CT, Liu TJ. Mitral regurgitation complicates postoperative outcome of noncardiac surgery. *Am Heart J*. 2007;153:712-717.
174. Boersma E, Poldermans D, Bax JJ, et al. Predictors of cardiac events after major vascular surgery: Role of clinical characteristics, dobutamine echocardiography, and beta-blocker therapy. *JAMA*. 2001;285:1865-1873.
175. Schouten O, Shaw LJ, Boersma E, et al. A meta-analysis of safety and effectiveness of perioperative beta-blocker use for the prevention of cardiac events in different types of noncardiac surgery. *Coron Artery Dis*. 2006;17:173-179.