Anesthesia for Valvular Heart Disease

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Normal cardiac valves permit unidirectional blood flow without causing obstruction or regurgitation, trauma to blood elements, thromboembolism, or excessive mechanical stress on the valve and heart (1). Valvular pathology disrupts this relationship. Maintaining cardiovascular stability with optimal hemodynamic parameters and adequate systemic perfusion pressure during the anesthetic management of patients with valvular heart disease can be extremely challenging. With the high incidence and severity of complications in this subgroup of patients, a concise understanding of all relevant factors affecting myocardial performance with valvular pathology is necessary. The scheme depicted in the figure below is useful for focusing on relevant factors that interact to maintain hemodynamic stability. Each of these factors has a variable effect on myocardial performance with valvular heart disease and will be interrelated to better understand the perioperative management of patients presenting for noncardiac surgery. Important factors that govern blood flow across a valve include: a) valve area; b) square root of the hydrostatic pressure gradient across the valve; and c) duration of flow whether systole or diastole. The valve area of many regurgitant lesions changes in response to loading conditions (preload, afterload) whereas valve area with stenotic lesions is generally fixed. Larger values of these factors will increase transvalvular flow; reducing these factors will decrease flow. With regurgitant lesions, the goal is to reduce or minimize regurgitant transvalular flow; with stenotic lesions, the goal is to maximize and enhance stenotic transvalular flow.

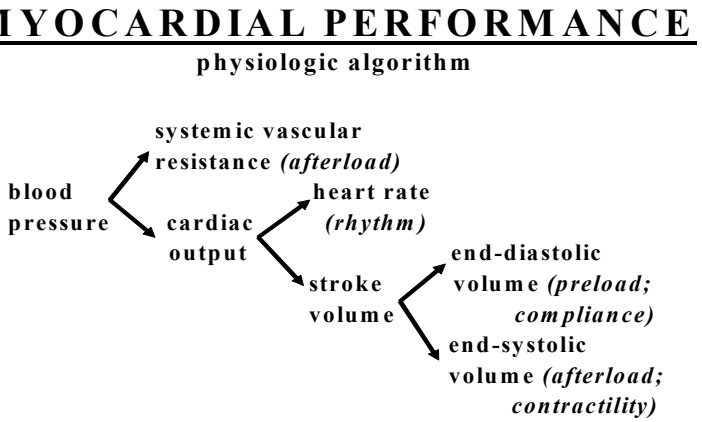

Figure 1. Relevant factors determining myocardial performance and systemic perfusion pressure.

MITRAL STENOSIS

The predominant causes of mitral stenosis (MS) include rheumatic heart disease > congenital > rheumatoid arthritis, lupus, and carcinoid syndrome. Normal mitral valve area is 4 to 6 cm^2 with mild stenosis < 2 cm^2 and severe stenosis < 1 cm^2 (2). The severity of flow obstruction with MS is affected by the valve orifice area, the mean diastolic pressure gradient between the left atrium and left ventricle, and the duration of diastole. As mitral valve orifice area decreases, the left atrial-ventricular pressure gradient must increase, causing atrial dilation with fibrillation in 30% - 70% of patients depending on patient age. Typical symptoms of MS include congestive failure and pulmonary edema, particularly with elevated heart and transmitral flow rates seen with exercise, pregnancy, anemia, infection, or atrial fibrillation with a rapid ventricular response. To manage the symptoms of left-sided heart failure, routine therapy consist of digoxin, diuretics, and anticoagulants for atrial fibrillation (2).

Anesthetic Implications

The size of mitral valve area with stenosis is relatively fixed during diastole with minimal flow-related valvular reserve (3). Secondary pulmonary hypertension with a 5- to 10- fold increase in pulmonary vascular resistance from medial and intimal thickening of the pulmonary arterioles can cause right ventricular failure and tricuspid regurgitation. Symptomatic relief may be obtained by percutaneous mitral balloon commissurotomy, which can benefit high-risk or pregnant patients with new onset of atrial fibrillation or moderate-severe pulmonary hypertension (4). Tachycardia can be particularly harmful because the period for diastolic filling is shortened. Since the mitral valve orifice area is fixed, left atrial pressure must increase causing pulmonary congestion. Although

sinus rhythm may contribute little to left ventricular end-diastolic volume with atrial dilation and MS, atrial fibrillation can precipitate pulmonary edema from an increase in heart rate. Digoxin should be continued perioperatively with the use of short-acting beta-blockers as necessary for heart rate control. If regional anesthesia is planned, careful consideration should be given to the hazard of bleeding from residual anticoagulation. Due to long term diuretic therapy, patients with MS require cautious volume expansion within the limits imposed by the stenotic mitral valve. Reduced preload from impaired filling and increased afterload from reflex vasoconstriction are the primary determinants of impaired contractile performance although rheumatic myocarditis with fibrosis may further decrease left ventricular compliance and filling (2). Any clinical scenario that causes further elevation of pulmonary vascular resistance, such as hypoxia, hypercarbia, lung hyperexpansion, or nitrous oxide, can worsen right heart failure. Oversedation should be avoided, and supplemental oxygen in the preoperative period by nasal cannula may be beneficial. If a pulmonary artery catheter is inserted, care should be taken to ensure proximal tip placement near the pulmonic valve to avoid the possibility of distal catheter tip migration and pulmonary artery rupture. Due to the inherent limitation of preload reserve across a stenotic valve (3), inotropic drug infusion with dobutamine or epinephrine may be necessary to maintain stroke volume as long as tachycardia is avoided. Anticipate bleeding complications from chronic anticoagulation in patients with atrial fibrillation.

MITRAL REGURGITATION

Mitral regurgitation (MR) is the most commonly encountered valve lesion in modern clinical practice (5). Primary MR results from abnormalities of the mitral valve, subvalvular apparatus, or cardiac skeleton caused by myxomatous degeneration, rheumatic disease, fenfluramine diet suppressants (>90 day medication), or endocarditis. Secondary MR is caused by functional lesions of the myocardium such as ischemia, infarction, or dilated cardiomyopathy (6, 7). MR results from ventricular remodeling after myocardial infarction (6). Several proposed mechanisms include a) papillary muscle dysfunction; b) reduced transvalvular closing force secondary to left ventricular contractile dysfunction; c) increased tethering forces by the chordae and papillary muscle secondary to dyskinesis; and d) mitral annular dilation. The posterior papillary muscle is exclusively fed by the posterior descending artery from the right or circumflex coronary arteries whereas the anterior papillary muscle receives its blood supply from two sources – the left anterior descending and circumflex coronary arteries (7). Consequently, the posterior papillary muscle is more prone to ischemia. In early systole, there is a failure of mitral leaflet coaptation causing regurgitation.

The amount of MR depends on the pressure gradient between the left ventricle and atrium, the instantaneous mitral valve orifice size, and the duration of systole. The regurgitant orifice serves as an escape valve to lessen the impedance to left ventricular ejection so that there is reduced isovolumic contraction which effectively reduces left ventricular afterload and can mask underlying contractile dysfunction. Patients with MR should be serially followed by transthoracic or transesophageal echocardiography. A reduction in left ventricular ejection fraction below 60% or an increase in end-systolic dimension exceeding 45 mm indicates the need for surgical intervention with valve repair or replacement. The presence of MR has been identified as a strong positive predictor of subsequent morbidity and mortality after myocardial infarction (6).

Anesthetic Implications

With MR, mitral valve orifice area is not constant but varies directly with ventricular loading conditions (8). These findings have important implications for patient management. Volume expansion or afterload augmentation with a vasoconstrictor increases mitral valvular orifice area and regurgitant volume. Afterload reduction or enhanced contractility reduces orifice area and regurgitant volume (8). Tachycardia decreases the regurgitant volume by reduced ventricular filling plus shortening of systole. These findings indicate that mitral annular size is dynamic and can be significantly altered by variable loading conditions.

Since total stroke volume consists of both forward and regurgitant volumes, ejection fraction values may overestimate left ventricular contractility. If a pulmonary artery catheter is used, v-wave height may not correlate with the severity of regurgitation, depending on the size and compliance of the left atrium. Longstanding MR can cause reactive pulmonary hypertension and right heart failure. Acute vasodilator therapy can be beneficial to decrease the systolic pressure gradient if the reduction in left ventricular pressure exceeds the reduction in left atrial pressure. With dynamic lesions, such as papillary muscle dysfunction, ruptured chordae, or dilated cardiomyopathy, the regurgitant orifice area as well as the transvalvular pressure gradient can be altered by vasoactive medications. In practice, under the influence of general or regional anesthesia, afterload reduction in combination with mild preload augmentation will enhance cardiac output and blood pressure. Since tachycardia reduces the regurgitant

volume/min, bradycardia is poorly tolerated due to prolongation of left ventricular filling time and should be avoided. Inodilators such as dobutamine may be especially useful due to the synergistic effects of positive inotropy and afterload reduction to reduce ventricular end-systolic size and regurgitant mitral flow.

OTHER MITRAL REGURGITANT LESIONS

With primary and secondary MR, regurgitant volume parallels ventricular size so that any therapy that reducing ventricular chamber size will decrease regurgitant flow. Two exceptions to this rule are mitral valve prolapse (MVP) and hypertrophic obstructive cardiomyopathy with MR.

MITRAL VALVE PROLAPSE

MVP is an inherited connective tissue disorder with myxomatous proliferation causing thickening and redundancy of the mitral valve producing nonspecific symptoms that include syncope, fatigue, palpitations, and atypical chest pain (9). Myxomatous degeneration is caused by dysregulation of mitral matrix protein synthesis and collagen degradation. MVP is defined as thickened leaflets (>5mm) with displacement (>2mm) into the left atrium during systole. Recently, the correlation between magnesium deficiency and MVP has been identified (10). MVP occurs in 0.6-2.4% of the general population and is the most common cause of mitral valve disease (10, 11). Complications from heart failure or sudden death are more frequent in older, male patients; atrial and ventricular arrhythmias are common. In general, the degree of MVP and regurgitation corresponds with the extent of leaflet thickening and redundancy although its effect in the general population is widely heterogenous and difficult to predict.

Anesthetic Implications
Prophylactic antibiotics are indicated with MVP and a murmur but not for a midsystolic click only (12). Patients with MVP should not be managed similar to patients with MR. Any reduction in left ventricular volume causes failure of the prolapsing leaflets to coapt and worsens the amount of regurgitation. Consequently, reductions in venous return and vascular resistance, tachycardia, or increased contractility are poorly tolerated. Patients should be adequately hydrated with intravenous fluids perioperatively. General anesthesia using volatile agents with careful volume replacement, vasoconstrictors to support blood pressure, and short-acting beta-blockers to control heart rate are recommended therapies.

HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY WITH MITRAL REGURGITATION

Hypertrophic cardiomyopathy is the most common genetically transmitted cardiac disorder. Inherited as an autosomal dominant trait, hypertrophic cardiomyopathy is a heterogeneous disease of the sarcomere producing more than 200 mutations in 11 different sarcomeric proteins (13). In response to the abnormal ventricular geometry and altered function, increased myocyte size (hypertrophy), increased fibroblast and collagen formation (fibrosis), and mal-alignment of sarcomeres occur (13). To manage these patients, it is essential to determine whether obstructive as opposed to non-obstructive symptomatology exists. In 25% of patients, dynamic left ventricular outflow obstruction results from mechanical impedance of the hypertrophied ventricular septum with abnormal systolic anterior motion of the mitral valve causing MR (14).
Diastolic dysfunction may ensue from impaired relaxation of a non-compliant ventricle coupled with shortening of diastole from prolonged systolic contraction. Patients can present with symptoms of congestive failure, angina, syncope, and palpitations. Risk factors for sudden cardiac death include a history of syncope, family history of sudden death, ventricular wall thickness >30 mm, outflow obstruction gradient >30 mmHg, and abnormal blood pressure response to exercise (15). Atrial fibrillation may result from atrial dilation and the loss of properly-timed atrial kick can precipitate severe hypotension and syncope. Chronic medical management consists of beta blockers to control heart rate and reduce outflow obstruction; calcium channel blockers to improve ventricular filling and reduce myocardial ischemia; disopyramide to reduce myocardial contractility; amiodarone for atrial dysrhythmias or fibrillation; internal defibrillator for ventricular dysrhythmias; dual chamber pacing which causes right ventricular preexcitation with asynchronous depolarization; ventricular septal myotomy or myectomy for severe outflow tract

gradient >50 mmHg at rest; and alcohol injection of the major septal perforator branches of the left anterior descending coronary artery to produce localized septal infarction (13).

Anesthetic Implications
Left ventricular outflow obstruction with hypertrophic cardiomyopathy is a dynamic process where the degree of outflow obstruction is directly linked to the muscular outflow tract sphincter and systolic anterior motion of the mitral valve. The midseptal bulge redirects the direction of outward flow which catches the redundant anterior leaflet from behind and pushes it toward the septum (14). Consequently, MR with hypertrophic cardiomyopathy occurs during early systole. The degree of obstruction is worsened by any reduction in left ventricular volume such as hypovolemia, positive pressure ventilation, positive end-expiratory pressure, and tachycardia. Any therapy that increases myocardial contractility or causes systemic vasodilation will also worsen the degree of obstruction. Left atrial enlargement secondary to MR makes these patients prone to atrial fibrillation. Maintaining sinus rhythm is essential since atrial contraction may contribute 30% to 40% of left ventricular end-diastolic volume. Careful volume replacement is necessary particularly in the fasted patient, and transient episodes of hypotension in the operating room should be aggressively managed with volume expansion and a vasoconstrictor such as phenylephrine. These patients can suffer significant perioperative morbidity with prolonged, major operations but surprisingly little mortality.

AORTIC STENOSIS

In the general population, the primary etiology of aortic stenosis (AS) has changed from rheumatic heart disease to idiopathic, calcific degeneration causing valve sclerosis (16). It is estimated that nearly half of all men over the age of 85 years have aortic sclerosis with significant stenosis in 4% (17). An increased incidence with aging is secondary to greater mechanical stress over time as well as longer risk factor exposure. These patients are generally older, hypertensive males with a prior history of smoking, diabetes, and hypercholesterolemia. Mechanical stress on the aortic valve is greatest on the aortic side of the leaflet with sparing of the noncoronary cusp due to absence of diastolic coronary flow (16). Potential benefit may be seen with statin therapy to slow disease progression and angiotensin converting enzyme inhibition to attenuate ventricular hypertrophy and remodeling (18). Less frequent cause of AS is bicuspid valvular stenosis which is also seen predominantly in men.
Although asymptomatic patients have a relatively good prognosis, nearly 75% of patients with AS develop symptoms within 5 years. Presenting symptoms include angina, congestive failure, and syncope, with the average time of onset from symptoms to death without intervening corrective therapy being 5, 3, and 2 years, respectively. Aortic blood flow velocity increases proportionately with AS severity so that patients can be followed by periodic echocardiographic examinations. Primary risk factors for AS are aortic jet flow velocity > 4.5m/sec and left ventricular ejection fraction <50%. Other associated factors include patient age (>50 years old), the extent of aortic calcification, and the annual serial progression of change in aortic flow velocity (>0.3 m/sec/yr). Recently, the severity of AS and left ventricular dysfunction have been correlated with serum levels of brain natriuretic hormone (16). In response to chronic pressure overload, the left ventricle undergoes concentric ventricular hypertrophy with parallel sarcomere replication and an increase in wall thickness (19). Gender differences exist as females develop less hypertrophy. The adaptive increase in wall thickness by myocyte hyperplasia reduces wall stress by the Laplace relationship. However, the increment in muscle mass has limited collateral perfusion and coronary vasodilator reserve that predisposes to subendocardial ischemia, particularly with the lengthening of systolic duration (20). Diastolic dysfunction develops early which further reduces subendocardial blood flow. Hypertension produces an additive load on left ventricular ejection and requires aggressive management.

Anesthetic Implications
AS flow depends on the systolic pressure gradient between the left ventricle and aorta, the duration of systole, and aortic valve area, which is typically fixed. Valvular obstruction increases antegrade blood flow velocity and pressure gradient across the valve. As the degree of stenosis worsens, the maximal velocity and pressure gradient tend to occur later in systole. Preoperative evaluation should include a transthoracic echocardiogram. Although several reports have suggested that patients with aortic stenosis can safely undergo noncardiac surgery, a recent review underscores the serious underlying morbidity in these patients (21). Individual operative risk depends on AS severity, concomitant coronary disease, and surgical procedure risk (22).
With diastolic dysfunction and impaired ventricular relaxation, atrial contraction may contribute 25% - 40% of end-diastolic volume. Consequently, maintaining normovolemia and sinus rhythm are essential; tachycardia and hypovolemia must be avoided (20, 22). Premedication should be light, and chest pain in the preoperative period

should be managed with supplemental oxygen and not nitrates because of venodilation. Systemic hypotension causes a reduction in coronary perfusion pressure should be vigorously managed with careful volume replacement and/or a vasoconstrictor such as phenylephrine (21). Postoperatively, effective pain management is essential, and patients should be appropriately monitored until fluid shifts have stabilized.

AORTIC REGURGITATION

Causes of aortic regurgitation (AR) include diseases that affect the aortic leaflets such as rheumatic heart disease, endocarditis, trauma, connective tissue disorders, and appetite suppressant medications as well as aortic root pathology secondary to annuloaortoectasia from aging and chronic hypertension. The latter mechanism is most common (1). AR produces combined pressure and volume overload, which significantly increases wall stress during both systole and diastole (19). Volume overload occurs secondary to the regurgitant volume per se; pressure overload results from systemic hypertension as a result of increased total aortic stroke volume ejected during systole (23).The left ventricle adapts with eccentric hypertrophy where sarcomeres are laid down in series and myofibrils elongate thereby preserving ventricular diastolic compliance. Once preload reserve is exhausted and the hypertrophic response with eccentric hypertrophy becomes inadequate, any further increase in afterload can reduce stroke volume and ejection fraction, thereby causing symptoms of exertional angina and congestive failure. Congestive failure is seen in 50% of patients within ten years of initial diagnosis. Both the symptoms and severity of AR correlate with an increase in left ventricular end-systolic diameter exceeding 55 mm or ejection fraction less than 50% (23, 24). Following patients with serial transthoracic echocardiography is helpful. The regurgitant volume depends directly on the regurgitant orifice area, the square root of the diastolic pressure gradient across the valve, and the diastolic time interval. Theoretically, increasing heart rate should improve net forward flow by decreasing the diastolic time interval. However, any reduction in regurgitant volume/beat is offset by the increase in beats/min so that total regurgitant volume/min remains constant. In experimental animals with AR, the effective orifice area appears dynamic, load-dependent, and directly proportionate to the transvalvular pressure gradient. A strong direct correlation exists between vascular resistance and regurgitant orifice area and both of those factors determine regurgitant volume.

Anesthetic Implications
Ejection phase indices of contractility with AR tend to be unreliable, since the increase in preload and reduction in afterload (low diastolic blood pressure) can mask impaired underlying contractility (24). Eccentric ventricular hypertrophy with AR elicits less coronary collateral development causing reduced vasodilator reserve. Coupled with ventricular dilation, hypertrophy, tachycardia, and decreased diastolic coronary perfusion pressure, these patients are prone to subendocardial ischemia. Acute afterload reduction can be beneficial if combined with preload augmentation. Patients with AR benefit intraoperatively from afterload reduction more than patients with mitral regurgitation; tachycardia is better tolerated than bradycardia. Although increasing heart rate does not alter total regurgitant flow or forward stroke volume, tachycardia decreases ventricular size and augments diastolic arterial pressure. Frequently, these patients have abnormal right ventricular relaxation which can also impair right-sided filling. Increasing left (and right) ventricular afterload should be avoided and the infusion of an inodilator such as dobutamine may be beneficial to reduce regurgitant flow.

ANTIMICROBIAL PROPHYLAXIS AGAINST ENDOCARDITIS

Any recommendation for antimicrobial prophylaxis in patients with valvular heart disease is complicated since clinical studies have defined what patients are at risk but the efficacy of treatment has only been assessed in animal studies. Recent guidelines published by the American Heart Association now stratify different cardiac conditions, according to the probability of contracting endocarditis as high-, moderate-, and negligible-risk categories (12). Patients with acquired valvular disease, hypertrophic cardiomyopathy, and mitral valve prolapse with a regurgitant murmur are in the moderate-risk category and mandate perioperative antimicrobial therapy based on the type, location, and severity of the operative procedure. In general, antimicrobial prophylaxis against *Streptococcus viridans* is necessary for dental, oral, and respiratory procedures, while antimicrobial prophylaxis against *Enterococcus faecalis* is indicated for genitourinary and gastrointestinal procedures. Appropriate antibiotic therapy should be initiated prior to the start of the surgical procedure.

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