Review Article

Valvular heart disease and anaesthesia

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ABSTRACT

Valvular heart disease presents as mixed spectrum lesion in healthcare settings in the third-world and developing countries. Rheumatic heart disease still forms the bulk of the aetiopathology of valve lesions. Mitral and aortic valve lesions top the list of valvular pathology. A thorough understanding of the pathophysiology of valvular heart disease is essential while planning anaesthesia and perioperative care for such patients. Meticulous use of optimal fluids, close monitoring of the changing haemodynamics and avoidance of situations that can cause major reduction of cardiac output and fluid shifts are mandatory to achieve good clinical outcome. We searched MEDLINE using combinations of the following: anaesthesia, aortic, mitral, regurgitation, stenosis and valvular heart disease. We also hand searched textbooks and articles on valvular heart disease and anaesthesia. This article mainly focuses on the understanding the pathophysiology of valvular heart disease in patients presenting for non-cardiac surgeries in secondary and tertiary care setting.

Key words: Anaesthesia, aortic, mitral, regurgitation, stenosis, valvular heart disease

INTRODUCTION

The incidence of heart disease ranges from 0.7% in 18–44 years age group up to 13.3% in individuals who are 75 years or older.[1] In industrialised countries, the prevalence of valvular heart disease is estimated at 2.5%.[2] A patient with a diseased heart valve can have associated heart failure or cardiac dysrhythmias such as atrial fibrillation which increase the risk of perioperative adverse events. Good perioperative optimisation and adequate monitoring help overcome haemodynamic disturbance which may occur during anaesthesia and surgery. A thorough understanding of the pathophysiology of valvular heart disease is mandatory for meticulous planning to achieve a favourable clinical outcome. Perioperative assessment includes a recent evaluation within 6 months along with echocardiography (ECHO) and detailed assessment of the progress of the symptoms. Single or multiple heart valves may be affected with isolated or mixed lesions.

Classification of valvular heart disease can be categorised based upon the aetiology:

1. Congenital valvular heart disease (atresia, stenosis, malposition, abnormalities of valve structure-bicuspid valves)
2. Acquired heart valve disease
   a. Endocarditis (regurgitation more common)
   b. Rheumatic heart disease: Mitral stenosis (MS), mitral regurgitation (MR), aortic stenosis (AS), aortic regurgitation (AR)
   c. Senile calcific AS
   d. Myxomatous mitral valve prolapse leading to regurgitation.

The most common valvular lesions in clinical settings are MS and AS.[3]

AORTIC STENOSIS

AS can be congenital or acquired. Idiopathic senile degeneration with sclerosis and calcification of the valve due to chronic inflammation accounts for the majority of acquired segment of AS. There is a clear association between the clinical risk factors for atherosclerotic

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disease and the development of AS, including the process of chronic inflammation.[4] Greater mechanical stress with age and risk factors such as hypertension, smoking, diabetes and hypercholesterolaemia contribute to 2%–4% of adults >65 years of age suffering from acquired AS.[4] Bicuspid congenital aortic valve may be noted in 1%–2% of the population born with an autosomal dominant pattern, and a variable penetrance and can develop scarring and calcification of the abnormal folding of the bicuspid leaflets, leading to AS in the later decades of life.[5,6]

Clinical features and diagnosis

A detailed history and physical examination, supplemented by ECHO, can elicit the diagnosis of AS. Symptoms such as decreased exercise tolerance, exertional dyspnoea, angina, congestive heart failure and syncope should raise suspicion of AS. Ejection systolic murmur with radiation to the carotids is often found on auscultation. ECHO is used to confirm the diagnosis and also to determine the multiple aspects of the pathophysiology of the aortic lesion. Normal aortic valve area (AVA) is 2.5–4 cm^2. The severity of the aortic valve stenosis is determined by the AVA [Table 1].

There is increased peak systolic wall stress of the left ventricle (LV) in the presence of an LV outflow tract obstruction, leading to chronic pressure overload with consequent development of concentric hypertrophy. This leads to diastolic dysfunction with an increase in LV end-diastolic pressure (LVEDP) and sub-endocardial ischaemia over time. The ejection fraction may be decreased over time, indicating reduced left ventricular contractility. In such cases, evaluation of the severity of AS can be complicated as the flow across the LV outflow tract and aortic valve is decreased due to poor contractility of the LV.[7] The pressure–volume correlation of AS is shown in Figure 1 which shows that due to increase in aortic resistance, the LV pressures are increased during ejection with increase in end-systolic volume and right shift of the loop.

ANAESTHETIC CONCERNS IN PATIENTS WITH AORTIC STENOSIS

Pre-operative ECHO generally reveals LV hypertrophy. Chest X-ray may show prominent ascending aorta due to post-stenotic dilation. ECHO may reveal the following pressure gradients and aortic velocities which are the most reproducible and the strongest predictors of clinical outcome as shown in Table 1.

Table 1: Classification of severity of aortic stenosis

Measurement	Mild	Moderate	Severe
Mean pressure gradient (mmHg)	<25	25-50	>50
Aortic valve area (cm^2)	1-1.5	0.75-1	<0.75

Patients with AS have a low fixed cardiac output. If there is sudden decrease in cardiac contractility or cardiac arrest, chest compressions will not maintain sufficient cardiac output. Thus, induction should focus on stable haemodynamics while achieving adequate anaesthetic depth. Due to diastolic dysfunction and impaired relaxation of the LV, the atrial contribution which accounts for nearly 40% of the total cardiac output should be preserved. Additionally, all efforts should be made to maintain normal sinus rhythm to get the 'atrial kick'.[8] Any possible arrhythmia should be avoided. It is wise to apply external defibrillator pads before induction of anaesthesia in case any shockable rhythm precipitates during induction of anaesthesia. Both tachycardia and bradycardia should be avoided. Bradycardia is undesirable because cardiac output may become unacceptably low in the presence of fixed aortic orifice. Any tachycardia can further jeopardise any pre-existing compromised coronary supply/demand relationship in the presence of ventricular hypertrophy and concomitant coronary disease.[9,10] Preload should be maintained adequately to fill the non-compliant LV. Afterload should be maintained or increased. Any systemic hypotension can cause reduced coronary perfusion pressure and should be rapidly managed with the early use of boluses of α-adrenergic agonists. Adequate contractility should be maintained. Good premedication helps prevent perioperative tachycardia in anxious patients. Perioperative monitoring should include electrocardiography (ECG) showing the anterior, lateral and inferior leads. There should be monitoring of invasive arterial blood pressure, central

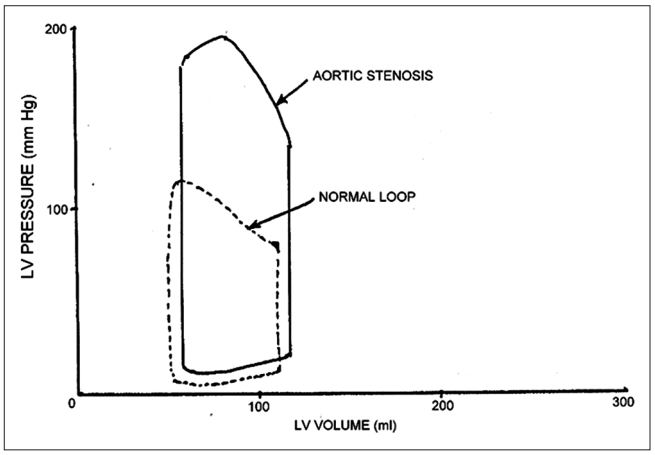

Figure 1: Left ventricular pressure–volume loop in aortic stenosis

venous pressures (CVP), pulse oximetry (SpO_2) and end-tidal carbon dioxide ($EtCO_2$). Transoesophageal ECHO (TOE) if available may be used to monitor the haemodynamics intraoperatively. Hypnosis could be achieved using low-dose benzodiazepines, fentanyl, etomidate and sevoflurane. Tracheal intubation may be achieved using vecuronium or rocuronium bromide with pancuronium top-ups to counter any slower heart rates with the combination of the former.

AORTIC REGURGITATION

In AR, the blood flows backwards into the LV during diastole. Chronic AR is more common than acute AR and has better long-term outcome. Common causes of AR include congenital lesions, connective tissue disorders, chronic inflammation, rheumatic disease and annular dilation from ageing and chronic hypertension. There is coaptation failure of the aortic valve (AV) leaflets due to chronic stress in the leaflets themselves or dilation of the AV annulus and the aortic root.[11] There is progressive volume overloading in chronic AR, leading to increase in end-diastolic wall tension. The LV undergoes a process of remodelling with the development of eccentric ventricular hypertrophy and chamber enlargement.[12] The LVEDP may be relatively normal because LV end-diastolic volume (LVEDV) increases slowly. In AR, forward flow is improved by peripheral vasodilation and ejection fraction is maintained by a large stroke volume.

Clinical features and diagnosis

The patients with chronic AR may remain asymptomatic for many years; however, they may eventually present with symptoms of left heart failure with increasing exercise intolerance, dyspnoea, paroxysmal nocturnal dyspnoea or orthopnoea. ECHO is the best diagnostic tool to note the severity of AR. The width of the AR jet at its origin provides the most reliable colour flow estimate of regurgitant severity.[8] A rough guideline for approximating severity is the width of the AR jet compared to the width of the LV outflow tract. If this ratio is <1/3, regurgitation is usually mild, 1/3–2/3 moderate and >2/3 is severe. Figure 2 shows the pressure–volume loop correlation in AR, where the loop has shifted to the right in patients with chronic AR. LVEDP remains relatively normal because LVEDV increases slowly over time.

Anaesthesia technique should aim at keeping a faster heart rate and avoiding bradycardia. Tachycardia limits the diastolic time so that the time for regurgitation is decreased leading to better forward flow. Sinus rhythm should be preserved. Reduced systemic vascular resistance (SVR) will promote forward flow. Good contractility needs to be maintained. In case inotropes are needed, inodilators such as milrinone or dobutamine are preferred.

MITRAL STENOSIS

Rheumatic heart disease is still the primary cause of MS in most developing countries. Other causes of MS are attributed to primary age-related degenerative valves and congenital mitral valvular abnormalities.

Clinical features and diagnosis

The severity classification as per the 2014 American Heart Association Guidelines for the Management of Patients with Valvular Heart Disease has been tabulated in Table 2.

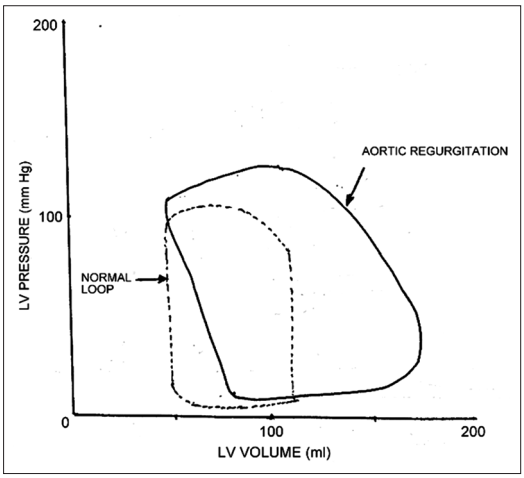

Figure 2: Left ventricular pressure–volume loop in aortic regurgitation

Table 2: Classification of severity of mitral stenosis

Stage	Definition	Anatomical	Haemodynamics
A	At risk of MS	Mild dooming during diastole	Normal transmural flow velocity
B	Progressive MS	Rheumatic changes with commissural fusion and diastolic dooming; MVA >1.5 cm^2	Increased flow velocity with diastolic pressure half-time <150 ms
C	Asymptomatic severe MS	Rheumatic changes with commissural fusion and diastolic dooming; MVA ≤1.5 cm^2	Diastolic pressure half-time ≥150 ms
D	Symptomatic severe MS	Rheumatic changes with commissural fusion and diastolic dooming; MVA ≤1.5 cm^2	Diastolic pressure half-time ≥220 ms with very severe MS

MS – Mitral stenosis; MVA – Mitral valve area

The diagnosis is confirmed by ECHO. As the MS progresses, there could be LV dysfunction due to LV muscle mass atrophy from the chronically under-filled state, leftward shift of interventricular septum due to RV hypertrophy and dysfunction, sub-valvular calcification, atrial fibrillation due left atrial dilation and enlargement. Thrombus can form in the atrium or left atrial appendage due to low-velocity blood flow. Patients with MS may be on treatment with anticoagulation with intravenous heparin, oral warfarin and drugs for rate control. Pulmonary venous and arterial pressures are elevated, secondary to long-standing elevated LA pressures. The pulmonary vasculature develops reactive pulmonary vasoconstriction secondary to chronic elevation in pulmonary artery pressure.[13] This leads to compensatory right ventricular (RV) hypertrophy. As the RV does not have enough muscle mass, chronic pulmonary hypertension can lead to progressive RV dilation and failure.[14,15] In MS, the LV always remains under filled. Although LV function or contractility is presumed to be normal in most patients with MS, it has been shown that LV dysfunction is common in patients with MS.[16] A slower heart rate is needed to transfer enough blood from the LA to fill the LV. Any fast atrial rate or arrhythmias such as atrial fibrillation diminishes the LV filling and thus the cardiac output. Transvalvular pressure gradient across the mitral valve is given by the Gorlin's formula: F = AVCc, where F = flow rate, A = area of the orifice, V = velocity of blood flow and Cc = Coefficient of orifice contraction. For mitral valve, the equation is modified into:

$$\Delta P = (CO/[[HR][DFP]]/[[MVA][44.3][0.85]])^2 \times 10.6$$

Where ΔP is the transmitral pressure gradient, CO = cardiac output, HR = heart rate, DFP = diastolic filling period and MVA = mitral valve area. Thus, when the heart rate is increased in a fixed small mitral orifice area, the gradient across the valve increases. Figure 3 shows the pressure–volume loops in MS patients. The loop is shifted to the left so that LVEDP and LVEDV are lower. The stroke volume is reduced in elevated heart rate and shortened diastolic filling intervals. There can be right-to-left ventricular septal shift due to the effect of pulmonary hypertension on the RV.[16]

Anaesthetic management in MS should focus on control of heart rate, ventricular preload, diminished RV and LV contractile function and coexisting pulmonary hypertension. Tachycardia is poorly tolerated because

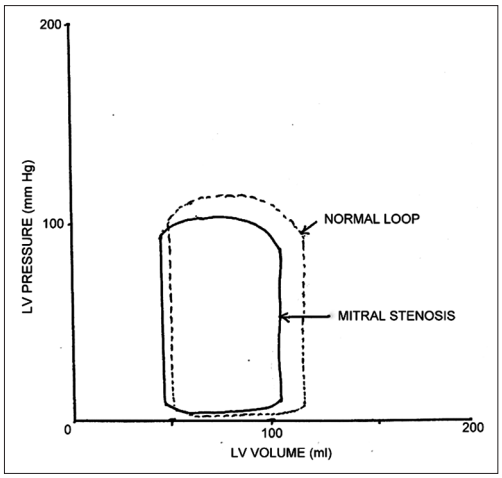

Figure 3: Left ventricular pressure–volume loop in mitral stenosis

of the decreased time for diastolic filling of LV and should be avoided. Critical MS is like a low-fixed CO state and precautions need to be taken to avoid any increase in heart rate during induction of anaesthesia or in the perioperative period. Sinus rhythm should be preserved. Any precipitation of atrial fibrillation will lose the 'atrial kick'. Elevated flow across the valve can occur during increased sympathetic activity from any stimulus and can suddenly increase the pressure gradient across the valve. This will elevate the LA pressures and subsequently the PA pressures. If the patient is on digoxin, it should be continued pre-operatively. Short-acting β-blockers can also be used perioperatively for heart rate control. Fluid should be judiciously administered so as to keep the right heart pressures and PA pressures low, as over transfusion can precipitate sudden pulmonary oedema in an already elevated chronic pulmonary hypertensive vasculature.[10] In MS, afterload reduction does not help in augmenting forward flow because stroke volume is determined by the mitral valve orifice area and the diastolic filling interval. LV contractility and SVR are usually preserved in MS although global systolic dysfunction develops in some MS patients.[14]

RV dysfunction is of major concern in patients of MS. All measures to avoid increases in pulmonary arterial (PA) pressures (e.g., avoid hypoxia, hypercarbia, acidosis, lung hyperexpansion and nitrous oxide) should be practiced. Oversedation in the preoperative period should be avoided to prevent hypoventilation and hypercarbia. Patients may be on anticoagulation for atrial fibrillation and clot formation. Coagulation profile may need to be checked (prothrombin time, activated partial thromboplastin time [APTT] and international normalised ratio [INR]). Most

non-cardiac surgeries of short duration may only need ECG, non-invasive blood pressure, SpO_2, $EtCO_2$ as standard monitoring modalities. In long surgeries with anticipated large fluid shifts and major tissue resection, invasive arterial blood pressures and CVP monitoring will prove useful. Inotropic support may be needed to augment the RV dysfunction.

MITRAL REGURGITATION

MR can either involve abnormalities in the valve or in sub-valvular components or functional abnormalities due to annular or LV dilation, leading to malcoaptation of the mitral valve leaflets.[17] Structural abnormalities in mitral regurgitant valve may include mitral valve prolapse, rheumatic mitral insufficiency, myxomatous degeneration, cleft valve associated with an AV septal defect and/or any infiltrative/fibrotic processes. Chronic ischaemic heart disease can cause a functional MR in patients with dilated cardiomyopathy or/and coronary artery disease. The valve morphology is usually normal in such patients. The incompetent mitral valve allows passage of blood from the LV into the left atrium during systole. The regurgitant volume is a function of the size of the mitral orifice, the pressure differential between the left atrium and the LV and the duration of the regurgitant cycle.[14] The MR could be acute or chronic, acute being more severe in terms of patient's clinical condition with sudden congestive heart failure needing immediate intubation, inotropes, diuresis and/or dialysis. In chronic MR, patient may complain of easy fatigability, palpitations and features of congestive heart failure. ECHO is used to quantitatively estimate the regurgitant fraction (the fraction of regurgitant volume in relation to total stroke volume).[18] ECHO also stratifies the MR depending on the width of the vena contracta, defined as the narrowest cross-sectional area of a jet [Table 3]. Note that even with similar ECHO features, clinical manifestations of a disease may differ e.g., mixed lesions or due to any sudden demand leading to worsening of haemodynamics.

The left atrium is subjected to both volume and pressure overload; however, the LA pressures do not increase as much as in MS due to gradual change of chamber dilatation. Atrial fibrillation may be present. Chronic severe MR will eventually lead to elevated PA pressures with RV dysfunction. Chronic MR can lead to eccentric hypertrophy of the LV, causing chamber enlargement without significant increases in wall thickness. Large stroke volume is ejected by the LV which comprises normal venous return into the left atrium plus the regurgitant volume from the previous cardiac cycle. Over a period, the LV systolic function deteriorates and the LV failure sets in. Figure 4 shows the effect on pressure–volume loops in MR. The area of the loop and the end-diastolic volume is grossly increased (shaded), there is the absence of isovolumic contraction phase and the LV volume starts decreasing as soon as the LV starts to contract.

Table 3: Classification of severity of mitral regurgitation

Grade	Definition	Anatomical	Haemodynamics
A	At risk MR	Mild mitral valve prolapse with normal coaptation; mild valve thickening and leaflet restriction	No MR jet or small central jet area <20% LA on Doppler; small vena contracta <0.30 cm
B	Progressive MR	Severe mitral valve prolapse with normal coaptation; rheumatic valve changes with leaflet restriction and loss of central coaptation	Central jet MR 20%-40% LA or late systolic eccentric jet MR; Vena contracta <0.7 cm; regurgitant volume <60 cc; Regurgitant fraction <50%; EROA <0.40 cm^2
C	Asymptomatic severe MR	Severe mitral valve prolapse with loss of coaptation or flail leaflet; rheumatic valve changes with leaflet restriction and loss of central coaptation	Central jet MR >40% LA or holo-systolic eccentric jet MR; Vena contracta ≥0.7 cm; regurgitant volume ≥60 cc; regurgitant fraction ≥50%; EROA ≥0.40 cm^2
D	Symptomatic severe MR	Severe mitral valve prolapse with loss of coaptation or flail leaflet; rheumatic valve changes with leaflet restriction and loss of central coaptation	Central jet MR >40% LA or holo systolic eccentric jet MR; Vena contracta ≥0.7 cm; regurgitant volume ≥60 cc; regurgitant fraction ≥50%; EROA ≥0.40 cm^2

MR – Mitral regurgitation; LA – Left atrium; EROA – Effective regurgitant orifice area

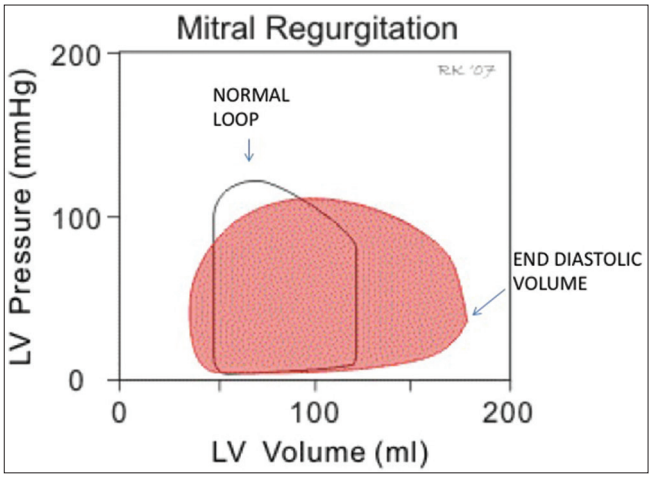

Figure 4: Left ventricular pressure–volume loop in mitral regurgitation

The primary anaesthetic goal in patients with chronic MR is maintaining forward systemic flow.[19] Higher heart rate should be maintained to decrease the regurgitant volume by shortening systole. Slow heart rate will increase the systolic period and prolong regurgitation, and also increase the diastolic filling interval, which would lead to LV distention. Maintaining sinus rhythm is useful to get the atrial contribution to cardiac output. Target should be to achieve afterload reduction to enhance forward cardiac output and blood pressure. Reduction of SVR with good anaesthetic depth, vasodilators and inodilators will promote forward flow. Higher SVR as in hypertension and hypervolemia will increase the regurgitant volume and worsen the MR. Hypotension in patients with significant MR can often be managed with inotropic support. Temporary use of small doses of ephedrine may be a better choice. Dobutamine, low-dose epinephrine, and milrinone are all acceptable inotropic choices for continuous infusion. Hypoxia, hypercarbia and acidosis are best avoided to prevent PA hypertension.

MIXED VALVULAR LESIONS

Often mixed valvular lesions such as MS and AR or AS and AR could be encountered in clinical settings. In such a case, an anaesthesiologist needs to understand which pathology is contributing mainly to the adverse haemodynamic challenge in perioperative setting and plan the anaesthetic management accordingly. However, the secondary lesion should also be kept in mind since it could modify the haemodynamics adversely.

Patients of valvular heart disease may often be found on the following medications

Antibiotic Prophylaxis

Prophylactic antibiotics may be needed in patients with valvular heart disease having increased risk of infective endocarditis (IE)[20,21] Recent guidelines for the prevention of IE recommend the maintenance of good oral health and hygiene rather than prescribing prophylactic antibiotic. Prophylaxis is recommended for patients with prosthetic cardiac valves, previous episode of IE, certain types of congenital heart disease and cardiac transplantation.[22]

Anticoagulation

Patients with valvular heart disease often require anticoagulation for associated finding such as atrial fibrillation. Non-cardiac surgery in prosthetic valve patients poses risk of IE, bleeding and acute and subacute valve thrombosis with interrupted anticoagulation. The current guidelines recommend withdrawal of oral anticoagulation 72 h before surgery to lower the INR to <1.5 and maintain anticoagulation with unfractionated heparin. The APTT is maintained twice the control value.[23]

Beta-blockade

The use of beta-blocker in patients with stenotic valvular lesions has to be made on case-to-case basis and correlated with haemodynamic variables. Generally, once indication of beta-blocker is established, practitioners have to titrate medications according to heart rates, which may differ between valvular lesions.[24]

Statins

Statins exert their effect by plaque stabilisation, anti-atherosclerotic, anti-thrombotic, vasodilative and anti-inflammatory properties.[25,26] Although there are no conclusive data to suggest the benefit of statin therapy in valvular heart disease, discontinuation of statin therapy is associated with worsened outcome.[26,27]

Recombinant BNP

Nesiritide is a recombinant brain-type natriuretic peptide (BNP), which decreases PA pressures and myocardial oxygen consumption while increasing coronary flow and urine output. In patients with severe MR, impaired LV function, and pulmonary hypertension, with a high operative mortality, the perioperative use of nesiritide has improved early outcomes in these high-risk patients. This may be due to improved ventricular loading conditions (decreased PA pressures, more effective diuresis) and/or a direct myocardial effect of BNP.[28]

This article did not specifically discuss the scope of regional anaesthesia. This could be used judiciously as site-specific regional anaesthesia, following proper screening for bleeding and haemodynamic profile of the patients and adhering to the haemodynamic goals for that patient.

CONCLUSION

Valvular heart disease is not uncommon in patients coming to the hospital for various interventions and surgeries. Most of the patients would need some forms of anaesthesia to undergo an uneventful surgical

encounter. Stenotic lesions do well with tight fluid control under general anaesthesia with appropriate monitoring and adhering to the haemodynamic goals. Smooth extubation of these patients with a pain-free post-operative period, judicious volume titration and cardiac support will go a long way for better clinical outcomes and uneventful recovery.

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Conflicts of interest

There are no conflicts of interest.

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