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Original Article

Arrhythmias in paediatric valvar disease*

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Abstract Valvar heart disease can be complicated by hemodynamic derangements, depending on the degree of the abnormality. Stenosis causes pressure overload of the chamber draining through the valve and regurgitation results in volume overload. Many lesions have a component of both, resulting in both pressure and volume overload. Increased wall stress causes myocardial stretching and fibrosis, resulting in scarring; a nidus for arrhythmia development. Arrhythmias can complicate the clinical picture and increase the morbidity and mortality in patients with both congenital and acquired valvar disease. In adults with congenital heart disease, arrhythmias are the most common cause of sudden death, followed by heart failure. Valvar stenosis and insufficiency certainly contribute to this. This article highlights the need for arrhythmia surveillance for high-risk valvar lesions.

Keywords: Arrhythmias; valvar heart disease; pediatrics

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Arrhythmia substrate in valvar disease

Myocardial hypertrophy and fibrosis results from chronic cyanosis and as a result of pressure or volume overload from valvar insufficiency and stenosis. Additionally, surgical scarring provides a nidus for arrhythmia development, especially in the atria. The hemodynamic loading of the cardiac chambers will vary depending on the type of congenital heart disease, competency of the cardiac valves, and type of surgery performed. As surgical and medical technology has improved over the last few decades, patients with even extremely complex intracardiac anatomy are surviving into adulthood. The arrhythmia burden in this patient population is high[1] and contributes significantly to their risk of heart failure and sudden death.[2,3] Therefore, it is important to understand the hemodynamic consequences and its role in arrhythmia formation while managing these patients.

Mitral valve prolapse

Mitral valve prolapse is a commonly diagnosed condition in which a portion of one or both leaflets of the mitral valve prolapse through the annular plane of the valve by 2 mm.[4] The diagnosis is made by echocardiography in the long-axis view only. As the mitral annulus has a saddle shape, the leaflets can appear to prolapse in the apical four-chamber view without true mitral valve prolapse. Prolapse results from the abnormal leaflet tissue, geometric disparities between the left ventricle and mitral valve annulus, and secondary to connective tissue disorders, such as Marfan syndrome.

The most common cause of mitral valve prolapse in adults is myxomatous degeneration, in which there are changes in the collagen matrix of the tissue, resulting in leaflet thickening, annular dilation, and chordal redundancy. Progressive myxomatous degeneration results in weakened leaflets and chordal structure, resulting in increased leaflet prolapse and mitral regurgitation over time. These patients are more likely to have hemodynamically significant mitral regurgitation, symptoms, and arrhythmias from left-sided dilation. This is fortunately uncommon in the paediatric population.

Prolapse can occur in structurally normal mitral valves. This can occur because of a disproportionate

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size of the left ventricle to the size of the valve and the chordal support structure. The redundant leaflet tissue or elongated chordae can cause mitral valve prolapse without degenerative histologic changes. This is well described in people with atrial septal defects, where the left-to-right shunt decreases the left ventricular volume and changes the left ventricular geometry. The mitral valve prolapse usually improves following repair of the atrial septal defect, likely related to increased ventricular volumes and normalisation of the left ventricular geometry.[5] These patients are therefore less likely to have an arrhythmogenic substrate and be at risk for sudden death.

Finally, mitral valve prolapse can occur in the setting of connective tissue disease. This is a result of both changes in left ventricular geometry as well as abnormalities in the leaflet structure. Like myxomatous degeneration of the valve, mitral valve prolapse and regurgitation is often progressive in the setting of connective tissue diseases and require regular follow-up. In addition to the morbidity caused by the underlying connective tissue disease, the hemodynamic derangements can result in arrhythmias and sudden death.

Older studies demonstrated an association with malignant arrhythmias and sudden death in adults with mitral valve prolapse, although not all causes of sudden death associated with mitral valve prolapse are arrhythmogenic.[6–8] In addition, patients with mitral valve prolapse were thought to commonly exhibit certain symptoms, such as palpitations, chest pain, and syncope, and clinical findings, such as a mid-systolic click, hypotension, and repolarisation abnormalities on an electrocardiogram, in what has been referred to as mitral valve prolapse syndrome.[9] However, most patients with mitral valve prolapse seem to have mild disease and no symptoms and their risk of sudden death is low, even in the adult population.[10] The underlying cause of the mitral valve prolapse is likely responsible for the arrhythmia risk. One study from Italy showed a significant number of young people who died suddenly with suspected isolated mitral valve prolapse had histologic evidence of arrhythmogenic right ventricular cardiomyopathy or myocarditis on autopsy.[11] Identifying which patients may be at risk for development of arrhythmias is important in determining subsequent follow-up and management of these patients.

Risk factors for arrhythmias and sudden death in association with mitral valve prolapse have been described. This includes the presence of moderate-to-severe mitral regurgitation, redundant chordal tissue, depressed left ventricular function, thickened mitral valve tissue (>5 mm), worsening regurgitation with exercise,[5] and bileaflet prolapse.[12] In the absence of these findings, significant arrhythmias and sudden death are exceedingly rare. Current guidelines regarding exercise restrictions concur with these findings.[13] Patients with mitral valve prolapse without symptoms, evidence of arrhythmias, impaired left ventricular systolic function, severe mitral regurgitation, or a concerning family history can participate in sports without any restrictions. In patients with normal mitral valve apparatus, worsening regurgitation due to progressive prolapse is rare and follow-up should be limited.

Tricuspid valve disease

Tricuspid valve disease can occur in isolation, such as with Ebstein's anomaly, or more commonly in conjunction with other congenital heart defects. Isolated tricuspid stenosis may occur in the setting of rheumatic heart disease, but is rare in most developed countries. Adults with CHD often have significant tricuspid valve insufficiency, leading to volume overload on the right heart chambers. As tricuspid insufficiency is so common following repair of CHD, the hemodynamic consequences can often be overlooked. Atrial fibrosis from chronic volume overload and surgical scarring results in diseased myocardium. This creates electrical heterogeneity within the atrial tissue allowing for macroreentrant atrial reentry tachycardias, such as typical atrial flutter and intraatrial reentrant tachycardia, also known as incisional atrial tachycardia or scar flutter. The ventricular response is highly variable with these tachycardias, given the variable degree of atrioventricular node disease in these patients and is often overlooked when the ventricular response is not robust. Intraatrial reentrant tachycardia often has a slower cycle length than typical flutter, and the P-waves are often distinct, which contributes to the difficulty in making the diagnosis (Fig 1).

Ebstein's anomaly results from an inferiorly displaced septal leaflet of the tricuspid valve, resulting in poor coaptation of the tricuspid leaflets and often significant tricuspid regurgitation. The most common arrhythmia associated with patients with Ebstein's anomaly is atrioventricular reentrant tachycardia owing to accessory atrioventricular pathways.[14] These patients often present during childhood with supraventricular tachycardia. Ventricular pre-excitation is not uncommon in these patients, as up to one-third have a Wolff–Parkinson–White pattern on their resting ECG.[15] Atrial arrhythmias in these patients can occur with rapid ventricular response causing hemodynamic instability and sudden death. Therefore, electrophysiology studies and catheter ablation should be strongly considered in these patients, even in the absence of documented arrhythmias. Unfortunately, these can be challenging procedures and recurrence is relatively high for these lesions, as the true tricuspid annulus can be challenging to identify, there may be

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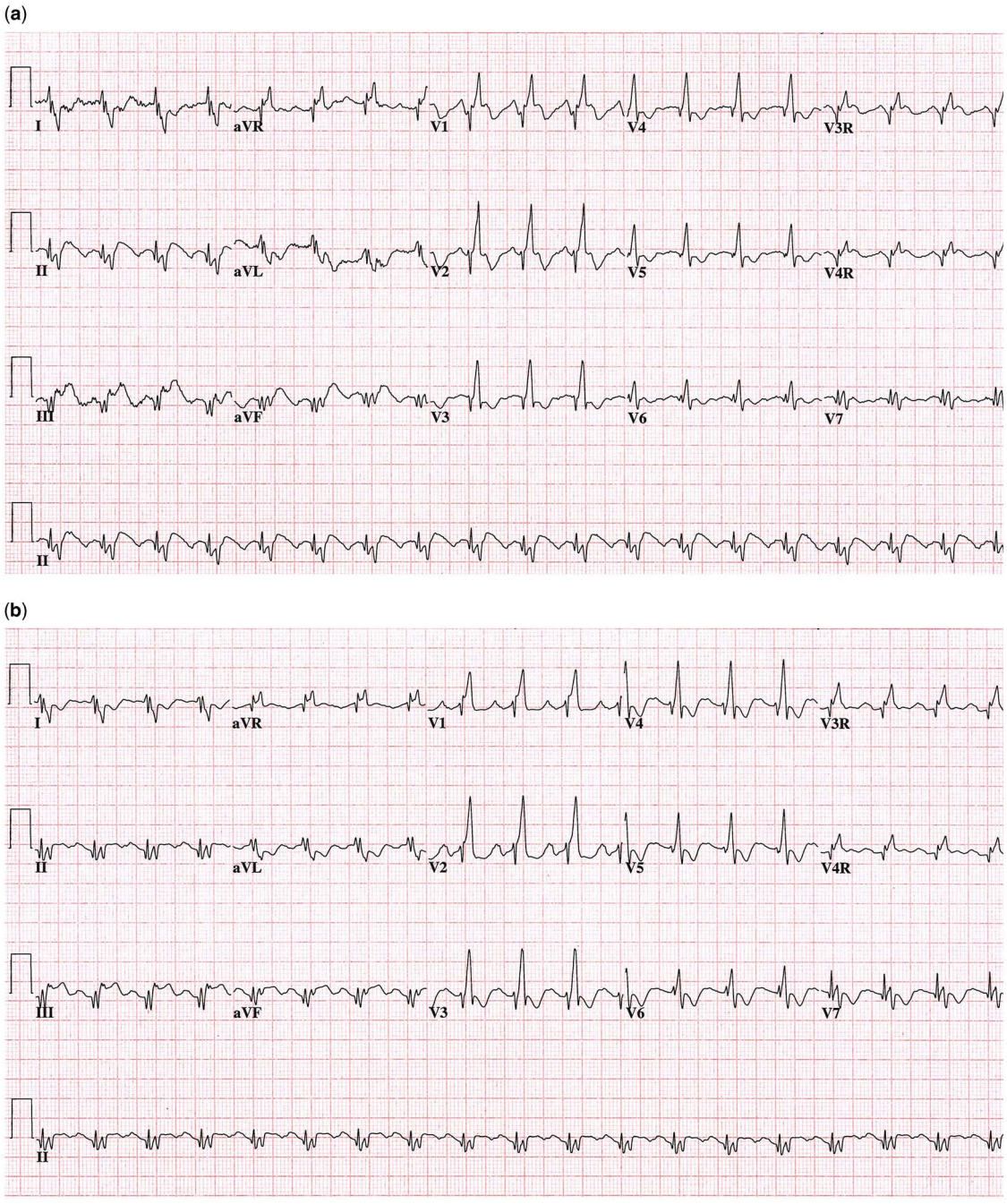

Figure 1.
Panel A shows an ECG showing intraatrial reentrant tachycardia with a right bundle branch block in a patient after a tricuspid valve replacement for Ebstein's anomaly. Panel B shows a repeat ECG in sinus rhythm. Note that the ventricular rate is not significantly higher in tachycardia likely owing to impaired atrioventricular node conduction. A slower rate obtained for palpitations in children with CHD does not exclude a tachyarrhythmia. ECG – electrocardiogram.

multiple accessory pathways, and significant tricuspid insufficiency affects catheter stability during the ablation.[16]

Tricuspid stenosis is rare in the paediatric population, but can be seen following tricuspid valve repair or with tricuspid valve replacement or as a result of endocarditis. Rheumatic heart disease resulting in tricuspid stenosis is rare in the United States, but is encountered in countries where access to health care is limited. Mild-to-moderate stenosis can lead to significant right atrial enlargement and atrial tachyarrhythmias.

In patients with atrial tachyarrhythmias from tricuspid valve disease, aggressive treatment is warranted,

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especially in the setting of CHD. Technological advances over the last decade in catheter ablation have improved success rates of eliminating these arrhythmias. However, recurrence is common because of multiple circuits and repeat procedures may be required.

Atrioventricular block can also occur during tricuspid valve repair or replacement, necessitating the need for pacing. In the setting of a prosthetic tricuspid valve, transvenous pacing is contra-indicated, and therefore epicardial pacing is currently the only option. Epicardial pacing should also be considered strongly in the setting of an annuloplasty as well, as the risk of stenosis may increase over time.

Aortic valve disease

Aortic stenosis can confer a high risk of ventricular arrhythmias and sudden death owing to significant strain on the left ventricle. The degree of aortic stenosis imposes an increase in the afterload of the ventricle with compensatory left ventricular hypertrophy. If left untreated, systolic function will become compromised leading to symptoms, an increase risk for arrhythmias, and sudden death. In neonates with critical aortic stenosis, decreased cardiac output leading to multiorgan system failure is a more common presentation than ventricular arrhythmias.

Ambulatory ECG monitoring from the Natural History Studies demonstrated that a significant number of patients with aortic stenosis had ventricular arrhythmias presumably leading to sudden death, highlighting the need for surveillance in this patient population.[17] In addition, there is an increase in QT dispersion, which predicts ventricular arrhythmia development, has been noted in children with aortic stenosis and left ventricular hypertrophy.[18]

Aortic valve replacement guidelines exist for moderate-to-severe aortic stenosis[19] and are extrapolated to the paediatric population. These guidelines are primarily symptom-based, which is not always obvious in our patient population. Symptoms may be a late finding and may not be the best determinant for intervention. In addition, symptoms may be subtle over time and go unrecognised. It is clear that dangerous arrhythmias, notably ventricular tachycardia, are the primary cause of sudden death in this patient population, particularly once heart failure has occurred. Therefore, other clinical parameters should be used to help guide timing of intervention. QRS duration has been shown to predict sudden death.[20] Positive stress testing has been predictive of sudden death in relatively asymptomatic patients with severe aortic stenosis and is useful in risk stratification[21] and is reasonable to perform routinely in age-appropriate patients.

Aortic regurgitation can be found following surgery for CHD, such as following arterial switch operation of transposition of the great arteries. It may be the result of endocarditis or rheumatic heart disease, and occurs in bicuspid aortic valve disease, although typically not in the paediatric age. Mild-to-moderate insufficiency is relatively well tolerated, but over time leads to left ventricular dilation. Left ventricular dysfunction often precedes arrhythmias, which is a later finding as a result of ventricular remodelling.

Pulmonary valve disease

The natural history studies showed that arrhythmias can occur in isolated pulmonary stenosis, some of which can result in sudden death,[17] although to a lesser extent than with aortic stenosis. It is important to note that neither medical therapy nor interventional therapy statistically changed the risk of serious arrhythmias or sudden death, but this observation was before interventional balloon valvuloplasty for pulmonary stenosis was routinely performed. Balloon pulmonary valvuloplasty is now commonly performed on neonates with moderate-to-severe pulmonary stenosis and evidence of right ventricular pressure overload. Pulmonary insufficiency is generally well tolerated and is uncommon in isolation. The arrhythmia risk depends on the degree of right ventricular dilation and/or dysfunction. Sudden death resulting from pulmonary valve disease is associated mostly with tetralogy of Fallot. Risk factors for the development of such are well described.[22] These patients require regular follow-up, as the risk of arrhythmias and sudden death increase over time.

Patient work-up

It cannot be stressed enough that arrhythmia surveillance is an important, and often overlooked, component to the management of children with heart disease and adults with CHD. Arrhythmias are one of the most common causes of sudden death in adults with CHD and cause significant morbidity in the paediatric population as well. Identifying which lesions are associated with malignant arrhythmias will dictate how aggressive the work-up of these patients. At every clinic visit, symptomatology should be assessed. However, the absence of perceived symptoms does not mean that arrhythmia surveillance should not be performed.

Electrocardiography is very useful in symptomatic patients who are actively in an arrhythmia, but may not identify patients with paroxysmal events. Comparison with previous electrocardiograms is important, paying particular attention to depolarisation changes – change in QRS duration – and the development of repolarisation abnormalities, suggestive of increasing myocardial strain. Exercise stress testing is another non-invasive

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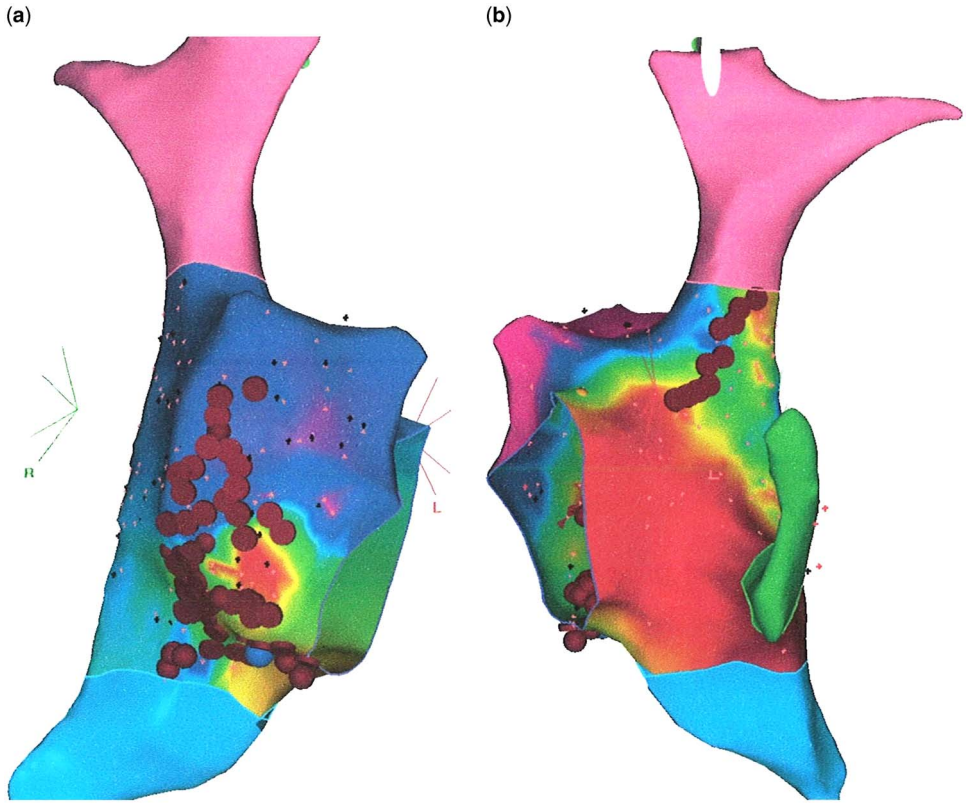

Figure 2.
Electroanatomical mapping of the right atrium in a patient who required a tricuspid annuloplasty years after a complete repair for an endocardial cushion defect. The red areas denote areas of small voltages, consistent with scar, correlating to the lateral atriotomy and ASD patch closure. The red points show ablation lines performed create areas of block to prevent flutter recurrence. An ablation line was made from an area of scar around the atriotomy to the IVC and from the posterior tricuspid annulus to the IVC, eliminating the circuit at the cavotricuspid isthmus, a critical part in the development of atrial flutter. An additional line was made from the atrial septal patch to the SVC. ASD = atrial septal defect, IVC = inferior vena cava, SVC = superior vena cava.

test easily conducted in an office that can yield clues to an underlying arrhythmia risk. As patients get older, routine testing should be conducted. In addition to just looking for ischaemic changes or arrhythmias, changes in exercise capacity may be helpful.

When symptoms are paroxysmal, ambulatory monitors such as event monitors can better document events. Routine use of 24-hour Holter monitor is less useful for paroxysmal symptoms, unless they occur almost daily, but can identify non-sustained arrhythmias that are not clinically detected.[23] Extended monitoring is available with event monitors, with the capability of continuous rhythm monitoring or just during symptoms. For rarer symptoms, implantable loop recorders can be implanted via a minimally invasive procedure and can last up to 3 years.

Treatment strategies

Prompt and aggressive treatment of arrhythmias in patients with valvar heart disease is warranted to minimise morbidity and mortality. Medical treatment consists of antiarrhythmic agents, catheter ablation, and device therapy when indicated. Understanding the hemodynamic derangements resulting in the arrhythmia may help guide therapy. Surgical options or interventions in the catheterization lab that can alleviate haemodynamic derangements should always be considered when arrhythmias arise. In addition, functional assessment is necessary. Often a rapid decline in function, especially in adults with CHD, has an arrhythmogenic origin. Unfortunately, patients with depressed function will not tolerate the hemodynamic effects of arrhythmias for prolonged periods.

Antiarrhythmic medication should be tailored to the specific arrhythmia. Sodium channel blocking – Vaughan-Williams classification IA agents – are useful for atrial arrhythmias. However, concern exists with the use of IC agents, such as Flecainide, in the setting of CHD because of early case reports[24,25] and an increase in mortality noted in adults with heart failure.[26] More recent data have shown a better safety profile in this patient population than previously thought.[27] Beta blocker therapy remains a mainstay

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of heart failure therapy and is commonly used as first-line treatment. They are often well tolerated even at higher doses. When these fail, the class III, potassium channel-blocking agents, such as sotalol, dronedarone, and amiodarone, are reasonable medications. There is currently a black box warning on dronedarone owing to an increase in mortality in patients with heart failure. Amiodarone is a powerful antiarrhythmic agent that can treat both atrial and ventricular arrhythmias, although the side-effect profile makes it less desirable for long-term treatment. The choice of antiarrhythmic therapy should be done in conjunction with a cardiologist with expertise in these medications.

Catheter ablation technology for both atrial and ventricular arrhythmias has improved markedly in the last 2 decades. Our understanding of arrhythmia substrates has allowed us to target specific sites in the myocardium to eliminate both focal and reentrant tachyarrhythmias with rising success rates. Recurrences can be common depending on the underlying heart disease, but these can be easier to control with medications even after failed ablations. Figure 2 shows an electroanatomical map of a patient who developed atrial flutter following a complete atrioventricular canal repair, who underwent tricuspid valve repair from tricuspid regurgitation. An ablation line was made from an area of scar around the atriotomy to the inferior vena cava and from the posterior tricuspid annulus to the inferior vena cava, eliminating the circuit at the cavotricuspid isthmus, a critical part in the development of atrial flutter.

For those patients with high-risk arrhythmias, usually ventricular tachycardia, especially in the setting of left ventricular dysfunction or left-sided obstructive lesions, such as aortic stenosis, implantable internal cardioverter-defibrillators can be life-saving devices. Indications for internal cardioverter-defibrillator implantation is well described in adults with valve disease.[28] These are less defined for the paediatric population and adults with CHD. In addition, implantation of such devices can be challenging in patients with limited venous access to the heart. Various surgical options have been described in these patients[29] and should not deter their use. The subcutaneous internal cardioverter-defibrillator is another option for patients who do not require pacing.[30] In addition, pacemakers may be necessary when atrioventricular conduction is impaired or chronotropic incompetence is present, usually after reparative surgery.

Conclusion

Arrhythmias do occur in various acquired and congenital valvar heart disease. The hemodynamic derangements they impose, in conjunction with the underlying heart disease and surgical history, can result in significant morbidity and sudden death. Arrhythmia surveillance for high-risk lesions should be performed routinely and aggressive treatment is warranted to minimise such morbidity and mortality.

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