

Ebstein's Anomaly

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ABSTRACT: Ebstein's anomaly is a malformation of the tricuspid valve with myopathy of the right ventricle (RV) that presents with variable anatomic and pathophysiologic characteristics, leading to equally variable clinical scenarios. Medical management and observation is often recommended for asymptomatic patients and may be successful for many years. Tricuspid valve repair is the goal of operative intervention; repair also typically includes RV plication, right atrial reduction, and atrial septal closure or subtotal closure. Postoperative functional assessments generally demonstrate an improvement or relative stability related to degree of RV enlargement, RV dysfunction, RV fractional area change, and tricuspid valve regurgitation.

BACKGROUND

Ebstein's anomaly (EA) is a malformation of the tricuspid valve (TV) with myopathy of the right ventricle (RV) that has variable presentation of the anatomic and pathophysiologic characteristics. The lesion is rare, with an incidence of approximately 1 in 20,000.¹ Anatomical features include (1) failure of TV leaflet delamination, (2) apical descent of the functional tricuspid orifice, (3) right ventricular dilation and "atrialization," (4) anterior leaflet abnormal fenestrations and tethering, and (5) right atrioventricular junction dilation (Figure 1).² The critical distinguishing feature of EA from other congenital regurgitant lesions is the degree of apical displacement of the septal leaflet (≥ 8 mm/m² body surface area).¹

Chordae are additionally variable and may be few to none, and leaflet fenestrations are common. Both atrialized (nontrabeculated myocardium between the anatomic and functional TV annulus) and trabeculated portions of the right ventricle are dilated. Patent foramen ovale and/or atrial septal defects are common, many with right-to-left shunting due to increased right-sided pressures and tricuspid regurgitation. These may contribute to cyanosis and/or paradoxical embolism, particularly in adult patients.³

Patient presentation is variable due to the underlying heterogeneity of disease anatomy and physiology. Although most patients are diagnosed in infancy or childhood, the initial diagnosis may also occur in adulthood. Arrhythmias are a common presenting feature in adults; atrial fibrillation, flutter, or ectopic atrial tachycardia may occur in up to 40% of newly diagnosed adult patients.¹

Initial presentation of EA in adulthood is common, and natural history demonstrates decreased survival with biventricular

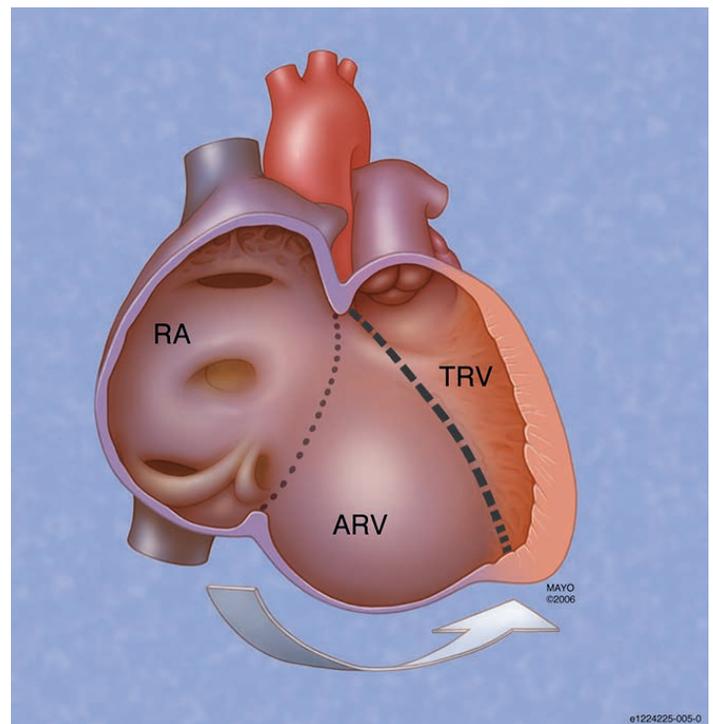


Figure 1.

Tricuspid valve displacement highlights rotation of tricuspid annulus towards the right ventricular outflow tract in addition to downward/apical displacement. ARV: atrialized right ventricle; RA: right atrium; TRV: true right ventricle. Copyright © Mayo Foundation for Medical Education and Research.

failure.⁴ Ventricular arrhythmias may lead to sudden cardiac death. In a study by Attie et al., the estimated overall survival in unoperated patients with time zero at 25 years of age was 89%, 81%, 76%, 53%, and 41% at 1, 5, 10, 15, and 20 years of follow-up, respectively.⁴

EVALUATION

Baseline testing in patients with EA includes electrocardiogram, chest radiograph, 24-hour Holter monitor, echocardiography, and as-needed cardiopulmonary exercise testing. Cardiac magnetic resonance is quite useful for quantification of RV size and function.^{5,6}

Electrocardiogram classically includes PR interval prolongation, tall P waves, and a degree of right bundle branch block.² Atrial tachycardia—including atrial fibrillation, atrial flutter, or ectopic atrial tachycardia—is present in 25% to 65% of patients, and 10% to 45% of patients have accessory pathways such as Wolff-Parkinson-White syndrome. Atrioventricular nodal reentrant tachycardia is present in approximately 10% of patients.⁷⁻⁹ Multiple (6% to 36%) accessory pathways are common and may increase the risk of sudden cardiac death.¹ Preoperative electrophysiologic assessment is indicated when a pre-excitation pathway is present, and most patients can be treated percutaneously.²

A globular appearance is classic on chest radiograph due to right atrial enlargement, although cardiac silhouette may appear relatively normal. Transthoracic echocardiography is the imaging standard in EA and provides a platform for TV leaflet and subvalvular characterization, determination of right-heart size and function (atrium and ventricle), and dynamic evaluation of intracardiac shunts and associated cardiac defects. Color flow Doppler is critical for assessing tricuspid regurgitation. Echocardiographic features favorable for TV repair include mobility of the anterior leaflet with a free leading edge and presence of septal leaflet tissue.² When planning for a circumferential (cone) reconstruction, any delamination of the inferior leaflet and septal leaflet facilitates successful repair. Conversely, leaflet tethering to

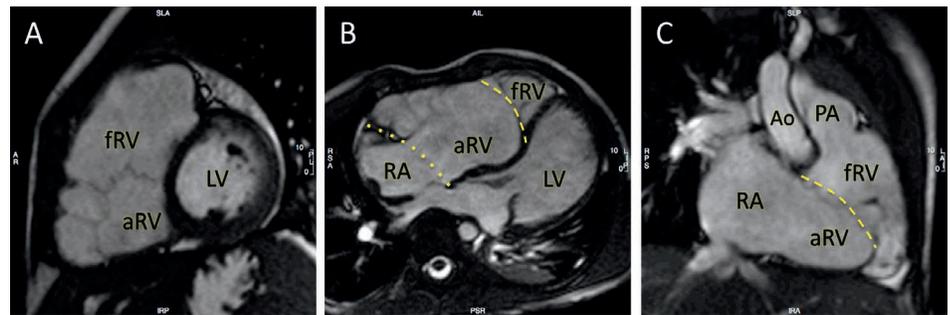


Figure 2.

Cardiac magnetic resonance imaging in Ebstein's anomaly. (A) Image of the ventricles in the short-axis plane at the mid-ventricular level. (B) Four-chamber view. (C) Right ventricular inflow-outflow view. The atrialized right ventricle (aRV) is between the atrioventricular junction (dotted line) and the functional tricuspid valve orifice (dashed line). The functional right ventricle (fRV) is the part of the right ventricle between the dashed line and the pulmonary valve. The anatomic right ventricle is a combination of both aRV and fRV. The functional orifice of tricuspid valve is rotated apically and superiorly toward the RV outflow tract. Ao: aorta; LV: left ventricle; PA: pulmonary artery; RA: right atrium. Copyright © Mayo Foundation for Medical Education and Research.

the endocardium with muscularization is indicative of a more difficult repair. Another feature in the adult that makes successful repair difficult is severe annular dilation, which can reach up to 8 or more centimeters.

Cardiac magnetic resonance imaging with gadolinium quantifies RV volumes and tricuspid regurgitation (Figure 2).^{6,10} The practice of including the atrialized RV in the quantification of RV volume and ejection fraction calculations varies among institutions and therefore must be considered when interpreting results. Quantification of tricuspid regurgitation is performed by velocity mapping perpendicular to the regurgitant jet, and a jet cross section ≥ 6 mm x 6 mm is considered severe.¹¹ The relationship between right-sided myocardial fibrosis and clinical outcomes has yet to be fully evaluated but has been shown to be related to supraventricular arrhythmias.¹²

MANAGEMENT

Asymptomatic patients may be managed medically with observation for many years. Assessment of arrhythmias, progressive RV enlargement, and/or

systolic function deterioration of the RV should be closely followed. Patients should be considered for operative intervention when they develop symptoms and/or worsening exercise capacity, cyanosis, paradoxical embolism, progressive RV dilation or dysfunction, and the onset of arrhythmias and when tricuspid repair is feasible and in a setting of low morbidity and mortality.^{2,5}

OPERATIVE INTERVENTION

Tricuspid valve repair is the goal of operative intervention; repair also typically includes RV plication, right atrial reduction, and atrial septal closure or subtotal closure. While tricuspid repair is generally the goal, it should be emphasized that the results of tricuspid replacement in adult patients indicate that it is safe and effective. Arrhythmia surgery is advised with guidance provided by an electrophysiologist knowledgeable in EA. Ventricular offloading with a bidirectional cavopulmonary shunt is performed selectively and generally reserved for cases of poor RV function.¹³

Tricuspid repair has evolved through many techniques and operative

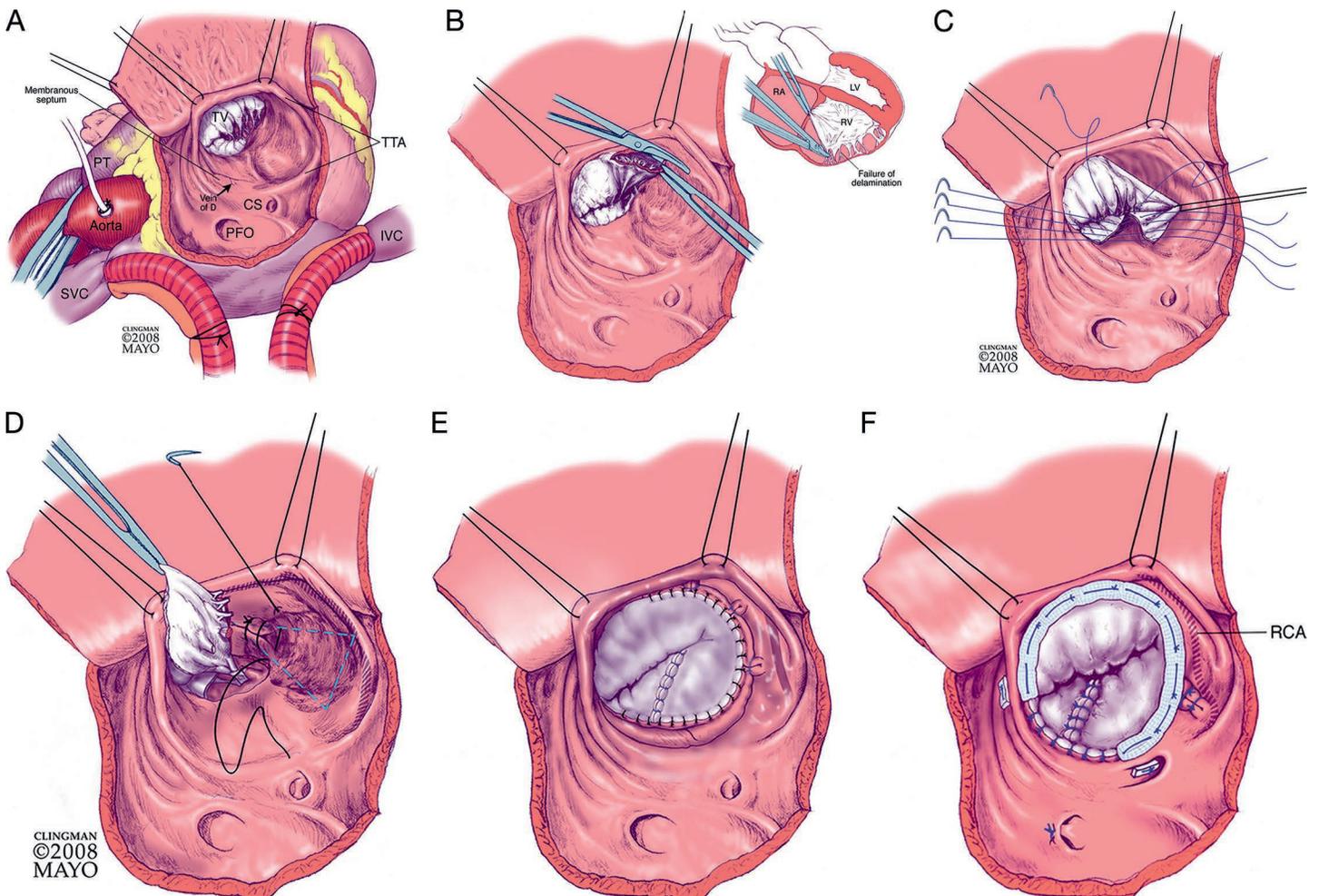


Figure 3.

Key components of cone repair. (A) Standard aortic and bicaval cannulation. Right atriotomy is parallel to the atrioventricular groove. Anatomic examination of tricuspid valve (TV) and atrialized right ventricle (RV). Membranous septum and atrioventricular (AV) node are marked by small vein (vein of D). (B) Delamination of the TV. First incision is made at 12 o'clock in the anterior leaflet a few millimeters away from the true annulus. Surgical delamination is the division of the fibrous and muscular attachments between the body of the leaflet(s) and the free wall of the RV. Delamination must continue to all attachments between the AV groove and the leading edge of the leaflets (close to the RV apex) while keeping the attachments at the leading edge of the leaflet intact. (C) Rotation of leaflet tissue. Following mobilization of all leaflet tissue, the inferior leaflet, or most medial aspect of the anterior leaflet, is rotated clockwise to meet the mobilized septal leaflet. These leaflets are approximated with a monofilament suture (either continuous or interrupted). At completion, the neo-tricuspid valve orifice should be composed of 360° of leaflet tissue. Prior to reattachment, the atrialized RV is examined to determine need for RV plication. (D) RV plication. Internal triangular plication of portions of the atrialized RV reduces tension on the repair, reduces size of the TV annulus, and eliminates noncontractile RV. Plication is completed with 4-0 or 5-0 monofilament, is started close to the RV apex, and proceeds to the AV groove. Suture line is partial thickness, primarily incorporating the endocardium. Care must be taken to avoid injury to the right coronary artery. (E) Attachment of neo-tricuspid valve to the true annulus. The septal leaflet is reattached to the ventricular septum (just caudal/ventricular side of the true annulus). (F) Repair can be reinforced with either a felt band (in younger children) or an annuloplasty band (older children and adults). CS: coronary sinus; IVC: inferior vena cava; LV: left ventricle; PFO: patent foramen ovale; RA: right atrium; right coronary artery; SVC: superior vena cava; TTA: true tricuspid annulus. Copyright © Mayo Foundation for Medical Education and Research.

modifications. Early repair techniques were centered on the anterior leaflet monocuspid valve.^{14,15} The original Danielson technique involved repositioning the true tricuspid annulus with plication of the atrialized portion of the RV free wall as well as right atrial reduction.¹⁴ Subsequent Danielson modifications include the addition of anterior papillary muscle approximation to the ventricular septum—using the Sebening stitch—to facilitate leaflet coaptation with the ventricular septum. The Carpentier-Chauvaud monocuspid repair technique focused on anterior leaflet mobilization with reattachment at the annulus anteriorly, use of an annuloplasty ring, and atrialized RV plication.¹⁵

The modern approach is the “cone reconstruction” method introduced in 2007 by da Silva (Figure 3).¹⁶ This technique was an extension of the Carpentier technique in that septal and inferior leaflet tissues were mobilized, and then the sides of all the mobilized leaflets were connected in a manner to create 360 degrees of leaflet tissue. The newly constructed “cone” was then reattached to the true annulus. This results in a near-anatomic repair.

Potential contraindications to cone reconstruction are older age (> 60 years), pulmonary hypertension, biventricular dysfunction (left ventricular ejection fraction < 30%), lack of septal leaflet tissue and minimal delaminated anterior leaflet tissue (< 50%), and severe enlargement of the RV with corresponding severe dilation of the right atrioventricular junction.² While the learning curve for a surgeon skilled in cone reconstruction is significant, early mortality is quite low (< 1%) with high rates of valve reparability (> 98%) in experienced centers.¹⁷ Tricuspid re-repair is feasible, particularly when the prior repair focused on annular maneuvers only and the subvalvar apparatus was untouched.¹⁸

Tricuspid valve replacement with a tissue prosthesis is an alternative when repair is not possible.^{2,19} Older patients with a severely enlarged RV or TV annular dilation in particular may benefit from TV replacement over repair due to the minimization of cross-clamp time (cross clamp can be removed after closure of the patent foramen ovale/atrial septal defect). Bioprosthetic valve function in the tricuspid position has relatively good durability, and chronic anticoagulation can generally be avoided.²⁰ Tricuspid valve-in-valve replacement strategies are becoming increasingly possible when bioprosthetic failure occurs.^{21,22} Mechanical valves are usually avoided in the setting of severe RV dysfunction due to risk of disc motion abnormalities and associated risk of valve thrombosis.²

Operative strategies related to coronary sinus drainage in relation to the valve suture line are outlined in Figure 4. When the coronary sinus is close to conduction tissue, the valve suture line is placed in the right atrium to avoid heart block.

A bidirectional cavopulmonary shunt (BCPS) is applied selectively in adult

patients to provide RV volume offloading in the setting of severe RV dysfunction.¹³ Pulmonary hypertension is rare in EA, so the BCPS is generally feasible even in the setting of moderate left ventricular (LV) dysfunction (LV ejection fraction 35%-40%). However, in the setting of hypertension or left-sided valve disease, BCPS should be used with caution as it may increase LV end-diastolic pressure. Indications for BCPS include both heart failure indications (RV end-diastolic volume > 250 mL/m², RV ejection fraction < 25%, D-shaped left ventricle, post-repair right atrial pressure to left atrial pressure ratio > 1.5:1, and post-repair cardiac output depression) and non-heart-failure indications (complex TV repair tension reduction and post-repair TV stenosis with a mean gradient > 8-10 mm Hg). BCPS contraindications related to pulmonary hypertension include a mean pulmonary artery pressure > 20 mm Hg, pulmonary arteriolar resistance > 4 Woods units, and elevated left heart pressures (LV end-diastolic pressure or left atrial pressure > 12 mm Hg).¹³

Another alternative to the BCPS is atrial septal fenestration by either subtotal atrial

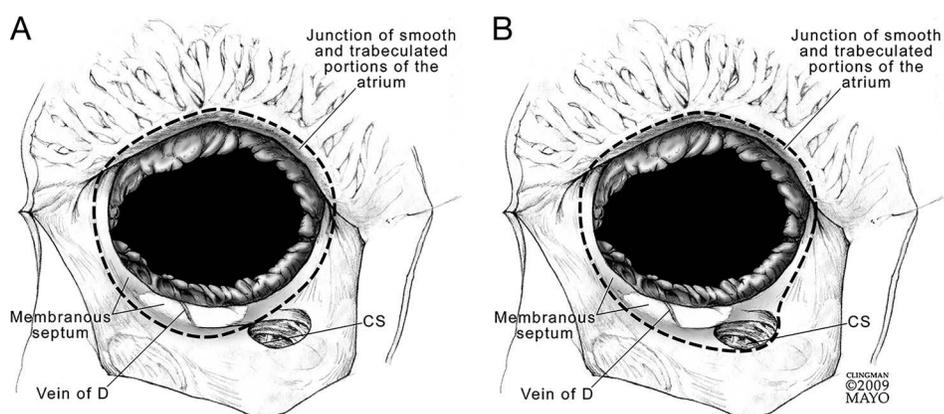


Figure 4.

Suture line placement for tricuspid valve repair in Ebstein's anomaly. (A) Coronary sinus (CS) can be left to drain normally into the right atrium (RA) if there is sufficient distance between the coronary sinus and atrioventricular node. (B) If coronary sinus and conduction tissue are close, the suture line can be deviated into the RA to avoid iatrogenic injury, and the coronary sinus then drains into the right ventricle. Copyright © Mayo Foundation for Medical Education and Research.

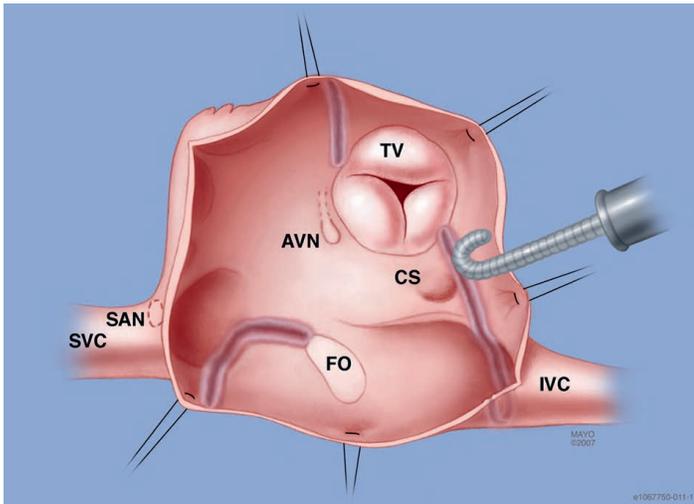


Figure 5.

Cryoablation for atrial flutter/fibrillation. AVN: atrioventricular node; CS: coronary sinus; FO: foramen ovale; IVC: inferior vena cava; SAN: sinoatrial node; SVC: superior vena cava; TV: tricuspid valve. Copyright © Mayo Foundation for Medical Education and Research.

septal defect closure or by leaving a patent foramen ovale open. This is applied more to infants and less often in the adult setting due to the risk of left heart dysfunction and risk of paradoxical embolism from right-to-left shunting.²

Intraoperative paroxysmal atrial fibrillation or atrial flutter can be managed with a modified right-sided maze or cavotricuspid isthmus ablation using either cryoablation or radiofrequency ablation (Figure 5). Continuous atrial fibrillation is best approached with a biatrial maze.²³

Although cardiac transplantation is rarely required in the adult patient with EA, it may be indicated in patients following single ventricle management strategies in the neonatal period. In a recent analysis from The Society of Thoracic Surgeons, there were no reported cases at the national level of cardiac transplant in adult patients with a primary diagnosis of EA.²⁴

LATE OPERATIVE OUTCOME

In the largest published series of late operative outcomes for EA, overall late survival was 98%, 94%, 90%, 86%, and 76% at 1, 5, 10, 15, and 20 years, respectively. Freedom from late reoperation was 97%, 91%, 82%, and 70% at 1, 5, 10, and 15 years, respectively.²⁵ Late cone reconstruction outcomes are limited due to the relatively recent application of this surgical strategy; however, adult-specific freedom from reoperation following cone reconstruction at 6 years is

98.8%.¹⁷ Independent predictors of late mortality include mitral regurgitation that requires surgical intervention, RV outflow tract obstruction (RVOTO), preoperative cyanosis as indicated by elevated hematocrit, > moderate RV dysfunction, and \geq moderate LV dysfunction.²⁵

Compared to the continuous decreased function in nonsurgical patients, postoperative functional assessments of patients following operative repair generally demonstrate improvement or relative stability related to degree of RV enlargement, RV dysfunction, RV fractional area change (FAC), and TV regurgitation.^{17,26} The majority of patients who underwent surgery in our center continue to be in New York Heart Association functional class I or II.²⁷ Patients with EA are at risk for late sudden death; factors associated with increased risk include prior ventricular tachycardia, heart failure symptoms, syncope, TV surgery, and pulmonary stenosis.²⁸ Exercise testing has not been standard in preoperative and postoperative evaluation of these patients, although we are now trying to do this in all of our adult patients.

Overall late functional assessments are limited. The largest study to date reported that late reoperation, rehospitalization, and atrial arrhythmias continue to be problematic for patients following surgical repair. Freedom from cardiac rehospitalization (including reoperation) at our center was 91%, 79%, 68%, 53%, and 35% at 1, 5, 10, 15, and 20 years, respectively.²⁵ This study is of patients in the period before cone repair; therefore, results may not be readily generalizable to current operative outcomes. Further assessment of outcomes is required in patients undergoing contemporary operative tricuspid repair interventions.

FUTURE DIRECTIONS

Therapeutic interventions to date have focused primarily on refinement and durability of surgical valve repair techniques and arrhythmia surgery in conjunction with improvement in timing of operative intervention. Although TV competence is improved and favorable RV remodeling has been suggested, the RV myopathy inherent to the disease process still remains and plays a role in late symptoms and arrhythmias and possibly in late sudden cardiac death. Cell-based regenerative therapies are being explored in congenital heart disease²⁹ and specifically in EA.³⁰ Initial results have demonstrated safety and rebound in RV function at 6-month follow-up; complete study follow-up and comparison between study treatment and control groups are not yet available.

Conflict of Interest Disclosure:

The authors have completed and submitted the *Methodist DeBakey Cardiovascular Journal* Conflict of Interest Statement and none were reported.

KEY POINTS

- Ebstein's anomaly is tricuspid valve and right ventricular malformation with variability in anatomy, pathophysiology, and clinical presentation.
- Echocardiography and magnetic resonance imaging are critical for both ongoing assessments and operative planning.
- Severe right ventricular dysfunction may augment operative strategies
- Late rehospitalizations are primarily due to atrial tachyarrhythmias and reoperation.

Keywords:

adult congenital heart disease, Ebstein's anomaly, tricuspid valve, arrhythmia

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