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REVIEW ARTICLE

# Ebstein's Anomaly: From Fetus to Adult—Literature Review and Pathway for Patient Care

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**Abstract**
Ebstein's anomaly, first described in 1866 by Dr William Ebstein, accounts for 0.3–0.5% of congenital heart defects and represents 40% of congenital tricuspid valve abnormalities. Ebstein's anomaly affects the development of the tricuspid valve with widely varying morphology and, therefore, clinical presentation. Associated congenital cardiac lesions tend to be found more often in younger patients and may even be the reason for presentation. Presentation can vary from the most extreme form in fetal life, to asymptomatic diagnosis late in adult life. The most symptomatic patients need intensive care support in the neonatal period. This article summarizes and analyzes the literature on Ebstein's anomaly and provides a framework for the investigation, management, and follow-up of these patients, whether they present via fetal detection or late in adult life. For each age group, the clinical presentation, required diagnostic investigations, natural history, and management are described. The surgical options available for patients with Ebstein's anomaly are detailed and analyzed, starting from the initial mono-leaflet repairs to the most recent cone repair and its modifications. The review also assesses the effects of pregnancy on the Ebstein's circulation, and vice versa, the effects of Ebstein's on pregnancy outcomes. Finally, two attached appendices are provided for a structured echocardiogram protocol and key information useful for comprehensive Multi-Disciplinary Team discussion.

**Keywords** Ebstein's anomaly · Tricuspid valve · Cone procedure

## Introduction

Ebstein's anomaly was first described in 1866 by Dr William Ebstein on the post-mortem examination of a young adult with cyanosis, dyspnea, and palpitations [1]. This condition affects the development of the tricuspid valve with widely varying morphology and subsequently clinical presentation. Patients can present from the most extreme form in the fetal life to late diagnosis in asymptomatic adults. The most symptomatic patients are those who need intensive care in the neonatal period.

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The literature on this condition was reviewed to enable creation of this pathway of care for Ebstein's patients from fetal life through to adult life and pregnancy. The anatomical basis of Ebstein's anomaly has been reviewed, including the cardiac and non-cardiac associations. For each age group the clinical presentation, required diagnostic investigations, natural history and management of these patients is described with particular focus on the available surgical options. This review focuses on Ebstein's anomaly only and other diseases of the tricuspid valve including tricuspid valve dysplasia.

For this pathway, neonate is defined as < 28 days, infant as 29 days to 1 year, child 1–11 years, and adolescent/adult > 12 years.

## Anatomical Definition of Ebstein's Anomaly

The hallmark of Ebstein's anomaly is inferior displacement away from the atrio-ventricular junction, of the hinge points of the septal and mural leaflets into the Right Ventricle (RV)

[2, 3]. This results from failure of delamination of both these leaflets [2–4]. The delaminated septal and mural leaflets usually form a combined leaflet. The antero-superior leaflet forms separately much earlier during fetal development compared to both septal and mural leaflets and so remains at a normal hinge-point position [2, 3].

The consequence of this embryological change is that the valve annulus and *functional* orifice are *rotationally displaced inferiorly* into the RV cavity. In the most severe form, this displacement can be into the RV outflow tract [2, 3]. The resulting combined septal-mural leaflet closes in a bifoliate configuration with the antero-superior leaflet.

Tricuspid regurgitation (TR) can occur due to non-delaminated leaflets having reduced/no motion which causes central regurgitation, or due to leaflet fenestrations [3].

Secondary to this leaflet displacement, part of the RV becomes incorporated into the right atrium (aiialized RV), and there is consequent functional RV hypoplasia [4].

## Epidemiology & Etiology

Ebstein's anomaly accounts for 0.3–0.5% of congenital heart defects and represents 40% of congenital tricuspid valve abnormalities [3]. No gender difference in incidence has been reported.

Initial studies from the Danish registry suggested an association between maternal Lithium use during pregnancy and Ebstein's anomaly. However, this association, though still prevalent, was not as frequent on follow-up studies [3–5].

## Associated Cardiac & Non-cardiac Abnormalities

### Structural Cardiac Abnormalities

Associated congenital cardiac lesions tend to be found more often in younger patients and may be the reason for presentation. Patients diagnosed later in life, unsurprisingly, tend to have less additional cardiac abnormalities. Associated lesions include

(1) Pulmonary stenosis or pulmonary atresia. Hypoplasia of the RV outflow tract is thought to be secondary to chronic reduced antegrade RV flow in fetal life.
(2) Interatrial communication is present in over 90% of patients, often with right-to-left shunting and resultant cyanosis [3, 4, 6].
(3) Prominent Eustachian valve, likely secondary to abnormal flow patterns in the right atrium (RA) [3, 4, 6].
(4) Tetralogy of Fallot
(5) Isolated ventricular septal defect
(6) Congenitally corrected transposition of the great arteries (ccTGA): up to 50% of cases of ccTGA present with variable tricuspid valve morphology which could be classified as Ebstein's anomaly [7].
(7) Abnormalities of left ventricle (LV) in up to 39% of patients, including abnormal LV morphology, volume, and function [3, 7]. This can be either primary myocardial dysfunction or secondary to abnormal septal interaction from the dilated RV to the LV. Left Ventricular Non-Compaction (LVNC) can also be present in up to 19% of patients [7].
(8) RV fibrosis. This is more frequently seen in adults, suggesting an acquired phenomenon secondary to chronic increased preload of the RV caused by TR.
(9) Mitral valve abnormalities including mitral valve prolapse, mitral cleft, double-orifice mitral valve, and parachute mitral valve.

### Arrhythmias

Ebstein's anomaly is the congenital heart defect most frequently associated with arrhythmias, which present both in childhood and later in life [8]. Thirty percent of patients have atrial arrhythmias [9]. Supra-ventricular tachycardia (SVT) is typically atrio-ventricular re-entry tachycardia (AVRT), secondary to Wolff–Parkinson–White (WPW) accessory pathways, with 25% having right sided and > 33% having multiple accessory pathways [4–8]. This may be due to discontinuity between the central fibrous body and septal atrio-ventricular ring [5]. Atrial arrhythmias can also occur secondary to increased dilation of the atrialized RV as well as dilation of the true RA. These arrhythmias can be precipitated by exercise, which is an important consideration for patient investigation.

SVT in the neonate can have drastic consequences in severe Ebstein's anomaly, as tachycardia can further impair the RV output, increasing RA pressure and further worsening cyanosis via right-to-left shunting across the atrial septal defect (ASD).

Patients can also get spontaneous ventricular tachycardia or fibrillation from the arrhythmogenic atrialized RV [5]. Ventricular and supra-ventricular ectopy are also seen in Ebstein's but more commonly in adolescents and adults [10].

As the patients get older, arrhythmias become more common in non-operated patients, with ~ 75% being SVT [3, 5] Onset of chronic atrial fibrillation (AF) is a poor prognostic sign with high mortality risk within 5 years [10]. From birth, rates of ventricular arrhythmias/sudden death were reported at 0.8% at 10 years, 8.3% at 50 years and 14.6% at 70 years [9].

Following tricuspid valve surgery, there is a higher incidence of ventricular arrhythmias, related potentially to ventriculotomy incisions [9, 11].

### Extracardiac Associations

Neonates with severe Ebstein's anomaly often have lung hypoplasia secondary to severe right atrial/ventricular dilation and cardiomegaly. The heart can occupy > 55% of the chest circumference (Fig. 1) with compression of the lungs and influencing lung development and function. Impaired cardiac output leads to redistribution of blood flow as seen in fetal hypoxemia where blood flow to the brain and heart is prioritized, at the expense of flow to placenta and other organs [6]. This can contribute to limited intrauterine growth, a risk factor for neonatal demise [6].

### Genetics

The majority of Ebstein's cases are not inherited, and genetic testing is not always performed in these patients [7]. However, there are familial Ebstein's cases with reports of genetic variants in the MYH7, TPM1, and NKX2-5 genes [12–14]. These are important to be aware of as MYH7 and TPM1 variants are commonly present in cardiomyopathies and so these Ebstein's patients may be more likely to have a co-existing cardiomyopathy including LVNC [12–14]. Variants in NKX2.5, in addition to Ebstein's, can also produce a phenotype of atrio-ventricular block, VSD, and Tetralogy of Fallot [12]. Genetic testing can, therefore, be helpful in Ebstein's anomaly and can guide monitoring for associated conditions.

## Presentation

Clinical presentation differs greatly between age groups.

### Fetal

Ebstein's anomaly may be detected on routine obstetric ultrasound or during fetal echocardiogram performed for screening high-risk pregnancies [15]. Some fetuses may be diagnosed after presenting with SVT or with hydrops.

The morphological spectrum of Ebstein's anomaly not only influences prenatal detection but also fetal pathophysiology and outcome. The greater degree of septal leaflet displacement and regurgitation leads to increased right atrial dilation and increased likelihood of earlier detection during screening compared to milder cases. Severe Ebstein's can have significant hemodynamic impact increasing the risk of in-utero demise or neonatal mortality. Severe displacement of the valve results in increased atrialization of the RV, influencing the right ventricle's ability to generate adequate RV pressure for anterograde flow across the pulmonary valve; the RV needs to generate systemic level pressures to overcome the high pulmonary vascular resistance in the lungs and systemic circulation because of the systemic-pulmonary circulation connection via the ductus arteriosus. If there is significant atrialization of the RV and severe TR, the pressure generated by the RV may be inadequate. RV pressures are proportional to gestational age, so for example, a 29-week gestational age fetus should have an RV pressure ≥ 29 mmHg (Fig. 2) [16].

Severe TR (Fig. 3) results in RA and RV dilation and may cause septal deviation impeding LV diastolic filling, which raises left atrial pressure. Increased left atrial pressure can lead to changes in foramen ovale size and flow, along with changes in RA and systemic venous pressures with consequential changes in ductus venosus, umbilical vein, and placental flow increasing the risk for hydrops.

Early morphological studies demonstrated that the most severe form of Ebstein's anomaly led to early in-utero

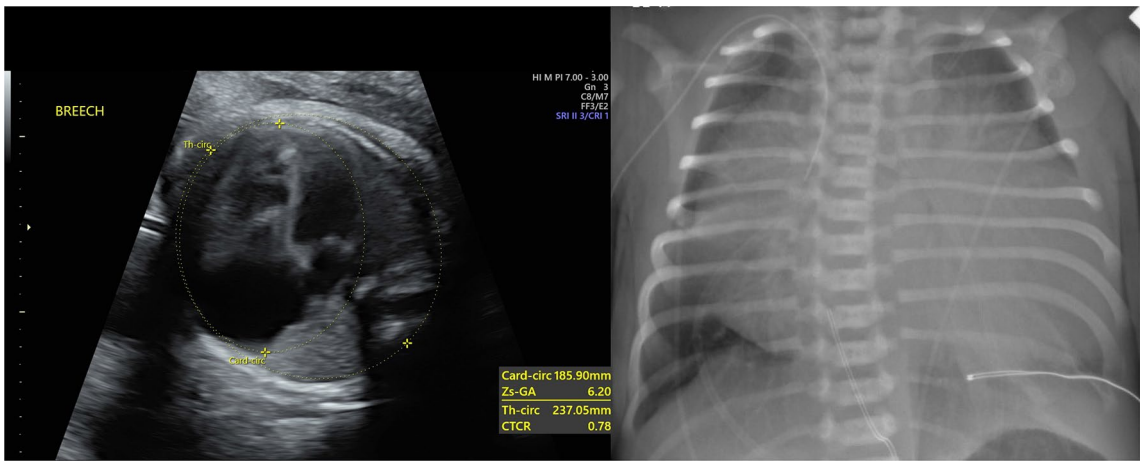


**Fig. 1** "Wall–wall" heart from severe Ebstein's shown on both fetal 2D echocardiogram and newborn CXR, respectively

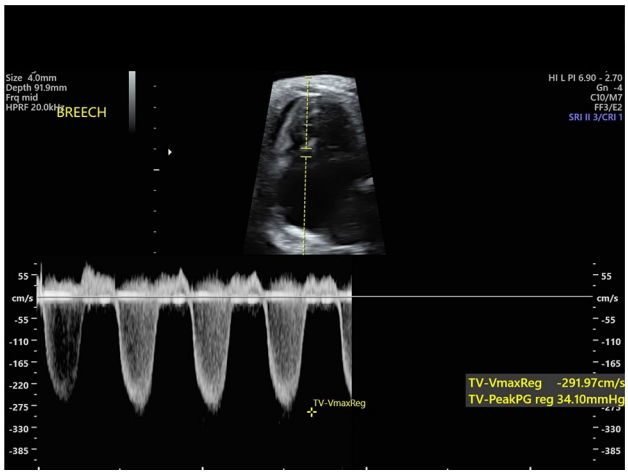


**Fig. 2** Fetal echocardiogram showing Ebstein's anomaly in a 32 + 4-week gestation fetus with prenatal TR jet Vmax 2.9 m/s (estimated RV pressure 34 mmHg)

demise. When evaluating risk factors for fetal and neonatal Ebstein's mortality, most studies also include tricuspid valve dysplasia lesions. Fetal risk factors for mortality at < 30 days of age include abnormal RV function predicted by low TR velocity and increase cardiothoracic ratio > 0.53 [17]. Contemporary multicenter data demonstrated independent fetal predictors of mortality at time of diagnosis include detection at < 32 weeks gestation, increased tricuspid valve annulus *z*-score, presence of pulmonary regurgitation, and pericardial effusion [18]. Non-survivors were more likely to have pulmonary regurgitation at any gestation and lower gestational age and weight at birth [18].

## Neonate and Infant

### History

Neonates not detected prenatally tend to present clinically only when it is on the severe spectrum of the disease. Often this is associated with pulmonary stenosis or atresia (functional or anatomic) [19]. In some cases, neonates with less severe forms of Ebstein's will be detected by pulse oximetry screening around 24 h of age [20].

The main features are usually cyanosis and congestive heart failure, which develop in the first few days of life [3, 4, 6, 19].

Atrial level right-to-left shunting is increased by the atrialized RV contracting during systole along with the rest of the functional RV, while the tricuspid valve is closed, causing retrograde flow of blood into the systemic veins and across the ASD into the left atrium [3].

With severe Ebstein's anomaly, during the first few days of life, while the patent ductus arteriosus (PDA) is open and the pulmonary vascular resistance (PVR) is high, with

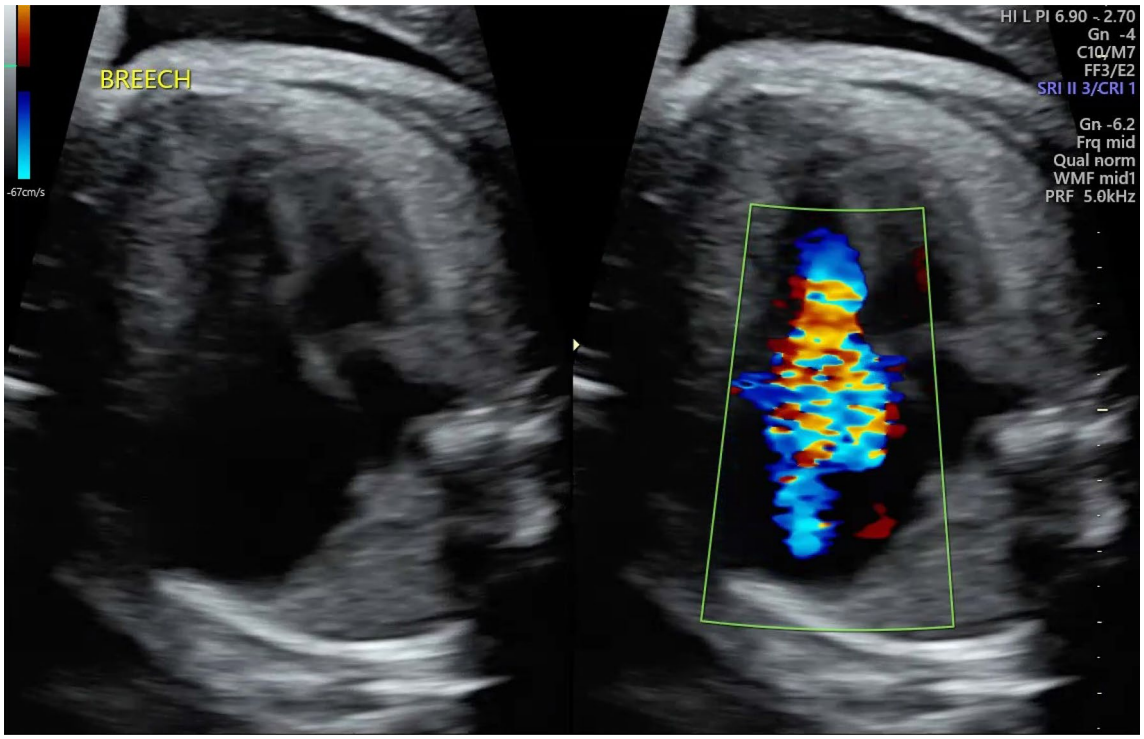


**Fig. 3** Fetal echocardiogram with color compares showcasing Ebstein's anomaly with severe tricuspid regurgitation

pulmonary artery pressures reaching systemic levels, the small functional RV may be unable to generate systolic pressure high enough to overcome the pulmonary diastolic pressure and open the pulmonary valve. Therefore, functional pulmonary atresia occurs [6].

Physiological closure of the PDA can either improve or worsen the condition of the neonate, and there must be careful monitoring at this time in severe Ebstein's anomaly [3, 4, 6]. If there is functional pulmonary atresia, there may be inadequate pulmonary blood flow, which may be further reduced after PDA closes, leading to worsening of cyanosis, and necessitating emergency intervention/surgery to maintain pulmonary blood flow [3, 6]. Conversely, if after PDA closes, the PVR drops, the RV may be able to overcome the lower pulmonary pressure and open the pulmonary valve. The resultant increased pulmonary blood flow may, therefore, improve cyanosis. Simultaneous reduction in RV afterload may reduce the degree of TR, with consequent reduced atrial right-to-left shunting, also reducing cyanosis.

LV volume and function may be impaired because of the dilated RA/RV. This may result in reduction of systemic output leading to metabolic acidosis and systemic hypotension [6].

Infants generally present with signs of heart failure or occasionally delayed detection of cyanosis, particularly if only mild [3, 4, 6, 19].

#### Examination Findings

This depends on the severity of Ebstein's anomaly and the presence/severity of right ventricular outflow tract (RVOT) obstruction, but usually there is varying degrees of cyanosis, prominent cardiac impulse, decreased intensity of 1st heart sound, single 2nd heart sound, soft holosystolic murmur of TR, and hepatomegaly secondary to severe TR.

### Adolescent/Adult

#### History

In younger children, the most common presentation is following an incidentally detected murmur, with echocardiogram revealing the diagnosis [3, 5, 19].

In older children and adults, the most common presentation is with palpitations and/or arrhythmias in up to 40% [6, 19]. An incidental murmur or exertional dyspnea is also a common feature. There may also be incidental finding of cardiomegaly on chest X-ray done for other reasons.

If there is an associated large ASD with mild Ebstein's anomaly, presenting features may be purely from the ASD.

Cyanosis may be a presentation in older patients. This can be either cyanosis on exercise (see below), or later in life may be due to rising RV end-diastolic pressure as the functionally abnormal RV becomes stiffer with resultant rise in RA pressure, causing bidirectional or right-to-left shunting across the ASD [5].

Older patients may even present with symptoms and signs of heart failure.

#### Examination Findings

Often there is a normal clinical examination, but clubbing may be present from chronic cyanosis. There may also have a soft pan-systolic murmur or hepatomegaly. If there is a significant ASD, patients may have fixed-split second heart sounds.

### The Effect of Exercise in Older Patients with Ebstein's Anomaly

Many patients with Ebstein's anomaly are asymptomatic with minimal cyanosis at rest. However, with exercise, they can become more cyanotic and have restriction of exercise tolerance. This happens for several reasons including

(1) an inability to increase RV output in response to exercise
(2) increased RV dilation during exercise from increased systemic venous return, further displacing the ventricular septum, worsening LV function which further impairs cardiac output, with resultant decreased oxygen delivery to tissues
(3) increased right-to-left shunting across the ASD during exercise producing cyanosis.

## Natural History

From fetal presentation, up to 27% of babies die before birth, with severe TR a significant risk factor [21]. The earlier Ebstein's is detected in pregnancy, the worse the outcome. From neonatal presentation, up to 18% of babies die in the neonatal period [4]. Risk factors include low birth weight, fetal diagnosis, tricuspid annulus $Z$ score $> 3$, and absent antegrade flow across the pulmonary valve. Thirty percent of patients die before the age of 10 years, with median mortality ~ 20 years [4].

Late effects of Ebstein's anomaly include RV failure, LV dysfunction, and increasing cyanosis. Heart failure was seen in 40% of adults in one early natural history study [22]. This heart failure can be due to either worsening RV dysfunction and impact on the LV, or from a combination of the underlying hemodynamics made worse by recurrent arrhythmia [22].

Arrhythmia also increases in frequency with age in unoperated Ebstein's anomaly. Sudden death from ventricular

arrhythmias is a recognized entity in both operated and non-operated patients. Patients can also develop endocarditis, cerebral abscesses, and stroke, especially in the presence of an ASD with right-to-left shunting.

## Diagnostic Investigations

### Fetal Echocardiogram

Fetal echocardiography allows for antenatal diagnosis of Ebstein's anomaly. This is important not only for prognostic counseling and planning of management but also is a key in attempting to differentiate Ebstein's anomaly from Tricuspid Valve dysplasia.

One key element of fetal counseling is attempting to predict and explain the likely prognosis. This has inherent difficulties but prognostic markers including the Celermajer index, the Simpson–Andrews–Sharland (SAS) score, and the recently published TRIcuspid malformation Prognosis Prediction (TRIPP) score can be used [23–25].

In addition, although this review focuses on Ebstein's anomaly, fetal echocardiographic differentiation from tricuspid valve (TV) dysplasia can be challenging. One sign that may help is in delineation of the origin of the tricuspid regurgitant jet [26]. In TV dysplasia, the regurgitant jet arises through the valve itself which is at the level of the TV annulus. This compares with Ebstein's where the jet origin is displaced inferiorly within the RV itself due to the leaflet displacement.

Following fetal diagnosis, associated pericardial/pleural effusion and hydrops fetalis should be excluded. The fetal rhythm should also be assessed due to the high incidence of arrhythmias. Some institutions advocate for fetal magnetic resonance imaging (MRI) to assess the lung volumes in those fetuses with severe cardiomegaly.

### Postnatal Investigations

Postnatally, diagnostic investigations are needed depending on the age group and whether the patient is being considered for surgical repair. Our recommendations are shown in Table 1.

### Investigation Details

#### ECG

12-Lead ECG can show variable findings depending on patient age, including right bundle branch block, RA hypertrophy with "Himalayan P Waves," shortened or prolonged PR interval secondary to either pre-excitation or prolonged atrial conduction in the enlarged RA.3 [4–6, 19], ECG changes may be related to conduction system abnormalities, as the atrio-ventricular node may be compressed with abnormal formation or fibrosis of the central fibrous body and the right bundle branch [7].

#### CXR

Mild cases may have normal radiographic findings, with severe cases conversely having a wall-to-wall heart from extreme cardiomegaly with pulmonary hypoplasia. The degree of cardiomegaly is usually proportional to severity

**Table 1** Essential and useful investigations stratified by age group

| | Neonate | Infant | Child | Adolescent/adult |
|---|---|---|---|---|
| Essential investigations | ECG | ECG | ECG | ECG |
| | CXR | CXR | CXR | CXR |
| | TTE | TTE | TTE | TTE |
| | Continuous telemetry monitoring (unless in extremis) | Holter | Holter | Holter |
| | | | | Cardiac MRI |
| | | | | CPET |
| Additional investigations | Cardiac CT to clarify pulmonary artery anatomy | Cardiac CT/Cardiac MRI | Cardiac CT/Cardiac MRI | Cardiac CT/Coronary Angiogram |
| | | Intra-operative TEE to guide surgical repair | Pre-operative TEE | Pre-operative TEE |
| | | | CPET | EPS |
| | | | EPS | |

*ECG* electrocardiogram, *CXR* chest X-ray, *TTE* trans-thoracic echocardiogram, *CPET* cardio-pulmonary exercise testing, *TEE* trans-esophageal echocardiogram, *EPS* electrophysiology study

of TR. Adults may have signs of a large ASD with prominent pulmonary vasculature.

### TTE

There are standard views that all patients with congenital heart defects should have on echocardiogram; however, in Ebstein's anomaly, the tricuspid valve may not be easily seen particularly if the valve is severely displaced, and visualization may require "off-axis" windows. A complete TTE protocol can be found in Appendix 1, but key features include

(1) Tricuspid valve leaflets (particularly antero-superior) are elongated, redundant, and dysplastic with abnormal chordal attachment.
(2) Apical displacement of the hinge point of the tricuspid valve septal leaflet, from the mitral valve insertion. Apical displacement of > 15 mm in children and > 20 mm in adults is diagnostic [27, 28]. The displacement index can also be calculated (Displacement index = displacement length/BSA), with diagnosis made when the displacement index is > 8 mm/m$^2$ in adults [27].
(3) Enlarged RA with atrialized RV and small functional RV. The anatomic severity of Ebstein's anomaly can be calculated using the Great Ormond Street (GOS) Equation, where the chamber area is measured at end-diastole in an apical four-chamber view [19].
    - Ratio: (RA + Atrialized RV)/(RV + LA + LV)
    - Four grades of increasing severity:
        - Ratio < 0.5 = grade 1
        - Ratio 0.5 to 0.99 = grade 2
        - Ratio 1 to 1.49 = grade 3
        - Ratio ≥ 1.5 = grade 4
    - Grades 3–4 are associated with worse prognosis
(4) Regurgitation of varying severity, which can often be underestimated due to the location of the jet.
    - Modified and off-axis echocardiographic views often necessary to accurately measure TR jet width and get an accurate Doppler index.
(5) RV outflow tract obstruction can occur secondary to redundant tricuspid valve tissue of the anterior leaflet
(6) There may be functional or anatomic pulmonary atresia
(7) An ASD may be present and is usually non-restrictive
(8) Impaired RV function may be present as well as LV dysfunction secondary to abnormal septal wall interaction

Echocardiography may also be used to determine the Carpentier grading of Ebstein's severity [29]:

- Type A: adherence of septal and posterior leaflets but without restricting volume of functional RV
- Type B: RV atrialized with normal anterior leaflet
- Type C: Severe restriction of anterior leaflet, which may cause RV outflow tract obstruction
- Type D: Almost complete atrialization of RV with just small residual infundibular component

Finally, advanced RV functional indices can be used on TTE, which correlate well with cardiac MRI including right ventricular global longitudinal strain (RVGLS), and 3D volumes and ventricular ejection fraction (EF) [30].

### TEE

It has a role both as a diagnostic investigation particularly for older patients, as well as in the intra-operative setting to guide surgical repair. Key views include

- Mid-esophageal 4-chamber view allows imaging of the anterior and septal leaflets
- RV inflow-outflow view is useful for Doppler assessment of TR
- Trans-gastric views allow identification of all three leaflets, with the best image of the chordae tendineae and papillary muscles in the trans-gastric RV inflow view
- Mid-esophageal views will also allow identification of atrial septal defects.
- 3D TEE helps in visualizing the tricuspid valve leaflets both from the atrial and ventricular perspectives

### Holter/Event Recorder

This has a key role in assessment of arrhythmias and detection of pre-excitation which may be intermittent. This is particularly important as the 70-year risk of sudden cardiac death is 15% or 0.2% risk/year [9]. Post-operatively 24-h ECG monitor can be useful as screening tool for atrial or ventricular arrhythmias.

### Cardiac Catheterization

Generally, this has little role in the pre-operative management of Ebstein's anomaly patients, unless there are PVR concerns. Catheterization may be necessary post-operatively if there are coronary artery concerns, particularly if extensive RV plication has been used as this may cause occlusion/twisting of the RCA. Catheterization is the gold standard for coronary artery anatomy delineation or if concerns about coronary artery disease in adults.

### Cardiac MRI

This is the gold standard for assessment of right ventricular volumes and has key advantages in investigating Ebstein's anomaly [31]. It has an important role particularly in older children and adults where TTE acoustic windows may be sub-optimal. The ability to assess the RV in orthogonal planes at any angle, means the tricuspid valve morphology, displacement, and regurgitation can be extensively interrogated [32].

A combination of the traditional short axis cine stack and trans-axial cine stack, as well as the four-chamber, two-chamber and RVOT cines, is helpful to delineate the apical displacement and effective volume (Fig. 4) [31]. Calculation of RV volume can be done both with and without inclusion of the atrialized RV, and this has the advantage of giving the surgeon an indication of likely RV volume following surgical repair [32].

A contiguous cine stack done parallel to the effective tricuspid valve plane can be particularly helpful to show the valve morphology "en-face" [31]. Late Gadolinium Enhancement may also be used to detect fibrosis in the atrialized portion of the RV; however, the relative thinness of the free wall makes this challenging.

### CPET

This provides a useful indicator of exercise capacity as well as maximal oxygen uptake. It can also show a patient's response to exercise, unmask exercise-related symptoms, and detect exertional cyanosis. Due to the need for patient engagement and co-operation, it is mainly useful in older children and adults.

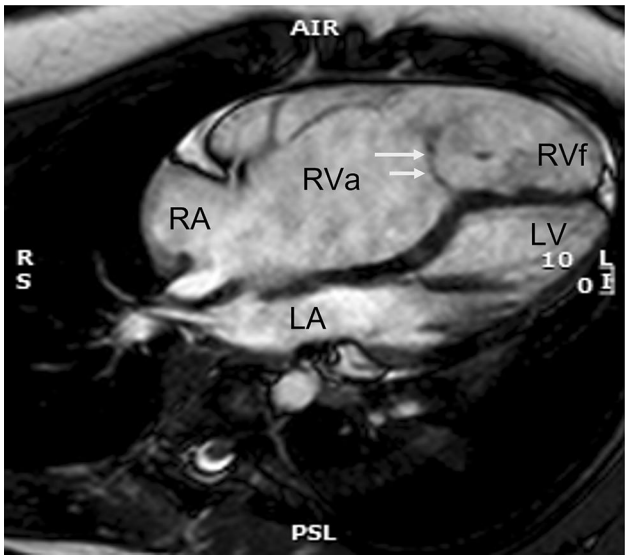


**Fig. 4** Steady-state free precession cardiac magnetic resonance imaging, four-chamber view, showing severe apical displacement of septal leaflet of tricuspid valve (white arrows). *RVf* functional right ventricle, *RVa* atrialized right ventricle, *RA* right atrium, *LA* left atrium, *LV* left ventricle

### EPS

Early publications demonstrated that for patients who underwent EPS to evaluate for an accessory pathway, 77% were right sided (40% right anteroseptal, 37% right free wall) [19]. The practice of doing an elective EPS prior to surgical repair has been suggested by the practices and publications from Boston Children's and Mayo Clinic groups [33, 34].

The Boston Children's practice is to perform an EPS in almost all Ebstein's patients prior to surgery, regardless of arrhythmia history. This followed review of their data showing 70% of Ebstein's patients had significant EPS findings [34].

The Mayo Clinic approach involves performing preoperative EPS in patients with WPW, known or suspected arrhythmias. In younger children; however, only selective EPS are done due to the increased associated risks [33].

2018 AHA guidelines suggest that EPS ± ablation can have a role in adults with Ebstein's where there is pre-excitation, as well as prior to having tricuspid valve surgery whether there is pre-excitation or not [35].

Our recommendations include

- Children should undergo elective EPS prior to surgical repair if they have WPW or documented arrhythmias and body weight is > 25 kg.
- There may be benefit in doing EPS for patients who are having palpitations but no documented evidence of WPW or arrhythmias. These patients may also benefit from implantable loop recorder to capture these episodes.
- EPS, although possible in patients who are 10–25 kg, is safer in patients > 25 kg particularly if they need ablation. The risks and benefit need to be carefully balanced.
- Adult patients should undergo elective EPS for symptomatic palpitations or overt pre-excitation.
- Routine EPS in asymptomatic patients or those without evidence of WPW/arrhythmias should be used selectively.

## Management

The approach to the management of patients with Ebstein's anomaly differs greatly depending on the age at presentation and the associated lesions. Management can be divided into medical, EPS/ablation for arrhythmias, and surgery.

Indications for surgery include

- Critically ill symptomatic neonates despite intensive medical management
- Severe or progressive cyanosis
- Progressive right heart dilation
- Congestive heart failure
- Deteriorating systolic function
- RV outflow tract obstruction
- Decreasing or severe limitation of activity (NYHA functional class 3–4)
- NYHA functional class 1–2 & cardiomegaly
- Paradoxical embolus
- Recurrent or intractable life-threatening arrhythmia with WPW syndrome

## Fetal Management

Unless there is antenatal SVT, requiring transplacental (maternal) therapy with antiarrhythmics, most programs proceed with expectant management.

Some institutions advocate for increased surveillance once fetuses reach 32-week gestation. This includes weekly surveillance with non-stress test, biophysical profile, and/or fetal echocardiogram to monitor for development of cardiac dysfunction, abnormal Doppler findings, effusions, and/or hydrops. If there is development of abnormal findings, multidisciplinary discussions with maternal fetal medicine, neonatology, and cardiology should determine optimal timing of delivery. The risks of morbidity and mortality associated with premature delivery need to be weighed against the risk of in-utero demise. Early delivery would have to be carefully managed with aggressive neonatal care including intubation, prostaglandin (PGE1), nitric oxide, diuresis, and drainage of effusions.

In the most severe cases where the RV is unable to generate adequate pressure to provide forward flow and pulmonary insufficiency is present, a circular shunt develops leading to potentially life-threatening fetal cardiac hemodynamics. In utero, a circular shunt involves pulmonary insufficiency, tricuspid regurgitation with right-to-left flow across the foramen ovale into the LV and aorta with retrograde flow in the ductus potentially compromising cerebral, systemic, and placental flow. In this scenario, perinatal ductal restriction may reduce ductal flow, reduce systemic steal, and therefore, improve both the fetal cerebral and systemic perfusion. This can be achieved by either maternal nonsteroidal anti-inflammatory drugs (NSAID) or chronic maternal hyperoxygenation therapy [36, 37]. NSAID use has been reported with enteral Indomethacin for between 11 and 49 days with encouraging results [36]. Maternal hyperoxygenation has similarly been reported using non-rebreathe facemask oxygen for twelve hours daily [37]. This not only results in constriction of the fetal ductus arteriosus but also may reduce pulmonary vascular resistance, increasing antegrade pulmonary blood flow in fetal life [37].

## Neonatal Management

### Medical Management

The initial priority is to stabilize the neonate if severely cyanotic, which may include a combination of ventilatory support, PGE1 infusion, inotropic support, and correction of metabolic acidosis. Neonates may also need sedation and paralysis to reduce PVR and reduce ventilator pressures [38]. PGE1 infusion may improve cyanosis by keeping the PDA open and increasing the pulmonary blood flow until the PVR naturally decreases. However as noted earlier, this can prolong functional pulmonary atresia with resultant worsening of TR and subsequently increased right-to-left shunting at the atrial level.

In general, neonates improve as PVR falls from increased forward flow through the RV and the pulmonary valve, with reduction of the right-to-left shunting at the atrial level. Some neonates may need nitric oxide as a pulmonary vasodilator to assist in this process [38].

If neonates are only mild to moderately cyanotic, they may not need intensive medical management and may just require watchful waiting until ductal closure. If neonates are asymptomatic, they may only need observation following confirmation of the diagnosis.

### Arrhythmia Management

Patients rarely develop arrhythmias in the neonatal period, but if they develop SVT, then anti-arrhythmic medication or cardioversion may be warranted.

### Cardiac Catheterization

Cardiac catheterization is rarely required in the neonatal period, but in certain situations ductal stenting may be an alternative to maintaining the baby on PGE1 infusion or instead of a surgical systemic-pulmonary shunt [39].

### Surgical Management

Neonatal indications for surgery include persistent mechanical ventilator dependency, right heart failure unresponsive to medical therapy, severe TR associated with severe cyanosis, persistent need for significant intravenous inotropic support, and PGE1-dependent circulation [40].

The Knott-Craig algorithms (Fig. 5) are the most widely quoted and respected management approach for neonatal Ebstein's anomaly [28–30]. This algorithm utilizes the

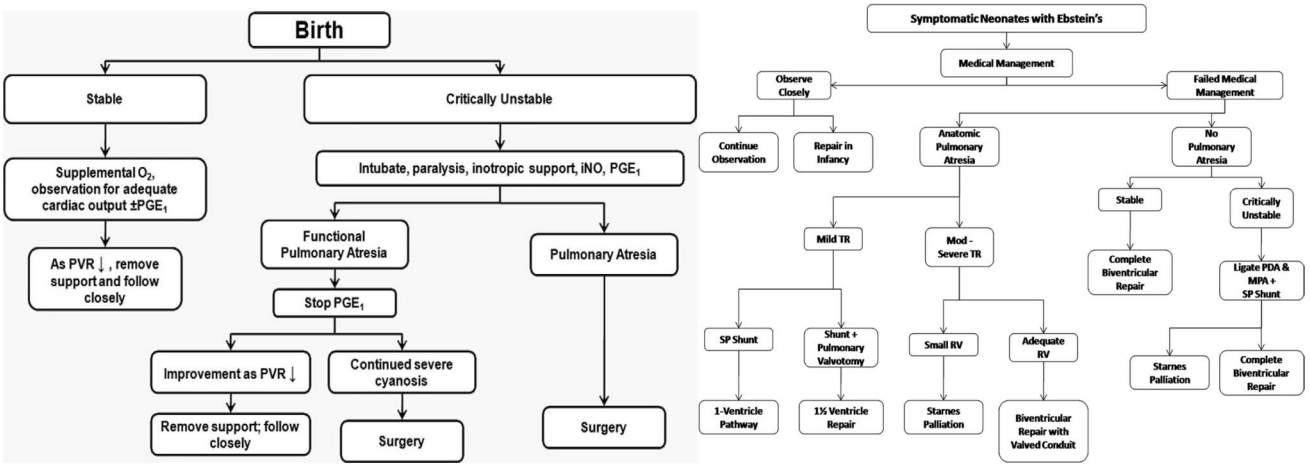


**Fig. 5** Knott-Craig algorithms for management of neonates with Ebstein's anomaly. Reproduced from Knott-Craig et al. [40]

cone repair as the surgical technique for 1&1/2 ventricular and biventricular strategies.

Compared to infants, neonates have higher mortality rates. Even when risk stratified by need for pre-operative extra-corporeal membrane oxygenation, mechanical ventilation, or cardiogenic shock, operative mortality was higher for neonates compared to all other age groups [41]. However, the Society of Thoracic Surgeons (STS) database suggests that there is no increased mortality risk for repeat operations during the neonatal period [42].

In addition to the above conventional approaches, recently we have introduced our own surgical management, based on a different perspective.

When a neonate is clinically stable, with morphology unfavorable for surgical repair and with ductus-dependent pulmonary blood flow, we either maintain the neonate on PGE1 infusion, or proceed to a systemic-to-pulmonary shunt. If the morphology is suitable for surgical repair, and a cone procedure is either not feasible or advisable, we prefer to avoid the Starnes approach toward a future univentricular type of repair. The reason is that, in our personal experience, the exclusion of the right ventricle from the circulation, by modifying the volume and pressure overload of the left ventricle, impairs the left ventricular function, and this is certainly a negative factor for the long-term outcome of future Fontan circulation. In addition, we generally try to keep all options open for future biventricular repair. Therefore, in these neonates, we repair the malformed tricuspid valve, to reduce as much as possible, the degree of the TR and right atrial volume, and close the inter-atrial communication with a fenestrated patch. The early results obtained with this approach in our recent group of patients are quite encouraging (Fig. 6).

## Management of the Patient Who Presents in Infancy

Patients who present during infancy, typically have less physiologic derangements than those who present during the neonatal period. If they develop signs of heart failure, they may need medical treatment with diuretics and/or digoxin. If there is LV dysfunction secondary to a dilated RV, right ventricular afterload reduction may help.

Arrhythmias: Anti-arrhythmic medications are the mainstay of treatment.

Cardiac catherization is rarely needed unless there are PVR concerns.

Surgical management: Clinicians usually must decide between 1 and 1/2 ventricular repair or biventricular repair. Univentricular repair is rarely indicated beyond the neonatal presentation. The reported mortality following surgery beyond the neonatal period is relatively low (4–23%) [42]. The cone repair should be the choice for biventricular repair in these patients, with selected cases suitable for plication of the atrialized chamber and tricuspid vale repair only.

## Management of the Patient Who Presents as a Child, Adolescent, or Adult

The general approach to adolescents and adults' management is broadly similar, with the caveat that as adults get older, consideration should be given to co-existing coronary artery disease. Heart failure should be managed medically. Good dental hygiene should be emphasized with dental inspection for patients undergoing interventional and/or surgical procedures.

The mainstay of arrhythmia treatment is with EPS ± ablation, or intra-operative ablation. This is a class 1 indication

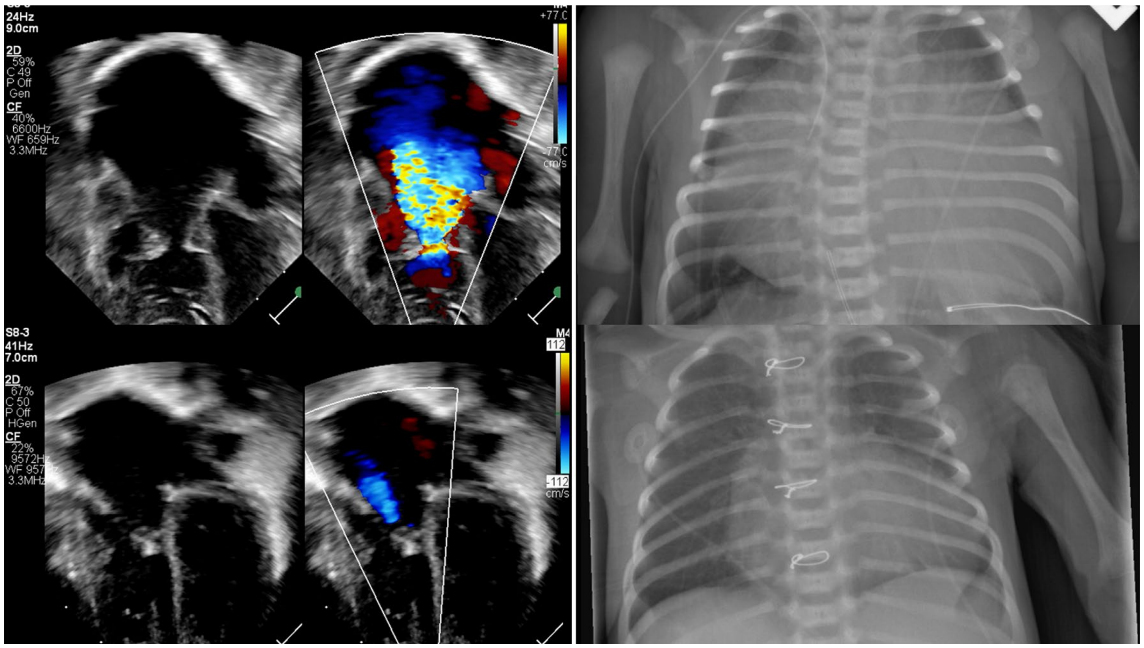

**Fig. 6** Pre- and post-operative echocardiograms using color compare, and CXR demonstrating changes in severity of tricuspid regurgitation and cardiomegaly post-Ebstein's repair in a 2-day-old neonate

from AHA guidelines where there is either high-risk pathway conduction or the presence of multiple accessory pathways [35]. Success rate is 95% for ablation of isolated right-sided accessory pathways and 76% for multiple pathways [4].

ICDs have a potential role in secondary prevention of Sudden cardiac death (SCD) in patients with Ebstein's anomaly who have previously had VF or cardiac arrest [9]. However there is no consensus on their use for primary prevention of SCD.

Cardiac catheterization has a role in adult patients, for PVR evaluation prior to surgery. Interventional ASD device closure can help improve oxygen saturations and stamina if there is significant cyanosis on exertion or reduced exercise tolerance. ASD closure can also help if Ebstein's is mild, and the main effect is volume loading from the ASD. For some patients with bioprosthetic valve failure, tricuspid valve-in-valve implantation (off label use of Melody (Medtronic, Minneapolis, USA) or Sapien valves (Edwards, Minneapolis, USA), can avoid or postpone reoperative cardiac surgery [43].

## Surgery

Most children should be able to have a biventricular repair. Rarely some patients will need 1&1/2 ventricular repair if the RV cavity or post-surgical tricuspid valve orifice are too small. Intra-operative anti-arrhythmic interventional catheter or surgical procedure may be necessary with either a MAZE or cryoablation.

Most patients should be able to undergo biventricular repair if presenting in adolescence or adulthood. The reported hospital mortality following surgical repair in adults was 0.7%, but evidently these outcomes were reached in a selected population, not including the most critically unwell patients who may have presented much earlier but only had surgery in adolescence/adulthood [42]. In our personal experience, when older patients with Ebstein's are referred for surgery, not infrequently the tertiary referral hospitals have to deal with very critically ill patients, due to prolonged severe cyanosis, RV dysfunction, and arrhythmias. In these cases, the combination of a superior cavo-pulmonary shunt (1&1/2 ventricle approach) with a perforated patch to close the inter-atrial communication is a safe surgical approach.

The European Society of Cardiology 2010 guidelines recommend ASD/PFO closure should be performed at the time of valve repair, with the following two indications for surgery in Ebstein's anomaly [44]:

(1) > Moderate TR & symptoms (NYHA class > II or arrhythmias) *or* if there is deterioration in CPET performance
(2) Asymptomatic but progressive RV dilation, reduced RV systolic function, or progressive cardiomegaly on CXR

Similarly, the 2018 AHA guideline recommendations for surgery are [35]:

(1) Class I indication where there is significant TR and at least one of symptoms of heart failure, objective documentation of reducing exercise capacity, or progressive echocardiographic evidence of RV systolic dysfunction
(2) Class IIa indication where there is significant TR and either progressive RV enlargement, right-to-left ASD shunting causing desaturation, paradoxical embolism, atrial tachyarrhythmias.

#### Cardiac Transplantation

Transplantation and the availability of organs is variable depending on the country and health system but is not a straightforward option and usually patients have to be significantly unwell to be given priority. However, referral for transplantation assessment should be considered for patients with Ebstein's anomaly, particularly where there is no clear surgical option, or in patients where there is severely impaired LV function [45].

#### The Asymptomatic Patient

These patients present a dilemma and should be investigated and managed very carefully. Although they may be incidentally picked up, often symptoms can be unmasked during detailed investigations including CPET. Many older adults may be used to and tolerant of their exercise limitation and objective evidence may be helpful in the decision making of these particularly challenging patients.

## Surgical Techniques

The surgical techniques used in Ebstein's anomaly have changed over time, progressing from initial mono-leaflet repair to circumferential repair with the cone procedure. This has since been subsequently modified in search of the "perfect" repair.

Surgical techniques include

(1) Mono-leaflet repair:
    (a) Danielson technique
    (b) Carpentier technique
(2) Modified Carpentier repair + ASD closure
(3) Cone Repair
(4) Tricuspid valve replacement
(5) 1&1/2 ventricular type of repair with bidirectional superior cavo-pulmonary shunt
(6) Univentricular approach
(7) Univentricular approach + RV exclusion (Starnes procedure)
(8) Surgical ablation of accessory pathway at time of operation in the presence of WPW

### Mono-leaflet Repair

In the first decades of surgical management for patients with Ebstein's anomaly, the traditional thinking of mono-leaflet repair was that the most important determinant of a durable mono-leaflet repair was a freely mobile antero-superior leaflet, particularly the leading edge. Outcomes were, therefore, poor if there was extensive adherence (> 50%) of the antero-superior leaflet to the ventricular myocardium.

The two main techniques were the Danielson technique from Mayo Clinic, Minnesota, and the Carpentier technique from Paris, France.

#### Danielson Technique

This was the first described mono-leaflet repair and could be applied to about 60% of patients [46]. It involved transverse/radial plication of the atrialized RV, and selective narrowing of the tricuspid valve orifice, by mobilizing only the antero-superior leaflet to create a mono-leaflet valve at the true morphological tricuspid valve annulus. The mural and septal leaflets were usually non-functional because of severe hypoplasia and not incorporated [47].

This has since been modified with transverse plication only used in selected cases of the thin/transparent-atrialized RV not effectively contributing to the RV function [48]. The tricuspid valve repair is now done at the *level of the functional annulus;* where the existing valve hinge point is within the RV. Finally, the ASD is closed.

This transverse plication modification was used in an attempt to reduce post-operative ventricular arrhythmias. These arrhythmias were believed to be due in part to suture lines in the plicated atrialized ventricular portion and/or interruption of small branches of the right coronary artery [48]. The modified Danielson technique has good long-term results for TR, with 74% < grade 2 TR at mean 12 years [48]. Additionally, the freedom from re-operation was 91% at 5 years and 61% at 15 years, with only 5% mortality [48, 49].

#### Carpentier Technique

This was developed in 1988 and could be applied to *most patients* [3, 8, 46]**.** It involved mobilization of the anterior leaflet with detachment from the annulus. The atrialized ventricle was then plicated longitudinally/vertically at right angle to the Danielson technique. The anterior leaflet was then reattached at *the true tricuspid valve annulus*, and the annulus remodeled and reinforced with a prosthetic ring, followed by ASD closure. The major issues, however, were the comparatively higher incidence of late complications

and reported 15% mortality (threefold higher vs the original Danielson technique) [3, 8, 46].

This technique was subsequently modified by Quaegebeur without the use of a prosthetic ring, with early results showing no deaths; however, 44% of patients had at least mild post-operative TR [46, 50].

## Cone Repair

This was developed in 1989 by Jose da Silva in Sao Paolo, as a modification of the Carpentier repair [46, 51]. The anterior and posterior leaflets were detached from their anomalous attachments as a single piece. The abnormal papillary muscles and other tissue between leaflets and corresponding RV wall were divided, aiming to preserve attachments to the leaflet-free edges. This essentially delaminates the leaflets. The overall effect was that aside from the septal leaflet, only the normal attachment of the anterior leaflet to the true tricuspid annulus and its subvalvular apparatus were left in place. The posterior leaflet-free edge was rotated clockwise and sutured to the anterior leaflet edge forming a new tricuspid valve, resembling a "cone." In some patients, the septal leaflet if sufficiently developed, was included.

The atrialized RV was longitudinally plicated, and a new annulus was constructed at the true morphological level by plicating the tricuspid annulus to closely match the circumference of the newly created cone-shaped valve, which was then sutured to the new annulus. Superficial suturing was performed near the expected location of the atrio-ventricular node to avoid complete heart block. *In our personal experience, because of the very thin-walled right atrium and atrialized RV portion, we reinforce with pledgeted sutures leaving the pledgets on the external side of the atrial wall.* This newly created cone-shaped valve allows central opening and blood inflow to the RV and closes with full leaflet coaptation. Additionally, a fenestrated ASD is created to allow atrial right-to-left shunting if needed.

The theoretical benefit of the "cone" repair compared to the mono-cuspid Carpentier repair is full circumferential attachment of the valve tissue to the annulus should further reduce TR. Using septal leaflet tissue would make the annulus wide enough to avoid tricuspid valve stenosis. Additionally, compared to the Danielson repair, there should be less need for tricuspid valve replacement (reported in up to 50% of those cases) [46, 52].

Modifications to the "cone" repair have been described by the Mayo Clinic group, using ringed annuloplasty for support and stabilization of the new "cone" annulus. In almost a third of cases, autologous pericardium is also used to both augment the anterior leaflet and increase the height of the leaflet, as well as to augment the circumference of the "cone" itself [52, 53].

The Wisconsin group also describes a modification whereby the entire annular leaflets are detached (360° detachment of tricuspid leaflets), the leaflets are then rotated 60° in a counterclockwise direction and then reimplanted [54]. This is done to both reduce and distribute tension on the reattached leaflets, as well as to reduce twisting of the papillary muscles and/or subvalvular apparatus that can be seen with the Cone procedure, resulting in better leaflet alignment, potentially better valve function with the aim of improved repair longevity [54].

### Outcomes of the Cone Repair

Several studies have shown no significant tricuspid valve stenosis, significant reduction of the degree of TR, reduction in RV size with time, and lower mortality following "cone" repair [30, 41, 46, 54–56]. However, Holst et al. reported decline in RV function in 32% ($p < 0.0001$), with some improvement on the late follow-up [41].

Using Cardiac MRI, the Boston group showed following cone repair, a decline in estimated TR fraction ($56 \pm 19\%$ to $5 \pm 4\%$, $p < 0.001$), reduced RV End-diastolic volume ($242 \pm 110$ ml/m$^2$ to $137 \pm 82$ ml/m$^2$, $p < 0.001$) and stroke volume ($101 \pm 35$ ml/m$^2$ to $51 \pm 7$ ml/m$^2$, $p < 0.001$), unchanged Right Ventricular Ejection Fraction, improved LV EDV ($68 \pm 13$ ml/m$^2$ to $85 \pm 13$ ml/m$^2$, $p < 0.001$) and stroke volume ($37 \pm 8$ ml/m$^2$ to $48 \pm 6$ ml/m$^2$, $p < 0.001$), unchanged Left Ventricular Ejection Fraction but improvement in LV synchronous contraction ($32 \pm 17$ ms vs. $21 \pm 9$ ms, $p = 0.02$) and basal septal circumferential strain ($16 \pm 7\%$ vs. $22 \pm 5\%$, $p = 0.03$) [57].

Through serial studies using echocardiography and then Cardiac MRI, the Great Ormond Street (GOS) hospital group showed decreased TR (69% to 10%; $p = 0.014$) and RA area (52.4 to 16.7 cm$^2$, $p = 0.04$), increased functional RV area (26.1 to 35.2 cm$^2$, $p = 0.021$), increased indexed LVEDV (50 to 69 ml/m$^2$; $p = 0.03$), and stroke volume (30.4 to 44.1 ml/m$^2$; $p = 0.015$), and significant reduction in GOS score ($1.07 \pm 0.24$ vs. $0.25 \pm 0.06$, $p = 0.007$) [58, 59]. Conversely, both tricuspid annular plane systolic excursion (TAPSE: $26.42 \pm 5.79$ mm vs. $8.75 \pm 3.18$ mm, $p < 0.001$) and RV fractional area change (FAC: $45.00 \pm 8.13\%$ vs. $35.46 \pm 5.76\%$, $p = 0.038$) were reduced post-op compared to pre-op. LV peak systolic strain ($-20.49 \pm 2.79$ vs. $-17.73 \pm 2.76$, $p = 0.041$) was also reduced but with medium-term recovery.

These studies clearly show the RV gets smaller with marked improvement in TR, directly related to the "cone" technique. This has been reflected in a direct comparison of the "cone" to conventional repair techniques from the Munich group [52].

The increase in LV volume and synchronous contraction can be explained by the improvement in septal interaction

to the LV from a less dilated RV. The deterioration in both LV and RV function is unlikely to be related to the actual "cone" repair and change in physiology but is more easily explained by the impact of cardio-pulmonary bypass and aortic cross-clamping. Ischemia–reperfusion injury affects mainly the endocardial layers of the myocardium in the early post-operative period. This consists predominantly of longitudinal fibers, which is reflected in impairment of longitudinal strain analysis, while radial strain and ejection fraction are conversely unchanged [58]. This functional impairment would likely be similar for other repair strategies, but there is a paucity of imaging data from other surgical techniques to prove this [58]. RV function deterioration can also be explained by the non-plicated atrialized RV now being included in the functional RV. This thin wall can become fibrotic over time, particularly in older patients who have had longstanding TR with resultant chronic increased RV preload [58]. Additionally, RV FAC and TAPSE are load dependent, and there is clear evidence that loading conditions change following "cone" repair with marked reduction in RV preload, potentially affecting the validity of these comparisons. Lastly, as Ebstein's anomaly embryologically forms from a failure of delamination of the RV, it intrinsically can be considered more an RV disease rather than solely of the tricuspid valve itself.

## Repair of Associated Pulmonary Atresia in the Neonate

One of the key dilemmas in Ebstein's surgery is neonatal presentation of Ebstein's anomaly and particularly with associated pulmonary atresia [60]. If there is anatomical pulmonary atresia, a systemic-to-pulmonary artery shunt is the traditional approach to management. Knott-Craig highlighted the importance of this in neonatal Ebstein's repair and also described RVOT patching to provide effective antegrade pulmonary blood flow. Aggressive reduction atrioplasty and fenestrated ASD closure were also incorporated, with good results including no cardiac mortality, sinus rhythm throughout, and all with < grade 2 TR.

## ASD Closure

Another key surgical consideration is simultaneous ASD closure. The majority of tricuspid repair techniques advocate ASD closure; however, in the context of small RV cavity/poor RV function/high PVR, fenestrated ASD closure would allow right atrial decompression [60].

In our personal experience, we prefer the safety of a fenestrated ASD patch, with future device closure of the residual defect if needed.

## Tricuspid Valve Replacement

If tricuspid repair fails or if valve leaflets are deemed unsuitable, then tricuspid valve replacement may be necessary. This has been reported in 20–30% of patients in conventional repair strategies, but with 5–20% hospital mortality, compared with 7% of patients post-cone repair [52, 61].

## One-and-Half Ventricular Repair (Bidirectional Glenn with Tricuspid Valve Repair)

In some patients, a bidirectional Glenn is used along with tricuspid valve repair to achieve better outcomes [62, 63]. This is usually done outside of the neonatal period once the PVR has dropped. The Glenn reduces preload on the dilated and poorly contracting RV, allowing an aggressive repair strategy [64]. The functional orifice of the tricuspid valve can be reduced and what would be a borderline valve becomes functionally adequate, as only 2/3rd of the previous systemic venous return passes through the valve. There is also reduced risk of tricuspid valve stenosis and progression of residual TR, from volume load reduction [49].

This one-and-half approach has been described by the Stanford group, as a planned procedure where there was inadequate RV function, shown by cyanosis at rest or with exercise [64, 65]. Also, as a salvage procedure, when coming off cardio-pulmonary bypass following tricuspid valve repair, there was either tricuspid valve stenosis or mean RA pressure exceeded $1.5 \times$ LA pressure, then a bidirectional Glenn was subsequently performed [64]. They showed an increase in mean oxygen saturation increase from $89.5 \pm 5.9\%$ to $96.9 \pm 3\%$ ($p = 0.003$), with no Glenn-related complications. Only three patients (9.7%) needed TV replacement [64].

2018 AHA guidelines recommend this one-and-half ventricular repair as a class IIb indication for ACHD patients where there is severe RV dilation and severe RV systolic dysfunction but where there is preservation of LV function along with non-elevated left atrial and LV end-diastolic pressure [35].

## Univentricular Approach

Despite all efforts, some patients may necessitate a univentricular pathway where there is inadequate functional RV to support the pulmonary circulation, an inadequate anterior leaflet, or co-existing anatomic pulmonary atresia.

In the first stage, an atrial septectomy is performed with modified Blalock-Taussig shunt, and consideration of PA banding/transection depending on severity of pulmonary valve regurgitation. The second stage is creation of a bidirectional Glenn and finally the endpoint, completion of the Fontan pathway [57].

### Univentricular Approach + RV Exclusion (Starnes Procedure)

In certain neonates where tricuspid valve repair is not feasible or has failed, then a univentricular approach combined with tricuspid valve closure and RV exclusion can be considered. This was first described by Vaughan Starnes in 1991, showing good initial results with 79% long-term survival [66]. The pathophysiology created is that of tricuspid atresia, with a patch attached at the level of the anatomic tricuspid valve annulus [58]. This patch includes a fenestration, to allow RV decompression of Thebesian venous drainage [58]. The coronary sinus is kept on the RA side of the patch to improve RV decompression and maintain exposure of the coronary veins to low pressure. A modified Blalock-Taussig shunt provides pulmonary blood flow and an atrial septectomy allows the drainage of the systemic venous return to the left side of heart [58].

The Starnes exclusion stops TR, which should also lead to the reduction in RV cavity size and reduce septal wall displacement, allowing the LV to return to its normal globular shape with normalization of LV function [6].

Performing a Starnes procedure technically commits the patient to a univentricular repair, but there have been case-reports of reversal, with either full biventricular or one-and-half ventricular repair achieved [59]. Additionally if there are RV arrhythmias, access for EPS/ablation catheters is restricted. Conversely, in the absence of ongoing RA enlargement, these patients may be less likely to have late arrhythmias.

### Surgical Ablation of Accessory Pathway

The potential need for simultaneous surgical electrophysiology ablation procedures should be considered, including surgical cryoablation or Cox-MAZE procedure. This is mainly right sided but occasionally patients may need bi-atrial.

## Post-operative Care

### Frequency of Review

Following hospital discharge, all pediatric patients should be reviewed within 4 weeks. Ongoing frequency of follow-up is patient specific but ideally should be every 3–6 months for the first post-operative year and then annually.

Adult patients should be seen within 3 months in an adult congenital heart disease (ACHD) clinic and at least annually thereafter.

### Post-operative Investigations

Due to the risk of arrhythmias, every patient should have an ECG at each clinic appointment. Additionally, to screen for ventricular arrhythmias, Holter monitoring should be performed annually in the first few years following surgery, particularly as the one-year risk of sudden death following Ebstein's surgery is 2% [9].

Trans-thoracic echocardiogram should be done at each clinic appointment.

Cardiac MRI is helpful to assess RV changes and LV volumes following tricuspid valve repair. Ideally this should be done 2–3 years following tricuspid valve repair but may be done more frequently when ultrasound acoustic windows are limited. Further follow-up cardiac MRI should be done every 3–4 years or at the discretion of the care team.

CPET should be considered every 2–3 years for assessing exercise tolerance and for arrhythmia surveillance.

### Medications

Short- and long-term medication usage is institution specific, with recommendations from the Mayo Clinic group for beta-blockers, ACE-Inhibitors, sildenafil in the case of elevated PVR, and amiodarone for 2–3 months if surgical RV plication was done or the patient-developed arrhythmias [61].

We suggest, therefore, all patients to be discharged on beta-blockers or ACE inhibitors for ventricular remodeling, and amiodarone or other anti-arrhythmic drugs depending on arrhythmia history and ablation procedures. Additionally, serious consideration should be given for sildenafil use if there are any PVR concerns in the peri-operative period.

## Ebstein's and Pregnancy

This review would not be complete without going full circle and considering the effect of pregnancy on the Ebstein's circulation. If the patient has a good functional status, then generally pregnancy is well tolerated [67].

For patients with Ebstein's anomaly, especially with more significant disease, there is an increased risk of prematurity and fetal loss [67]. If women are cyanotic, there is significantly lower birth weight of the liveborn baby, at 2.53 kg in Ebstein's anomaly vs 3.14 kg in controls ($p < 0.001$) [67]. Additionally, there is up to 6% risk of congenital heart disease in the baby [67].

Conversely, pregnancy does not put a significant strain on the Ebstein's heart, with no significant maternal arrhythmias, complications, or death [67]. The cardiothoracic ratio and TR pressure gradient can significantly increase during

pregnancy compared to prepregnancy values, but these differences tend to resolve following delivery, indicating temporary pregnancy-related hemodynamic effects [67].

Therefore, in accordance with 2018 AHA guidelines, women with Ebstein's anomaly should receive MDT prepregnancy counseling on impact of pregnancy on the maternal heart as well as on obstetric and fetal risks, as well as any potential maternal long-term risks [35]. In addition, exercise testing can be helpful for Ebstein's patients to feed into risk assessment for any women considering pregnancy [35].

Initial presentation of Ebstein's is possible during pregnancy following development of new onset cyanosis. This is secondary to increased RV end-diastolic pressure (and therefore increased RA pressure) from an RV becoming functionally inadequate secondary to increased volume loading from pregnancy [5]. The plasma volume increases by 30–50% by the third trimester of pregnancy [67].

Regarding mode of delivery of the fetus, some studies suggest assisted delivery with either elective C-section or epidural use for painless vaginal delivery may reduce complications from labor [67]. This is to prevent Valsalva maneuver during delivery which may increase the risk of a paradoxical embolus from atrial level right-to-left shunting in those Ebstein's patients with ASD. This is a controversial concept in obstetrics and seems unnecessary.

## Conclusion

In summary, Ebstein's anomaly is a rare but complex congenital heart defect, with widely varying anatomy and pathophysiology. The clinical course of these patients has been reviewed and a clear pathway for investigation, management, and follow-up has been proposed. Two attached appendices are provided for a structured echocardiogram protocol and key information that could be useful for comprehensive Multi-Disciplinary Team conferences.

## Appendix 1: Trans-Thoracic Echocardiogram Protocol

(a) General assessment:

(i) Abdominal Situs
(ii) Systemic veins

(1) Single/Dual SVC and Bridging vein
(2) Dual/interrupted IVC and Azygous continuation

(iii) Distinguish left and right ventricle
(iv) Assess Atrio-ventricular and Ventriculoarterial Concordance
(v) Pulmonary veins and connection to left Atrium
(vi) Atrial Communication size
(vii) Ventricular communications
(viii) Mitral Stenosis/regurgitation

(1) Pulse-Wave (PW) doppler of mitral valve inflow for E/A ratio
(2) Continuous-Wave (CW) doppler of Mitral Regurgitation for Dp/Dt

(ix) LVOT:

(1) PW and CW to look for laminar flow & the presence of AS/AR
(2) Pressure half-time for AR and width of vena contracta and whether jet hits AMVL

(x) RVOT:

(1) PW and CW to look for laminar flow
(2) PR and grade severity including flow reversal in PAs.
(3) Maximum gradient at end of pulmonary regurgitation doppler gives indicator of diastolic PA pressure

(xi) Branch Pulmonary Arteries:

(1) Size and gradient in branch PAs

(xii) Coronary artery origins/flow and branching
(xiii) Aortic arch:

(1) Presence of coarctation
(2) Branching pattern and arch sidedness

(b) Tricuspid valve leaflets:

(i) Septal—Best seen on A4C
(ii) Antero-Superior—Best Seen on A4C, PSAX, and PLAX from RV inflow view
(iii) Inferior/Posterior/Mural—Best seen on PLAX from RV inflow view
(iv) subcostal short axis and long axis demonstrate the anterior and septal leaflets well
(v) Subcostal en-face view shows all three leaflets in one image.

(c) TV vs MV

(i) Apical displacement of the hinge point of the septal leaflet of the tricuspid valve
(ii) Measure on Apical 4-chamber view

(1) Look for Displacement index (Distance/BSAm2):

(a) TV displaced toward apex by more than 8 mm/m2 from MV insertion.

(d) Tricuspid valve key areas to look at

(i) Morphology and movement of each leaflet

(1) Hinge point and distal attachments
(2) Freely moving vs restricted movement
(3) Fenestrations in each leaflet
(4) Mobility vs adherence of the antero-superior leaflet

(ii) Tricuspid Valve Chordae
(iii) Tricuspid Valve Papillary muscles
(iv) Direct muscular insertions into the antero-superior leaflet
(v) Competence and lack of coaptation of the tricuspid valve
(vi) Size of tricuspid valve annulus and *z*-score (and compare to Mitral valve)
(vii) Severity of TR as well as central/single vs multiple jets
(viii) Presence of membrane above tricuspid valve
(ix) Size of ASD

(e) LV and RV functional assessment
(f) Degree of RA and RV dilation
(g) Degree of Pulmonary stenosis/functional atresia
(h) Associated VSD
(i) Color Doppler
(i) Regurgitation: number of jets and grading of TR

(1) Keep on low Nyquist to look for low-velocity jets
(2) Look for jets from fenestrations in valve

(j) CW Doppler:

(i) Tricuspid valve regurgitation
(ii) Estimated RVSP

(k) Hepatic vein and IVC inflow
(i) Look at flow profile with PW for estimation of RA pressure and severity of TR
(l) Right Atrium
(i) Apical 4 chamber just before TV Opens—measure RA major and minor length and RA area in 4 chamber
(m) Atrialized Right Atrium
(i) Area
(n) Anatomic severity of Ebstein: GOS Eq. 8, 9

(i) Calculation of chamber area ratio in apical 4 chamber at End-diastole
(ii) (RA + Atrialized RV)/( RV + LA + LV)
(iii) Four grades of increasing severity:

(1) ratio < 0.5 = grade 1
(2) ratio 0 0.5 to 0.99 = grade 2
(3) ratio 1 to 1.49. = grade 3
(4) ratio ≥ 1.5. = grade 4

(iv) ≥ 1 Indicates poor prognosis

(o) Atrial septum

(i) PFO/ASD
(ii) Direction of shunting on color Doppler

(p) Ventricular volumes & function

(i) RV:

(1) RV FAC
(2) RV Volumes

(ii) LV:

(1) MAPSE
(2) Simpson's Biplane
(3) M-Mode

(a) Look at relationship of ventricular septum during systole and diastole

(4) LV volumes

(q) Pulmonary valve

(i) Pulmonary Stenosis or Atresia
(ii) Functional vs True Atresia
(iii) CW Doppler

(1) PR Vendmax (estimation of PA diastolic pressure)

(r) Pulmonary Arteries
  (i) Size including *z*-scores
(s) Associated lesions

## Appendix 2: Key Information for Multi-disciplinary Team Conference

### Fetal

(1) CT ratio
(2) TV annulus size
(3) Tricuspid regurgitation severity and jet velocity to estimate RV pressure
(4) Pulmonary anterograde flow, ductal flow directionality, and pulmonary regurgitation severity
(5) Atrial communication size
(6) Cardiac function
(7) Effusions and/or hydrops
(8) Extracardiac
  (i) Doppler findings
  (ii) Lung volume assessment by U/s or fetal MRI
  (iii) Fetal growth restriction

### Neonate

(1) Whether antenatal diagnosis and any history of antenatal arrhythmia
(2) Key information on condition at birth and need for respiratory/inotropic support
(3) Need for PGE1
(4) ECG and CXR
(5) Detailed Trans-thoracic Echocardiogram
(6) 24-h tape to assess rhythm.

### Infant

(1) Whether antenatal diagnosis and any history of antenatal arrhythmia
(2) Symptoms of heart failure
(3) Presence of arrhythmia
(4) Weight trend
(5) ECG and CXR
(6) Detailed Trans-thoracic Echocardiogram
(7) 24-h tape to assess rhythm.

### Child

(1) Mode of presentation
(2) Symptoms of heart failure or cyanosis at rest
(3) Cyanosis on exercise
(4) ECG
(5) Chest X-ray
(6) Detailed Trans-thoracic Echocardiogram
(7) 24-h tape
(8) CT Angiogram/Cardiac MRI if necessary
(9) Exercise testing for older children
(10) Associated arrhythmia and results of EP study if indicated

### Adolescent/Adult

(1) Mode of presentation
(2) Whether symptomatic
(3) Associated arrhythmia and history of anti-arrhythmic need
(4) Cyanosis at rest or on exercise
(5) ECG
(6) Chest X-ray
(7) Trans-Thoracic Echocardiogram
(8) TEE results if indicated
(9) 24-h tape
(10) Exercise testing
(11) CT Angiogram/Cardiac MRI results if indicated
(12) EP Study result if indicated

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