The American Association for Thoracic Surgery (AATS) 2024 expert consensus document: Management of neonates and infants with Ebstein anomaly

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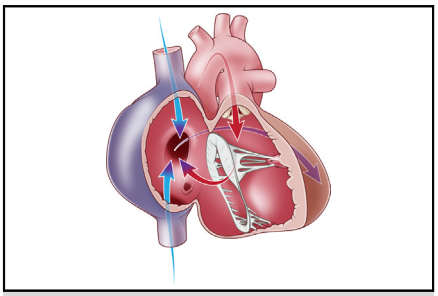
ABSTRACT

Objectives: Symptomatic neonates and infants with Ebstein anomaly (EA) require complex management. A group of experts was commissioned by the American Association for Thoracic Surgery to provide a framework on this topic focusing on risk stratification and management.

Methods: The EA Clinical Congenital Practice Standards Committee is a multinational and multidisciplinary group of surgeons and cardiologists with expertise in EA. A citation search in PubMed, Embase, Scopus, and Web of Science was performed using key words related to EA. The search was restricted to the English language and the year 2000 or later and yielded 455 results, of which 71 were related to neonates and infants. Expert consensus statements with class of recommendation and level of evidence were developed using a modified Delphi method, requiring 80% of members votes with at least 75% agreement on each statement.

Results: When evaluating fetuses with EA, those with severe cardiomegaly, retrograde or bidirectional shunt at the ductal level, pulmonary valve atresia, circular shunt, left ventricular dysfunction, or fetal hydrops should be considered high risk for intrauterine demise and postnatal morbidity and mortality. Neonates with EA and severe cardiomegaly, prematurity (<32 weeks), intrauterine growth restriction, pulmonary valve atresia, circular shunt, left ventricular dysfunction, or cardiogenic shock should be considered high risk for morbidity and mortality. Hemodynamically unstable neonates with a circular shunt should have emergent interruption of the circular shunt. Neonates in refractory cardiogenic shock may be palliated with the Starnes procedure. Children may be assessed for later biventricular repair after the Starnes procedure. Neonates without high-risk features of EA may be monitored for spontaneous closure of the patent ductus arteriosus (PDA). Hemodynamically stable neonates with significant pulmonary regurgitation at risk for circular shunt with normal right ventricular systolic pressure should have an attempt at medical closure of the PDA. A medical trial of PDA closure in neonates with functional pulmonary atresia and normal right ventricular systolic pressure (>20-25 mm Hg) should be performed. Neonates who are hemodynamically stable without pulmonary regurgitation but inadequate antegrade pulmonary blood flow may be considered for a PDA stent or systemic to pulmonary artery shunt.

Conclusions: Risk stratification is essential in neonates and infants with EA. Palliative comfort care may be reasonable in neonates with associated risk factors that may include prematurity, genetic syndromes, other major medical comorbidities, ventricular dysfunction, or sepsis. Neonates who are unstable with a circular shunt should have emergent interruption of the circular shunt. Neonates who are unstable are most commonly palliated with the Starnes procedure. Neonates who are stable should undergo ductal closure. Neonates who are stable with inadequate pulmonary flow may have ductal stenting or a systemic-to-pulmonary artery shunt. Subsequent procedures after Starnes palliation include either single-ventricle palliation or biventricular repair strategies. (J Thorac Cardiovasc Surg 2024;168:311-24)



Cardiac anatomy of a neonate with Ebstein anomaly and circular shunt.

CENTRAL MESSAGE

Symptomatic neonates with Ebstein anomaly may require emergent surgery. Initial treatment may best be accomplished by the Starnes procedure, yet a paradigm shift for biventricular repair is emerging.

PERSPECTIVE

Symptomatic neonates with Ebstein anomaly are a heterogeneous group. Neonates with a circular shunt represent the most severe end of the spectrum and will often require emergent management. Initial management may best be accomplished by the Starnes procedure, yet a paradigm shift for biventricular repair is emerging.

Abbreviations and Acronyms

BCPS = bidirectional cavopulmonary shunt
BT = Blalock-Taussig
COR = classification of recommendation
COX = cyclooxygenase
EA = Ebstein anomaly
ECMO = extracorporeal membrane oxygenation
EO = expert opinion
LD = limited data
LOE = level of evidence
LV = left ventricle/ventricular
MRI = magnetic resonance imaging
NR = nonrandomized
PA = pulmonary artery
PDA = patent ductus arteriosus
PR = pulmonary regurgitation
RV = right ventricle/ventricular
RVSP = right ventricular systolic pressure
TR = tricuspid regurgitation
TV = tricuspid valve

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Surgical management of symptomatic neonates and infants with Ebstein anomaly (EA) represents a difficult problem, as these patients are relatively rare, heterogeneous, and often present in a poor clinical state. A Society of Thoracic Surgeons database study on surgical treatment of neonatal EA demonstrated an overall mortality rate of 27.4%, and the mortality related to the primary repair was 39.9%.[1] A more recent study has also reported a high mortality of 37.5% within 1-year follow-up.[2] The European Congenital Heart Surgeons Association reported a mortality of more than 50% in their neonates and infant's subgroup.[3] Right ventricular (RV) exclusion (Starnes procedure) has proven to be a simple and reproducible procedure to improve survival in unstable neonates.[4,5] The Starnes procedure has been successfully applied to low-weight neonates with good results.[6] Recent reports suggest that the Starnes procedure does not necessarily commit the child to a single-ventricle pathway as successful tricuspid repair after the Starnes procedure has been performed.[7-11] Modifications to the Starnes procedure have been described to help facilitate subsequent biventricular repair.[11,12] Primary neonatal biventricular repair of EA has also been described and may result in good outcomes in selected patients if a tailored strategy is applied.[13-19] Patients who survive beyond 1 year of age generally do well but may require further surgical management.[2]

An expert panel of surgeons and cardiologists was assembled to provide guidance to practitioners regarding the management of neonates and infants with EA. Currently available literature was reviewed and a framework developed to base initial risk categorization and treatment options for symptomatic patients. Areas in which data are lacking and further research is needed were identified.

METHODS

The American Association for Thoracic Surgery Congenital Clinical Practice Standard Committee identified EA in neonates and infants as a topic that could benefit practitioners by providing an expert consensus document created by review of the currently available data, supplementation with expert opinion where the data are lacking, and identification of areas that would most benefit from future research. An international panel of experts consisting of 12 practicing pediatric cardiothoracic surgeons and 2 pediatric cardiologists was selected by the writing group chairs (I.K. and P.C.). The final manuscript was then reviewed by 12 additional surgical and medical experts in management of EA. Attempts were made to identify all currently available relevant data about EA in neonates and infants. A robust search was performed using PubMed, Embase, Scopus, and Web of Science using key words related to EA with the assistance of a medical librarian.

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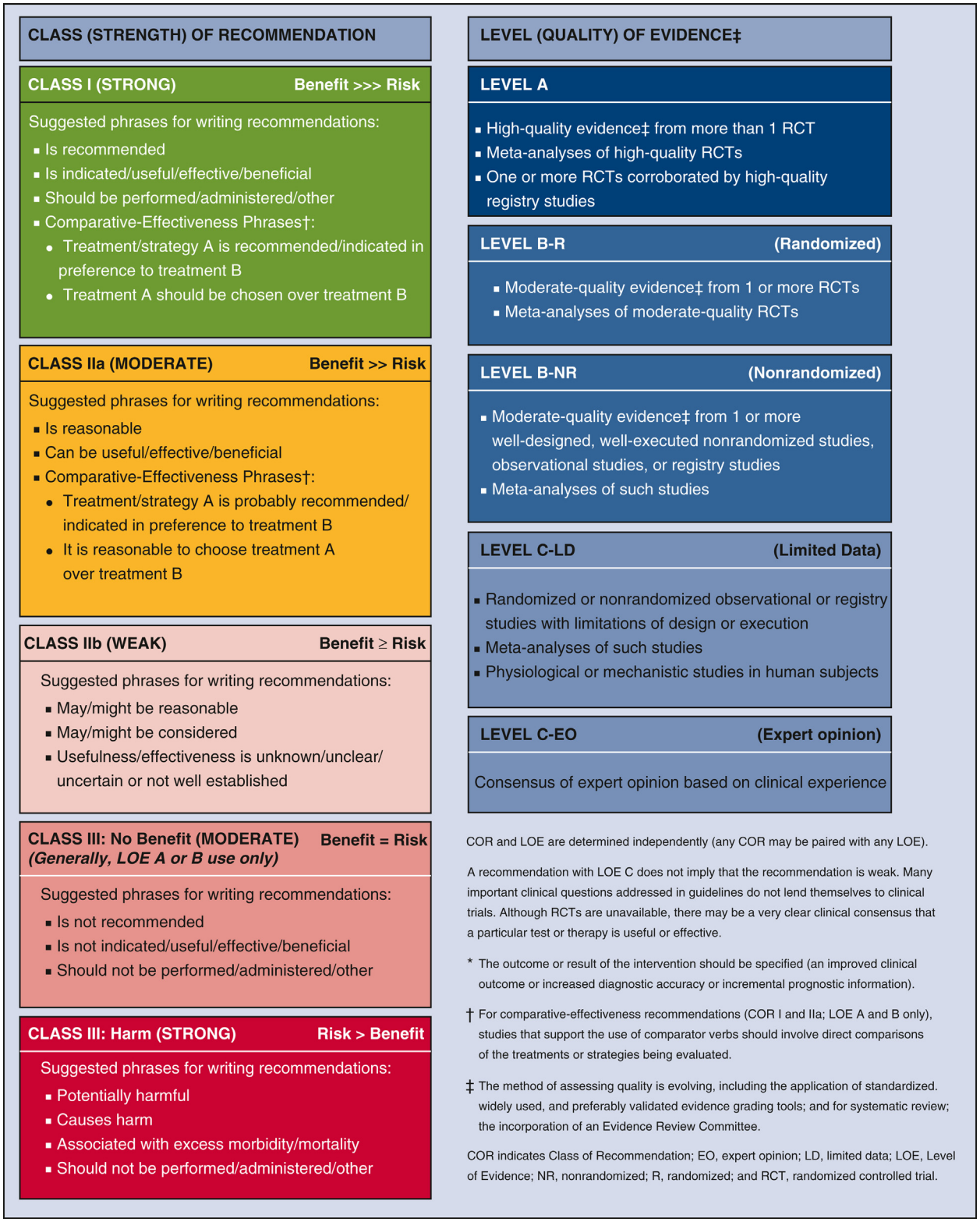

FIGURE 1. American College of Cardiology/American Heart Association recommendation system: applying class of recommendation (*COR*) and level of evidence (*LOE*) to clinical strategies, interventions, treatments, or diagnostic testing in patient care.* (Updated May 2019). *RCT*, Randomized controlled trial; *R*, randomized; *NR*, nonrandomized; *LD*, limited data; *EO*, expert opinion. Reprinted with permission, 2016 American Heart Association, Inc. https://cpr.heart.org/en/resuscitation-science/cpr-and-ecc-guidelines/tables/applying-class-of-recommendation-and-level-of-evidence. Halperin JL, Levine GN, Al-Khatib SM, et al. Further evolution of the ACC/AHA clinical practice guideline recommendation classification system: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2016;133(14):1426-1428.

The search was restricted to the English language and the year 2000 or later and yielded 455 results, of which 71 were related to neonates and infants After these articles were reviewed, clinical questions were designed using the patient intervention comparison outcome format.[20] Expert consensus statements with classification of recommendation (COR) and the level of evidence (LOE) were developed using a modified Delphi method requiring 80% of members votes with at least 75% agreement on each statement. Consensus was required before finalizing the COR or LOE for each statement with the same voting requirement. The entire group of authors has met on multiple occasions, created, voted on, re-discussed the statements, reviewed, and revised the manuscript as per the American Association for Thoracic Surgery consensus guidelines. The language for each statement was chosen to be consistent with that recommended by the American College of Cardiology and American Heart Association (Figure 1).[21] When a recommendation lacked sufficient evidence to allow for a formal statement, it was included as a Best Practices Statement.

Once the recommendations and their COR and LOE were determined, a narrative was written to help fully inform readers as to the intent and meaning of each statement, as well as the main points and counterpoints. The narration also supplies readers with the data used to make each recommendation. Areas lacking data and other areas for future research were noted. Finally, because of often-limited data on the surgical management of EA in neonates and infants, the discussion was aimed at describing the current trends and technical innovations and is not intended to give definitive recommendations.

Limitations and Bias

The evaluation of different treatment strategies for neonates and infants with EA has been somewhat hampered by a heterogeneous and relatively rare patient population, significant variations in management techniques, and the lack of randomized controlled studies.

Terminology

- **Circular shunt** in neonates with EA results from the pulmonary regurgitation (PR) causing the blood to flow from the aorta to the pulmonary artery (PA) through a patent ductus arteriosus (PDA), then to the RV, the right atrium from tricuspid valve regurgitation, to the left atrium across the patent foramen ovale, to the left ventricle (LV) and aorta, and back to the PDA (Figure 2, *A*).[18,19,22-28] It is important to emphasize that fraction of the circular shunt can be different, thus creating the spectrum of hemodynamics from hemodynamically stable patients to those in cardiogenic shock.
- **Functional pulmonary atresia** in neonates with EA should have no or minimal antegrade pulmonary blood flow and include those with mild (1-2/4) associated PR. These patients are a different subgroup from those with a hemodynamically significant circular shunt (Figure 2, *B*).[29-33]
- **Palliative comfort care:** Comfort care without any intervention.
- **Palliative procedure:** Surgical or catheter-based procedure, short of a complete biventricular repair performed with intent to ensure survival.
- **Neonate:** Age younger than 1 month.
- **Infant:** Age younger than 1 year.

EXPERT CONSENSUS STATEMENT AND BEST PRACTICES

On the basis of the available data, the expert consensus writing group developed recommendations for neonates and infants with EA in terms of the timing of surgical intervention, the strategy of surgical and catheter-based interventions, technical aspects of the surgical intervention, and the projections for further interventions in the future. Because of the rarity of the lesion and lack of randomization of surgical strategies, many of the recommendations relied on individual expert opinions and nonrandomized descriptive analyses of moderate-sized series from individual institutional experiences.[1,15,24,27,30-36] Several statements were presented to the writing group, and consensus was obtained often with several modifications before the consensus opinion was adopted. All statements are presented herein.

Regular and thorough fetal and neonatal echocardiography should be performed when severe EA is suspected and a multidisciplinary team, including pediatric cardiothoracic surgeons, pediatric cardiologists, and pediatric cardiac intensive care specialists, must be available on delivery of high-risk neonates: Best Practices Statement.

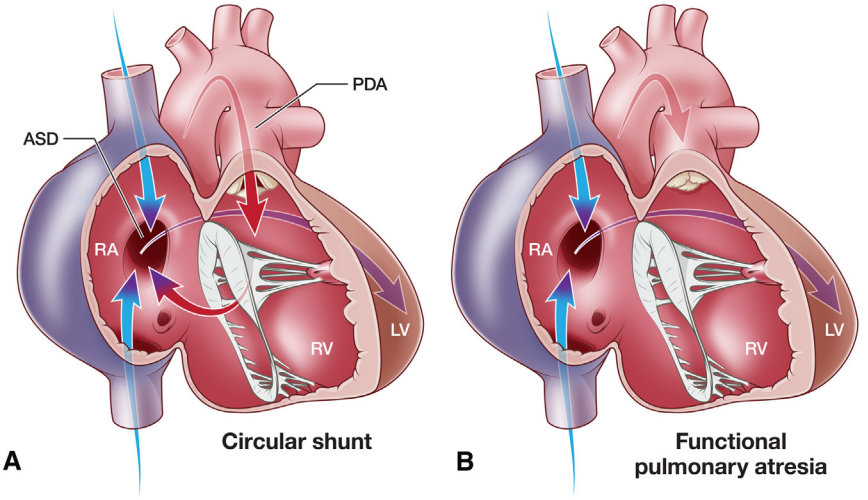

FIGURE 2. A, Anatomy of the heart with Ebstein anomaly and a circular shunt. B, Anatomy of the heart with Ebstein anomaly and functional pulmonary atresia. *ASD*, Atrial septal defect; *PDA*, patent ductus arteriosus; *RA*, right atrium; *RV*, right ventricle; *LV*, left ventricle.

Recommendations Regarding Preoperative Assessment and Risk Stratification

When evaluating fetuses with EA, those with severe cardiomegaly in early gestation, bidirectional shunt at the ductal level, anatomic or physiologic pulmonary valve atresia, circular shunt, LV dysfunction, low right ventricular systolic pressure (RVSP; <20-25 mm Hg), or fetal hydrops should be considered high risk for intrauterine demise and postnatal morbidity and mortality (class I, level B-nonrandomized [NR]).

EA in the fetus and neonate represents a spectrum of disease ranging from mild apical displacement of the tricuspid valve septal leaflet with minimal or no tricuspid insufficiency to severe cardiomegaly typically associated with severe tricuspid regurgitation (TR) with variable degrees of septal leaflet displacement with/without posterior leaflet displacement. The milder end of the spectrum, which represents the minority of those encountered prenatally, usually causes no hemodynamic compromise before and after birth and may even go unrecognized for years; however, when encountered in the first or mid-trimesters, there may be evolution to more severe disease warranting surveillance through later gestation.[37,38] Conversely, fetuses with the more severe EA, the majority of EA encountered prenatally, are at high risk of evolving hydrops/heart failure and spontaneous intrauterine demise, with rates most recently reported as high as 15% to 20% among continued pregnancies.[35,39] Those with severe disease who are liveborn have ongoing high risks of mortality, with 25% to 32% neonatal demise in contemporary series,[35,39] and significant morbidity.

Severe cardiomegaly, severe and low velocity TR suggesting low RVSP (<20-25 mm Hg), no antegrade pulmonary flow associated with functional or anatomical pulmonary atresia, LV dysfunction and significant PR, all of which may be progressive, have been identified as risk factors for worse fetal and neonatal outcomes.[35,38-40] How these features contribute to fetal and neonatal loss is best understood through an appreciation of the pathophysiology. As a start, severe cardiomegaly evolves secondary to volume loading of the right heart, largely through significant TR, most often involving the right atrium and atrialized RV, which can occupy most of the fetal chest. Massive cardiomegaly, particularly when present earlier in gestation, can affect pulmonary growth with low lung weights documented on fetal autopsy and reduced observed to expected fetal lung volumes measured by ultrasound and magnetic resonance imaging (MRI).[37] Some affected fetuses will have anatomical pulmonary outflow obstruction as the result of distal linear anterior tricuspid valve (TV) leaflet attachments, pulmonary valvar stenosis, or membranous pulmonary atresia. In the presence of a patent pulmonary valve, functional pulmonary atresia can evolve when the RV is unable to generate sufficient pressure (systemic in the fetus) to open the pulmonary valve due to severe TR and/or an insufficiently sized functional RV. In this context, there is usually retrograde or, with little forward flow, bidirectional flow in the ductus arteriosus. The presence of PR provides a clue to pulmonary valve patency. Significant pulmonary insufficiency, however, with a patent ductus in utero, can steal from the fetal and placental circulation contributing to fetal hypoxemia, and further volume loads the RV. Early experience with judicious use of nonselective cyclooxygenase (COX) inhibitor (indomethacin) to induce premature ductal constriction in those with significant pulmonary insufficiency, particularly at nonviable gestations and with severe placental steal, has shown promise in improving outcomes for this subgroup.[23,41,42] More work is needed to better understand optimal timing and consequences, including risks of acute fetal renal vasoconstriction and to maternal labor and delivery, of nonselective COX inhibition.[43-45] Furthermore, significant constriction or closure of the PDA in utero may result in acute compromise at birth that requires coordinated delivery planning and availability of emergent medical and surgical supports for resuscitation.[46]

The fetal circulation requires at least one ventricle that can fill at low pressures and eject the equivalent of the combined cardiac output. Most congenital heart defects, including the functional single RV and LV, can maintain a normal or near-normal combined cardiac output through redistribution of the cardiac preload with an augmented atrial kick, and an increase in their short axis dimension with augmented circumferential or short-axis contractility.[47,48] In severe EA, however, the LV output is often low, despite the requirements of a functional single ventricle.[49,50] Evolving right heart volume load, particularly coupled with an atrialized RV and ventricular septum, most notable in those without forward pulmonary blood flow, is associated with LV dyssynchrony, an inability of the LV to augment its circumferential contractility as well as altered diastolic filling due to adverse ventricular-ventricular interaction.[49,51] This contributes to cardiovascular compromise, affecting the combined cardiac output and ultimately cardiac filling pressures. It also contributes to reduced cerebral oxygen delivery, which may have an important impact on long-term neurodevelopment.[50] As proof that this adverse ventricular-ventricular interaction is a critical aspect of the pathophysiology of severe EA, the performance of Starnes procedure results in an acute augmentation of LV circumferential contractility and improved synchrony.[52] In addition, the right atrium, which receives most of the cardiac preload, has also been shown to be dysfunctional in severe fetal EA, contributing further to an inability to redistribute flow to the left heart and to the evolution of hydrops.[53] Finally, fetal and neonatal EA can be associated with supraventricular arrhythmias including atrial flutter, ectopic atrial ectopy, atrioventricular reentry tachycardia, and atrial ectopy, some as a consequence of

severe right atrial dilation, and all of which may further acutely compromise an already-fragile circulation.[37]

When evaluating fetuses with EA, serial echocardiography (frequency every 2-4 weeks earlier and every 1-2 weeks after 32 weeks) should be performed as most high-risk features manifest later in gestation (class I, level B-NR).

Given the high risks of cardiovascular compromise, the development of hydrops with additional risks of mirror syndrome to the mother, and fetal loss, close serial surveillance with fetal echocardiography is recommended particularly for moderate-to-severe EA, with a frequency of 2 to 4 weeks in the previable gestational periods, with more frequent surveillance in the third trimester.[54] In addition to fetal echocardiography, frequent obstetrical surveillance may also be considered including nonstress testing, MRI, biophysical profiles and biometry assessment to ensure fetal well-being.[55] Further work is needed to fine-tune optimal intervals of follow-up and the constellation of surveillance methods that best improve perinatal outcomes. Any changes suggestive of evolving compromise in a third-trimester fetus should prompt discussions around urgent delivery if neonatal management can improve the hemodynamics. Anticipated preterm delivery before 34 weeks should also prompt maternal administration of corticosteroids to facilitate fetal lung maturation. Fetal growth restriction, hydrops, cardiomegaly, reduced fetal MRI observed/expected lung to head ratio, and total fetal lung volume ratio are potential prognosticators of poor outcomes in severe EA.[56]

Fetuses with EA and high-risk features should be born via a planned delivery at a center with expertise in multiple specialties including intensive care, extracorporeal membrane oxygenation (ECMO) service and cardiac surgery (class I, level C-expert opinion [EO]).

Delivery of most pregnancies complicated by EA should occur in a tertiary or quaternary care center with the availability of cardiologists and cardiovascular surgical expertise. This is particularly critical for the fetus with more severe EA at risk for ongoing LV dysfunction and dyssynchrony after birth, which is associated with worse outcomes, or compromise from a severe circular shunt.[57] With delivery discontinuation of the low-resistance placental circulation acutely increases the biventricular afterload which can jeopardize the LV function further. In addition, the presence of a PDA, increases the pressure faced by the RV and tricuspid and pulmonary valves, contributing, in those with a patent pulmonary valve, to worsening valve insufficiency and increased RV volume loading, compromising LV filling and systolic function further and ultimately increasing central venous pressures.[58] Decreasing pulmonary vascular resistance that occurs in the transition, and may be augmented through mechanical ventilation and pulmonary vasodilators, results in increased pulmonary venous return and left atrial pressure. This, in turn, may jeopardize the obligate right-to-left atrial shunt in severe EA necessary to maintain LV preload and the cardiac output. Increasing pulmonary blood flow through the PDA will also overload an already-compromised LV. Low cardiac output and evolution of right heart failure, essentially hydrops after birth, are typical features of severe neonatal EA when appropriate intervention is not offered. When there is severe pulmonary insufficiency, further systemic steal can be observed that can acutely jeopardize the circulation in more severe neonatal EA. Given the risks of acute cardiovascular compromise and even neonatal death, it is imperative that the delivery of affected pregnancies occur where the expertise and resources are present to acutely resuscitate and provide medical and surgical intervention, including the availability of ECMO support.[59-62] When preparing for delivery of the greatest risk fetal EA, presenting the case to the perinatal and cardiosurgical team with clear plans for delivery timing, location and mode, and acute medical and surgical management can ensure the right place and time of the delivery, prepare the team and ultimately reduce delays in critical care.[62]

When evaluating neonates with EA, those with severe cardiomegaly, prematurity (less than 30-32 weeks), intrauterine growth restriction, anatomic or functional pulmonary valve atresia, circular shunt, LV dysfunction, or cardiogenic shock should be considered high risk for morbidity and mortality (class I, level B-NR).

Neonates without high-risk features of EA (and those with high-risk features who can be initially stabilized) should be allowed to undergo spontaneous closure of ductus arteriosus in a monitored setting to potentially avoid neonatal surgical intervention (class I, level C-limited data [LD]).

Neonates without high-risk features of EA in whom the RV is generating sufficient pressure to eject should be allowed to undergo spontaneous closure of the ductus arteriosus.[58,63] Even if there is mild cyanosis caused by right-to-left atrial shunting, antegrade pulmonary flow will be augmented with ductal closure if anatomical pulmonary atresia is not present. In addition, the consequent decrease in the pulmonary pressures after ductal closure may lead to reduction in the severity of tricuspid and even pulmonary insufficiency. In some patients, supplemental oxygen or even pulmonary vasodilators after the ductus arteriosus begins to constrict can promote forward flow from the RV. Although noninvasive monitoring is reasonable, excessive invasive monitoring including placement of umbilical arterial and venous lines can add morbidity including aortic and renal artery thrombosis, to these infants and should be avoided when they are clinically well.[64]

Recommendation Regarding the Care of Unstable Neonate

Hemodynamically unstable neonates with EA and a circular shunt should have emergent interruption of the circular shunt (class I, level B-NR).

Hemodynamically unstable neonates with EA and a circular shunt usually present within the first few hours of life and are most often in cardiogenic shock. Emergent interruption of the circular shunt may be best achieved with a Starnes single-ventricle palliation if an operating room and cardiopulmonary bypass is immediately available.[1,5,6,30,35] Alternatively, if patient or hospital system coordination prevents immediate intervention, the circular shunt may be interrupted by ligation of the main PA and placing bilateral branch pulmonary bands maintaining oxygenation through the PDA.[18,25,31,65] Although this strategy can be life-saving, a more definitive palliation is usually needed within 2 to 3 days secondary to the development of progressive dynamic LV outflow tract obstruction resulting from the nondecompressed RV.[5,18,52,57,66] In this scenario, a rapid 2-stage Starnes single-ventricle palliation is associated with the most predictable positive outcome.[5,25,28,31,65] The alternative is ECMO support with occlusion of the PDA followed by definitive biventricular repair or Starnes palliation.[2,23,36,59]

Neonates with EA who present in refractory cardiogenic shock (on inotropic support, ventilated, and on PGE for ductal dependent pulmonary blood flow) should be palliated with the Starnes procedure (class I, level C-LD).

Severely symptomatic neonates who are on significant inotropic support and full positive-pressure ventilation and remain in refractory cardiogenic shock usually represent the most severe form of EA or have a circular shunt present. Initial palliation is most reliably achieved with a Starnes operation with an anticipated mortality of 10% to 20%.[4,5,10,24,32,36,67] Importantly, the Starnes procedure results in early improvements in LV dysfunction and dyssynchrony, not observed after PDA closure in neonates with severe EA.[52] A simplified biventricular repair, also known as Knott-Craig repair, provided comparable results in a large series of neonates and young infants, but these results have not been widely duplicated by other institutions except in anecdotal cases and small series.[2,11,13,18,19,31] Even though a successful "cone" biventricular repair, also known as Da Silva repair, has been sporadically reported in neonates, this form of biventricular repair is best reserved for older infants after the initial neonatal Starnes palliation[2,8,11,16,27,68-71] Knott-Craig has reported a 90% early and late survival with the simplified version of the biventricular repair for this subgroup of neonates provided there is no associated *anatomical* pulmonary atresia.[13,15,33,72,73] In general, it should be kept in mind that operative mortality associated with neonatal repair of EA is high and the Starnes operation appears to give most consistent and predictable outcomes, particularly if the neonatal procedure is performed outside the institutions with significant expertise in neonatal biventricular repair.[1,5]

Neonates with EA and circular shunt with hemodynamic instability and low RVSP (<20-25 mm Hg) should undergo ligation/occlusion of the main PA and Starnes procedure (class I, level C-EO). Similarly, severely symptomatic neonates with anatomical pulmonary atresia should undergo a Starnes operation as the first intervention.[4,10,24,36,67] This is the most widely reproducible palliation and is associated with a better mortality than that of initial neonatal biventricular repair.[2] A 22% incidence of complete heart block has been reported.[2] This can be decreased dramatically or eliminated by suturing the inflow occlusion patch to the ligamentum of Todaro, leaving the coronary sinus to the atrial or ventricular side (Figure 3).

Although a PDA ductal stent or a Blalock-Taussig (BT) shunt may be an option in some cases, this is a less-optimal palliation because the RV is not decompressed with the aforementioned strategies and as a result may cause significant dynamic LV outflow tract obstruction and low cardiac output.[5,18,52,57,66] Neonates with mild-to-moderate pulmonary valve stenosis may be successfully palliated with an open pulmonary valvotomy and simple biventricular repair.[13,18]

Exceptions to this recommendation is a small subgroup of symptomatic neonates with EA and anatomical pulmonary atresia who have adequate size and function of the RV, as judged by an estimated RVSP >25-30 mm Hg. In these patients, it may be reasonable to do a simple biventricular repair with the addition of an RV-to-PA valved conduit.[72,73]

Palliative comfort care may be reasonable in neonates with significant associated lesions that may include significant prematurity, genetic syndromes, major medical comorbidities, severe LV dysfunction, or sepsis (class II, level C-EO).

Severely symptomatic neonates with significant associated cardiac and noncardiac lesions may be unsuitable for any form of intervention, and palliative comfort care may be the most reasonable option. These comorbidities may include significant prematurity (less than 32 weeks of gestation), genetic syndromes, and major medical comorbidities such as sepsis, etc. Exceptions to these exclusion criteria would include neonates with EA and perimembranous ventricular septal defects, atrioventricular canals, and LV noncompaction associated with a large ventricular septal defect, all of which have been successfully addressed with a biventricular repair in early infancy or during the neonatal period.[13,16,18,72]

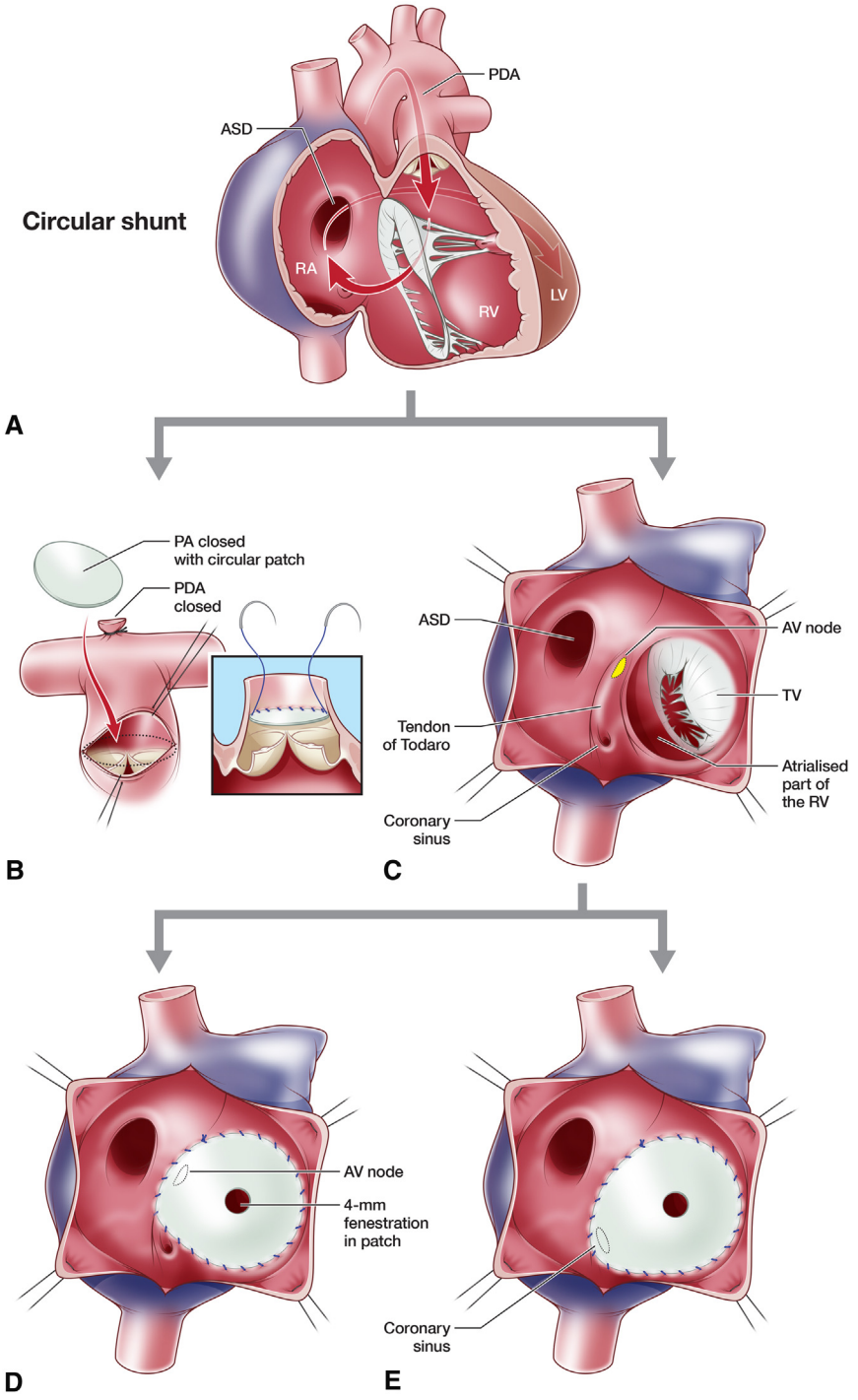

FIGURE 3. Modified Starnes operation to facilitate subsequent biventricular repair. A, Circular shunt in a neonate with Ebstein anomaly; (B) intraluminal patching of the main pulmonary artery; (C-E) the right ventricular inflow closure with a fenestrated patch placed into the supravalvular position and sutured to the tendon of Todaro to avoid damage to conduction system or tricuspid valve. Tricuspid valve is closed with a fenestrated patch leaving coronary sinus draining to the atrium (D) or to the ventricle (E). *ASD*, Atrial septal defect; *PDA*, patent ductus arteriosus; *RA*, right atrium; *RV*, right ventricle; *LV*, left ventricle; *PA*, pulmonary artery; *AV*, atrioventricular, *TV*, tricuspid valve.

Recommendation Regarding the Care of Stable Neonate

A medical trial of ductal closure in neonates with functional pulmonary atresia and normal RVSP (>20-25 mm Hg) should be performed. If the first attempt fails, subsequent attempts can still be made within the first 2 weeks of life (class I, level C-LD).

In many neonates with severe EA, the RVSP may suffice to provide enough pulmonary blood flow to maintain viable O_2 saturations once the ductus arteriosus is closed.[58] However, when maintaining ductal patency, the RV faces systemic pressure and may not be able to eject. Labile O_2 saturations likely reflect variability in pulmonary blood flow, right-to-left atrial shunting, and cardiac output (mixed venous O_2 saturations). Echocardiographic evaluation and serial assessment of ductal patency, flow through the pulmonary valve, severity of tricuspid and pulmonary insufficiency, and estimated RV systolic pressure based on the tricuspid insufficiency jet velocity relative to the systemic blood pressure are critical to understanding the medical and surgical needs of an affected neonate. Assessment of LV function and degree of dyssynchrony may also be helpful, and correlates with outcome, although its role in acute care is still evolving.[57] Although an exact cut-off has not been clearly defined, those with an RVSP of one-third to one-half that of the systemic blood pressure (ie, 20-25 mm Hg) should have a trial of spontaneous ductal closure. If the pulmonary valve is patent but PDA closure does not happen spontaneously, the use of COX inhibitors or even surgical closure of the PDA should be considered. If uncertainty exists regarding the patency of the pulmonary valve and PDA closure is needed, attempted balloon occlusion of the PDA in the catheterization laboratory would provide more certainty of pulmonary valve patency and tolerance of PDA closure.[58] With PDA constriction and closure but not before, the use of pulmonary vasodilators can assist in driving down the pulmonary vascular resistance and pressures and facilitating RV ejection into the pulmonary circulation. Some reduction in O_2 saturation may occur initially with ductal closure, but as the pulmonary vascular bed transitions fully, improvements in RV ejection and degrees of tricuspid and pulmonary insufficiency should lead to a reduction in right-to-left atrial shunting. Ductal constriction can also unmask critical pulmonary outflow obstruction both with insufficient systemic O2 saturations and with the finding of a high PDA gradient suggesting sufficiently low pulmonary pressures, but an RVSP that should be able to eject. Most of the children with RVSP >20 to 25 mm Hg will likely be best served with biventricular repair, although, of course, Starnes procedure can also be performed.[33]

Neonates with EA and significant PR who are at risk for development of a circular shunt but are hemodynamically stable and have RVSP of >20-25 mm Hg should have an attempt at *medical* closure of the PDA (class I, level C-LD).

Even in more severe EA associated with a circular shunt, PDA closure should be attempted, particularly if the neonate can be stabilized and the RVSP is at least 20-25 mm Hg.[58] However, a lengthy waiting period to allow PDA closure may contribute to worsening of the hemodynamics and end-organ failure, even in preterm infants.[6] Trialing COX inhibitors or even surgical closure may be considered to urgently reduce the burden of PDA patency and improve the hemodynamics of an affected neonate. In contrast to the neonate with greater RVSP based on the tricuspid insufficiency jet, those with lower RVSP and enlarged heart should be considered for a Starnes procedure which has even been successfully performed early in infants born more preterm.[22]

In neonates with EA who are hemodynamically stable but have inadequate antegrade pulmonary blood flow, a ductal stent or BT shunt may be considered as the first intervention as an alternative to primary biventricular repair (class IIA, level C-LD).

In symptomatic neonates who are stable hemodynamically but cannot be weaned from positive pressure ventilation or remain prostaglandin-dependent because of inadequate antegrade pulmonary blood flow (arterial oxygen saturations <80%), a ductal stent or BT shunt may be considered as a first palliation, deferring more definitive repair until 3 to 5 months of age. Alternatively, a simplified primary biventricular repair can be performed with an expected mortality of around 10%, similar to that of BT shunt or ductal stent. Although doing the simplified biventricular repair advocated by Knott-Craig, it is important not to "cut-and-sew" the fragile tricuspid valve leaflets during the early neonatal period when the pulmonary vascular resistance is still elevated.[13,14,31] Nevertheless, it should be noted that occasional case reports of a successful early neonatal cone repair have been reported in the literature even in neonates with a circular shunt.[8,16,19,27,68-71] Attempts at repair should be performed by surgeons with significant experience with this technique and a personalized approached to neonates that require surgery must be applied.[6,10,17,18]

The 1-year mortality for patients with EA who required surgery in neonatal period has recently been reported at 37%, with roughly two-thirds of them having undergone the Starnes repair.[2] Clearly, severely symptomatic neonates may not have an option to avoid Starnes procedure. Yet, whenever possible, biventricular repair for symptomatic neonates with EA, with or without prior Starnes procedure, should be deferred until 3 to 4 months of age, when a post-bidirectional cavopulmonary shunt (BCPS) can be safely added to unload the RV.[31,34,72,74,75] At 3 to 5 months of age, a simplified TV repair as advocated by Knott-Craig is reproducible and associated with low mortality.[13,15,17,72,74,76] At this age, a cone repair may also be safely undertaken in experienced hands.[1,8,11,36] Patients who underwent an initial Starnes palliation should also undergo stage 2 single-ventricle palliation around 3 to 5 months of age or be converted to a biventricular repair with takedown of the Starnes' palliation (Figure 4) before involution of the RV.[2,8,9,11]

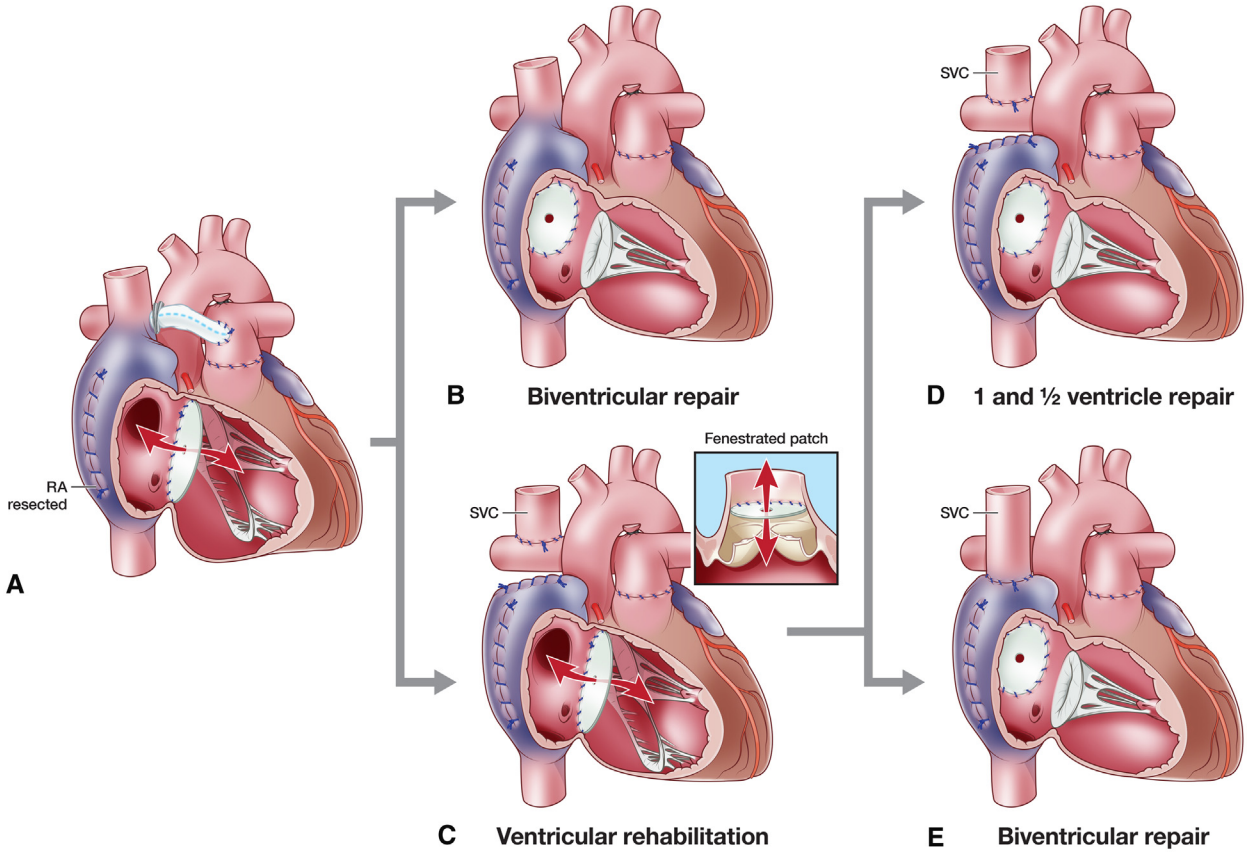

FIGURE 4. Modified Starnes operation (A) with intraluminal pulmonary artery banding for subsequent biventricular repair (B) or ventricular rehabilitation pathway (C) with subsequent 1 and ½ ventricle (D) or biventricular repair conversion (E). After removal of the intraluminal pulmonary artery patch, the inflow patch is removed, tricuspid valve is reconstructed, and atrial septal defect is closed with a patch and 4-mm fenestration. If the right ventricle appears small, then intraluminal pulmonary artery patch is fenestrated (C) at the time of bi-directional cavo-pulmonary shunt placement to achieve ventricular loading and rehabilitation. *RA*, Right atrium; *SVC*, superior vena cava.

Recommendations Regarding Subsequent Procedures After Neonatal Palliative Intervention

Subsequent procedures after a Starnes palliation should include continued staging toward a single-ventricle palliation or conversion to a biventricular repair (class I, level C-EO).[2,8-11,23] In view of desirability of avoiding the long-term consequences of a single-ventricle circulation, 2 major considerations come to the forefront. First, there is the concern that the RV may involute rapidly upon fenestrated tricuspid valve closure, potentially diminishing the size of the RV over a short period. Given the importance of RV size in establishing a biventricular circulation, careful monitoring is essential to determine the optimal timing for conversion from a single ventricle pathway to a biventricular pathway, ensuring intervention occurs before the RV becomes overly small. It appears that the optimal timing for such conversion will be in infancy or shortly after infancy, when the PA resistance drops and, thus, allows the option of BCPS added to biventricular conversion if required. The second consideration involves the technical aspect, namely, determining the most effective approach to PA closure/ligation in cases of functional pulmonary atresia (ie, not anatomical pulmonary atresia); strategies to consider are outlined below. Ideally, preserving the native pulmonary valve and avoiding the need for a RV-to-PA conduit at the time of biventricular conversion is a preferred outcome. Strategies to achieve this are outlined below, yet further experience is needed to gain clarity on these issues.

The Starnes procedure serves as an important initial intervention for stabilizing critically ill neonates, especially in institutions with limited experience managing neonates with EA. Although successful neonatal biventricular repair is achievable with a skilled team, the Starnes procedure offers stabilization for most cases. Importantly, undergoing the Starnes procedure does not rule out future biventricular repair or 1.5-ventricle repair post-BCPS. It is advocated that all patients who undergo the Starnes operation should also undergo evaluation for potential subsequent biventricular repair.[5-10,21] This recommendation emphasizes the necessity of careful consideration and evaluation, ensuring that patients are not automatically directed toward a

univentricular pathway without proper assessment. The staged management prompts critical questions about optimizing the Starnes procedure to facilitate future biventricular repair, criteria for selecting candidates for such repair, and determining the ideal timing for biventricular or 1.5-ventricle repair.

Given this uncharted territory, it seems fitting to share some thoughts and considerations. Since the decision to proceed to biventricular repair or BCPS is made in infancy, modifying the original Starnes operation is essential for optimal preservation of pulmonary and tricuspid valves, along with ensuring age-appropriate growth of the RV cavity (Figure 3, *A-E*). Preserving the pulmonary valve involves intraluminal patching of the main PA above the native pulmonary valve (Figure 3, *B*) and placing a fenestrated polytetrafluoroethylene patch farther from tricuspid valve leaflets to reduce potential leaflet scarring to the patch and aid subsequent tricuspid valvuloplasty and biventricular repair. Historically, this is accomplished by suturing the patch above the tricuspid valve annulus along the Todaro's ligament (Figure 3, *C*) and usually leaving the coronary sinus orifice in the right atrium (Figure 3, *D*). This strategy allows some involution of the RV, advantageous for a univentricular pathway. However, leaving the coronary sinus on the RV side (Figure 3, *E*) may facilitate sufficient RV growth for a future biventricular repair.

Ideally, biventricular repair should be considered in almost all patients following the modified Starnes procedure (Figure 4, *A-E*) and ideally should be performed while the patient is an infant. However, if the RV seems too small as the infant outgrows the original systemic-to-pulmonary artery shunt, a fenestration can be added to the intraluminal pulmonary artery patch during BCPS (Figure 4, *C*) to facilitate RV volume loading and potential growth, achieving subsequent 1.5- or 2-ventricle circulation (Figure 4, *D* and *E*).

Atrial septal defect closure typically involves a patch with a 4-mm central fenestration (Figure 4, *B*, *D*, *E*). Although plication of the atrialized RV is common in older children and adolescents, it is often not necessary at the time of complete repair during infancy, particularly after the Starnes procedure when size of the RV may be marginal for a complete 2-ventricle repair. In this situation a 1.5-ventricle repair is an excellent alternative (Figure 4, *D*). Right reduction atrioplasty is performed routinely when the right atrium is dilated.

The technique of TV repair in neonates and infants may include the monocusp repair (Figure 5) or, preferably, the cone repair (Figure 6) techniques. This is largely dependent on surgeon's experience. Advantages of the monocusp repair include simplified annular reduction maneuvers, avoiding manipulations in the area of conduction system, and the relative ease to use of the Sebening stitch (ie, approximation of anterior papillary muscle(s) to the ventricular septum) (Figure 5, *E*) if required, although the latter can be used in both repairs.[77-80] The tissues are typically sturdy in older children. Thus, the simplified monocusp repair can be more reproducible in neonates or when the surgeon is less experienced. In contrast, the cone procedure is more anatomic, but also has a more difficult learning curve. Importantly, dissection and manipulation of fragile leaflet tissue with subsequent leaflet to leaflet approximation can result in dehiscence in this young age. For these reasons, the cone procedure in neonates and infants should ideally be reserved for surgeons and programs with satisfactory experience. Details of both monocusp and cone repairs are described elsewhere.[7,12-14,77-80]

Close clinical and imaging surveillance after the Starnes procedure should be done at 2- to 4-week intervals. Imaging should include routine transthoracic echocardiography and MRI (at 3-4 months) that can provide more objective analysis of RV size and function. The specific assessment modes, algorithms, and timing for biventricular repair post-Starnes operation are yet to be elucidated. Conceptually, it is timely to emphasize making every effort to

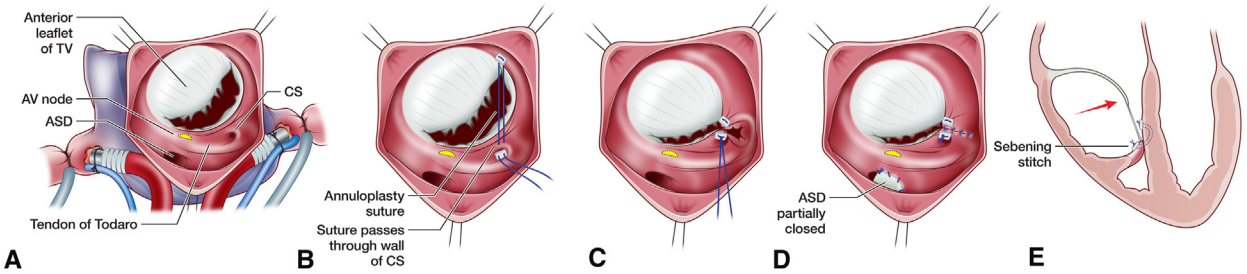

FIGURE 5. Principles of Knott-Craig monocusp repair. A, Anatomy of the tricuspid valve (*TV*) in Ebstein anomaly. B, The pledgetted suture is placed through the annulus at the junction of the anterior and the absent or nondelaminated posterior leaflet and is brought via the medial wall of the coronary sinus. C, The suture is tied over a second pledgett, creating a double-orifice opening. D, The smaller orifice is closed. Atrial septal defect (*ASD*) is partially closed. E, If significant TV insufficiency is still present, it can be easily be corrected by placing a pledgetted suture from the tip of the papillary muscle to the midportion of the interventricular septum (also known as a Sebening stitch). *AV*, Atrioventricular; *CS*, coronary sinus.

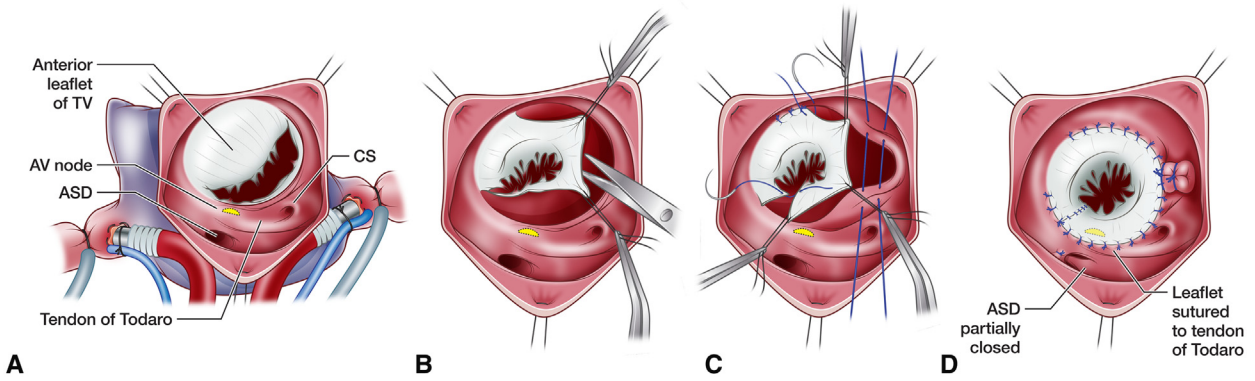

FIGURE 6. Principles of Da Silva cone repair. A, Anatomy of the tricuspid valve (*TV*) in Ebstein anomaly. B, The delaminated portion of the TV is detached. C, The TV annulus is plicated. D, TV is reconstructed in a "*cone*" shape and reattached to a newly created annulus. It is most crucial to sutures the newly reconstructed valve to the ligamentum of Todaro (ie, above the atrioventricular [*AV*] node to avoid damage to conduction system). Atrial septal defect (*ASD*) is partially closed. *CS*, Coronary sinus.

potentially enable biventricular repair in children after the initial Starnes operation.

Future directions. Precise indications and timing of biventricular conversion after Starnes operation remain unclear. Risk stratification, timing of interventions, and the outcomes need further clarification.

CONCLUSIONS

Risk stratification is essential in neonates and infants with EA. Palliative comfort care may be reasonable in neonates with associated high-risk features that may include prematurity, genetic syndromes, other major medical comorbidities, LV dysfunction, or sepsis. Unstable neonates with a circular shunt should have emergent interruption of the circular shunt. Unstable neonates are commonly palliated with the Starnes procedure. Stable neonates should undergo ductal closure. Stable neonates with inadequate pulmonary flow may have ductal stenting or a systemic-to-pulmonary artery shunt. Subsequent procedures after a Starnes palliation should include continued staging toward a single-ventricle palliation or conversion to a biventricular repair.

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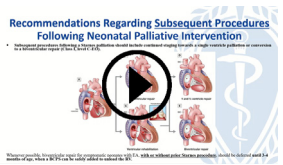

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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