The American Association for Thoracic Surgery (AATS) 2023 Expert Consensus Document: Recommendation for the care of children with trisomy 13 or trisomy 18 and a congenital heart defect

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ABSTRACT

Objectives: Recommendations for surgical repair of a congenital heart defect in children with trisomy 13 or trisomy 18 remain controversial, are subject to biases, and are largely unsupported with limited empirical data. This has created significant distrust and uncertainty among parents and could potentially lead to suboptimal care for patients. A working group, representing several clinical specialties involved with the care of these children, developed recommendations to assist in the decision-making process for congenital heart defect care in this population. The goal of these recommendations is to provide families and their health care teams with a framework for clinical decision making based on the literature and expert opinions.

Methods: This project was performed under the auspices of the AATS Congenital Heart Surgery Evidence-Based Medicine Taskforce. A Patient/Population, Intervention, Comparison/Control, Outcome process was used to generate preliminary statements and recommendations to address various aspects related to cardiac surgery in children with trisomy 13 or trisomy 18. Delphi methodology was then used iteratively to generate consensus among the group using a structured communication process.

Results: Nine recommendations were developed from a set of initial statements that arose from the Patient/Population, Intervention, Comparison/Control, Outcome process methodology following the groups' review of more than 500 articles. These recommendations were adjudicated by this group of experts using a modified Delphi process in a reproducible fashion and make up the current publication. The Class (strength) of recommendations was usually Class IIa (moderate benefit), and the overall level (quality) of evidence was level C-limited data.

Conclusions: This is the first set of recommendations collated by an expert multidisciplinary group to address specific issues around indications for surgical intervention in children with trisomy 13 or trisomy 18 with congenital heart defect. Based on our analysis of recent data, we recommend that decisions should not be based solely on the presence of trisomy but, instead, should be made on a case-by-case basis, considering both the severity of the baby's heart disease as well as the presence of other anomalies. These recommendations offer a framework to assist parents and clinicians in surgical decision making for children who have trisomy 13 or trisomy 18 with congenital heart defect. (J Thorac Cardiovasc Surg 2024;167:1519-32)

Trisomy 13 (Patau syndrome) and trisomy 18 (Edwards syndrome).

CENTRAL MESSAGE

Providing expert consensus opinions can assist clinicians and parents in decision making concerning children with trisomy 13 or trisomy 18.

PERSPECTIVE

Expert consensus documents are critical to the practice of medicine when peer-reviewed data are insufficient to create clinical practice guidelines. The management of infants with trisomy 13 or trisomy 18 who have an associated congenital heart defect lacks consistency. The variability in practice leads to discontent and distrust among parents and clinicians and to potentially suboptimal patient care.

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Received for publication Sept 9, 2023; revisions received Nov 27, 2023; accepted for publication Nov 30, 2023; available ahead of print Jan 27, 2024.

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0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2023.11.054

Abbreviations and Acronyms

ASD = atrial septal defect
CCS = Comprehensive Care Services
CHD = congenital heart defect
CMC = children with medical complexity
COR = classification of recommendation
CPAP = continuous positive airway pressure
HFNC = high-flow nasal cannula
ICR = intracardiac repair
LOE = level of evidence
PDA = patent ductus arteriosus
PH = pulmonary hypertension
PPC = pediatric palliative care
PVD = pulmonary vascular disease
STAT = The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery
STS = The Society of Thoracic Surgeons
T13 = trisomy 13
T18 = trisomy 18
VSD = ventricular septal defect

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1. INTRODUCTION

1.1 Preamble

Trisomy 13 (T13) and trisomy 18 (T18) are rare genetic syndromes caused by the addition of a chromosome (aneuploidy) 13 or 18, respectively. Given the multiple congenital anomalies and associated functional problems, the 2 conditions generate management challenges. T13 and T18 are often associated with miscarriage and stillbirth, in addition to restricted intrauterine growth and extreme prematurity. T13 (Patau syndrome) affects approximately 1 out of 16,000 live births. Congenital heart disease (CHD) is present in up to 80% of the live born babies. Associated problems include limb abnormalities, respiratory control problems, functional airway disease, orofacial clefts, nervous system anomalies, hypotonia, and abdominal wall defects. T18 (Edwards syndrome) affects approximately 1 out of 5000 live births. CHD is present in 80% to 90% of these babies born alive. Associated problems include limb abnormalities, nervous system anomalies, orofacial clefts, micro-retrognathia, respiratory control problems, functional airways disease, esophageal atresia, and abdominal wall defects. In the past, when such babies received only comfort care, survival to 1 year was 10% to 15%. More recent data from centers that provide life-prolonging treatment suggest survival rates for babies who receive life-prolonging treatment are higher.

1.2 Association with CHD

Whereas all CHD types and complexities have been reported in T13 and T18, the most common are patent ductus arteriosus (PDA) (32%), atrial septal defect (ASD) (27%), ventricular septal defect (VSD) (28%), and tetralogy of Fallot (9%) in T13, and VSD (42%), PDA (33%), and ASD (19%) in T18. Polyvalvular dysplasia is common in both disorders. Associated CHDs are categorized by complexity as mild, moderate, or severe[1] (Table 1).

1.3 Justification for Recommendations and a Writing Group

The paucity of clinical recommendations and lack of consensus in the medical and surgical cardiac care of these children motivated the American Association for Thoracic Surgery to convene a group of experts to address surgical decision making. This group consisted of clinicians and researchers in the fields of medical genetics, bioethics, cardiac surgery, pediatric cardiology and pulmonology, and cardiac and neonatal intensive care. The goal was to provide recommendations that could assist physicians and families in making decisions.

TABLE 1. Case complexity designations

Mild complexity congenital heart disease
Atrial septal defects
Patent foramen ovale
Persistent ductus arteriosus
Pulmonary valve stenosis
Moderate complexity congenital heart disease
Coarctation of the aorta
Atrioventricular septal defect
Tetralogy of Fallot
Total anomalous pulmonary venous connection
Ventricular septal defect
Sinus venosus atrial septal defect
Ebstein anomaly
Severe complexity congenital heart disease
Functional single ventricle anatomy
Hypoplastic left Heart Syndrome
Tricuspid atresia
Mitral atresia
Double outlet right ventricle
Transposition of the great arteries
Pulmonary atresia with ventricular septal defects
Truncus arteriosus
Pulmonary atresia with Intact ventricular septum

1.4 Methodology

This project was performed under the auspices of the American Association for Thoracic Surgery Congenital Heart Surgery Evidence-Based Medicine Taskforce. A subgroup of the taskforce met regularly to identify key questions related to the care of these children using the PICO Framework (patients/population, intervention, comparison/control, outcome). Using a list of key words, the group created a library of abstracts from a literature search of PubMed, Embase, Scopus, and Web of Science. Each abstract was reviewed by the entire writing group and graded on predefined criteria to address an overall set of goals for the project. Nine PICO Framework questions were formulated from this process. Full-length articles were then reviewed by at least 2 members of the writing group. Expert consensus statements with classification of recommendations (COR) and level of evidence (LOE) were developed using a modified Delphi method. To consider the statement having reached consensus, 80% of the members must have voted, with 75% of the members who voted casting a vote of "agree" or "strongly agree."

1.5 COR and LOE

COR and LOE, along with the language used for each statement, were determined based on guidance provided by the American College of Cardiology and the American Heart Association (Figure 1). In brief, COR reflects the magnitude of the treatment effect or likelihood of benefit relative to risk of harm. LOE estimates the certainty of that effect based on available data. When there were inadequate data for a consensus statement, a Best Practices Statement was created.

After the statements were drafted, the manuscript was constructed with a narrative following each statement to highlight the data and rationale behind the statement, including the strengths and limitations of the studies considered.

2. INDICATIONS BASED ON CLINICAL STATUS

2.1 Recommendation: Mild-to-Moderate Complexity CHD

	COR	LOE
In infants with T13 or T18 and CHD of mild or moderate complexity, who are confined to the hospital or neonatal intensive care unit, cardiac surgery is *reasonable* if the hemodynamic consequence of the CHD prohibits discharge.	**IIa**	**C-LD**

Until recently, congenital heart surgery was not offered because of the high mortality in children with T13 or T18 presumably caused by central apnea. A study from 1996 concluded that because CHD was not the direct cause of death, congenital heart surgery would not improve survival and was therefore "not justified."[2] A long era of "no surgery" followed this publication. Recent studies, single-institution case series and multi-institution database cohort studies, showcase acceptable perioperative outcomes and improved survival, refute the belief that T13 and T18 are universally "lethal," and call into question the "futility" of cardiac surgery.[3-12]

The earliest evidence of improved survival after palliative or corrective cardiac surgeries came in the late 1990s. Although initially believed to be near fatal or even "lethal" with a 5% to 10% survival to age 1 year based on population studies,[13] reports of longer survival in T13 and T18 prompted a review and revision of health care delivery.[14] This era effect is clearly demonstrated in studies from Japan comparing early (2008-2012) with late (2013-2017) survival of infants with T18. Survival to discharge significantly increased from 28% to 82% with simultaneous increase in CHD surgeries from 59 (17 out of 29) to 96% (26 out of 27) from the early to later years of this study.[15]

The majority of infants in this cohort had VSD and PDA, and the most common surgeries were pulmonary artery banding and PDA closure. In the United States, an evaluation of surgical experience from the Pediatric Cardiac Care Consortium demonstrated 91% survival to discharge following cardiac surgery (ascertainment bias should be considered because this database is voluntary).[16] VSD

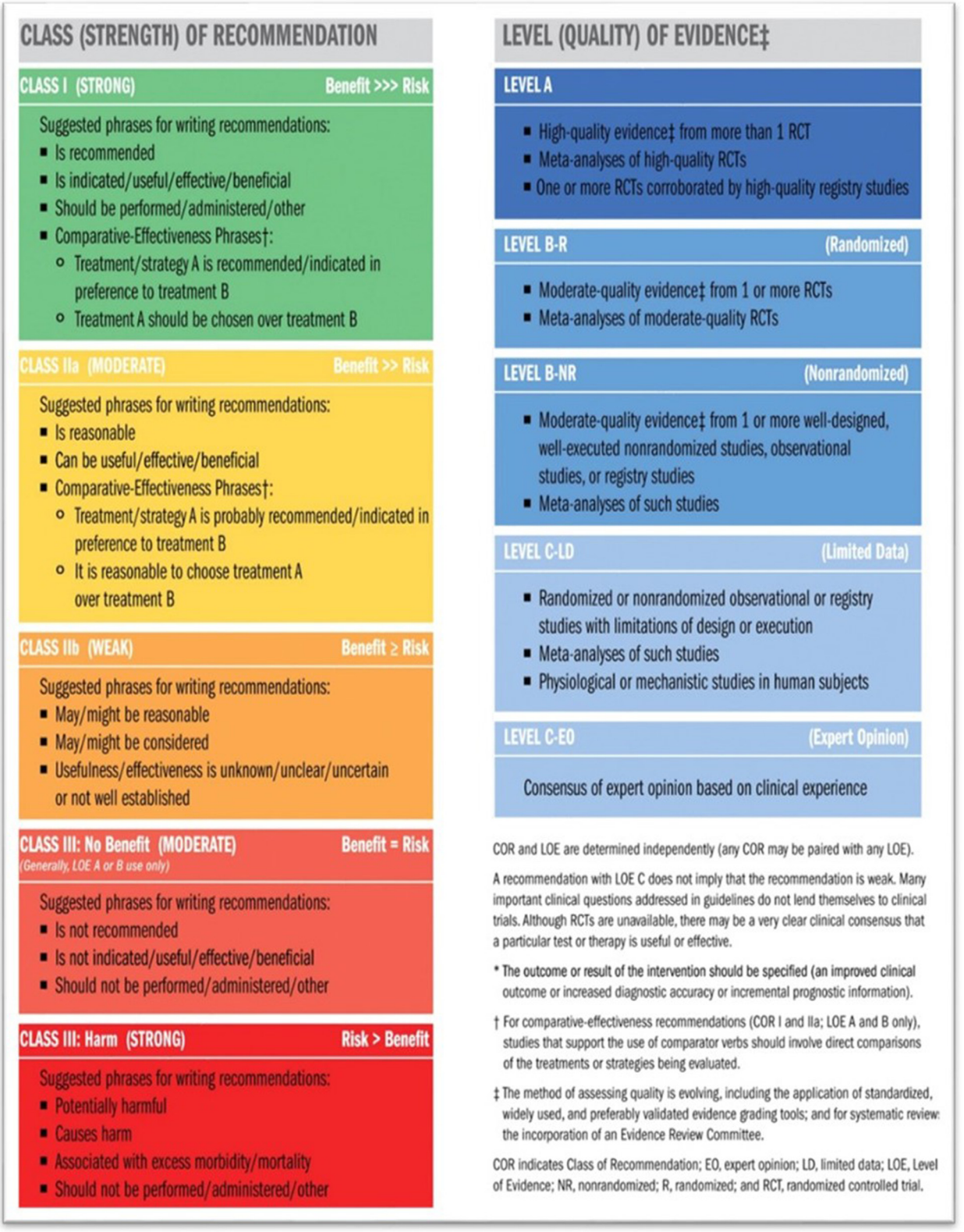

FIGURE 1. American College of Cardiology/American Heart Association recommendation system: applying Class of Recommendation and Level of Evidence to clinical strategies, interventions, treatments, or diagnostic testing in patient care. (Updated May 2019.) Reprinted with permission, ©2019 American Heart Association, Inc. https://cpr.heart.org/en/resuscitation-science/cpr-and-ecc-guidelines/tables/applying-class-of-recommendation-and-level-of-evidence. *RCT*, Randomized controlled trial; *COR*, class of recommendation; *LOE*, level of evidence.

was the most common lesion, followed by tetralogy of Fallot, coarctation, PDA, and atrioventricular canal defect. This study demonstrates the feasibility of palliative and corrective repair of CHD and improvement in survival with an intention-to-treat approach. A single-center study about the same time (2008-2013) examined mortality after cardiac surgery compared with supportive management and found a 29% mortality rate in the surgical group and a 50% mortality rate in the expectant management group.[17]

Increasing CHD surgery is a temporal trend across many countries, including the United States; it varies from 7% (US Pediatric Health Information System database)[6] to 26% (Japan)[4] and as high as 54%.[9] The number and regional distribution of surgical centers performing cardiac surgery are also increasing—with 70% of The Society of Thoracic Surgeons (STS) participating surgical centers performing surgery between 2010 and 2017.[18]

In a recent STS study, in-hospital mortality of children with T13 and T18 undergoing cardiac surgery for all levels of complexity exceeded the mortality rate of the overall group (15% vs 3%). Yet, this study importantly revealed that about 85% children with T13 and T18 undergoing various cardiac surgeries survived to discharge.[18] Similarly, a US Pediatric Health Information System database study reviewing 1020 infants with T18 and 648 infants with T13 from 2004 to 2015 showed improved in-hospital survival compared with expectant management.[6]

High early mortality and respiratory failure among children with T13 and T18 influence surgical decision making. Apnea is a noted confounder in this group, yet the etiologies and prognosis are varied. For example, seizures may play an unrecognized role in apnea as noted by a study showing improved survival with positive-pressure ventilation.[18] Positive-pressure ventilation allowed a subsequent diagnosis of seizures, which then improved with anti-epileptic drugs.[19,20] Median length of stay was longer (16 days in T13 or T18 vs 7 days in the overall STS cohort) and with increased surgical complexity.[18] When including all patients with T13 and T18, surgery may be accompanied by shorter hospital stays.[6]

Although patient age at the time of cardiac surgery varies tremendously across studies, most are reported between 2 and 4 months, in step with the presentation of heart failure symptoms. Such a presentation may manifest in an infant with T13 or T18 as failure to thrive despite adequate or optimal caloric intake, increased oxygen or diuretic requirement, tachypnea, tachycardia, hepatomegaly, cardiomegaly on chest radiograph, and echocardiographic findings consistent with a large left-to-right shunt.

Addressing metabolic needs may require nasogastric tube and gastrostomy placement. Separating the hemodynamic effects of CHD from coexistent extracardiac issues may delay progress and lengthen time to discharge, adding to provider and family frustrations. Gastrostomy tube placement is associated with improved survival,[7] demonstrating the importance of nutrition and growth. Persistent elevation in pulmonary arterial pressures or a delayed drop is well described and may minimize pulmonary overcirculation in a neonatal intensive care unit, allowing for discharge but later readmission. As with trisomy 21, pulmonary hypertension (PH) is likely to become nonreactive with time and result in increased morbidity and mortality following delayed surgical repair (as discussed in 6.1).

For all these reasons, repair of simple CHD of mild and moderate complexity should be thoroughly discussed in a multidisciplinary group and within a shared decision-making model with parents.[21] Surgical and medical management can then be aligned with goals of care established by this group and in a timely manner.

Palliative procedures such as pulmonary artery banding, followed by improved symptoms may facilitate discharge, although the same may be accomplished with definitive surgery and is in fact the preferred approach in many centers.[17]

2.2 Recommendation: Severe Complexity/ Functional Single Ventricle CHD

	COR	LOE
In infants with T13 or T18 and the diagnosis of CHD of severe complexity or functional single ventricle anatomy, it *might be reasonable* NOT to offer cardiac surgery based on anticipated early and late risks (demographic, physiologic, and clinical).	**IIb**	**C-LD**

The literature on outcomes following neonatal repair of complex CHD (eg, transposition of the great arteries, pulmonary atresia, and VSD) is limited and scant for single ventricle palliation.[5,14] It is possible that most infants with T13 or T18 who underwent single ventricle palliation did so before their genetic syndrome was identified. The STS report identified 343 index operations in 304 children with T13 and T18. The majority were The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery (STAT) 1 and 2 (64%), encompassing mild-to-moderate CHD. Only 2% were STAT 5, which comprises the most complex CHD. For STAT 5 operations, in-hospital mortality was almost triple that in children with T13 and T18 (43% vs 15%).[5] Although the same STS report indicated that a handful of T13 or T18 patients underwent Glenn and Fontan palliation, there is no report of long-term survival following single ventricle palliation in these children.[22-24]

Our statement that it is reasonable not to offer single ventricle palliation to infants with T13 or T18 is therefore based essentially on extremely limited data on surgery, data on nonsurvival in this population, as well as current

overall single ventricle palliation results. Our statement is also influenced by extracardiac risk factors in children with T13 and T18 on early and late outcomes.

Several studies that have examined current risk factors for mortality following single ventricle palliation identified several patient characteristics associated with operative, interstage, and late mortality. These include premature birth, low birth weight, low weight at time of first-stage palliation, genetic syndromes, and extracardiac anomalies—all uniformly common in children with T13 and T18.[2,13,15-18,25-35] Additional clinical risk factors for single ventricle palliation include respiratory failure, mechanical ventilation, and other organ involvement (eg, central nervous, and gastrointestinal) and are frequently encountered in children with T13 and T18.[7,9,36-39]

Single ventricle palliation success is largely dependent on well-functioning lungs and low pulmonary vascular resistance. The high prevalence of pulmonary vascular disease (PVD) in patients with T13 and T18 is well documented, and the pathophysiology of this PVD is not clearly explained.[4,7,10,19,20,40-42] This vulnerability may be inherent in these patients and likely to be excerbated by factors including apnea, respiratory insufficiency/failure, aspiration, and mechanical ventilation. Persistent PVD was noted to be associated with increased mortality following repair of simpler lesions such as VSD in children with T13 and T18; therefore, it seems rational to conclude that increased PVD would preclude successful single ventricle palliation outcomes in patients with T13 and T18.[4,7,10,19,20,40-42]

3. TIMING OF ELECTIVE REPAIR

3.1 Recommendation: Early Elective Repair

	COR	LOE
In infants and children with T13/T18 and CHD of mild or moderate complexity, who are at home or need recurrent hospital admissions, timely elective cardiac surgical repair is *reasonable* to decrease late cardiac morbidity mortality and to improve quality of life	**IIa**	**C-EO**

Some children with T13 or T18 can be discharged home after birth and are monitored in the outpatient setting for heart failure symptoms in shunting lesions (PDA, VSD, or ASD) or evidence for decreasing cardiac output (right- or left-sided obstructive lesions). Medical therapy such as caloric fortification, feeding rehabilitation, and diuretic therapy may be initially pursued until surgery is clearly indicated from a hemodynamic perspective. This approach is similar to management of nonaneuploidy patients, in whom standard of care is to medically manage as far as reasonably possible. Definitive surgery is pursued when medical therapy has been maximized, attempting to avoid the morbidity of repeat hospitalizations for unmanageable symptoms or intercurrent chest infections.

Children with T13 and T18 undergoing congenital heart surgery show improved in-hospital survival compared with those managed expectantly. Kosiv and colleagues[6] showed a lower in-hospital mortality following congenital heart surgery in children with T13 and T18 (45% lower in T13 and 64% lower in T18), and this survival benefit persisted throughout the 2-year follow-up. Since 2008, there has been a more than 3-fold increase in the number of cardiac surgeries performed in children with T13 and T18,[10] mostly for mild-to-moderate complexity lesions. In a single-center study comparing complete repairs with palliative repairs, Peterson and colleagues[8] described patients undergoing complete repair as older (median age, 9.2 months) and bigger (median weight, 5.2 kg) with no deaths before discharge and longer out-of-hospital survival. Most of these patients were initially managed as outpatients and admitted for surgery from home. These outcomes are superior to the surgical mortality and longevity of patients with T13 and T18 who need surgery as a newborn infant and cannot be discharged home after birth. However, other children will need cardiac surgery before discharge.

4. ASSOCIATED NONCARDIAC DEFECTS

4.1 Recommendation: Extracardiac Defects

	COR	LOE
While associated extracardiac defects such as esophageal atresia and abdominal wall defects are associated with higher morbidity and mortality in infants with T13/T18, repair of CHD of mild-to-moderate complexity *may be considered* once these other defects are adequately addressed.	**IIb**	**C-LD**

In addition to CHD, children with T13 and T18 are frequently diagnosed with multiple extracardiac anomalies. The presence of these anomalies contribute to postoperative morbidity and mortality following cardiac surgery, thus further complicating surgical decision making.[3-5] Pont and colleagues[24] examined the prevalence of congenital anomalies and their influence of mortality in children with T13 and T18. Among babies with T13, in-hospital death occurred in 54% with CHD, 49% with gastrointestinal anomaly, 58% with nervous system anomaly, 81% with abdominal wall defect, 42% with limb abnormality, and 50% with orofacial anomaly. Among babies with T18, in-hospital death occurred in 50% with CHD, 73% with gastrointestinal anomaly, 60% with nervous system anomaly, 72% with abdominal wall defect, 45% with limb abnormality, and 50% with orofacial anomaly.[24] It is important to note that most of the babies have multiple anomalies and thus fall into multiple groups. This increased

mortality supports the idea that extracardiac anomalies should be addressed before offering cardiac surgery.

Surgical procedures to address extracardiac anomalies in children with T13 and T18 have increased in parallel with surgery for CHD. Nelson and colleagues[27] reported an increase in surgical intervention in Canada with >24% of T13 and 14% of T18 patients undergoing 1 or more surgeries. Ear, nose, and throat procedures (excluding tracheostomy) were most common in children with T13, followed by gastrostomy. Gastrostomy was the most common procedure performed in children with T18.[27] Similar reports have been published in the United States and Japan, showing that a substantial number of patients with T13 and T18 received surgery before discharge, and that a considerable number of those required home medical care.[43,44]

Moreover, higher complexity surgical repair is performed in children with T13 and T18. Acharya and colleagues[45] reviewed the Children's Hospitals National Consortium and in 2021 reported on medical and surgical interventions in US neonatal intensive care units (50). Among babies with T13 and T18, 41% had at least 1 surgery of which omphalocele repair (silo and primary repair), tracheoesophageal ligation, esophageal atresia repair (staged and primary repair), gastroschisis repair, ventriculoperitoneal shunt, myelomeningocele repair, and congenital diaphragmatic hernia repair were noted.[45]

Although early results of these surgeries were acceptable, reported attrition following discharge remains high. Nishi and colleagues[46] documented intervention to address esophageal atresia in 24 patients with T18 of whom more than 50% underwent repair, either single or stepwise. Although there were no intraoperative deaths, 1-year survival was only 17%, with cardiac complications being the most common cause of death. Additional studies demonstrated unrepaired CHD to be among the most common causes of death in these patients.[46-48]

In other sections, we discuss the evidence that children with T13 and T18 and repaired CHD of mild-to-moderate complexity have better survival; we suggest that this should be the case for those with adequately repaired extracardiac anomalies.

There is an appropriate concern that extracardiac anomalies increase the risk of cardiac surgery. Several studies have shown that extracardiac anomalies do increase the early and late risks of neonatal cardiac surgery.[49-51] In the STS CHD refined risk prediction model, common noncardiac anomalies carried increased odds of mortality: omphalocele (adjusted odds ratio [aOR], 3.4), gastroschisis (OR, 3.1), congenital diaphragmatic hernia (OR, 2.6), and tracheoesophageal fistula (OR, 1.6).[52] In 2021, Kosiv and colleagues[53] presented a model to predict survival in children with T13 and T18. In this validated survival prediction model, abdominal wall defect (including omphalocele) was associated with increased mortality (hazard ratio, 1.32). Other earlier studies that examined outcomes of cardiac surgery in patients with T13 and T18 showed that extracardiac anomalies or previous tracheoesophageal surgery did not affect survival to discharge.[8]

Although extracardiac defects are associated with higher risk and longer recovery, we suggest that the correction of mild-to-moderate CHD in children with T13 and T18 be considered after additional defects have been adequately treated. Conversely, for children with T13 and T18 and moderate-to-major CHD, it is reasonable to recommend against cardiac surgical correction in the setting of significant extracardiac anomalies.

4.2 Recommendation: Ventilator Dependence and CHD Surgery

	COR	LOE
In infants with T13 and T18 who are ventilator-dependent (with or without tracheostomy) due to central apnea, airway, or lung disease, surgical repair of a congenital heart defect of mild-or-moderate complexity *may be considered*, if the severity of the respiratory disease is not prohibitive. An increased likelihood for long-term tracheostomy and higher mortality risks for these patients should be clearly explained to parents.	**IIb**	**C-LD**

Children with T13 and T18 represent a heterogeneous population with multifaceted reasons for chronic respiratory failure, including central apnea, aspiration, hypoventilation, pulmonary hypoplasia, abdominal wall defects, and congenital cardiac anomalies resulting in pulmonary overcirculation; all of which can contribute to chronic ventilator dependence.[7,8,54] Small physique, thoracic deformities, and scoliosis are also common in patients with T13 or T18 and can influence pulmonary dynamics and make supine position difficult for cardiac surgical procedures.[54,55]

Mechanical ventilation before cardiac interventions in infants with T13 and T18 has been associated with higher postoperative morbidity and mortality, as summarized in a 2020 review.[6] In a cohort of 304 children from the STS CHD Surgery database, 11 out of 16 (69%) children with T13 who received mechanical ventilation survived to discharge compared with 54 out of 57 (94%) who did not receive mechanical ventilation and survived.[18] Similarly, in children with T18, 52 out of 82 (63%) who were receiving mechanical ventilation at the time of surgery survived to discharge compared with 176 out of 188 (94%) who were not receiving mechanical ventilation. With 2 out of every 3 children who need mechanical ventilation preoperatively surviving to discharge, based on this large surgical cohort, ventilation alone should not be a criterion

for refusing to offer surgery for mild-to-moderate complexity lesions, particularly because surgical treatment of overcirculation may actually improve chances for weaning from ventilator support.

A single-center review of 17 children with T18, which included 10 who underwent cardiac surgery, reported clinical outcomes[56]; 3 had required preoperative mechanical ventilation, and each received tracheostomy later in their hospital course. Two of these children were discharged home with the tracheostomy, and 1 died after a prolonged hospital course.[56] A similar single-center review of 19 children with T13 and T18 who had cardiac surgeries included 5 children who had never been discharged home before surgery. Two out of the 19 had a preoperative tracheostomy, and 6 were receiving high-flow nasal cannula (HFNC) support from 1 to 7 L/m. This report does not specify the need for postoperative respiratory support; but the 1-year survival was 80%, and the 5-year survival was 67%.[12] Another recently published single-center report of 14 children with T13 and T18 who had surgery focused on the pulmonary outcomes.[8] This included 4 who were receiving mechanical ventilation preoperatively and 6 receiving either continuous positive airway pressure (CPAP)/HFNC or nasal cannula supplemental oxygen. Postoperatively, 7 of the 14 required mechanical ventilation for more than 7 days, and 6 of the 14 required CPAP/HFNC for more than 7 days. In this cohort, there was 1 in-hospital death of a child who had required preoperative mechanical ventilation; all others were discharged home. Two of the 14 received a tracheostomy before discharge.

Accompanying editorials to that article[8] highlighted the potential to interpret the meaning of these data divergently. In 1 editorial, palliative care, in lieu of surgical correction of cardiac anomalies, was suggested for children with T13 and T18, who remain on chronic mechanical ventilation.[57] The other editorial recommended that proceeding with surgery should be predicated on clear communication with family to set expectations for prolonged respiratory course and the potential for tracheostomy.[58] This divergence of interpretation may be a consequence of differing interpretations of quality of life among clinicians of using prolonged mechanical ventilation at home, as well as the inherent uncertainly in predicting outcome based on need for preoperative mechanical ventilation alone.

Families and clinicians need to consider 2 important issues in deciding about cardiac surgery in children with T13 and T18 who also have airway or respiratory disease. First, surgical intervention to address excess pulmonary blood flow may be useful to facilitate weaning from the ventilator for some of these patients.[59] Second, discharge home with tracheostomy may be considered by some families to be an acceptable, if not a positive, outcome for their child; parents appreciate when tracheostomy is presented in a balanced fashion.[60] Although some children will need long-term mechanical ventilation because of central apnea or tracheomalacia, home ventilation is not necessarily a problematic outcome; it is a standard intervention in children with complex respiratory issues that is accepted by many parents.

Individualized consideration of cardiac surgery for patients with children who would benefit from chronic mechanical ventilation is therefore important; issues to consider include appraising overall clinical condition, the underlying reasons for lung disease, expected benefits of cardiac interventions, and a focus on optimizing holistic outcomes and quality of life.[61] Preoperative planning and conversations with families should include the potential for prolonged intubation and chronic ventilation, even after sedation for minor procedures and radiographic imaging studies.[54] Higher morbidity and mortality risks following cardiac surgery, including potential tracheostomy and chronic ventilator dependence, have been reported[9,12,56] and should be discussed with families before committing to any cardiac surgical interventions. Home ventilation is among the most challenging home-based interventions that families are required to support. As part of shared decision making, it is very important to provide balanced information to parents for a clear and complete discussion.

5. PALLIATIVE VERSUS DEFINITIVE REPAIR

5.1 Recommendation

	COR	LOE
In infants and children with T13 or T18, surgical repair of CHD of mild-to-moderate complexity is associated with better outcomes than palliation; however, initial palliation (eg, pulmonary artery banding) *is recommended* in those with significant associated morbidity.	**I**	**C-LD**

Much of the surgical literature referenced thus far suggests that for children with T13 or T18 and concomitant CHD of mild-to-moderate complexity, surgical repair, definitive and palliative, leads to decreased cardiac morbidity and late mortality in the absence of extracardiac issues. In 2009, Kaneko and colleagues[62] published a report of 17 children with T18 who underwent cardiac surgery, 14 of whom underwent an initial palliative strategy. All of the patients had a VSD (except for 1 atrioventricular SD), and most of the infants weighed <2.5 kg at the time of surgery. Four infants proceeded to staged intracardiac repair. Median postoperative survival in the palliation group was 257 days, and only 1 child in that group died of heart failure-related complications. These results suggest that palliative surgery that is potentially followed by staged intracardiac repair can offer these children acceptable survival and, importantly, protect most of these children from dying as the result of the sequelae of heart failure.

In a 2019 STS analysis, the most frequent surgeries were in the lowest risk classification of STAT 1 (including VSD repair in 30%, ASD repair in 3%, coarct repair in 3%, and tetralogy of Fallot repair in 7%) followed by STAT 4 (pulmonary artery banding in 17% and Blalock-Thomas-Taussig shunt in 3%).[18] This indicates the complete repairs are being undertaken twice as frequently as palliative procedures in most reporting centers.[17]

Although palliative procedures may not have as long a bypass run or include any hypothermic circulatory arrest, they are not free from risk and have their own attendant immediate and intermediate complications; they are therefore placed in the higher surgical risk category of STAT 4 compared with definitive repairs that typically fall under STAT 1.[39] With waning expertise in some of these procedures, particularly aortopulmonary shunts, a case-by-case decision needs to be made by the care team and family. If a cardiac palliation does not facilitate growth or improvement in comorbidity, definitive surgical intervention without delay is considered reasonable (Class IIa, LOE C-EO) according to a review of contemporary practice.[63]

Palliative procedures such as pulmonary artery banding followed by improved symptoms may facilitate discharge to home or other care facility, which may be the goal of initial inpatient care. Somatic growth and time may permit the family and clinicians to plan forward-looking decisions about staged repair or ongoing expectant management, making palliative surgery a reasonable option if definitive surgery cannot be performed.

6. ASSOCIATED PVD

6.1 Recommendation

	COR	LOE
Infants and children with T13 or T18 are prone to develop early pulmonary hypertension due to an intrinsic arteriopathy, among other reasons. Therefore, early cardiac surgery *is reasonable* for mild-to-moderate complex congenital heart defects.	**IIa**	**B-NR**

Estimating the actual incidence of PVD and PH in children with T13 and T18 is challenged by heterogeneity of clinical status, surgical management, and timing of repair. It is clear that PVD has an important influence on long-term survival. Peterson and colleagues[8] looked at 50 children with T13 and T18 from the Pediatric Cardiac Care Consortium database from 1982 to 2008 who had undergone cardiac intervention in the United States and Canada. PH complicated in-hospital and out-of-hospital mortality. Nonsurvivors following VSD repair had higher pulmonary artery pressures and pulmonary vascular resistance compared with those who survived to discharge. Causes of postdischarge death were, in order: cardiac, respiratory disease, and PH. If treatments are being offered to extend the life of children with T13 or T18, careful attention must be given to the role of PH.[9]

Research suggests that there is an increased prevalence of PVD among children with T13 and T18. In 1989, Van Praagh and colleagues[64] reviewed 41 autopsies of children with T18, 25 of whom also had lung histology available. The authors identified significant medial hypertrophy and intimal proliferation in 8 (32%) cases. Most of these children had VSDs without pulmonary outflow tract obstruction. Six children were younger than age 2 months, and all were younger than age 7 months, leading the authors to conclude that children with T18 had a predisposition to develop a pulmonary vasculopathy earlier than typical children without a genetic syndrome.[64]

An additional study of 31 infants with T13 or T18 between 1983 and 1988 with VSDs demonstrated echocardiographic data (such as right ventricular end-diastolic dimensions and right ventricular free wall thickness) believed to be out of proportion with the cardiac lesions and patient age when compared with other infants.[64] This was believed to indicate an underlying predisposition to elevated pulmonary vascular pressures.[64] It is now generally accepted that children with T13 and T18 are at higher risk for developing PVD and PH, and this is a major contributor to higher mortality rates when CHD is not treated.

Tahara and colleagues[65,66] evaluated lung biopsies, taken at the time of palliative surgery, from 28 children with T18 and identified 4 children (14.3%) with medial wall defects of the small pulmonary arteries. Medial wall defects predispose a vessel to significant intimal proliferation and lumen narrowing. It is rare in other children without T18 and T13 (0.6%). Some patients in the Tahara study[67] also had pulmonary artery hypoplasia (46.4%), alveolar hypoplasia (53.6%), and alveolar wall thickening (75%.) The authors suggest that the PH found in children with T18 is not associated with medial hypertrophy, but rather a decreased pulmonary vascular bed size with higher resistance. Additionally, the alveolar hypoplasia with wall thickening likely influences vascular tone and remodeling, in addition to limiting gas exchange. Because of the underlying pathology that may predispose a child with T18 to develop PH, Tahara and colleagues[66] conclude that, if parents are requesting surgical intervention, it be done early to limit the development or progression of disease.

Can early surgery, then, modify the development of PH? An increasing amount of data are supporting that it can. A study by Kaneko and colleagues[61] looked at 17 children with T18 who underwent surgical correction for VSD or AVSD, with or without PDA. The children had either palliation with a pulmonary artery band alone, a staged repair, or primary complete intracardiac repair (ICR). Palliative surgery with or without secondary ICR had a statistically

significant association with longer postoperative survival when compared with primary ICR. It is suggested that this is partially related to controlling excessive pulmonary blood flow. Kaneko and colleagues[61] concluded that palliative surgery alone may be adequate to prevent cardiac deaths. Subsequent studies dispute the conclusion that palliative surgery alone is adequate,[34] but the study by Kaneko and colleagues[61] does support the benefit of early palliation to limit pulmonary blood flow on survival.

Overall, it must be recognized the patients with T13 and T18 may have a predisposition to the development of PVD, particularly with cardiac lesions with increased pulmonary blood flow. Because cardiac interventions are being considered, children must be monitored closely for signs of developing PH. In children with mild-to-moderately complex CHD with increased pulmonary blood flow, early surgery should be considered to mitigate the development of PH. When contraindications exist for early primary ICR, a staged approach with early palliation to limit pulmonary blood flow should be considered.

7. CARE MODELS

7.1 Recommendation: Multidisciplinary Care Team

	COR	LOE
In the management of children with T13 or T18, *multidisciplinary teams* including palliative care, *are recommended* as a component of an overall comprehensive care plan to enhance decision making for families considering cardiac surgery.	**I**	**C-LD**

Comprehensive care services (CCS) and pediatric palliative care teams have become integral health care partners for children with medical complexity. Children with medical complexity (CMC), the consensus designation for this group of high-risk children,[67] are characterized by chronic health problems involving multiple organ systems, functional limitations, and increased health care resource use. Infants and children with T13 or T18 meet this definition because of their medical fragility, high frequency of technology dependence, functional limitations, and increased health care needs.

In 2012, the American Academy of Pediatrics recommended "interdisciplinary and coordination plans that address the child's many healthcare needs."[68] Comprehensive care services for CMC encompass a team comprising physicians, surgeons, nurse practitioners, social workers, and care coordinators. A growing body of evidence, including 2 clinical trials, indicates that comprehensive care serving CMC and focusing on care coordination improve health care quality, decrease hospital costs and emergency department visits, and are acceptable and valuable to families.[69-72] Ellzey and colleagues[70] surveyed 191 families of CMC participating in a comprehensive care team; 85% considered their child's quality of life as excellent, very good, or good; and 87% reported "satisfaction with their child's health care." Additionally, Elgen and colleagues[73] describe a novel iterative approach for their interdisciplinary team that applies a bio-psycho-social model to the management of CMC.

A group of 507 children at a single children's hospital included children with T13 and T18 with chronic conditions.[72] Two articles discuss children with T13 and T18 specifically in the context of a comprehensive care team strategy. While commenting on the investigation of outcome of cardiac surgery by Kosiv and colleagues,[5] Jenkins and Roberts[74] stated that counseling about decisions for cardiac surgery "must be part of a comprehensive treatment plan." The timely and relevant review by Weaver and colleagues[75] describes the Interdisciplinary Trisomy Translational Program at the Children's Hospital and Medical Center, Omaha, Neb. The Interdisciplinary Trisomy Translational Program includes representatives from cardiology, cardiothoracic surgery, neonatology, otolaryngology, intensive care, neurology, social work, chaplaincy, palliative care, nursing, and medical genetics. The team aims to integrate the family's goals of care within the context of shared decision making.

Similar to CCS, pediatric palliative care (PPC) is an established discipline in pediatrics and essential to the management and support of families and children with chronic diseases and life-limiting conditions. The American Academy of Pediatrics 2013 Policy Statement provided comprehensive guidelines for interdisciplinary PPC teams. More recently, perinatal palliative care has become an integral part of prenatal care with the growth of fetal centers in the United States and the increasing ability to make fetal diagnoses of this genetic condition. PPC aims to meet the needs of children with medical complexity and life-limiting conditions, as well as supporting their families. PPC teams strive to relieve physical and psychological suffering, assist in care coordination, and facilitate informed decision making.

Because of the increased neonatal and infant mortality associated with T13 and T18,[76] children with these conditions and their families are ideal for referral to PPC for guidance. The limited data on the topic include the retrospective study of PPC referrals for children with T18 in children's hospitals, 1 in the United States and 1 in the United Kingdom, over an 11-year period.[77] There were 20 referrals in the United States and 38 in the United Kingdom. Of note, no cardiac surgeries were performed in the UK hospital cases, whereas 7 of the 20 children had cardiac surgery in the US hospitals. The authors recommended more research on the topic because they predict that more PPC clinicians will likely care for children with T13 and T18 in the future. Leuthner and Acharya[78] review the literature on current outcomes in T13 and T18 with the goal of providing

information to support parental decision making during perinatal counseling. The authors conclude that "there needs to be balanced decision making between parents and providers for the appropriate care" of the infant and mother and that perinatal palliative care consultation incorporate the knowledge of outcome with parental values.[78]

In conclusion, CCS for children with medical complexity and PPC teams have become integral to the care and management of children with chronic and life-limiting conditions. These service models should be provided to children with T13 and T18 and their families. There is growing evidence that the involvement of an interdisciplinary team can improve the physical, psychological, and emotional well-being of the patient and family as they are followed throughout the health care continuum. Additional research is needed about the effect on long-term outcomes.

7.2 Recommendation: Holistic Care Plan

	COR	LOE
Parents carrying a suspected or confirmed fetus with T13 or T18 and the diagnosis of a congenital heart defect *should* participate in the development of a holistic care plan for their child with input from maternal fetal medicine, neonatology, genetics, pediatric cardiology/cardiac surgery, and other necessary subspecialties involved in the future care of their child. This plan should reflect the parental goals for the pregnancy.	**I**	**C-LD**

Traditionally T13 and T18 have been described as a "lethal" anomaly. Parents receiving a prenatal diagnosis of T13 or T18 historically encountered almost universally negative prenatal counseling from health care professionals, including that their fetus was "incompatible with life."[79-84,85] For parents who choose to continue their pregnancy, concerns for a diminished quality of life and profound neurologic impairments give rise to clinical approaches that may focus on life-limiting interventions.[86] Social media and online parent support groups have emboldened parents and provided a different narrative, which describes improved survival, quality of life, and valuable and enriching life.[20,84-86]

Physicians involved in the perinatal care of families influenced by a suspected or confirmed diagnosis of T13 or T18 in the fetus must be abreast of the current survival and outcome data[20,60,76] and present balanced information about potential clinical trajectories for this heterogeneous population.[20,60,86,87] Goals of care may range from termination of pregnancy and comfort interventions to a pursuit of life-prolonging interventions, including surgery and technological dependence (eg, gastrotomy tube, tracheostomy, and home mechanical ventilation).[87] Decision making requires an individualized approach which recognizes that harms of certain interventions will outweigh benefits for some patients, and vice versa, based on unique clinical features.[88,89] Engaging in a process of shared decision making that communicates a range of outcomes, related uncertainties, and accounts for parental values regarding quality of life is essential.[87]

Centers providing comprehensive treatment to children with T13 and T18, including surgical and procedural interventions to address CHDs, must have robust multidisciplinary subspecialty support to develop synergistic care plans. Options presented to parents should reflect reasonable options based on current studies.[87] If some institutions do not offer surgery, that information should be transparent and referrals provided to support that family's personal goals for the pregnancy and care of their infant. Prenatal conversations about outcomes should be balanced, providing a reasonable range of possible outcomes and clinical challenges confronting all children with T13 and T18. In-depth conversations about cardiac surgery or committing to a definitive plan to offer a surgical intervention should be avoided prenatally because some infants may not achieve requisite clinical stability for surgical interventions to be feasible.[88,89] Shared decision making in these contexts, above all, should focus on building a trusting relationship with the family, clarifying their values and preferences, and developing shared goals for their infant.[90-93]

8. CONCLUSIONS

Our interdisciplinary working group provides an expert consensus document that can serve as a framework to care for children with T13 and T18 and a CHD that may be useful to families and providers, and potentially improve patient outcomes. We recognize that some treatment strategies may differ from current institutional practices. Because this is the first iteration of these guidelines, we anticipate ongoing multi-institutional collaborations to guide treatment.

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 manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

The authors thank Jill Colsch for her expert guidance and patience in completing the manuscript. The authors also thank the families of patients and the colleagues who have been inspirational in the care of these children.

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Key Words: trisomy 13, trisomy 18, congenital heart defects, mortality, indications for surgery