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REVIEW ARTICLE

Cardiac Surgery in Trisomy 13 and 18: A Guide to Clinical Decision-Making

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Abstract

There has been substantial controversy regarding treatment of congenital heart defects in infants with trisomies 13 and 18. Most reports have focused on surgical outcomes versus expectant treatment, and rarely there has been an effort to consolidate existing evidence into a more coherent way to help clinicians with decision-making and counseling families. An extensive review of the existing literature on cardiac surgery in patients with these trisomies was conducted from 2004 to 2020. The effects of preoperative and perioperative factors on in-hospital and long-term mortality were analyzed, as well as possible predictors for postoperative chronic care needs such as tracheostomy and gastrostomy. Patients with minimal or no preoperative pulmonary hypertension and mechanical ventilation undergoing corrective surgery at a weight greater than 2.5 kg suffer from lower postoperative mortality. Infants with lower-complexity cardiac defects are likely to benefit the most from surgery, although their expected mortality is higher than that of infants without trisomy. Omphalocele confers an increased mortality risk regardless of cardiac surgery. Gastrointestinal comorbidities increased the risk of gastrostomy tube placement, while those with prolonged mechanical ventilation and respiratory comorbidities are more likely to require tracheostomy. Cardiac surgery is feasible in children with trisomies 13 and 18 and can provide improved long-term results. However, this is a clinically complex population, and both physicians and caretakers should be aware of the long-term challenges these patients face following surgery when discussing treatment options.

Keywords Trisomy 13 · Trisomy 18 · Cardiac surgery · Risk factors · Outcomes

Introduction

Trisomy 13 (T13) and trisomy 18 (T18) are the two most common aneuploidies after trisomy 21, with a reported prevalence of 1.42/10,000 and 3.19/10,000 pregnancies, respectively, in the United States [1, 2]. Both syndromes have been considered "universally lethal," with around 70% of first-trimester pregnancies diagnosed with T18 and nearly 50% of those diagnosed with T13 resulting in fetal demise [3, 4]. Mortality remains high among live newborns, with a reported survival of 11.5% for T13 and 13.4% for T18 at one year of age [5]. The primary causes of death are either respiratory or cardiovascular, although medical interventions have been shown to increase one-year survival [6–9].

Congenital heart disease (CHD) is one of the most frequent problems these patients face; consequently, heart failure resulting from untreated CHD is one of the primary causes of mortality among affected individuals [9, 10]. Although controversial, cardiac surgery has become more common in patients with T13 and T18 [11, 12]. A number of studies have been published regarding outcomes of cardiac surgery in T13 and T18 with varied results due to population size, patient characteristics, and follow-up time constraints. The diversity of factors affecting patient survival has limited congruency in recommendations. To the best of our knowledge, these studies have not produced a salient guide to decision-making for clinicians that encompasses the complex factors influencing outcomes. This review purposes to offer a nuanced analysis of the literature to provide the clinician guidance in an area of ongoing debate.

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Methods

An extensive literature search was conducted on PubMed for all articles pertaining to congenital heart surgery in T13 or T18, as well as additional relevant studies in patients without heart surgery between January 2004 and January 2020. The resulting studies were screened for the characteristics of their surgical population and identified risk factors for negative outcomes after cardiac surgery. The most commonly mentioned risk factors were organized by preoperative and perioperative factors. Resulting studies were comprised of both multicenter database analyses and single-institution reports. A summary of these and their characteristics can be found in Table 1. The primary databases reported include the Pediatric Health Information Systems (PHIS), Pediatric Cardiac Care Consortium (PCCC), Kid's Inpatient Database (KID), and the Society of Thoracic Surgeon's (STS) Congenital Heart Surgery Database.

Results

Preoperative Factors

Trisomy Presentation

The most common presentation of T13 and T18 is full trisomy, where individuals have three copies of the affected chromosome in all of their somatic cells. However, 1% of affected patients present with mosaic trisomy, in which only some cells have the supernumerary chromosome, and 8% have partial trisomy, characterized by Robertsonian translocations [13]. These variations have been associated with greater survival: a seven-year study in England and Wales found one-year survival of 80% in mosaic T13, 70% in mosaic T18, and 29% in partial T13, with no partial T18 cases [14]. The low prevalence and improved outcomes for these variants is reflected in cardiac surgery populations. Results from the PCCC population, which included 18 mosaic/partial T13 and 10 analogous T18 patients, provide a favorable panorama. In this study, a lower in-hospital mortality rate (5.6% vs 54.5% for T13 and 0% vs 11.9% for T18) and significantly longer median survival (16.7 vs 14.5 years) were associated with mosaic/partial diagnoses compared to those with full trisomy [15]. Unfortunately, additional database studies used ICD-9 codes for the identification of T13/18 patients and were thus unable to differentiate between trisomy presentations [16, 17]. Single-center studies provide some additional information, although their mosaic/partial populations are small. Of the two mosaic patients in Costello et al.'s study, one died postoperatively and the other survived to discharge [18]. Meanwhile, Muneuchi et al. found that mosaicism negatively influenced rates of survival to discharge, but did not affect long-term survival for the three patients with mosaic T18 in their cohort of nine surgical patients [19]. Despite the improved odds of survival following cardiac surgery observed in patients with mosaic and partial trisomy presentations, further studies with larger populations are needed in order to strengthen these observations [14, 20].

Extracardiac Anomalies

Heart defects affect up to 60–80% of infants with T13 and T18. However, the syndromic nature of these diseases implicates multiple organ systems with a wide range of defects beyond the heart. Extracardiac anomalies have been well described as a risk factor for operative mortality in the general CHD surgical population [21]. The majority of these babies (T13: 78%; T18: 58%) are affected by anomalies in at least two organ systems [10]. Extracardiac anomalies can vary by disease: in T13, the most common are limb deformities (48%), oro-facial clefts (45%), neurological (39%), and ophthalmological defects (30%), while the most common extracardiac anomalies in T18 include limb deformities (28%), neurological (21%), digestive and urinary tract defects (each 18%) [10]. Of these, eye, ear, limb, and genitourinary anomalies are associated with the lowest rates of in-hospital mortality for both T13 and T18 [22]. Abdominal wall (81%) and central nervous system (58%) defects were more commonly seen in T13 infants who did not survive to discharge, while gastrointestinal (73%) and abdominal wall (72%) defects were more preponderant among their T18 counterparts [22].

In particular, esophageal atresia and omphalocele have been implicated in multiple reports as important risk factors for mortality. In a multicenter study from Japan, esophageal atresia was found in 37% of T18 infants who died prior to discharge ($p = 0.02$), with similar rates of CHD among hospital survivors and non-survivors [23]. Although surgical intervention for esophageal atresia in T18 is feasible, the postoperative survival rate at one year for these patients is 17% [24]. Meanwhile, an analysis of T13 and T18 babies born across nine states found that the presence of omphalocele significantly increased the risk of death for infants with T18 at one and twelve months [5]. Notably, all of these studies cited CHD as an important factor for mortality. Therefore, it can be surmised that the combination of the aforementioned defects with CHD would further augment the risk of in-hospital mortality.

Table 1 Summary of included studies analyzing outcomes of cardiac surgery in patients with T13 and T18

Study	Author and year	Type of study	Trisomy	Number of patients	Weight at surgery (kg)	Age at surgery	Palliative surgery	Corrective surgery	Preoperative ventilation	Discharged home	Hospital mortality	Late mortality	Survival
Cardiac Surgery in Patients with Trisomy 13 and 18: An Analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database [30]	Cooper DS, Riggs KW, Zafar F, Jacobs JP, Hill KD, Pasquali SK, et al. (2019)	Multicenter, retrospective cohort (STS Congenital Heart Surgery Database)	13	73	4.8 (3.5–9.4)	4.5 (1.4–18.6) months	13 (17.8%)[a]	39 (53.4%)[b]	16 (21.9%)	65 (89%)	8 (11%)	n/a	n/a
			18	270	3.5 (2.5–5.6)	3.7 (1.5–9.4) months	55 (20.4%)[a]	172 (63.7%)[b]	82 (30.4%)	228 (84%)	42 (16%)	n/a	n/a
Mortality and resource use Following Cardiac Interventions in Children with Trisomy 13 and Trisomy 18 and Congenital Heart Disease [40]	Domingo L, Carey JC, Eckhauser A, Wilkes J, Menon SC (2019)	Multicenter, retrospective cohort (PHIS)	13	49[c]	n/a, 1 (2.0%) low birth weight	10.7 (1.29, 26.57) weeks	14 (28.6%)	22 (44.9%)	n/a	26 (53%)	16 (33%)	n/a	n/a
			18	140[c]	n/a, 6 (4.3%) low birth weight	19.4 (7.79, 42.93) weeks	10 (7.1%)	101 (72.1%)	n/a	85 (61%)	31 (22%)	n/a	n/a

Table 1 (continued)

Study	Author and year	Type of study	Trisomy	Number of patients	Weight at surgery (kg)	Age at surgery	Palliative surgery	Corrective surgery	Preoperative ventilation	Discharged home	Hospital mortality	Late mortality	Survival
Trisomy 18 and Congenital Heart Disease: Single-Center Review of Outcomes and Parental Perspectives [34]	Davisson NA, Clark JB, Chin TK, Tunks RD (2018)	Single-center retrospective	18	9	3.2 (1.5–12.2)	4.3 (0.2–23.4) months	1 (11.1%)	8 (88.9%)	3/9 (33.3%)	6 (66.7%)	3 (33.3%)	0 (0%)	50 (5–91) months
Congenital Heart Surgical Admissions in Patients with Trisomy 13 and 18: Frequency, Morbidity, and Mortality [42]	Ma MH, He W, Benavidez OJ (2019)	Multi-center, retrospective cohort (KID)	13	22	n/a	n/a	n/a	n/a	n/a	19 (86%)	3 (14%)	n/a	n/a
			18	58	n/a	n/a	n/a	n/a	n/a	51 (88%)	7 (12%)	n/a	n/a

Table 1 (continued)

Study	Author and year	Type of study	Trisomy	Number of patients	Weight at surgery (kg)	Age at surgery	Palliative surgery	Corrective surgery	Preoperative ventilation	Discharged home	Hospital mortality	Late mortality	Survival
Trisomy 18 and Congenital Heart Disease: Single-Center Review of Outcomes and Parental Perspectives [34]	Davisson NA, Clark JB, Chin TK, Tunks RD (2018)	Single-center retrospective	18	9	3.2 (1.5–12.2)	4.3 (0.2–23.4) months	1 (11.1%)	8 (88.9%)	3/9 (33.3%)	6 (66.7%)	3 (33.3%)	0 (0%)	50 (5–91) months
Factors Influencing Outcomes After Cardiac Intervention in Infants with Trisomy 13 and 18 [28]	Peterson R, Calamur N, Fiore A, Huddleston C, Spence K (2018)	Single-center retrospective	13 and 18	16	5.2 (3.7, 6)	9.2 (6.2, 18.3) months	-	11	0 (0%)	11 (100%)	0 (0%)	3 (27%)	25.8 (13.3–47) months
					2.5 (2.0, 2.7)	1.7 (0.3, 1.9) months	7	-		4 (57%)	2 (29%)	4 (57%)	2.6 (1–3.5) months
Long-Term Outcomes of Children With Trisomy 13 and 18 After Congenital Heart Disease Interventions [15]	Peterson JK, Kochilas LK, Catton KG, Moller JH, Setty SP (2017)	Multi-center, retrospective cohort (PCCC)	13	29	3.8 (3.2, 7.3)	3.2 (0.6–8.6) months	8	21	4 (13.8%)	21 (72.4%)	8 (27.6%)	23 (23%)	14.8 (12.3–25.6) years
			18	69	4.3 (2.7, 6.4) kg	6.2 (1.4–16.7) months	21	48	9 (13%)	60 (87%)	9 (13%)		16.2 (12–20.4) years

Table 1 (continued)

Study	Author and year	Type of study	Trisomy	Number of patients	Weight at surgery (kg)	Age at surgery	Palliative surgery	Corrective surgery	Preoperative ventilation	Discharged home	Hospital mortality	Late mortality	Survival
Congenital Heart Surgery on In-Hospital Mortality in Trisomy 13 and 18 [16]	Kosiv KA, Gossett JM, Bai S, Collins RT (2017)	Multicenter, retrospective cohort (PHIS)	13	37	n/a, birth weight 2.8 (2.3–3.2)	n/a, 0 (0–1) days (admission)	21	24	36 (97.3%)	26 (70%)	11 (30%)	n/a	141 (46–571) days
			18	63	n/a, birth weight 2.4 (2.1–2.9)	n/a, 0.5 (0–1) days (admission)	14	64	63 (98.4%)	53 (84%)	10 (16%)	n/a	278 (63–1029) days
Survival and Surgical Interventions for Children With Trisomy 13 and 18 [20]	Nelson KE, Rosella LC, Mahant S, Guttmann, A (2016)	Multicenter, administrative and demographic databases in Ontario	13	6	n/a	0.7 (0.1–9.8) years	n/a	n/a	n/a	n/a	n/a	n/a	8.3 (0–11.3) years
			18	6	n/a	0.7 (0–2.6) years	n/a	n/a	n/a	n/a	n/a	n/a	7.4 (0.1–15.0) years
Effectiveness of cardiac surgery in patients with trisomy 18: A single-institutional experience [31]	Nakai Y, Asano M, Nomura N, Matsumae H, Mishima A (2016)	Single-center retrospective	18	10	2.1 (1.5–2.7)	47 (6–123) days	10	1	n/a	9 (90%)	1 (10%)	3 (30%)	495.4 ± 512.6 days

Table 1 (continued)

Study	Author and year	Type of study	Trisomy	Number of patients	Weight at surgery (kg)	Age at surgery	Palliative surgery	Corrective surgery	Preoperative ventilation	Discharged home	Hospital mortality	Late mortality	Survival
A Contemporary, Single-Institutional Experience of Surgical Versus Expectant Management of Congenital Heart Disease in Trisomy 13 and 18 Patients [18]	Costello JP, Weiderhold A, Louis C, Shaughnessy C, Peer SM, Zurakowski D, et al. (2015)	Single-center retrospective	13	1	n/a	43 days	0	1	n/a	1 (100%)	0 (0%)	0 (0%)	798 days
			18	7	1.8 + 0.3	105 ± 94 days	2	5	n/a	5 (71%)	2 (29%)	1 (20%)	106 (13–1778) days
Inpatient Hospital Care of Children With Trisomy 13 and Trisomy 18 in the United States [17]	Nelson KE, Hexem KR, Feudtner C (2012)	Multi-center, retrospective cohort (KID)	13	34 procedures	n/a	1.2 (0–13) years (admission)	n/a	n/a	n/a	n/a	n/a	n/a	n/a
			18	120 procedures	n/a	0.7 (0–6) years (admission)	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Outcomes of cardiac surgery in trisomy 18 patients [19]	Muneuchi J, Yamamoto J, Takahashi Y, Watanabe M, Yuge T, Ohno T, et al. (2011)	Single-center retrospective	18	9	2.4 (1.5–3.2)	50 (14–295) days	6	3	3 (33%)	5 (56%)	2 (22%)	2 (22%)	22.4 (3.3–241) months

Table 1 (continued)

Study	Author and year	Type of study	Trisomy	Number of patients	Weight at surgery (kg)	Age at surgery	Palliative surgery	Corrective surgery	Preoperative ventilation	Discharged home	Hospital mortality	Late mortality	Survival
Radical surgery for a ventricular septal defect associated with trisomy 18 [47]	Kobayashi J, Kaneko Y, Yamamoto Y, Yoda H, Tsuchiya K (2010)	Single-center retrospective	18	5	1.6 (1.4–3.2)	14.5 (7–194) days	4	-	n/a	-	-	-	-
					4 (3.6–5.1)	349 (258–402) days	-	5	n/a	4 (80%)	1 (20%)	2 (40%)	815 ± 389 days
Cardiac surgery in patients with trisomy 18[d] [26]	Kaneko Y, Kobayashi J, Achiwa I, Yoda H, Tsuchiya K, Nakajima Y, Kawakami T (2009)	Single-center retrospective	18	17	1.96 (1.0–4.06)	66 (7–258) days	14	7	n/a	14 (82%)	3 (18%)	8 (47%)	324 (12–1384) days
Intensive cardiac management in patients with trisomy 13 or trisomy 18 [25]	Kaneko Y, Kobayashi J, Yamamoto Y, Yoda H, Kanetaka Y, Nakajima Y, Kawakami, T (2008)	Single-center retrospective	13	1	n/a	72 days	1	0	1 (100%)	1 (100%)	0 (0%)	1 (100%)	207 days
			18	3	Kaneko 2009								

Table 1 (continued)

Study	Author and year	Type of study	Trisomy	Number of patients	Weight at surgery (kg)	Age at surgery	Palliative surgery	Corrective surgery	Preoperative ventilation	Discharged home	Hospital mortality	Late mortality	Survival
Effectiveness of cardiac surgery in trisomies 13 and 18 (from the Pediatric Cardiac Care Consortium) [29]	Graham EM, Bradley SM, Shirali GS, Hills CB, Atz AM (2004)	Multicenter, retrospective cohort (PCCC)	13	11	3.8 (2.8–11.3)	77 (4–2,375) days	14	25	9 (25.7%)	11 (100%)	0 (0%)	n/a	n/a
			18	24	3.6 (2.1–16.0)	145 (6–2,479) days				21 (86%)	4 (14%)		

Only patients with cardiac surgery included unless otherwise noted. Palliative and corrective surgeries are not mutually exclusive. For patients who underwent palliative and then corrective surgery, only the weight and age at initial surgery were taken into account. Results reported as n (%), mean ± standard deviation, median with interquartile range (Q1, Q3), or median with range (minimum–maximum), as reported in each study

[a]Only includes palliative procedures for which numbers are given

[b]Only includes corrective procedures for which numbers are given

[c]Number of patients who underwent all cardiac interventions (surgical and catheter-based)

[d]Patients also found in Kaneko 2008 and Kobayashi 2010

Pulmonary Vascular Disease and Pulmonary Hypertension

Pulmonary hypertension is often cited as a complication or coexisting risk factor for these infants. However, few studies provide clarity as to true nature of pulmonary vascular disease with hemodynamic data. By definition, all infants with unrestrictive ventricular septal defect (VSD) physiology would have "pulmonary hypertension," i.e., expected pulmonary artery (PA) pressure would be the same as the right ventricle, which in turn is the same as the left ventricular pressure. However, this does not equate to pulmonary vascular disease. The majority of published literature simply cites pulmonary hypertension without providing supportive data; others use ICD-9 coding (primary vs. secondary), which is also unreliable in this regard. Overall, only three papers have specifically described patient hemodynamics and assessed pulmonary vascular resistance in infants with T13 and T18.

In the first study to report hemodynamic data in these infants, Kaneko et al. banded the PA in four patients at an early age (first 2 weeks up to 2 months of age) [25]. Although all patients were effectively banded, they continued to demonstrate increased pulmonary vascular resistance (PVR) on their follow-up catheterizations. For instance, one patient banded on day of life 10 had a PVR of 4.0 Woods units/m^2 on her catheterization evaluation prior to VSD repair, nearly a year later. Using the PCCC data, Peterson and colleagues analyzed the hemodynamics of a subset of patients (14/33 patients with VSD) [15]. They found that patients who died in-hospital ($n=3$) after VSD closure had a higher median PVR (5.05 Woods units/m^2) than survivors ($n=11$, PVR = 3.45 Woods units/m^2) and mean PA pressure (45 vs 38 mmHg). Moreover, PH accounted for 78% of Kaneko et al.'s mortalities prior to hospital discharge (especially among those without cardiac surgery), and 13% of post-discharge mortalities in the PCCC surgical cohort [15, 26].

Similarly, a survey of hospitals affiliated with the Japanese Society of Pediatric Cardiology and Cardiac Surgery reported a preoperative prevalence of pulmonary hypertension of 93% among T18 infants and half of the T13 population seen in Japan between 2005 and 2008, although it is unclear whether the diagnosis of pulmonary hypertension was based on catheterization data or not [27]. In many of these infants, pulmonary hypertension can persist postoperatively. This is evidenced in Peterson, Calamur, et al.'s study, where patients had a median right ventricular to left ventricular systolic pressure ratio of 0.5 (IQR 0.3–0.67) following cardiac surgery, with the highest ratio being 0.9. Further, among survivors, 27% were discharged on pulmonary vasodilators and 45% on supplemental oxygen [28]. Higher preoperative mean pulmonary pressure has been associated with postoperative mortality for infants with T13 and T18 [15]. Collectively, those with PVR ≥ 5.0 Woods units/m^2 have done poorly following surgery. These data suggest that (1) perhaps T13/T18 patients are more at risk for pulmonary vascular disease than other newborns; (2) determination of PVR preoperatively can help in risk assessment; and (3) postoperative management should strongly consider the possibility of pulmonary hypertensive crises for these infants.

Mechanical Ventilation

Due to the high prevalence of respiratory conditions, such as central apnea, and their substantial role on mortality, patients with T13 and T18 often require preoperative mechanical ventilation [9, 20, 23]. The influence of preoperative mechanical ventilation on patient outcomes is dependent on a variety of factors including length of intubation, type of surgery, and successful ventilator wean.

In one of the first studies analyzing this population, Graham et al. found that patients who required more than two days of mechanical ventilation preoperatively had an increased mortality or need for mechanical ventilation at discharge [29]. Similarly, Peterson, Calamur et al. found that preoperative mechanical ventilation greater than two days was associated with continued postoperative ventilator use [28]. The presence of preoperative mechanical ventilation as a risk factor for operative mortality is further supported by data from the STS database, which establishes an eightfold in-hospital mortality risk for patients intubated prior to surgery [30]. Finally, patients undergoing palliative procedures have been described as requiring more prolonged mechanical ventilation postoperatively than those with complete repair [28]. Nevertheless, surgical palliation offers a better possibility of extubation than conservative treatment [31].

These results indicate that preoperative mechanical ventilation is an important risk factor for in-hospital mortality. Minimal (< 2 days) or no preoperative ventilation may reduce postoperative ventilation and mortality [29]. Surgical intervention overall offers improved survival and extubation rates, with corrective surgery offering shorter postoperative mechanical ventilation times than palliative procedures.

Perioperative Factors

Weight at Surgery

Patient weight at surgery is a well-documented risk factor for mortality in non-syndromic patients [32]. Non-syndromic patients who weigh less than 2.5 kg at the time of surgery are shown to experience higher rates of in-hospital mortality regardless of surgical complexity or procedure performed [33]. Similarly, a majority of studies performed on patients with T13 and T18 have associated higher weight with greater survival to discharge and longer survival overall [16, 18,

20, 27, 34, 35]. Unfortunately, the prevalence of low (1500-2500 g) and very low (< 1500 g) birth weight in T13 and T18 patients has been reported in over half of patients in multicenter studies [36, 37]. These patients have been shown to experience longer hospital stays and higher mortality rates than those with higher birth weights [36–38].

A majority of studies performed on patients with T13 and T18 have described greater weight as one of the most important factors for a positive outcome. Most centers are clearly inclined to offer surgery to patients with higher birth weights [15, 16], which appears to be associated with greater survival to discharge and longer survival overall [16, 18, 20, 27, 34, 35]. In many of these reports, higher mortality can be observed in patients with lower weights, especially under 3 kg. Even when pursuing palliative intervention, it appears lower weight is a significant risk factor; in Nakai et al.'s report, the mean weight at surgery for infants who died was 1.88 kg vs. 2.26 kg for survivors [31, 34]. It appears most clinicians have already incorporated this knowledge into their practice: the median weight at surgery for patients in the STS database [T13: 4.8 (3.5–9.4); T18: 3.5 (2.5–5.6)] is significantly higher than their birth weight [T13: 2.7 (2.4–3.1); T18: 2.0 (1.8–2.4)], suggesting that surgery is typically postponed until weight is over 3 kg [30].

Collectively, these results demonstrate the important impact of weight on outcomes. The implications are twofold: (1) as in other arenas of pediatric cardiac surgery, in the case of prenatal diagnosis, it behooves surgeons to have conversations early with maternal–fetal medicine and/or obstetricians caring for these moms to delay birth until 40 or 41 weeks of gestation; (2) surgical intervention is most likely to result in an optimum outcome if the patient is ≥ 3 kg; palliative intervention can be considered (and should be considered early) in patients that weigh much less to allow for possible weight gain while awaiting complete repair [28].

Age at Surgery

Age and weight are inextricably linked, as weight increases with age. In non-syndromic neonates (< 30 days at surgery), higher operative mortality and complication rates exist compared to older patients [39]. Analyses of T13 and T18 patient populations have similarly highlighted the importance of age on surgical outcomes.

Most authors believe that older age at the time of surgery significantly improves patient survival. Nakai et al. found that long-term survivors were significantly older at the time of surgery (69.7 ± 37.3 vs 23.0 ± 17.3 days), although there was no impact on survival to hospital discharge [31]. In Peterson, Calamur, et al.'s cohort, patient age at surgery significantly impacted survival, with those undergoing complete repair at an average of 9.2 months surviving a mean of 25.8 months. Infants with increased risk for surgical repair were palliated at an average age of 1.7 months, with a mean survival of 2.6 months [28]. Patients reviewed from the STS database had an older median age at surgery of 4.5 (1.4–18.6) for those with T13 and 3.7 (1.5–9.4) months for those with T18 [30]. Similarly, analysis of the PHIS database showed older age at the time of surgery was linked to improved long-term survival, contrasting a higher 30-day mortality among patients who were operated on at a median age of 1 week for both T13 and T18 with survivors whose median age at operation was 6.3 weeks for T13 and 17 weeks for T18 [40]. Of note, however, the latter data also highlighted that older age at admission was associated with lower mortality rates, suggestive that older babies may be more stable, having already survived to hospital discharge as a newborn [16].

In general, age in and of itself is a useful predictor of long-term outcomes for these infants. Overall, patient survival to 28 days is only 26% for T13 and 37% for T18 [5]. However, those who make it to 28 days have a 60% and 71% probability of survival to one year, respectively, for T13 and T18 infants [5]. Notably, the improved survival in patients operated at a minimum three months of age, even in light of prolonged exposure to pulmonary overcirculation, suggests in general that delaying surgery for a month or two, when the patient's clinical status allows for it, would be a reasonable approach to optimize outcomes.

Surgical Approach

The spectrum of cardiac defects found in T13 and T18 are routinely approached in three manners: "definitive" palliative surgery, corrective surgery, and delayed corrective surgery following an initial palliative intervention. Discussions surrounding corrective versus palliative surgery in patients with T13 or T18 have evolved in recent literature. Consistent with the general approach in pediatric cardiac surgery currently, complete surgical repair of CHD has shown the best outcomes compared to palliative surgery, with improved in-hospital and long-term survival [15, 18, 19, 28]. However, a number of single center reports have shown successful outcomes with initial surgical palliation followed by corrective surgery [26, 28, 29, 41].

Due to the short life expectancy associated with these syndromes, older studies preferred surgical palliation for relief of symptoms. This approach resulted in improved survival compared to expectant treatment, although survival to discharge remains inferior to that of infants undergoing complete surgical repair [28]. Consequently, recent publications favor corrective surgery for improved survival. According to data from the STS, between 2010 and 2019, the majority of CHD surgeries for patients with T13 and T18 performed

in North America were corrective [30]. However, a significant percentage of patients (T13: 21.9%; T18: 16.3%) underwent multiple cardiac procedures, suggesting surgical palliation frequently occurred prior to corrective procedures. Interestingly, results from the STS study found significantly improved operative survival following a staged approach in patients with T18, but not T13 [30]. Thus, these infants stand to benefit the most from corrective cardiac surgery, with a staged approach providing improved outcomes compared to surgical palliation alone.

Surgical Complexity

Over 60% of surgeries performed on T13/T18 infants between 2010 and 2017 in the STS database were classified as STS/European Association for Cardiothoracic Surgery Congenital Heart Surgery Mortality (STAT) categories 1 and 2 [30]. These are considered low-risk procedures, such as patent ductus arteriosus ligation, vascular ring repair, atrial septal defect closure, or VSD closure. Higher-complexity STAT 4 and 5 procedures comprised about a quarter of reported surgeries and were performed more often in T13 (36% vs 24%) and comparably in T18 (27% vs 24%) relative to the entire STS population [30]. Since 2010, there has been a steady increase in the number of procedures performed every year on patients with T13 and T18 [30]. Reports on high-complexity lesions, such as hypoplastic left heart syndrome, are rare, with only two reported cases in both the STS and PHIS databases [16, 30].

An analysis of the KID found that a Risk Adjustment for Congenital Heart Surgery-1 (RACHS-1) score greater than 2 (higher complexity) was associated with increased rates of postoperative complications and hospital death [42]. Results from the STS database demonstrate that low complexity/low-risk procedures (STAT 1) have favorable results for T13 patients compared to the overall STS population (although the sample was limited to 25 patients), but not so for T18 (10% mortality vs. expected mortality of 0–0.5%). This increased risk became more prominent for STAT 2 procedures, with 29% of T13 patients and 17% of T18 patients suffering from operative mortality (versus the expected mortality of 1–2%) [30]. In general, patients with T18 experienced significantly higher in-hospital mortality at every STAT category [30]. Although this finding was only statistically significant for STAT 2 among children with T13, this is likely due to the smaller population size even in this comprehensive report from North America. Additional reports from large-scale database studies such as PHIS and PCCC have similarly found higher operative mortality rates for these patients [15, 40]. This observation remained true even for low complexity score surgeries such as STAT 1 and STAT 2 (6.4% vs 0.6% and 25% vs 2.4%, respectively), as well as the most common and straightforward procedure, VSD repair (9% vs 0.6%), when compared to the general population [15, 40]. In general, collective results suggest an operative mortality 10–20-fold higher than usual for even simple procedures, which should be taken into consideration when counseling families. Data on single ventricle palliation, considered the upper limit of surgical complexity for CHD, remain scarce, and most centers do not currently offer such procedures to infants with T13 and T18 due to concerns with causing prolonged affliction in affected infants, given these procedures' association with high baseline mortality and significant postoperative morbidity [43].

Postoperative Concerns

Tracheostomy

One of the most common concerns parents of T13 and T18 patients have, beyond cardiac surgery, is the necessity for additional life-sustaining treatments. Of these, the two most commonly performed are tracheostomies for respiratory support and gastrostomies in order to facilitate feeding [34, 44].

Tracheostomies are often performed in T13 patients with unstable respiratory conditions or who require long-term respiratory support [45, 46]. An analysis of the prevalence of surgical procedures in the United States between 1997 and 2009 found that approximately 3% of T13 patients and 5% of T18 patients undergo a tracheostomy [17]. The primary indications in this population include lower airway obstructions, such as bronchomalacia and tracheomalacia, upper airway obstructions, such as laryngomalacia and rhinocephaly, persistent respiratory failure, and central or obstructive apnea [7, 24, 45]. Tracheostomies are more commonly performed among patients who undergo surgical rather than expectant treatment, as seen in both Kosiv and Davisson's results [16, 34]. This likely reflects the increased treatment intensity surgical patients receive, as well as their complicated hospital course with an increased probability of requiring a tracheostomy. In general, the need for tracheostomy is higher for T13 than for T18 patients, as seen in Peterson, Kochilas, et al. (6.9% vs 4.6%) and Domingo et al. (12.2% vs 3.6%), although a higher total of T18 patients undergo tracheostomy during their first admission likely because a larger percentage are offered interventions or survive [15, 40]. As noted previously, the likelihood of needing protracted respiratory support is greatly increased in patients who have had prior prolonged ventilator support. Discussion with families regarding the high likelihood of needing such support post-surgery and the implications of being able to go home with such intensive therapy is paramount in decision-making.

Gastrostomy

Another life-sustaining surgical procedure commonly performed in T13 and T18 patients is gastrostomy tube placement. In addition to facilitating feeding in patients with intolerance to oral feeds, this procedure is often performed in patients with tracheoesophageal fistulae or esophageal atresia as a bridge to definitive surgical repair [38, 45]. The wide range of indications for this procedure makes it the most prevalent surgery for both T18 and T13, and its use has gradually increased over time [17, 34, 44, 46].

The approach towards gastrostomy in single-center reports depends largely on each institution's experience, and reports are therefore varied. For example, 100% of Davisson's 17 patients had a gastrostomy tube, regardless of whether they received surgical or expectant treatment [34]. In contrast, the only patient to undergo gastrostomy in Costello et al.'s cohort was managed expectantly [18]. Results from larger database studies paint a clearer picture. In both PHIS (T13: 21.6% vs 7.7%; T18: 25.4% vs 15.9%) and PCCC databases (9.2% vs 6.8%), the presence of gastrostomy tube feeding was higher in patients with cardiac surgery than those treated expectantly [15, 16]. Unplanned gastrostomy following cardiac surgery was rare among the PCCC cohort, with only 3.4% of T13 and 10.8% of T18 patients undergoing this procedure [15]. Domingo et al. found that gastrostomy tube placement was more prevalent among T13 than T18 patients (18% versus 6%), although similar studies have not found a significant difference in the distribution of this procedure between trisomic populations [16, 40]. More recently, Cooper et al. found that 24.7% of T13 and 22.6% of T18 patients in the STS database had a preoperative gastrostomy [30]. In all of these instances, gastrostomy tube placement was not linked to any adverse outcomes in patients with cardiac surgery and was actually associated with improved survival among T18 patients in the STS database [30].

Overall, parents and caretakers should be aware that on average a quarter of patients require gastrostomy tube placement, depending on each individual's digestive comorbidities and ability to tolerate oral feeds. As in the case of tracheostomy, gastrostomy tube placement occurs more commonly in surgical patients due to their longer survival and increased treatment intensity.

Conclusion

As the care of patients with T13 and T18 evolves, these diagnoses are no longer considered uniformly fatal. A growing body of evidence suggests that these patients benefit from undergoing cardiac surgery, though physicians remain reticent to pursue cardiac surgery due to the perceived lethality of these syndromes [11]. Through the analysis of results from various studies detailing the clinical outcomes of patients who undergo cardiac surgery, weight > 2.5 kg, older age at surgery, complete surgical repair rather than palliation, and reduced or no preoperative mechanical ventilation all support an improved prognosis. Careful management of preoperative complications, such as pulmonary hypertension, also results in better postoperative outcomes. Excluding a few reported cases, patients with partial or mosaic trisomy appear to have longer survival than their full trisomy counterparts. Information regarding patients with high-complexity CHD and the effect of associated comorbidities remains scarce, providing an important area of opportunity for further research. As more data become available, surgeons will be able to more knowledgably anticipate the expected outcomes for cardiac surgery in patients with T13 and T18.

The recommendations in this article are limited to the data on trisomic populations as reported in the existing literature. Results from hospitals performing cardiac surgery without sharing their experience and outcomes could not be analyzed. This limitation is mitigated by the inclusion of papers analyzing multicenter databases, such as STS, PHIS, and PCCC. Another limitation is the possibility for selection bias in the studies discussed, with healthier patients being offered surgical treatment. The number of papers included in this review diminishes any outsize effect of specific variables on small populations, though data from larger, more diverse surgical populations are necessary in order to improve our understanding of cardiac surgery outcomes in these populations.

Author Contributions

HC involved in literature search, drafting of the manuscript, and revision of the manuscript. CC performed review of the literature and drafting and revision of the manuscript. JM and BR contributed to drafting and revision of the manuscript. PE involved in study design, revision of the manuscript, and project supervision.

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