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Congenital heart management in Trisomy 13 and 18: Survey of pediatric cardiology providers

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ABSTRACT

Best practices for the care of patients with Trisomy 13 and Trisomy 18 are not well defined. The aim of this work is to identify current perspectives and practices of pediatric cardiac practitioners regarding the care and procedural management of these patients. A survey was distributed to all 412 members of the American Academy of Pediatrics Section on Cardiology and Cardiac Surgery. Respondents were asked about the appropriateness of interventional catheterization and surgical procedures for patients with Trisomy 13/18. Other questions focused on provider perceptions regarding Trisomy 13/18 quality of life, decision making, and other measures of care. 103 respondents met inclusion threshold. With the exception of patent ductus arteriosus stenting, over half agreed or somewhat agreed that various interventional catheter procedures were appropriate for Trisomy 13/18 patients. A majority agreed or somewhat agreed that Risk Adjustment for Congenital Heart Surgery (RACHS) categories 1 (71%) and 2 (58%) procedures were appropriate in Trisomy 13/18, with steep reductions in this sentiment for subsequent RACHS categories. Most respondents did not feel that extracorporeal membrane oxygenation is reasonable in this population. 59% reported that their institution has no written or generally agreed upon policies for the care of this population. Overall, findings demonstrate variability regarding the perceived appropriateness of specific interventions for patients with Trisomy 13/18, with most providers feeling that lower-risk interventions may be appropriate. Providers, pediatric heart centers, and families may benefit from better defined institutional approaches to the management of these patients.

1. Introduction

While Trisomy 13 (T13) and Trisomy 18 (T18) are relatively rare, with an incidence of 0.85 and 1.29 per 10,000 live births respectively, a prenatal diagnosis is made in over 80% of patients born with one of these conditions [1,2]. This allows families more time to explore the options for the care of their child with T13/T18. However, outcomes and management decisions for patients with T18 and T13 are not well tracked. Data from the Pediatric Health Information System database published by Kosiv et al. indicates that T13 median survival is 5–13 days and T18 median survival is 6–15 days [3]. Between 1999 and 2007, the 5-year survival was 9.7% for T13 and 12.9% for T18, with gestational age being the strongest predictor of mortality [4]. Common non-cardiac morbidities associated with T13/T18 include orofacial anomalies, brain abnormalities, tracheoesophageal fistula, diaphragmatic hernia, spina bifida, abdominal wall defects, and limb defects.

In addition to numerous non-cardiac complications, many of these patients have congenital heart defects (CHD), with ventricular septal defects (VSDs), atrial septal defects (ASDs), and Tetralogy of Fallot (TOF) being the most common [1]. Given the same CHD diagnosis, patients with T13/T18 tend to have more significant co-morbidities and higher mortality rates than children without T13/T18 [1,5]. However, recent data has demonstrated an association between congenital heart surgery and decreased in-hospital mortality in these patients [3]. Other work has demonstrated nearly two-fold increased hospitalization cost amongst patients with T13/T18 undergoing congenital heart surgery relative to non-T13/T18 peers, with surgical intervention yielding admission mortality rates of 14% and 12%, respectively [6]. At the present time, medical and surgical treatment standards for T13/T18 are controversial, as was outlined in a recently published ethical review of treatment of a child with T18 and hypoplastic left heart syndrome [7].

Previous research, based on data from 2008, as well as a more

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recent small Canadian survey, has shown that pediatric cardiology providers would often recommend low-risk cardiac surgical interventions or procedures in the setting of Trisomy 13 or 18, with high-risk interventions less frequently recommended [8,9]. Over the last decade, standards of care for patients with T13 and T18 have continued to evolve and vary substantially both across and within institutions. Trends in the literature indicate that increasingly complex cardiovascular interventions for patients with T13/T18 are being performed but remain controversial [10,11]. The aim of this work is to evaluate the current opinion and practice of pediatric cardiology providers across the United States. Our goal is to understand the range of care for these patients. We hypothesize that low-risk interventions are often perceived as acceptable and that, as interventional complexity increases, there may be cut-offs amongst most respondents in perceived acceptability.

2. Methods

This study was designed as a cross-sectional survey that was distributed to all 412 members of the American Academy of Pediatrics Section on Cardiology and Cardiac Surgery (AAP-SOCCS). The AAP-SOCCS and the University of Wisconsin Health Sciences Institutional Review Board reviewed and approved this research. The survey was designed and administered using the Qualtrics online survey platform (Provo, Utah) and distributed to members as an electronic link sent by email on March 6, 2018, with one additional email reminder sent two weeks later. Survey respondents were informed that the survey would take about 10 min to complete. There were no incentives to complete the survey, and no personal information was collected. Prior to distributing the survey, it was tested by the authors for usability and technical function.

The survey design did not preclude participants from distributing it to colleagues or encouraging other members to complete the survey. A QR-code link was also publicized and distributed to attendees at the Midwest Pediatric Cardiology Society 2018 annual meeting as well as the AAP-SOCCS 2018 meeting.

A 28-item questionnaire was developed by the authors, based on review of published literature and expert opinion. The first survey page focused on provider demographic questions. Providers who did not complete at least one question on survey page two, related to policies and perspectives on the care of patients with T13/T18, were excluded from analysis. Survey questions focused on provider perspectives regarding the appropriateness of specific catheter interventions and Risk Adjustment for Congenital Heart Surgery (RACHS) surgical category interventions in patients with non-mosaic Trisomy 13 or Trisomy 18 and presumed spontaneous respiration without the presence of apnea. For these questions, providers were asked if they agreed that the intervention or intervention category in the question was appropriate. Reponses were scored numerically as follows: agree (+2), somewhat agree (+1), neutral (0), somewhat disagree (−1), disagree (−2), and would not offer procedure to family (−3). Additional questions focused on provider perspectives on quality of life for T13/T18, provider comfort with medical decision making for these patients, prenatal management, and consideration of extracorporeal membranous oxygenation (ECMO).

2.1. Statistical analysis

Categorical variables were summarized using frequencies and percentages; years in practice were characterized in terms of median and interquartile range (IQR; range of central half-sample). The (Mann-Whitney) Wilcoxon rank-sum test was used to explore whether a physician's level of agreement for RACHS-2/3 procedures was associated with his/her involvement in prenatal care, gender, and institutional surgical volume exposure (≥300 patients per year vs less). Spearman's rank correlation coefficient and associated test was used to assess for an association between years of practice and agreement for RACHS-2/3 procedures. Significance level was pre-set to 0.05 and no adjustment for multiplicity was made for this hypothesis-generating research; associated confidence intervals have 95% coverage. Statistical analyses were performed using R, version 3.5.1.

3. Results

119 individuals initiated the survey. Of these, 103 (88%) were included in the analysis, having completed at least one question related to the care of patients with T13/T18 from the second survey page. A total of 99 respondents (83% of those who initiated) completed the survey in its entirety. Of the 103 respondents who answered any questions related to the care of patients with T13/T18, 62% were male. Years in practice was provided for all but two respondents and ranged from 0 to 50 years, with half of respondents indicating at least 12 years in practice (IQR 4–25 years). Men tended to report more years of practice than women, with means of 17.8 years and 10.7 years, respectively ($p = .003$). More than half of the respondents (55%) indicated that they were directly involved with prenatal management of patients with T13/T18, and prenatal involvement was not found to differ by gender. Most (74%) respondents indicated that they practiced in a university hospital practice setting. The majority reported specialization in non-interventional pediatric cardiology (74%), although there were also respondents from interventional pediatric cardiology (12%), pediatric intensive care (5%), and cardiac surgery (3%). Over half (53%) of respondents reported working in centers with annual surgical volume of at least 300 patients.

No respondents reported that their institution had a written policy for the care of patients with T13/T18; 40% reported unwritten, but generally accepted policies, while 59% reported no policy whatsoever. Most respondents indicated that the respiratory status of patients with T13/T18 does (29%) or may (64%) affect institutional recommendations for intervention. Of the 30 respondents who indicated that respiratory status does affect recommendations, 90% reported that patients need to have demonstrated sustained spontaneous respiration before cardiac interventions and 80% reported that the presence of apnea precludes cardiac interventions.

If a patient with T13/T18 can breathe spontaneously and is without apnea, over 50% of respondents agreed or somewhat agreed that each catheterization procedure would be appropriate if applicable, with the exception of PDA stenting (Fig. 1). When asked about the appropriateness of RACHS surgical category procedures in these patients, over 50% of respondents agreed or somewhat agreed that RACHS-1 and RACHS-2 category procedures were appropriate, with a steep reduction in this sentiment for RACHS-3 and further reduction for RACHS categories 4 through 6 (Fig. 2). Given the shift in perceptions between RACHS-2 and RACHS-3 procedures, these were examined further. Although more providers agreed or somewhat agreed that surgical procedures were appropriate at RACHS level 2 (58.4%) than at RACHS level 3 (22.8%), there was no statistically significant difference in their responses based on gender, years in practice, involvement in prenatal care, or the surgical volume of their institution.

Most (70%) respondents felt that ECMO was never reasonable in patients with T13/T18 prior to cardiovascular intervention. Similarly, 60% of respondents indicated that ECMO is never reasonable after cardiac surgery, while 61% indicated that it is never reasonable after cardiac catheterization.

Only 3% of respondents reported that T13/T18 can have a good quality of life, while 76% reported feeling somewhat or very comfortable in helping to make medical decisions for patients with T13/T18. 85% of respondents indicated that they would never advocate for a cardiovascular intervention to be performed against parental request.

The 50 respondents who reported active involvement in the prenatal care of patients with T13/18 were asked about recommendations for termination of pregnancy in eight scenarios of increasingly complex congenital heart disease (Table 1). With increasing complexity of

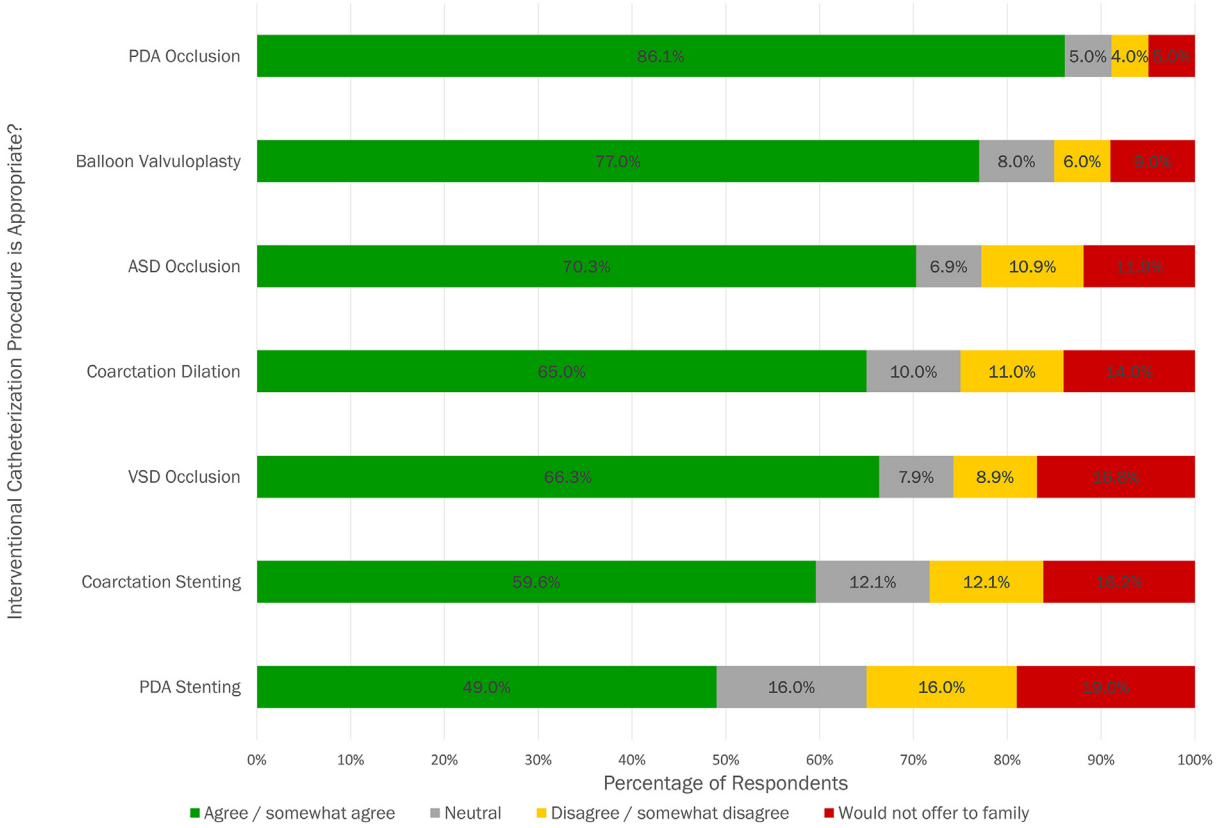

Fig. 1. Provider agreement and disagreement with the appropriateness of catheter interventions, as well as refusal to offer intervention, in T13/T18.

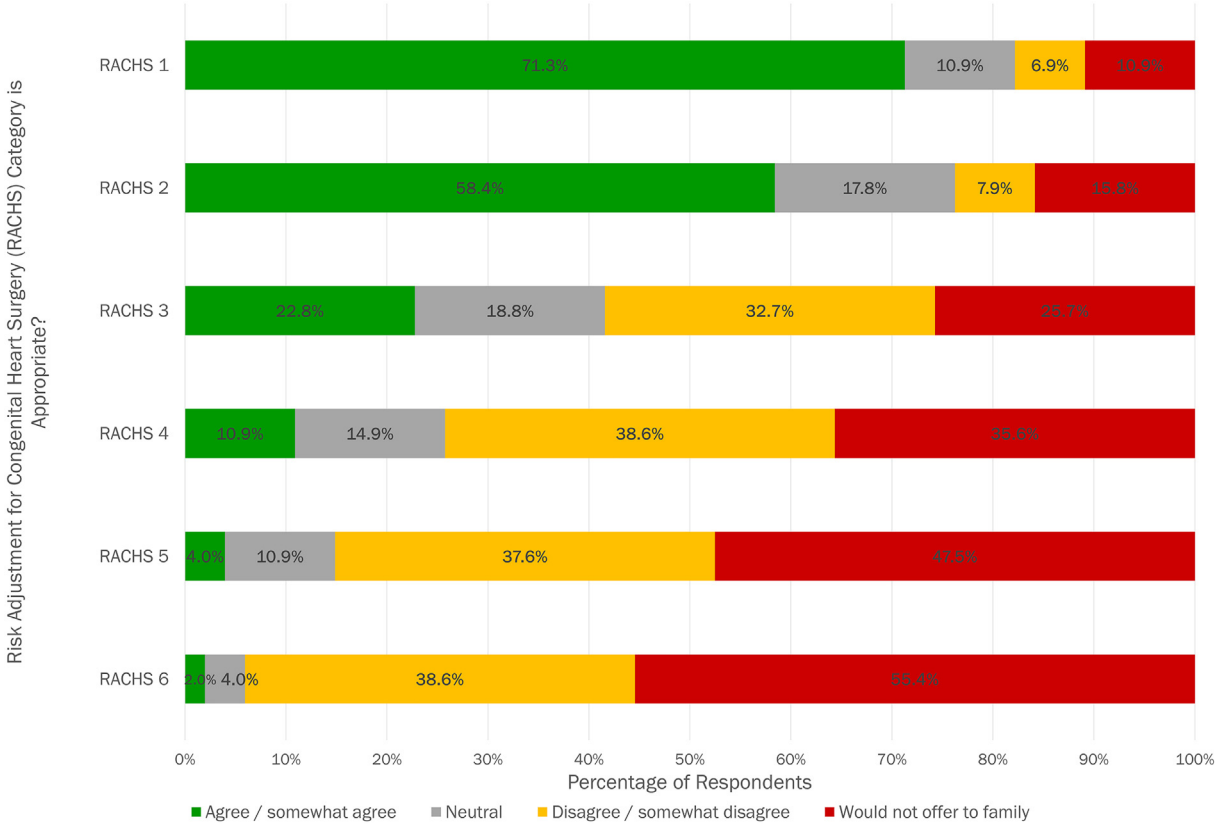

Fig. 2. Provider agreement and disagreement with the appropriateness of surgical interventions by RACHS category, as well as refusal to offer intervention, in T13/T18.

Table 1
Prenatal providers who would always or never recommend termination of a pregnancy with T13/T18 and cardiac lesions.

Cardiac lesion termination	Always recommend termination	Never recommend
No CHD	14%	30%
ASD or common atrium	14%	26%
VSD	14%	26%
Coarctation	16%	26%
Tetralogy of Fallot	18%	22%
AV canal	22%	22%
Transposition of the great arteries	26%	20%
Single ventricle	29%	20%

Abbreviations: ASD, atrial septal defect; AV, atrioventricular; CHD, congenital heart defect; VSD, ventricular septal defect.

congenital heart disease, the number who would always recommend termination increased and the number who would never recommend termination decreased.

All respondents were asked about their recommendations for comfort care in a newborn with normal respiratory status and the same eight scenarios of increasingly complex congenital heart disease (Table 2). With increasing complexity of congenital heart disease, the number who would always recommend comfort care increased and the number who would never recommend comfort care decreased.

4. Discussion

As recently as 2010, the American Heart Association and American Academy of Pediatrics removed T18 from a list of diagnoses for which it is ethical to not initiate resuscitation after birth. Previous research has found that different medical subspecialties may have different perspectives on care for these patients, with neonatologists being less optimistic than pediatric pulmonologists about the prognosis of T18, more likely to recommend comfort care, and less likely to recommend intervention [12]. Although T18 and T13 are two distinct entities, there is significant overlap in the ethical and physiologic features of these conditions.

One small survey of Canadian cardiologists in 2013 found that providers expressed more willingness to intervene for simpler cardiac lesions than for those with more complexity in patients with T18 [8]. This seems to parallel a 2007–8 survey in which 32% of cardiologists would recommend low-risk intervention, as scored by the Risk Adjustment for Congenital Heart Surgery (RACHS-1) criteria, for patients with T13 or T18 [9]. The same survey data demonstrated that cardiologists were more likely to recommend low-risk interventions (32%) as compared to neonatologists (7%) or geneticists (20%), while parental request for intervention resulted in a 3-fold increase in physician respondents recommending intervention [9].

Table 2
Providers who would always or never recommend comfort care for a child with T13/T18 and cardiac lesions with normal respiratory status.

Cardiac lesion comfort care	Always recommend comfort care	Never recommend
No CHD	28%	10%
ASD or common atrium	26%	4%
VSD	23%	2%
Coarctation	26%	2%
Tetralogy of Fallot	39%	3%
AV canal	42%	3%
Transposition of the great arteries	59%	1%
Single ventricle	78%	3%

Abbreviations: ASD, atrial septal defect; AV, Atrioventricular; CHD, congenital heart defect; VSD, ventricular septal defect.

Our work shows that most of the cardiovascular professionals who completed the survey agree or somewhat agree with the appropriateness of various cardiac catheterization procedures in patients with T13/T18 who have spontaneous respiration and are without the presence of apnea. An exception to this was PDA stenting, in which less than half of those surveyed felt that the intervention is appropriate, likely due to the temporizing nature of this procedure. Perceived appropriateness of the RACHS surgical procedures was above 50% for both RACHS 1 and RACHS 2 categories with a steep drop for RACHS 3-RACHS 6, representing a possible cut point in provider perspectives. This suggests an increased perceived appropriateness of intervention in these patients as compared to the results from 2007 to 8 [9]. As RACHS categories increased, the percentage of providers who disagree or somewhat disagree with the appropriateness of the intervention in T13/T18 also increased, as did the percentage of those who would not offer the procedure to the family. The clinician's perceived appropriateness of RACHS 2 and 3 level surgical procedures does not appear to be influenced by gender, years in practice, center's surgical volume, or direct participation in prenatal counselling. Despite what appears to be an increasing level of perceived appropriateness of lower risk surgical and catheterization procedures, many providers recommend termination of pregnancy or comfort care in the setting of T13/T18, even in the absence of CHD.

In a recent survey of worldwide ECMO program directors, 69% of those surveyed indicated that they would not offer ECMO in the setting of trisomy 18 and acute respiratory distress syndrome. The scenario presented was of an infant with a history of respiratory infections, implying that the child had survived the immediate newborn period. There was significant variation by specialty, with 50% of pediatric cardiothoracic surgeons willing to offer ECMO [13]. Our survey of a different provider population and clinical scenario yields a different perspective, with most respondents indicating that ECMO is generally not reasonable in patients with T13/T18 and only a few indicating that it may be reasonable after cardiac surgery.

To date, most respondents report that their center does not have an institutional policy for management and intervention in T13/T18. Most providers report that respiratory drive may affect recommendations for intervention but that this varies by provider or case to case. Although providers are split as to quality of life in patients with T13/T18, most feel very or somewhat comfortable helping families to make medical decisions and would never advocate for a procedure to be performed against parental request. Surveyed providers are more likely to recommend comfort care in patients with more complex congenital heart disease, such as single ventricle physiology or transposition of the great vessels. Similarly, providers involved in prenatal management are more likely to recommend termination in the setting of more complex congenital heart disease. However, the number of providers who would always recommend termination in T13/T18 with any given congenital heart disease never exceeds 29%. Another 20% of providers would never recommend termination, even in the setting of T13/T18 and single ventricle physiology. Differences between providers and centers in recommendations and offered procedures may represent a significant ethical justice issue, as parents may be unaware that recommendations can vary so significantly.

This work highlights variability in perspectives across providers, even as trends of relative perceived appropriateness of lower-complexity procedures and surgeries emerge for the survey group overall. Evolving and varying perspectives should encourage providers and centers to maintain open and frequent dialogue regarding care for these patients. In an era of increasing transparency regarding procedural outcomes in congenital heart disease, families of patients with T13/T18 may want to know an institution's position on the care of children with these trisomies from the time of initial diagnosis. With advances in prenatal diagnosis of both aneuploidy and CHD, discussions regarding the care of children with T13/T18 frequently begin before birth. This

can be challenging, as the physiologic impact of the suspected CHD and the degree of respiratory pathology cannot be fully defined prior to birth.

Although precise, formal policies on the care of children with T13/T18 are difficult to articulate, miscommunications and inappropriate expectations are more likely when an institution does not have a uniform approach to children with T13/T18 and congenital heart disease. We recommend that providers consider broadly defining their institutional approach to the management of these patients, with a transparent and consistent framework for their care.

4.1. Limitations

This study was completed in survey form and is limited by its relatively small sample size. It is possible that there is a sampling bias via networking effect, as providers with interest may have forwarded it to like-minded colleagues. Additionally, respondents who completed the survey may have had a particular interest in this topic or strong views, which would bias results to extreme respondents. This work specifically excluded patients with mosaic T13/T18, reducing its utility for these populations.

4.2. Conclusion

Patients with Trisomy 13 or 18 are medically complex, and there is significant controversy regarding cardiac interventions and management in these patients. Our findings suggest that most providers perceive catheterization interventions as appropriate in the setting of Trisomy 13 or Trisomy 18. Perceived appropriateness falls with surgical procedures that exceed the RACHS-1 and 2 categories, as well as with the use of ECMO. Perspectives regarding intervention in these patients appear to be evolving, but significant variability remains amongst providers. Providers and centers may benefit from developing an institutional approach to the management of these patients in order to ensure that the framework for their care is consistent and transparent.

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Declaration of competing interest

The authors have no commercial or other associations that might pose a conflict of interest in connection with the submitted article. The authors of this work report no relationships with industry and other entities.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ppedcard.2019.101169.

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