THE JOURNAL OF PEDIATRICS • www.jpeds.com

Perinatal Outcomes of Fetuses and Infants Diagnosed with Trisomy 13 or Trisomy 18

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Objectives To identify factors associated with prenatal, perinatal, and postnatal outcomes, and determine medical care use for fetuses and infants with trisomy 13 (T13) and trisomy 18 (T18).

Study design This population-based retrospective cohort study included all prenatal and postnatal diagnoses of T13 or T18 in the greater Cincinnati area from January 1, 2012, to December 31, 2018. Overall survival, survival to hospital discharge, medical management, and maternal, fetal, and neonatal characteristics are analyzed.

Results There were 124 pregnancies (125 fetuses) that were identified, which resulted in 72 liveborn infants. Male fetal sex and hydrops were associated with a higher rate of spontaneous loss. The median length of survival was 7 and 29 days, for infants with T13 and T18, respectively. Of the 27 infants alive at 1 month of age, 13 (48%) were alive at 1 year of age. Only trisomy type (T13), goals of care (comfort care), and extremely low birthweight were associated with a shorter length of survival. A high degree of variability existed in the use of medical services, with 28% of infants undergoing at least 1 surgical procedure and some children requiring repeated (≤29) or prolonged (>1 year) hospitalizations.

Conclusions Although many infants with T13 or T18 did not survive past the first week of life, nearly 20% lived for more than 1 year with varying degrees of medical support. The length of survival for an infant cannot be easily predicted, and surviving infants have high health care use throughout their lifespans. *(J Pediatr 2022;■:1-8)*.

Trisomy 13 (T13) and trisomy 18 (T18) are among the most common fetal life-limiting diagnoses, with a combined prevalence of roughly 1 in 1800 pregnancies, or 1.68 per 10 000 births for T13 and 4.08 per 10 000 births for T18.[1-4] Each condition has been referred to as lethal, with near universal descriptions of profound neurodevelopmental impairment. Historically, invasive medical interventions were considered futile by many, and a comfort care approach was the only option presented to families. Recent debate within the medical community and diverse perspectives of families have challenged these views.[5-9] A growing number of institutions are offering a range of medical and surgical interventions for children with T13 or T18, and families are increasingly electing to pursue interventions for their children.[10,11]

Significant variability remains in the choices families make regarding prenatal and postnatal care and the medical care provided following a diagnosis of T13 or T18.[12-14] Some families choose to continue the pregnancy, with the hope of meeting their child alive. After birth, some choose to focus on comfort measures only, and others elect for intensive medical interventions with the goal of prolonging life. Families appreciate balanced and personalized information from healthcare providers who respect their choices and provide support throughout the process.[7,15-17]

To meet these needs, it is important that providers understand outcomes of pregnancies and neonates with T13 or T18. Rates of spontaneous pregnancy loss are variable, ranging from 32% to 87%. Fetal intrapartum death and intolerance of labor are high, with 64%-80% of deliveries resulting in cesarean delivery.[18] Although the median survival of infants with T13 or T18 is 1-3 weeks, some live for years; 46% are discharged home and 9.7% and 12.3% of infants with T13 and T18, respectively, survive to 5 years.[19-23] An increasing number of individuals with T13 or T18 are receiving a range of medical interventions.[5,23]

The variation in pregnancy outcomes, survival outcomes, treatment, and goals of care is likely due in part to variation in counseling, care practices, and medical interventions offered for individuals with T13 or T18. These factors are interrelated and the evolution in practice makes it challenging for healthcare providers to counsel families with accurate information.[9,17,20,24-27] The objective of this retrospective cohort study of pregnancies and neonates with a diagnosis of T13 or T18 in the greater Cincinnati region over a 7-year period was to identify factors associated with prenatal, perinatal, and postnatal outcomes, and to determine the medical care use for

CHD	Congenital heart disease
NICU	Neonatal intensive care unit
T13	Trisomy 13
T18	Trisomy 18

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D.S. received funding from National Institutes of Health R01HL156860 during the study period. The authors declare no conflicts of interest.

https://doi.org/10.1016/j.jpeds.2022.04.010

fetuses and infants with T13 or T18 to better understand outcomes and facilitate high quality counseling and shared decision-making.

Methods

This study was approved by the Institutional Review Board at Cincinnati Children's Hospital Medical Center and each participating obstetric hospital. Patients were identified through genetic counselors, regional cytogenetics laboratories, referrals to perinatal hospice, and EPIC data query of *International Classification of Disease* codes at each institution between January 1, 2012, and December 31, 2018. All prenatal and postnatal diagnoses of T13 or T18 in every delivery hospital in the greater Cincinnati region (1 level IV neonatal intensive care unit [NICU], 4 level III NICUs, and 10 level I/II delivery hospitals) were included to minimize ascertainment bias. The 2012-2018 epoch was chosen to ensure the medical management and treatments offered reflect current clinical practice. Each diagnosis was confirmed by manual review of cytogenetics reports. Patients were excluded if medical records were not available, all care after diagnosis was provided outside of the region, or chromosomal mosaicism or more complex chromosomal rearrangements were present. A detailed retrospective chart review was performed to determine outcomes of pregnancies and neonates.

Data Collection

Manual data extraction was performed from January 1, 2020, to June 30, 2020, providing a minimum of 1 year follow-up. Data were entered into a REDCap database that consisted of 153 variables spanning demographic, maternal, prenatal, perinatal, and postnatal outcomes. A review of medical records and the National Death Index was performed at the end of data collection to verify deaths and ascertain the reported cause of deaths.

Data Analyses

De-identified data were exported and analyses were performed using the R statistical software package. Descriptive statistics were calculated using the "Rcmdr" package. Survival was calculated from birth and death dates. Living children were censored on the day of the last chart review and National Death Index query. Univariate and multivariate Cox regression analysis of factors associated with duration of survival was performed using the "survival" R package; reported *P* values reflect the Wald test. Kaplan-Meier survival plots were also generated. The associations between 2 categorical variables were tested using Fisher exact test and associations between 2 groups with continuous variables were tested using the Wilcoxon rank-sum test. Differences between groups were considered statistically significant when the *P* value was less than .05. The World Health Organization criteria for classification of birthweights and prematurity were used. Where appropriate, the Centers for Disease Control and Prevention definition was applied to classify structural abnormalities as a major congenital malformation.[28] Structural anomalies were considered a major surgical malformation when the standard of care for infants involved surgery (eg, congenital diaphragmatic hernia, gastroschisis, omphalocele, myelomeningocele). Comfort care was defined to include hospice care and/or medical interventions only intended to provide relief for symptoms such as pain, agitation, or air hunger (but not any medical interventions that were provided with the intent of prolonging life). Noninvasive therapies were defined as interventions such as nasal cannula, a nasogastric feeding tube, or antibiotics, which could be provided outside of an intensive care setting, and were administered with the explicit goal of prolonging life or evaluating the clinical response to aid in decision-making. Invasive interventions were defined to include continuous positive airway pressure or mechanical ventilation, other medical interventions that required an intensive care unit setting to provide, and/or any surgical procedure with the goal of prolonging life.

Results

Genetic Testing and Counseling

Most diagnoses were made during the prenatal period (79% for T13, 82% for T18). In total, 71% of women underwent amniocentesis (1 monochorionic-diamniotic twin pregnancy, both twins affected with T18), 9% underwent chorionic villus sampling, and 1 had a karyotype performed after a spontaneous abortion. Of the 24 postnatal diagnoses, 2 had low-risk cell-free fetal DNA (both T18), 1 had a high-risk quad screen for trisomy 21, and 1 had a normal level II ultrasound examination without additional prenatal testing. The remaining participants either declined prenatal diagnostic testing despite high-risk screening results or had noninvasive testing that technically failed. Less than one-half of the families prenatally met with a neonatologist (38%), pediatric cardiologist (31%), multidisciplinary fetal care team (16%), and/or pediatric palliative care specialist (Table I). An additional 13% (n = 16) met with the palliative care team after delivery.

Pregnancy Characteristics

A total of 125 fetuses or infants with T13 (n = 38) or T18 (n = 87) were identified (Table I). The total birth prevalence (live births, spontaneous abortions at <20 weeks, intrauterine fetal demises at ≥20 weeks, and elective termination of pregnancy) for T13 was 1.62 per 10 000 live births and the prevalence among live births was 1.00 per 10 000 live births. The total birth prevalence for T18 was 3.76 per 10 000 live births and the prevalence among live births was 1.86 per 10 000 live births. The mean maternal age was 33 years (range, 14-46 years), and the mean gravida was 3 (range, 1-14). Most identified as Caucasian. Complete demographic data are outlined in Table I. Just fewer than one-half had a prior pregnancy loss with 17% having 2 or more losses. Five percent had a prior

Table I. Prenatal characteristics

Characteristics	T13 (n = 38)*	T18 (n = 87)†	All (n = 125)†	*P* value
Maternal characteristics				
Maternal age, years	30.5 (26.0-37.0)	34 (27-39)	33 (26-39)	NS
Gravida	3 (2-4)	3 (2-4)	3 (2-4)	NS
Maternal race				NS
Asian	1 (2.6)	1 (1.1)	2 (1.6)	–
Black	8 (21)	9 (10.5)	17 (13.7)	–
Hispanic	3 (7.9)	4 (4.7)	7 (5.6)	–
Caucasian	25 (66)	73 (84)	98 (79)	–
Caucasian/AI-AN	1 (2.6)	0	1 (0.8)	–
Pregnancy/fetal characteristics				–
Prenatal diagnosis	30 (79)	71 (82)	101 (81)	NS
Male sex	18 (47)	37 (43)	55 (44)	NS
Abnormalities on ultrasound examination	36 (95)	87 (100)	123 (98)	NS
Malformations (by organ system)				–
Cardiac	27 (71)	64 (74)	91 (73)	NS
Neurologic	23 (64)	27 (31)	50 (40)	<.01
Craniofacial	19 (53)	25 (29)	44 (35)	<.05
Pulmonary/thoracic	4 (11)	8 (9)	12 (10)	NS
GI	11 (31)	19 (22)	30 (24)	NS
Renal/GU	11 (31)	15 (17)	26 (21)	NS
Musculoskeletal	21 (58)	28 (32)	49 (39)	<.01
Ophthalmologic	3 (8)	1 (1)	4 (3)	NS
Constitutional/minor	20 (56)	77 (89)	97 (78)	<.001
Consultative services received				–
Neonatology	19 (50)	28 (33)	47 (38)	NS
Pediatric cardiology (prenatal)	9 (24)	29 (34)	38 (31)	NS
Palliative care	16 (42)	41 (48)	57 (46)	NS
Multidisciplinary fetal care	5 (13)	15 (17)	20 (16)	NS
Birth plan created	22 (58)	47 (55)	69 (56)	NS
Pregnancy outcome				NS
Spontaneous abortion	3 (8)	5 (6)	8 (6)	–
Intrauterine fetal demise	5 (13)	19 (22)	24 (19)	–
Elective termination	5 (13)	16 (18)	21 (17)	–
Live birth	25 (66)	47 (54)	72 (58)	–

AI-AN, American Indian/Alaskan Native; *GI*, gastrointestinal; *GU*, genitourinary; *NS*, not significant.
Values are median (IQR) or number (%).
*No prenatal imaging for 2 pregnancies; n = 36 used for calculations where appropriate.
†A total of 125 fetuses from 124 pregnancies (1 twin pregnancy, both fetuses with T18).

pregnancy or child impacted by a genetic diagnosis (eg, G6PD deficiency, factor V deficiency, 22q11.2 microdeletion syndrome, trisomy 21, Turner syndrome, partial 14q deletion). At least 1 abnormality was seen on prenatal imaging in 98% of pregnancies, including the 2 pregnancies with low-risk cell-free fetal DNA screens. The number of organ systems with at least 1 structural malformation was higher for fetuses with T13 (**Table I**). The incidence of congenital heart disease (CHD) was similar between the 2 groups (71% in T13 vs 74% in T18). Specific congenital heart lesions identified during the prenatally are listed in **Table II** (available at www.jpeds.com).

Pregnancy Outcomes

Of the 125 pregnancies, 6% ended in a spontaneous loss, 19% ended in an intrauterine fetal demise, 17% ended in a termination of pregnancy, and 58% resulted in a live birth (**Table I**). Nearly one-half of deliveries were via cesarean delivery (**Table III**; available at www.jpeds.com). One-half of women had scheduled deliveries or went into labor spontaneously, 14% went into preterm labor, 17% had deliveries for maternal indications (eg, preeclampsia), and 17% had deliveries owing to concern for fetal well-being. In univariate analyses, male fetal sex, lower maternal gravida, and the presence of hydrops were associated with a higher incidence of spontaneous pregnancy loss. The percentage of fetuses with prenatally diagnosed CHD was higher among the pregnancies resulting in a liveborn infant than those that resulted in a spontaneous loss ($P < .01$) (**Table IV**; available at www.jpeds.com). Compared with women whose pregnancy ended in a live birth or spontaneous loss, those whose pregnancy ended in termination were significantly less likely to have a prenatal consultation with neonatology or palliative care (**Table V**; available at www.jpeds.com). For live births, a slight majority of families with or without subspecialty consultation had a birth plan in place at the time of delivery. Ninety-two percent were offered postnatal resuscitation. When interventions were not offered, major anomalies or other comorbidities (eg, proboscis, hydrops, extreme prematurity) that impacted mortality were present.

Neonatal Characteristics and Survival

Birth and delivery data are summarized in **Table III**, and postnatal care outcomes and location of care are depicted in **Figures 1** and **2** (available at www.jpeds.com). Of the 125 fetuses, 72 (58%) were liveborn. Infants with T18

weighed significantly less than infants with T13, even though the median gestational age of the 2 groups was not significantly different. Families were divided in electing a comfort care approach after birth (47%) or choosing to pursue invasive treatment with the goal of extending life (43%). The remaining 10% of families chose a trial of noninvasive therapies, such as nasal cannula and/or nasogastric feeds. Nearly one-half of the infants received positive-pressure ventilation in the delivery room and 8% received endotracheal intubation. No infants received chest compressions, emergent intravenous access, or cardiac medications (**Table III**). Regardless of the location of birth, just fewer than one-half of the infants were admitted to a NICU.

The median length of survival was 7 days and 29 days, for infants with T13 and T18, respectively (**Figure 3**, A and B). The 30-day and 1-year survival rates for children with T13 were 12% and 8%, respectively; for children with T18, 49% and 25%; and, for the combined cohort, 36% and 19%. Of the 4 infants with T13 and 23 infants with T18 who were alive at 1 month of age, 50% of the infants with T13 and 48% of the infants with T18 were alive at 1 year of age, with a median length of survival of 111 days and 590 days, respectively. In univariate analyses, the type of trisomy (T13), a birthweight of less than 1000 grams, very or extremely low-gestational age, and choosing comfort-measures only were associated with a shorter length of survival (**Figure 3**, C-F; **Table VI** available at www.jpeds.com). In multivariate regression analysis, gestational age no longer remained significantly associated with the length of survival (**Table VII**; available at www.jpeds.com). Of note, the 1-month and 1-year survival rates for children managed initially with comfort care was 15% and 6%, respectively.

Neither the number of organ systems impacted by 1 or more malformations nor the presence of CHD were associated with length of survival. Malformations never associated

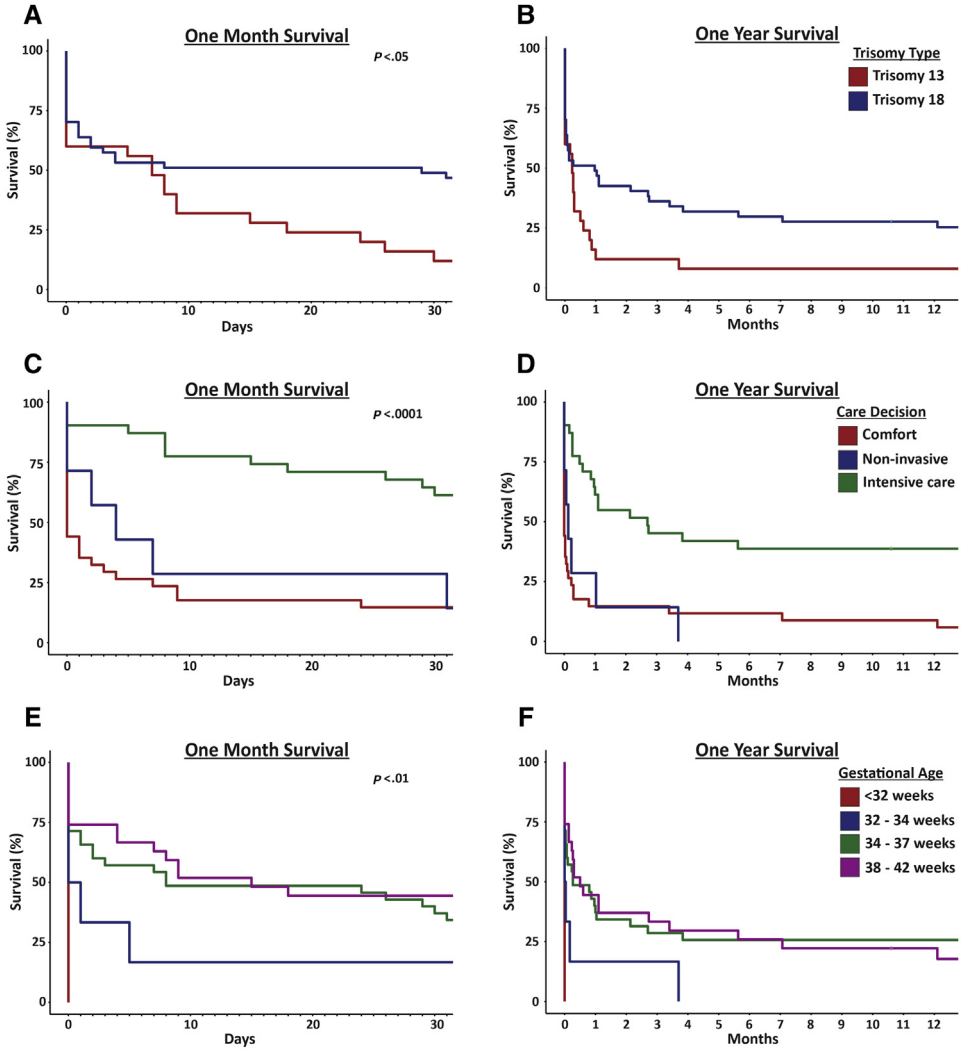

Figure 3. Kaplan-Meier survival analysis for T13 and 18. Kaplan-Meier survival curves for T13 and 18 are shown in 1-month and 1-year intervals, with comparisons made by, **A** and **B,** trisomy type, **C** and **D,** care decision, and **E** and **F,** gestational age at the time of delivery.

with survival beyond the first week of life or survival included congenital diaphragmatic hernia (n = 40) and hypoplastic left heart syndrome (n = 5). Moreover, all infants born at less than 32 weeks of gestation or less than 1000 g died within the first week of life. There was no significant association between myelomeningocele or cleft lip/palate on length of survival (**Figure 4**; available at www.jpeds.com). Prenatal consultation with neonatology, fetal care, or palliative care was not associated with a change in the overall duration of survival. However, prenatal consultation with a pediatric cardiologist was associated with an increased length of survival ($P < .01$) (**Table VIII**; available at www.jpeds.com).

Perinatal and Postnatal Hospital Course

Just fewer than one-half of all liveborn infants and two-thirds of those admitted to the NICU were discharged home (**Figures 1** and **2**). More infants with T18 were discharged home from the NICU than those with T13 (74% vs 44%) (**Table IX**; available at www.jpeds.com). Overall, the median initial hospital stay was 16 days (range, 1-531 days). Of the 32 patients discharged home, nearly one-half were readmitted to the hospital at least once (range, 1-29 rehospitalizations). The length of hospital stay for readmissions varied widely, ranging from 1 to 713 days. Respiratory insufficiency and apnea were frequent morbidities contributing to the need for and length of hospitalization. Most infants (88%) in the cohort were diagnosed with either central, obstructive, or mixed apnea at some point in their life. Just fewer than one-half (47%) required some degree of respiratory support and 24% required mechanical ventilation for a median of 8 days (range, 1-515 days) (**Table IX**).

Just fewer than one-half of liveborn infants had a postnatal echocardiogram. Although CHD was suspected prenatally in 90% of liveborn infants, significant cardiovascular pathology was identified in all but 1 postnatal study. Cardiac abnormalities seen are summarized in **Table X** (available at www.jpeds.com). Most liveborn infants with CHD confirmed (60% for T13, 72% for T18) developed cardiac symptoms that required medications (eg, diuretics). Five children with T18 had surgical repair of an atrial septal defect, ventricular septal defect, and/or patent ductus arteriosus. No children with T13 or children with more complex CHD underwent cardiac surgery. Ten children (14%) received a tracheostomy. All neonates who received invasive interventions required a nasogastric or gastrostomy tube for enteral nutrition. More than one-quarter (28%) of children with T13 or T18 underwent at least 1 noncardiac surgical procedure at some point (median, 3; range, 1-17), at a median age of 233 days (range, 0-2173 days). The most common procedures performed were gastrostomy tube and tracheostomy placement (**Table XI**; available at www.jpeds.com).

Discussion

Our large regional retrospective cohort study provides a detailed overview of the prenatal, perinatal, and postnatal outcomes of fetuses and infants with T13 or T18.

Significant variation in the outcomes of pregnancies involving a fetus with T13 or T18 that have been reported in the literature likely reflect the evolving choices made by families and medical providers. Between 2% and 55% of families elect for pregnancy termination.[14,18,29] For those who elect to continue their pregnancies, the rates of spontaneous abortions or fetal demise remain high.[3,18,30,31] However, our data and those of Winn et al highlight that, even though there is an increased risk of pregnancy loss, the majority of pregnancies result in a liveborn infant.[14] Male sex and the presence of fetal hydrops were the only factors associated with a higher incidence of spontaneous loss. When counseling families, it is important to note that, regardless of the goals of care, many will meet their infant alive. Both obstetric and pediatric providers need to be prepared to guide families through this process.

Families cannot make care decisions or adequately prepare for the neonatal period without an accurate prenatal diagnosis. In our cohort, a small number of cases had a false-negative screening. As such, especially in the context of abnormalities on imaging, providers must communicate the limitations of screening tests. Although many families in our cohort elected for prenatal diagnostic testing, some deferred diagnostic genetic testing until after birth. Even in the absence of a definitive diagnosis, establishing a high suspicion for either T13 or T18 may impact counseling during and goals of care for the pregnancy, including the timing and mode of delivery. In 1 study, patients who elected for a comfort care approach were more likely to deliver vaginally and have an elective induction of labor.[32] Other studies have reported a higher rate of cesarean delivery.[18] In our cohort, the rate of cesarean delivery for infants with T13 was comparable with the national average (28.0% vs 31.7%), but was much higher for infants with T18, at nearly 60% of deliveries.[33]

Many families consider rates of survival when determining the goals of care. Although several studies have provided insights to survival rates, interpreting these data in the context of the highly varied treatment pathways that families choose remains complicated.[5,6,34,35] In our cohort, the median survival time of 7 days for infants with T13 and 29 days for infants with T18 are consistent with published survival statistics.[19] However, it is clear from both our data and the recently published literature that a significant minority of infants with T13 or T18 live well beyond the neonatal period, with some children living for many years.[19-21] Also consistent with published data, we found that prematurity and low birth weight were associated with a decreased length of survival, particularly for birthweights of less than 1000 grams. The lack of significant effect on mortality for more modest decreases in birthweight may be related to the

relatively high incidence of intrauterine growth restriction that may not directly impact mortality. In our study, infants with T18 had overall higher rates of survival compared with infants with T13. This finding is consistent with some, but not all, reports in the literature.[6,36,37] The factor most strongly associated with the overall length of survival in our study was the level of support chosen by families and providers. Compared with infants who received intensive interventions, infants who received noninvasive support or comfort care only were more than twice as likely to die. Although these analyses corrected for multiple factors and morbidities, it is likely that the observed associations are confounded by additional medical morbidities and factors that impact families' and medical providers' care decisions. In these situations, the limitations of care should not be interpreted to mean that, had interventions been offered, the length of survival would have been improved. These results contrast with previous studies that reported parental goals of care did not affect the length of survival.[38,39] It is possible that the larger number of patients in our study, differences in comorbidities, associated anomalies, and when interventions were offered account for the differences. Neonatal intensive care can prolong the length of survival for many infants with T13 or T18.[9] Applying the term futility to medical interventions for these infants is inappropriate and the potential impact of interventions on survival is important to convey to families as they are navigating goals of care.

Infants who survive beyond the first week of life have high rates of healthcare use throughout the remainder of their lifespan. Our study shows readmission rates are high and hospital stays can be lengthy. The need for respiratory support, nutritional support, and invasive surgical procedures are relatively common. In Japan, a national database was used to review hospital admissions and medical procedures in patients with T13 and T18 over a 3-year period. The majority of patients who were discharged required home medical care ranging from tube feedings to oxygen or mechanical ventilation.[35] Other studies have highlighted that invasive surgical procedures are offered for children with T13 or T18, with significant variability in patient outcomes and impact on overall survival.[5,6,26,37,39,40] The burden of CHD in infants and children with T13 or T18 is high; most surviving children developed symptoms requiring medical or surgical management. Deciding when surgical intervention is the best option for children remains challenging for families and providers. Although CHD is a common finding in individuals with T13 or T18, the type of defect, approach to intervention, if interventions are offered, and reported outcomes remains variable.[41-43] Consistent with data from our study, a model shows certain variables, including cardiac surgery, gastrostomy, parenteral nutrition, and mechanical ventilation, are predictive of survival to 6 months of age.[44] An individual approach is necessary in determining which patients could potentially benefit from invasive interventions and discussing these options with families.[45] The expected neurodevelopmental outcomes, level of functioning, and degree of interaction that families have with their children are important factors that must be considered. Despite profound neurodevelopmental impairments, these children meet early developmental milestones and have meaningful interactions with their families.[46,47]

Given the complexity of medical decision-making, open and transparent discussions based on the best available objective data are needed. With the changing approach to care for patients with T13 or T18, providers may feel distress or disagree with the goals of care and treatment pathways families wish to pursue.[48] To appropriately counsel families, it is important that providers understand the values and goals of the family, as well as the anticipated outcomes and disease trajectory, for each fetus or neonate with T13 or T18. In this cohort, fewer than one-half of families met with a pediatric provider or multidisciplinary fetal care team during their pregnancy. We hypothesize that the association between prenatal consultation with pediatric providers and lower termination rates (but a lack of an association between prenatal counseling and postnatal survival) reflects referral selection bias. Families are making initial decisions about goals of care before meeting with pediatric care providers. Whether these decisions are based on counseling from their primary obstetrician, maternal-fetal medicine specialists, their personal views, or perspectives obtained from their family and community support remains unknown. Similarly, we speculate that our observation that prenatal consultation with a fetal cardiologist is associated with increased survival may be the result of referral bias. Families motivated to pursue invasive interventions are being referred at higher rates. Because most pregnancies result in a live birth, this outcome may leave some families incompletely prepared for the experiences and decisions that they will face after birth. This situation is compounded by the fact that only a slight majority of infants in this study had a birth plan in place at the time of delivery. Specialized centers frequently have perinatal palliative care services available to women with a fetal life-limiting diagnoses, but many families are not referred to such programs.[4,13] The involvement of a palliative care team early on allows for families to explore their values and views of quality of life and incorporate the medical information into their decision-making framework. The unique and individualized approach to care allows families and medical providers to work collaboratively to develop a care plan that aligns with the family's wishes.[12,43,49-51] We also hope that these data highlight the evolving role of pediatricians in perinatology and the importance of close collaboration to optimally care for families with genetic disorders identified during the prenatal period.

Our study has several limitations. We excluded mosaicism and more complex chromosomal rearrangements, which is important to consider when using these data to counsel families. Although the integrated nature of newborn care across the greater Cincinnati region allows for an opportunity to perform outcomes research across a large population and we made every effort to ascertain all prenatal and postnatal case of T13 or T18, we recognize the data may not be complete. However, the number of patients identified is

consistent with reported rates and the authors were able to find outcomes for all patients. Although retrospective cohort studies have limitations, owing to the relatively rare nature of these diagnoses the time needed to complete a comparably sized prospective observational study would require a concerted multicenter effort, and a controlled trial randomizing infants to different treatment pathways would be unethical.

This study should serve as a useful frame-of-reference to facilitate counseling families of fetuses and neonates with T13 or T18. Research is needed to better understand what information families are using prenatally and postnatally to establish goals of care, the long-term medical and developmental outcomes for children after the first month of life, the relationship between these children and their families, and optimal approaches to the medical management of these children. ■

Submitted for publication Oct 8, 2021; last revision received Mar 31, 2022; accepted Apr 8, 2022.

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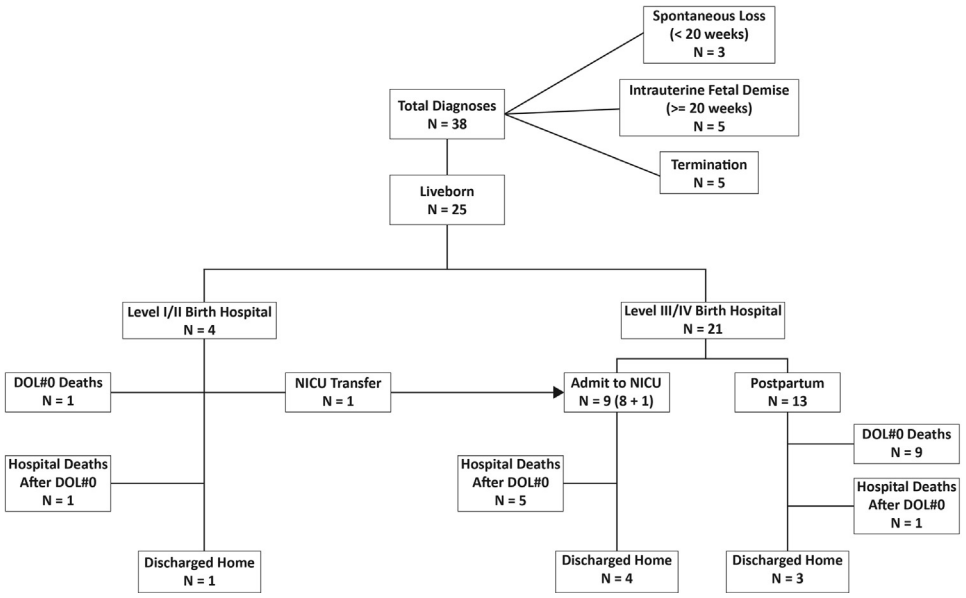

Figure 1. Postnatal outcomes flow diagram for T13. Outcomes for fetuses and infants diagnosed with T13 are represented at each stage of the perinatal and neonatal course. *DOL*, day of life.

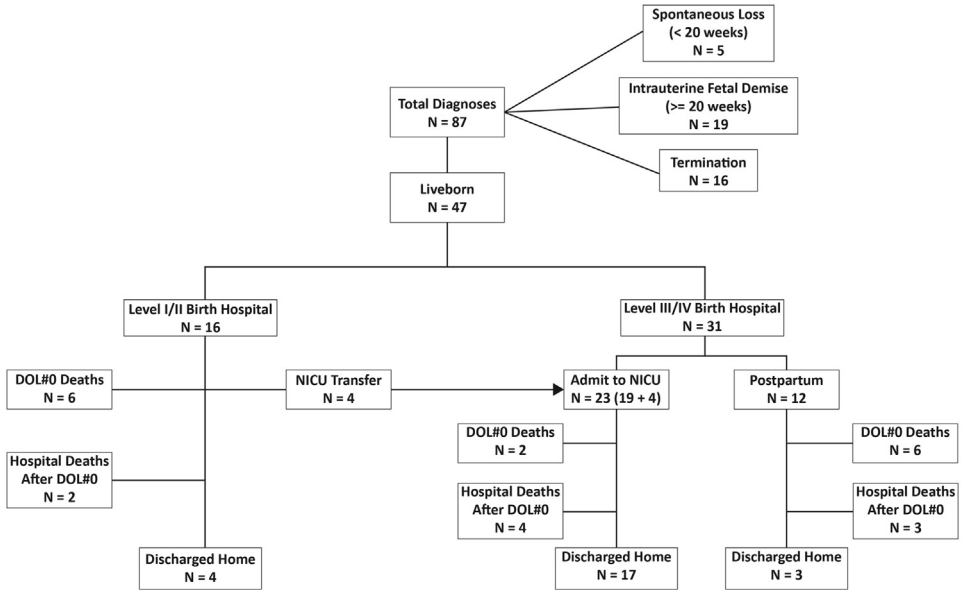

Figure 2. Postnatal outcomes flow diagram for T18. Outcomes for fetuses and infants diagnosed with T18 are represented at each stage of the perinatal and neonatal course.

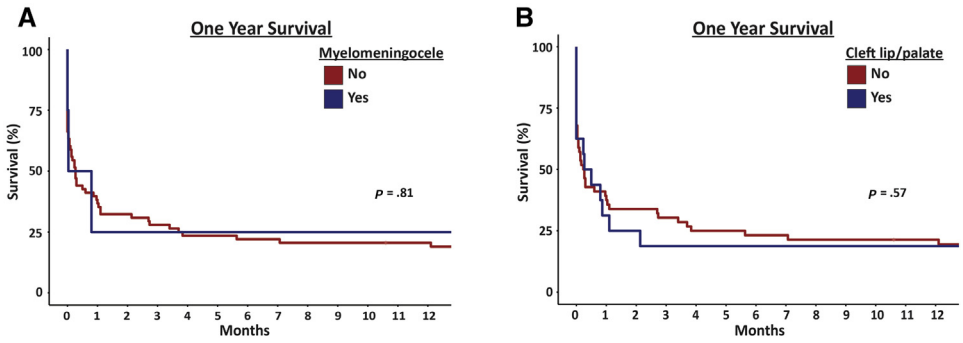

Figure 4. Survival analysis for selected congenital anomalies. Kaplan-Meier survival curves for T13 and 18 are shown, comparing outcomes for infants with or without, **A,** myelomeningocele or **B,** cleft lip/palate.

Table II. Prenatal cardiac findings

Primary cardiac abnormalities	T13	T18	All
Isolated VSD	7	18	25
Double outlet right ventricle	0	10	10
Tetralogy of Fallot	1	8	9
Valvular abnormalities	3	4	7
HLHS/single ventricle	6	2	8
VSD with additional findings	1	5	6
AV canal defect	1	3	4
Possible coarctation/arch abnormality	2	2	4
Cardiomegaly	1	2	3
Atrial and ventricular septal defects	0	2	2
AS/PS + biventricular dysfunction	0	2	2
AV canal + d-TGA	0	1	1
d-TGA	0	1	1
Heterotaxy	1	0	1
Complex CHD - NOS	5	9	14

AS, aortic stenosis; *AV*, atrioventricular; *d-TGA*, (dextro-) transposition of the great vessels; *HLHS*, hypoplastic left heart syndrome; *NOS*, not otherwise specified; *PS*, pulmonary stenosis; *VSD*, ventricular septal defect.

Table III. Characteristics and delivery room management of liveborn infants

Characteristics	T13 (n = 25)	T18 (n = 47)	All (n = 72)
Birthweight, grams	2245 (1900-2857)	1890 (1572-2115)	1976 (1605-2295)
Gestational age, weeks	$36^{6/7}$ ($34^{2/7}$-$38^{2/7}$)	$37^{2/7}$ ($36^{0/7}$-$38^{2/7}$)	$37^{1/7}$ ($35^{3/7}$-$38^{2/7}$)
Mode of birth			
Vaginal delivery	18 (72)	19 (40)	37 (51)
Cesarean delivery	7 (28)	28 (60)	35 (49)
Location of birth			
Level I/II facility	4 (16)	16 (34)	20 (28)
Level III facility	21 (84)	31 (65)	52 (72)
NICU admission	9 (36)	23 (49)	32 (44)
Offered attempt at resuscitation	23 (92)	43 (91)	66 (92)
Initial treatment decision			
Comfort care	12 (48)	22 (47)	34 (47)
Full intensive care	11 (44)	20 (43)	31 (43)
Trial of noninvasive therapies	2 (8)	5 (11)	7 (10)
Delivery room interventions			
Blow-by oxygen	3 (12)	9 (19)	12 (17)
Positive-pressure ventilation	6 (24)	28 (60)	34 (47)
Intubation	6 (16)	2 (4)	6 (8)
Select congenital malformations			
Congenital diaphragmatic hernia	1 (4)	3 (6)	4 (6)
Myelomeningocele	2 (8)	2 (4)	4 (6)
Anorectal malformation	1 (4)	2 (4)	3 (4)
Omphalocele	2 (8)	3 (6)	5 (7)
Gastroschisis	0	0	0
Cleft lip/palate	9 (36)	7 (15)	16 (22)
Holoprosencephaly	8 (32)	3 (6)	11 (15)

Values are median (IQR) or number (%).

Table IV. Factors associated with spontaneous loss

Variables	Spontaneous loss (n = 32)	Liveborn (n = 72)	*P* value
Maternal age, years, median	34	33	NS
Gravida, median	2	3	NS
Fetal sex, male	59%	36%	<.05
Trisomy type (T13)	25%	35%	NS
Organ systems affected*	3	3	NS
Hydrops*	16%	3%	<.05
CHD*	61%	88%	<.01

NS, not significant.
*Based on n = 31, owing to 1 early loss with no imaging data available.

Table V. Association between antenatal counseling and pregnancy outcome

Variables	Liveborn/ spontaneous loss (n = 104)	Termination (n = 21)	*P* value
Neonatology consult	46 (48%)	1 (4.8%)	<.001
Fetal care consult	18 (19%)	2 (10%)	NS
Cardiology consult	37 (39%)	1 (4.8%)	<.01
Palliative care consult	56 (58%)	1 (4.8%)	<.001

Table VI. Factors associated with mortality (univariate analysis)

Variables	Hazard ratio (95% CI)	*P* value
Sex	1.58 (0.94-2.65)	NS
Trisomy type (T13 vs T18)	1.72 (1.01-2.94)	<.05
Birthweight		
≥2500 g	Reference group	
Low birthweight (1500-2499 g)	1.01 (0.52-2.0)	NS
Very low birthweight (1000-1499 g)	1.04 (0.41-2.61)	NS
Extremely low birthweight (<1000 g)	6.21 (1.84-21.0)	<.01
Prematurity		
Term (38-42 weeks)	Reference group	
Late preterm (34-37 weeks)	0.96 (0.55-1.65)	NS
Moderate preterm (32-24 weeks)	2.31 (0.93-5.73)	NS
Very/extremely low gestational age neonate (<32 weeks)	6.64 (1.47-29.92)	<.05
No. of organ systems affected	1.05 (0.8906-1.233)	NS
Major malformation	1.4 (0.73-2.36)	NS
Surgical malformation	1.51 (0.66-2.674)	NS
Postnatal CHD	0.77 (0.37-1.63)	NS
Support decision		
Full Interventions	Reference group	
Noninvasive support	3.12 (1.30-7.48)	<.05
Comfort measures only	3.67 (2.09-6.45)	<.001

Table VII. Factors associated with mortality

Variables	Hazard ratio (95% CI)	*P* value*
Sex	1.44 (0.81-2.58)	NS
Trisomy type (T13 vs T18)	2.09 (1.09-4.00)	<.05
Birthweight		
≥2500 g	Reference group	
Low birthweight (1500-2499 g)	1.71 (0.81-3.62)	NS
Very low birthweight (1000-1499 g)	2.80 (0.91-8.65)	NS
Extremely low birthweight (<1000 g)	6.28 (1.63-24.22)	<.01
Prematurity		
Term (38-42 weeks)	Reference group	
Late preterm (34-37 weeks)	1.00 (0.81-3.62)	NS
Moderate preterm (32-24 weeks)	1.22 (0.35-4.25)	NS
Very/extremely low gestational age neonate (<32 weeks)†	NA	NA
No. of organ systems affected	1.07 (0.90-1.27)	NS
Major malformations	0.96 (0.50-1.86)	NS
Surgical malformations	1.06 (0.49-2.31)	NS
Postnatal CHD	1.90 (0.74-4.89)	NS
Support decision		
Full interventions	Reference group	
Noninvasive support	2.47 (0.87-7.01)	NS
Comfort measures only	4.31 (2.16-8.61)	<.001

NA, not applicable.
*Wald test.
†Insufficient total numbers in this group.

Table VIII. Prenatal consultation and postnatal survival

Variables	Hazard ratio (95% CI)	*P* value
Neonatology	0.9841 (1.016-1.621)	NS
Fetal care	1.22 (0.6168-2.412)	NS
Fetal cardiology	0.4334 (0.2532-0.7418)	<.01
Palliative care	0.9621 (0.5842-1.584)	NS
Birth plan	1.345 (0.7682-2.356)	NS

Table IX. Medical interventions, hospitalizations, and survival of liveborn infants

Variables	T13 (n = 25)	T18 (n = 47)	All (n = 72)
Admitted to the NICU	9 (36)	23 (49)	32 (44)
Discharged home	8 (32)	24 (51)	32 (44)
Readmitted to the hospital*	3 (38)	12 (50)	15 (47)
Respiratory			
Apnea	20 (80)	43 (91)	63 (88)
Respiratory support	13 (52)	21 (45)	34 (47)
Mechanical ventilation	9 (36)	8 (17)	17 (24)
CHD (any)	19 (76)	42 (89)	61 (85)
Cardiology			
Postnatal echo	10 (40)	25 (53)	35 (49)
Symptomatic needing medications*	6 (60)	18 (72)	24 (69)
Pulmonary hypertension*	5 (50)	13 (52)	18 (51)
Surgical interventions	3 (12)	17 (36)	20 (28)
Approach to care			
Comfort care	12 (48)	22 (47)	34 (47)
Invasive interventions	11 (44)	20 (43)	31 (43)
Noninvasive interventions	2 (8)	5 (11)	7 (10)
Do not resuscitate orders	24 (96)	37 (79)	61 (85)
At birth*	14 (58)	23 (62)	37 (61)
After a trial of interventions*	7 (29)	8 (22)	15 (29)
Just before death*	3 (13)	6 (16)	9 (15)
Died	23 (92)	40 (85)	63 (88)
At home*	5 (22)	12 (30)	17 (27)
In the hospital*	18 (78)	27 (68)	45 (71)
In the ambulance*	0	1 (2)	1 (2%)
Alive	2 (8)	7 (15)	9 (13)
Median (range), days	584 (531-637)	1394 (318-2762)	1366 (318-2762)

Numbers for each intervention reflect whether the child received that therapy (eg, respiratory support) at any point during their life.
Values are number (%) unless otherwise noted.
*The relevant denominator was used to calculate percentages for each category, which may not equal all liveborn infants with T13 or T18 (eg, percentage of infants readmitted to the hospital is referenced to the total number of infants discharged home).

Table X. Postnatal echocardiogram findings

Cardiac lesions	T13 (n = 10)	T18 (n = 25)	Totals (n = 35)
Ventricular septal defect	7	23	30
Atrial septal defect/patent foramen ovale	5	16	21
Valvular abnormalities	4	14	18
Patent ductus arteriosus	5	7	12
Double outlet right ventricle	0	4	4
Tetralogy of Fallot	3	1	4
Coarctation/arch abnormalities	1	2	3
d-Transposition of the great vessels	0	2	2
Hypoplastic left heart syndrome	1	0	1
Truncus arteriosus	0	0	0
Atrioventricular canal defect	0	0	0

Table XI. Surgical procedures for children with T13 or 18

	T13			T18		
Organ system and surgery type	**No. of surgeries**	**No. of infants**	**Age range***	**No. of surgeries**	**No. of infants**	**Age range***
Gastrointestinal						
Major	3	2	23-246	21	11	1-1526
Minor	6	1	72-325	23	12	28-1526
Ears/nose/throat						
Major	2	2	174-246	8	8	28-1586
Minor	1	1	627	6	5	521-1304
Cardiology						
Major	0	0	n/a	5	5	49-283
Minor	0	0	n/a	2	2	79-228
Plastics						
Major	1	1	261	2	2	655-1613
Neurosurgery						
Major	0	0	n/a	3	1	27-50
Other						
Major	0	0	n/a	8	3	134-2173
Minor	0	0	n/a	13	7	5-1526

Specific surgeries by trisomy type	**T13**	**T18**
Gastrointestinal		
Gastrotomy tube	3	15
GT/GJ revision	2	6
Bowel Resection	2	3
Nissen	0	4
Ladds	1	3
Paraesophageal hernia	0	3
Embolize liver tumor/liver biopsy	0	3
Tracheoesophageal fistula	0	2
Umbilical hernia	1	1
Pyloroplasty	0	1
Hepatic resection/cholecystectomy	0	1
Omphalocele closure	0	1
Meckel's	0	1
Cardiology		
ASD/VSD/PDA closure	0	4
Cath (1 attempted VSD/ASD closure)	0	3
Ear/nose/throat		
Tracheostomy	2	8
Myringotomy tubes	1	4
Adenoidectomy/tonsillectomy	0	2
Plastics		
Cleft lip/palate	1	1
Craniotomy	0	1
Neurosurgery		
EVD/VP shunt	0	2
MMC	0	1
Other		
Botox	0	5
Central lines	0	3
ECMO (1 failed cannulation)	0	2
Chest exploration	0	2
Aortopexy	0	1
Diaphragm plication	0	1

ASD/VSD/PDA, atrial septal defect/ventricular septal defect/patent ductus arteriosus; *ECMO*, extracorporeal membrane oxygenation; *EVD/VP*, external ventricular drain/ventriculoperitoneal drain; *GT/GJ*, gastrostomy tube/gastrostomy-jejunostomy tube; *n/a*, not applicable.

*Ages are listed in days. A GT/GJ revision is the conversion of a gastrotomy tube to a gastrojejunostomy tube.