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Perinatal and perioperative factors associated with mortality and an increased need for hospital care in infants with transposition of the great arteries: a nationwide 11-year population-based cohort

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Conflict of interest

None

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ABSTRACT

Introduction: Newborns with transposition of the great arteries (d-TGA) need immediate care for an optimal outcome. This study comprised a nationwide 11-year population-based cohort of d-TGA infants, and assessed whether the implementation of a nationwide systematic fetal screening program, or other perinatal - or perioperative factors, are associated with mortality or an increased need for hospital care. **Material and Methods:** The national cohort consisted of all live-born infants with simple d-TGA (TGA +/- small ventricular septal defect, n = 127) born in Finland during 2004–2014. Data were collected from six national registries. Prenatal diagnosis and perinatal and perioperative factors associated with mortality and length of hospitalization were evaluated. **Results:** Preoperative mortality was 7.9%, and the total mortality was 8.7%. The prenatal detection rate increased after introducing systematic fetal anomaly screening from 5.0% to 37.7% during the study period ($P < 0.0001$), but the total mortality rate remained unchanged. All prenatally diagnosed infants (n = 27) survived. Lower gestational age (OR 0.68, $P = 0.012$) and higher maternal age at birth (OR 1.16, $P = 0.036$) were associated with increased mortality in multivariable analysis. The older infant age at time of operation ($P = 0.002$), longer aortic clamp time ($P < 0.001$), and higher maternal BMI ($P = 0.027$) were associated with longer initial hospital stay. An extended need for hospital care during the first year of life was multi-factorial. **Conclusions:** In our cohort, none of the prenatally diagnosed d-TGA patients died. Due to the limited prenatal detection rates, however, the sample size was insufficient to reach statistical significance. D-TGA infants born with lower gestational age and to older mothers had increased mortality.

Keywords

Transposition of the great arteries, Transposition of great vessels, Prenatal diagnosis, Mortality, Hospitalization, Maternal BMI,

Abbreviations

d-TGA = (dextro-) transposition of the great arteries

LOS = length of hospital stay

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BMI = body mass index

BAS = Rashkind balloon atrial septostomy

IQR interquartile range

OR odds ratio

CI confidence interval

Key message

In our 11-year national cohort of d-TGA infants, prenatal detection rates increased in time, and none of the prenatally diagnosed d-TGA infants died. Older maternal age and lower gestational age were associated with increased mortality.

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INTRODUCTION

Transposition of the great arteries (d-TGA) is a critical heart malformation that can be fatal. However, excellent outcomes are usually achieved with optimal management strategies.[1] Prenatal diagnosis of d-TGA enables the centralization of these births to tertiary centers with 24-hour pediatric cardiology services and intensive care facilities, reducing mortality and morbidity in these infants.[2-4] Furthermore, recent evidence from multicenter studies indicates that preoperative management, such as the correct timing of arterial switch operation, may improve outcomes.[5,6] Since an increasing number of d-TGA patients reach adulthood, more research into maternal and perinatal risk factors and postoperative care is needed to further optimize outcomes.

A nationwide fetal anomaly screening program has the potential to diminish mortality. Previous studies on the impact of prenatal diagnosis are mainly based on regional cohorts or single-center data, and nationwide data are scarce. We have recently demonstrated improved prenatal detection rates of severe cardiac defects after the implementation of a national fetal anomaly screening program in Finland.[7] The first aim of this study was to evaluate how the improved detection rates associated with the mortality of infants with d-TGA. The second aim was to assess how perinatal factors and the perioperative management of simple d-TGA infants are associated with mortality and hospitalizations during the first year of life.

MATERIAL AND METHODS

Data source

We obtained 11-year nationwide, retrospective, population-based observational data on all cases with simple d-TGA in Finland from January 1, 2004, to December 31, 2014. A description of the implementation of a free-of-charge systematic nationwide fetal anomaly screening and its impact on the prenatal detection of d-TGA rates (including complex d-TGA infants) has been published previously.[7] All pregnant women are offered two screening ultrasounds (the first between gestational weeks 11 and 13, followed by a fetal anatomy scan between weeks 18 and 22) and combined serum screening for chromosomal defects.[7] The basic data were generated from different national registries, five of which were as follows: 1) the National Register of Pediatric Cardiac Surgery maintained by the Children's Hospital at Helsinki University Hospital, which

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encompasses three registries at the Finnish Institute for Health and Welfare; 2) the Register of Congenital Malformations; 3) the Register of Induced Abortions; 4) the Medical Birth Register; and 5) the Cause-of-Death Register maintained by Statistics Finland.[8] After the cohort was established, the length of hospital stay (LOS) was retrieved from the inpatient episodes from 6) the Care Register for Health Care, maintained by the Finnish Institute for Health and Welfare.

Study population

From 2004 to 2014, 651 969 children were born in Finland, 649 971 of whom were live births. A total of 184 d-TGA cases were diagnosed. Diagnoses were evaluated and confirmed.[7] Simple d-TGA was defined as transposition of the aorta and pulmonary trunk with or without small ventricular septal defect. More complex d-TGA forms with associated cardiac lesions were excluded. We further excluded all pregnancy terminations, all stillbirths, and infants born with major extra-cardiac malformations according to EUROCAT guidelines[9] (n = 4). None of the live-born infants had a chromosomal anomaly. When analyzing the factors that may have contributed to the differences in the LOS, we only included children who survived infancy (first year of life) (Figure 1).

Data characteristics

Data on prenatal detection, pregnancy, birth, and the infant were retrieved from the registries above. The characteristics included were: 1) **prenatal diagnosis** of d-TGA (yes/no); **2) maternal** age, body mass index (BMI), obesity, smoking, diabetes; 3) **birth**: mode of birth (vaginal, instrumental birth, cesarean section; elective, urgent (30 to 120 minutes decision-to-delivery interval), or emergency (under 30 minutes)), and type of maternity hospital (university hospital, central hospital, regional hospital); and 4) **infant** sex, birthweight, 1-minute Apgar scores, and gestational age at birth. In addition, we assessed age in full hours when the patient arrived at the pediatric cardiac surgery unit at Helsinki University Hospital (describes the diagnostic delay from birth to arrival), septostomy (yes/no), and perioperative factors (infant age at operation (days), weight at operation, and aortic clamp time) (Table 1).

Maternal BMI was calculated from the register data of height and pregestational weight recorded during the first prenatal visit, on average, at gestational week 8. A BMI $\geq$30 kg/m^2 was considered obese. Smoking during pregnancy also included mothers who had ceased smoking during the first

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trimester. Data were complete for all variables except maternal weight (117/127, 92%), maternal smoking (125/127, 98%), and aortic clamp time in surgery (106/116, 91%).

Perinatal management.

All congenital heart surgery and catheter interventions (including Rashkind balloon atrial septostomy (BAS)) in Finland are centralized in one tertiary center, namely, the pediatric cardiac unit at Helsinki University Hospital.

All infants with a prenatal diagnosis of a critical congenital heart defect are delivered in Helsinki regardless of maternal residence. Pulse oximetry screening was initiated gradually in 2005 and has been fully operational since 2007 in Finland. In d-TGA, the treatment target-saturation before arterial switch operation is >80% (measured from the right upper arm), and this is accomplished by adjuvant therapies, such as BAS, prostaglandin infusion, mechanical ventilation, inotropic agents, and inhaled nitric oxide.

Outcome measurements: Mortality and length of hospital stay.

We assessed total mortality (all deaths after live birth until December 31, 2017), preoperative mortality (death before operation) and postoperative mortality (deaths after operative care) until the age of 3 years (Figure 1). In addition to the total mortality of the whole study period from 2004 to 2010, the total mortality was assessed at the beginning of the study period and at the end of the study period, specifically, before implementation of the free-of-charge systematic fetal screening program (from 2004 to 2006) and during the fully operational fetal screening program (from 2010 to 2014). The initial length of stay (initial LOS) included the time in days from the beginning of postnatal hospitalization over the arterial switch operation period at Helsinki University Hospital until discharge to another hospital or home care. We further assessed the complete first-year hospitalization, the total number of days spent in the hospital (first-year LOS) during the first year of life. The type of maternity hospital was not included in the evaluation of survivor's need for care due to the small number of patients and high mortality in regional hospitals.

Statistical analyses

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Statistical analyses were performed with IBM SPSS Statistics, version 25 (IBM Corp., Armonk, NY, USA). Frequencies and percentages were used to describe categorical variables. Continuous variables were described with medians and interquartile ranges (IQRs) or means and standard deviations (SDs). The differences in categorical variables were compared using the chi-square test or Fisher's exact test. An independent samples t-test for normally distributed variables and a Mann-Whitney U test for non-normally distributed variables were used for group comparisons. Univariate associations between continuous outcomes and continuous factors were analyzed with Spearman correlation coefficients. Factors with $P<0.1$ in univariate analysis were included in multivariable models. Hospitalization variables were positively skewed outcomes and values were natural log-transformed for multivariable analysis. Associations of multiple factors with hospitalization variables were analyzed with multivariable linear models. Mortality was analyzed with multivariable binary logistic regression. The results are expressed using odds ratios (ORs) and 95% confidence intervals (CIs). Two extreme outliers (patients with a first-year LOS of 336 and 365 days) were excluded from the multivariable linear models. Post-hoc power analysis was performed to estimate the sample size of infants needed for clinical trials of prenatal diagnosis to reduce the mortality with increasing prenatal detection rates. *P*-values <0.05 were considered statistically significant, and no adjustments were made for multiplicity. All statistical tests were two-sided.

Ethical approval

The Ethics Committee of the Helsinki University Hospital approved the study (April 20, 2017, HUS/1938/2016). The Finnish Institute for Health and Welfare authorized the use of the health register data in this study, as required by the national data protection legislation. Participants were not contacted; no informed consent was required.

RESULTS

Mortality and prenatal diagnosis

In this cohort of isolated simple d-TGA, 127 patients were born alive in Finland in 2004–2014 (Figure 1). The prenatal detection rate increased due to implementation of systematic nationwide fetal anomaly screening from 5.0% (2/40, before the program; 2004–2006) to 37.7% (20/53, during the fully operational screening program; 2010–2014) ($P < 0.0001$). In total, the prenatal

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detection rate of simple d-TGA was 21.3% (27/127), and all infants with a prenatal diagnosis were born in Helsinki University Hospital. The total mortality was 8.7% (11/127). Three of the 11 infants (27.3%) who died were born prematurely before 37 gestational weeks, compared to five of the 116 survivors (4.3%). All of the survivors weighed >2000 grams. Preoperative mortality was 7.9% (10/127), and postoperative mortality was 0.9% (1/117) ($P = 0.008$) (Figure 1). Seven of the preoperatively deceased patients died within 24 hours, and the rest died within 48 hours after birth. The only postoperative death occurred at 18 days of age. The median (IQR) arrival age of the undiagnosed patient in the pediatric cardiac surgery unit was 8 (4.5–12.5) hours. There were no significant differences in the demographic, perinatal, or perioperative variables in those with and without a prenatal diagnosis (Table 1). The total mortality was 0% (0/27) in prenatally diagnosed patients and 11.0% (11/100) in postnatally diagnosed patients ($P = 0.119$). In total, 91% (116/127) of the patients were alive at the age of three years. The implementation of a national fetal anomaly screening program did not change the total mortality: before the program (2004–2006), the total mortality was 7.5% (3/40); and during the fully operational screening program (2010–2014), the total mortality was 7.5% (4/53) ($P = 1.00$). The demographics of the survivors and the deceased are presented in Table 2.

Post-hoc power analysis estimated the total sample size of 150 infants needed for clinical trials of prenatal diagnosis to reduce the mortality by 11% (0% vs 11%) when prenatal detection rates are approximately 40% as at the end of the present study ($\alpha = 0.05$, power = 0.80).

Associations with mortality

The data on factors associated with outcomes are presented in Table 1. The results of univariate analysis are shown in Table 3. Maternal age and the number of previous births were strongly associated, and of these two, maternal age was included in the multivariable analysis. The multivariable analysis showed that lower gestational age (OR 0.68, 95% CI 0.50–0.92, $P = 0.012$), and higher maternal age at birth (OR 1.16, 95% CI 1.01–1.33, $P = 0.036$) were associated with higher mortality. When comparing the mortality between hospital types, the differences were statistically non- significant; in the regional hospitals (23.0%, 3/13) in comparison to the university hospitals (5.5%, 3/55) (OR 5.20, 95% CI 0.91–29.55, $P = 0.06$) or the central hospitals (8.5%, 5/59) (OR 3.24, 95% CI 0.67–15.77, $P = 0.15$).

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Associations with the length of hospital stay

The univariate analysis results are presented in Table 4. The median (IQR) initial LOS was 22 (18–27) days. Obesity (BMI ≥30 and higher maternal BMI as a continuous variable was associated with longer first-year LOS in univariate analysis, and the continuous variable was chosen to multivariable analysis. The patients who did not need BAS (6%, 7/116) were born earlier (median 38.0 gestational weeks, IQR 33.6–39.7 vs 39.7 gestational weeks, IQR 38.6– 40.7, $P = 0.004$) and were smaller (median 2810 grams, IQR 2050– 2925 vs median 3400 grams, IQR 3100– 3819, $P = 0.001$). According to multivariable analysis, older age at operation, longer aortic clamp time in surgery and increasing maternal BMI were associated with longer initial LOS (Table 5). The median (IQR) first-year LOS was 25 (20–32) days. Seven factors were associated with extended first-year LOS, details in Table 5. The prenatal diagnosis of d-TGA was not associated with the length of the initial LOS or first-year LOS.

DISCUSSION

We have previously shown that the implementation of a free-of-charge fetal screening program increased the detection rates of severe congenital heart defects. Antenatal diagnosis enables the centralization of these deliveries to tertiary units with optimal management directly after birth. In a Finnish national cohort of all infants born with simple d-TGA, we show that none of the infants died who had received an antenatal diagnosis and who were thus delivered in a tertiary center. However, this was a statistically non-significant finding due to the limited prenatal detection rate in our cohort. In addition, lower gestational age, and higher maternal age at birth were associated with increased mortality in this patient population. Future research is warranted for our finding that high maternal pre-pregnancy BMI was associated with a prolonged initial hospital stay and hospitalization during the first year of life.

Blyth et al. described a “hidden mortality” for newborns with d-TGA without an antenatal diagnosis. Lack of prenatal planning leads to the death of affected infants soon after birth, before transfer to the surgical center.[10] Our study demonstrates similar hidden mortality in infants with d-TGA who lack prenatal diagnosis. Preoperative mortality is high, and only one of the ten preoperatively deceased infants reached the operative unit, partly due to restrictive atrial septum and partly due to misdiagnosis leading to a poor outcome. However, the mortality difference

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between pre- and postnatally diagnosed patients remained statistically non-significant. This could be due to small sample size, low prenatal detection rate, or low mortality in general.

We have previously reported that the total and live-birth prevalence of d-TGA are similar, and prenatal detection rates have increased over time in Finland, as they have in other countries.[7] The implementation of systematic screening significantly increased the prenatal detection of d-TGA (5.0% to 38%). As in the regional cohort assessing the implementation of fetal screening from the Netherlands,[4] the increase did not reduce total mortality, as the prenatal detection rate is still suboptimal. The current practice of postnatal saturation screening plays a crucial role in the detection of infants with cyanotic heart defects after birth and may be critical in reducing postnatal mortality. However, an increased risk of preoperative death among patients without prenatal diagnosis has been reported in the analogous national single-center system in New Zealand[11]. Indeed, in the current era, overall postoperative mortality has been decreasing among these infants.[5,11,12] Prematurity and low birthweight are known to increase operative mortality.[13-15] Accordingly, in this study, three postnatally diagnosed premature newborns died in the maternity hospital; the other six patients born between 32 and 37 gestational weeks were successfully operated on. None of the newborns who weighed <2000 grams survived.

Every infant with d-TGA receives similar care in Finland; operations are centralized to a single tertiary center. Septostomy was performed often (94%), similar to cohorts from Canada[16] and France[17]. The frequency of BAS varies greatly among the centers (48–93%).[4-6,16,17] Consistent with the latest multicenter studies, these nationwide data showed that patients with BAS had a shorter first-year LOS in general during the first year of life,[5] although BAS has previously been associated with higher morbidity.[18,19] However, the small sample size and the characteristics of patients who did not need septostomy can affect these results. In our study, the patients who did not need BAS were born earlier and were smaller. Yet, prematurity is related to a relatively larger size of the foramen ovale and was further associated with longer first-year LOS in our study. This confounding factor of prematurity may also explain the association between the lack of BAS and longer first-year LOS.

Maternal obesity is a risk factor for congenital heart defects[20-23] and, in a population of healthy infants, is associated with a lower 1-minute Apgar score, macrosomia[24] and increased

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hospitalization during the first years of life.[25-27] Interestingly, we observed an association between maternal BMI and longer initial LOS (adjusted β 0.015) and first-year LOS (adjusted β 0.016) in d-TGA infants, meaning that ten units higher pre-pregnancy BMI increases the initial LOS by 16% (exp(10x0.015) = 1.16) and first-year LOS by 17% (exp(10x0.016) = 1.17). However, for initial LOS, it could be as little as 2% (0.4 days median) to as high as 32% (7.0 days median) and for first-year LOS from 0.2% (0.1 days median) to 38% (9.5 days median), respectively.

To our knowledge, this is the first time that maternal obesity has been associated with infant morbidity in children with congenital heart disease. However, we must point out that the finding may reflect the association of higher maternal BMI with the longer first-year LOS in infants operated for any reason and not arterial switch operation in particular. The mechanisms underlying this association are unclear; we speculate that higher colonization of bacteria in the birth canal[28] and an altered immune biomarker profile of obese parent offspring[29] may adversely impact infant recovery from cardiac surgery. The association is not explained by a lower prenatal detection rate among obese mothers; no significant differences were found between obese and normal-weight mothers.[7] A decreasing maternal age at birth was also associated with longer first-year LOS. This may not be due to the morbidity of these infants, but rather to the younger mother feeling less confident in her ability to take care of the sick child at home.

Finnish registries are mandatory, comprehensive, and have high quality standards. These qualities facilitated the collection of complete population-based data, including data from infants who did not reach the pediatric cardiac surgery unit. All infants in this national cohort were operated on in the same tertiary hospital. Centralization allowed for the assessment of factors that are associated with endpoints when the standard of care is similar for every newborn with TGA.

There were several limitations. Peripartal factors were not recorded extensively. In particular, newborns with prenatal diagnosis often lack a 5-minute Apgar score and umbilical artery pH, whist for postnatally diagnosed infants, the highest preoperative lactate measurements from the maternity hospitals were not accessible. The reasons behind later hospitalization during the first year of life were not comprehensively recorded, leading to information on the need for hospital care in general, not only due to the heart defect. Most importantly, our study sample is quite small despite being a national cohort over several years. We also conducted several analyses without

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correction for multiple testing. This may have resulted in the identification of spurious associations and should be just viewed as hypothesis-generating rather than a cause and effect relationship. Associations identified in our study should be examined in other cohorts before any conclusion regarding their association can be made.

CONCLUSION

None of the prenatally diagnosed d-TGA patients died. However, due to the limited prenatal detection rates, the sample size was insufficient to reach statistical significance. D-TGA infants born to older mothers and infants with lower gestational age had an association with increased mortality.

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Figure Legend

Figure 1. Flow chart on data formation. TGA = transposition of the great arteries, TOPFA = termination of pregnancy due to fetal anomaly.

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Table 1. Measured characteristics and differences between prenatally and postnatally diagnosed infants with simple (dextro-) transposition of the great arteries (d-TGA).

	Cohort	**Prenatal diagnosis**	**Postnatal diagnosis**	
Characteristics	**n = 127**	**n = 27**	**n = 100**	***P*-value** [a]
Total mortality	9%, 11/127	0%, 0/27	11%, 11/100	0.119
Male sex	73%, 93/127	78%, 21/27	72%, 72/100	0.547
Elective cesarean	9%, 11/127	7%, 2/27	9%, 9/100	1.00
Vaginal birth	76% 96/127	67% 18/27	78% 78/100	0.224
Operative birth	16% 20/127	26%, 7/27	12%, 13/100	0.102
Vacuum extraction	5% 6/127	7.4% 2/27	4% 4/100	0.607
Urgent cesarean	5% 6/127	15% 4/27	2% 2/100	0.018
Emergency cesarean	6% 8/127	4% 1/27	7% 7/100	1.00
Apgar score 1 minute	8 (7–9)	8 (8–9)	8 (7–9)	0.704
Gestational age, weeks	39.7 (38.6–40.6)	39.4 (38.6–40.3)	39.7 (38.6–40.7)	0.326
Birthweight, grams	3395 (3040–3800)	3560 (3080–3800	3370 (3033–3796)	0.491
Survivors	**n = 116**	**n = 27**	**n = 89**	
Septostomy	94%, 109/116	100%, 27/27	92%, 82/89	0.198
Age at operation, days	8 (6–12)	8 (7–10)	8 (5–12)	0.847
Weight at operation, grams	3527 [559]	3645 [551]	3492 [360]	0.347
Aortic clamp time, minutes	110 [23]	111 [25]	110 [22]	0.813
Initial LOS, days	22 (18–27)	21 (19–23)	23 (18–30)	0.267
First-year LOS, days	25 (20–32)	22 (19–28)	25 (21–34)	0.054
Maternal characteristics	**n = 127**	**n = 27**	**n = 100**	
Age, years	30.1 [5.1]	30.7 [5.3]	29.0 [5.1]	0.524
BMI, kg/m^2	23.9 (26.2–34.3)	22.2 (20.9–27.7)	24.3 (21.9–27.2)	0.158
BMI ≥30 kg/m^2	12% ,15/117	12%, 3/25	13%, 12/92	1.00
Previous pregnancies	1 (0–2)	1 (0–2)	1 (0–2)	0.863
Previous births	1 (0–2)	1 (0–2)	1 (0–2)	0.323
Smoking	17%, 21/125	11%, 3/27	18%, 18/98	0.562
Diabetes				1.00
Type 1	3%, 4/127	4%, 1/27	3%, 3/100	
GDM with insulin treatment	2%, 2/127	0%, 0/27	2%, 2/100	
GDM with diet treatment	14%, 18/127	15%, 4/27	14% 14/100	

Values are median (IQR) or mean [SD] or percentages

[a] *P*-value for the difference between prenatal and postnatal diagnosis

LOS = length of hospital stay, BMI = body mass index

GDM = Gestational diabetes

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Table 2. Measured characteristics and differences between survivors and deceased infants with simple (dextro-) transposition of the great arteries (d-TGA).

Characteristics	Survivors n = 116	Deceased n = 11	*P*-value [a]
Male sex	74%, 86/116	64%, 7/11	0.452
Elective cesarean	8% 9/116	18%, 2/11	0.240
Vaginal birth	77%, 89/116	64%, 7/11	0.334
Operative birth	16%, 18/116	18%, 2/11	0.817
Vacuum extraction	5%, 6/116	0%, 0/11	1.00
Urgent cesarean	4%, 5/116	9%, 1/11	0.426
Emergency cesarean	6%, 7/116	9%, 1/11	0.526
Apgar score 1 minute	8 (7–9)	7 (5–9)	0.057
Gestational age, weeks	39.7 (38.6–40.7)	38.9 (36.0–40.0)	0.030
Birthweight, grams	3398 (3045–3800)	3330 (1760–3500)	0.302
Maternal characteristics			
Age, years	29.9 [5.1]	33.1 [4.8]	0.049
BMI, kg/m^2	23.9 (21.4–27.2)	23.9 (21.4–27.2)	0.973
BMI ≥30 kg/m^2	12%, 13/107	20%, 2/10	0.615
Previous pregnancies	1 (0–2)	2 (2–4)	0.015
Previous births	1 (0–2)	2 (1–3)	0.044
Smoking (yes)	21%, 21/114	0%, 0/11	0.209
Diabetes			0.789
Type 1	3%, 3/116	0%, 0/11	
GDM with insulin treatment	2%, 2/116	0%, 0/11	
GDM with diet treatment	14%, 16/116	18%, 2/11	

Values are median (IQR) or mean [SD] or percentages

[a] *P*-value for the difference between survivors and deceased

BMI = body mass index, GDM = Gestational diabetes

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Table 3. Univariate analysis of mortality

Factor	**Cohort** **n = 127**	**Survivors** **n = 116**	**Dead patients** **n = 11**	
	Median (IQR)/ Mean [SD] or n (%)	Median (IQR)/ Mean [SD] or n (%)	Median (IQR)/ Mean [SD] or n (%)	*P*-value
Gestational age, weeks	39.7 (38.6–40.6)	39.7 (38.6–40.7)	38.9 (36.0–40.0)	0.030
Maternal age, years	30.1 [5.1]	29.9 [5.1]	33.1 [4.8]	0.049
Previous births	1 (0–2)	1 (0–2)	2 (1–3)	0.044

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Table 4. Univariate analysis of hospitalization outcomes

Factor	**Initial LOS, days** [a] **n = 116** Median (IQR) or r	*P*-value	**First-year LOS days** [a] **n = 116** Median (IQR) or r	*P*-value
Prenatal diagnosis		0.267		0.054
Yes	21 (19–23)		22 (19–28)	
No	23 (18–30)		25 (21–34)	
Gestational age, weeks	-0.16	0.090	-0.16	0.094
Birthweight, grams	-0.14	0.140	-0.13	0.153
Maternal age, years	-0.31	0.001	-0.31	0.001
Maternal BMI, kg/m^2	0.18	0.066	0.22	0.024
Maternal BMI		0.056		0.046
<30	22 (18–27)		24 (19–32)	
≥30	25 (21–33)		30 (24–33)	
Previous births	-0.12	0.219	-0.15	0.114
Age in pediatric cardiac surgery unit, hours	0.12	0.216	0.17	0.070
Septostomy (yes/no)		0.004		<0.001
Yes	22 (18–27)		24 (24–31)	
No	29 (25–35)		41 (33–160)	
Age at operation, days	0.53	<0.001	0.44	<0.001
Aortic clamp time, minutes	0.23	0.016	0.27	0.005

[a] Median (IQR) for categorical variables and Spearman correlation coefficient r for continuous variables.

LOS = Length of hospital stay

BMI = Body mass index

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Table 5. Multivariable analysis of hospitalization outcomes.

Factor	Initial LOS, days [a] n = 97			First-year LOS, days [a] n = 97		
	Adjusted β	95% CI	*P*-value	Adjusted β	95% CI	*P*-value
Prenatal diagnosis (yes/no)				-0.122	-0.266 to 0.021	0.094
Gestational age, weeks	-0.018	-0.053 to 0.017	0.299	-0.064	-0.106 to -0.022	0.003
Maternal age, years	-0.008	-0.018 to 0.003	0.146	-0.014	-0.027 to -0.001	0.031
Maternal BMI, kg/m^2	0.015	0.002 to 0.028	0.027	0.016	0.0002 to 0.032	0.047
Age in final care unit, hours				-0.001	-0.002 to 0.000	0.005
Septostomy (yes/no)	-0.167	-0.417 to 0.083	0.187	-0.314	-0.618 to -0.010	0.043
Age at operation, days	0.016	0.007 to 0.025	<0.001	0.024	0.010 to 0.037	<0.001
Aortic clamp time, minutes	0.004	0.001 to 0.006	0.002	0.004	0.001 to 0.006	0.010

Adjusted β = regression coefficient for the effect of a one-unit increase in continuous factors on the log-transformed outcomes and mean the difference in the log-transformed outcome values between groups (yes vs no) for dichotomous factors. β coefficients are adjusted for other variables included in the linear model. Example of interpretation of regression coefficient in log-transformed outcomes;

For initial LOS, maternal BMI regression coefficient (Adjusted β) is 0.015, one unit increase of BMI corresponds to exp(0.015) = 1.015 times increase (i.e. 1.5% increase) in the initial LOS.

[a] Log-transformed outcome values were used in statistical analysis.

Data are expressed as mean differences as a recurrently infected group minus hypertrophic group.

LOS = Length of hospital stay

BMI = Body mass index

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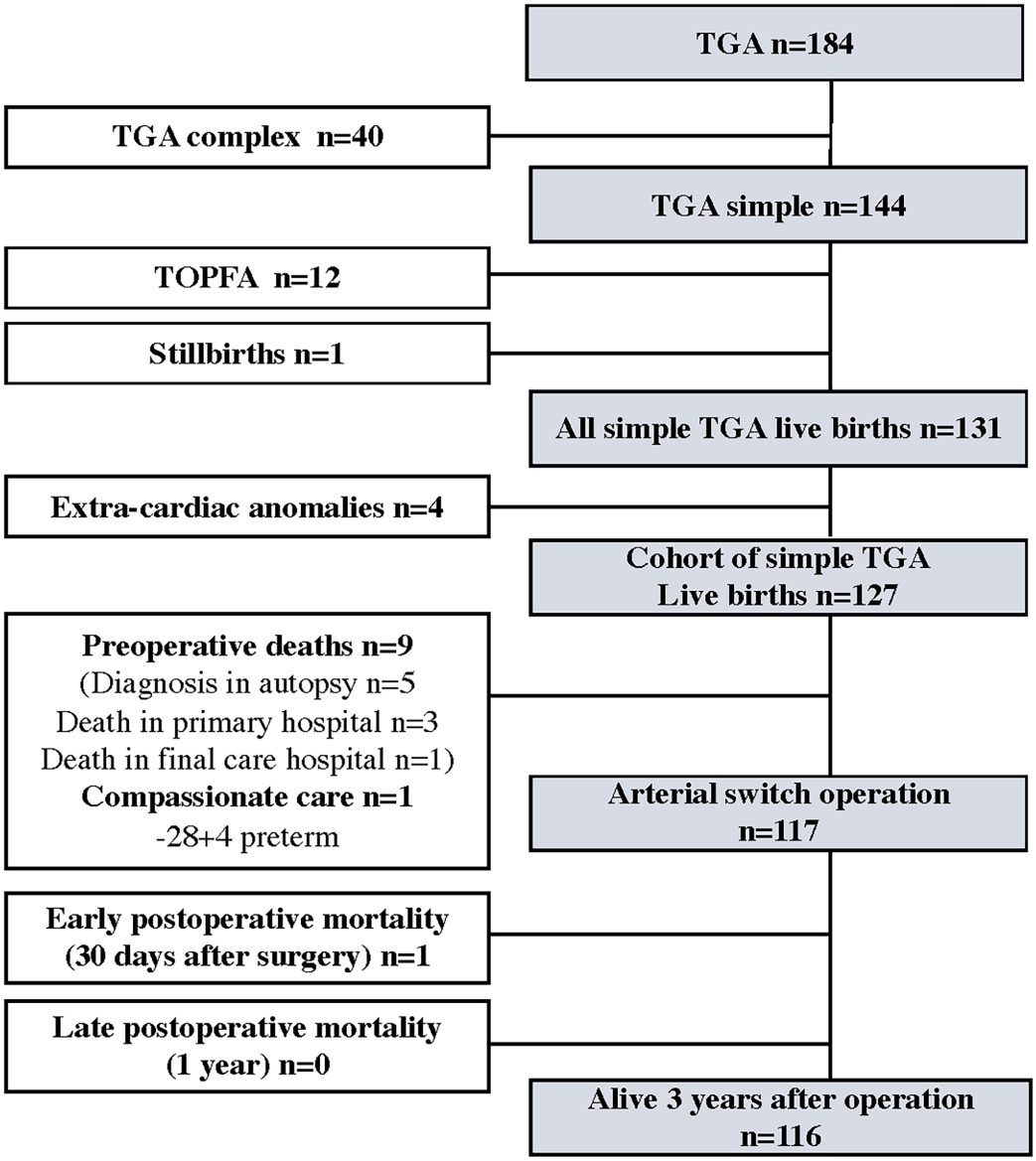

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