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Original Article

Perinatal and early postnatal outcomes for fetuses with prenatally diagnosed *d*-transposition of the great arteries: a prospective cohort study assessing the effect of standardised prenatal consultation

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Abstract *Background:* The aim of this study was to explore perinatal and early postnatal outcomes in fetuses with prenatally diagnosed *d*-transposition of the great arteries and impacts of standardised prenatal consultation. *Methods:* All fetuses with prenatally diagnosed *d*-transposition of the great arteries prospectively enrolled at South China cardiac centre from 2011 to 2015. Standardised prenatal consultation was introduced in 2013 and comprehensive measures were implemented, such as establishing fetal CHD Outpatient Consultation Service, performing standard prenatal consultation according to specifications, and establishing a multidisciplinary team with senior specialists performing in-person consultations. Continuous follow-up investigation was conducted. Perinatal and postnatal outcomes were compared before and after consultation including live birth, elective termination of pregnancy, spontaneous fetal death, stillbirths, referral for surgery, and survival. *Results:* In all, 146 fetuses were enrolled with 41 (28%) lost to follow-up. Among 105 remaining fetuses, 29 (28%) were live births and 76 (72%) were terminated. After consultation, live birth rate was higher (50 versus 33%) and termination rate was lower (50 versus 76%), although there was no statistical significance. Excluding three live births without postnatal *d*-transposition of the great arteries, 65% (17/26) underwent arterial switch operation within 30 days. A total of three in-hospital deaths occurred and during the 10-month follow-up period, one death was observed. In one case, the switch procedure was performed at 13 months and the infant survived. Out of eight infants without arterial switch operation, two died. *Conclusions:* Live birth rate increased after consultation; however, termination remained high. Combining termination, patients without arterial switch operation, and operative mortality, outcomes of *d*-transposition of the great arteries infants can be improved. Standard consultation, multidisciplinary collaboration, and improved perinatal care are important to improve outcomes.

Keywords: CHD; transposition of the great arteries; prenatal diagnosis

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The incidence of *d*-transposition of the great arteries is ~2.5/10,000 live births and is one of the most common causes of cyanotic CHD.[1] *d*-Transposition of the great arteries accounts for ~5–7% of all CHD.[2] Most frequently, in this form of CHD, the karyotype is normal and extracardiac abnormalities are relatively unusual.[3] The expected prognosis for *d*-transposition of the great arteries is poor, with 50% of infants dying within 1 month and 90% dying before the age of 1 year.[4]

Prenatal diagnosis was proposed as an effective strategy to improve outcomes for CHD, especially for critical CHD such as *d*-transposition of the great arteries.[5,6] In a report from Boston Children's Hospital, over a 20-year period, rates of prenatal diagnosis of *d*-transposition improved, but remained imperfect.[7] Traditional ultrasound screening for CHD, which included the four-chamber view, but not the examination of the great arteries, showed the prenatal diagnosis rate for *d*-transposition of the great arteries was low and ranged from 10% in the United States to 50–70% in Europe.[8–11] Introducing an outflow tract view into the screening protocol, a 20–30% improvement in the detection rate of CHD in general, and *d*-transposition of the great arteries in particular, has been demonstrated.[12–15]

Evidence concerning the impact of prenatal diagnosis on perinatal maternal–fetal and early postnatal fetal outcomes is scarce. Limited sample size and difficulty in following up are the main barriers.[16] With these limitations, currently published results are contradictory. In addition, data on the effect of a strategy to standardise prenatal consultation on the outcomes of *d*-transposition of the great arteries are limited. To fill this gap, we conducted a prospective cohort study to explore the perinatal and early postnatal outcomes for fetuses after prenatal diagnosis of *d*-transposition of the great arteries and compared the outcomes before and after initiation of a standardised prenatal consultation.

Materials and methods

Standardised prenatal consultation

In our centre, a formalised Outpatient Consultation Service for fetal CHD has been established and a standardised prenatal consultation procedure has been carried out for mothers with a diagnosis of fetal CHD, including *d*-transposition of the great arteries, since 2013. The prenatal consultation standard for fetal CHD in Guangdong province has been previously described.[17] A multidisciplinary team including experts on Prenatal Diagnosis, Genetic Counseling, Pediatric Cardiology, Cardiac Surgery, Obstetrics, Neonates and Pediatrics, Cardiac Imaging, and Epidemiology was established. Two senior specialists of Pediatric Cardiology were responsible for face-to-face consultation. During every consultation, consultants need to fulfil the following comprehensive criteria: inform the diagnosis of fetal *CHD* according to the results of echocardiography and the difference from the normal fetal heart using an imaging technique; explain the impact of fetal CHD and the potential associated other birth defects and genetic anomalies on intrauterine fetal growth, pregnancy outcomes, delivery, neonates' symptoms, and development after birth; provide current treatment options such as medications, interventional therapy, cardiac surgery, and more, as well as provide information on the short- and long-term prognostic outcomes after treatments; and provide prenatal consultation suggestions for the affected family. According to the 2016 report of European Association of Cardio-Thoracic Surgery, which our centre joined in 2009, the 30-day mortality was 10.10% for arterial switch operation and 10% for arterial switch operation and ventricular septal defect repair in our centre. This mortality rate was higher than that in Europe (3.69 and 6.48%), but was comparable to the results from other large cardiac centres in China. On the one hand, during consultation, the specialists for consultation emphasise the continuous improvement of arterial switch operation technique; on the other hand, a mortality risk is introduced. Mothers with a prenatal diagnosis of fetal *d*-transposition of the great arteries were generally counselled to continue their pregnancies based on improved treatment techniques, decreased mortality, and better postoperative outcomes for *d*-transposition of the great arteries in the current era. Recommendation for elective termination of pregnancy was suggested only for extremely complex cases of *d*-transposition of the great arteries: for example, for cases in which it was coexisting with other chromosomal anomalies. For mothers who chose to continue the pregnancy, follow-up echocardiography was conducted every 4 weeks. Repeated prenatal consultation was conducted according to the results of echocardiographic and obstetric examination. Live births with *d*-transposition of the great arteries were followed up annually for their prognostic outcomes with or without treatments.

Study design

This was a prospective cohort study from a major tertiary referral centre for maternal–fetal medicine and CHD treatment in southern China. All fetuses with prenatally diagnosed *d*-transposition of the great arteries in the Department of Maternal-Fetal Cardiology from December, 2011 to October, 2015 were enrolled.

Prenatal diagnosis of CHD was made using echocardiography according to the fetal cardiac

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ultrasound technology standard in Guangdong province.[18] Standard views include four-chamber, right and left ventricular outflow tract, and long-axis views of the aortic arch. Echocardiography was performed using ALPHA 7 and ALPHA 10 equipment (HITACHI-ALOKA Co., Japan). Experienced paediatric cardiologists were responsible for the initial examination. The final diagnosis of CHD in fetuses was confirmed by the Senior Director of the Department of Maternal-Fetal Cardiology. Re-examination of any suspected lesion was performed if images were inadequate for diagnosis.

d-Transposition of the great arteries subtypes were coded according to the International Classification of Diseases, 10th Revision (Q20.000–Q28.000). Fetuses with prenatal diagnosis code Q20.302 were selected as our study population. We excluded patients with a prenatally diagnosed single ventricle combined with *d*-transposition of the great arteries.

Consequently, the study population was divided into two groups: before standard consultation (2011–2013) and after standard consultation (2014–2015). Outcomes were compared between these two groups.

Within the two cohorts, simple and complex *d*-transposition of the great arteries were further subcategorised. *d*-Transposition of the great arteries cases with an intact ventricular septum and no associated cardiac defects other than a patent oval window and a patent ductus arteriosus were classified as simple *d*-transposition of the great arteries. In contrast, complex transposition included all the cases with coexisting malformations, such as ventricular septal defects, left ventricular outflow tract obstruction, aortic arch anomalies, and anomalous venous systemic return.[19]

Perinatal outcomes of our study included live birth – including neonatal death in 7 days after birth – elective termination of pregnancy, spontaneous fetal demise or abortions, and stillbirths. Live births were defined as when a fetus, at any gestational age, exits the maternal body and subsequently shows any sign of life, such as voluntary movement, heartbeat, or pulsation of the umbilical cord, however, briefly and regardless of whether the umbilical cord or placenta are intact.[20] Elective termination of pregnancy, referred to as induced abortion, was undertaken when the fetus was prenatally diagnosed with *d*-transposition of the great arteries. Spontaneous fetal demise and abortion were defined as fetal death in utero without intervention before 28 weeks of gestation and stillbirth was defined as fetal deaths occurring after 28 weeks of gestation. Early postnatal outcomes included referral for surgery and survival.

Questionnaires, clinical records, and telephone surveys were used as the data sources for this prospective cohort study. As the referral centre for fetal echocardiographic examination, our centre accepted fetuses with suspected cardiac anomalies found on basic screening using obstetrical ultrasound. A structured, standardised questionnaire with basic maternal demographic characteristics was filled by the mother with prenatally diagnosed fetal CHD. The Secretary of the Department of Maternal-Fetal Cardiology completed the prenatal diagnosis section of the questionnaire according to the echocardiographic examination report, and copies of the report were attached. According to the expected date of delivery, perinatal outcomes were obtained by a research coordinator from the Division of Epidemiology, Department of Cardiac Surgery. Hospital outcomes were initially assessed from the Hospital Information System. Once the patient was confirmed in the Hospital Information System, clinical records were obtained to gather additional information on outcomes. Finally, the outcome information for those not followed up at our hospital was obtained through phone calls. Annual follow-up examination was performed thereafter for all live births.

Statistical analysis

Quantitative variables were expressed as mean ± standard deviation or median (range), as appropriate. Qualitative variables were expressed as percentage or numbers. The Student's t-test was used for comparison of normally distributed data, whereas the Mann–Whitney U-test was used for non-normally distributed data. The χ^2 test was used for categorical variables. SPSS® 22.0 (IBM Co. Ltd) was used for all computation.

Ethics statements

This study was approved by the Ethics Committee of Guangdong General Hospital. Informed consent was acquired from every mother with an affected fetus.

Results

From December, 2011 to October, 2015, 185 fetuses were prenatally diagnosed with *d*-transposition of the great arteries. Excluding 39 cases with single ventricle combined with *d*-transposition of the great arteries, the enrolment rate was 100% of eligible patients. Thus, 146 patients were enrolled in the study, 64 (44%) in the before standard consultation group and 82 (56%) in after standard consultation group. Overall, there were 26 (18%) fetuses with simple *d*-transposition of the great arteries and 120 (82%) with complex *d*-transposition of the great arteries (Table 1).

Maternal sociodemographic characteristics

Maternal sociodemographic characteristics are presented in Table 2. No significant difference in

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Table 1. Associated lesions of the 120 patients with complex *d*-transposition of the great arteries.

Lesions	Number (%)
Ventricular septal defect	58 (55%)
Pulmonary stenosis	27 (26%)
Atrial septal defect	22 (21%)
Atrioventricular septal defect	16 (15%)
Pulmonary valve stenosis	8 (8%)
Taussig–Bing-type double-outlet right ventricle	7 (7%)
Dextrocardia	5 (5%)
Mesocardiac	5 (5%)
Pulmonary atresia	4 (4%)
Common atrium	2 (2%)
Total anomalous pulmonary venous return	2 (2%)

maternal sociodemographic characteristics were found between the before standard consultation and after standard consultation groups, except in gravidity and parity. There were more singly gravid women in the before standard consultation cohort (65 versus 42%, $p = 0.024$), and the proportion of nulliparous mothers was higher in after standard consultation group (77 versus 58%, $p = 0.020$). Notably, 61% of the subjects – 53% in the before standard consultation and 67% in the after standard consultation groups – were transferred from other health providers for fetal echocardiography.

Perinatal outcomes of fetuses with prenatally diagnosed d-transposition of the great arteries

Among the 146 enrolled fetuses, 41 (28%) were lost to follow-up after prenatal diagnosis of *d*-transposition of the great arteries. The basic maternal demographic characteristics and anatomic diagnosis – that is, simple and complex *d*-transposition of the great arteries type – were compared between fetuses lost to follow-up and those not lost, and no significant differences were found. The anatomic distribution of the 41 patients lost to follow-up between before standardised consultation (2011–2013) and after standardised consultation (2014–2015) was also compared and there was no significant statistical difference ($\chi^2 = 0.819$, $p = 1.000$). Therefore, outcomes of the remaining 105 fetuses who were followed up are likely representative of the entire enrolled population. The potential risk for results being biased because of loss to follow-up was minimal when comparing the perinatal outcomes between the before standardised consultation (2011–2013) and after standardised consultation (2014–2015) groups. In total, there were 29 (28%) live births and 76 (72%) cases of elective termination. No spontaneous fetal demise and abortions or stillbirths were observed. There were no trends over time from 2011 to 2015 for either live birth or elective termination rate when considering overall, simple, or complex *d*-transposition of the great arteries (Fig 1). The rates of live birth and elective termination were compared for before standard consultation and after standard consultation group, and for overall, simple, and complex *d*-transposition of the great arteries (Fig 2). Overall, there were no differences detected in rates of live birth or elective termination between the various groups.

Importantly, only 7% (5/76) elective termination occurred in our centre, and it was significantly lower than the proportion of live births of 76% (22/29, $p = 0.000$). In our centre, there were no significant differences between before standard consultation and after standard consultation groups in the proportion of elective termination (6 versus 7%, $p = 1.000$) or live births (90 versus 68%, $p = 0.367$).

Postnatal outcomes for live births

There were 29 live births following prenatal diagnosis of *d*-transposition of the great arteries. Of these live births, three were found to have postnatal diagnoses other than *d*-transposition of the great arteries and were excluded. Among the remaining 26, five (19%) were male, five (19%) were one of twins, five (19%) weighed less than or equal to 2.5 kg, three (12%) were premature – that is, gestational age <37 weeks – and eight (31%) had simple *d*-transposition of the great arteries.

Of the 26 lives births, the overall mortality was 23% (6/26). There was no significant difference between infants with simple and complex *d*-transposition of the great arteries [13% (1/8) versus 28% (5/18), $p = 0.628$] or when comparing before standard consultation and after standard consultation periods [38% (3/8) versus 17% (3/18), $p = 0.330$]. The flow chart of the operative status and survival of the 26 live births with prenatally diagnosed *d*-transposition of the great arteries is illustrated in Figure 3. Among the 26 live births, 17 (65%) underwent arterial switch operation during the same hospitalisation period as for their birth and within 30 days of age. There were three in-hospital deaths (18%, 3/17). During a median follow-up of 10 months (range, 2–53), one additional death was observed in the operative cohort. The four postoperative deaths are detailed in Table 3. An additional infant underwent arterial switch operation at 13 months of age and was alive at the last follow-up instance.

In all, eight patients have declined surgery and, at the last follow-up instance, two have died. Of them, one died at 7 days of age without surgery, for a total non-operative mortality of 25% (2/8).

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Table 2. Maternal sociodemographic characteristics, before standard consultation and after standard consultation in Guangdong, China 2011–2015.

Characteristics	Overall (n = 146)	Before standard consultation (2011–2013) (n = 64)	After standard consultation (2014–2015) (n = 82)	p
TGA type				
Simple TGA	26 (18%)	9 (14%)	17 (21%)	0.296
Complex TGA	120 (82%)	55 (86%)	65 (79%)	
Gestational age at prenatal diagnosis				
<28 weeks	98 (67%)	42 (66%)	56 (68%)	0.734
⩾28 weeks	48 (33%)	22 (34%)	26 (32%)	
Maternal age				
<20	1 (1%)	0	1 (1%)	0.642
20–29.99	94 (64%)	43 (67%)	51 (62%)	
30–34.99	37 (25%)	14 (22%)	23 (28%)	
35+	14 (10%)	7 (11%)	7 (9%)	
Maternal race				
Han	144 (99%)	64 (100%)	80 (98%)	0.504
Minority	2 (1%)	0	2 (2%)	
Maternal education				
Middle school or below	19 (13%)	12 (19%)	7 (9%)	0.170
High school	86 (59%)	37 (58%)	49 (61%)	
College or above	40 (28%)	15 (23%)	25 (31%)	
Maternal occupation				
Factory worker	6 (7%)	0	6 (8%)	1.00
Other	84 (93%)	11 (100%)	73 (92%)	
Migrants				
Yes	21 (15%)	13 (21%)	8 (10%)	0.065
No	124 (86%)	50 (79%)	74 (90%)	
Maternal residence				
City	127 (88%)	56 (88%)	71 (88%)	0.978
Country	18 (12%)	8 (13%)	10 (12%)	
Gravidity				
1	80 (55%)	27 (42%)	53 (65%)	0.024**
2	44 (30%)	24 (38%)	20 (24%)	
⩾3	22 (15%)	13 (20%)	9 (11%)	
Parity				
0	100 (69%)	37 (58%)	63 (77%)	0.020**
1	40 (27%)	25 (39%)	15 (18%)	
⩾2	6 (4%)	2 (3%)	4 (5%)	
Maternal abnormal reproductive history*				
Yes	6 (4%)	3 (5%)	3 (4%)	1.00
No	140 (96%)	61 (95%)	79 (96%)	
Household income (Yuan)				
1–2500	17 (12%)	12 (19%)	5 (6%)	0.060
2501–5000	105 (72%)	42 (66%)	63 (77%)	
5001+	24 (16%)	10 (16%)	14 (17%)	
Referrals for fetal echocardiography				
Yes	89 (61%)	34 (53%)	55 (67%)	0.086
No	57 (39%)	30 (47%)	27 (33%)	

TGA = *d*-transposition of the great arteries
*Included stillbirth, spontaneous abortion, or baby with any congenital abnormality
**Statistically significant

Discussion

To our knowledge, this is the first cohort of prenatally diagnosed *d*-transposition of the great arteries prospectively studied to evaluate the effects of a standardised prenatal consultation on perinatal and postnatal outcomes.

For the overall study duration from 2011 to 2015, there were no differences in the measured perinatal and postnatal outcomes for fetuses prenatally diagnosed with *d*-transposition of the great arteries, including in rates of live birth and elective termination. Comparing the before standard consultation (2011–1013) and after standard consultation periods

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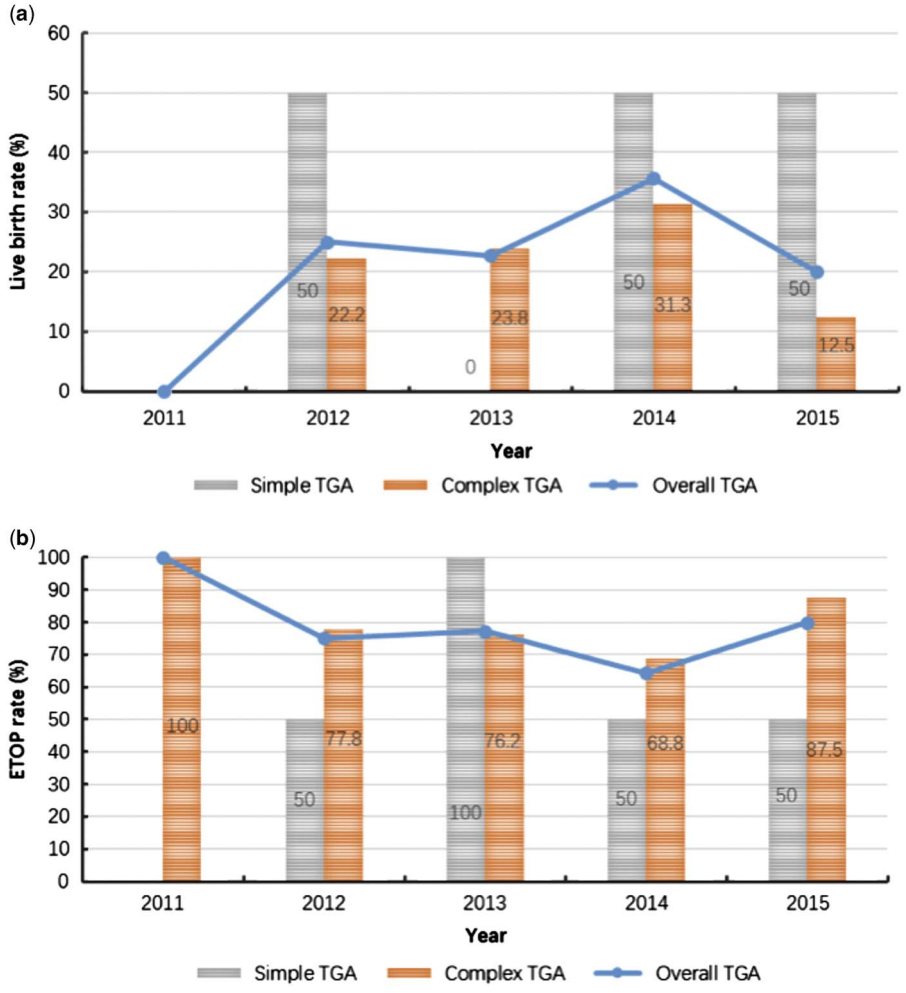

Figure 1.
*Perinatal outcomes for fetuses with prenatally diagnosed d-transposition of the great arteries (TGA) by year in Guangdong, China during 2011–2015. (**a**) Live birth rate of overall, simple, and complex TGA from 2011 to 2015. (**b**) elective termination of pregnancy (ETOP) rate of overall, simple, and complex TGA from 2011 to 2015.*

(2014–2015), there were no changes in the rates of live births and elective termination. The overall live birth rate was relatively low at <30%, whereas the elective termination rate was over 70%, even after standardised consultation was initiated. There was no difference in elective termination rate comparing simple with complex *d*-transposition of the great arteries. However, for simple *d*-transposition of the great arteries, the live birth rate was higher and the elective termination rate was lower in the after standard consultation period, although no statistical significance could be shown because of small numbers.

Reports on perinatal outcomes of fetuses with prenatally diagnosed *d*-transposition of the great arteries are limited. Dhanardhono et al reported a single-centre experience from Singapore. Among 9834 fetuses, three were diagnosed with *d*-transposition of the great arteries; one of them was terminated and the other two were live births.[21] Khoo et al published the outcomes for 103 fetuses who were prenatally diagnosed with CHD. Neither elective termination nor stillbirths were observed in the overall cohort, and of the four fetuses with *d*-transposition of the great arteries, one neonatal death occurred.[22] Yang et al presented the results of a study from Beijing in 2009. In the 14 fetuses with prenatally diagnosed *d*-transposition of the great arteries, 11 (79%) were terminated.[16] This finding was comparable to the elective termination rate in our study.

Several reasons could potentially account for the higher rate of elective termination in China compared with other countries, including ethical and religious issues, insurance system, and unique social policies. For example, elective termination is legal in China, whereas in most regions of the United States of America, termination of pregnancy is only legal before 24 weeks of gestation and in Japan, elective termination is forbidden by law after the 22nd week

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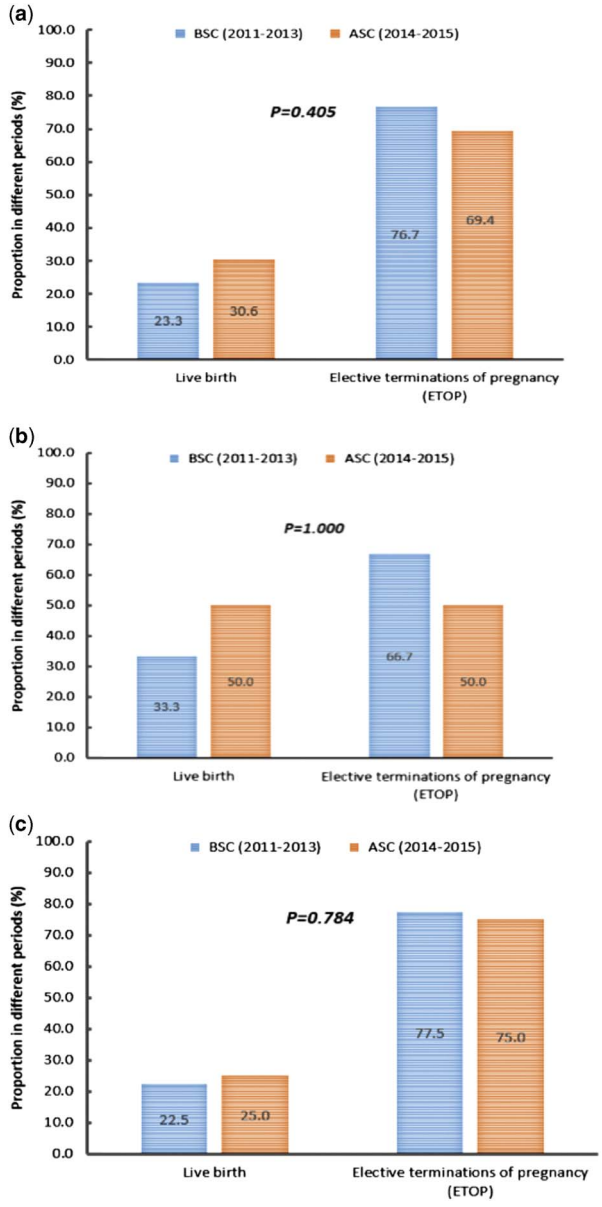

Figure 2.
*Perinatal outcomes for fetuses with prenatally diagnosed overall, simple, and complex d-transposition of the great arteries (TGA), before standardised consultation (BSC) (2011–2013) versus after standardised consultation (ASC) (2014–2015) in Guangdong, China during 2011–2015. (**a**) Perinatal outcomes for all fetuses with prenatally diagnosed TGA. (**b**) Perinatal outcomes for fetuses with prenatally diagnosed simple TGA. (**c**) Perinatal outcomes for fetuses with prenatally diagnosed complex TGA.*

of gestation. Religious objections are also less common in China where there are few Catholics. In addition, medical expenses for treating CHD are not totally covered by the current Chinese insurance system, which results in the affected families being responsible for most of the medical expenses related to treating their CHD-afflicted children. This factor is especially important in extremely damaging lesions such as *d*-transposition of the great arteries. Finally, from 1979 to 2015, a strict policy of family planning that allowed each couple only one child was in effect in China, placing great emphasis on giving birth to a healthy baby. For all of the above reasons, elective termination is considered to be an acceptable consequence of a prenatal *d*-transposition of the great arteries diagnosis.

With this specific culture and social background, it may be difficult to vary the outcomes after prenatal diagnosis and decrease the elective termination rate;[8,23,24] however, the fact that the live birth rate in cases of simple *d*-transposition of the great arteries in the current study was higher after standardised consultation is encouraging. This was particularly true for patients followed up throughout their prenatal course at our centre, rather than for those returning to their local providers. Indeed, continuous professional care and follow-up examinations have been identified as critical components in a family's decision regarding elective termination.[25] Therefore, collaborating with local hospitals to develop standardised consultation and education for the care and follow-up of prenatally diagnosed *d*-transposition of the great arteries cases, especially of simple *d*-transposition of the great arteries cases, could potentially achieve a lower rate of elective termination and higher live birth rates. Another factor that may aid in decreasing elective termination rates would be the availability of funds to support affected families, which should be alluded to during the prenatal consultation. In addition, a universal two-children-per-family policy was enacted in China in November, 2015. All these changes could impact the outcomes for fetuses prenatally diagnosed with *d*-transposition of the great arteries and could increase the live birth rate.

Theoretically, prenatal diagnosis may impact not only the incidence of surgery, but also the survival. Termination can affect neonatal outcomes by decreasing the number of complex patients with multiple congenital anomalies, thus creating a bias towards more favourable outcomes in postnatal results. Prenatal diagnosis also allows optimisation of pregnancy management by allowing tailoring of the timing, location, or mode of delivery; however, results regarding the effect of prenatal diagnosis on the preoperative mortality or early postoperative outcomes among neonates with *d*-transposition of the great arteries have not been consistent. Some studies reported the positive protective effects of prenatal diagnosis on the preoperative and postoperative mortality of patients with *d*-transposition of the great arteries, whereas others reported negative results.[26] Calderon et al found that prenatal diagnosis of *d*-transposition of the great arteries was associated with better neurocognitive outcomes and that time of

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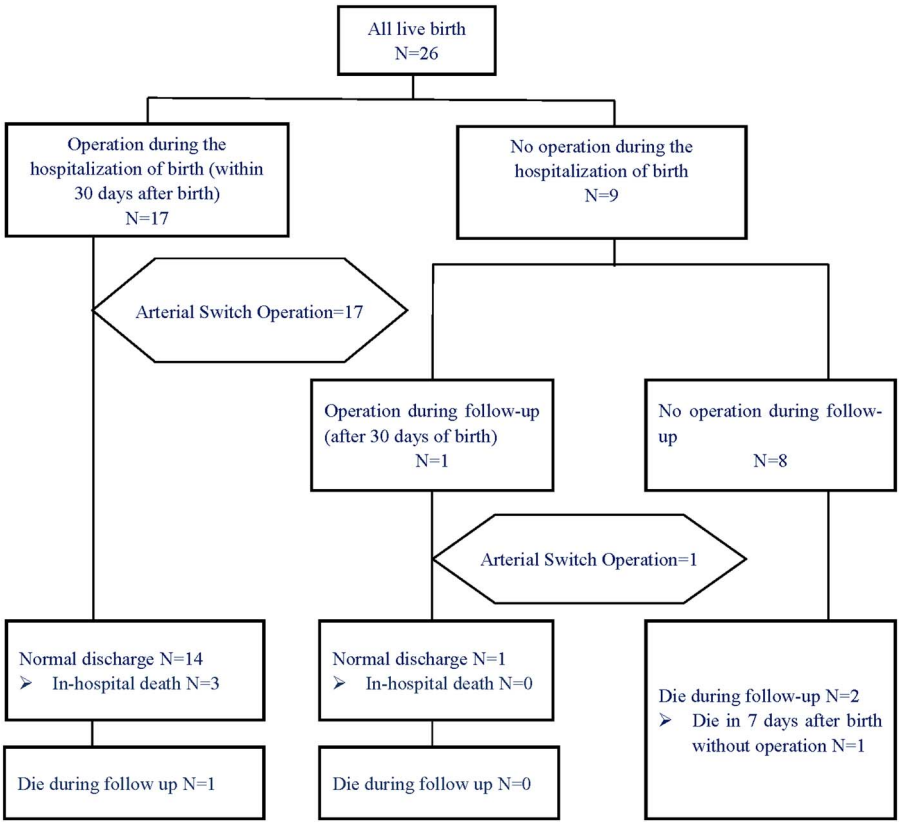

Figure 3.
Flow chart of the early postnatal outcomes and intermediate follow-up of the 26 live births with prenatally diagnosed d-transposition of the great arteries in Guangdong, China during 2011–2015.

diagnosis might influence the development of early complex cognitive skills, such as executive functions.[6]

The mortality in our study was higher than that in some previously reported studies. Several reasons could account for this. Previous studies only included patients with *d*-transposition of the great arteries operated on at a single institution or at multiple tertiary referral cardiac centres. It is possible that the population at these centres was subject to selection bias. For example, extremely complex cases may not survive to be transferred to the centre, or families may elect not to seek treatment. In contrast, all the neonates with *d*-transposition of the great arteries delivered in our hospital were offered surgical treatments. Indeed, the four postoperative deaths were in complex cases of *d*-transposition of the great arteries; however, there is still ample room for improvement in the management of and treatments for neonates with *d*-transposition of the great arteries.

There were several limitations to our study. First, postnatal outcomes of patients with *d*-transposition of the great arteries without prenatal diagnosis were not acquired. Hence, the effect of prenatal diagnosis on the postnatal outcomes of *d*-transposition of the great arteries could not be explored. Second, the number of patients lost to follow-up was relatively high. In order to improve the rate of follow-up, we will be developing a system for specialised follow-up and consultation at the time of initial registration and provide the patients with a streamlined system for their follow-up visits. Finally, *d*-transposition of the great arteries follow-up information on the perinatal and postnatal outcomes occurring in other hospitals relied on oral reports, which may not be totally accurate. Collaboration with other health providers to get more accurate outcome information will be necessary. This information gathering will be improved by our Guangdong Registry of Congenital Heart Disease network, which will also provide a basis for collaboration in future studies.[27]

With an overarching goal of improving the outcomes for fetuses diagnosed with *d*-transposition of the great arteries, there is an important chain of prenatal diagnosis, consultation, preparation for pregnancy, and postnatal treatments. Any institution or department in the chain will impact the prenatal choices made by the family and postnatal outcomes of the baby, and thus multidisciplinary and inter-institutional cooperation are crucial. We remain

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Table 3. Details of the four postoperative deaths.

N	Birth weight (g)	Gestational age at prenatal diagnosis (weeks + days)	Prenatal diagnosis	Preoperative condition	Operation age (days)	Diagnosis confirmed by operation	Coronary artery pattern	Days from operation when dead	Death reasons
1	3180	28 + 4	TGA, VSD	Mechanically ventilated	8	TGA, PDA, ASD, PH, TR	Intramural, 2 RLCx	20	Low cardiac output, severe infection, capillary leak syndrome
2	2990	30 + 2	TGA	One of the twins; IVF-ET; mechanically ventilated	8	TGA, VSD, CoA/IAA, ASD, PDA, PH	Normal (1 LCx–2 R)	12	Severe low cardiac output
3	3090	23 + 6	TGA, VSD	IVF-ET; mechanically ventilated	12	TGA, ASD, VSD, PDA, PH	1 LR-2 Cx	7	Severe low cardiac output, kidney failure, liver damage, capillary leak syndrome
4	3300	30	TGA	Mechanical ventilated	10	TGA, VSD, PFO, PDA	Intramural, 2 RLCx (RCA)	64	Cardiac arrest; die in home during follow-up

ASD = atrial septal defect; CoA = coarctation; IAA = interrupted aortic arch; Cx: left circumflex; IVF-ET = in vitro fertilisation and embryo transfer; L = LAD, left anterior descending; PDA = patent ductus arteriosis; PFO = patent foramen ovale; PH = pulmonary hypertension; R = RCA, right coronary artery; TGA = *d*-transposition of the great arteries; TR = tricuspid regurgitation; VSD = ventricular septal defect

optimistic, that in concert with these collaborations, establishment of a policy of standardised consultation will achieve better perinatal and postnatal outcomes after fetal diagnosis of *d*-transposition of the great arteries.

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Conflicts of Interest

None.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation in China and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the Ethics Committee of Guangdong General Hospital.

References

1. Botto LD, Correa A, Erickson JD. Racial and temporal variations in the prevalence of heart defects. Pediatrics 2001; 107: E32.
2. Khairy P, Clair M, Fernandes SM, et al. Cardiovascular outcomes after the arterial switch operation for D-transposition of the great arteries. Circulation 2013; 127: 331–339.
3. Quartermain MD. Transposition of the great arteries. In: Rychik J, Tian Z (eds). Fetal Cardiovascular Imaging: A Disease-Based Approach, Elsevier Inc., Philadelphia, PA, 2012; 153–163.
4. Liebman J, Cullum L, Belloc NB. Natural history of transposition of the great arteries. Anatomy and birth and death characteristics. Circulation 1969; 40: 237–262.
5. Van Velzen CL, Haak MC, Reijnders G, et al. Prenatal detection of transposition of the great arteries reduces mortality and morbidity. Ultrasound Obstet Gynecol 2015; 45: 320–325.
6. Calderon J, Angeard N, Moutier S, Plumet MH, Jambaque I, Bonnet D. Impact of prenatal diagnosis on neurocognitive

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outcomes in children with transposition of the great arteries. J Pediatr 2012; 161: 94–98.e1.
7. Escobar-Diaz MC, Freud LR, Bueno A, et al. Prenatal diagnosis of transposition of the great arteries over a 20-year period: improved but imperfect. Ultrasound Obstet Gynecol 2015; 45: 678–682.
8. Khoshnood B, De Vigan C, Vodovar V, et al. Trends in prenatal diagnosis, pregnancy termination, and perinatal mortality of newborns with congenital heart disease in France, 1983-2000: a population-based evaluation. Pediatrics 2005; 115: 95–101.
9. Raboisson MJ, Samson C, Ducreux C, et al. Impact of prenatal diagnosis of transposition of the great arteries on obstetric and early postnatal management. Eur J Obstet Gynecol Reprod Biol 2009; 142: 18–22.
10. Bertagna F, Rakza T, Vaksmann G, et al. Transposition of the great arteries: factors influencing prenatal diagnosis. Prenat Diagn 2014; 34: 534–537.
11. Blyth M, Howe D, Gnanapragasam J, Wellesley D. The hidden mortality of transposition of the great arteries and survival advantage provided by prenatal diagnosis. BJOG 2008; 115: 1096–1100.
12 Sklansky MS, Berman DP, Pruetz JD, Chang RK. Prenatal screening for major congenital heart disease: superiority of outflow tracts over the 4-chamber view. J Ultrasound Med 2009; 28: 889–899.
13. Carvalho JS, Mavrides E, Shinebourne EA, Campbell S, Thilaganathan B. Improving the effectiveness of routine prenatal screening for major congenital heart defects. Heart 2002; 88: 387–391.
14. Ogge G, Gaglioti P, Maccanti S, Faggiano F, Todros T. Prenatal screening for congenital heart disease with four-chamber and outflow-tract views: a multicenter study. Ultrasound Obstet Gynecol 2006; 28: 779–784.
15. Levy DJ, Pretorius DH, Rothman A, et al. Improved prenatal detection of congenital heart disease in an integrated health care system. Pediatr Cardiol 2013; 34: 670–679.
16. Yang XY, Li XF, Lu XD, Liu YL. Incidence of congenital heart disease in Beijing, China. Chin Med J 2009; 122: 1128–1132.
17. Guangdong General Hospital GCI, Guangdong Eugenics Association Congenital Heart Disease Committee. Prenatal consultation specification of fetal congenital heart disease in Guangdong province. Int Med Health Guidance News 2015; 21: 1033–1036.
18. Guangdong General Hospital GCI, Guangdong Eugenics Association Congenital Heart Disease Committee. Fetal cardiac ultrasound technology specification in Guangdong province. Int Med Health Guidance News 2015; 21: 739–741.
19. Martins P, Castela E. Transposition of the great arteries. Orphanet J Rare Dis 2008; 3: 27.
20. Oganization WH. International Statistical Classification of Diseases and Related Health Problems. Tenth Revision. Vol. 2. World Health Organization, Geneva, Switzerland, 1993, 129 pp.
21. Dhanardhono T, Thia E, Wei X, Saktini F, Dewi PK, Yeo GS. Incidence and outcome of prenatally diagnosed, chromosomally normal congenital heart defects in Singapore. Singapore Med J 2012; 53: 643–647.
22. Khoo NS, Van Essen P, Richardson M, Robertson T. Effectiveness of prenatal diagnosis of congenital heart defects in South Australia: a population analysis 1999-2003. Aust N Z J Obstet Gynaecol 2008; 48: 559–563.
23. Khoshnood B, Lelong N, Andrieu T, et al. Assessing socio-demographic differences (or lack thereof) in prenatal diagnosis of congenital heart defects: a population-based study. BMJ Open 2016; 6: e009353.
24. Lee JE, Jung KL, Kim SE, Nam SH, Choi SJ, Oh SY, et al. Prenatal diagnosis of congenital heart disease: trends in pregnancy termination rate, and perinatal and 1-year infant mortalities in Korea between 1994 and 2005. J Obstet Gynaecol Res 2010; 36: 474–478.
25. Donofrio MT, Moon-Grady AJ, Hornberger LK, et al. Diagnosis and treatment of fetal cardiac disease: a scientific statement from the American Heart Association. Circulation 2014; 129: 2183–2242.
26. Bonnet D, Coltri A, Butera G, et al. Detection of transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. Circulation 1999; 99: 916–918.
27. Qu Y, Liu X, Zhuang J, et al. Incidence of congenital heart disease: the 9-year experience of the Guangdong Registry of Congenital Heart Disease, China. PloS One 2016; 11(7): e0159257.