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Original Research

Pregnancy outcomes in women with congenitally corrected transposition of the great arteries

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Summary

The aim of this study was to define the pregnancy outcomes in women with congenitally corrected transposition of the great arteries (cc-TGA). The medical databases at Anzhen Hospital between January 2011 and March 2018 were retrospectively reviewed. Data of 12 pregnant women with cc-TGA were collected. One patient was lost at 35 weeks of gestation. There were 8 (72.7%) term births and 3 (27.3%) premature births. Of the 11 deliveries, 2 (18.2%) were vaginal and 9 (81.8%) were cesarean. The baseline New York Heart Association (NYHA) functional class was I - II in 11 patients, II - III in 7 patients, and III - IV in 5 patients in the third trimester ($P = 0.037$). In the third trimester, 6 (50%) patients became symptomatic and experienced heart function deterioration compared with asymptomatic patients (6 *vs.* 0, $P = 0.002$). In the third trimester, tricuspid regurgitation (TR) was identified in 11 patients: 2 with mild TR, 4 with moderate TR, and 5 with severe TR. Five symptomatic patients developed severe TR, in which the rate of TR was significantly higher than that of asymptomatic patients (5 *vs.* 0, $P = 0.015$). No difference was found in NYHA class between the third trimester and 1 week after delivery ($P > 0.05$). One patient died of ventricular fibrillation at 3 months postpartum. Successful pregnancy can be achieved by most women with cc-TGA. The deterioration of right ventricular function is common among pregnant women with cc-TGA, and severe TR is a high risk factor resulting in deterioration of the right ventricular function.

Key words: pregnancy; congenitally corrected transposition of the great artery; systemic right ventricle.

Introduction

Congenitally corrected transposition of the great arteries (cc-TGA) is a rare cardiac disorder that accounts for 1/33,000 of live births and for 0.05% of all congenital cardiac diseases [1]. It is characterized by atrioventricular and ventricular–great arterial discordance. Pulmonary venous return enters the left atrium, which is connected to the "thin-walled" morphological right ventricle (RV) guarded by a tricuspid valve. The morphological RV supports the systemic circulation. The systemic venous return enters the right atrium, passes through the mitral valve, and flows into the morphological left ventricle, which pumps it into the pulmonary artery. cc-TGA may be an isolated defect, and may be associated with other congenital defects, including ventricular septal defects, pulmonary stenosis, Ebstein's malformation, dextrocardia, and atrial septal defects. Long-term survival rates are good for both simple and complex cc-TGA, which at 40 years of age are estimated to be 84% [2]. Thus, most women with cc-TGA reach childbearing age. The long-term risk depends on the severity of coexistent lesions and function of the systemic RV. However, dysfunction of the systemic RV and tricuspid regurgitation are encountered in 30-50% of patients at an earlier age [3]. Impaired systemic right ventricular function reduces peak oxygen uptake and is related to reduced exercise capacity [4].

During pregnancy, childbirth, and puerperium, the systemic RV is exposed to dramatic hemodynamic changes, including a 50% increase in blood volume, increased cardiac output, reduction in cardiovascular resistance, and rapid fluid shifts during delivery [5]. The morphologic RV is not designed to support systemic circulation and may not be adaptable to these physiological changes and increases the maternal and fetal risks [6]. Bowater et al. [7] recently proved that women with cc-TGA are at greater risk to experience cardiac symptoms during pregnancy. Patients with cc-TGA may carry an increased risk of maternal mortality and severe morbidity [8]. Based on the systemic ventricular function, the systemic RVs are assigned to the modified World Health Organization classification (m-WHO) of maternal cardiovascular risk class III or IV [9]. Recently, a few case reports [10-12]and retrospective studies on pregnancies with cc-TGA [13, 14] show that patients with cc-TGA may achieve successful pregnancy and some patients may live a long lifespan. However, most studies paid attention to the outcomes of pregnancy and few studies described the changes of systemic RV function due to the hemodynamic loading effect of pregnancy and delivery. This study has examined a cohort of pregnant women with cc-TGA and observed the right ventricular function and TR during preg-

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nancy and after delivery. Both cardiac and obstetric outcomes have been examined allowing us to counsel these women more accurately as to the potential risks and outcomes of pregnancy.

Materials and Methods

Study subjects

The medical databases of Anzhen Hospital between January 2011 and March 2018 were retrospectively reviewed for female patients with a confirmed diagnosis of cc-TGA, who had been pregnant. Only pregnancies that went beyond the second trimester were included. All medical records were reviewed in all patients. The diagnosis of cc-TGA and coexistent cardiac defects in the study group was established by echocardiography. All patients were managed by multidisciplinary teamwork, and patients and newborn babies were followed up for 3 months– 3 years. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Anzhen Hospital. Written informed consent was obtained from all participants.

Cardiac outcome

The baseline data was recorded and included the age at pregnancy, parity, pre-pregnancy New York Heart Association (NYHA) functional class, and medical history of any prior surgical and cardiac complications. Heart functional class and echocardiographic parameters, including ejection fraction of systemic RV and tricuspid regurgitation (TR) in the third trimester and 1 week postpartum, were analyzed. According to the results of echocardiography, TR was assessed visually and graded as none/trivial, mild, moderate, and severe [15, 16].

Cardiac complications

Cardiac complications included pulmonary artery hypertension, cyanosis, reduced NYHA functional class from baseline, arrhythmia, maternal cardiac death, and invasive cardiac intervention during the pregnancy or follow-up after delivery.

Obstetric outcome

Obstetric and neonatal complications were noted. Other information recorded included the timing of delivery, birthweight, and incidence of cardiac defects in offspring.

Statistical Analysis

Data analysis was performed using SPSS 18. Descriptive statistics are reported as the frequency, or mean value and interquartile range or standard deviations, as appropriate. Between-group frequencies were compared via Fisher's exact test. P-values < 0.05 were considered statistically significant.

Results

Characteristics of the study population

There were 14 pregnant women with cc-TGA on the databases. Twelve patients whose pregnancy progressed to 28 weeks gestation were included in the study, and the other two patients were excluded because of induced abortion in the first trimester. According to the segmental analysis of the heart, 1 (8.3%) patient in the study cohort was classified as having IDD and 11 (91.7%) were classified as having SLL. The mean age at pregnancy of the study population were 27.1 $\pm$ 3.7 (21-34) years old. Eight (66.7%) patients were nulliparous and 4 (33.3%) were multiparous. Five (41.7%) women had isolated cc-TGA and seven (58.3%) women had associated cardiac defects, which included dextrocardia, pulmonary atresia (PS) or pulmonary atresia, ventricular septal defects (VSDs), atrial septal defects (ASDs), truncus arteriosus communis, ventricular septal aneurysms (VSAs), Ebstein's anomaly, and Bicuspid aortic valves associated with mild aortic valve stenosis. Patient No. 1 experienced cyanosis before pregnancy. Four patients had associated sustained arrhythmia not requiring treatment: one had complete right bundle branch block (CRBBB), two had atrial premature beats (APB), and one had second-degree atrioventricular block (II-AVB). Baseline NYHA functional class was I in 9 (75%) patients and II in 3 (25%) patients. Patient No. 10 underwent mitral valve replacement with a mechanical prosthetic valve and tricuspid valvuloplasty before pregnancy and accepted anticoagulation therapy with warfarin after the operation. All patients were asymptomatic before pregnancy. Baseline characteristics of the patients are shown in Table 1.

Cardiac complications in the third trimester

Six (50%) patients became symptomatic and experienced palpitations and shortness of breath in the third trimester. Cardiac complications were diagnosed in these patients during pregnancy, including cyanosis and pulmonary artery hypertension in 1 patient (No. 1), sinus tachycardia in 3 patients, pulmonary artery hypertension in 1 patient, reduced NYHA functional class in 6 patients, and heart failure (HF) in 1 patient. One patient (No. 6) died of ventricular fibrillation after 3 months postpartum. Clinical data of the patients during pregnancy are shown in Table 2.

Systemic RV function changes in the 3^{rd} trimester and after delivery

In the third trimester, five (41.7%) patients had an NYHA class III - IV and required admission to the hospital. After pregnancy, the study population had a significant deterioration in NYHA functional class, compared with that in baseline ($P = 0.037$). No difference in the deterioration of heart function was found between patients with simple cc-TGA or cc-TGA complicated with other cardiac defects in the third trimester ($P > 0.05$). Heart functional class improvement was observed in two patients in the puerperium, but no difference in the NYHA class between the third trimester and 1 week after delivery was identified ($P > 0.05$). Information on systemic RV function class in the third trimester and 1 week after delivery is shown in Table 3.

Table 1. — *Baseline characteristics in women with cc-TGA*

Patient Number	Age	Parity	Type of TGA	Other cardiac defect and arrhythmia	NYHA class before pregnancy
1	27	0	IDD	Dexiocardia, pulmonary atresia, VSD, ASD truncus arteriosus communis, CRBBB	II
2	24	1	SLL	VSA, ASD	II
3	21	0	SLL	VSA, ASD	I
4	30	0	SLL	APB	I
5	34	1	SLL	APB	I
6	23	0	SLL	VSD, PS	I
7	30	1	SLL	Ebstein's Anomaly, II-AVB	I
8	27	0	SLL	-	I
9	30	1	SLL	-	I
10	29	0	SLL	Dexiocardia	I
11	24	0	SLL	-	II
12	26	0	SLL	Bicuspid aortic valve associated with mild aortic valve stenosis	I

Table 2. — *Clinical data during pregnancy*

Patient number	Symptom	Occurrence time	Cardiac complication	Bnp (pg/ml)	SpO_2 (%)	Obstetrical complication
1	Yes	31	PAH	-	84	-
2	No	-		38	98.8	-
3	No	-		-	95.8	-
4	Yes	36	Sinus tachycardia	87	98.9	-
5	Yes	28	HF	2760	99.6	Sever PE
6	Yes	36	Sinus tachycardia	123	98	-
7	No	-		55	97.3	-
8	No	-	-	-	98.3	GDM
9	No	-	-	84	98.9	
10	No	-	-	168	96.1	
11	Yes	25		62	98.3	
12	Yes	33	Sinus tachycardia	96	97.7	

PE: pre-eclampsia; GDM: gestational diabetes mellitus

Tricuspid regurgitation in the 3rd trimester and after delivery

In the third trimester, TR was identified in 11 patients: 2 mild TR, 4 moderate TR, and 5 severe TR. Five out of six symptomatic patients during pregnancy developed severe TR, in which the rate of TR was significantly more than that of asymptomatic patients (5 *vs.* 0, $P = 0.015$). All symptomatic patients experienced a deterioration of heart function and none of the asymptomatic patients did (6 *vs.* 0, $P = 0.002$). The degree of TR was relieved in 4 cases after delivery. Echocardiographic records on TR in the third trimester and 1 week after delivery are shown in Table 3.

Obstetric complications

There were two pregnancy-related disorders: severe preeclampsia in patient No. 5 and gestational diabetes mellitus in patient No. 8. Patient No. 5 was complicated with heart failure. After her heart function improved with magnesium sulfate, digoxin, and furosemidum treatment, a cesarean section was performed. No. 8 was managed by lifestyle changes to maintain normal blood glucose levels during pregnancy and experienced no complications.

Obstetric outcomes

One patient (No. 11) was loss to follow-up at 35 weeks of gestation. Two patients (18.2%) delivered vaginally, and nine patients (81.8%) accepted a cesarean section, of which two patients were due to scared uterine and seven patients due to cardiac disease. There were 8 (72.7%) term births and 3 (27.3%) premature births among eleven patients. All premature births were attributed to maternal heart function deterioration. No cardiac defect was identified in the offspring. Information on the maternal and fetal outcomes is shown in Table 4.

Discussion

Significant hemodynamic and physiologic changes during pregnancy may adversely affect the hemodynamic status of women with cc-TGA. The women with a systemic RV are more likely to develop cardiovascular complications during pregnancy or the postpartum period, as well as adverse pregnancy-related events, than women with a systemic left ventricle [17]. A systemic RV is assessed as

Table 3. — *Heart function class and Echocardiographic parameters in 3rd trimester and 1 week after delivery*

Patient	NYHA class		EF of SRV (%)		Degree of TR	
Number	3rd trimester	1 week after delivery	3rd trimester	1 week after delivery	3rd trimester	1 week after delivery
1	III	III	55	52	Moderate	Mild
2	II	II	53	50	Moderate	Moderate
3	I	I	60	50	Moderate	Moderate
4	II	II	60	60	Severe	Mild
5	IV	IV	53	46	Severe	Moderate
6	III	III	40	-	Severe	Severe
7	I	I	50	55	Moderate	Mild
8	I	I	60	60	Mild	Mild
9	I	I	-	-	Mild	Mild
10	I	I	56	55	None	None
11	IV	-	45	-	Severe	-
12	III	III	55	59	Severe	Severe

Table 4. — *Mode of delivery, use of anaesthesia, and fetal outcome*

Patient Number	Gestational age at birth	Mode of delivery	Anaesthesia	Birthweight (g)	Apgar score
1	31^{+3}	CS	Epidural	1520	2010/10/10
2	37	CS	Epidural	3030	2010/10/10
3	39	CS	Spinal	3660	2010/10/10
4	38	CS	Epidural	3930	2010/10/10
5	30^{+6}	CS	Epidural	980	2007/8/9
6	38	CS	Epidural	3530	2010/10/10
7	38+	CS	Epidural	3630	2010/10/10
8	40	VD	-	3700	2010/10/10
9	39	VD	-	3350	2010/10/10
10	38^{+}	CS	Spinal	2930	2010/10/10
11	Loss of follow-up		-		
12	34^{+}	CS	Epidural	2850	2010/10/10

high risk by the WHO classification of maternal cardiovascular. But these studies collected cases including cc-TGA and surgical TGA and thus, were under representative of women with cc-TGA [7, 8, 18]. A recent study showed that pregnancy does not seem to impair systematic RV function and successful pregnancy may be achieved by most women with cc-TGA [13].

The results of the present study indicate that pregnancy contributed to systemic RV failure in women with cc-TGA, and worsened RV function did not recover during early puerperium. The cardiac functional deterioration in the third trimester was more likely experienced by symptomatic women with cc-TGA during pregnancy, most of whom also suffered from severe TR. Heart failure occurred in 1 patient with severe TR and preeclampsia in the 28^{th} gestational week, which may be attributed to cc-TGA and preeclampsia. One cardiac death occurred 3 months after delivery. Our findings are in agreement with previous studies [7, 8, 18, 19]. Women with a systemic RV after surgically and congenitally corrected transposition of the great arteries encountered mild-moderate RV dysfunction during pregnancy [8]. Another study of patients (including 28 pregnant women) with systemic RV showed that RV dysfunction is sometimes irreversible. The researchers found that the functional class and RV systolic dysfunction and dilation progressed during pregnancy and after delivery did not recover in some patients to the levels of pre-pregnancy [19].

TR may be a predictor of maternal cardiac complications. Our observation on the deterioration of right ventricular function differs from that reported by Kowalik et al. [13]. More cases with reduced heart function during pregnancy were found. We noted differences in the rate of patients with moderate-severe TR between the two studies, which was 6 of 13 pregnant women with cc-TGA in Kowalik's study and 9 of 12 pregnant women in our study. Traditionally, TR was considered secondary to morphological RV dysfunction, which cannot sustain the systemic circulation [20]. Therefore, TR should be regarded as a high risk factor for pregnant women with cc-TGA, due to the increased volume load of the RV in cc-TGA. The degree of TR may deteriorate during pregnancy [19]. Mutual effects of hemodynamic changes during TR may lead to right ven-

tricular dysfunction in women with cc-TGA.

In this group of women with cc-TGA, most patients achieved successful pregnancy. Term pregnancies was achieved by most women with cc-TGA except 3 patients. The iatrogenic preterm deliveries resulting from right ventricular dysfunction were performed in those patients. These observations are in agreement with other studies [13, 14], which show that most women with cc-TGA can achieve a term pregnancy. The rate of cesarean section (81.8%) in the study group was higher than the 26% and 12% described by Kowalik et al. [13] and Connolly et al. [14], respectively, which may be due to more cases with poor heart function in our data. The fetal outcome in this group of women with cc-TGA is in accordance with previous studies [7, 18]. There are increased risks in comparison with the general population, with higher preterm delivery and low birth weight rates.

There were several limitations to our study. The retrospective design of the study should involve collection of all medical data including those not included in the electronic archives; however, some data items could not be collected. The present study had a small sample size, which limited the statistical analyses performed. The study population was from an expert center for pregnancy and cardiac disease. Patients with more severe cardiac complications may choose not to proceed with pregnancy, and patients not progressing to 28 weeks of gestation were not included; thus, patient samples were also subject to selection bias. Therefore, our study population may represent a subset of women with cc-TGA with lower cardiac risk. We were unable to ascertain the risks of miscarriage before 28 weeks.

In summary, the analysis demonstrates that successful pregnancy can be achieved by women with cc-TGA. Reduced systemic right ventricular function is common among pregnant women with cc-TGA, and severe TR is a high risk factor resulting in the deterioration of right ventricular function. TR may be regarded as a factor to predict maternal cardiac risk. Pregnant women with cc-TGA should be monitored closely by a multidisciplinary team that includes, at minimum, obstetricians, cardiologists, and anesthetists.

Conflicts of interest

The authors declare no conflict of interest.

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