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Original article

Pregnancy outcomes and mid-term prognosis in women after arterial switch operation for dextro-transposition of the great arteries – Tertiary hospital experiences and review of literature

Chinami Horiuchi (MD)[a,b,*], Chizuko A. Kamiya (MD, PhD, FJCC)[a], Hideo Ohuchi (MD, PhD, FJCC)[c], Takekazu Miyoshi (MD, PhD)[b], Mitsuhiro Tsuritani (MD, PhD)[a], Naoko Iwanaga (MD, PhD)[a], Reiko Neki (MD, PhD)[a], Koichiro Niwa (MD, PhD, FJCC)[d], Kenichi Kurosaki (MD)[c], Hajime Ichikawa (MD, PhD)[e], Tomoaki Ikeda (MD, PhD)[b], Jun Yoshimatsu (MD, PhD)[a]

[a] Departments of Perinatology and Gynecology, National Cerebral and Cardiovascular Center, Suita, Osaka, Japan
[b] Departments of Obstetrics and Gynecology, Mie University School of Medicine, Mie, Japan
[c] Departments of Pediatric Cardiology, National Cerebral and Cardiovascular Center, Suita, Osaka, Japan
[d] Cardiovascular Center, St. Luke's International Hospital, Tokyo, Japan
[e] Departments of Pediatric Cardiovascular Surgery, National Cerebral and Cardiovascular Center, Suita, Osaka, Japan

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ABSTRACT

Objective: Arterial switch operation (ASO) for dextro-transposition of the great arteries (d-TGA) has gradually replaced the atrial switch operation and has become the standard operation. To date, the outcomes of pregnant women with d-TGA after this new operation have not been investigated. In this study, we investigated the impact of ASO on pregnant outcomes and mid-term prognosis in women with d-TGA and compared with the atrial switch operation through the literature review.

Methods and results: There were 20 pregnancies in 10 women with d-TGA after ASO and 6 resulted in abortion. Among 14 successful pregnancies in 10 women, 11 pregnancies achieved the term delivery and 3 pregnancies, including 1 twin pregnancy, resulted in preterm labor. Maternal cardiovascular events occurred in 4 (heart failure and arrhythmias in 3 and arrhythmia in 1), and all were controllable with medications. Risk factors for the peripartum cardiac events were older age at ASO and delivery, and higher concentration of brain natriuretic peptide (BNP) at first trimester ($p < 0.05$). In 7–60 month-follow-up after delivery, no case showed deterioration of functional class and systemic ventricular function. According to the literature review, women after ASO demonstrated a better prognosis than those after the atrial switch operation.

Conclusions: The majority of women with d-TGA after ASO tolerated pregnancy and delivery well. The older age at ASO, an elderly pregnancy, and higher BNP levels at the first trimester were possibly risk factors of peripartum cardiovascular events among the group. The literature reviews and this study may indicate the advantage of systemic left ventricle compared with systemic right ventricle in long-term outcomes after delivery.

Introduction

Dextro-transposition of the great arteries (d-TGA) is a congenital heart disease characterized by a combination of concordant atrioventricular and discordant ventricular arterial connections. This condition leads to severe hypoxia in the early neonatal period. From the late 1950s to early 1960s, atrial switch operation (Mustard and Senning procedures) was the operation of choice in d-TGA without severe pulmonary stenosis. At that time, most women with d-TGA had undergone atrial switch operation. However, the past studies have described that these patients were at high risk of systemic right ventricular dysfunction, atrial arrhythmias, and cardiac death at long-term follow-up [1]. Pregnancy with

* Corresponding author at: Department of Perinatology and Gynecology, National Cerebral and Cardiovascular Center, 5-7-1 Fujishiro-dai, Suita, Osaka 565-8565, Japan.
E-mail address: chinami@ncvc.go.jp (C. Horiuchi).

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d-TGA after atrial switch operation resulted in severe cardiac complications such as maternal death or cardiopulmonary arrest (CPA) during pregnancy and by mid-term follow-up after delivery [2–4].

In 1975, Jatene et al. reported the first arterial switch operation (ASO) for d-TGA [5]. Since its introduction, a two-stage repair was introduced comprising first stage of pulmonary artery banding supplemented by a systemic-pulmonary shunt subsequent to the second-stage of ASO. In the late 1980s, the primary ASO in neonates and early infants had become the standard operation for d-TGA because this procedure was a complete anatomical repair [6]. Advances in neonatal management and pediatric surgery made it possible for women with d-TGA to reach childbearing age.

The progression to ASO had positive impact on systemic ventricular function, morbidity, and exercise capacity long-term follow-up [7,8]. The systemic left ventricle could be treated with better mid- and long-term outcomes, compared to the systemic right ventricle. However, there have been no reports comparing pregnancy outcomes and mid-term prognosis after delivery between systemic left and right ventricles. To date, there has been little study to investigate the outcomes of pregnant women with d-TGA after this operation. The number of pregnant women with cardiovascular disease has increased in recent decades. Cardiovascular diseases have been one of the leading causes of maternal mortality, although its prevalence rate is relatively low [9,10]. The purpose of this study was to investigate the pregnancy outcomes and mid-term prognosis in women with d-TGA after ASO and to compare them with those after the atrial switch operation through the literature review.

Methods

Subjects

Pregnancies in women after ASO for d-TGA between 2006 and 2017 at the National Cerebral and Cardiovascular Center in Osaka, Japan were reviewed and labor cases were included in the analysis. All data were collected retrospectively using medical records. Baseline data were obtained for age, basic cardiac anatomy, history of prior surgery, age at ASO, re-intervention after ASO, cardiac and vascular residua before pregnancy, cardiac events, medications, and smoking habit. At our center, the first ASO was performed in 1977 and since the late 1980s, the primary ASO was performed. New York Heart Association (NYHA) functional class, chest radiography, and transthoracic echocardiography were reviewed from 1 year before pregnancy to last follow-up after delivery. Plasma concentrations of brain natriuretic peptide (BNP) were reviewed from the 1st trimester to 1 year after delivery. All study protocols were conducted with the approval of the Ethics Committee of the National Cerebral and Cardiovascular Center.

Echocardiography

Echocardiographic data from the last available report before pregnancy until the last follow-up after delivery were reviewed. Ventricular dimensions such as left ventricular end-diastolic diameter (LVDd) and left ventricular end-systolic diameter (LVDs) were measured from M-mode echocardiography in parasternal long- or short-axis views. Percent fractional shortening (%FS) was calculated from LVDd and LVDs. The presence and severity of valvular regurgitation were categorized as mild, moderate, or severe based on the appearance of the regurgitation jet on color-flow Doppler imaging. Hemodynamic assessment of the right ventricle and pulmonary circulation were performed within the guidelines [11]. The degree of pulmonary stenosis was defined as above, with moderate defined based on the Doppler-derived systolic pressure gradient across the pulmonary valve $\geq$36 mmHg and/or estimated right ventricular systolic pressure $\geq$50 mmHg [12].

Definitions of events

Adverse cardiovascular events included cardiac death, new onset of arrhythmia, heart failure, coronary events, and thromboembolic events. Arrhythmia was defined as a significant tachy- or bradyarrhythmia that occurred during pregnancy for the first time. Heart failure was defined as deterioration of NYHA function class and/or pulmonary edema diagnosed by chest X-ray and treated with pharmacotherapy.

Obstetric complications included threatened premature delivery, fetal growth restriction (FGR) (estimated fetal weight $<$10th percentile), hypertensive disorders of pregnancy, premature labor (spontaneous onset of labor $<$37 weeks of gestation), very premature labor (spontaneous onset of labor $<$34 weeks of gestation), and postpartum hemorrhage [$>$500 ml with vaginal delivery or $>$1000 ml with Cesarean section (CS)].

Neonatal complications included premature birth ($<$37 weeks of gestation), small-for-gestational-age birth weight (SGA) ($<$10th percentile), heavy-for-gestational-age birth weight (HGA) ($>$90th percentile), transient tachypnea of newborn (TTN), respiratory distress syndrome (RDS), and congenital heart disease [13].

Statistical analyses

Descriptive data are expressed as mean $\pm$ standard deviation (SD) and as percentages. Differences in potential risk factors between two groups with or without cardiac events during pregnancy and the postpartum period were evaluated. Continuous variables were compared using Student's *t*-test if data were normally distributed and with the Mann–Whitney *U*-test if they were not. The chi-square test or Fisher's exact test with the cell number including zero were used to test for differences between frequencies of occurrence. Two-tailed probability values $<$0.05 were considered statistically significant.

Literature reviews

We conducted a search using PubMed database on November 22, 2016. We used the following search strategy to PubMed database: “pregnancy outcomes” and “transposition of the great arteries” or “arterial switch operation” or “atrial switch operation” or “Mustard operation” or “Mustard procedure” or “Mustard repair” or “Senning operation” or “Senning procedure” or “Senning repair” [14]. The analysis was restricted to articles in English and the publication data were restricted to reports from January 1, 2000.

The screening of articles and abstracts was performed by 1 author by the following criteria: (1) case report and review article were excluded; (2) the publication reported the cardiovascular events developed during peripartum periods and $\geq$3 months after delivery. For the purpose of the review, ASO group make comparison of maternal cardiac events during pregnancy and in the postpartum period and neonatal outcome, as well as mid-term cardiac complications subsequent to delivery with atrial switch group.

Results

Baseline characteristics

Twenty pregnancies occurred in 10 women after ASO. Five pregnancies in 2 women were electively aborted due to social

Table 1
Baseline clinical characteristics before pregnancy ($n = 10$).

Case	Associated malformations	Prior palliation		Year of ASO	Age at ASO (days)	Shaher classification	Re-intervention		Cardiovascular lesions	Medication
		Age (days)	Details				Age (years)	Details		
1	VSD			1981	351	2A	22	RVOT patchplasty, Infundibulectomy	PR mod	
2		3	BAS	1982	90	1			PS mod	
3		21 90	BAS, PAB, lt. BTS	1985	196				AR mild PS mild	
4		6 210	BAS PAB, lt. BTS	1985	334	1			Aortic root dilation AR mod PR mod	β-Blocker
5	VSD	60	BAS	1986	576	1	11	Mitral valvuloplasty Aortic valvuloplasty	MR mod AR mod Residual VSD	Diuretics
6	VSD, RAA	17	BAS	1987	169	1	12 12	PTPA Patch angioplasty of main lt. PA, RVOT reconstruction	lt. PS mild	
7		1	BAS	1988	6	1	1.5 1.8	PTPA Patch plasty of PA	AR mild PS mild	
8		9	BAS	1989	15	1	6	PA plasty, Infundibular myotomy, Pulmonary valvar commissurotomy	PS mild	
9				1990	20	1			AR mod	
10		45 90	BAS PAB, lt. BTS	1995	92	2A			lt. PS mod	

AR, aortic regurgitation; BAS, balloon atrial septostomy; BTS, Blalock-Taussig shunt; MR, mitral regurgitation; PA, pulmonary artery; PAB, pulmonary artery banding; PR, pulmonic regurgitation; PS, pulmonic stenosis; PTPA, percutaneous transluminal pulmonary angioplasty; RAA, right aortic arch; RVOT, right ventricular outflow tract; VSD, ventricular septal defect.

reasons and there was 1 spontaneous abortion. Overall, 14 successful pregnancies in 10 women were seen between 2006 and 2017. Baseline characteristics of the enrolled 10 women are summarized in Table 1. The early era of ASO was performed at older age compared with the more recent era. Lecompte's maneuver in the ASO was applied in 80% of cases. Eight had undergone cardiopulmonary exercise testing and/or the coronary angiogram using the computed tomography or cardiac catheterization before their first pregnancy. None of them had ischemic changes at the examinations. Two of the ten women received cardiac medications before pregnancy: one case of β-blocker for aortic root dilatation (54 mm); and another case of diuretics for moderate mitral regurgitation. All women were NYHA function class I before pregnancy.

Obstetric and neonatal outcomes

Table 2 shows obstetric and neonatal outcomes and complications for the successful pregnancies. Mean gestational age at delivery was 37.3 ± 3.2 weeks. Eleven (79%) of 14 pregnancies reached full term, while 3 pregnancies (21%) resulted in preterm labor: due to fetal growth arrest ($n = 1$) and spontaneous labor

Table 2
Obstetric and neonatal outcomes for 14 pregnancies.

Case	Number of pregnancies	Obstetric complications	Delivery				Neonatal complications
			Gestational weeks	Birth weight (g)	Mode	Indication for CS	
1	1		37.6	2290	CS	Labor arrest	SGA
2	1		39.7	3056	Vaginal, F		
	2		38.3	2790	Vaginal, V, E		
3	1		41.0	4062	CS	Labor arrest	HGA
	2		38.1	2646	CS		
4	1		37.7	2832	CS	Dilated aortic root	
5	1	Twin pregnancy Fetal growth restriction	34.7	1720 1781	CS	Fetal growth arrest	SGA, TTN SGA, TTN
6	1		37.0	2518	CS	Breech presentation	
7	1	Hypertensive disorders of pregnancy, Postpartum hemorrhage	38.4	2830	Vaginal		
8	1		39.4	2610	Vaginal		
	2		39.3	2340	Vaginal, E		SGA
	3		36.8	2342	Vaginal, V, E	Labor onset	
9	1		27.1	1189	Vaginal	Labor onset	RDS
10	1		37.7	2804	Vaginal, E		

CS, Cesarean section; E, vaginal delivery with epidural spinal anesthesia; F, forceps-assisted delivery; HGA, heavy-for-gestational age birth weight; RDS, respiratory distress syndrome; SGA, small-for-gestational age birth weight; TTN, transient tachypnea of the newborn; V, vacuum-assisted delivery.

Table 3
Cardiovascular complications during pregnancy and postpartum period.

Case	Number of pregnancies	During pregnancy			Postpartum		
		Gestational weeks	Details	Treatments	Days	Details	Treatment
1	1	24	NSVT (150 bpm, 5 beats)	β-blocker	3	Heart failure	Diuretics
2	2	37	New onset AT (123 bpm, 1 min)				
3	1	28			1	Heart failure	Diuretics
5	1	28	NSVT (180 bpm, 11 beats)	β-blocker	0	Heart failure	Diuretics
		29	New onset AT (123 bpm, 1.5 min)		7	NSVT (170 bpm, 17 beats)	ACE-I

ACE-I, angiotensin-converting enzyme inhibitor; AT, atrial tachycardia; NSVT, non-sustained ventricular tachycardia; bpm, beats per minute.

onset ($n = 2$). In the twin pregnancy, FGR was documented after 31 gestational weeks and CS was performed at 34 gestational weeks.

In 5 pregnancies (36%), delivery was performed by CS. In four of these five cases, CS was performed due to obstetric indications. In one remaining case, CS was performed because of aortic dilatation (54 mm). Postpartum hemorrhage due to a retained placental fragment in one woman was treated with blood transfusions and interventional radiology. Mean birth weight was 2521 ± 638 g. No neonatal deaths or congenital heart disease were encountered. Four neonates (27%) were SGA, including three neonates whose mothers took β-blockers (carvedilol).

Cardiovascular outcomes

Peripartum cardiovascular events are summarized in Table 3. Cardiovascular events occurred in 4 pregnancies (29%) in 4 women. No cardiac death or coronary and thromboembolic event was encountered. One (Case 5 in Table 3) of the three pregnancies who showed complications of both arrhythmia and heart failure showed moderate aortic and mitral regurgitation and dilated left ventricle before twin pregnancy. She displayed complications with atrial tachycardia (AT) with a palpitation and recurrent non-sustained ventricular tachycardia (NSVT) and was started on carvedilol to prevent recurrence of the arrhythmias. Moreover, serial echocardiography showed an increase in LVDd (58 mm before pregnancy, up to 65 mm at 33 gestational weeks) and a decrease in left ventricular contraction. The serial pressure gradient of tricuspid regurgitation (TRPG) gradually elevated (23 mmHg before pregnancy, 29 mmHg at 29 gestational weeks, 32 mmHg at 32 gestational weeks). In addition, serial plasma BNP concentrations gradually increased (39.1 pg/ml before pregnancy, 79.7 pg/ml at 28 gestational weeks, 163.9 pg/ml at 32 gestational weeks). At 34 gestational weeks, CS was performed due to obstetric indications including arrest of fetal growth and fetal transverse presentation. Cardiac catheterization was subsequently performed, and neither changes in the severity of aortic regurgitation/tricuspid regurgitation nor coronary artery stenosis were seen.

Patient characteristics/history, echocardiographic parameters, and plasma concentrations of BNP levels were compared between pregnancies with and without cardiovascular events to analyze risk factors of maternal cardiac events (Table 4). Age at ASO and at pregnancy were significantly older and plasma BNP concentrations at the first trimester were significantly higher in pregnant women with cardiac events. In addition, plasma BNP concentrations just before cardiovascular events in women with the events tended to be higher compared to the peak plasma BNP concentrations in those without (106.2 ± 40.8 pg/ml vs. 44.9 ± 18.3 pg/ml, $p = 0.076$). Women with the cardiovascular events tended to have higher TRPG in the postpartum than that at the first trimester (47.3 ± 15.9 mmHg vs. 34.0 ± 9.9 mmHg, $p = 0.088$).

Mid-term follow-up after delivery

Recent clinical records including echocardiography were available for all women for 7–60 months after childbirth (Table 5).

Table 4
Comparison of patient characteristics and echocardiographic parameters between pregnancies with and without cardiovascular events.

	Event (+) $n = 4$	Event (−) $n = 10$	p-Value
Patient characteristics			
TGA with IVS	2 (50%)	9 (90%)	0.176
with VSD	2 (50%)	1 (10%)	
Median age at ASO (days)	273.5 (170–407)	55 (15–150)	0.031
Re-operation after ASO	2 (50%)	3 (30%)	0.580
Cardiac medications before pregnancy	1 (25%)	1 (10%)	0.506
Mean age at pregnancy (years)	29.8 ± 2.5	23.9 ± 4.5	0.019
Multipara	1 (25%)	3 (30%)	1.00
Mean BNP level at first trimester (pg/ml)	49.7 ± 13.4	23.4 ± 10.3	0.033
Smoking	1 (25%)	2 (20%)	1.00
Echocardiographic parameters before pregnancy or at first trimester			
Reduced LV function (%FS ≤30)	2 (50%)	2 (20%)	0.521
Mitral valve regurgitation (moderate or severe)	1 (25%)	0 (0%)	0.286
Aortic valve regurgitation (moderate or severe)	0 (0%)	2 (20%)	1.000
Neo-aortic root dilatation (>40 mm)	0 (0%)	2 (20%)	1.000
Pulmonary valve regurgitation (moderate or severe)	1 (25%)	2 (20%)	1.000
Pulmonary artery or lateral pulmonary artery stenosis (PG ≥50 mmHg)	1 (25%)	2 (20%)	1.000
Left ventricular end-diastolic diameter (≥50 mm)	3 (75%)	3 (30%)	0.245
Tricuspid valve regurgitation PG ≥30 mmHg	2 (50%)	3 (30%)	0.580

Data given as n (%), median (interquartile range) or mean ± SD. ASO, arterial switch operation; BNP, brain natriuretic peptide; FS, fractional shortening; IVS, intact ventricular septum; LV, left ventricle; PG, pressure gradient; TGA, transposition of the great arteries; VSD, ventricular septal defect.

Table 5
Clinical and echocardiographic data before pregnancy and mid-term after delivery.

Case	Duration from last delivery (months)	NYHA functional class		Coronary artery events	Ventricle function	Progression of valve lesions[a]		Aortic root dilatation	
		Before pregnancy	Last follow-up		Last follow-up	Before pregnancy	Last follow-up	Before pregnancy	Last follow-up
1	27	I	I	None	Preserve	Mod.	Severe		
2	7	I	I	None	Preserve	–	–		
3	27	I	I	None	Preserve	–	–	38 mm	39 mm
4	30	I	I	None	Preserve	–	–	54 mm	54 mm
5	60	I	I	None	Preserve	–	–		
6	13	I	I	None	Preserve	–	–		
7	46	I	I	None	Preserve	Mild	Mod.		
8	18	I	I	None	Preserve	–	–		
9	8	I	I	None	Preserve	–	–		
10	10	I	I	None	Preserve	–	–		

–, less than mild; Mod., moderate; NYHA, New York Heart Association.
[a] Progression of valve lesion led to regurgitation by the aortic valve and stenosis or regurgitation by the pulmonary artery.

Echocardiography showed progression of pulmonary regurgitation at 27 months in Case 1 and progression of aortic regurgitation at 46 months in Case 7 after delivery. No women showed progression of systemic ventricular dysfunction, pulmonary stenosis, or aortic dilation after delivery. In addition, no women showed any deterioration in NYHA functional class or experienced ischemic events after delivery.

Literature reviews for pregnancy and mid-term outcomes in women with d-TGA

The eight articles were classified as describing pregnancy outcomes after atrial switch operation (seven reports) and outcomes after ASO (one report) (Fig. 1) [2–4,13,15–18]. A total of 8 articles and this study were reviewed. Table 6 shows a comparison of cardiac event rates during the peripartum period and at mid-term follow-up after delivery and neonatal events between women after ASO and women after atrial switch operation. No differences were identified between the groups in terms of cardiac complications during pregnancy, such as arrhythmia with medications and heart failure.

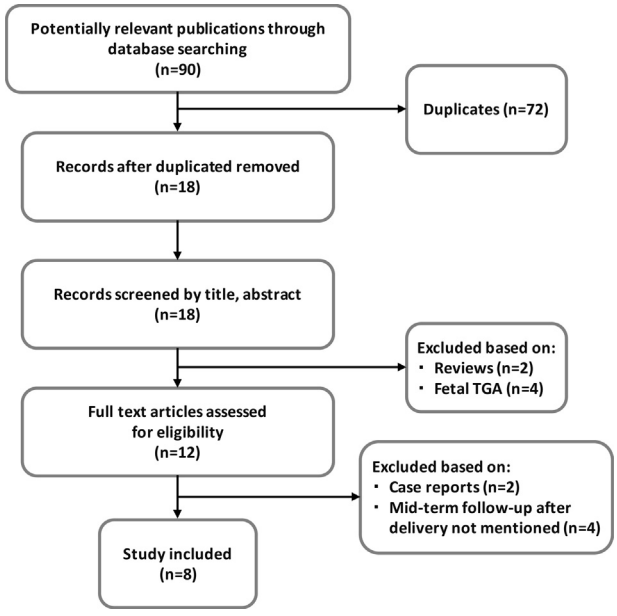

Fig. 1. Process of study selection. Studies' flow chart for study inclusion and exclusion. Eight reports were included for the literature review. TGA, transposition of the great arteries

However, women in the atrial switch group showed a higher risk of deterioration in NYHA functional class and progression of systemic ventricular dysfunction ≥moderate during pregnancy relative to those in the ASO group. In addition, progression of valve lesion of ≥moderate severity during pregnancy occurred more frequently for tricuspid lesions in the atrial switch group. Cardiac complications at the mid-term follow-up after delivery tended to be present much more frequently in the atrial switch group compared with the ASO group. Some cases of the atrial switch group had not recovered from systemic ventricular dysfunction at the mid-term follow-up after delivery. Moreover, six women in seven reports of the atrial switch group showed more severe cardiac complications, such as maternal death or CPA during pregnancy and at the mid-term follow-up after delivery, while no maternal death has been reported among arterial case [2–4,13].

The incidences of preterm birth and SGA were similar in the ASO group in the two groups. No intrauterine fetal demise or neonatal death were encountered in the ASO group.

Discussion

The present study has suggested the risk factors for maternal cardiac events such as cardiac failure and tachyarrhythmias in women with d-TGA after ASO. The risk factors were older age at ASO, elderly pregnancy, and high BNP concentrations at first trimester. To our knowledge, there is only one report that has demonstrated pregnancy outcomes in these women [13]. We have demonstrated the risk factors for maternal cardiovascular events and mid-term impact of delivery for the first time. Although women with d-TGA after ASO had higher risk for cardiovascular and obstetric events than the healthy pregnant women, the cardiovascular events were well-treatable and mid-term prognosis after delivery is good [19].

Pregnancy outcomes

The present study showed that most pregnancies in women after ASO were well tolerated: Most pregnancies resulted in appropriate term delivery such as delivery at over 36 gestational weeks. Four of fourteen pregnancies (29%) were complicated with tachyarrhythmias and/or heart failure during pregnancy and in the postpartum period. Only one previous study reported pregnancy outcomes in women after ASO [13]. In that report, two pregnancies (15%) developed cardiac complications during pregnancy (NSVT in 1 patient, mechanical valve thrombosis in 1 patient). No maternal or fetal/neonatal deaths were seen in our study or in the previous

Table 6
Comparison of cardiac events during pregnancy and mid-term events after delivery between ASO versus atrial switch operation; literature review and this study.

	ASO 19 women/27 pregnancies [13,this study]	Atrial switch operation 143 women/234 pregnancies [2–4,15–18]
Cardiac events during pregnancy		
Deteriorated NYHA	0	31/143 (21.7%)
Arrhythmia with medication	3/27 (11.1%)	22/234 (9.4%)
Heart failure	2/27 (7.4%)	12/234 (5.1%)
Death/CPA	0	3/234 (1.3%)
Progression of valve lesions (≥moderate)	0[a]	28/102 (27.5%)[b]
Progression of systemic ventricular dysfunction (≥moderate)	1/27 (3.7%)[c]	37/147 (25.2%)[d]
Neonatal events		
Preterm birth (<37 weeks of gestation)	4/15 (26.7%)	44/158 (27.8%)
Small for gestational age	4/15 (26.7%)	21/109 (19.3%)
Intrauterine fetal demise	0	6/158 (3.8%)
Neonatal death	0	3/158 (1.9%)
Mid-term events after delivery		
Deteriorated NYHA	0	17/114 (14.9%)
Death/CPA	0	3/140 (2.1%)
Progression of valve lesions (≥moderate)	2/19 (10.5%)[a]	12/96 (12.5%)[b]
Progression of systemic ventricular dysfunction (≥moderate)	1/19 (5.3%)[c]	10/96 (10.4%)[d]

Data are given as *n* (%). ASO, arterial switch operation; NYHA, New York Heart Association; CPA, cardiopulmonary arrest.
[a] Mitral and aortic regurgitation and pulmonary stenosis or regurgitation were included.
[b] Tricuspid valve regurgitation was included.
[c] Systemic ventricular dysfunction ≥moderate was considered as left ventricular ejection fraction ≤40%.
[d] Systemic ventricular dysfunction ≥moderate was assessed qualitatively or as ventricular pressure over time (dP/dt) <1000 mmHg/s.

report. The rate of peripartum cardiac complications was higher than in the previous study, presumably because this study included new-onset arrhythmia with and without medication, whereas the previous study included only arrhythmia with medication.

Older age at pregnancy, older age at ASO, and higher BNP concentration in the first trimester were the risk factors for maternal cardiac events. In this study, older age at ASO and older maternal age related to the earlier surgical era.

The risk factors, such as older age at ASO and elderly pregnancy might be associated with degree of exercise performance in the patients. Previous studies demonstrated a significant relationship between pre-pregnancy exercise capacity and pregnancy outcome [20,21]. A previous study also showed that exercise capacity in patients with ASO varied according to the surgical era. The exercise capacity of patients on whom ASO was performed in the earlier surgical era was reduced, compared to those on whom the primary ASO was performed in neonates or early infants [22].

The previous studies reported that plasma BNP concentrations were negatively correlated with exercise capacity [23]. Our findings are consistent with the previous studies. Increasing BNP concentrations could be a reflection of current cardiac condition and useful for prediction of pregnancy outcomes. Increased BNP concentrations might reflect subclinical heart failure that might manifest clinically due to the hemodynamic stress [24]. The previous study found that BNP concentrations ≤100 pg/ml during pregnancy had a high negative predictive value for adverse maternal cardiac events [23]. Our study also supported that plasma BNP concentrations may be useful when managing pregnancy cases with cardiac disease.

In addition, women with cardiac events tended to show higher TRPG throughout the pregnancy. High TRPG indirectly indicates high pressure in the right ventricle, which may correspond to left atrial pressure elevation or the relative pulmonary stenosis with the volume load during pregnancy, and the cause may be different with each person. Case 5 was complicated with moderate mitral regurgitation with higher left atrial pressure and no progressive pulmonary stenosis during pregnancy, therefore TRPG elevation in this case is mainly due to high LA pressure elevation. The others showed the pulmonary stenosis with volume overload during pregnancy, therefore, TRPG elevation should be due to relative pulmonary stenosis. Echocardiography is useful for assessing cardiac function before and during pregnancy. Generally, the dynamic cardiovascular adaptation and neurohormonal changes seen during pregnancy and postpartum lead to significant stress on the cardiovascular system. In women with moderate to severe congenital heart disease, hemodynamic changes could exceed compensatory capacity, resulting in cardiac complications. Elevated right ventricular pressure and right ventricular blood volume load are likely to induce arrhythmia during pregnancy [25,26]. A previous study showed that pregnancy itself increased right ventricular dilatation. The rate of increase in right ventricular volume during pregnancy was about 20%, compared with about 6% in the left ventricle in healthy women [27]. In this study, women with cardiovascular events showed higher right ventricular pressure during pregnancy, although no significant pulmonary valve lesions or pulmonary hypertension had been seen before pregnancy. Pregnancy-related volume overload might therefore cause high right ventricular pressure subsequent to relative pulmonary stenosis and/or right remodeling in those women.

Prognosis after delivery

During follow-up after delivery, no woman showed deterioration of NYHA functional class or systemic ventricular dysfunction, with the exception of increased pulmonary or aortic regurgitation in 2 cases. Several authors reported that ASO survivors show better cardiac function, exercise performance, self-reported quality of life, and fewer somatic complaints compared to Mustard patients [8,21,7]. Because the systemic ventricle was corrected to the left ventricle, physiological loads such as pregnancy may have a reduced adverse impact on cardiac function in women after ASO, compared to a systemic right ventricle such as in the atrial switch group.

Comparisons of outcomes between women after ASO and atrial switch operation

After the atrial switch operation, the systemic circulation is supported by the right ventricle, which can lead to cardiac

complications such as right ventricular dysfunction increasing the risk of tricuspid regurgitation, heart failure, arrhythmia, and sudden death. Women with systemic right ventricle are in the high-risk category for pregnancy, showing increased risks of preeclampsia and fetal complications compared with normal pregnancy [28]. Cardiac function in atrial switch cases continued to be affected after delivery, and sometimes the effects were irreversible. Pregnancy reportedly has negative effect on the right ventricle more than the left ventricle [27–30]. The review of the literature therefore showed that women who have undergone ASO achieve better mid-term outcomes after delivery compared to women who have undergone the atrial switch operation. Pregnancy surely affects the systemic right ventricle more than the left ventricle.

Study limitations

Several limitations of this study should be acknowledged. First, the present study had a small sample size, was retrospective, and was a single-center study. Selection bias could not be excluded because of including repeated pregnancies in the same woman. The retrospective design of this study did not allow for a standard analysis of plasma BNP levels before pregnancy because the patients were referred to our hospital in the early weeks of pregnancy. The insufficient statistical power due to the small sample size did not allow, as previously, determination of the impact of the maternal cardiovascular events during pregnancy. The multivariate analysis of the risk factors to identify reliable independent predictors for safer pregnant outcome were not possible. The retrospective design of this study, however, has clear definition of medical treatment and obstetric management.

Second, there were no women with coronary artery lesions in this study, although the literature reported the incidence of late coronary artery stenosis after ASO to be 7% [31]. Therefore, we were not able to demonstrate the peripartum cardiovascular and obstetric events in women with coronary artery lesions after ASO.

Third, without a control group, whether the cardiovascular events and changes shown on echocardiography are due to pregnancy or represent the natural course remains unclear. Further long-term follow-up after pregnancy is warranted. Adding to the literature reports concerning ASO and the atrial switch operation, in this study the ASO group had less mortality during and after pregnancy rather than the atrial switch group. However, a variety of definitions of cardiovascular events were used in the literature, and statistical analysis was not performed.

Further investigation in multiple centers using standardized definitions is thus needed.

Conclusion

In summary, some pregnancies in women with d-TGA after ASO had peripartum cardiovascular and obstetric complications. However, all of the cardiovascular events were well-treatable. Women with older age at ASO, elder pregnancy, and higher BNP at the first trimester warrant careful management during the peripartum period. The literature reviews and the study may indicate the clinical importance of the systemic left ventricle in long-term outcomes after delivery.

Authors' contributions

Data collection, PubMed database searching, literature review: C.H.

Data analysis/interpretation: C.H., C.K., H.O., K.N., J.Y.

Article drafting: T.M., M.T., N.I., R.N., H.O., K.N., T.I., K.K, H.I, T.I.

Statistical analysis: C.H.

Concept/design: C.H., C.K.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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