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SYSTEMATIC REVIEW AND META-ANALYSIS

Outcome of Pregnancy in Women With D-Transposition of the Great Arteries: A Systematic Review

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BACKGROUND: Information on maternal and fetal outcomes of pregnancy in women with D-transposition of the great arteries is limited. We conducted a systematic literature review on pregnancies in women with transposition of the great arteries after atrial and arterial switch operations to better define maternal and fetal risk.

METHODS AND RESULTS: A systematic review was performed on studies between 2000 and 2021 that identified 676 pregnancies in 444 women with transposition of the great arteries. A total of 556 pregnancies in women with atrial switch operation were tolerated by most cases with low mortality (0.6%). Most common maternal complications, however, were arrhythmias (9%) and heart failure (8%) associated with serious morbidity in some patients. Worsening functional capacity, right ventricular function, and tricuspid regurgitation occurred in ≈20% of the cases. Rate of fetal and neonatal mortality was 1.4% and 0.8%, respectively, and rate of prematurity was 32%. A total of 120 pregnancies in women with arterial switch operation were associated with no maternal mortality, numerically lower rates of arrhythmias and heart failure (6% and 5%, respectively), significantly lower rate of prematurity (11%; $P<0.001$), and only 1 fetal loss.

CONCLUSIONS: Pregnancy is tolerated by most women with transposition of the great arteries and atrial switch operation with low mortality but important morbidity. Most common maternal complications were arrhythmias, heart failure, worsening of right ventricular function, and tricuspid regurgitation. There was also a high incidence of prematurity and increased rate of fetal loss and neonatal mortality. Outcome of pregnancy in women after arterial switch operations is more favorable, with reduced incidence of maternal complications and fetal outcomes similar to women without underlying cardiac disease.

Key Words: atrial switch operation ■ arterial switch operation ■ congenital heart disease ■ D-transposition of the great arteries ■ pregnancy

Many women with surgically corrected D-transposition of the great arteries (D-TGA) survive to adulthood and strive to have children.[1] A significant proportion of these patients have residua and/or sequelae associated with important long-term complications.[2–4] Women who had the atrial switch operation (ATSO) reaching childbearing age can have complications, including moderate to severe degrees of systemic/right ventricular (RV) systolic dysfunction, tricuspid valve regurgitation (TR), atrial arrythmias, and baffle leak/obstruction.[1,5,6] Because of the substantial increase in hemodynamic burden as well as an elevated thrombogenic and arrhythmogenic risk, pregnancy presents a challenge to patients with this condition and to their clinicians. The arterial switch operation (ASO) that restores the normal anatomic arrangement of the circulation for transposition of the great arteries (TGA) has become the preferred surgical correction for patients with D-TGA. There is significant long-term survival with this procedure; however, it is not without complications, such as valvular dysfunction, neoaortic dilatation, and coronary artery stenosis.[1,7]

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CLINICAL PERSPECTIVE

What Is New?

- The modified World Health Organization classification of maternal cardiovascular risk predicts significant increased risk of maternal mortality in women with complex congenital heart disease.
- This study, however, shows that most women with D transposition of the great arteries with atrial switch tolerate pregnancy, and mortality rate is low. Pregnancy, however, can be associated with worsening right ventricular function, tricuspid regurgitation, and decreased functional capacity; in some patients, it can be associated with heart failure and arrhythmias, which can be associated with serious morbidity; main fetal complications are increased rate of prematurity, fetal loss, and neonatal mortality.
- Outcomes of pregnancy in women with D transposition after arterial switch is more favorable, with lower reported incidence of maternal complications, no mortality, and normal fetal outcome.

What Are the Clinical Implications?

- Multidisciplinary evaluation is recommended preconception in women with D-transposition of the great arteries to identify and treat patients at high risk for complications during pregnancy.
- A close follow-up is required during pregnancy and early postpartum for early diagnosis and management of hemodynamic deterioration.
- Women with atrial switch need to be aware of the potential effect of their condition on fetal outcome, and premature delivery should be anticipated.

Nonstandard Abbreviations and Acronyms

ASO	arterial switch operation
ATSO	atrial switch operation
CS	cesarean section
D-TGA	D-transposition of the great arteries
NYHA	New York Heart Association
TGA	transposition of the great arteries
TR	tricuspid valve regurgitation

The modified World Health Organization classification commonly used for assessment of pregnancy risks categorizes D-TGA in class III as part of complex heart disease with a significantly increased risk of maternal mortality or severe morbidity.[8] The value of this classification as well as other available risk predictors, such as the Zahara[9] and Cardiac Disease in Pregnancy (CARPREG) Risk Score[10] for prediction of risk of pregnancy in women with TGA, is limited because of underrepresentation and the heterogeneous nature of these conditions. Individual risk stratification and counseling of women with D-TGA require a more lesion-specific understanding of the anticipated effects of pregnancy. The aim of this study was to review and analyze recent data from a large number of pregnancies in patients with D-TGA and to define maternal and fetal risks associated with pregnancy after both ATSO and ASO and provide management recommendations.

METHODS

The systematic review protocol was created with the International Prospective Register of Systematic Reviews (PROSPERO) formatting, and in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. A librarian designed searches on PubMed and Embase using keywords and subject headings relating to D-TGA and pregnancy (see Data S1 for full list of search terms). Studies met inclusion criteria if they were written in English, published between 2000 and 2021, reported maternal and fetal outcomes in women with D-TGA who underwent pregnancy, and were original research studies. Studies were excluded if they had <5 women with D-TGA, did not report maternal and fetal outcomes, or data from women with D-TGA could not be reliably extracted when multiple congenital conditions were included. Our criteria were aimed at identifying a wide range of studies reporting current and relevant pregnancy outcomes, within a historical time frame to include women with both ATSO and ASO given the temporal changes in surgical corrective approach.

Articles were reviewed by 2 independent reviewers (J.P., J.D.) on Covidence, and discrepancies were resolved by a third reviewer (U.E.). Data were hand extracted by 3 physician reviewers (J.P, J.D., U.E.). All data and supporting materials have been provided with the published article. Variables analyzed included the following: standard demographic metrics (number of patients/pregnancies, age, and location), type of repair, additional congenital defects, prior cardiac surgeries or arrhythmias, systemic ventricular dysfunction, New York Heart Association (NYHA) functional class, and presence of valvular or baffle complications. Maternal outcomes analyzed included the following: maternal mortality, arrhythmias, heart failure (HF), worsening functional class, worsening systemic ventricular function, and worsening valvular regurgitation. Fetal outcomes included the following: live births, spontaneous abortions, elective abortions, cesarian section rate, duration of pregnancy, birth weight, small for gestational age, preeclampsia, preterm labor or delivery,

fetal mortality (mortality occurring after 20 weeks' gestation), neonatal mortality (mortality occurring after complete delivery up to 28 days), and neonatal congenital heart disease.

Statistical Analysis

Extracted data and descriptive statistics were compiled into Tables 1 through 7, with missing data denoted with NR (Not Reported). Comparison of maternal and fetal outcomes between ATSO and ASO cohorts were analyzed by χ^2 test or stratified Fisher exact test (expected value in any of the cells was <5). Significance was set at $P<0.05$.

RESULTS

In total, 1028 studies were screened, and 17 were selected for inclusion (see Preferred Reporting Items for Systematic Reviews and Meta-Analysis diagram; Figure 1 and Tables 1 and 5). In total, 676 pregnancies in 444 women with TGA were identified for analysis.

Total TGA With Atrial Switch (ATSO) Procedure

A total of 556 pregnancies resulting in 353 live births in 358 women have been reported in 12 retrospective studies, which included between 17 and 121 pregnancies in 10 to 121 patients each (Table 1).[11–22] Type of surgery was reported in 186 women, of whom it should be 146 (72%) had a Mustard procedure and 58 (28%) had a Senning operation. Additional congenital heart defects (CHDs), including ventricular septal defect, pulmonic stenosis, and coarctation of the aorta, were detailed in 35 (23%) of patients with these data available, and additional operations before pregnancy, including pulmonary artery (PA) banding, repair of venous obstruction, coarctation of the aorta, or baffle revision, occurred in close to a third of the women (Table 1). NYHA class before pregnancy was reported in 213 pregnancies; 181 (85%) were in class I, 21 (15%) were in class II, and 1 was in class III (0.5%). Medical history included arrhythmias in 102 patients (34%), pacemaker in 29 cases, and implantable cardioverter-defibrillator in 1 patient. Echocardiographic data on RV function were reported in 132 patients, with dysfunction reported in 109 (83%), which was severe in only 3 cases (3%). TR was reported in 168 (83%) of the 201 women with available data and was severe in only 2 (1%) cases. Baffle leak or obstruction was reported in 11 patients (<3%) at baseline.

Maternal Cardiovascular Complications

There were 45 women (9%) who developed arrhythmias during pregnancy (Table 2); most were supraventricular, including atrial fibrillation or flutter, atrial tachycardia, or supraventricular tachycardia, and occurred mostly in the third trimester. Medications used to treat these arrhythmias included β blockers, digoxin, and unspecified antiarrhythmic drugs. The development of arrhythmias led to hospital admission in 2 patients and to urgent early cesarean section (CS) delivery in another. One woman received a permanent pacemaker for junctional bradycardia. There were 3 resuscitated cardiac arrests: 2 during delivery and 1 at 48 hours postpartum. There were 3 instances of maternal mortality (see Table 3 for complete description): 1 at 27 weeks' gestation and 2 at 6 weeks and 6 months postpartum. HF developed in 8% of pregnancies (n=39), mostly during third trimester or early postpartum, and resulted in hospital admissions, emergency deliveries, and pregnancy termination in a few patients and cardiac arrest in 1 woman.

Information on functional class during pregnancy was available in 8 of the studies.[11,13,15–19,21] Deterioration was reported in 19% (n=47) of the patients. Bowater et al[15] reported significant deterioration of group mean NYHA class values, with only partial improvement at 4 years of follow-up. Deterioration of RV function during pregnancy was reported in about 19% (n=36) of the patients[16,17,19] and persisted postpartum in some of the patients. Metz et al[13] reported a significant decrease in mean RV dP/dt (a ratio of pressure change in the ventricle during the isovolumic contraction period) group value in 10 women during pregnancy, with only partial improvement postpartum. In contrast, Zentner et al[14] found no difference in RV function or exercise duration in postpregnancy women compared with nonpregnant control. Rate of worsening degree of TR varied between studies and ranged between 0%[19] and 52%.[17] Metz et al[13] reported a transient progression of TR, which was not severe in any of the patients and improved after the delivery, and Bowater et al[15] found no difference in degree of TR during pregnancy compared with nonpregnant control. Other inconsistently reported complications included: new baffle obstruction in 7 patients, and new baffle leak in 9 patients, with significant decrease in oxygen saturation in 1. Other severe complications included a stroke in 1 patient, thromboembolism in 5 patients, and hemoptysis in 2 patients.

Fetal Complications

Miscarriage was reported in 13% (n=46) of available pregnancies, and elective abortions were reported in 4%. Mean pregnancy duration was reported in 10 studies and was 37 weeks (range,24–42 weeks). Preeclampsia was reported in 5% of pregnancies. Prematurity (<37 weeks) was reported in 32% of reported cases. Mean birth weight (7 studies) was 2776

Table 1. Baseline Characteristics of Patients With D-TGA and ATSO

Author, year	Study design, country	No. of patients	No. of pregnancies	Age, mean±SD, y	Mustard repair	Senning repair	No. of patients with additional congenital defects	Additional cardiac surgeries before pregnancy	No. of patients with history of arrhythmia	RV dysfunction	NYHA functional class	Valvular dysfunction and baffle complications
Bowater, 2012[15†]	Retrospective cohort United States	18	31	25.5±5.2	5	9	NR	NR	NR	Mild-moderate: 19 Severe: 1	I: 18[††]	TR: none: 1; mild-moderate: 26; severe: 1
Canobbio, 2006[12]	Retrospective cohort United States	40	70	NR	36	4	VSD: 1; PS: 3; VSD and PS: 5	Reoperations for baffle leaks or pulmonary venous obstructions: 6	Atrial flutter: 5; SVT: 5; junctional: 3; AF: 1; VT: 1; ectopy: 1; PPM: 13	Mild-moderate: 18; severe: 1	I: 31; II: 8; III: 1	TR: none: 9; mild-moderate: 21; severe: 1
Cataldo, 2015[17]	Retrospective matched cohort United States, Italy	21	34	26±6	11	10	NR	Percutaneous intervention for venous pathway obstruction: 2 Baffle revision at age 2 y: 1	CHB: 2 (PPM: 1); junctional/atrial tachycardia: 4; SVT: 1	Mild: 6	I: 18; II: 3; III: 0	TR: moderate: 3 Baffle leak: 2 Baffle obstruction: 5
Drenthen, 2005[11]	Retrospective cohort The Netherlands	28	69	25.8±3.5	25	3	VSD: 4	NR	21	NR	I: 43; II: 6; III: 0	TR: none: 5; minor: 34; moderate: 10; severe: 0
Fabre-Gray, 2020[20]	Retrospective cohort United Kingdom	19	38	24.5 (16–36)	NR	NR	NR	NR	NR	NR	NR	NR
Guedes, 2004[21]	Retrospective cohort Canada	16	28	27±5	16	0	NR	NR	SVT: 5; PPM for SSS: 5	Mild-moderate: 4; severe: 1	I: 21; II: 7	Baffle occlusion: 1
Juan, 2016[18]	Retrospective cohort United States, Canada	17	17	31±6	17	0	VSD: 4; coarctation of aorta: 1	NR	NR	NR	I: 17; II: 0; III: 0	TR: none: 0; mild: 10; moderate: 5; severe: 0 Baffle leak: 1
Lipczyńska, 2016[19]	Retrospective cohort Poland	15	24	23.5	1	14	1	NR	7	Normal-mild:15 Moderate-severe: 0	I: 14; II: 1; III: 0	TR: none-mild: 15; moderate-severe: 0
Metz, 2011[13]	Retrospective cohort United States	10	21	23.4±3.6	NR	NR	NR	NR	NR	Mild: 3;	I: 9; II: 1; III: 0	TR: none: 5 mild: 5; moderate: 0

(*Continued*)

Table 1. Continued

Author, year	Study design, country	No. of patients	No. of pregnancies	Age, mean±SD, y	Mustard repair	Senning repair	No. of patients with additional congenital defects	Additional cardiac surgeries before pregnancy	No. of patients with history of arrhythmia	RV dysfunction	NYHA functional class	Valvular dysfunction and baffle complications
Trigas, 2014[16]	Retrospective cohort Germany	34	60	25	17	17	14	Reoperation attributable to pulmonary venous obstruction, baffle leak, coarctation of the aorta, or banding of the pulmonary artery: 4	SND: 14; Aflut: 2; VT: 1 PPM: 3 ICD: 1	Normal: 23; mild- moderate: 21; severe: 0	I: 28; II: 5; III: 0	TR: none: 4; mild: 36; moderate: 4; severe: 0 Baffle leak: 2
Tutarel, 2021[22]	Eu (ROPAC) Prospective review	121	121	29.1	NR	NR	NR	NR	Pacemaker rhythm: 7	35	NR	TR: none-mild: 33; moderate-severe: 14
Zentner, 2012[14]	Retrospective matched cohort Australia, New Zealand	19	43	37±4	18	1	VSD and/or PS: 2	NR	NR	NR	NR	NR
Total*		358	556	27.8	146 (72%)	58 (28%)	35 (23%)	13 (14%)	102 (34%)	Normal-moderate: 144/147 (97%) Severe: 3/147 (2%)	I: 181/213 (85%); II: 21/213 (15%); III: 1/213 (0.5%)	TR: none: 33/201 (16%); mild- severe: 168/201 (≈83%) Baffle leak/ obstruction: 11

AF indicates atrial fibrillation; Aflut, atrial flutter; ATSO, atrial switch operation; CHB, complete heart block; D-TGA, D-transposition of the great arteries; NR, not reported; NYHA, New York Heart Association; PPM, permanent pacemaker; PS, pulmonary stenosis; RV, right ventricular; SND, sinus node dysfunction; SSS, sick sinus syndrome; SVT, supraventricular tachycardia; TR, tricuspid valve regurgitation; VSD, ventricular septal defect; and VT, ventricular tachycardia.

*Percentages are calculated as that of total number of patients/pregnancies with available data on each respective outcome; incomplete data and discrepancies in reporting style limit the accuracy of synthesized information.

†Excluded from final calculation due to inability to synthesize into predefined categories.

††Based on average functional class.

Table 2. Maternal Outcomes of Women With D-TGA and ATSO

Primary author, year	Maternal mortality	Arrhythmia		Heart failure		Worsening of FC/persistent	Worsening RV function	Worsening of valvular regurgitation	Other complications
		No. of cases	Onset/management	No. of cases	Onset/management				
Bowater, 2012[15]	0	AF: 1	Admitted during pregnancy. Ablation before second pregnancy.	2	1 wk before delivery/ admitted for bedrest for shortness of breath: 2	9 /NR	18	NR	
Canobbio, 2006[12]	1	AF/flutter: 7	AF/flutter developed almost exclusively in the third trimester	11	30–33 wk/HF: 6. Four emergency deliveries for HF at <34 wk, unknown management in 1 woman	NR/NR	NR	NR	Hemoptysis: 2 Baffle leak: 1
		Cardiac arrest: 1	6 wk postpartum in setting of new HF, mortality		2 d-6 wk postpartum/HF postpartum: 5. One SCD at 6 wk postpartum, 1 patient admitted until cardiac transplantation				
Cataldo, 2015[17]	0	AT: 2	NR	0	NR/NR	3 /NR	6	11	Baffle leak: 4 Baffle obstruction: 1 Thromboembolism: unspecified: 1 TIA/stroke: 1
		AF: 1							
Drenthen, 2005[11]*	0	AF: 6	Verapamil, propranolol, nadroparin, acenocoumarol, sotalol, verapamil, digoxin, amiodarone	2	NR/Both successfully treated with diuretic therapy	17 /4	NR	NR	Thromboembolism: DVT: 1; PE: 1; CVA: 0
		Atrial flutter: 1	Quinapril						
		SVT: 1	NR						
		VT: 3	Propranolol						
Fabre-Gray, 2020[20]	0	NR	NR	NR	NR	NR/NR	NR	NR	Thromboembolism: PE: 1
Guedes, 2004[21]	0	Bradycardia: 1	PPM placement for junctional bradycardia	2	Over 3 pregnancies deterioration NYHA class II-III, severe RV dilation: 1 Cesarian section for HF, no further data: 1	6 /2	4	8	NR
		SVT: 1	No treatment						

(*Continued*)

Table 2. Continued

Primary author, year	Maternal mortality	Arrhythmia		Heart failure		Worsening of FC/persistent	Worsening RV function	Worsening of valvular regurgitation	Other complications
		No. of cases	Onset/management	No. of cases	Onset/management				
Juan, 2016[18]	0	AT: 2	Third trimester: both patients treated with unspecified medication	2	Third trimester /sustained atrial tachyarrhythmia, HF, treated with antiarrhythmic therapy: 1	0/NR	3	1	Thromboembolism: 0 DVT: 1 Stroke: 0
		Resuscitated cardiac arrest: 1	48 h postpartum; resuscitated successfully, in setting of HF		48 h postpartum, Postresuscitation, treated with diuretics and ACEI: 1				
		Mortality: 1	No further information						
Lipczyńska, 2016[19]	0	0	N/A	0	NR	3 /NR	1	1	Thromboembolism: 0
Metz, 2011[13]	0	SVT: 1	Required hospitalization for medication initiation at 22 wk	1	NR	2 /NR	NR	NR	Baffle obstruction: 5
Trigas, 2014[16]	0	SVT: 2	NR	5	NR/NR: 1	7 /5	4	3	Baffle leak: 4 Baffle obstruction: 1
		VT/VF: 1	ICD implantation: 1		8 wk postpartum/sudden HF, eventual VF/ICD: 1				
		Resuscitated cardiac arrest:1	During delivery, tachycardic rhythm, resuscitated successfully		Second trimester/HF, cesarean section 29 wk, arrest at delivery: 1				
		Resuscitated cardiac arrest:1	During delivery, resuscitated successfully, ICD implantation		Third trimester/HF developed in setting of atrial arrythmia, BB treated, cesarean section 36 wk, arrest at delivery, ICD: 1				
					NR/medical abortion at 16 wk: 1				
Tutarel, 2021[22]	0	SVT: 5 VT: 4	NR	11	NR	NR/NR	NR	NR	Thromboembolism: 1

(*Continued*)

Table 2. Continued

Primary author, year	Maternal mortality	Arrhythmia		Heart failure		Worsening of FC/persistent	Worsening RV function	Worsening of valvular regurgitation	Other complications
		No. of cases	Onset/management	No. of cases	Onset/management				
Zentner, 2012[14]	2	AT: 1	NR	3	During gestation/admission: 2	NR/NR	NR	NR	NR
		SCD: 2	SCD: occurred at home. 6 wk postpartum with pregnancy complicated by atrial arrhythmias, mortality SCD: occurred at home. 27 wk in a patient who had reported palpitations, mortality		3d postpartum/admission: 1				
Totals, n (%) [95% CI]*	3 (0.6) [−14.3 to 15.4]	45 (9) [−50.7 to 69.5]		39 (8) [−47.8 to 64.1]		Worsening FC: 47 (19) [−66.7 to 105.3]	36 (19) [−69.1 to 111.7]	24 (17) [−66.8 to 105.5]	Baffle leak: 9 Baffle obstruction: 7 Hemoptysis: 2 Thromboembolism: 5 TIA/stroke: 1

ACEI indicates angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; AT, atrial tachycardia; ATSO, atrial switch operation; BB, beta-blocker; CVA, cerebrovascular accident; D-TGA, D-transposition of the great arteries; DVT, deep venous thrombosis; FC, functional class; HF, heart failure; ICD, implantable cardioverter-defibrillator; NR, not reported; NYHA, New York Heart Association; N/A, not applicable; PE, pulmonary embolism; PPM, permanent pacemaker; RV, right ventricular; SCD, sudden cardiac death; SVT, supraventricular tachycardia; TIA, transient ischemic attack; VF, ventricular fibrillation; and VT, ventricular tachycardia.
*Percentages are calculated as that of total number of patients/pregnancies with available data on each respective outcome; incomplete data and discrepancies in reporting style limit synthesized information.

g, and 19% of the newborn were small for gestational age. There were 4 neonatal deaths attributable to extreme prematurity, and 7 cases of in utero death, representing 0.8% and 1.4% of pregnancies, respectively. None of the newborns were reported to have CHD. Total fetal loss (miscarriage, elective abortion, or fetal death) was 12.4%, and rate of CS delivery was 34% (Table 4).

Total TGA With Arterial Switch Procedure (ASO)

Our review identified 120 pregnancies in 86 women with TGA and a history of ASO (Table 5).[23–26] Prior palliative procedures were reported in about a third of the patients, including atrial balloon septostomy, PA banding, ventricular septal defect closure, PA interventions, aortic coarctation repair, and LeCompte procedure. Of the patients, 28% had interventions after the initial ASO, including a relief of RV outflow tract obstruction and PA stenosis, ascending aorta angioplasty, mitral valve repair and replacement, and RV to PA conduit. Valvular regurgitation (pulmonic, aortic, and tricuspid) was common, with moderate severity in 15 patients.

No maternal mortality was reported in any of the studies (Table 6). Arrhythmias were reported in 7 pregnancies (6%), mostly in the second and third trimesters, including atrial tachycardia, atrial fibrillation, and nonsustained ventricular tachycardia. One patient developed a mechanical prosthetic valve thrombosis 3 weeks postpartum, requiring mitral valve replacement complicated by successfully resuscitated cardiac arrest.[23] Symptomatic HF was reported in only 5% of the pregnancies, mostly shortly after the delivery. All arrhythmic and HF episodes were managed with medications.

Rate of preeclampsia was 7%, and fetal outcome was favorable, with a 91% live birth rate (Table 7). There was 1 fetal and no neonatal death, and rate of prematurity and small for gestational age was 9% each. Mode of delivery was reported in 95 pregnancies, and the rate of CS delivery was 42%. Cesarean delivery was indicated because of aortic dilatation in 3 cases.

Comparison Between D-TGA With ATSO and ASO

The incidences of arrhythmias and HF were numerically lower in patients with ASO (Figure 2 and Figure 3). The difference, however, did not reach statistical significance. In contrast, there was a statistically significant difference in the rate of prematurity ($P<0.001$).

DISCUSSION

Our review provides information on maternal and fetal outcomes associated with pregnancy in a large

Table 3. Maternal Mortality: Clinical Details Across All Studies

Study: primary author	Resuscitated cardiac arrest	Maternal mortality	Details
Canobbio[12]	0	1	A woman with D-TGA developed HF at 30th week gestation and died suddenly 6 wk after delivery Of note: a second death was reported over 4 y after delivery and was thus excluded from our analysis
Juan[18]	1	0	A woman who was diagnosed with pulmonary edema, admitted to the hospital, and treated with diuretics and angiotensin-converting enzyme inhibitor therapy. She was on β-blocker therapy before pregnancy, but this medication was discontinued during pregnancy. She had a resuscitated sudden death event 48 hours following cesarean delivery.
Trigas[16]	2	0	Case 1: A woman with HF and AF treated with β blockers during pregnancy. She underwent cesarean section in the 36th week gestation and developed a tachycardic rhythm disorder with cardiac arrest during the delivery. After successful resuscitation, an ICD was implanted. Case 2: A woman with TGA, complex VSD, and mild pulmonary vein stenosis who experienced a clinical deterioration to functional class III during pregnancy. The patient had a cardiac arrest during cesarean delivery in the 30th week gestation with successful resuscitation. Of note: Not included because outside peripartum timeline: Resuscitation 18 mo postpartum attributable to ventricular fibrillation
Zentner[14]	0	2	Case 1: A woman with a history of palpitations and syncope during pregnancy 3 wk prior, awaiting Holter monitoring. Patient had a sudden cardiac death at home at 27th week gestation. Presumed to be arrhythmic. Case 2: A woman with a history of HF and atrial arrythmia before pregnancy. Enalapril and sotalol were discontinued before conception. Patient was admitted for HF and atrial arrythmia during pregnancy. She was discharged home but experienced sudden cardiac death six months postpartum.
Totals	3	3	

AF indicates atrial fibrillation; D-TGA, D-transposition of the great arteries; HF, heart failure; ICD, implantable cardioverter-defibrillator; and VSD, ventricular septal defect.

number of women with D-TGA after both ATSO and ASO that should be useful in counseling these patient populations before pregnancy and for the design of appropriate management plans during pregnancy, labor and delivery and the postpartum period.

D-TGA After ATSO

Although ATSO has been gradually replaced by ASO in children with D-TGA, there are women with history of Mustard or Senning procedure in the childbearing age who plan to have children.[7,22,27–29] The modified World Health Organization classification for prediction of pregnancy risk includes D-TGA as a class III and predicts significant risk of maternal mortality or severe morbidity.[30] This classification often affects major decisions, including advising against conception, early termination of pregnancy, interventions during pregnancy, as well as early CS delivery.[19] The results of this review indicate that although pregnancy in women with TGA after ATSO can be associated with important maternal complications and have a significant effect on fetal outcome, it is well tolerated in most women and risk of maternal mortality is small. Important complications were reported in a minority of patients but could have serious consequences. The main cardiovascular events were symptomatic HF and arrhythmias, both reported in <10% of the cases. Worsening HF mostly occurred late in pregnancy and during delivery but also in the early postpartum period and resulted in hospital admissions, emergency deliveries, pregnancy termination, and even cardiac arrest in some patients. Symptomatic deterioration late in pregnancy is most likely attributable to increased hemodynamic burden, evidenced by the reported increase in brain natriuretic peptide levels.[31] Development of HF after the delivery is attributable to increased venous return to the heart after the removal of the inferior vena cava compression by the fetus as well as auto transfusion of blood during uterine contractions and mobilization of extravascular fluid into the intravascular space.[32] In addition, increased systemic vascular resistance attributable to removal of the low-resistance placental circulation further contributes to deterioration of ventricular performance.[32]

Patients with D-TGA and ATSO are at a risk of both bradyarrhythmias and tachyarrhythmias.[1,33] This is reflected by a prepregnancy history of arrhythmias, pacemakers, and implantable cardioverter-defibrillator in about 34% of all patients in this review. One of 10 patients developed arrhythmias during pregnancy, which were mostly atrial (atrial tachycardia, fibrillation, or flutter and supraventricular tachycardia). Ventricular arrhythmias were uncommon but had severe consequences, including cardiac arrest and sudden death in some patients.

Table 4. Fetal Outcomes in Pregnancies in Women With D-TGA and ATSO

Primary author, year of source	Live births	Spontaneous abortions	Elective abortions	Cesarean section	Pregnancy duration, mean±SD or range, wk	Birth weight average, g	SGA	Preeclampsia/ PIH	Preterm labor / delivery	Fetal mortality	Neonatal mortality	CHD
Bowater, 2012[15]	31	0	0	14	30–41	NR	6	NR	11	0	1	0
Canobbio, 2006[12]	54	10	6	15	36.7±3.6	2714	NR	4	28	0	0	0
Cataldo, 2015[17]*	26	NR	NR	4	37 (30–40)	2525	10	NR	19	0	0	0
Drenthen, 2005[11]	47	17	3	8	36.4±4.5	NR	10	9	16	4	2	0
Fabre-Gray, 2020[20]	38	NR	NR	3	37.1 (32.2–40)	2515	25	1	15	0	0	NR
Guedes, 2004[21]*	18	0	0	3	38.1±1.5	3040	NR	NR	NR	0	0	0
Juan, 2016[18]	17	0	0	NR	38 (24–39)	2770	NR	NR	3	0	1	0
Lipczyńska, 2016[19]	22	2	0	20	37.2 (26–41)	NR	6	1	2	0	0	0
Metz, 2011[13]	14	6	1	3	35.6 (26–40)	NR	NR	NR	7	0	0	0
Trigas, 2014[16]	44	11	5	24	39 (29–42)	2910	5	1	15	0	0	0
Tutarel, 2021[22]	NR	NR	NR	54	NR	NR	22	3	26	1	0	NR
Zentner, 2012[14]	42	0	0	NR	NR	2700	NR	NR	8	2	0	0
Total n (%) [95% CI]*	353 (85) [–95.5 to 265.2]	46 (13) [–57.7 to 83.8]	15 (4) [–36.2 to 44.6]	148 (34) [–80.4 to 148.9]	Average: 37.1	Average: 2776	74 (19) [–66.8 to 105.5]	19 (5) [–40.5 to 51.6]	150 (32) [–79.0 to 143.4]	7 (1.4) [–22.0 to 24.8]	4 (0.8) [–17 to 18.6]	0 (0)

ATSO indicates atrial switch operation; CHB, complete heart block; D-TGA, D-transposition of the great arteries; NR, not reported; PIH, pregnancy-induced hypertension; and SGA, small for gestational age.

*Fetal outcome data are available for fewer than the number of reported pregnancies. Percentages are calculated as that of total number of patient/pregnancies with available data on each respective outcome; incomplete data and discrepancies in reporting style limit the accuracy of synthesized information.

Table 5. Baseline Characteristics of Patients With Total TGA and ASO

Primary author, year	Design of study/ country of publication	No. of pregnant patients	No. of pregnancies	No. of live births	Age, mean±SD, y	Other congenital defects	Additional cardiac surgeries before pregnancy	Arrhythmia	Valvular dysfunction	NYHA FC
Tobler, 2010[23]	Retrospective/ Canada	9	17	13	22±4	Aortic dilatation (37 mm, 44 mm): 2 Left circumflex coronary artery from RCA: 2 LVD: 2 Single coronary pattern: 2 VSD: 4	Arterioplasty of ascending aorta, conduit replacement, and PA angioplasty: 1 Insertion of monocusp RVOT patch: 1 Lecompt maneuver: 6 MV repair, subaortic muscle bundle resection, and MV replacement: 1 PA homograft reconstruction and redo surgery and aortopulmonary window repair: 1 RVOT patch extending PA angioplasty: 1 RVOT patch with insertion of homograft and balloon angioplasty of left PA: 1	Atrial flutter: 2	PR: 3 PS: 2	NR
Stoll, 2018[29]	Retrospective/United Kingdom	15	25	24*	23±3.9	Coarctation of aorta: 1 Neoaortic root dilatation: 5 RV outflow tract obstruction: 1 VSD: 5	NR	NR	AR: mild: 4; moderate: 2 PR: mild: 3; moderate: 1 PS: mild: 4 TR: mild: 3; moderate: 2	NR
Fricke, 2019[24]	Retrospective/ Australia	11	17	17	29.3±3.4	VSD: 6 Taussig-Bing anomaly: 1	AV replacement: 1 Pacemaker: 1 Residual VSD closure, ARR, RVOT obstruction resection, and ICD: 1 RVOT obstruction resection and PV replacement: 1	NR	AR: mild: 3; moderate-severe: 1 PR: mild – 2; moderate – 2	I: 9; II: 2; III: 0

(*Continued*)

Table 5. Continued

Primary author, year	Design of study/ country of publication	No. of pregnant patients	No. of pregnancies	No. of live births	Age, mean±SD, y	Other congenital defects	Additional cardiac surgeries before pregnancy	Arrhythmia	Valvular dysfunction	NYHA FC
Horiuchi, 2019[25]	Retrospective/Japan	10	20	14	29.8±2.5	Right aortic arch: 1 VSD: 3	Mitral and aortic valvuloplasty: 1 PA patchplasty: 1 PA patchplasty, infundibular myotomy, and PV commissurotomy: 1 Patch angioplasty of left PA and RVOT reconstruction: 1 PTPA: 2 RVOT patchplasty and infundibulectomy: 1 RVOT reconstruction: 1	NR	AR: mild: 2; moderate: 3 MR: moderate: 1 PR: moderate: 2 PS: mild: 4 (1 left); moderate: 1	I: 10; II: 0; III: 0
Tutarel, 2021[26]	Prospective/United States	41	41	40	26.7±3.9	Aortic dilatation: 4 Coarctation of aorta: 2 LVD: 1 PDA: 4 VSD: 13	NR	NR	AR: mild: 14; moderate: 1 PS: 14	I: 38; II: 2; III: 1
Total		86	120	108	Average: 26			2 (22%)	AR: 10/86 (12%) MR: 1/86 (1%) PR: 13/86 (15%) PS: 11/86 (13%) TR: 5/86 (6%)	I: 57/62 (92%) II: 4/62 (6%) III: 1/62 (2%)

Percentages are of total number of pregnant patients with data on each respective variable. AR indicates aortic regurgitation; ARR, aortic root replacement; ASO, arterial switch operation; AV, aortic valve; FC, functional class; LVD, left ventricular dysfunction; MR, mitral regurgitation; MV, mitral valve; NR, not reported; NYHA, New York Heart Association; PA, pulmonary artery; PDA, patent ductus arteriosus; PR, pulmonary regurgitation; PS, pulmonary stenosis; PTPA, percutaneous transluminal pulmonary angioplasty; PV, pulmonary valve; RCA, right coronary artery; RV, right ventricular; RVOT, RV outflow tract; TGA, transposition of the great arteries TR, tricuspid valve regurgitation; and VSD, ventricular septal defect.

*One ongoing pregnancy at time of publication.

Table 6. Maternal Outcomes in Pregnancy in Women With D-TGA and ASO

Primary author, year of source	Arrhythmia			Symptomatic heart failure			Worsened FC	Worsened ventricular function	Other complications
	Case	Onset	Management	Case	Onset	Management			
Tobler, 2010[23]	Recurrent NSVT with mild LVD: 1	16 wk GA	Amiodarone	None	N/A	N/A	NR	2	Mechanical MV thrombosis postpartum, with subsequent MVR* complicated by cardiac arrest, with successful resuscitation resulting in moderate LVD (EF from 60% to 48%): 1 TIA/stroke: 0
Stoll, 2018[29]	None	N/A	N/A	None	N/A	N/A	0	0	Thromboembolism: NR TIA/stroke: NR
Fricke, 2019[24]	Rapid atrial flutter and fibrillation: 1	2 d postpartum	NR	Symptomatic deterioration of HF in a patient with AR: 1	31 wk GA	NR	0	1	Thromboembolism: NR TIA/stroke: NR
Horiuchi, 2019[25]	NSVT and later HF at 3 d postpartum: 1	24 wk GA	β-Blockers	HF, unspecified: 2	1 d postpartum 3 d postpartum	Diuretics	0	0	Thromboembolism: 0 TIA/stroke: 0
	New-onset AF: 1	37 wk GA	β-Blockers	HF on day of delivery with reduced EF in a patient with AR and MR: 1	0 d postpartum	Diuretics Carvedilol			
	NSVT and new-onset AT: 1	28 wk GA (NSVT),29 wk GA (AT)	NR						
	NSVT and HF on day of delivery: 1	7 d postpartum	ACEI						
Tutarel, 2021[26]	Ventricular tachycardia: 1	Second and third trimester	Metoprolol	Hospital admission for HF (EF 45%) in patient with a prepregnancy history of HF: 1	3 mo postpartum	NR	NR	0	Thromboembolism: 0 TIA/stroke: 0
Total, n (%) [95% CI]†	7 (6) [−43.2 to 56.1]			5 (5) [−37.4 to 46.6]			0	3 (6)* [−0.4 to 0.5]	Thromboembolism: 1 (1) TIA/stroke: 0

ACEI indicates angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; AR, aortic regurgitation; ASO, arterial switch operation; AT, atrial tachycardia; D-TGA, D-transposition of the great arteries; EF, ejection fraction; FC, functional class; GA, gestational age; HF, heart failure; LVD, left ventricular dysfunction; MR, mitral regurgitation; MV, mitral valve; MVR, mitral valve replacement; NR, not reported; NSVT, nonsustained ventricular tachycardia; N/A, not applicable; and TIA, transient ischemic attack.

*Number of pregnancies with available echocardiographic data.

†Percentages are calculated as that of total number of patients/pregnancies with available data on each respective outcome; incomplete data and discrepancies in reporting style limit the accuracy of synthesized information.

Table 7. Fetal Outcomes in Pregnancy in Women With D-TGA and ASO

Primary author, year of source	Live births	Spontaneous abortions	Elective abortions	GA, mean±SD, wk	Birth weight, mean±SD, g	SGA	Preeclampsia/ PIH	Preterm delivery	Fetal mortality	Neonatal mortality	Neonatal CHD	Cesarean delivery
Tobler, 2010[23]	13	4	0	NR	3300±500	1	NR	0	0	0	VSD: 1	NR
Stoll, 2018[29]	24*	0	0	38.5±2.0	3184±447	NR	NR	1	0	0	0	7 (2 for aortic dilatation, 1 for maternal choice)
Fricke, 2019[24]	17	0	0	38.5±2.2	3600±300	NR	2	1	0	0	0	8
Horiuchi, 2019[25]	14	1	5	37.3±3.2	2521±638	4 (3 took β-blockers)	1	3	0	0	0	6 (1 for aortic dilatation 54 mm)
Tutarel, 2021[26]	40	0	0	39	2962±100	1	2	7	1	0	0	19
Total, n (%) [95% CI]	108 (91) [–95.3 to 276.8]	5 (4) [–36.0 to 44.4]	5 (4) [–36 to 44.4]	Average: 38.3	Average: 3113	6 (9) [–49.7 to 67.6]	5 (7) [–44.9 to 59]	12 (11) [–54.2 to 76.4]	1 (0.8) [–17.1 to 18.8]	0	1 (0.8) [–17.1 to 18.8]	40 (42) [–84.8 to 169.0]

Percentages are of number of pregnancies with data on each respective outcome. ASO indicates arterial switch operation; CHD, congenital heart defect; D-TGA, D-transposition of the great arteries; GA, gestational age; NR, not reported; PIH, pregnancy-induced hypertension; SGA, small for gestational age; and VSD, ventricular septal defect.
*One ongoing pregnancy at time of publication.

Dysfunction of the systemic RV is a common long-term complication after the Mustard or Senning operations.[1,28,34] RV dysfunction, mostly mild to moderate, was reported in most women before pregnancy. Decrease in RV function during pregnancy was reported in 6 studies[11,16–18,21] and ranged between 0% and 25%, with an average of 10%, and persisted after pregnancy in some of the cases. However, information on long-term impact of pregnancy on ventricular function is conflicting. Guedes et al[21] described deterioration of RV function in 25% of 16 women during pregnancy with no recovery at 3 years after the delivery in 75% of the cases. Similar incidence of RV disfunction, however, was also seen in a group of 6 women without a history of pregnancy. Cataldo et al[17] followed up 21 pregnant women and 15 matched controls for an average of 55 months and reported worsening of RV function in almost a third of women in both groups. Similarly comparable rates of clinical and RV functional deterioration over an average follow-up of almost 7 years were described by Lipczynska et al,[19] who compared 15 women with 24 pregnancies to the same number of nulliparous women. Bowater et al[15] compared a group of 18 pregnant women with D-TGA to a matched group of men and a group of nulliparous women with atrial switch and found a significant deterioration of both RV function and NYHA functional class at 1 year only in the pregnancy group, but no difference between the groups at a 3- to 4-year follow-up.

Tricuspid valve regurgitation is also common in patients with TGA after ATSO because of the change in geometry of the ventricular septum.[28] Mild or moderate TR was reported in most patients before pregnancy. Information on change in the severity of the TR was provided by Cataldo et al,[17] who reported worsening in >50% of the patients compared with none in control women without pregnancy history.[17] Pregnancy-related TR did not recover after pregnancy in 36% of the patients because of RV dilatation. Guedes et al also reported progression of TR in half of the patients but a recovery at follow-up in two-thirds of the patients.[21]

Prepregnancy functional class was described as normal (NYHA class I) in most cases. Worsening of functional class during pregnancy was reported in a fifth of the patients with available data and persisted after pregnancy in 11 women. Although decreased functional class during pregnancy is often seen in healthy women[35,36] and is not a reliable indication for hemodynamic deterioration, persistence of symptoms after the delivery is a better indication for pregnancy-associated progression of cardiac dysfunction.

Baffle leaks and obstruction are also important complications after Mustard and Senning operations.[1] Although most are not hemodynamically significant, severe cases can lead to pulmonary hypertension (obstruction) or intracardiac shunts with RV volume

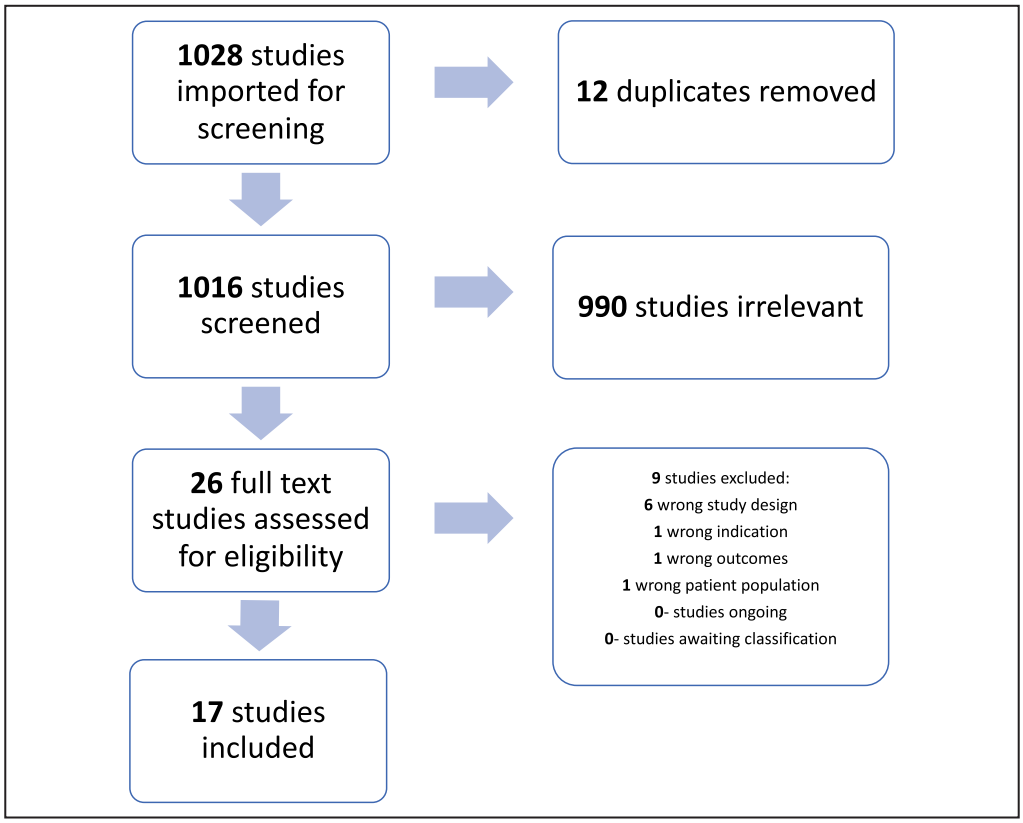

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis diagram and flowchart of included studies.

overload or systemic desaturation (leak) and require reintervention. Several patients in this group required surgical repair of pulmonary venous obstruction or baffle leak before pregnancy, and a few patients developed a new baffle leak or obstruction during pregnancy, which did not seem to affect pregnancy outcome.

The results of this study also demonstrate an important impact of the cardiac condition on fetal outcomes. The main obstetrical complication was a high rate of prematurity, which was 3-fold higher than the reported global preterm birth rate and resulted in 4 cases of newborn mortality.[37] The incidence of miscarriage, however, was comparable to that of normal population and substantially lower than that reported in women with other complex CHD, such as Fontan circulation or cyanotic CHD.[38,39]

Rate of CS delivery varied considerably between the different reports. The average rate was 34%, which is only slightly higher than that reported in normal pregnancies in North America and Europe[40] and considerably lower than that reported in patients with valvular disease or other CHD.[38,41] Rate of CS was high in 2 of the studies (55%[16] and 91%[19]). Although the reasons were not specified, it was probably attributable to clinician's preference of a CS delivery in women with cardiac disease even without obstetrical or cardiac indications. Lower rate of CS deliveries in the other studies[11–13,17,21] supports this assumption. Because of increased risk of maternal morbidity associated with planned CS compared with planned vaginal delivery,[42] CS delivery in women with TGA and ATSO should be limited to patients with maternal or fetal instability.[43]

Contrary to previously reported 2% recurrence rate of TGA in offspring of women with the same condition,[44] none of the newborns included in this study was reported to have CHD.

Arterial Switch Operation

The ASO that restores the normal anatomic arrangement of the circulation for TGA has become the preferred surgical correction in children with D-TGA. There is a significant long-term survival with this procedure which is, however, not without complications,[1,7] including distortion of RV outflow tract and pulmonary arteries, neoaortic dilatation, valvular regurgitation, and coronary artery stenosis that can lead to myocardial infarction or sudden death.[1] Information about the outcome of pregnancy is still limited. Our review identified 120 pregnancies in 86 women with TGA and ASO.[23–25] More than half of the patients

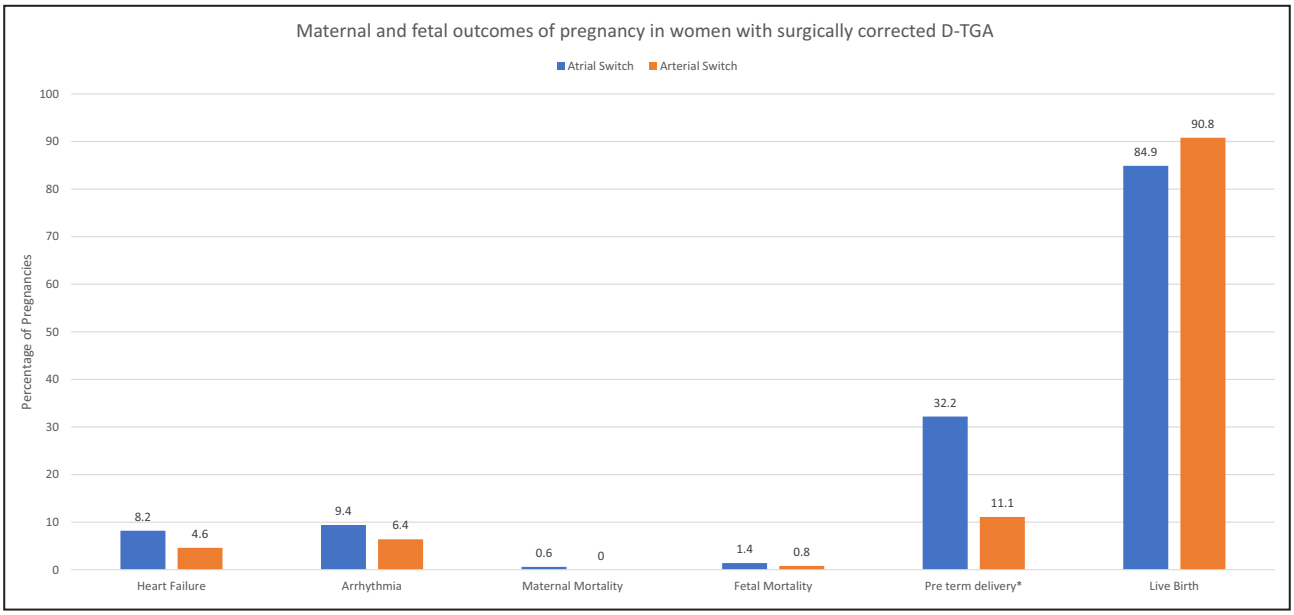

Figure 2. Maternal and fetal outcomes with pregnancy in women with corrected D-transposition of the great arteries (D-TGA).
*Indicates *P* value<0.001.

had prior palliative procedures, and about a third of the patients had further interventions since ASO (Table 4). The outcome of women with ASO seemed to be superior compared with those after ATSO. There was no maternal mortality, and the incidence of HF and arrhythmias, which were the main cardiac events, was about half of that reported in women with ATSO. Arrhythmias were not life threatening and, like HF episodes, were manageable with medications. Plasma brain natriuretic peptide levels measured in one study[25] were significantly higher in women with these cardiac events. This finding supports a previous study by Kampman et al,[45] who demonstrated that increased NT-proBNP (N-terminal pro-B-type natriuretic peptide) levels during gestation were an independent risk predictor of cardiovascular events during pregnancy in women with CHD and suggests the value of a routine monitoring of brain natriuretic peptide levels during pregnancy.

Rate of cesarean deliveries was slightly higher in women with ASO compared with ATSO. This finding is surprising because only a minority of the patients had a cardiac indication (aortic dilatation) for the procedure. This finding supports the tendency of clinicians to prefer a cesarian delivery in women with cardiac disease even without cardiac indications.

Fetal outcome was also more favorable with a high rate of live birth and <10% abortion rates, which was attributable to social rather than medical reasons. There was no fetal or neonatal death, and the rates of prematurity and small for gestational age were comparable to that reported in healthy women.[46]

Study Limitations

Because of the retrospective design of most studies included in our review, the information provided is not complete and several reports did not include all the pregnancy characteristics or end points of interest. Furthermore, lack of uniform definitions in maternal and fetal events limited the accuracy of data synthesis. In addition, most of the patients in the included studies were asymptomatic or mildly symptomatic before gestation. It is therefore possible that women with more severe cardiac conditions were advised not to proceed with pregnancy or have early termination. The result of our study therefore may not be applicable to higher-risk women with TGA.

CONCLUSIONS AND RECOMMENDATIONS

Experience in a large number of patients with D-TGA with ATSO indicates that pregnancy in asymptomatic or mildly symptomatic women is well tolerated in the majority and mortality is low. Concurrently, this condition can be associated with clinically important maternal complications, including HF, arrhythmias, thromboembolic events, worsening of RV function, and TR, which may persist after delivery with possible long-term effect. Multimodality evaluation is recommended preconception or early in pregnancy to identify high risk for complications during pregnancy. This evaluation should include a careful history of cardiac events before pregnancy, physical examination, transthoracic

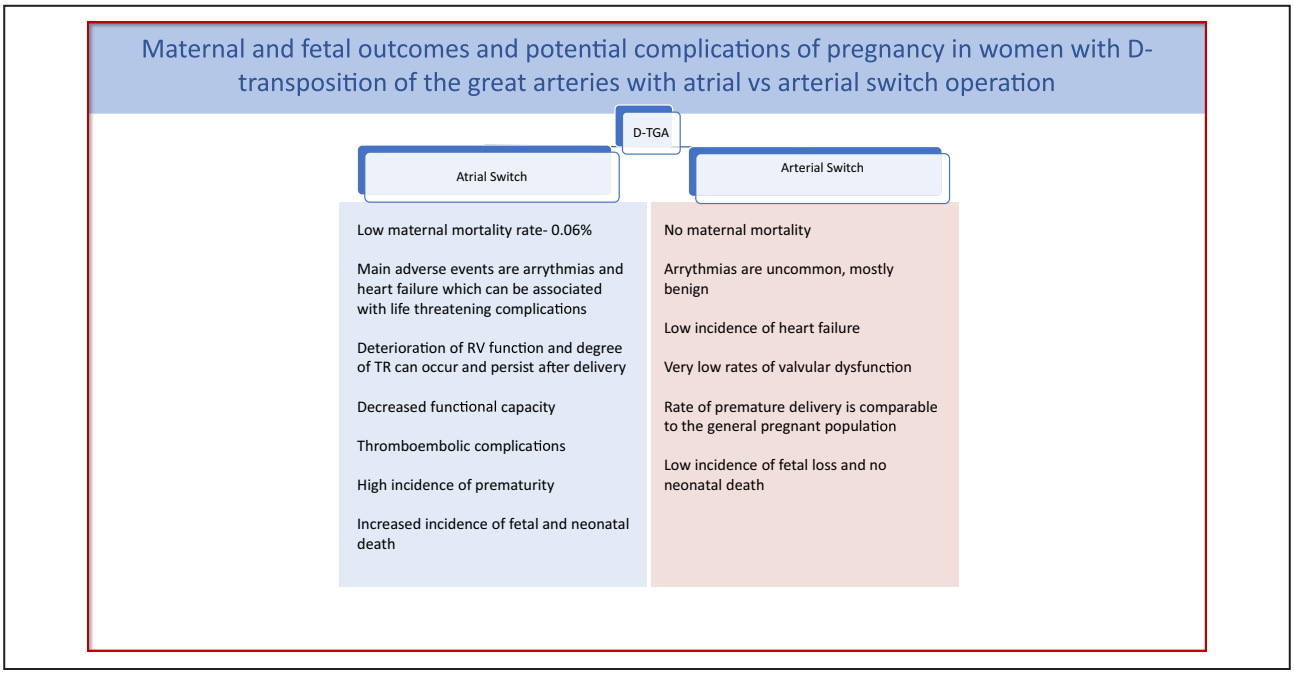

Figure 3. Pregnancy outcomes in women with D-transposition of the great arteries (D-TGA).

echocardiography, and, if needed, magnetic resonance imaging for assessment of cardiac function, the presence and severity of valvular disease, and aortic dilatation, exercise testing for objective assessment of functional capacity and level of brain natriuretic peptide, and, if necessary, invasive hemodynamic evaluation for assessment of the presence and severity of pulmonary hypertension.[47] A close follow-up is required during pregnancy and postpartum by a multidisciplinary group experienced in the management of pregnant women with cardiac disease for prevention or early diagnosis and management of hemodynamic deterioration. Frequency of follow-up should be increased after the 30th week of gestation, and hemodynamic deterioration after the delivery should be anticipated and prevented by increased diuresis before and immediately after the delivery. Women should be made aware of the fact that fetal outcome can also be influenced by the underlying disease with an increase in the rate of prematurity and fetal and neonatal death.

Women with TGA after ASO seem to be at a lower risk compared with those after ATSO. Pregnancy was well tolerated in most cases without mortality, and the incidence of HF and arrhythmias was lower compared with women with ATSO, and these complications were manageable with medical therapy. Fetal outcome was also favorable, with incidence of prematurity and small for gestational age comparable to those seen in healthy women. Despite the overall favorable outcome, the development of cardiac events during the latter part of pregnancy and early postpartum in some of the patients suggests the need for a careful preconceptual evaluation and close follow-up during pregnancy in this patient population as well.

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Supplemental Material

Appendix S1

REFERENCES

1. Warnes CA. Transposition of the great arteries. *Circulation.* 2006;114:2699–2709. doi: 10.1161/CIRCULATIONAHA.105.592352
2. Hornung T, O'Donnell C. 51 - transposition of the great arteries. In: Gatzoulis MA, Webb GD, Daubeney PEF, eds. *Diagnosis and management of adult congenital heart disease (third edition)*. Elsevier; 2018:513–527. doi: 10.1016/B978-0-7020-6929-1.00051-4
3. Dennis M, Kotchetkova I, Cordina R, Celermajer DS. Long-term follow-up of adults following the atrial switch operation for transposition of the great arteries - a contemporary cohort. *Heart Lung Circ.* 2018;27:1011–1017. doi: 10.1016/j.hlc.2017.10.008
4. Moe TG, Bardo DME. Long-term outcomes of the arterial switch operation for d-transposition of the great arteries. *Prog Cardiovasc Dis.* 2018;61:360–364. doi: 10.1016/j.pcad.2018.08.007
5. Couperus LE, Vliegen HW, Zandstra TE, Kiès P, Jongbloed MRM, Holman ER, Zeppenfeld K, Hazekamp MG, Schalij MJ, Scherptong RWC.

Long-term outcome after atrial correction for transposition of the great arteries. *Heart.* 2019;105:790–796. doi: 10.1136/heartjnl-2018-313647
6. Graham TP Jr, Bernard YD, Mellen BG, Celermajer D, Baumgartner H, Cetta F, Connolly HM, Davidson WR, Dellborg M, Foster E, et al. Long-term outcome in congenitally corrected transposition of the great arteries: a multi-institutional study. *J Am Coll Cardiol.* 2000;36:255–261. doi: 10.1016/S0735-1097(00)00682-3
7. Kiener A, Kelleman M, McCracken C, Kochilas L, St Louis JD, Oster ME. Long-term survival after arterial versus atrial switch in d-transposition of the great arteries. *Ann Thorac Surg.* 2018;106:1827–1833. doi: 10.1016/j.athoracsur.2018.06.084
8. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomström-Lundqvist C, Cífková R, De Bonis M, Iung B, Johnson MR, Kintscher U, Kranke P, et al. 2018 ESC guidelines for the management of cardiovascular diseases during pregnancy. *Eur Heart J.* 2018;39:3165–3241. doi: 10.1093/eurheartj/ehy340
9. Drenthen W, Boersma E, Balci A, Moons P, Roos-Hesselink JW, Mulder BJ, Vliegen HW, van Dijk AP, Voors AA, Yap SC, et al. Predictors of pregnancy complications in women with congenital heart disease. *Eur Heart J.* 2010;31:2124–2132. doi: 10.1093/eurheartj/ehq200
10. Silversides CK, Grewal J, Mason J, Sermer M, Kiess M, Rychel V, Wald RM, Colman JM, Siu SC. Pregnancy outcomes in women with heart disease: the CARPREG II study. *J Am Coll Cardiol.* 2018;71:2419–2430. doi: 10.1016/j.jacc.2018.02.076
11. Drenthen W, Pieper PG, Ploeg M, Voors AA, Roos-Hesselink JW, Mulder BJ, Vliegen HW, Sollie KM, Ebels T, van Veldhuisen D, et al. Risk of complications during pregnancy after senning or mustard (atrial) repair of complete transposition of the great arteries. *Eur Heart J.* 2005;26:2588–2595. doi: 10.1093/eurheartj/ehi472
12. Canobbio MM, Morris CD, Graham TP, Landzberg MJ. Pregnancy outcomes after atrial repair for transposition of the great arteries. *Am J Cardiol.* 2006;98:668–672. doi: 10.1016/j.amjcard.2006.03.050
13. Metz TD, Jackson GM, Yetman AT. Pregnancy outcomes in women who have undergone an atrial switch repair for congenital d-transposition of the great arteries. *Am J Obstet Gynecol.* 2011;205:273.e271–273.e275.
14. Zentner D, Wheeler M, Grigg L. Does pregnancy contribute to systemic right ventricular dysfunction in adults with an atrial switch operation? *Heart Lung Circ.* 2012;21:433–438. doi: 10.1016/j.hlc.2012.04.009
15. Bowater SE, Selman TJ, Hudsmith LE, Clift PF, Thompson PJ, Thorne SA. Long-term outcome following pregnancy in women with a systemic right ventricle: is the deterioration due to pregnancy or a consequence of time? *Congenit Heart Dis.* 2013;8:302–307. doi: 10.1111/chd.12001
16. Trigas V, Nagdyman N, Pildner von Steinburg S, Oechslin E, Vogt M, Berger F, Schneider KTM, Ewert P, Hess J, Kaemmerer H. Pregnancy-related obstetric and cardiologic problems in women after atrial switch operation for transposition of the great arteries. *Circ J.* 2014;78:443–449. doi: 10.1253/circj.CJ-12-1051
17. Cataldo S, Doohan M, Rice K, Trinder J, Stuart A, Curtis S. Pregnancy following mustard or senning correction of transposition of the great arteries: a retrospective study. *BJOG.* 2016;123:807–813. doi: 10.1111/1471-0528.13508
18. Jimenez Juan L, Valente AM, Silversides CK, Geva T, Colman JM, Roche SL, Siu SC, Wald RM. Cardiac magnetic resonance imaging characteristics and pregnancy outcomes in women with mustard palliation for complete transposition of the great arteries. *Int J Cardiol Heart Vasc.* 2016;10:54–59. doi: 10.1016/j.ijcha.2016.01.001
19. Lipczyńska M, Szymański P, Trojnarska O, Tomkiewicz-Pająk L, Pietrzak B, Klisiewicz A, Kumor M, Podolec P, Hoffman P. Pregnancy in women with complete transposition of the great arteries following the atrial switch procedure. A study from three of the largest adult congenital heart disease centers in Poland. *J Mater-Fetal Neonatal Med.* 2017;30:563–567. doi: 10.1080/14767058.2016.1177821
20. Fabre-Gray A, Curtis S, Trinder J. Obstetric outcomes following atrial and arterial switch procedures for transposition of the great arteries (TGA) - a single, tertiary referral centre experience over 20 years. *Obstet Med.* 2020;13:125–131. doi: 10.1177/1753495X19825964
21. Guédès A, Mercier LA, Leduc L, Bérubé L, Marcotte F, Dore A. Impact of pregnancy on the systemic right ventricle after a mustard operation for transposition of the great arteries. *J Am Coll Cardiol.* 2004;44:433–437. doi: 10.1016/j.jacc.2004.04.037
22. Tutarel O, Baris L, Budts W, Gamal Abd-El Aziz M, Liptai C, Majdalany D, Jovanova S, Frogoudaki A, Connolly HM, Johnson MR, et al. Pregnancy outcomes in women with a systemic right ventricle and transposition of the great arteries results from the ESC-EORP registry of pregnancy and cardiac disease (ROPAC). *Heart.* 2021;108:117–123.
23. Tobler D, Fernandes SM, Wald RM, Landzberg M, Salehian O, Siu SC, Colman JM, Sermer M, Silversides CK. Pregnancy outcomes in women with transposition of the great arteries and arterial switch operation. *Am J Cardiol.* 2010;106:417–420. doi: 10.1016/j.amjcard.2010.03.047
24. Fricke TA, Konstantinov IE, Grigg LE, Zentner D. Pregnancy outcomes in women after the arterial switch operation. *Heart Lung Circ.* 2020;29:1087–1092. doi: 10.1016/j.hlc.2019.07.016
25. Horiuchi C, Kamiya CA, Ohuchi H, Miyoshi T, Tsuritani M, Iwanaga N, Neki R, Niwa K, Kurosaki K, Ichikawa H, et al. 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. *J Cardiol.* 2019;73:247–254. doi: 10.1016/j.jjcc.2018.11.007
26. Tutarel O, Ramlakhan KP, Baris L, Subirana MT, Bouchardy J, Nemes A, Vejlstrup NG, Osipova OA, Johnson MR, Hall R, et al. Pregnancy outcomes in women after arterial switch operation for transposition of the great arteries: results from ROPAC (Registry Of Pregnancy and Cardiac Disease) of the European Society of Cardiology EURObservational research programme. *J Am Heart Assoc.* 2021;10:e018176, DOI: 10.1161/JAHA.120.018176
27. Venkatesh P, Evans AT, Maw AM, Pashun RA, Patel A, Kim L, Feldman D, Minutello R, Wong SC, Stribling JC, et al. Predictors of late mortality in D-transposition of the great arteries after atrial switch repair: systematic review and meta-analysis. *J Am Heart Assoc.* 2019;8:e012932. doi: 10.1161/JAHA.119.012932
28. Storsten P, Eriksen M, Remme EW, Boe E, Erikssen G, Smiseth OA, Skulstad H. Dysfunction of the systemic right ventricle after atrial switch: physiological implications of altered septal geometry and load. *J Appl Physiol (1985).* 2018;125:1482–1489. doi: 10.1152/japplphysiol.00255.2018
29. Stoll VM, Drury NE, Thorne S, Selman T, Clift P, Chong H, Thompson PJ, Morris RK, Hudsmith LE. Pregnancy outcomes in women with transposition of the great arteries after an arterial switch operation. *JAMA Cardiology.* 2018;3:1119–1122. doi: 10.1001/jamacardio.2018.2747
30. Davis MB, Arendt K, Bello NA, Brown H, Briller J, Epps K, Hollier L, Langen E, Park K, Walsh MN, et al. Team-based care of women with cardiovascular disease from pre-conception through pregnancy and postpartum: JACC focus seminar 1/5. *J Am Coll Cardiol.* 2021;77:1763–1777. doi: 10.1016/j.jacc.2021.02.033
31. Miller E, Cannobio M, Koos B. Pregnancy outcomes in women with d-transposition of the great arteries after atrial switch. *J Am Coll Cardiol.* 2019;73:591–591. doi: 10.1016/S0735-1097(19)31199-4
32. Havakuk O, Elkayam U. Hemodynamics and cardiac function. Cardiac problems in pregnancy. 2019:1–16.
33. Görler H, Ono M, Thies A, Lunkewitz E, Westhoff-Bleck M, Haverich A, Breymann T, Boethig D. Long-term morbidity and quality of life after surgical repair of transposition of the great arteries: atrial versus arterial switch operation. *Interact Cardiovasc Thorac Surg.* 2011;12:569–574. doi: 10.1510/icvts.2010.253898
34. Dos L, Teruel L, Ferreira IJ, Rodriguez-Larrea J, Miro L, Girona J, Albert DC, Gonçalves A, Murtra M, Casaldaliga J. Late outcome of senning and mustard procedures for correction of transposition of the great arteries. *Heart.* 2005;91:652–656. doi: 10.1136/hrt.2003.029769
35. Milne JA, Howie AD, Pack AI. Dyspnoea during normal pregnancy. *Br J Obstet Gynaecol.* 1978;85:260–263. doi: 10.1111/j.1471-0528.1978.tb10497.x
36. Elkayam U. Cardiovascular evaluation during pregnancy. In: Elkayam U, ed. *Cardiac problems in pregnancy.* Weily Blackwell; 2019:17–31. doi: 10.1002/9781119409861.ch2
37. Walani SR. Global burden of preterm birth. *Int J Gynecol Obstet.* 2020;150:31–33. doi: 10.1002/ijgo.13195
38. Ropero AG, Baskar S, Roos Hesselink JW, Girnius A, Zentner D, Swan L, Ladouceur M, Brown N, Veldtman GR. Pregnancy in women with a fontan circulation: a systematic review of the literature. *Circ Cardiovasc Qual Outcomes.* 2018;11:e004575. doi: 10.1161/CIRCOUTCOMES.117.004575
39. Presbitero P, Somerville J, Stone S, Aruta E, Spiegelhalter D, Rabajoli F. Pregnancy in cyanotic congenital heart disease. Outcome of mother and fetus. *Circulation.* 1994;89:2673–2676. doi: 10.1161/01.CIR.89.6.2673
40. Betrán AP, Ye J, Moller AB, Zhang J, Gülmezoglu AM, Torloni MR. The increasing trend in caesarean section rates: global, regional and national estimates: 1990-2014. *PLoS One.* 2016;11:e0148343. doi: 10.1371/journal.pone.0148343

41. Orwat S, Diller GP, van Hagen IM, Schmidt R, Tobler D, Greutmann M, Jonkaitiene R, Elnagar A, Johnson MR, Hall R, et al. Risk of pregnancy in moderate and severe aortic stenosis: from the multinational ROPAC registry. *J Am Coll Cardiol.* 2016;68:1727–1737. doi: 10.1016/j.jacc.2016.07.750
42. Liu S, Liston RM, Joseph KS, Heaman M, Sauve R, Kramer MS. Maternal mortality and severe morbidity associated with low-risk planned cesarean delivery versus planned vaginal delivery at term. *CMAJ.* 2007;176:455–460. doi: 10.1503/cmaj.060870
43. Elkayam U, Goland S, Pieper PG, Silversides CK. High-risk cardiac disease in pregnancy: part II. *J Am Coll Cardiol.* 2016;68:502–516. doi: 10.1016/j.jacc.2016.05.050
44. Digilio MC, Casey B, Toscano A, Calabrò R, Pacileo G, Marasini M, Banaudi E, Giannotti A, Dallapiccola B, Marino B. Complete transposition of the great arteries: patterns of congenital heart disease in familial precurrence. *Circulation.* 2001;104:2809–2814. doi: 10.1161/hc4701.099786
45. Kampman MAM, Balci A, van Veldhuisen DJ, van Dijk APJ, Roos-Hesselink JW, Sollie-Szarynska KM, Ludwig-Ruitenberg M, van Melle JP, Mulder BJM, Pieper PG, et al. N-terminal pro-b-type natriuretic peptide predicts cardiovascular complications in pregnant women with congenital heart disease. *Eur Heart J.* 2014;35:708–715. doi: 10.1093/eurheartj/eht526
46. McCormick MC, Litt JS, Smith VC, Zupancic JA. Prematurity: an overview and public health implications. *Annu Rev Public Health.* 2011;32:367–379. doi: 10.1146/annurev-publhealth-090810-182459
47. Elkayam U. How to predict pregnancy risk in an individual woman with heart disease*. *J Am Coll Cardiol.* 2018;71:2431–2433. doi: 10.1016/j.jacc.2018.03.492

SUPPLEMENTAL MATERIAL

Data S1.

Supplemental Methods

The search was designed by a librarian using a variety of keywords and subject headings describing transposition of the great arteries, surgical techniques, and pregnancy. The search was conducted in PubMed, Embase, and CINAHL Complete on October 21, 2021. See appendix for full search strategies. Searches were limited to materials published in journals and in the English language between 1/1/2001 and 12/31/2021. Results were de-duplicated in EndNote software. After de-duplication, the librarian reviewed abstracts manually to remove materials labeled as conference abstracts, and remaining abstracts were imported into Covidence for screening.

PubMed. Searched https://pubmed.ncbi.nlm.nih.gov on October 21, 2021 using the advanced search interface.
1 "transposition of the great vessels" OR "transposition of the great arteries" OR "transposition of great vessels"[MeSH Terms] OR "transposition of great arteries" OR "transposition of great vessels" OR d-tga OR dtga OR "atrial switch" OR "arterial switch" OR "Arterial Switch Operation"[Mesh] OR mustard[tiab] OR senning[tiab] OR jatene[tiab]
2 "pregnancy"[MeSH Terms] OR "pregn*"[Title/Abstract] OR "pregnancy complications, cardiovascular"[MeSH Terms] OR "pregnancy outcome"[MeSH Terms] OR "pregnancy, high risk"[MeSH Terms] OR "obstetric*"[Title/Abstract]
3 #1 AND #2
Filters applied: English, published from 2001/1/1 - 2021/12/31

Embase. Searched embase.com on October 21, 2021 using the advanced search interface, unselecting all mapping options.
1 ‘transposition of the great vessels' OR 'transposition of the great arteries' OR 'great vessels transposition'/exp OR 'transposition of great vessels' OR 'transposition of great arteries' OR dtga OR 'd tga' OR 'atrial switch' OR 'arterial switch' OR 'arterial switch operation'/exp OR mustard:kw,ab,ti OR senning:kw,ab,ti,de OR jatene:kw,ab,ti OR 'atrial switch operation'/exp
2 ‘pregnancy'/exp OR pregn*:ti,ab,kw,de OR 'pregnancy complication'/exp OR 'pregnancy outcome'/exp OR obstetric*:kw,ti,ab
3 #1 AND #2
4 #3 AND (2001:py OR 2002:py OR 2003:py OR 2004:py OR 2005:py OR 2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py OR 2021:py)
5 #4 AND [english]/lim
6 #5 AND [embase]/lim NOT ([embase]/lim AND [medline]/lim)
7 #6 AND ('article'/it OR 'article in press'/it OR 'conference paper'/it OR 'conference review'/it OR 'review'/it)

CINAHL Complete. Searched using EBSCOhost interface on October 21, 2021 using the advanced search screen. Prior to entering search terms, select the following: the “Boolean/Phrase” search mode, English language limit, and the published dates of January 2001 through December 2021.

In the first search box, leave the input as “select a field.” Input these words/phrases: MH "Transposition of Great Arteries+" OR (AB Mustard OR TI mustard) OR (AB senning OR TI senning) OR (AB jatene OR TI jatene) OR "transposition of the great vessels" OR "transposition of the great arteries" OR "transposition of great arteries" OR "transposition of great vessels" OR dtga OR "d tga" OR d-tga OR "atrial switch" OR "arterial switch"

Clear the search box, leaving the input as “select a field.” Input these words/phrases: (MH "Pregnancy+") OR (AB pregn* OR TI pregn*) OR (MH "Pregnancy Complications, Cardiovascular") OR (MH "Pregnancy Outcomes") OR (AB obstetric* OR TI obstetric*)

Use the search history. Combine search 1 and search 2 using AND. On the results screen, select the Source Type limit of “academic journals.”