



# Cardiac magnetic resonance imaging characteristics and pregnancy outcomes in women with Mustard palliation for complete transposition of the great arteries



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## ABSTRACT

**Background:** Women with transposition of the great arteries (TGA) following atrial redirection surgery are at risk of pregnancy-associated arrhythmia and heart failure. The cardiovascular magnetic resonance imaging (CMR) characteristics of these women and the relationship of CMR findings to pregnancy outcomes have not been described.

**Methods:** We included 17 women with atrial redirection surgery and CMR within 2 years of delivery.

**Results:** All women were asymptomatic at baseline (New York Heart Association Class 1). CMR studies were completed pre-pregnancy in 3, antepartum/peripartum in 2, and postpartum in 12 women. Three women (3/17, 18%) experienced major cardiovascular events related to pregnancy: cardiac arrest (n = 1) and symptomatic atrial arrhythmia (n = 2). Median gestational age at delivery was 38 weeks (24–39 weeks) and birth weight was 2770 g (2195–3720 g). Complications were seen in 3 offspring (3/17, 18%): death (n = 1) and prematurity (n = 2). CMR characteristics included median right ventricular end diastolic volume 119 mL/m<sup>2</sup> (range 85–214 mL/m<sup>2</sup>) and median right ventricular ejection fraction (RVEF) 37% (range 30–51%). All women with cardiovascular complications had an RVEF <35% (range 32–34%). The association between RVEF <35% and cardiovascular complications trended towards statistical significance (p = 0.05). No statistically significant differences in CMR measurements were found between those with and without neonatal complications.

**Conclusions:** While the majority of women in this cohort had successful outcomes following pregnancy, important cardiovascular complications were seen in a significant minority, all of whom had an RVEF <35%. The preliminary findings of our study provide impetus for a larger prospective study to evaluate the prognostic role of CMR in pregnant women with atrial redirection surgery.

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## 1. Introduction

Right ventricular (RV) systolic dysfunction is a predictor of mortality in non-pregnant adults with a systemic RV [1–3]. Given

**Abbreviations:** ACHD, Adult congenital heart disease; BP, Blood pressure; CMR, Cardiovascular magnetic resonance imaging; EF, Ejection fraction; NYHA, New York Heart Association; RVEDV, Right ventricular end diastolic volume; RVEF, Right ventricular ejection fraction; RV, Right ventricle; SSFP, Steady state free precession; TGA, Transposition of the great arteries; TR, Tricuspid valve regurgitation.

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invariable hemodynamic adaptations to pregnancy, including prolonged augmentation of cardiac output, pregnant women with atrial redirection (Mustard or Senning operations) for underlying transposition of the great arteries (TGA) are at increased risk of heart failure and arrhythmias [4–7]. Accordingly, contemporary guidelines suggest in general terms that women with “more than moderate systemic RV dysfunction” should be advised against pregnancy [8]. In contradistinction to those with systemic left ventricular systolic dysfunction where adverse cardiovascular events in pregnancy are known to be more common with an ejection fraction (EF) less than 40% [9], a precise threshold RVEF for the systemic RV has not been defined, as all published studies to date have examined RV function only qualitatively using echocardiography alone [4–7].

Although cardiovascular magnetic resonance imaging (CMR) is considered to be the reference standard for quantification of RV volumes and function [10,11], there are as yet no data available regarding the CMR characteristics of women following atrial redirection surgery who undergo pregnancy. In this study, we sought to evaluate the relationship between CMR measurements of systemic RVEF and pregnancy outcomes in women who underwent atrial redirection surgery. We hypothesized that systemic RV dysfunction would be associated with increased risk of maternal and fetal/neonatal adverse events.

## 2. Methods

### 2.1. Study design

Women born with complete (D-loop) TGA palliated with atrial redirection surgery were retrospectively identified from institutional databases at two large Adult Congenital Heart Disease (ACHD) centers in Toronto (University Health Network/Mount Sinai Hospital) and Boston (Boston Children's Hospital/Brigham and Women's Hospital) from 1996 until 2011. The study cohort included consecutive women with atrial redirection surgery who had CMR imaging completed within 2 years of their delivery date [5]. Patients were excluded if CMR datasets were incomplete. The Research Ethics Boards of each respective institution approved this study.

### 2.2. Patient population

Baseline demographic data were recorded at the first clinic visit in the first trimester of pregnancy, including age, New York Heart Association (NYHA) functional class, baseline blood pressure (BP), parity status, associated cardiovascular lesions, medications, and history of previous cardiovascular events. A completed pregnancy was defined as >20 weeks gestation. Follow-up clinical data were obtained from available maternal and pediatric records. Maternal echocardiographic reports at baseline (prior to pregnancy or in first trimester), during pregnancy (second or third trimester) and post delivery (preferably >6 months post-partum) were reviewed for ventricular dimensions, ventricular systolic function, baffle stenosis/leak, outflow obstruction, and degree of tricuspid (systemic atrioventricular) valve regurgitation (TR). Severity of TR was graded as none, mild, moderate or severe according to published criteria [12].

### 2.3. Adverse outcomes

Adverse outcomes were classified as cardiovascular, obstetric and fetal/neonatal outcomes, as previously defined [9]. Cardiovascular events were defined as: 1) pulmonary edema (documented on chest radiograph or by crackles heard over more than one-third of posterior lung fields), 2) decline in NYHA functional class ( $\geq 2$  classes) compared with baseline or need for urgent invasive cardiac procedures during pregnancy or within 6 months of delivery, 3) sustained tachyarrhythmia requiring medical therapy or intervention, 4) stroke, and 5) cardiac arrest and/or cardiac death. Obstetric events were defined as: 1) pregnancy-induced hypertension (blood pressure increase of systolic pressure  $\geq 30$  mm Hg and diastolic pressure  $\geq 15$  mm Hg over pregnancy values), 2) pre-eclampsia (de novo hypertension with BP  $\geq 140$  mm Hg or diastolic BP  $\geq 90$  mm Hg and accompanied by new-onset proteinuria  $> 0.3$  g/24 h) or eclampsia [8], 3) pre-term labor, 4) post-partum hemorrhage (blood loss  $> 500$  mL after vaginal delivery or  $> 1000$  mL after cesarean section warranting transfusion or a drop in hemoglobin  $\geq 20$  g/L), and 5) non-cardiac obstetric maternal death. Fetal/neonatal events were defined as: 1) fetal death (categorized as stillbirth if  $\geq 20$  weeks gestation or spontaneous abortion if  $< 20$  weeks gestation) or neonatal death (within 28 days of birth), 2) premature delivery ( $< 37$  weeks of gestation), 3) small for gestational weight

( $< 10$ th percentile), 4) respiratory distress syndrome, and 5) cerebral hemorrhage.

### 2.4. Cardiovascular magnetic resonance imaging (CMR)

All CMR studies were performed on commercially available 1.5 T whole-body scanners with phased array surface coils. All CMR datasets were acquired in expiratory breath-hold. Retrospectively ECG gated cine steady state free precession (SSFP) in axial and short-axis slice orientation was acquired with contiguous volume coverage (6–8 mm slice thickness with 2 mm interslice gap). Representative spatial resolution was  $1.3 \times 1.3 \times 0.8$  mm and temporal resolution was  $\leq 50$  msec. Systemic RV and subpulmonic left ventricular volumes were contoured on SSFP cine imaging according to previously described methodology [13]. For the purposes of this study, all images were analyzed by a single experienced observer (LJJ) using a dedicated workstation and commercial software (Argus, Siemens Healthcare, Erlangen, Germany) in a core laboratory at the University Health Network, Toronto. Moderate RV systolic dysfunction was defined as RVEF  $< 35\%$  as previously established in non-pregnant adults with atrial redirection surgery for complete TGA [3,14–16].

### 2.5. Statistical analysis

Statistical analysis was performed using SPSS software version 20 (IBM SPSS Statistics 20, 2011). Continuous variables were described using means and standard deviation or medians and ranges, as appropriate. Categorical variables were described using frequencies and percentages. Multiple cardiovascular complications in a woman or multiple fetal/neonatal complications in a baby were counted as a single outcome event in the mother or child, respectively. The relationship between continuous variables was evaluated using the Spearman correlation co-efficient. The Mann–Whitney U test was used to compare CMR measurements in those with and without adverse events in pregnancy. Univariate logistic regression analysis was used to examine the effect of RVEF on the odds of an adverse outcome of pregnancy. Fisher exact test was used to assess the association between various RVEF thresholds and adverse cardiovascular events in pregnancy and likelihood ratios were used to obtain the optimal cut-off. McNemar Bowker test was used to compare echocardiographic parameters at baseline, during pregnancy and post-partum. A  $P$  value  $< 0.05$  was considered statistically significant.

## 3. Results

### 3.1. Clinical characteristics

A total of 17 women with 17 completed pregnancies met inclusion criteria (7 from Boston and 10 from Toronto). Women with atrial redirection surgery comprised approximately 9% of the overall cohort of pregnant women with congenital heart disease followed in Boston [17] and 4% of the pregnant women followed in Toronto [9]. Atrial redirection surgery consisted of the Mustard palliation for all of the women included in this study. None of the women had a Senning procedure for atrial redirection. All women were asymptomatic at baseline assessment (NYHA functional class 1). Clinical characteristics of the study population are summarized in Table 1. Echocardiographic data at baseline, antepartum, and post-partum are shown in Table 2. The majority of women did not have appreciable changes in RV global systolic function on echocardiography, as demonstrated by Fig. 1, although 3 women with mild RV systolic dysfunction at baseline had moderate RV systolic dysfunction following pregnancy.

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