



## Location matters: left heart obstruction in pregnancy



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### ABSTRACT

**Objectives:** Left heart obstruction in pregnancy is associated with higher rates of morbidity/mortality. The primary aim of this study was to evaluate maternal cardiovascular, obstetric, and fetal/infant events in pregnant women with left heart obstruction.

**Study design:** Pregnant women with current or repaired left heart obstruction were retrospectively analyzed (2000–2014): mitral stenosis, left ventricular outflow tract obstruction (subvalvar, valvar, supra-valvar), and coarctation of the aorta. Maternal cardiovascular events were defined as: heart failure, arrhythmia, urgent/emergent cardiac surgery or percutaneous transcatheter intervention, transient ischemic attack/cerebrovascular accident, and death up to 6 months postpartum.

**Results:** There were 90 pregnancies in 67 women (29 ± 7 years old) who had 15 maternal cardiovascular events. Isolated mitral stenosis ( $n = 6$ ) or >1 serial left heart obstructive lesion ( $n = 6$ ) were the source of the event in the majority pregnancies. Women with isolated mitral stenosis had increased cardiovascular events compared to other single left heart obstructive lesions (OR 18.6, 95% CI: 3.8–91.1). If >1 serial obstructive lesion was present, there was also an increased risk of maternal cardiovascular events (OR 6.8, 95% CI: 1.6–29.1), however isolated mitral stenosis carried similar risk to serial left heart obstructive lesions (OR 2.7, 95% CI: 0.7–11.2).

Baseline characteristics associated with events included: New York Heart Association functional class >2 (27% vs. 0,  $p < 0.001$ ), any current left heart obstruction (73% vs. 36%,  $p = 0.01$ ), severe left heart obstruction (40% vs. 29%,  $p < 0.001$ ), and higher Cardiac Disease in Pregnancy (“CARPREG”) score ( $1.2 \pm 0.7$  vs.  $0.5 \pm 0.7$ ,  $p = 0.01$ ). There was no difference in rate of obstetric/fetal/infant complications in women with cardiovascular events; however, term birth weight was lower ( $2.7 \pm 0.5$  vs.  $3.1 \pm 0.6$  kg,  $p = 0.01$ ). There was no maternal mortality.

**Conclusions:** Isolated mitral stenosis and serial (>1) left heart obstructive lesions carry the highest risk of maternal cardiovascular events. We are the first to show higher event rates in women with serial left heart obstructive lesions. The data supports the need for specialized and experienced high-risk obstetric-cardiac teams to care for women with left heart obstruction, and demonstrates excellent outcomes in a complex cohort of pregnant women with all types of left heart obstruction.

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### Introduction

Increased cardiovascular demand in the setting of pregnancy is accomplished in part by augmenting cardiac output with higher heart rate and increased stroke volume. For women

with pre-existing left heart obstruction, meeting the demand for increased stroke volume can be difficult. Individual types of left heart obstruction, such as aortic stenosis, have been evaluated in pregnancy. No group, however, has evaluated maternal cardiovascular, obstetric, and fetal/infant events in a comprehensive group of women with all types of left heart obstruction (current or history of obstruction) who undergo pregnancy, labor, and delivery. The goal of the present study was to evaluate maternal cardiovascular, obstetric, and fetal events in pregnant women with current or prior left heart obstruction.

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## Methods

Pregnant women with left heart obstruction were retrospectively analyzed (2000–2014). Cardiovascular lesions causing left heart obstruction included: mitral stenosis (MS), left ventricular outflow tract obstruction (LVOTO: subvalvar, valvar, supra-valvar), Coarctation of the Aorta (CoA), and combination disease with more than one level of left heart obstruction. Patients with current or surgically corrected left heart lesions were included. All women were seen by a multi-disciplinary team which included: high risk maternal fetal medicine obstetricians, cardiologists with expertise in the management of adult congenital heart disease and pregnancy, and cardiac anesthesiologists, as well as nurses and social workers from each of these disciplines.

Basic demographic data was collected and included: age, number of pregnancies, height, weight, tobacco use history, presence of hypertension prior to pregnancy, history of prior cardiac event [1] (heart failure, transient ischemic attack, cerebrovascular accident, or arrhythmia), left ventricular ejection fraction, prior heart surgery, and medication history. Additionally, we collected and analyzed pre-pregnancy (up to 12 weeks gestation) and post-pregnancy echocardiograms as well as advanced cardiac imaging (cardiac computed tomography or magnetic resonance imaging) to evaluate mean and peak gradients, valve area when applicable, and heart function. Current left heart obstruction was defined as: mitral valve area  $<2\text{ cm}^2$  with mean gradient  $>5\text{ mmHg}$   $\pm$  pulmonary artery pressure  $>30\text{ mmHg}$ , aortic valve area  $<1.5\text{ cm}^2$  with LVOT mean/peak gradient  $\geq 20/36\text{ mmHg}$ , or in the case of CoA a peak isthmus gradient  $\geq 20\text{ mmHg}$ . Severe left heart obstruction was defined by previously published criteria including aortic valve (subvalvar, valvar, supra-valvar) mean/peak gradient  $\geq 40/60\text{ mmHg}$  or valve area  $\leq 1.0\text{ cm}^2$ , mitral valve mean gradient  $\geq 10\text{ mmHg}$  or valve area  $\leq 1.0\text{ cm}^2$ , or CoA peak gradient  $\geq 30\text{ mmHg}$  [2,3].

Each pregnancy was evaluated independently to determine if there were any maternal cardiovascular events (CV event) up to 6 months post-partum. Cardiovascular events were defined as: heart failure (New York Heart Association/NYHA functional class  $>2$ , pulmonary edema, new or increasing diuretic dose), arrhythmia, urgent/emergent cardiac surgery or percutaneous trans-catheter intervention, transient ischemic attack or stroke, and death.

Obstetric events evaluated included: antepartum hemorrhage ( $>24$  weeks gestation), pregnancy induced hypertension ( $>140/90\text{ mmHg}$  after 20 weeks gestation), pre-eclampsia ( $>300\text{ g/L}$  24 hours proteinuria or  $++$  dipstick), eclampsia (preeclampsia plus seizures), gestational diabetes, preterm premature rupture of membranes ( $<37$  weeks gestation), pre-term labor ( $<37$  weeks gestation), postpartum hemorrhage ( $>500\text{ mL}$  vaginal or  $1000\text{ mL}$  cesarean section delivery), and venous thromboembolism. Descriptive characteristics of the type of labor and assistance in the second stage of labor were also collected. Fetal and infancy complications evaluated were: preterm birth (24–37 weeks gestation), small for gestational age ( $<5$ th percentile), birth weight, respiratory distress syndrome, intraventricular hemorrhage, fetal demise (death  $>20$  weeks gestation), perinatal mortality (still birth  $>24$  weeks to death 1 week post-birth), and neonatal mortality (death up to 1 month of age). Respiratory distress syndrome and intraventricular hemorrhage were assessed from the clinical chart and recorded if listed in the diagnosis.

The local institutional review board approved this retrospective study. Descriptive data for maternal, obstetric, and fetal events were generated. Comparisons were made between pregnancies with or without cardiovascular event. Continuous variables were evaluated with independent *T*-tests, and categorical and ordinal variables were evaluated with Fisher's exact tests. Risk of specific type of obstructive lesion was evaluated with an

odds ratio. Pre-pregnancy echocardiographic data and post-partum echo data were compared in all patients when available and assessed with paired *T*-tests. All significance tests were evaluated with a type I error rate of 5% ( $\alpha = 0.05$ ). Data are presented as means with standard deviation and/or frequency (%). The data were analyzed using SPSS (IBM Corp. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY).

## Results

There were 90 pregnancies in 67 women with left heart obstruction ( $29 \pm 7$  years, Gravida  $2.3 \pm 1.3$ ). All women had a current or prior (repaired) diagnosis of at least one lesion causing left heart obstruction (Bicuspid aortic valve/BAV = 34, Unicuspid aortic valve/UAV = 2, CoA = 28, MS = 13, Other = 13). Diagnoses in women with "other" types of obstruction included: subaortic membrane, Shone's complex [4], combination MS and AS, AS post AVR, and transitional AV canal defect with AS. Within this cohort, there were 25 pregnancies in women with at least two left heart obstructive lesions (second lesion: BAV = 16, CoA = 2, Other = 7). There were 3 patients with Shone's complex. Of the 90 pregnancies that occurred, 15 were complicated by maternal cardiovascular events. Table 1 outlines baseline characteristics of the entire cohort and of those with and without maternal cardiovascular events.

Mitral stenosis was the single most common isolated diagnosis ( $n = 6$ ) present in the 15 (17%) pregnancies complicated by a maternal cardiovascular event. However, an equal number of women ( $n = 6$ ) had serial left heart obstructive lesions associated with a maternal cardiovascular event. The absolute risk of a maternal CV event with each diagnosis was: single non-mitral left heart obstructive lesion: 4/100 pregnancies,  $>1$  serial left heart obstructive lesions 24/100 pregnancies, and isolated mitral stenosis 46/100 pregnancies. Women with isolated MS had increased CV events compared to women with other single left heart obstructive lesions (OR 18.6, 95% CI: 3.8–91.1). In pregnancies complicated by  $>1$  serial obstructive lesion, there was also an increased risk of maternal CV events (OR 6.8, 95% CI: 1.6–29.1), however isolated MS carried similar risk to serial left heart obstructive lesions (OR 2.7, 95% CI: 0.7–11.2). Specific details regarding maternal cardiovascular events in pregnancy are detailed in Table 2.

Women were more likely to have a CV event during pregnancy if they had elevated baseline NYHA functional class (27%(4) vs. 0(0),  $p < 0.001$ ), any current left heart obstruction (73%(11) vs. 36%(28),  $p = 0.01$ ), current severe left heart obstruction (60%(9) vs. 10%(5),  $p < 0.001$ ), and higher baseline CARPREG score ( $1.2 \pm 0.7$  vs.  $0.5 \pm 0.7$ ,  $p = 0.01$ ) (Table 1, Fig. 1). There was no difference in adverse CV events in women with prosthetic mechanical valves (7% vs. 3%,  $p = 0.42$ ). Specific cardiac diagnoses associated with a CV event, as compared to rates of these diagnoses in women without CV events are listed in Fig. 2.

There was no significant difference in obstetric complications in those with or without a maternal cardiovascular event. Rates of vaginal delivery and Cesarean section were similar in women with and without cardiovascular events. Fetal/infant complications were not different between these two groups. However, term birth weight was lower in women with a cardiovascular event ( $2.7 \pm 0.5$  vs.  $3.1 \pm 0.6\text{ kg}$ ,  $p = 0.01$ ). One patient (BAV without current left heart obstruction) had intrauterine fetal death at 29 weeks gestation due to trisomy 18 in the fetus (accounting for the 1 case of fetal demise and perinatal mortality). Neonate death occurred at 3 weeks of age in the offspring of a patient with a normal functioning BAV. This infant had severe congenital aortic stenosis with successful percutaneous intervention, but died after the procedure due to severe sepsis (Table 3).

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