Mitral valve regurgitation in the fetus
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Significance/Background: Moderate to severe mitral valve regurgitation is rare in the fetus and is often secondary to primary mitral valve disorders. Among this is mitral valve dysplasia complex (MVD C), is a unique and rare form of left-sided heart disease that is characterized by a restrictive or intact atrial septum, dysplastic and incompetent mitral valve, aortic annular hypoplasia and dilated left ventricle. Patients with a prenatal diagnosis of MVDS have previously been reported to have an extremely poor prognosis with a high rate of fetal demise and neonatal death. The published literature on mitral valve regurgitation in the fetus, however, is limited. Clear predictors of outcomes are not available, and management strategies appear to be highly varied.

Specific Aims:
1) To describe a large cohort of fetuses with moderate to severe mitral valve regurgitation.
2) To determine what prenatal echocardiographic features in mitral valve regurgitation are associated with fetal demise and neonatal death.

Improved knowledge of the population and outcomes with mitral valve regurgitation will help 1) aid in prenatal counseling, and 2) guide future management decisions for fetuses diagnosed with mitral valve regurgitation. We propose that identification of this unique cardiovascular finding will allow us to develop novel strategies to improve outcomes for this patient population.

Brief Approach:
1. Study design: Retrospective cohort study. We will evaluate maternal and fetal variables as well as fetal echocardiographic variables, and their associations with outcomes listed. All echocardiographic measurements will be re-measured in a core lab fashion at our lab.
2. Study population:
   a. Inclusion criteria: All fetuses with normal cardiac connections and moderate to severe mitral valve regurgitation
   b. Exclusion criteria: Atrioventricular septal defects, twin-twin transfusion syndrome, tricuspid valve atresia, pulmonary valve atresia
3. Time period to be studied: 2005-2016
4. Independent /Intervention variables: List variables to be studied:
   a. Quantitative assessment of left and right heart structures: LA dimensions, MV annulus in diastole, LV length (diastole and systole), LV
volume (using the bullet method), aortic valve and ascending aorta diameters, tricuspid valve (TV) and pulmonary valve annulus diameter, RV end-diastolic length, CT ratio. *All reported z-scores are based on gestational age.*

**b. Qualitative assessment of MV, LV, PVs, FO:**

i. **MV**-- morphology, the presence of accessory chordal attachments, and echogenic papillary muscles,

ii. **LV**-- presence or absence and severity of endocardial fibroelastosis

iii. **Pulmonary veins**-- normal, dilated, or compressed,

iv. Patency and size of the **foramen ovale**.

**c. Cardiac Doppler evaluation:**

i. **Intracardiac Doppler measurements:** MV and TV inflow patterns and durations, MV and TV regurgitant jet color Doppler vena contracta width, LV pressure (maximum instantaneous MR jet velocity), and maximum instantaneous AS gradient and color Doppler jet width, direction of patent foramen ovale flow, cardiac output (RV, LV, combined when available)

ii. **Extracardiac Doppler measurements:** Resistance measures and flow patterns in the middle cerebral artery, umbilical artery, umbilical vein, and ductus venosus, VTI ratio in pulmonary veins

d. **Fetal biometry:** Measurement of the bi-parietal diameter, head circumference, femur length, and abdominal circumference. Fetal weight should be estimated using the method of Hadlock et al.

e. **Fetal interventions performed:** Aortic valvuloplasty, atrial septal intervention, antiarrhythmic therapy

f. Are there any special skills that will be necessary at centers that enroll patients? No

g. How will the PI “certify” centers regarding these skills (e.g. novel measurement or intervention)? Not applicable; re-measuring to be done by our center

5. Outcomes/Dependent variables:

a. **Primary outcome:** Fetal demise

b. **Secondary outcomes:**

i. Fetal or neonatal demise

ii. Improvement with fetal aortic valvuloplasty for cases in which the aortic valve is stenotic

6. Timeline: 1 years