Pregnancy and Heart Disease for the Generalist
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DISCLOSURES

I have no disclosures relevant to today’s talk
Cardiovascular Effects of Pregnancy

- Anatomic
  - Ventricular muscle mass increases (1st trimester)
  - End-diastolic volume increases (2nd and 3rd trimester)
  - End-systolic volume unchanged

- Physiologic
  - Plasma Volume
  - Blood Volume

Plasma Volume

- 45% increase above non-pregnant values
  - 1200 to 1600 mL in total

- Unclear mechanism
  - Possible initiated by nitric oxide–mediated vasodilation
  - Stimulating renin-angiotensin-aldosterone system
  - Possibly adaptive in reducing hemodynamic instability after blood loss
**Blood Volume**

- Plasma volume increases disproportionately to red blood cell mass
- Mild net anemia
- Maximal in the middle of the third trimester
- Possibly adaptive by decreasing viscosity
  - Countering increased thrombotic risk
  - Improved intervillous perfusion

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**Increased Cardiac Output**

Vascular changes

- General softening of vascular collagen
- Hypertrophy of the smooth muscle component
- Net increased compliance
- Further accentuated by vasodilator effects
  progesterone and prostaglandin

### Hemodynamic Changes During Normal Pregnancy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1st Trimester</th>
<th>2nd Trimester</th>
<th>3rd Trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood volume</td>
<td>↑</td>
<td>↑↑</td>
<td>↑↑↑</td>
</tr>
<tr>
<td>Cardiac volume</td>
<td>↑</td>
<td>↑↑ to ↑↑↑</td>
<td>↑↑↑ to ↑↑</td>
</tr>
<tr>
<td>Stroke volume</td>
<td>↑</td>
<td>↑↑↑</td>
<td>↑, ↔, or ↓</td>
</tr>
<tr>
<td>Heart rate</td>
<td>↑</td>
<td>↑</td>
<td>↑↑ or ↑↑↑</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>↔</td>
<td>↓</td>
<td>↔</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Pulse pressure</td>
<td>↑</td>
<td>↑</td>
<td>↔</td>
</tr>
<tr>
<td>SVR</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>
How do we risk stratify patients?

- No large randomized studies
- No standardized, evidence-based guidelines
- CARPREG score
- ZAHARA scoring
- WHO classification

Low Maternal/Fetal Risk

- Asymptomatic Aortic Stenosis
  - Low mean gradient less than 25 mmHg
  - Valve area greater than 1.5 cm²
  - Normal LV systolic function (EF > 50%)
- Aortic Regurgitation
  - NYHA functional class I or II
  - Normal LV systolic function
- Mitral Regurgitation
  - NYHA functional class I or II
  - Normal LV systolic function
Low Maternal/Fetal Risk

- Mitral Valve Prolapse
  - Up to mild to moderate MR
  - Normal LV systolic function
- Mild mitral stenosis
  - MVA greater than 1.5 cm²
  - Mean gradient less than 5 mmHg
  - Without severe pulmonary hypertension
- Mild to moderate pulmonary valve stenosis

High Maternal/Fetal Risk

- Severe AS with or without symptoms
- Aortic Regurgitation
  - NYHA functional class III-IV symptoms
- Mitral Stenosis
  - NYHA functional class II-IV symptoms
- Mitral Regurgitation
  - NYHA functional class III-IV symptoms
High Maternal/Fetal Risk

- Aortic and/or mitral valve disease
  - Resulting in severe pulmonary hypertension (>75% systemic)
  - Severe LV dysfunction (EF < 40%)
- Mechanical prosthetic valve requiring anticoagulation
- Marfan syndrome with or without AR
- Pulmonary hypertension
- Cyanotic heart disease

Marfan’s

- Collagen and vascular changes in pregnancy
- Increased risk for dissection for aorta > 4-4.5 cm in diameter
- Continue beta blockers
- Surveillance echocardiography imaging every 6-8 weeks
- Invasive arterial pressure monitoring and assisted second stage
CARPREG Study

- Prospective study of 562 pregnant women with heart disease in Canada between 1994-1999.
- 546 women underwent 599 pregnancies.
- Live birth rate-98%
- 27% C-section
  - 96% for obstetrical reasons

CARPREG – Four Risk Factors

- Prior cardiac event
  - Heart failure
  - TIA or CVA
  - Arrhythmia
- Baseline NYHA class III-IV or cyanosis
- Left heart obstruction
  - MV area <2 cm²
  - AV area <1.5 cm²
  - Peak LVOT gradient >30 mmHg
- Myocardial dysfunction
  - Ejection fraction <40%
  - Hypertrophic cardiomyopathy
  - Restrictive cardiomyopathy
CARPREG Risk Index

ZAHARA I Study

- Retrospective study of 1802 patients with congenital heart disease
- Cardiac complications
  - Arrhythmia
  - Heart failure
  - Thrombo-embolic events/MI/CVA
  - Endocarditis
- Obstetric complications
  - Pregnancy induced hypertension
  - Preeclampsia/Eclampsia/HELLP
  - Premature labor
  - Post-partum hemorrhage
- Neonatal Complications
  - Premature delivery
  - SGA
  - Offspring mortality

TABLE 4. Accuracy of Risk Index

<table>
<thead>
<tr>
<th>No. of Predictors</th>
<th>Rate of Primary Cardiac Events</th>
<th>Rate of Primary or Secondary Cardiac Events, Revised Index</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimated Risk, %</td>
<td>Derivation Group, Revised Index</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Revised Index</td>
</tr>
<tr>
<td>0</td>
<td>5</td>
<td>7/249 (3%)</td>
</tr>
<tr>
<td>1</td>
<td>27</td>
<td>27/111 (24%)</td>
</tr>
<tr>
<td>&gt;1</td>
<td>75</td>
<td>15/25 (6%)</td>
</tr>
<tr>
<td>C statistic (95% CI)</td>
<td>0.83</td>
<td>0.80</td>
</tr>
</tbody>
</table>


THE OHIO STATE UNIVERSITY
WILLIAMSAW MEDICAL CENTER
ZAHARA I Results

- 1302 completed pregnancies

<table>
<thead>
<tr>
<th>Complication</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>7.6%</td>
</tr>
<tr>
<td>Obstetrical</td>
<td>24%</td>
</tr>
<tr>
<td>Neonatal</td>
<td>25%</td>
</tr>
</tbody>
</table>

--Drenthen W et al. Eur Heart J 2010;31:2124-2132

ZAHARA I Scoring

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of arrhythmias</td>
<td>1.50</td>
</tr>
<tr>
<td>Cardiac medication before pregnancy</td>
<td>1.50</td>
</tr>
<tr>
<td>NYHA class prior to pregnancy &gt;= II</td>
<td>0.75</td>
</tr>
<tr>
<td>LHO (PG &gt; 50 mmHg or AVA &lt; 1.0 cm2)</td>
<td>2.50</td>
</tr>
<tr>
<td>Systemic AV valve regurgitation (moderate/severe)</td>
<td>0.75</td>
</tr>
<tr>
<td>Pulmonary AV valve regurgitation (moderate/severe)</td>
<td>0.75</td>
</tr>
<tr>
<td>Mechanical valve prosthesis</td>
<td>4.25</td>
</tr>
<tr>
<td>Cyanotic heart disease (corrected/uncorrected)</td>
<td>1.00</td>
</tr>
<tr>
<td>TOTAL POSSIBLE</td>
<td>13.00</td>
</tr>
</tbody>
</table>

--Drenthen W et al. Eur Heart J 2010;31:2124-2132
ZAHARA I

Prospective study involving women with structural heart disease

2008-2010

ZAHARA II
WHO Classification

- Based on underlying diagnosis in addition to any other co-morbidity
- It includes contra-indications for pregnancy not found in other scoring systems
- Recommended by European Society of Cardiology (ESC)
WHO Classification

<table>
<thead>
<tr>
<th>Risk class</th>
<th>Risk of pregnancy by medical condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>No detectable increased risk of maternal mortality and moderate increase in morbidity.</td>
</tr>
<tr>
<td>II</td>
<td>Small increased risk of maternal mortality or moderate increase in morbidity.</td>
</tr>
<tr>
<td>III</td>
<td>Significantly increased risk of maternal mortality or severe morbidity. Expert counselling required. If pregnancy is decided upon, intensive specialist cardiac and obstetric monitoring needed throughout pregnancy, childbirth, and the puerperium.</td>
</tr>
<tr>
<td>IV</td>
<td>Extremely high risk of maternal mortality or severe morbidity; pregnancy contraindicated. If pregnancy occurs termination should be discussed. If pregnancy continues, care as for class III.</td>
</tr>
</tbody>
</table>

WHO I: Low-risk

- Cardiology follow-up may be limited to 1-2 visits throughout pregnancy

- Conditions in which pregnancy risk is WHO I
  - Uncomplicated, small or mild pulmonary stenosis
  - Patent ductus arteriosus
  - Mitral valve prolapse
  - Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage)
  - Atrial or ventricular ectopic beats, isolated
WHO II: Low/Moderate Risk

- Follow-up once a trimester

WHO II (If otherwise well and uncomplicated)

- Unoperated atrial or ventricular septal defect
- Repaired tetralogy of Fallot
- Most arrhythmias

WHO II-III (depending on individual)

- Mild left ventricular impairment
- Hypertrophic cardiomyopathy
- Native or tissue valve heart disease not considered WHO I or IV
- Marfan syndrome without aortic distortion
- Aorta <45 mm in aortic disease associated with bicuspid aortic valve
- Aortic coarctation

WHO III: High Risk

- Monthly-to-bimonthly cardiology and OB follow-up

WHO III

- Mechanical valve
- Systemic right ventricle
- Fontan circulation
- Cyanotic heart disease (unrepaired)
- Other complex congenital heart disease
- Aortic dissection 40-45 mm in Marfan syndrome
- Aortic dissection 45-50 mm in aortic disease associated with bicuspid aortic valve
WHO IV: Pregnancy Contra-indicated

Conditions in which pregnancy risk is WHO IV (pregnancy contra-indicated)

- Pulmonary arterial hypertension of any cause
- Severe systemic ventricular dysfunction (LVEF <30%, NYHA III–IV)
- Previous peripartum cardiomyopathy with any residual impairment of left ventricular function
- Severe mitral stenosis, severe symptomatic aortic stenosis
- Marfan syndrome with aorta dilated >45 mm
- Aortic dilatation >50 mm in aortic disease associated with bicuspid aortic valve
- Native severe coarctation

Imaging in Pregnancy

- Echo
- MRI
- X-ray
- CT
- Nuclear Imaging
- Angiography

No Radiation Exposure; Tests of Choice
Iodizing Radiation

- Majority of fetal exposure from cardiothoracic imaging is from scatter (Compton) radiation
- Shielding fetus is of little value

**TABLE 3: Cardiac Imaging with Radiography, Fluoroscopy, and CT**

<table>
<thead>
<tr>
<th>Examination</th>
<th>Estimated Fetal Dose (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest radiography</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Pulmonary CTA</td>
<td>0.01–0.66</td>
</tr>
<tr>
<td>Coronary CTA (prospective gating)</td>
<td>~ 1</td>
</tr>
<tr>
<td>Coronary CTA (retrospective gating)</td>
<td>~ 3</td>
</tr>
<tr>
<td>Abdominal pelvic CTA</td>
<td>6.7–56</td>
</tr>
<tr>
<td>Direct fluoroscopy for groin-to-heart catheter passage*</td>
<td>0.004–0.244/min</td>
</tr>
<tr>
<td>Coronary angiography</td>
<td>0.074</td>
</tr>
<tr>
<td>Complex electrophysiologic intervention</td>
<td>0.0923–0.012/min</td>
</tr>
</tbody>
</table>

*Note—Reasonable estimates are presented. Fetal exposure increases as the fetus grows and ascends toward the maternal thorax. Larger patients requiring greater peak kilovoltage and tube current will have greater secondary fetal exposure. CTA = CT angiography.

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Radionuclide Exposure

**TABLE 4: Doses to the Fetus From Nuclear Medicine Examinations**

<table>
<thead>
<tr>
<th>Examination</th>
<th>Activity(nCi)</th>
<th>Radionuclide and Exposure</th>
<th>Early Pregnancy Fetal Dose (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung perfusion</td>
<td>5.5(203)</td>
<td>99mTc-macroaggregated albumin (P)</td>
<td>0.56</td>
</tr>
<tr>
<td>Lung ventilation</td>
<td>30(1000)</td>
<td>123I gas</td>
<td>0.0105</td>
</tr>
<tr>
<td>Lung ventilation</td>
<td>30(1000)</td>
<td>123I Tc aerosol</td>
<td>0.1–1.9</td>
</tr>
<tr>
<td>Myocardial perfusion</td>
<td>30(1000)</td>
<td>99mTc Tc-estradiol (P)</td>
<td>1.2</td>
</tr>
<tr>
<td>Myocardial perfusion</td>
<td>30(1000)</td>
<td>99mTc-teledosin (P)</td>
<td>0.45</td>
</tr>
<tr>
<td>Gated blood pool</td>
<td>55(500)</td>
<td>99mTc-tagged RBCs (P)</td>
<td>5.0</td>
</tr>
<tr>
<td>PET viability</td>
<td>19(567)</td>
<td>18F-FDG (P, F, A)</td>
<td>0.5–3.8</td>
</tr>
<tr>
<td>PET perfusion</td>
<td>85(2560)</td>
<td>18F-FDG (P, F, A)</td>
<td>&gt; 2</td>
</tr>
</tbody>
</table>

*Note—Data from [30, 32]. Values in parentheses are megabecquerels. Minimal hydration and frequent voiding can reduce the fetal dose after administration of a number of radiopharmaceuticals, especially 123I-macroaggregated albumin, 99mTc sestamibi, 99mTc tetrofosmin, and 18F-FDG. P = likely to enter amniotic circulation. A = likely to cross placental barrier. F = likely to enter fetal circulation.

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## Radiation Exposure

### TABLE 2: Recommendations Regarding Fetal Irradiation

<table>
<thead>
<tr>
<th>Fetal Estimated Exposure (mGy)</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 (total gestation)</td>
<td>General public limit</td>
</tr>
<tr>
<td>&lt; 5 (0.50/mo)</td>
<td>Nuclear Regulatory Commission fetus exposure limit</td>
</tr>
<tr>
<td>Fetal dose &lt; 50</td>
<td>Fetal risk negligible</td>
</tr>
<tr>
<td>Fetal dose &lt; 100</td>
<td>Termination not justified</td>
</tr>
<tr>
<td>Fetal dose 100–150</td>
<td>Consider individual circumstances</td>
</tr>
<tr>
<td>Fetal dose &gt; 150</td>
<td>Possible fetal damage; termination should be seriously considered</td>
</tr>
<tr>
<td>Fetal dose &gt; 200</td>
<td>Termination generally recommended</td>
</tr>
</tbody>
</table>


## Contrast Agents

- **Iodinated contrast**
  - Readily cross placenta
  - Pregnancy Class B
  - Use only if necessary
- **Gadolinium-based contrast**
  - Easily cross placenta
  - Pregnancy Class C
  - Avoid if possible
  - Enters breast milk
FDA Drug Classification for Pregnancy

- Class A: Controlled clinical studies in humans show safety
- Class B: Human data reassuring (animal positive), animal studies show no risk.
  - Dobutamine
  - Normal saline
- Class C: Human data lacking, animal studies positive or not done (67%)
  - Adenosine
  - Echo contrast agents (Definity, Optison)
- Class D: Human data show risk, benefit may outweigh risk.
- Class X: Animal or human data positive for unacceptable risk.

Agitated saline (Bubble) studies and Pregnancy

- There is currently no data looking at the safety of bubble studies in pregnant women
- Generally felt as safe based on concept that normal saline is a category B drug to use in pregnancy (considered safe)
- Case reports of CVA/TIA in patients undergoing bubble studies
- Would wait until after first trimester if feasible
Residual Intracardiac Shunting

- Theoretical risk of paradoxical emboli
- Aspirin 81 mg daily
- IV filters

References

THANK YOU