Cardiac Disease in Pregnancy

Outline

- Scope of the “problem”
- Physiology of pregnancy
- Cardiac risk in pregnancy
- Pregnancy management
- Contraception
Mortality in Pregnancy


http://www.cdc.gov/reproductivehealth/MaternalInfantHealth/PMSS.html#m8

Mortality in Pregnancy


http://www.cdc.gov/reproductivehealth/MaternalInfantHealth/PMSS.html#m8
Changing face of congenital heart disease

Figure 1: Distribution of Age at Death in Patients With Congenital Heart Disease in 1993-1998 and 2004 to 2005

Khairy et al. JACC 2010; 56:1149-57

Pregnancy Physiology
Physiology of Pregnancy

- Heart rate
- Cardiac output
- Plasma volume
- RBC Mass
- Hematocrit

% change from prepregnancy value

Duration of pregnancy (weeks)

Labor Stages

1. Onset of painful, regular contractions until full cervical dilation

2. Full cervical dilation until birth

3. Birth until expulsion of the placenta and membranes
Valsalva Maneuver

1.Expiration against closed glottis: ↑ intrathoracic pressure, baroreceptor activation
2. ↑HR, ↓CO and BP
3. ↑Vascular tone and BP recovers
4. Overshoot of MAP and reflex ↓HR
   • Decreased preload, increased afterload
   • Increased myocardial oxygen consumption
   • Decreased uterine perfusion

What do we know about cardiac risk in pregnancy?
CARPREG Study

- Prospective multicenter study of pregnancy outcomes in women with heart disease
  - 562 women enrolled; total of 599 pregnancies not ending in miscarriage

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N</th>
<th>(%)</th>
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<tbody>
<tr>
<td>Age 18-35</td>
<td>532</td>
<td>(86)</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>359</td>
<td>(58)</td>
</tr>
<tr>
<td>NYHA FC I-II</td>
<td>575</td>
<td>(96)</td>
</tr>
<tr>
<td>Prior HF, TIA, CVA</td>
<td>24</td>
<td>(4 )</td>
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<tr>
<td>No cardiac medications</td>
<td>550</td>
<td>(89)</td>
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</table>


<table>
<thead>
<tr>
<th>Congenital heart disease</th>
<th>N</th>
<th>(%)</th>
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<tbody>
<tr>
<td>Shunts</td>
<td>142</td>
<td>(24)</td>
</tr>
<tr>
<td>AS/BAV</td>
<td>83</td>
<td>(14)</td>
</tr>
<tr>
<td>Pulmonary stenosis</td>
<td>58</td>
<td>(10)</td>
</tr>
<tr>
<td>TOF or DORV</td>
<td>53</td>
<td>(9 )</td>
</tr>
<tr>
<td>Coarctation</td>
<td>51</td>
<td>(9 )</td>
</tr>
<tr>
<td>D-TGA</td>
<td>25</td>
<td>(4 )</td>
</tr>
<tr>
<td>Ebstein anomaly</td>
<td>12</td>
<td>(2 )</td>
</tr>
<tr>
<td>Marfan syndrome</td>
<td>10</td>
<td>(2 )</td>
</tr>
<tr>
<td>L-TGA</td>
<td>6</td>
<td>(1 )</td>
</tr>
<tr>
<td>Fontan</td>
<td>5</td>
<td>(1 )</td>
</tr>
<tr>
<td>Cyanotic</td>
<td>4</td>
<td>(0.5)</td>
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<table>
<thead>
<tr>
<th>Acquired cardiac lesion</th>
<th>N</th>
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<tr>
<td>Valvular</td>
<td>81</td>
<td>(14)</td>
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<tr>
<td>Dilated CM</td>
<td>23</td>
<td>(4 )</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>21</td>
<td>(4 )</td>
</tr>
<tr>
<td>Ischemic</td>
<td>11</td>
<td>(2 )</td>
</tr>
<tr>
<td>Hypertrophic CM</td>
<td>9</td>
<td>(2 )</td>
</tr>
<tr>
<td>Sick sinus syndrome</td>
<td>6</td>
<td>(1 )</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>3</td>
<td>(0.5)</td>
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</table>
### CARPREG outcomes

#### Primary cardiac events
- Pulmonary edema
- Sustained arrhythmias
- CVA/TIA
- Cardiac arrest, cardiac death

#### Neonatal events
- Premature birth (< 37 weeks)
- SGA
- Respiratory distress syndrome
- Intraventricular hemorrhage
- Fetal death
- Neonatal death

#### Secondary cardiac events
- Change in NYHA class
- Need for an invasive procedure

#### Obstetric events
- Non-cardiac death
- Pregnancy-induced hypertension
- Post-partum hemorrhage

### CARPREG: cardiac events

- Primary cardiac event in 80 (13%) pregnancies
  - 91% were CHF or arrhythmia

- Embolic stroke in 4
  - Dilated cardiomyopathy
  - MVR with subtherapeutic INR
  - Mitral stenosis
  - D-TGA after Mustard with severe systemic ventricular dysfunction

- Death in 3: Sudden death x 2 (dilated cardiomyopathy, severe PHTN), postpartum heart failure (D-TGA after Mustard procedure)
CARPREG score & event rate

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR (95% CI)</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Prior cardiac event or arrhythmia</td>
<td>6.0 (3-14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NYHA FC &gt; II or cyanosis</td>
<td>6.0 (2-22)</td>
<td>0.009</td>
</tr>
<tr>
<td>Left heart obstruction</td>
<td>6.0 (3-14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systemic ventricular dysfunction</td>
<td>11.0 (4-34)</td>
<td>&lt;0.001</td>
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</table>

Alternate: ZAHARA score

<table>
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<tr>
<th>Risk factor</th>
<th>Points</th>
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<tr>
<td>Arrhythmia</td>
<td>1.5 pt</td>
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<tr>
<td>Cardiac meds</td>
<td>1.5 pt</td>
</tr>
<tr>
<td>NYHA&gt;II</td>
<td>0.75 pt</td>
</tr>
<tr>
<td>LHO</td>
<td>2.5 pt</td>
</tr>
<tr>
<td>Syst Av/VR (mod/lev)</td>
<td>0.75 pt</td>
</tr>
<tr>
<td>PR (mod/sev)</td>
<td>0.75 pt</td>
</tr>
<tr>
<td>Mechanical valve</td>
<td>4.25 pt</td>
</tr>
<tr>
<td>Cyanotic heart disease</td>
<td>1.0 pt</td>
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</table>

Drenthen et al. EHJ 2010; 31:2124-32
### WHO Classification

<table>
<thead>
<tr>
<th>WHO Class</th>
<th>Definition</th>
<th>Examples</th>
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<tr>
<td>WHO I</td>
<td>No increased risk of mortality</td>
<td>Mild PS</td>
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<tr>
<td></td>
<td>No/mild increased risk of morbidity</td>
<td>Repaired ASD/VSD</td>
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<tr>
<td>WHO II</td>
<td>Small increase in risk of mortality OR Moderate increase in risk of morbidity</td>
<td>Unoperated ASD/VSD</td>
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<tr>
<td></td>
<td></td>
<td>Repaired TOF</td>
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<tr>
<td>WHO III</td>
<td>Significantly increased risk of mortality or severe morbidity</td>
<td>Systemic RV Fontan circulation</td>
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<td></td>
<td></td>
<td>Cyanotic Marfan with root 40-45 mm</td>
</tr>
<tr>
<td>WHO IV</td>
<td>Pregnancy contraindicated</td>
<td>Pulmonary hypertension Systemic ventricle dysfunction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• EF &lt; 30%</td>
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<tr>
<td></td>
<td></td>
<td>• NYHA Class III-IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Severe AS or MS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Native severe coarctation</td>
</tr>
</tbody>
</table>

Brickner ML. Circulation 2014; 130:273-82/

### Other factors

- Mechanical valves
- Aortopathy
Mechanical valves: historical

- Maternal mortality rate 1-4%
  - Risk of valve thrombosis:
    - Warfarin alone: 3.9%
    - UFH in first trimester followed by warfarin: 9.2%
    - LMWH appears to be more efficacious and safer than UFH (~5-10% risk of thrombosis)
    - Contemporary data is limited
  - Warfarin crosses the placenta while heparin does not
    - Embryopathy (defects in cartilage and bone)
    - CNS abnormalities
    - Increased late fetal deaths
    - Hemorrhagic risk (mother and fetus)


Contemporary data

- Registry of pregnancy and cardiac disease (ROPAC)
- Multicenter, multinational
- Prospective enrollment
- 2008-2014

Summary of initial ROPAC results

- 212 women with mechanical valves
  - 10 patients with valve thrombosis, 5 of whom had been switched to heparin

- 23% rate of maternal hemorrhage

- VitK use in 1st trimester associated with 29% (vs 9%) miscarriage rate and 7% risk of late fetal death (vs 0.7%)

- Only 58% chance of pregnancy free of serious adverse event

Aortic disease in pregnancy

- Hormonal changes in pregnancy lead to changes in aortic histology
  - Increased risk of dissection
  - Most commonly in the 3rd trimester (50%) or early postpartum (33%)

- Risk depends on etiology of aortopathy
Pregnancy and CHD: Examples

Spectrum of ACHD complexity

**Simple**
- AV disease
- MV disease*
- PFO
- Small ASD or VSD
- Repaired PFO, ASD, VSD
- Mild PS

**Moderate**
- PAPVR, TAPVR
- AV Canal
- Coarctation
- Ebstein’s
- Sinus venosus ASD
- Primum ASD
- Tetralogy of Fallot
- RVOT obstruction
- Significant PV disease

**Great complexity**
- Conduits
- Cyanotic CHD
- Double outlet RV
- Fontan
- Eisenmenger
- PVOD
- TGA
- Truncus arteriosus
- Heterotaxy

Case #1

28 year old female with repaired Tetralogy of Fallot, severe PR, mildly decreased RV function

Tetralogy of Fallot

- 10% of all CHD
- Long-term considerations
  - Pulmonary regurg
  - RV dilation/dysfunction
  - LV dysfunction
  - Residual VSD
  - Arrhythmias
  - Aortic root dilated
TOF & Pregnancy

• General principles
  – Unrepaired women are high risk
  – Significant residual hemodynamic abnormalities should be addressed before pregnancy

• Reported cardiac event rates range from 7-20%
  – Most events occur in patients with severe RV dilation or dysfunction but others are still at risk


TOF: Does pregnancy increase long-term risk?

– Possible increased risk of adverse long-term outcomes in women who have been pregnant

FIGURE 1
Kaplan-Meier curve comparing parous women with nulliparous, nonpregnant controls

Parous women were more likely at any point in time to have or long-term composite adverse cardiac outcomes

Case #1: Recommendations

28 year old female with repaired Tetralogy of Fallot, severe PR, mildly decreased RV function

Case #2

32 year old with L-transposition of the great arteries, mild systemic right ventricular dysfunction and mild TR
L-TGA

- Congenitally-corrected

- Long-term sequelae
  - Systemic RV dysfunction
  - Tricuspid regurgitation
  - Heart block

L-TGA and pregnancy

- Systemic RV has an impaired ability to tolerate workload and increased demand of pregnancy
  - Higher risk of arrhythmia and HF
  - ~10% have an irreversible decline in RV function

- Severe TR, NYHA III-IV, systemic EF <40% should be counseled against pregnancy

Therrien et al. AJC 1999; 84:820-824
Connolly et al. AJC 1999; 33:1692-5
Kowalick et al. IJGO 2014; 124:154-7
Case #2: Recommendations

32 year old with L-transposition of the great arteries, mild systemic right ventricular dysfunction and mild TR

Case #3

30 year old with Marfan syndrome and aortic root= 4.8 cm
Specific aortic syndromes and risk in pregnancy

- **Marfan**
  - Normal root: risk of dissection 1%
  - Risk factors for dissection:
    - aortic root > 4 cm
    - Increasing aortic size during pregnancy
  - Pregnancy contraindicated with aorta > 4.5 cm
  - Dissection of residual aorta can occur after root replacement

- **Bicuspid aortic valve**
  - Risk of dissection not well understood
  - Pregnancy contraindicated if aorta > 5.0

- **Ehlers-Danlos Type IV**
  - Pregnancy contraindicated because of risk of uterine rupture

- **Turner syndrome**
  - Assess concomitant cardiac malformations
  - Dissection can occur without aortic dilatation
  - **Absolute** aortic size not helpful
    - Indexed aortic diameter > 27 mm/m² is associated with high risk of dissection
Case #3: Recommendations

30 year old with Marfan syndrome and aortic root= 4.8 cm

Case #4

38 year old female with severe valvular AS, normal LV function. Dyspnea with climbing stairs.
Aortic stenosis

• Pregnancy risk related to AS severity
  – Mild or moderate: well tolerated
  – Severe
    • <10% risk of heart failure
    • Up to 25% risk of arrhythmias*
    • Rare mortality
    • *Outcomes better in more contemporary series

AS & pregnancy

• Risk assessment
  – Pregnancy contraindicated if symptoms, impaired LV function
  – Pre-pregnancy exercise testing helpful to assess for symptoms, BP response
  – Aortic size > 50 mm pre-pregnancy → consider surgery (BAV)

• Pregnancy management of severe AS
  – Frequent monitoring
  – Percutaneous balloon valvuloplasty can be considered
  – Cesarean section with general anesthesia (possible)
Case #4: Recommendations

38 year old female with severe valvular AS, normal LV function

Pregnancy management and counseling
Preconception

• What is the risk of the pregnancy?
  – What, if anything, can be done to decrease it?
• What are the long-term risks to the woman?
• What is the risk of transmission of CHD?
  – ~3-5% in absence of a syndrome
• Are there acceptable alternatives to pregnancy?

Preconception

• What is the risk of the pregnancy?
  – History: symptoms, functional status?
  – Echocardiogram +/- MRI
    • Image entire aorta in aortopathy
  – Cardiopulmonary exercise test
  – Calculate CARPREG, ZAHARA or WHO score
  – Literature for disease-specific risk
### Risk of CHD transmission

- 3-5% of CHD is associated with a genetic syndrome

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Usual inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turner</td>
<td>Sporadic*</td>
</tr>
<tr>
<td>Trisomy 21</td>
<td>Sporadic</td>
</tr>
<tr>
<td>22q11 (DiGeorge)</td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td>Williams</td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td>Noonan’s</td>
<td>Autosomal dominant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Usual inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>VATER</td>
<td>Sporadic</td>
</tr>
<tr>
<td>Holt-Oram</td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td>Alagille</td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td>CHARGE</td>
<td>Autosomal dominant*</td>
</tr>
</tbody>
</table>

* Associated with reduced fertility

Bernier and Spaetgens. Cardiol Clinics 2006; 557-69.

### Pregnancy management

- Echo: 1<sup>st</sup> and 3<sup>rd</sup> trimester
- Fetal echo: 18-20 weeks
- Vaginal delivery usually preferred except:
  - Marfan with dilated root
  - Known dissection
  - Intractable heart failure
  - Oral anticoagulants in preterm labor
- Epidural anesthesia preferred
- Consider passive second stage in some cases
- Close postpartum follow-up! (High risk of events early postpartum)
Contraception

• Avoid estrogen containing contraceptives if increased risk of thrombosis
  – Arrhythmias
  – Mechanical valves
  – Single ventricles

• Vasovagal a risk with IUD insertion; may need to occur in hospital in severe lesions

Take home points

• Risk scores can be useful but individualized assessment is essential

• Best to assess risk and counsel prior to pregnancy
  • Start discussion early!

• Long-term risks are important but are currently hard to quantify
OHSU Maternal Cardiac Program

- Comprehensive care for women with known or suspected cardiac disease who are pregnant or contemplating pregnancy

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