Pregnancy and Heart Disease: approaches to risk
38th Hellenic Congress of Cardiology

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Heart Disease in Pregnancy: Growing Issue

• Leading cause of maternal death is maternal CVD
  – Rare 0.2-4% of pregnancy c/b CVD

• Congenital Heart Disease
  – Advances in early diagnosis and definitive treatment, women are living better and longer

• Acquired Heart Disease
  – Women are having children later in life
  – Access to care, immigration
26 yo w/ occasional DOE and moderate-severe mitral stenosis
38 yow with a dilated aorta

moderate aortic insufficiency
30 yow w/ asymptomatic, severe mitral regurgitation

32 yow w/ mechanical mitral valve replacement
Pregnancy and Heart Disease

Normal Pathophysiology
- Hemodynamic changes
- Structural & functional changes

Congenital & Acquired Heart Disease
- Preconception risk assessment:
  - Lesion & functional assessment
- Peripartum management
  - High vs low risk groups
Hemodynamic Changes in Pregnancy: Preload & Afterload

- **30-50% increase** in blood volume
  - plateaus 3rd trimester

- **10-20% decrease** in afterload
  - SBP 10mmHg
  - TPR 600 dynes/sec/cm²

Bonica & McDonald. Principles and Practice of Obstetric Analgesia and Anesthesia
Cardiac Output in Pregnancy

- 30-50% ↑ in cardiac output
- 10-20% ↑ in heart rate

Poppas Circ.1997
Cardiac Structural Changes

- Increase chamber dimensions
  - Atria and ventricles: 10-15% increase
- Small Pericardial effusions are common
  - 36-69% by 3rd trimester
- Contractility unchanged
  - Function (EF) increased
- Return to nml postpartum
  - Hemodynamics: 6 wks, structure: by 6mos

- Katz Circ ’78, Duvekot AJ Ob Gyn ’93, Robson Br J Ob Gyn ’87 & AJP ‘89
Normal Cardiovascular Adaptations to Pregnancy

- Hemodynamic Changes
  - Preload, afterload & CO
- Structural changes
  - Ventricle and effusions
- Functional changes
  - EF & contractility
Heart Disease in Pregnancy: How to approach individual patients

• Approach based on pathophysiology
  – Grouped based on defects, anticipated response to known physiologic changes
  – Similar outcomes, treatments, L&D rec

• Approach based on high risk markers
  – Studies have defined markers of maternal and neonatal morbidity and mortality
  – Ideal for preconception counseling

• Practical approach:
  – Who is at high risk? Who is at low risk?
Pathophysiology of pregnancy: Volume loaded defects well tolerated

• Physiology of Shunts: ASD, VSD, PDA
  – Increased volume offset by decrease afterload

• Caution:
  – Filters on IV
  – Epidural anesthesia for large shunts

• Exceptions:
  – Pulmonary HTN
  – Reduced EF
Thromboembolic risk with ASD:

Drenthen retrospective 2,491 pregnancies, 5% emboli/PE
Siu, prospective: 569 pregnancies, 76 shunts, no CVA

JACC 2007;49:2303
Pathophysiology: **mild** pressure loaded defects are well tolerated

- Afterload & HR negative effects
- Stenotic Valves:
  - Congenital Aortic and Rheumatic Mitral
- Hypertrophic Cardiomyopathy

- Exceptions:
  - Severe stenosis
  - Pulmonary HTN
  - Reduced LVEF
Severe, Symptomatic Mitral Stenosis

Increase in HR, flow, LAP

**Gradient** increases by sq. root of CO, 1.5x results in 2.3x increase gradient

Patients usually worsen during pregnancy and delivery, may be first diagnosed
Pregnancy and Mitral Stenosis

- Mortality < 1% women with minimal symptoms
  - Hameed A. JACC.2001

- Maternal risk related to severity
  - Most pts increase by one NYHA class
    - CHF: 26% mild, 38% moderate, 67% severe MS
      - Silversides AJC 2003;91:1382.

- Medical treatment: betablockade
  - 92% improved (NYHA I-II)
Pathophysiology: cyanotic defects are poorly tolerated

- Complex congenital patients with *uncorrected* shunts
  - Tetrology of Fallot
  - Ebsteins
  - Transposition of great arteries
- Exceptions:
  - Risk correlates with degree of cyanosis (O2 Sat & Hg)
Systemic RV: poorly tolerated

- After Mustard or Senning (usually for cTGA)
  - High risk of arrhythmias, CHF
  - 20-30% risk of deterioration of systemic ventricle and many do not recover postpartum
  - 12% neonatal mortality
    - JACC 2004 Jul 21;44(2):433-7
Pulmonary Hypertension: Eisenmengers

- 50% maternal mortality
  - Thrombosis/PE periphereim
  - Circulatory collapse,
  - Risk with termination
- Fetal morbidity and mortality
  - Related to O2 saturation/Hg

- Idiopathic Pulmonary HTN
  - 17-40% maternal mortality
  - NOT predicted by duration or sPAP
  - Case reports 73 pts
Other conditions: Hemodynamic stress worsens function and structure

• Dilated Cardiomyopathy:
  – Increase in volume and chamber dilation worsens function and symptoms

• Marfans
  – Increased heart rate and vascular changes
  – Risk of dissection=10%
38 yo w/ 5cm dilated aorta and moderate aortic insufficiency
Sporadic Marfan’s: HIGH RISK
Marfan’s in Pregnancy

- 10% Dissection, MOST in aorta > 40mm
- Three prospective studies (101 pts)
  - Dutch: 78 pregnancies in 44 pts
    - 3/5 dissections in aorta > 40mm

- Recommendations:
  - Mortality < 1%, Ao < 40mm and no CV abnormalities
  - Surgical correction pre-pregnancy
  - Betablockers based on nonpregnant data
    - ESC guidelines, EHJ 2013. Shores J, NEJM ‘94
Summary:
Congenital Heart Disease

Well-tolerated (with monitoring):
- Shunts:
  - ASD
  - VSD
  - PDA
- Corrected Tetrology

Poorly-tolerated
- Complex & Uncorrected lesions
- Cyanotic patients
- Poor functional class
- Marfan’s w/ aorta >40mm
- Eisenmengers (PHTN)
Summary:
Acquired Heart Disease

Well-tolerated
• Regurgitant valves
• Mild-Moderate stenosis
• CAD w/o ischemia

Poorly-tolerated
• LV dysfunction
• Poor functional class
• Severe stenosis
• Mechanical valves
Valvular Lesions Associated with: High Maternal/Fetal Risk

- Severe Aortic stenosis
- Moderate-severe mitral stenosis, NYHA II-IV
- Aortic regurgitation, NYHA III-IV
- Mitral regurgitation, NYHA III-IV
- Any valve with LVEF<40%
- Any valve with severe PHTN (75%SBP)
- Mechanical prosthetic valve
- Marfan syndrome: aortic dilation, aortic regurgitation

AHA/ACC Guidelines 2014
Asymptomatic (normal LVEF and NYHA), severe mitral regurgitation is well tolerated

Mechanical Valve Risks:
- Thrombosis (4%-9%)
- Bleeding (23%)
- Death (2-3%)
<table>
<thead>
<tr>
<th><strong>Mechanical valves</strong></th>
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</thead>
<tbody>
<tr>
<td>OACs are recommended during the second and third trimesters until the 36th week.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Change of anticoagulation regimen during pregnancy should be implemented in hospital.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>If delivery starts while on OACs, caesarean delivery is indicated.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>OAC should be discontinued and dose-adjusted UFH (a PTT ≥2× control) or adjusted-dose LMWH (target anti-Xa level 4–6 hours post-dose 0.8–1.2 U/mL) started at the 36th week of gestation.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>In pregnant women managed with LMWH, the post-dose anti-Xa level should be assessed weekly.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>LMWH should be replaced by intravenous UFH at least 36 hours before planned delivery. UFH should be continued until 4–6 hours before planned delivery and restarted 4–6 hours after delivery if there are no bleeding complications.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Immediate echocardiography is indicated in women with mechanical valves presenting with dyspnoea and/or an embolic event.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Continuation of OACs should be considered during the first trimester if the warfarin dose required for therapeutic anticoagulation is &lt;5 mg/day (or phenprocoumon &lt;3 mg/day or acenocoumarol &lt;2 mg/day), after patient information and consent.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Discontinuation of OAC between weeks 6 and 12 and replacement by adjusted-dose UFH (a PTT ≥2× control; in high risk patients applied as intravenous infusion) or LMWH twice daily (with dose adjustment according to weight and target anti-Xa level 4–6 hours post-dose 0.8–1.2 U/mL) should be considered in patients with a warfarin dose required of &gt;5 mg/day (or phenprocoumon &gt;3 mg/day or acenocoumarol &gt;2 mg/day).</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Discontinuation of OACs between weeks 6 and 12 and replacement by UFH or LMWH under strict dose control (as described above) may be considered on an individual basis in patients with warfarin dose required for therapeutic anticoagulation &lt;5 mg/day (or phenprocoumon &lt;3 mg/day or acenocoumarol &lt;2 mg/day).</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Continuation of OACs may be considered between weeks 6 and 12 in patients with a warfarin dose required for therapeutic anticoagulation &gt;5 mg/day (or phenprocoumon &gt;3 mg/day or acenocoumarol &gt;2 mg/day).</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>LMWH should be avoided, unless anti-Xa levels are monitored.</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>
Congenital and Acquired Heart Disease in Pregnancy

Preconception Risk Assessment and Counseling

• Evaluation
  – Functional assessment
  – Structural assessment
    • Echocardiogram
    • MRI, cardiac catheterization

• Optimization
  – Medications
  – Percutaneous correction
  – Surgical repair or correction
CAPREG: Predictors of Cardiac Risks

1. NYHA functional class >II, or cyanosis
2. Myocardial dysfunction:
   - LVEF<40%
   - Complex CHD
3. Left heart obstruction
   - MS, MVA<2 cm2
   - AS, AVA<1.5cm2, LVOT P>30mmHg
4. Prior Cardiac events:
   - CHF
   - TIA/CVA
   - Arrhythmias requiring therapy

CHD: Cardiac Events Predicted by Lesion

- Literature Review, >1985, 2,491 pregnancies
- complications=11%
  - 4.8% CHF  4.5% arrhythmias
- Cardiac Events =2%
  - MI, CVA, death (mortality underestimated by survival cohorts)

Drenthen W. JACC 2007;49:2303 and ZAHARA EHJ 2010;312124
<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 no/mild 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>
<tr>
<td>Conditions in which pregnancy risk is WHO I</td>
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<td>------------------------------------------</td>
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<tr>
<td>- Uncomplicated, small or mild</td>
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<tr>
<td>- pulmonary stenosis</td>
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<tr>
<td>- patent ductus arteriosus</td>
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<tr>
<td>- mitral valve prolapse</td>
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<tr>
<td>- Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage).</td>
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<tr>
<td>- Atrial or ventricular ectopic beats, isolated</td>
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<tr>
<th>Conditions in which pregnancy risk is WHO II or III</th>
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<tbody>
<tr>
<td><strong>WHO II</strong> <em>(if otherwise well and uncomplicated)</em></td>
</tr>
<tr>
<td>- Unoperated atrial or ventricular septal defect</td>
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<tr>
<td>- Repaired tetralogy of Fallot</td>
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<tr>
<td>- Most arrhythmias</td>
</tr>
<tr>
<td><strong>WHO II–III</strong> <em>(depending on individual)</em></td>
</tr>
<tr>
<td>- Mild left ventricular impairment</td>
</tr>
<tr>
<td>- Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>- Native or tissue valvular heart disease not considered WHO I or IV</td>
</tr>
<tr>
<td>- Marfan syndrome without aortic dilatation</td>
</tr>
<tr>
<td>- Aorta &lt; 45 mm in aortic disease associated with bicuspid aortic valve</td>
</tr>
<tr>
<td>- Repaired coarctation</td>
</tr>
<tr>
<td><strong>WHO III</strong></td>
</tr>
<tr>
<td>- Mechanical valve</td>
</tr>
<tr>
<td>- Systemic right ventricle</td>
</tr>
<tr>
<td>- Fontan circulation</td>
</tr>
<tr>
<td>- Cyanotic heart disease (unrepaired)</td>
</tr>
<tr>
<td>- Other complex congenital heart disease</td>
</tr>
<tr>
<td>- Aortic dilatation 40–45 mm in Marfan syndrome</td>
</tr>
<tr>
<td>- Aortic dilatation 45–50 mm in aortic disease associated with bicuspid aortic valve</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Conditions in which pregnancy risk is WHO IV <em>(pregnancy contraindicated)</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Pulmonary arterial hypertension of any cause</td>
</tr>
<tr>
<td>- Severe systemic ventricular dysfunction (LVEF &lt; 30%, NYHA III–IV)</td>
</tr>
<tr>
<td>- Previous peripartum cardiomyopathy with any residual impairment of left ventricular function</td>
</tr>
<tr>
<td>- Severe mitral stenosis, severe symptomatic aortic stenosis</td>
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<tr>
<td>- Marfan syndrome with aorta dilated &gt; 45 mm</td>
</tr>
<tr>
<td>- Aortic dilatation &gt; 50 mm in aortic disease associated with bicuspid aortic valve</td>
</tr>
<tr>
<td>- Native severe coarctation</td>
</tr>
</tbody>
</table>
WHO class most predictive for CHD

Balci A. Heart 2014;100:1372
Cardiovascular Disease and Pregnancy

Normal Pathophysiology
• Hemodynamics: HR, load, CO
• Structural & functional changes

Congenital & Acquired Heart Disease
• Preconception risk assessment:
  – Define: defect, function, events
• Pathophysiology, WHO high risk:
  – stenosis, cyanosis, Ao, PHTN
  – functional class: >II, LVEF<40%
ευχαριστώ!
Extra slides
Multicenter Prospective Study: 599 pregnancies

13% AE (1% CVA/mortality)

*10/24 TAB for CVD

3 deaths: 1 CHF, 2 SCD
4 CVA: CM, MVR, MS

Siu S. Circ. 2001; 104: 515.
What are the risks of AS?

- **CAPREG**: AVA > 1.5 cm$^2$ conferred increased risk
  - 57 AS (AVA = 0.9 cm$^2$): 4CHF, 1SVT
  - 599 pregnancies but 10 TAB, 7 for stenosis
    - Siu et al. Circ 2001

- **ZAHARA**: AVA < 1 cm$^2$ or PG > 50 mmHg, OR13
  - 81 AS (1302 pregnancies):
    - 18/81 severe: 32% AE, 63 moderate: 16% AE
      - Drenthen et al. EHJ 2010

- **EU registry**: No deaths in AS (4 MS)
  - 1321 patients: 66% CHD, 25% valvular
Moderate AS is well tolerated

49 pregnancies in 39 women
- >90% NYHA I and normal LVEF
- 33% moderate, 59% severe (PG≥64)
- 37% mod or sev AI, 29% repaired coarctation

- 6% maternal AE (all in severe pts)
  - Silversides CK et al. AJC 2003;91:1386.

53 pregnancies in 35 women
- 93% NYHA class I
- 41 mild-mod: 3 SVT
- 12 severe (peak velocity>4 m/s): 2CHF

- 9% maternal cardiac AE
  - Yap SC et al. ZAHARA Int J Cardiol. 2008;126:240.
Neonatal Risks in Women with Heart Disease

- 13 centers: 302 women with heart disease (HD)
  572 healthy controls (NML)
- Neonatal events: HD 18% vs NML 7%
  - age 20-35; no smoking, anticoagulants, OB risks:
    - 5% HD vs 4% NML
  - age <20 >35 & smoking, multi gestations or OB risks:
    - 27% HD vs 11% NML
  - Siu SC. Circ. 2002;105:2179.
Obstetric Complications Predicted by Lesion

Obstetric events underreported
- 2% thromboembolism
  - PE
- Hypertensive disorders
- Preterm Labor

Review: 2,491 pregnancies

Drenthen W. JACC 2007;49:2303
Fetal complications: Review: 2,491 pregnancies

- Premature = 16% (but increased in Complex CHD = 22-65%)
- Mortality = 4%
- (15% miscarriages, 5% elective terminations)

Drenthen W. JACC 2007;49:2303
Hemodynamic Effects of Labor and Delivery

• Increased BP during contractions:
  – related to intensity, pain and positioning
• Increased cardiac output
  – 50% during contractions, 50% in second stage
  – 80% early postpartum, autotransfusion
• Increase in oxygen consumption 3x
• Second stage (pushing) mimics valsalva
  – Phase 2, decrease preload, reflex increase HR
• Cesarean Section
  – variable, wide fluctuations
### FIGURE 4 Maternal Composite Outcome

<table>
<thead>
<tr>
<th>Alternative strategy</th>
<th>Favors Alternative</th>
<th>Favors VKA</th>
<th>Ratio [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>LMWH</td>
<td></td>
<td></td>
<td>3.1 [1.3, 7.5]</td>
</tr>
<tr>
<td>LMWH + VKA</td>
<td></td>
<td></td>
<td>3.2 [0.9, 8.8]</td>
</tr>
<tr>
<td>UFH + VKA</td>
<td></td>
<td></td>
<td>3.1 [1.5, 7.4]</td>
</tr>
</tbody>
</table>

Ratio of the meta-analytic averaged risk for the maternal composite outcome between a VKA regimen and each alternative regimen. Abbreviations as in Figures 1 and 2.
ESC Guidelines 2011: Take-home

2. Congenital Heart Disease
   - Most women with congenital heart disease tolerate pregnancy well. The risk depends on the underlying heart disease and its complexity, in particular on ventricular and valvular function, functional class and cyanosis.
   - All patients should be seen by the end of the first trimester and an individualized follow-up plan should be established. Vaginal delivery can be planned in most patients.
   - Pregnancy is contraindicated in patients with pulmonary hypertension or Eisenmenger syndrome due to high risk of maternal mortality.
   - Cyanosis poses a significant risk to the fetus, with a live birth unlikely (<12%) if maternal oxygen saturation is <85%.
   - An irreversible decline in systemic ventricular function is seen in 10% of patients with TGA corrected with Mustard / Senning repair.
   - Although successful pregnancy is possible in selected patients after Fontan operation, these are moderate to high risk pregnancies.
3. Aortic Disease

- Pregnancy is a high risk period for all patients with aortic pathology.
- Dissection occurs most often in the last trimester of pregnancy (50%) or the early postpartum period (33%).
- The diagnosis of aortic dissection should be considered in all patients with chest pain during pregnancy.
- In women with Marfan syndrome and aortic root diameters >45 mm pregnancy should be discouraged.
- Approximately 50% of the patients with a bicuspid aortic valve and aortic stenosis have dilatation of the ascending aorta. Dissection does occur, although less frequently than in Marfan patients.
- Caesarean delivery should be considered when the aortic diameter exceeds 45 mm.
4. Valvular heart disease

- Moderate and severe mitral stenosis are poorly tolerated during pregnancy and should be treated interventionally pre-pregnancy.
- During pregnancy percutaneous commissurotomy should only be considered when symptoms persist despite medical therapy.
- In aortic stenosis intervention pre-pregnancy is indicated in case of symptoms, LV dysfunction or symptoms during exercise testing.

- Regurgitant lesions are better tolerated than stenotic lesions. Pre-pregnancy intervention is only indicated when severe regurgitation is accompanied by refractory heart failure or severe ventricular dilatation or dysfunction.
- Mechanical valve prosthesis: Oral anticoagulation (OAC) with vitamin K antagonists is the safest therapy to prevent valve thrombosis and is therapy of choice during the second and third trimester. During the first trimester continuation of OAC should be considered when the required daily dose is low (warfarin <5 mg). Pregnant patients on higher warfarin dose should be considered for unfractionated heparin or low molecular weight heparin (LMWH) with strict dose-adjustment according to aPPT or anti-factor Xa levels (weekly control). At the 36th week of gestation OAC should be discontinued and replaced by dose-adjusted unfractionated heparin or LMWH. When delivery starts while still on OAC, caesarean delivery is indicated to prevent fetal cerebral bleeding.
Cardiac Evaluation is difficult

- Normal Symptoms
  - fatigue, dyspnea, lightheadedness
  - *Not* orthopnea
- Normal Signs (hyperdynamic state)
  - vigorous PMI
  - palpable P2, S3 or S4
  - $SEM < 2/6$
  - bounding pulses
  - JVP (mild)
  - Lower extremity edema

*The Third Commandment of Pregnancy: Thou shalt not go shopping with skinny non-pregnant women*