Pregnancy and Cardiovascular Disease

Cindy M. Martin, M.D.
Co-Director, Adult Congenital and Cardiovascular Genetics Center

No Disclosures
Objectives

• Discuss the hemodynamic changes during pregnancy
• Define the low, medium and high risk cardiac lesions as related to pregnancy
• Review use of cardiovascular drugs in pregnancy
Pregnancy and the Heart

• 2-4% of pregnancies in women without preexisting cardiac abnormalities are complicated by maternal CV disease
• In 2000, there were an estimated 1 million adult patients in the US with congenital heart disease (CHD), with the number increasing by 5% yearly
• In 2005, the number of adult patients with CHD surpassed the number of children with CHD in the United States
• CV and CHD disease does not always preclude pregnancy but may pose increase risk to mother and fetus
Hemodynamic Changes during Pregnancy

- Blood Volume – increases 40-50%
- Heart rate – increases 10-15 bpm
- SVR and PVR – decreases
- Blood Pressure – decreases 10mmHg
- Cardiac Output – increases 30-50%
  - Peaks at end of second trimester and plateaus until delivery
- These changes are usually well tolerated
Physiologic Changes in Pregnancy
Hemodynamic Changes in Labor and Delivery

• CO increases an additional 50% with each contraction
  – Uterine contraction displaces 300-500ml blood into the general circulation
  – Possible for the cardiac output to be 70-80% above baseline during labor and delivery
• Mean arterial pressure also usually rises
• Volume changes
  – Increased blood volume with uterine contraction
  – Increase venous return
  – Volume loss during delivery (300-400ml for vaginal delivery, 500-800ml for cesarean section)
CV Exam During Pregnancy

- Brisk and full carotid upstroke
- JVP normal or mildly increased
- Displaced and enlarged apical impulse
- 96% will have SEM (usually not loud)
- 88% will have wide loud split S1
- 84% will have a loud S3
- Not normal to have S4, DM, or fixed split S2
Contraindications To Pregnancy

- Severe Pulm HTN (30-50% maternal mortality)
- Severe obstructive lesions
  - AS, MS, PS, HCM, Aortic Coarctation
- Ventricular dysfunction
  - Class III or IV CHF, EF < 40% (>7% maternal mortality and >30% maternal morbidity)
  - Prior peripartum cardiomyopathy with depressed EF
- Dilated or unstable aorta
  - Marfan with aorta root ≥ 40mm
- Severe cyanosis
Prospective Multicenter Study of Pregnancy Outcomes in Women with Heart Disease

- Cardiac Disease in Pregnancy (CARPREG) Investigators
- Circulation 2001; 104:515
Low Risk Cardiac Lesions of Pregnancy (Mortality < 1%)

- Atrial Septal Defect, uncomplicated
- Ventricular Septal Defect, uncomplicated
- Patent ductus arteriosus, uncomplicated
- Asymptomatic AS with low mean gradient (<50mmHg) and nrl LVEF
- AR with normal LV function and NYHA Class I or II
- Mitral Valve Prolapse (isolated or with mild or moderate MR and normal LV function)
- MR with normal LV function and NYHA Class I or II
- Mild or moderate MS (MVA > 1.5cm², mean gradient < 5mmHg) without severe pulmonary HTN
- Mild or moderate PS
- Repaired cyanotic CHD without residual cardiac dysfunction
Intermediate Risk Cardiac Lesions of Pregnancy (Mortality 5-15%)

- Large left to right shunt
- Coarctation of aorta, uncomplicated
- Marfan syndrome with normal aortic root
- Moderate or severe MS
- Mild or moderate AS
- Severe PS
High Risk Cardiac Lesions of Pregnancy (Mortality 25-50%)

- Eisenmenger’s syndrome
- Severe pulmonary HTN
- Complex cyanotic CHD (TOF, Ebstein’s anomaly, TA, TGA)
- Coarctation of aorta, complicated
- Marfan syndrome with aortic root replacement or valve involvement
- Bicuspid aortic valve with aortic root ≥ 40mm
- Severe AS with or without symptoms
- Aortic or mitral valve disease with LVEF ≤ 40%
- NYHA Class III or IV a/w with any valvular dz or CM
- History of prior peripartum cardiomyopathy
Predictors of Cardiac Events

- Prior CHF, TIA, stroke or sustained arrhythmia
- Baseline NYHA III, IV or cyanosis
- Left heart valvular or outflow tract obstruction
  - $\text{AVA} < 1.5\text{cm}^2$, $\text{MVA} < 2\text{cm}^2$ or
  - $\text{LVOT peak gradient} > 30\text{mmHg}$
- Decreased systemic ventricular function ($\text{EF} < 40\%$)

- Maternal cardiac events rates for 0 points = 5%,
- 1 point = 27%, >1 point = 75%
Peripartum Cardiomyopathy

- New diagnosis of LV dysfunction which occurred during last trimester or within 6 months postpartum without any other identifiable cause
- Incidence in US: 1 in 1500 to 3000 pregnancies
- Increase in frequency
  - Multi-fetal pregnancy
  - Multi-parity
  - Tocolytics
  - Age > 30 yrs
  - African America women
  - Gestational HTN
Peripartum Cardiomyopathy

• Etiology Unknown
  – Myocarditis, Immune, Hemodynamic
  – Increased cytokine and Fas (apoptosis-signaling receptor)

• Prognosis – variable
  – Major cause of pregnancy related death in US
  – Increased mortality with continued depressed EF > 6 mos postpartum
  – ~50% of patients improve in 6 months
Peripartum Cardiomyopathy

• Management
  – Deliver fetus when identified before delivery if refractory to medical management
  – If EF < 35% some recommend anticoagulation 2/2 hypercoagulopathy of pregnancy
  – Standard CHF therapy
    • Conservative tx - ↓ salt, bed rest
    • Digoxin, hydralazine, diuretic if necessary
    • ACE inhibitors, ARBs and aldosterone antagonists contraindicated
  – ?IV immune globulin, pentoxifylline
  – Transplantation
Peripartum Cardiomyopathy

• Subsequent Pregnancies???
• Elkayam et al; NEJM 2001
  – 44 women with PPCM
    • Group 1 – 28 pregnancies occurred with nrl LVEF
    • Group 2 – 16 pregnancies occurred with ↓ LVEF
  – Total cohort had ↓ mean LVEF
  – CHF sx: group 1= 21%, group 2 = 44%
  – Mortality: group 1 = 0%, group 2 = 19%
Peripartum Cardiomyopathy

- Subsequent Pregnancies???
  - If LV dysfunction and/or dilation persists – risk is high and subsequent pregnancy is not recommended
  - If LV function has normalized would perform dobutamine stress echo
    - If abnormal – risk is moderate and subsequent pregnancy is not recommended
    - If normal – risk is low and subsequent pregnancy is not contraindicated
Coarctation of Aorta and Pregnancy
Coarctation of Aorta and Pregnancy

- Women with h/o coart regardless of repair status need to undergo imaging prior to pregnancy.
- Even in the absence of residual stenosis or aneurysm there is increased risk of aortic dissection.
  - This risk is even higher in patients with bicuspid aortic valve.
- Pregnancy will frequently be complicated by hypertension (25-35%).
- Blood pressure should be monitored closely and treated aggressively during pregnancy.
Coarctation of Aorta and Pregnancy

• Vaginal delivery is the preferred method of delivery unless patient has significant systemic hypertension, dilated aorta, or significant residual stenosis

• Fetus should undergo cardiovascular ultrasound as left sided heart lesions (coarc and hypoplastic left heart) have one of the highest reported risks of recurrence in offspring
Fontan Physiology and Pregnancy

Fontan Procedure
For heart with only one usable ventricle
(In this illustration Tricuspid Atresia)

R.A. R.A.
AO L.A.
P.A. L.V.

stiches
artificial wall to make chamber
inferior vena cava
Fontan Physiology and Pregnancy

- Fontan physiology historically considered contraindication to pregnancy
- Recent studies have challenged this as a universal recommendation
- In 1996, Canobbio et al published a case report series which described that although there was a high rate of spontaneous abortion, 13/14 completed pregnancies were well tolerated
Fontan Physiology and Pregnancy

- High spontaneous abortion rate ~50%
- If pregnancy sustained after 14 weeks fetal outcome is usually good
- Common to see decrease in maternal ventricular function (40-50% of pts) which almost always recovers after delivery
- High incidence of atrial arrhythmias (~25%)
- High incidence of premature delivery (~40%)
All patients considering pregnancy should undergo imaging (echo +/- cardiac MRI, CPX, and holter testing).

If patients have preserved ventricular function, acceptable exercise tolerance and limited arrhythmia burden then pregnancy can be considered.

Long term effects on maternal cardiovascular outcome is unknown.
Cardiac Drugs in Pregnancy

- Most CV drugs cross placenta and secreted in breast milk
- Weigh risk/benefit ratio – avoid when possible
- Use drugs with long safety record
- Prescribe lowest dose for shortest duration
- Avoid multi-drug regimens
- No drug completely safe
Cardiac Drugs in Pregnancy

FDA Classification

• A – no disclosed fetal risks
• B – animal studies suggest risk
• C – animal studies suggest adverse fetal effects
• D – evidence of human fetal risk
• X – documented fetal abnormalities
Beta-blocker in Pregnancy

• Effective and relatively safe
  – Metoprolol and Labetolol

• Indications
  – Arrhythmias, aortic disease, HOCM, HTN

• Concerns – fetal and neonatal
  – IUGR, apnea, ↓HR, hypoglycemia

• Atenolol
  – adverse fetal effects when used early in pregnancy (LBW, premature delivery)
  – Unsafe during lactation – concentrates is breast milk
Calcium Channel Blockers in Pregnancy

• Relatively safe for mother and fetus
• Tocolytic effect – stop near term
  – Dysfunctional labor, postpartum hemorrhage
• May ↓ uteroplacental perfusion
• Beta-blockers preferred if tolerated
Diuretics in Pregnancy

- Best not to use during pregnancy
  - Fetal electrolyte and platelet effect
  - Fetal hyponatremia and increased uric acid
  - Decreased maternal intravascular volume
  - Decreased utero-placental perfusion
- Use only in setting of CHF
- Better to start prior to pregnancy
Cardiac Drugs in Pregnancy

• Other drugs safe to use in pregnancy
  – Alpha methyldopa – for HTN
  – Hydralazine – for HTN, CHF
  – Digoxin – for CHF or arrhythmias
Delivery Options

• Vaginal Delivery
  – Feasible and preferable in most cases
  – Facilitate 2\textsuperscript{nd} stage

• C-section indications
  – OB reasons
  – Coumadin anticoagulation
  – Severe PHT
  – Fixed obstructive lesions (sudden BP change dangerous)
    • Spinal and even epidural anesthesia can cause significant hypotension 2/2 abrupt vasodilatation
  – Unstable aorta
Anticoagulation in Pregnancy

• Hematologic changes in pregnancy
  – Increased clotting factor concentration
  – Increased platelet adhesiveness
  – Decreased fibrinolysis and protein S activity

• Increased risk of thrombosis and embolism
Anticoagulation in Pregnancy

• Warfarin
  – Low molecular weight – crosses placenta
  – Greater AC effect in fetus 2/2 ↓ vit K dependent factors in fetal liver
  – ↑ risk of fetal loss, permaturity, stillbirth, fetal intracranial hemorrhage
  – Retroplacental hemorrhage
  – Embryopathy risk
  – Package insert – warfarin CI in pregnancy
Warfarin Embryopathy

- Bone and cartilaginous abnormality
  - Lack of vitamin K dependent protein prevents calcification of cartilage
  - Chondrodysplasia, nasal hypoplasia, optic atrophy with microphthalmia, blindness, ↓IQ, CNS dysfunction, seizures
- Exposure 6-12 weeks gestation
- Past reported 30% risk, 1995 study found incidence 4-10%
- Dose related – low risk with dose <5mg/day
UF Heparin in Pregnancy

• High molecular rate – does not cross placenta
• Short half-life, variable response
• For ↑ risk pt goal PTT 2.5 - 3.5 x control otherwise PTT 2 – 3 x control
• May require TID or even QID dosing
• Treatment of choice in late pregnancy, delivery
• Long-term use not recommended
  – Osteoporosis ~30%, sterile abscesses, ↓ plts, alopecia
Low-Molecular Weight Heparin

- Uncertainty regarding LMWH and pregnancies
- Does not cross placenta
- When compared to UF heparin
  - ↑ Bioavailability, administration ease
  - ↓ Osteoporosis and thrombocytopenia
- However studies have shown weight based dosing inadequate in pregnancy
- Measurement of anti-Xa activity necessary to ensure adequate AC in pregnancy
  - Peak (4 hr post dose) anti-Xa level goal 0.7-1.2 U/ml
Anticoagulation in Pregnancy

- Decision regarding AC in pregnancy requires detailed discussion
- Insufficient data to reliably predict efficacy and safety of any regimen
- Meticulous monitoring must be emphasized
- Choose UFH or LMWH until 12th week, warfarin 12th – 35th week, then UFH or LWMH until delivery; UFH throughout pregnancy or LMWH throughout pregnancy
- For high-risk: Add ASA 81-325mg daily
Pregnancy and the Heart

- Growing number of pregnancies complicated by cardiovascular disease
- Pregnancy usually well tolerated but there are conditions in which pregnancy poses high risk
- Physiologic changes of pregnancy peak at end of second trimester
- Not normal to have S4, DM or fixed split S2
- Many CV meds “okay” during pregnancy
- Anticoagulation complicated during pregnancy
Adult Congenital and Cardiovascular Genetics Clinic