Considerations in Pregnancy for Women with Marfan & Loeys-Dietz Syndrome

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Marfan Pregnancy Webinar
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Goals of Today’s Talk

• Discuss pregnancy’s effects on a connective tissue disorder and the risks associated with pregnancy

• Learn things to consider if you are wanting to get pregnant

• Acquire tools and resources to assist you in having safe and healthy pregnancy
Connective Tissues Disorder

A **connective tissue disorder** involves ligaments, bones, blood vessels.

- Connective tissues - extensive extracellular matrix –framework- collagen & elastin
- Connective Tissue = Heart, eyes, blood vessels, skeleton

The **aorta** is the main artery from the heart that carries blood to entire body.

- CTDs –**Aneurysm** “dilation” at Aortic Root
- **Dissection**- Tear in intima layer and creates false lumen and bleeds into false lumen
Normal Cardiovascular Changes in Pregnancy:

Hemodynamic Changes in Pregnancy

- Cardiac output
- Blood volume
- Heart rate
- Stroke volume

ESC Guidelines on Cardiovascular Diseases during Pregnancy 2016

Hormonal Changes in Pregnancy

- HCG
- Progesterone
- Estrogen

Histology Large Arteries
- Loss of reticulin
- Decreased Mucopolysaccharide
- Loss of corrugation fibers

Timing and Risk Factors for Aortic Dissection in Pregnancy

Overall rate of aortic dissection in pregnancy/postpartum period 5-6%*
- Majority of aortic complications occur in the 3rd trimester or postpartum period

Aortic Root Size significantly affects risk of dissection
- >4cm risk of dissection 10%
- <4cm risk of dissection 1%

Other risk factors:
- Rapid aortic root growth
- HTN disorders/preeclampsia

Aortic Dissection in Pregnancy

A rare but significant event if it occurs….

- 3rd most frequent cause of maternal death from cardiovascular disease

- High mortality for mother and fetus (15 and 30%)

- Delays in diagnosis and treatment can be difference between life or death
  - Mortality rate for untreated proximal aortic dissection increases 1-3% per hour following presentation

Knight et al 2015; Immer et al 2003; Jovic et al 2014
Connective Tissues Disorder

Signs of aortic dissection:
Chest pain, Back Pain, Dyspnea, Stroke sx, Syncope, focal neurological signs

Table 4 - Symptoms and physical findings in aortic dissection.

- Pulse deficit
- Systolic blood pressure limb differential > 20 mmHg
- Focal neurological deficits
- Aortic regurgitation
- Pericardial tamponade
- EKG—ST-segment elevation
- Syncope
## Risk Factors for Long-Term Adverse Outcomes After Pregnancy

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Protective Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aorta &gt;4 cm</td>
<td>Prospective care</td>
</tr>
<tr>
<td>Rate of aortic root change</td>
<td>Medications</td>
</tr>
<tr>
<td>Initial aortic root size</td>
<td></td>
</tr>
<tr>
<td>Number of pregnancies</td>
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</tbody>
</table>

### Table 2

Risk factors for long-term outcome after pregnancy in women with Marfan syndrome. Modified from Donnelly et al.23

<table>
<thead>
<tr>
<th>Associated factors with long-term adverse outcome:</th>
<th>Odds ratios</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic size</td>
<td>1.3 (1.11–1.61)</td>
</tr>
<tr>
<td>Number of pregnancies</td>
<td>1.5 (1.15–1.97)</td>
</tr>
<tr>
<td>Prospective care</td>
<td>0.1 (0.05–0.39)</td>
</tr>
<tr>
<td>Medication</td>
<td>0.3 (0.14–0.92)</td>
</tr>
<tr>
<td>Aorta &gt; 4 cm</td>
<td>3.8 (1.11–13.3)</td>
</tr>
<tr>
<td>Independent correlates</td>
<td></td>
</tr>
<tr>
<td>Initial aortic size</td>
<td>1.8 (1.07–3.07)</td>
</tr>
<tr>
<td>Rate of aortic change (log)</td>
<td>7.4 (1.32–41.22)</td>
</tr>
</tbody>
</table>
The Decision to Become a Parent

- Pregnancy
- In Vitro Fertilization
- Surrogacy
- Adoption
- Plant Parent
- Pet Parent
Considerations in Pregnancy for Women with Marfan or Loeys-Dietz syndrome

1. Plan Ahead
2. Assemble your Team
3. To Test or Not to Test…….
4. Protect aorta- meds/imaging
5. Delivery decisions- how, when where
6. Is breast the best?
PREGNANCY MANAGEMENT GUIDELINES

Women with Marfan or Loeys-Dietz syndrome

- Preconception counseling
- Antepartum care
- Anesthesia considerations
- Delivery recommendations
- Postpartum surveillance
PLAN AHEAD - Pre-conception Counseling

- Titration off of Angiotensin-Receptor Blocker (ARB) onto Beta-Blocker
- Imaging Studies- CV imaging (CTA vs MRA) and Spinal Imaging
- Genetic counseling of heritability risk and genetic testing options
- Counseling about risks of pregnancy- Meet with Maternal-Fetal Medicine Specialist
  - Cardiovascular risks, obstetric risks and potential effect on long term health
- Discussion of Contraceptive Options:
  - *Discuss prophylactic Aortic Root Replacement (ARR) before pregnancy (4-4.5 cm)
Consideration of Prophylactic Aortic Root Replacement

• Discussion about prophylactic aortic root replacement 4-4.5 cm
  • ONLY for Marfan, Loeys-Dietz syndrome and BAV

• Mitigates future type A dissection
  • Potential risk for type B dissection beyond the graft
  • Surveillance in pregnancy- imaging of entire aorta- beyond echocardiograms
# Marfan and Loeys-Dietz Syndrome

## Risks to Discuss in Relation to Pregnancy

<table>
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<tr>
<th>OBSTETRIC</th>
<th>CARDIAC</th>
<th>vEDS</th>
</tr>
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<tr>
<td>• PTB/ PPROM</td>
<td>• Aortic root growth</td>
<td>• Arterial dissection</td>
</tr>
<tr>
<td>• Fetal growth restriction</td>
<td>• Aortic dissection</td>
<td>• Maternal mortality 6-50%</td>
</tr>
<tr>
<td>• Postpartum Hemorrhage</td>
<td>• Arrhythmias</td>
<td></td>
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<tr>
<td>• VTE (Blood clot)</td>
<td>• Aortic root growth</td>
<td></td>
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<tr>
<td>• Spontaneous pneumothorax</td>
<td>• Aortic dissection</td>
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<tr>
<td></td>
<td>• Hollow organ rupture (bowel, liver, spleen)</td>
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Assemble Your Team

Multi-Disciplinary Approach

• Team includes:
  o Maternal-Fetal Medicine, Cardiology
  o CV surgery, Anesthesia, NICU
  o Nursing leaders and nurses from all specialties

• Delivery at hospital with Cardiothoracic Surgery

• Education, Contingency Plans & Simulation
To Test or Not to Test: Genetic Testing Options in Pregnancy

Before Pregnancy
Preimplantation Genetic Diagnosis (PGD)

During Pregnancy
CVS or Amniocentesis

After Pregnancy
Test child after delivery
### Protection of Aorta and Risks to the Fetus

#### Antepartum Care during Pregnancy

**Aorta and Vascular Management & Surveillance**
- Beta-blockade during pregnancy – metoprolol preferred
- Maternal echocardiogram
  - Frequency depends on severity (q trimester to q 4-8 weeks)
- Assessment of entire vascular tree (MRA)

#### Fetal Surveillance
- Level II ultrasound
- Growth ultrasounds q 4 weeks
- +/- Fetal echocardiogram

### Prenatal Ultrasound Findings in Aortopathy Syndromes

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<thead>
<tr>
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<th>Marfan</th>
<th>Loeys-Dietz</th>
<th>vEDS</th>
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<tbody>
<tr>
<td>No fetal findings</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><em>Neonatal Marfan</em></td>
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<td></td>
<td></td>
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<tr>
<td>Aortic/Pulmonary dilation</td>
<td></td>
<td>Other CHD</td>
<td>Club feet</td>
</tr>
<tr>
<td>Clefts</td>
<td>Club feet</td>
<td>Other CHD</td>
<td>Amniotic band</td>
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Anesthesia Considerations

- Spinal imaging: scoliosis, dural ectasia, cervical spine stability (LDS)

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<th>vEDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scoliosis</td>
<td>Scoliosis</td>
<td>Vascular anomalies</td>
</tr>
<tr>
<td>Dural ectasia</td>
<td>Dural ectasia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vascular anomalies</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cervical spine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>instability</td>
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</table>

- Regional vs General Anesthesia
- Dural ectasia

**Table 1. Factors Considered When Choosing EA Versus GETA**

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<thead>
<tr>
<th></th>
<th>EA</th>
<th>GETA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speed of onset</td>
<td>Slow, controlled—our plan for elective cesarean delivery only</td>
<td>Fast—our plan for emergent cesarean delivery</td>
</tr>
<tr>
<td>Inadequate surgical anesthesia</td>
<td>Possible, but safe EA for cesarean delivery in LDS had been reported.</td>
<td>Possible but monitoring available for level of anesthesia</td>
</tr>
<tr>
<td>Trauma to c-spine</td>
<td>Negligible risk unless intubation required</td>
<td>Possible if c-spine instability exists</td>
</tr>
<tr>
<td>Aspiration</td>
<td>Negligible risk since patient is awake. Neuraxial is preferred anesthetic for nonemergent cesarean deliveries.</td>
<td>At risk, especially with pregnancy altering the airway, and requiring rapid sequence intubation</td>
</tr>
<tr>
<td>Hemodynamic instability</td>
<td>Possible—controlled or mitigated by incrementally establishing surgical level block</td>
<td>Possible—controlled with smooth induction/intubation</td>
</tr>
<tr>
<td>Dural puncture with vascular complications</td>
<td>Possible—theoretic risk of decreased intracranial pressure with CSF leakage secondary to intrathecal insertion may increase arterial transmural pressure facilitating rupture of vascular malformation¹⁴</td>
<td>No risk</td>
</tr>
<tr>
<td>Uterine atony</td>
<td>Not enhanced by EA</td>
<td>Possible with volatile anesthetics</td>
</tr>
<tr>
<td>Experience of childbirth</td>
<td>Possible—this patient declined any sedative medication</td>
<td>Not possible</td>
</tr>
</tbody>
</table>

Kapoor R, Mann DG, Mossad EB. AA Case Reports. 2017
# Delivery Recommendations- How, When and Where

<table>
<thead>
<tr>
<th>Mode of Delivery</th>
<th>Marfan and Loeys-Dietz</th>
</tr>
</thead>
</table>
| Vaginal vs Cesarean | • Ao Root  
|                   | • Institution  
|                   | • Vaginal Considerations  
|                   | • Ao root <4-4.5cm  
|                   | • Regional Anes  
|                   | • Operative Delivery  |

### How…..Vaginal vs C-section
- Depends on institution, aortic root size
- Vaginal– Forcep or vacuum –decreases time/effort pushing (Vaginal <4-4.5cm)
- Cesarean delivery- >4.5 cm, rapid growth

### When…. 37- 39 weeks

### Where….Hospital w/ Cardiovascular Surgery
- Tertiary care center
- Cardiologist, CV surgeon

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Timing of Delivery

Plan at 39 weeks *36-39 weeks No consensus
Postpartum Recommendations
Is the Breast Best????

Postpartum Management
• Inpatient observation for 48-72 hrs
• Imaging prior to discharge- echocardiogram vs CTA/MRA
• Echocardiogram at 3-6 months PP

Breast Feeding- the Potential Risks
• Mouse model demonstrates potential detrimental effects of oxytocin

Oxytocin levels rise through pregnancy, peaking in the third trimester and remain elevated with lactation

Oxytocin antagonism prevents pregnancy-associated aortic dissection in a mouse model of Marfan syndrome

Marfan Mouse Model
15% normal fibrillin
Are there similar effects in humans???
Oxytocin levels rise through pregnancy, peaking in the third trimester and remain elevated with lactation.
Summary Points about Pregnancy

• Women with CTD can have successful pregnancies with close management

• Whether to pursue a pregnancy is an individualized decision

• The optimal delivery method (vaginal vs C-section) and whether breast feeding is detrimental is not yet known

• Current and Future Research:
  To better understand the mechanisms of how pregnancy effects the cardiovascular system
  To be able to better predict who will develop cardiovascular and obstetrical complications in pregnancy
Summary Points about Pregnancy

- **Plan Ahead**
  - See your obstetrician before you decide to get pregnant
  - Birth control plan – to prevent unplanned pregnancy

- **Assemble your Team**
  - MFM, Cardiology, CV surgery, anesthesia, nursing specialists, genetics counselors, intensive care specialists

- **Get care through the Pregnancy**
  - Protect aorta with meds and surveillance
  - Protect aorta with good anesthesia and safe delivery plan
  - Protect aorta with close post-delivery surveillance