Management of Multifetal Pregnancies

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Disclosures

- I have no relevant financial relationships to disclose or conflicts of interest to resolve.

- I will not discuss any unapproved or off label, experimental or investigational use of a product, drug, or device.
Multifetal Gestations

- Twins
  - Dichorionic (70%)
    - Dichorionic-diamniotic; zygote division day 1-3
  - Monochorionic (30%)
    - Monochorionic-diamniotic; zygote division day 4-8
    - Monochorionic-monoamniotic (1%); division day 8-12
    - Conjoined twins; zygote division day 13+
Incidence

- Significant increase over past few decades
  - Twins increased from 18.9/1000 (1980) to 33.3/1000 (2009)
  - 76% increase
    - Martin et al. NCHS Data Brief 2012; 80:1-8

- Higher order (3+) rose 400% to peak 193.5/100,000 (1998)
- Recent modest decrease to 153.4/100,000 (2009)
Incidence Increasing

- Increasing maternal age of conception
  - <20 yo multifetal gestation rate 16.3/1000
  - 40+ yo multifetal rate increases to 71.1/1000

- Increasing utilization of assisted reproduction
  - Cycles completed in 2010
  - 26% resulted in twin gestation
  - 1.3% resulted in triplets or more
    - SART data
  - Recently decreasing with single embryo transfer
Increased Fetal/Neonatal Risk

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Singleton</th>
<th>Twin</th>
<th>Triplet</th>
<th>Quadruplet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BW</td>
<td>3296 g</td>
<td>2336 g</td>
<td>1660 g</td>
<td>1291 g</td>
</tr>
<tr>
<td>Mean GA</td>
<td>38.7 wks</td>
<td>35.3 wks</td>
<td>31.9 wks</td>
<td>29.5 wks</td>
</tr>
<tr>
<td>Del &lt;37 wks</td>
<td>10.4%</td>
<td>58.8%</td>
<td>94.4%</td>
<td>98.3%</td>
</tr>
<tr>
<td>Del &lt;32 wks</td>
<td>1.6%</td>
<td>11.4%</td>
<td>36.8%</td>
<td>64.5%</td>
</tr>
<tr>
<td>CP rate/1000 LB</td>
<td>1.6</td>
<td>7</td>
<td>28</td>
<td>---</td>
</tr>
<tr>
<td>Infant mort/1000 LB</td>
<td>5.4</td>
<td>23.6</td>
<td>52.5</td>
<td>96.3</td>
</tr>
</tbody>
</table>
Increased Maternal Risk

- HE, anemia, GDM, hypertension, CS, PPH, pp depression
- Hypertension risk increases with number of fetuses
  - Singleton 6.5%
  - Twin 12.7%
  - Triplet 20%
- Higher risk for complications due to hypertension
  - Delivery <35 wks (34.5% twins vs 6.3% in singleton)
  - Abruption (4.7% twins vs 0.7% in singletons)
    - Sibai et al. AJOG 2000; 182:938-42
Diagnosis

- Must be made with US
  - Ideally late first or early second trimester

- Clinical diagnosis insufficient
  - RADIUS trial (routine antenatal diagnostic imaging w/ US)
  - 37% of twins diagnosed after 26 wks
  - 13% diagnosed intrapartum
    - LeFevre et al. AJOG 1993; 169:483-9

- Establishes number, dating and chorionicity
Chorionicity

- **Dichorionic**
  - Discordant genders
  - Separate placentas
  - Twin peak sign amnion (lambda or delta sign)

- **Monochorionic**
  - Same gender
  - Single placenta
  - T sign amnion
  - Thin (<3 mm) amnion
Chorionicity by Ultrasound
Twin Peak Sign
Monochorionic vs Dichorionic

T sign = Monochorionic
Twin peak = Dichorionic

T Sign

Twin Peak
Monochorionic Risks Increased

- Increased risk
  - Fetal and neonatal death
  - Congenital anomalies
  - Preterm delivery
  - Fetal growth restriction
  - Twin-twin transfusion (10-15%)
    - Glinianaia et al. Human Reprod 2011; 26:2549-57
Increased Risks During Pregnancy

- Stillbirth: 5X risk
- Neonatal death: 7x risk
- Delivery <37 wks: 6X risk
- Delivery <32 wks: 13x risk
- Increased costs in first year for preterm vs term
  - Up to 10X greater
How to Monitor for Preterm Risk?

- Serial cervical lengths 16-24 wks?
  - No proven effective interventions

- Serial digital exams?
  - Not accurate

- Serial fetal fibronectins?
  - Not in asymptomatic patients

- Home uterine monitoring?
  - Not effective
How to Reduce Risk for Preterm?

- Interventions that have not proven effective include
  - Prophylactic cerclage
  - Routine bedrest or hospitalization
  - Prophylactic tocolytics
  - Prophylactic pessaries
  - 17 OH-P
  - Vaginal progesterone

- None have reduced neonatal morbidity or mortality
Prophylactic Cerclage

- Routine cerclage ineffective in twins/triplets
  - Rebarber et al. AJOG 2005; 193:1193-6

- Cerclage for short cervix in twins increased risk (RR 2.2)
Routine Bedrest

- No benefit for uncomplicated twin pregnancy
  - Crowther et al. Cochrane System Rev 2010; Issue 7

- Increased maternal risks
  - Venothromboembolism
  - Bone demineralization
  - Deconditioning
    - ACOG. Committee Opinion Dec 2015; 650
Prophylactic Tocolytics

- Prolonged oral betamimetics ineffective
  - No reduction in PTD, LBW or Neo mortality

- Associated with increased maternal risks
  - Pulmonary edema
  - Gestational diabetes
  - Maternal cardiac stress
  - Maternal death
    - FDA 2011
Prophylactic Pessaries

- No evidence of benefit in unselected multifetal gestations.
- Recent RCT >800 pts w/ twins 16-20 wks (Arabin pess) -
  - 13% poor outcome (death or severe morbidity) pessary
  - 14% poor outcome control group (RR 0.98; CI 0.7-1.4)
Progestosterone

- 17-OHP ineffective in twins and triplets
  - Rouse et al. NEJM 2007; 357:454-61
  - Combs et al. AJOG 2011; 204:221
  - Combs et al. AJOG 2011; 204:166

- 17-OHP ineffective in twins with short cervix
  - RCT or asympt twins with CL <2.5 cm
  - 500 mg IM twice weekly
    - Senat et al. AJOG 2013; 208:194

- Vaginal progesterone ineffective (200 and 400 mg)
  - Serra et al. BJOG 2013; 120:50-7
What is Effective?

- Single embryo transfer
- Carefully monitored stimulated ovulation
- Multifetal reduction for triplets or more
  - Less preterm births
  - Less low birth weight infants
  - Less neonatal mortality
    - Dodd et al. Cochrane System Rev 2012; Issue 10
- Selective termination has increased risk
  - Unintended loss rate 11.1% for triplets vs 2.4% for twins
    - Eddleman et al. AJOG 2002; 187:1168-72
Fetal Aneuploidy Screening

- Decreased sensitivity of serum screening in multiples
  - Analyte levels estimated by mathematical modeling
  - Twin serum analytes essentially averaged together
  - Detection rate midtrimester screening DS 63%; FP 11%

- Nuchal translucency
  - 75-85% detection DS
  - 67% detection Tri 18
  - FP 5%
Ultrasound

- Detailed fetal anatomic survey at 18-22 wks
- Fetal echo 24 wks if monochorionic or ART
- Serial growth US every 4-6 wks for growth
  - More frequent if IUGR with Dopplers as well
- Twin-twin screen every 2 wks if monochorionic
## Staging for Twin-Twin Transfusion

<table>
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<tr>
<th>Stage 1: mono-di with oligo (&lt;2 cm) and poly (&gt;8 cm); bladders seen</th>
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<tbody>
<tr>
<td>Stage 2: oligo-poly with absent bladder in donor</td>
</tr>
<tr>
<td>Stage 3: abnormal Dopplers on either twin (AEDV, REDV or venous abnl)</td>
</tr>
<tr>
<td>Stage 4: hydrops of either twin</td>
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<tr>
<td>Stage 5: death of one or more twins</td>
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</tbody>
</table>
Growth Discordance

- 20% or more significant; especially if monochorionic
  - Less concerning if both are AGA
    - Kilie et al. J Perinat 2006; 26:268-72
  - Increased major neo morbidity (7x incr) if one IUGR
  - Higher perinatal M&M compared to IUGR singleton
Antenatal Testing

- No benefit of testing or Dopplers in uncomplicated di/di
  - Giles et al. BJOG 2003; 110:593-7
- Reserve for maternal or fetal abnormalities
  - Hypertension
  - Diabetes
  - IUGR
  - Monochorionic
Preterm Labor

- Antenatal steroids 24-34 wks reduces Neo M&M
  - Roberts et al. Cochrane System Rev 2006; Issue 3
- May be effective as early as 23w0d, but not less
  - Carlo et al. JAMA 2011; 306:2348-58
- Tocolytics short-term (48 hrs)
  - Indocin or nifedipine first line therapy
- Magnesium for neuroprotection <32 wks
  - Reduces mod to severe CP
Timing of Delivery

- Average gest age for twins about 36 wks
- Increased risk for perinatal mortality at 38 wks (di-di)
  - Cheung et al. Am J Epidemiol 2000; 152; 1107-16
- Uncomplicated dichorionic-diamniotic twin
  - Deliver at 38 wks
- Uncomplicated monochorionic-diamniotic twin
  - Deliver at 34-37 wks
- Uncomplicated monochorionic-monoamniotic twin
  - Deliver at 32-34 wks
Route of Delivery

- Twins alone not an indication for CS unless mono-mono
- Eligible for vag delivery if presenting twin cephalic
  - Crowther et al. Cochrane System Rev 2011; Issue 12
- Recent trial of planned CS vs planned vag del 32+ wks
  - No reduction in Neo death or serious morbidity
  - 2.2% CS and 1.9% vag del (OR 1.16; CI 0.77-1.74)
    - Barret et al. NEJM 2013; 369:1295-305
- Epidural anesthesia recommended
Monoamniotic Twins

- 1% of all twin pregnancies

- Historically high perinatal mortality up to 30-70%
  - Primarily from cord entanglement

- Significant improvement with inpt surveillance
  - 10X reduction in fetal death with inpt monitoring
  - 3/178 inpt (1.7%) vs 21/130 oupt (16.1%)
  - Persisted even if intensive outpt 4x/wk NST; 2x/wk US
  - Estimated NNT 13 admissions to prevent single fetal death
Summary

- No effective means to prolong gestation
- Prevention of higher order multiples important
- Chorionicity critical for surveillance
- Effective interventions to reduce Neo M&M
  - Steroids, magnesium neuroprotection, TTTS, MFR
- Don’t abandon the option of vaginal delivery