The Management of Monochorionic-Diamniotic Twins

Carla Ransom, MD
Vanderbilt University
November 30, 2012
The changing face of pregnancy
Learning objectives

• To understand the biology of twinning
• To understand the complications associated with monochorionic gestation
• To recognize the development of twin-twin transfusion syndrome (TTTS)
• To understand the therapeutic options for TTTS
• To understand the antenatal management of monochorionic gestation
Session 1
- Diagnosis of twin gestation
- Maternal & fetal morbidity
- Prevention of PTB
- Special situations: TTTS, death of one twin

Session 2
- Prenatal diagnosis in twins
- Antenatal testing
- Delivery timing
Disclosures

• None
U.S. Twin Births

With advancing age, FSH/LH rise, as does DZ twinning
Maternal Age Association with Multiples

- At <20 yo - multiple births represents 16 per 1000 live births
- At ≥ 40yo - 70 per 1000 live births
Effect of Multiple Births

• 3% of all live births

• 17% preterm births (<37 wks)

• 23% very preterm births (<32 wks)

• 24% of low birthweight (<2500g)

• 26% very low birthweight (<1500g)

Financial cost

Singleton: $9,845

Twins: $37,947 ($18,974 per baby)

Triplets: $109,765 for triplets ($36,588 per baby)

N Engl J Med. 1994 Jul 28;331(4):244-9
Importance of Ultrasound in Multiples

- Changes management of the pregnancy
  - Prognosis
  - Counseling
  - Selective reduction options
  - Appropriate follow up schedule

- Having an accurate description of the number of:
  - Amnions
  - Chorions
  - Fetuses
Accuracy of Referral Diagnosis

- Incidence of wrong diagnosis of multiples at time of referral
  - 46% of twins unassigned
  - 66% of triplets unassigned
  - 44% of 289 referrals to USCD had accurate assignment of amnionicity and chorionicity

- Wrong assumptions (with IVF or other)

The biology of twinning

Zygosity
Amnionicity & chorionicity
Placentation
Zygosity
Chorionicity
Zygosity = Genetic Makeup

Dizygotic – ovulation & fertilization of 2 oocytes

- 69% of all twin births
- Always results in diamniotic, dichorionic placentation
- Usually 2 separate placentas

Monozygotic - ovulation and fertilization of a single oocyte, with subsequent division of the zygote

- 31% of all twin births
- Timing of zygote division determines placentation although factors responsible for timing of egg division are not known
Risk factors for occurrence

**Dizygotic**
- Ethnicity
  - 1:1000 Japan
  - 8:1000 Europe
  - 50:1000 Nigeria
- Maternal age
- Race
- Parity
- ART: multiple follicle development, >1 embryo

**Monozygotic**
- Advanced maternal age
- ART: multiple follicle development
Amnionicity & Chorionicity- ? zygosity

Placentation: Di Di

Zygosity:
- DZ
- MZ with division within 3 days post fertilization

Placentation: Di Di with fused single placenta

Zygosity:
- DZ with fused placenta
- MZ with division within 3 days post fertilization

Placentation: Mono Di

Zygosity:
- MZ: division 4-8 days post fertilization
Cleavage timing: monozygotic

Creasy & Resnick, 6th ed, p 57
Significance of Amnionicity & Chorionicity

Monochorionicity more important than zygosity

• 10 to 15 % of mono/di twins will develop twin-twin transfusion syndrome

• MC twins are at increased risk of neurologic morbidity, discordant birth weight, and co-twin in utero death

• Selective reduction of one twin:
  – only an option for dichorionic/diamniotic
  – selective termination can result in death of co-twin
SONOGRAPHIC SIGNS OF CHORIONICITY - DICHOORIONIC PLACENTATION
Separate placentas
Twin peak/lambda sign
Thick dividing membrane

Egan JF, Ultrasound in Twins, AIUM lecture series, 2012
Gender discordance
SONOGRAPHIC SIGNS OF CHORIONICITY - MONOCHORIONIC PLACENTATION
T-sign

Egan JF, Ultrasound in Twins, AIUM lecture series, 2012
Thin wispy membrane

Egan JF, Ultrasound in Twins, AIUM lecture series, 2012
Di/Di vs Di/Mo
1st trimester membranes
Di-Mo Twins - 13 weeks
3-D Imaging of Di/Mo and Di/Di Twins
Di/Di vs Di/Mo
22 wks MVP with Membrane
Di/Mo
Di/Mo 2\textsuperscript{nd} Trimester, Thin Membrane
Pitfalls of Membranes

- Not appreciating the draping or cocooning of membranes.
- Fetal movement (changing position)
- Wispy vs. thick membranes, especially with advancing gestation.
- Synechiae
- Mistaking umbilical cord for a membrane
  - Vessels in the membranes
Draping Membranes
Draping Membranes Around Extremities
Helpful Hints About Membranes

- Changing maternal position.
- Looking at the “corners” of the fetus
  - Chin and chest
  - Shoulder
  - Behind knees
  - Between feet
- Amniotic fluid density
- Cord insertions near membranes
  - Marginal
  - Velamentous
MATERNAL COMPLICATIONS
<table>
<thead>
<tr>
<th></th>
<th>Singleton (%)</th>
<th>Twin (%)</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>3.4</td>
<td>12.5</td>
<td>3.7</td>
</tr>
<tr>
<td>GDM</td>
<td>2.3</td>
<td>4</td>
<td>2.2</td>
</tr>
<tr>
<td>Threatened abortion</td>
<td>18.6</td>
<td>26.5</td>
<td>1.4</td>
</tr>
<tr>
<td>Thromboembolism</td>
<td>0.1</td>
<td>0.5</td>
<td>3.3</td>
</tr>
<tr>
<td>Antepartum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postpartum thromboembolism</td>
<td>0.2</td>
<td>0.6</td>
<td>2.6</td>
</tr>
<tr>
<td>Hyperemesis</td>
<td>1.7</td>
<td>5.2</td>
<td>3.0</td>
</tr>
</tbody>
</table>

*Campbell DM, Templeton A: Maternal complications of twin pregnancy. Int J Gynecol Obstet*

FETAL COMPLICATIONS
Adverse Outcomes in Twins

- Abnormal Fetal Growth
- Preterm Birth
- Fetal Demise
- Premature Rupture of Membranes
- Twin-twin transfusion syndrome
- Aneuploidy & malformations
- Malpresentation
## M&M

<table>
<thead>
<tr>
<th></th>
<th>Singleton</th>
<th>Twins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean birthweight</td>
<td>3298 g</td>
<td>2323 g</td>
</tr>
<tr>
<td>Low birthweight (&lt;2500g)</td>
<td>6.5 %</td>
<td>57.2 %</td>
</tr>
<tr>
<td>Very low birthweight (&lt;1500g)</td>
<td>1.1%</td>
<td>10.2%</td>
</tr>
<tr>
<td>Delivery &lt; 32 weeks</td>
<td>1.6 %</td>
<td>12.1 %</td>
</tr>
<tr>
<td>Average gestational age</td>
<td>38.7 weeks</td>
<td>35.2 weeks</td>
</tr>
<tr>
<td>Risk of cerebral palsy</td>
<td>---</td>
<td>4 times higher</td>
</tr>
<tr>
<td>Risk death by age 1 year</td>
<td>---</td>
<td>7 time higher</td>
</tr>
</tbody>
</table>

ACOG practice bulletin #56

Fetal Growth in Twins

• Same as singletons during 1\textsuperscript{st} & 2\textsuperscript{nd} trimesters

• Generally follow singleton ultrasound growth charts

• Likely slower growth during 3\textsuperscript{rd} trimester
Fetal Growth Restriction (FGR)

- Placental crowding
- Anomalous cord insertion
- 14 – 25% of twins < 10\textsuperscript{th} percentile birth weight
Discordant Fetal Growth

- ~ 15% of twins will be discordant
- Higher incidence of FGR
- Increased risk of neonatal death with ≥15% discordance
- Discordance ranging 15 – 40% predictive of adverse outcome
Preterm Birth in Twins

• 17% of all preterm births

• 57% of all twins are born < 37 weeks

• Not all spontaneous preterm births
  – Preeclampsia, diabetes, nonreassuring fetal status
Prediction of Preterm Birth

Cervical length measurement

• CL of ≤ 25mm between 24-28 weeks
  — OR PTB prior to 32 weeks: 6.9 (95% CI 2-24.2)
  — Risk PTB 27% in women with CL of ≤ 25mm compared to 5% if CL ≥ 25mm

Am J Obstet Gynecol, 1996; 175: 1047
Prediction of PTB prior to 32 weeks in twins by cervical length

<table>
<thead>
<tr>
<th>Cut off for CL</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV %</th>
<th>NPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment at 21 to 24 weeks of gestation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>42</td>
<td>85</td>
<td>22</td>
<td>94</td>
</tr>
<tr>
<td>25</td>
<td>54</td>
<td>86</td>
<td>27</td>
<td>95</td>
</tr>
<tr>
<td>30</td>
<td>46</td>
<td>89</td>
<td>19</td>
<td>97</td>
</tr>
<tr>
<td>Assessment at 25 to 28 weeks of gestation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>56</td>
<td>76</td>
<td>16</td>
<td>95</td>
</tr>
<tr>
<td>25</td>
<td>63-100</td>
<td>70-84</td>
<td>13-18</td>
<td>96-100</td>
</tr>
</tbody>
</table>

Vayssiere, AJOG, 2002; 187:1596.
Prediction of Preterm Birth

• Cervical length measurement

• Fetal fibronectin
Fetal Fibronectin in Twins

- N = 147 twin pregnancies
- fFN at 2-week intervals between 24 - 30 weeks
- 30% with a positive test at 28 weeks delivered < 32 weeks vs. 4% with a negative result
- When fFN was performed at 30 wks, 38% with a positive test vs. 1% with a negative test delivered < 32 weeks
- However, only 13 of the 147 women delivered before 32 weeks

Goldenberg RL et al, AJOG1996 Oct;175(4 Pt 1):1047-53
# fFN + cervical length

- **155 twin pregnancies**
- **fFN + CL q2-3 weeks from 22-32 weeks**

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Mean GA at delivery</th>
<th>Risk for spontaneous pretermbirth, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;28 wk</td>
<td>&lt;30 wk</td>
</tr>
<tr>
<td>All negative</td>
<td>120</td>
<td>36.1 ± 2.3</td>
<td>1.6</td>
</tr>
<tr>
<td>1 positive</td>
<td>24</td>
<td>34.8 ± 3.1</td>
<td>13.3</td>
</tr>
<tr>
<td>Both positive</td>
<td>11</td>
<td>32.5 ± 3.8</td>
<td>50</td>
</tr>
<tr>
<td>P-value</td>
<td></td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
Prevention of Preterm Birth

- Bedrest
- Home uterine activity monitoring
- Cerclage
- Progesterone supplementation
- Tocolytics
Bedrest

• Cochrane review of 6 RCTs:
  – 600 women, 1400 babies
  – Routine hospitalized bedrest offers NO BENEFIT in multiples

• Home bedrest?
  – No prospective trials in multiples
Bedrest- what’s the downside?

• Increased risk thromboembolism
• Decreased bone mineralization
• Economics
• Depression, mood disorders
• ? Worse outcomes
  – Risk of PTB <34 weeks increased in women on bedrest (OR 1.84, 95% CI 1.01-3.34)

Crowther, Cochrane Database Syst Rev, 1 (2001
Home uterine activity monitors

- Meta analysis of 6 trials
- No difference in the rate of PTB (RR 1.01, 95% CI 0.79-1.30)
- Decreased risk PTL with cervix >2cm (RR 0.44, 95% CI 0.25-0.78)
- No difference in infant birthweight or NICU admission

Take home point: no role for HUAM in twins

• Prophylactic in twins: doesn’t work
• Twins + cervical shortening: no clear benefit
• Meta analysis (2005):
  – Twins WITH cerclage had HIGHER rates of:
    • Delivery prior to 35 weeks (75 % vs 36%)
    • RR 2.15 (95% CI 1.15-4.01)

Berghella, Obstet Gynecol, 2005
## Progesterone

<table>
<thead>
<tr>
<th>Author</th>
<th>Multiples</th>
<th>Primary Outcome</th>
<th>Intervention (Drug vs placebo)</th>
<th>Results RR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Briery</td>
<td>Twins N=30</td>
<td>PTB &lt; 35 wk</td>
<td>17-OHP [20-30 until 34 wk]</td>
<td>2.24 [0.8-6.3]</td>
</tr>
<tr>
<td>Rouse</td>
<td>Twins N=661</td>
<td>Delivery or death &lt; 35wk</td>
<td>17-OHP [16-20 until 34 wk]</td>
<td>1.1 [0.09-1.3]</td>
</tr>
<tr>
<td>Norman</td>
<td>Twins N=500</td>
<td>PTB or death &lt;34 wk</td>
<td>Vaginal progesterone gel</td>
<td>1.27 [0.91-1.78]</td>
</tr>
</tbody>
</table>
Tocolytics

Prophylactic tocolysis:
- 5 RCTs with 344 twin pregnancies
- RR of birth <37 weeks 0.85 (95% CI 0.65-1.10)
- RR of birth <34 weeks = 0.47 (95% CI 0.15-1.50)
- RR neonatal low birthweight = 1.19 (95% CI 0.77-1.85)
- RR neonatal mortality = 0.80 (95% CI 0.35-1.82)

*Take home point:* do not use prophylactic oral betamimetics in twins

Tocolytics for PTL

• No difference in:
  – Delivery within 7 days of treatment
  – Perinatal or neonatal death
  – Neonatal complications: RDS, NEC, Cerebral palsy

• Increased side effects in women with twins
  – Risk pulmonary edema
TWINS: SPECIAL SITUATIONS
Management of the death of one fetus
Fetal Demise

Higher rate of stillbirth than singletons

• Placental insufficiency
• Anomalous cord insertion
• Monochorionicity – placental vascular connections
• Preeclampsia
Management of the death of one fetus

- 2-7% in spontaneous twin gestations
- 25% in multiple gestations from ART.
- Vanishing twin: death of one fetus 1st trimester
  - Dickey et al
    - “Vanishing twin” in 36% of twins, 53% triplets, 65% quads.
  - Landy et al
    - 21% vanishing twin

Mortality in co-twin

• Fetal death at >20 weeks
  – 2.6% twins
  – 4.3% triplets
• Same-sex twin
  – Fetal death 20-24wk: 8% survival
  – Fetal death >37 weeks: 85% survival
• Opposite sex twins
  – Fetal death 20-24wk: 12% survival
  – Fetal death >37 weeks: 98% survival
Morbidity in co-twin

- DIC
- Thromboemboli
- Hypotension
- Ischemic damage leading to structural defects
  - Intestinal atresia
  - Gastroschisis
  - Limb amputation
  - Aplasia cutis
  - Porencephalic cyst, hydranencephaly, or microcephaly
- Cerebral palsy

Semin Diagn Pathol 1993; 10:222
Obstet Gynecol 1991; 78:517
Lancet 2000;355:1597
Twin-twin transfusion syndrome
Twin to Twin Transfusion Syndrome - TTTS

From, Fisk & Galea, NEJM 351:182, 2004
Twin to Twin Transfusion Syndrome - TTTS

Twin to Twin Transfusion Syndrome - TTTS
Twin to Twin Transfusion Syndrome - TTTS

Twin to Twin Transfusion Syndrome - TTTS

2250 g  TTTS  850 g DiMo

Courtesy of Dr. Kurt Benirschke
Twin to Twin Transfusion Syndrome - TTTS

Courtesy of Dr. Kurt Benirschke
TTTS Staging

- Four published staging systems:
  - Quintero
  - Cincinnati *
  - Cardiovascular profile scoring *
  - Children’s Hospital of Philadelphia *

*Fetal echocardiogram findings included
# Quintero Staging

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>Donor DVP</th>
<th>Recipient DVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20 wks</td>
<td>≥ 8cm</td>
<td>&lt; 2cm</td>
</tr>
<tr>
<td>≥ 20 wks</td>
<td>≥ 10cm</td>
<td>&lt; 2cm</td>
</tr>
</tbody>
</table>

Concurrently with:

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
<th>Stage IV</th>
<th>Stage V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder filling in donor</td>
<td>Absent bladder filling in donor</td>
<td>Abnormal Dopplers: • AEDF in donor • Reverse DV a-wave</td>
<td>Hydrops in one or both twins</td>
<td>Death of one or both twins</td>
</tr>
</tbody>
</table>
# Cincinnati Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Donor DVP</th>
<th>Recipient DVP</th>
<th>Recipient Cardiomyopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>&lt; 2cm</td>
<td>≥ 8cm</td>
<td>No</td>
</tr>
<tr>
<td>II</td>
<td>Bladder not visible</td>
<td>Bladder visible</td>
<td>No</td>
</tr>
<tr>
<td>IIIA</td>
<td></td>
<td></td>
<td>Mild *</td>
</tr>
<tr>
<td>IIIB</td>
<td></td>
<td></td>
<td>Moderate *</td>
</tr>
<tr>
<td>IIIC</td>
<td></td>
<td></td>
<td>Severe *</td>
</tr>
<tr>
<td>IV</td>
<td>Hydrops</td>
<td>Hydrops</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>Death</td>
<td>Death</td>
<td></td>
</tr>
</tbody>
</table>

* Cardiac Variables

Cardiomyopathy: Mild, Moderate, Severe
AV regurgitation: Mild, Moderate, Severe
RV/LV thickness: >2 + Z-score, >3 + Z-score, >4 + Z-score
MPI: >2 + Z-score, >3 + Z-score

Severe biventricular dysfunction
<table>
<thead>
<tr>
<th>Findings</th>
<th>Normal +2 points each</th>
<th>1 Point Deduction</th>
<th>2 Point Deduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrops</td>
<td>None</td>
<td>Ascitis; pleural and pericardial effusion</td>
<td>Skin edema</td>
</tr>
<tr>
<td>Venous Doppler</td>
<td>Normal</td>
<td>DV atrial systolic reversal</td>
<td>Umbilical venous pulsation</td>
</tr>
<tr>
<td>Cardiothoracic ratio</td>
<td>&lt; 0.35</td>
<td>&gt;0.35 and &lt;0.5</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>Cardiac Function</td>
<td>Ventricular SF &gt;0.28 and valve regurgitation</td>
<td>SF &lt; 0.28 or TR or semilunar valve regurgitation</td>
<td>TR plus dysfunction or any mitral regurgitation</td>
</tr>
<tr>
<td>Arterial Doppler</td>
<td>Normal</td>
<td>AEDF</td>
<td>REDF</td>
</tr>
</tbody>
</table>
### CHOP Staging

<table>
<thead>
<tr>
<th>Category</th>
<th>0 points</th>
<th>1 point</th>
<th>2 points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recipient</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ventricular Findings</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac enlargement</td>
<td>None</td>
<td>Mild</td>
<td>&gt; Mild</td>
</tr>
<tr>
<td>Systolic dysfunction</td>
<td>None</td>
<td>Mild</td>
<td>&gt; Mild</td>
</tr>
<tr>
<td>Ventricular hypertrophy</td>
<td>None</td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td><strong>Valve Function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tricuspid regurgitation</td>
<td>None</td>
<td>Mild</td>
<td>&gt; Mild</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>None</td>
<td>Mild</td>
<td>&gt; Mild</td>
</tr>
<tr>
<td><strong>Venous Doppler findings</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tricuspid valve inflow</td>
<td>2 peaks</td>
<td>1 peak</td>
<td></td>
</tr>
<tr>
<td>Mitral valve inflow</td>
<td>2 peaks</td>
<td>1 peak</td>
<td></td>
</tr>
<tr>
<td>Ductus venousus</td>
<td>All forward</td>
<td>Decreased atrial contraction</td>
<td>Reversal</td>
</tr>
<tr>
<td>Umbilical vein</td>
<td>No pulsation</td>
<td>Pulsations</td>
<td></td>
</tr>
<tr>
<td><strong>Great Vessel findings</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outflow tracts</td>
<td>PA &gt; AO</td>
<td>PA = AO</td>
<td>PA &lt; AO, RVOTO</td>
</tr>
<tr>
<td>Pulmonary Insufficiency</td>
<td>Absent</td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td>Donor Twin Umbilical Artery</td>
<td>Normal</td>
<td>Decreased diastole</td>
<td>Ab</td>
</tr>
</tbody>
</table>
Consensus Statement

• The Quintero staging system should be retained until a superior system has been appropriately validated.
• Cardiac indices and markers of systemic hemodynamic alterations may improve prediction of disease progression and/or perinatal outcomes...[but] should be assessed and validated individually and in combination within a clinical trial.

Stage I
Poly-Oli Sequence
Stage I
Poly-Oli Sequence
Stage II
Poly-Oli Sequence with Absent Bladder
Stage III
Abnormal Doppler Studies

- Reverse DV a-wave
- Elevated MCA

Recipient
Donor
Stage III
Cardiac Changes
CT Ratio: 0.74
Stage IV
Hydrops with Tricuspid Regurgitation
What is the optimal interval for TTTS screening?

Thorson 2011

• Restrospective look at 108 MC pregnancies
  – 42 with TTTS
• Peak incidence occurred at 18 0/7- 18 6/7 weeks
• 2/3 were diagnosed before 22 0/7 weeks
• Screening interval >14 days associated with late Quintero stage at diagnosis (OR 9.45)

Incidence of twin-twin transfusion syndrome by gestational age
Twin-Twin Transfusion Checks
Di/Mo Twins, Every Two Weeks if Normal

• Maximum vertical pockets*
  – Discordant fluid volumes.
  – 2 x 2 cm pockets with membrane in view
• Bladder*
• Evidence of hydrops, presence of effusions, ascites*
• Doppler studies as indicated.
• Cardiac size*
• Cord diameter
• Discordant placental size

*“TTTS check” components
TTTS Treatment Options

• No treatment
• Serial amnioreduction
• Septostomy
• Selective Laser Photocoagulation (SLPC)
• Cord ligation
In summary

DIAGNOSIS- chorionicity matters!
NUTRITION- follow weight gain goals
REFERRAL TO MFM- for any high risk developments
TTTS- occurs in 10-15% . Important to screen for this every 1-2 weeks throughout.
Thank you!