“Management of Complicated Monchorionic Twins”

Anthony Johnson, DO
Professor
University of Texas Health Science Center
Houston, TX

Disclosures

- I have no relationships with commercial companies that could be perceived as a conflict of interest.
- I will be discussing the use of products that are investigational or approved devices that are being used “off label”
  - Bipolar cauterization
  - Radiofrequency ablation
  - Fetoscopes

Twins Overview


 Twins/1,000 births
Dizygotic/Monozygotic ~ 3:1
MZ: Mono/Dichorionic ~ 3:1
US Live births 4,112,052 ~ 24,286 MCDA cases/yr

1980                         2009

Complications in Monochorionic Multi-Fetal Pregnancies

- Twin-Twin Transfusion Syndrome
- Twin Reverse Arterial Perfusion
- Growth Discordance
- Discordant malformations
  - Structural
  - Chromosomal
- Monoamnioitc

"There is NO diagnosis of twins.
The only diagnosis is a monochorionic or dichorionic twin gestation.
This should be written in capital red letters on the front of the chart at 8 - 10 weeks".

K Nicolaides, 02/27/09

Diagnosis

- - - - -

K Nicolaides, 02/27/09
Multifetal Pregnancies ~ Establish chorionicity 10 - 14 weeks

"TT" sign
Monochorionic

Twin Peak (lambda)
Dichorionic

Amnionicity and chorionicity should be documented for all multiple gestations when possible.
ACOG Practice Bulletin, NUMBER 101, FEBRUARY 2009

Twin Pregnancies ~ Chorionicity 10 - 14 weeks

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Sens</th>
<th>Spec</th>
<th>Sens</th>
<th>Spec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speulveda et al 1996</td>
<td>360</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Carroll et al 2002</td>
<td>165</td>
<td>97</td>
<td>100</td>
<td>98</td>
<td>98</td>
</tr>
<tr>
<td>Lee et al 2006 &lt; 14wks</td>
<td>410</td>
<td>90</td>
<td>99</td>
<td>88</td>
<td>95</td>
</tr>
<tr>
<td>2nd tri</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

56% ACOG optimal time for Dx chorionicity 1st trimester; 62% Manage all twins without MFM consultation
Cleary-Goldman J et al 2004

Outcome of MCDA twin gestations in the era of invasive fetal therapy (a prospective cohort study)

<table>
<thead>
<tr>
<th>Survival</th>
<th>Twin live births</th>
<th>172</th>
<th>85%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Singleton</td>
<td>15</td>
<td>7%</td>
</tr>
<tr>
<td></td>
<td>Double demise</td>
<td>15</td>
<td>7%</td>
</tr>
<tr>
<td>Complication</td>
<td>TTTs</td>
<td>18</td>
<td>9%</td>
</tr>
<tr>
<td></td>
<td>sIUGR</td>
<td>30</td>
<td>15%</td>
</tr>
<tr>
<td>Losses</td>
<td>Total</td>
<td>11%</td>
<td>(TTTs ~ 42%)</td>
</tr>
<tr>
<td></td>
<td>&lt; 24 weeks</td>
<td>84%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 24 weeks</td>
<td>16%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt; 32 weeks</td>
<td>1%  (2/160)</td>
<td></td>
</tr>
</tbody>
</table>

Lewi et al. 2008

Monochorionic Twins Management of Anomalies

Risk of in utero death of affected twin

- No benefit from acute delivery
- 12% of cases associated with IUFD of co-twin
- 1.4X over dichorionic twins
- 18% of survivors with neurologic sequelae
- 1.4X over dichorionic twins

Ong et al. BJOG 2006;113:992-8
Bahityar MO, J Ultrasound Med 2007;26:1491

Ong et al. BJOG 2006;113:992-8

Review: Prevalence of CHD in MC/DAC Twin Gestations: A Systematic Literature Review
CHD prevalence in MCDA twin gestation compared to population by Fusi et al.
OB

Bekirayar MO, J Ultrasound Med 2007;26:1491
MANAGEMENT OF MONOCHORIONIC TWIN PREGNANCY

- Twin pregnancies should be offered ultrasound at 10-14 weeks to assess viability, chorionicity, major malformation and nuchal translucency.
- Fetal ultrasounds assessment should be take place every 2-3 weeks in uncomplicated MC pregnancies from 16 weeks.
  - Abdominal circumference
  - Fetal brain
  - Amniotic fluid assessment (MVP)
  - UA Doppler studies

**Monochorionic Twins**

**Ultrasound Surveillance**

- All twins: Ultrasound for anomalies at 18 – 20 weeks
- Dichorionic: Ultrasounds Q 4 weeks for serial growth
- Monochorionic twins: Ultrasounds alternate Q 2 weeks, 16 wks
  - Amniotic fluid volume, bladder
  - Fetal growth
  - Doppler
  - UA +/- DV, UV
  - MCA after 28 weeks
- Fetal echocardiography

**Therapeutic Options**

- Thermal Vascular Occlusion
  - Bipolar cauterization
  - Radiofrequency ablation
- Amnioreduction
- Microseptostomy with AR
- Laser ablation of vessels

**Acardiac Twin**

- Incidence 1/35,000
- Earliest form of TTTS
- Reverse Arterial Perfusion – acardiac*
- Co-twin anomaly – 10%
- Perinatal M&M – 50%
- Growth AT:PUMP 70%
- Polyhydramnios
- Cardiac decompensation in pump twin

**Complicated Monochorionic Twins Outcomes following Bipolar Occlusion for Selective Reduction**

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>PROM</th>
<th>GA @ Delivery</th>
<th>% Live</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lewis et al.*</td>
<td>80</td>
<td>38%</td>
<td>35.4</td>
<td>83%</td>
</tr>
<tr>
<td>Robyr et al.</td>
<td>46</td>
<td>23%</td>
<td>33.0</td>
<td>74%</td>
</tr>
<tr>
<td>Johnson et al</td>
<td>87</td>
<td>21%</td>
<td>36</td>
<td>82%</td>
</tr>
</tbody>
</table>

* 92% normal at 1 yr of age

Everest Medical 3.0 mm (3.3 mm trocar)
5.0 mm
Imagyn 2.0 mm
TRAP ~ Radiofrequency Ablation

Selective Reduction
Bipolar vs. RFA

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>GA Procedure</th>
<th>GA Delivery</th>
<th>PPROM</th>
<th>Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roman, 2010 Bipolar</td>
<td>40</td>
<td>22 (15-26)</td>
<td>39 (19-40)</td>
<td>23%</td>
<td>88%</td>
</tr>
<tr>
<td>Roman, 2010 RFA</td>
<td>20</td>
<td>20 (17-29)</td>
<td>36 (26-40)</td>
<td>9%</td>
<td>87%</td>
</tr>
<tr>
<td>Bebbington, 2010 Bipolar</td>
<td>89</td>
<td>21 (+/- 2.7)</td>
<td>35 (29-39)</td>
<td>28%</td>
<td>87%</td>
</tr>
<tr>
<td>Bebbington, 2010 RFA</td>
<td>58</td>
<td>20 (+/- 2.2)</td>
<td>33 (23-38)</td>
<td>29%</td>
<td>72%</td>
</tr>
</tbody>
</table>

Monochorionic Twins
Epidemiology of TTTS

• Complicates 9 – 15% of MCDA twins
• 1 in 58 twin pregnancies
• 1 in 4,170 pregnancies
• Presentation < 26 weeks ~ 90% perinatal mortality


Twin-twin Transfusion Syndrome

Net transfer of blood or other vasoactive substance from one fetus (donor) to the other (recipient) via placental vascular communications
– Arterio-arterial
– Veno-venous
– Arterio-venous - Deep, unidirectional flow
Pathophysiologic evidence is indirect

Twin Twin Transfusion Etiology

Twin Twin Transfusion Syndrome Diagnosis

Single placenta
Polyhydramnios (8cm) / oligohydramnios (2cm)
Concordant for sex
Discordant for size and placental echogenicity
Recipient persistent enlarged bladder
Donor small or non-visible bladder
Prediction of Twin Twin Transfusion

- Nuchal Translucency
- Discordant AFV*
- Folding Intertwin Membrane
- Arterio-arterial anastomoses

Twin-Twin Transfusion Syndrome Staging

**Stage I**
- Oligohydramnios (<2 cm) with Polyhydramnios (>8 cm)

**Stage II**
- Discordant fluid volume
- No bladder in the donor twin

**Stage III**
- Doppler flow: absent or reversed in umbilical artery or ductus venosus, pulsatile flow in the umbilical vein

**Stage IV**
- Hydrops in one or both fetuses

**Stage V**
- One or both fetuses have died


Intervention for the treatment of TTTS Laser vs. Amnioreduction

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Laser</th>
<th>Amnioreduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative Risk (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dual Death</td>
<td>0.33</td>
<td>(0.16-0.67)</td>
</tr>
<tr>
<td>Overall Death</td>
<td>0.71</td>
<td>(0.56-0.92)</td>
</tr>
<tr>
<td>Less Perinatal Death</td>
<td>0.59</td>
<td>(0.40-0.87)</td>
</tr>
<tr>
<td>Neonatal Death</td>
<td>0.29</td>
<td>(0.14-0.61)</td>
</tr>
<tr>
<td>Neurologically intact at 6 months</td>
<td>1.66</td>
<td>(1.17-2.35)</td>
</tr>
</tbody>
</table>

Intervention for the treatment of TTTS Laser vs. Amnioreduction

Outcome

- Relative Risk (95% CI)
- Dual Death: 0.33 (0.16-0.67)
- Overall Death: 0.71 (0.56-0.92)
- Less Perinatal Death: 0.59 (0.40-0.87)
- Neonatal Death: 0.29 (0.14-0.61)
- Neurologically intact at 6 months: 1.66 (1.17-2.35)

*Unpublished data

Neonatal Survival Rates TTTS Post Laser

- Study: Dalto et al, 1999-2000
- N: 101
- Post-laser: 13%

- Study: Habli, 2009
- N: 152
- Post-laser: 2%

- Study: Lopriore, 2009
- N: 113
- Post-laser: 5%

- Study: Lewi et al, 2009
- N: 202
- Post-laser: 5%

- Study: Slagehekke, 2010
- N: 276
- Post-laser: 8%

Larger intertwin hemoglobin difference w/o signs of TOPS
- Intertwin blood transfusion w/o hormonal imbalance
- Post laser: ex-recipient anemic w/ ex-donor polycythemic ~ 77%

Twin Anemia-Polycythemia Sequence (TAPS)

Larger intertwin hemoglobin difference w/o signs of TOPS
Intertwin blood transfusion w/o hormonal imbalance
Post laser: ex-recipient anemic w/ ex-donor polycythemic ~ 77%

**Study** | **N** | **Post-laser**
----------|-------|----------------|
Dalto, 1999 | 101 | 13%            |
Habli, 2009  | 152 | 2%             |
Lopriore, 2010 | 276 | 8%            |
Lewi et al, 2009 | 202 | 5%            |
Slagehekke, 2010 | 113 | 5%            |

Larger intertwin hemoglobin difference w/o signs of TOPS
Intertwin blood transfusion w/o hormonal imbalance
Post laser: ex-recipient anemic w/ ex-donor polycythemic ~ 77%
**TAPS: Antenatal Management**

- Expectant observation
- Induction of labor
- Intrauterine transfusion
- Selective reduction
- Laser photocoagulation

**Solomon Technique**

After identification and coagulation of each individual anastomoses, the complete vascular equator is coagulated from one placental margin to the other

**TTTS Intervention By ~ Staging**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Poly/Oligo</th>
<th>Donor Absent Bladder</th>
<th>Abnormal Doppler</th>
<th>Hydrops</th>
<th>Demise</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>II</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>III</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>IV</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>V</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Laser

Observe/IUT

“...in the only randomized study that included sufficient cases to address the issue of survival after primary treatment with either laser surgery or amnioreduction, survival rates were higher...and morbidity in the survivors was lower following selective laser surgery at all stages...”

**Survival Rates for Stage 1 TTTS**

<table>
<thead>
<tr>
<th>Case Series</th>
<th>N</th>
<th>Both Survive</th>
<th>One Survive</th>
<th>ALOS</th>
<th>Overall Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huber, 2006</td>
<td>29</td>
<td>76%</td>
<td>17%</td>
<td>93%</td>
<td>84%</td>
</tr>
<tr>
<td>Middeldorp, 2007</td>
<td>10</td>
<td>90%</td>
<td>10%</td>
<td>100%</td>
<td>95%</td>
</tr>
<tr>
<td>Total</td>
<td>39</td>
<td>79%</td>
<td>15%</td>
<td>94%</td>
<td>87%</td>
</tr>
<tr>
<td>QvsAR Bebbington, 2010</td>
<td>42</td>
<td>70%</td>
<td>22%</td>
<td>92%</td>
<td>82%</td>
</tr>
<tr>
<td>Wagner, 2009</td>
<td>30</td>
<td>77%</td>
<td>20%</td>
<td>97%</td>
<td>87%</td>
</tr>
<tr>
<td>Total</td>
<td>72</td>
<td>76%</td>
<td>15%</td>
<td>91%</td>
<td>84%</td>
</tr>
</tbody>
</table>

**Management of Stage 1 TTTS**

The Cochrane Collaboration 2008
- Review suggested laser improved outcome in Quintero Stage 1 and 2 however available studies were not powered to test hypothesis
- Randomized evaluation of interventions (AR, septostomy and laser) in milder forms of TTTS (Quintero stage 1) are required

Stamilio et al 2010: NAFTNet Consensus Conference
- Current evidence indicates that decision between observation and intervention (laser, AR or septostomy) fulfills criteria for normative equipoise
- Randomized clinical trials should be initiated to identify the optimal treatment for mild TTTS
- Primary outcomes: perinatal survival and infant morbidity (dual intact survival of both twins > 2yrs)

Randomized Controlled Trial
Comparing a Conservative Management and Laser Surgery (TTTS1)
This study is currently recruiting participants.
Verified on June 2011 by Assistance Publique - Hôpitaux de Paris
Selective IUGR

Monochorionic Twins
Selective IUGR

- 10-15% of monochorionic twins
- Perinatal mortality & long term morbidity
  - Smaller twin: IUFD 30-40% Neurologic 15-40%
  - Cotwin twin: IUFD 25-30% Neurologic 20-30%
  - iatrogenic prematurity
  - - acute feto-feto transfusion
- Smaller twin EFW < 10%tile for gestational age
- Weight discordance > 25% [(Large + small)/ Large]
- Unequal placental sharing
- +/- Unbalanced intertwin vascular flow

Monochorionic Twins
Classification sIUGR

<table>
<thead>
<tr>
<th>Type</th>
<th>Umbilical Artery</th>
<th>IUFD</th>
<th>Neurologic Compromise</th>
<th>In Utero Deterioration</th>
<th>GA Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal</td>
<td>2-4%</td>
<td>&lt;5%</td>
<td>Rare</td>
<td>34-35</td>
</tr>
<tr>
<td>II</td>
<td>Ductus Venosus</td>
<td>30-40%</td>
<td>14%</td>
<td>50% Ductus Venous Dopplers</td>
<td>≤ 30</td>
</tr>
<tr>
<td>III</td>
<td></td>
<td>15%</td>
<td>15-40%</td>
<td>Rare</td>
<td>32+</td>
</tr>
</tbody>
</table>

Risk of IUFD in sIUGR Twin ~ 40%

Observation

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Survival</th>
<th>Neurologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>14/17 (82%)</td>
<td>3/22</td>
</tr>
<tr>
<td>Laser</td>
<td>8/11 (72%)</td>
<td>0/12</td>
</tr>
</tbody>
</table>

Quintana, R, et al 2001

Monochorionic Twins
Selective Growth Retardation

MCDA Twins
Selective Growth Retardation

Intervention | Survival | Neurologic |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>14/17 (82%)</td>
<td>3/22</td>
</tr>
<tr>
<td>Laser</td>
<td>8/11 (72%)</td>
<td>0/12</td>
</tr>
</tbody>
</table>

Monochorionic Twins
Selective IUGR

<table>
<thead>
<tr>
<th>Type</th>
<th>Gest Age @ delivery</th>
<th>Survival of IUGR twin</th>
<th>Survival of co-twin</th>
<th>Survival of both twins</th>
<th>PVL in co-twin</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td></td>
<td>25/31 (81%)</td>
<td>29/31 (94%)</td>
<td>25/31 (81%)</td>
<td>4/28 (14%)</td>
</tr>
<tr>
<td>II</td>
<td>31.0</td>
<td>6/18 (33%)</td>
<td>17/18 (94%)</td>
<td>5/18 (28%)</td>
<td>1/17 (6%)</td>
</tr>
<tr>
<td>III</td>
<td>32.6</td>
<td>0.32</td>
<td>0.97</td>
<td>&lt; 0.001</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Gratacos et al. Ultrasound Obstet Gynecol 2008;31:669-75

Expectant Observation
- Fetal monitoring
  - Biophysical profile
  - Ductus venosus Doppler blood flow studies in Type II
- Early delivery
- Selective reduction
- Laser ablation placental anastomoses ~ RCT

* Laser only possible in 88% of cases; 12% required second laser procedure
Conclusion

Increase awareness of risks associated with MC pregnancies to Ob/Gyn and patients

- No Dx Twins
- Establish chorionicity early
- Risk stratify multifetal pregnancies DC vs. MC

- MC pregnancies serial ultrasound beginning at 16 weeks
  - Limited (MVP, UA and bladder)
  - Growth studies with Doppler assessment

- MFM/Fetal Treatment Center referral consultation for
  - Targeted ultrasound/echo
  - Signs of discordance growth or AFV

Update ACOG Practice Bulletin
#56 October, Multiple Gestation: Complicated Twins, Triplets and High-Order Multifetal Pregnancy