The diagnosis and management of complicated twins

Joanne Stone MD
Director, Maternal Fetal Medicine
Mount Sinai Health System
Professor OB/GYN at Icahn School of Medicine at Mount Sinai

PRACTICE BULLETIN
Multifetal Gestations: Twin, Triplet, and Higher-Order Multifetal Pregnancies

Compared with dichorionic twins, monochorionic twins have a higher frequency of fetal and neonatal mortality, as well as morbidities, such as fetal and congenital anomalies, prematurity, and fetal growth restriction (10.

Unique Risks of Monochorionic Twins
- Fetal loss
- Fetal anomalies – 2-4X increased risk
- Twin Twin Transfusion Syndrome (TTTS)
- Unequal placental sharing
- Discordant twin growth
- Selective Intrauterine Growth Restriction (sIUGR)
- Twin Anemia Polycythemia Syndrome (TAPS)
- Twin Reversed Arterial Perfusion (TRAP)
- Monoamniotic Monochorionic Twins (MA/MC, MoMo)
- Conjoined twins
- Death of one twin

Other important facts about MC twins
- 100% have vascular connections
- Cerebral Palsy rate is 1.5%
- White matter injury incidence 25% in MC twins after co-twin death
Establishing Chorionicity
- Diagnosis best in 1st trimester
- 98% accurate
- Single placenta, T sign, membrane thickness < 1.5-2 mm

Dating a twin pregnancy
- Use known date of conception if ART used
- Ideally date CRL at 11+0 – 13+6 weeks
- For spontaneous twins, larger CRL should be used

Follow-up after diagnosing MC twins
- MFM consultation
- US every 1-2 weeks
  - MVP (maximum vertical pocket) to assess amniotic fluid
  - Bladder
  - Umbilical artery and ductus venosus dopplers as appropriate
  - MCA (middle cerebral artery dopplers)
  - Early and routine anatomy survey
  - Fetal echocardiograms

Survival rates in MC twins
- When both fetuses alive at 12 weeks, chance of delivering at least one or two live-borns:
  - DC twins: 98% or 96%
  - MC/DI twins: 92% or 86%
  - MC/MA twins: 67% or 67%

Predictors of adverse outcome
- NT, CRL, EFW discordance
- Velamentous cord insertion in 1 or both twins increases risk adverse outcome and TTTS
• CRL discordance ≥ 10% or NT ≥ 20% perform detailed US and karyotype
• For MCDA: increased NT found in 25% MC twins and risk early intrauterine demise or development TTTS > 30% but poor PPV and NPV

Fetal Anomalies

- 3-5x increase risk congenital anomalies in MZ twins
- 20% concordant – especially CHD and NTDs
- MZ twins are NOT “IDENTICAL”
• Post-zygotic genetic/epigenetic and environmental events
• Unequal blastomere allocation
• Genetic/epigenetic discordance

Pathophysiology of complications of MC twins

• “chorio-angio-pagus” - (placenta-vascular-conjoined)
• Angioarchitecture explains pathophysiology behind unique complications and reasoning for management
• Explains how both are affected by complications

Complications of MC twins

- Majority are uncomplicated
- 10 - 15% have TTTS
- 3% have spontaneous TAPS
- 15% have sFGR
  - Unbalanced division of the placenta -> sFGR
  - Can have combination of unbalanced intertwin blood flow and unequal placental share
Diseases associated with **unbalanced** intertwin blood flow

- Twin-twin transfusion syndrome (TTTS)
- Twin anemia polycythemia sequence (TAPS)

Diseases associated with **unequal partitioning of placenta**

- Selective FGR or discordant fetal growth
- Can have both TTTS and sFGR co-existing

Unbalanced AV anastomoses and partitioning

- TTTS
- TAPS
- TTTS and sFGR
- TTTS and sFGR and TAPS

TTTS

- Complicates 8-10% of MCDA twins
- Untreated TTTS has 70-100% loss rate – esp early severe disease
- High neurologic morbidity in survivors (10-30%)

Angioarchitecture in TTTS

- Intertwin transfusion
  - Unequal sharing of blood flow due to unbalanced deep AV anastomoses
  - Changes in cardiac function

Imbalance of A-V anastomoses in one direction – donor “transfuses” volume to recipient

Dx: twin poly-oligo (MVP ≤ 2cm, ≥ 8cm)
Ultrasound findings in TTTS

- 1st trimester
  - CRL discordance
  - NT > 95th percentile or discordance >20%
  - Reversal or absence of ductus venosus A wave
- 2nd trimester findings
  - Abdominal circumference discordance
  - Membrane folding
  - Velamentous placental cord insertion in donor

TTTS Quintero Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Ultrasound parameter</th>
<th>Categorial criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Fetal hydrops</td>
<td>MPR &lt; 2 cm in donor, MPR &gt; 1 cm in recipient</td>
</tr>
<tr>
<td>II</td>
<td>Fetal hydrops</td>
<td>Non-appearance of fetal hydrops in donor over 60 min of observation (Figure 2)</td>
</tr>
<tr>
<td>III</td>
<td>Fetal hydrops</td>
<td>Absent or reversed fetal hydrops; absent or reversed umbilical artery Dopplers; normal ductus venosus A wave</td>
</tr>
<tr>
<td>IV</td>
<td>Fetal hydrops</td>
<td>Absent or reversed fetal hydrops</td>
</tr>
</tbody>
</table>

Some centers incorporate fetal echocardiography (recipient cardiomyopathy) into staging.

TTTS Management

- Delivery
- Expectant management
  - Majority stage I remain stable or regress
  - Serial amnioreduction
  - Laser photocoagulation
    - Superior to AR in RCT
    - Treatment of choice for dual survival
  - Selective termination of one fetus
  - Pregnancy termination

TTTS outcomes with laser therapy

- 85% chance 1 survivor
- 65% chance 2 survivors
- 10% chance of no survivors
- 54% chance donor demise in Stage III with abnormal Dopplers and sFGR
- Mean GA delivery – 33 weeks
- 10-20% chance neurologic morbidity of survivors by age 2

Management options in TTTS

- Pregnancy termination
  - Early or advanced stage TTTS
  - Complete termination or umbilical cord occlusion
- Amnioreduction
  - > 26 weeks
  - Decline unavailable fetoscopic laser therapy
- Laser photocoagulation of communicating vessels
  - 18 – 26 weeks
  - Generally more advanced stage TTTS
- Delivery for late presentation

TTTS Quintero Staging


Some centers incorporate fetal echocardiography (recipient cardiomyopathy) into staging.

TTTS Management


TTTS outcomes with laser therapy

NAFNet: what to do about stage I

- Multicenter retrospective observational study
- 124 cases stage I TTTS
- Expectant mgmt. vs. AR vs Laser
- Risk factors for progression
- Outcome data
  - Good: 2 survivors ≥ 30 weeks
  - Mixed: Single survivor or delivery 26-29.9 weeks
  - Poor: Double fetal demise or delivery < 26 weeks

Stage I TTTS: data from North American Fetal Therapy Network

- Regressed to normal
- No survivors
- Spontaneous preterm birth
- Progressed to stage I

Expectant management group

- Average of 11 days until change in status (regress, progress, termination, etc)
- No factors at diagnosis predictive of disease outcome
- AR or laser protected against no survivors
- Laser protected against poor outcome

TAPS (Twin Anemia Polycythemia Sequence)

- A chronic form of feto-fetal transfusion
- Can be spontaneous or after laser
- Involves small peripheral vessels on placental surface

TAPS

- Large inter-twin Hb difference w/o AF discordance
- Small unidirectional unbalanced AV anastomoses near perimeter of placenta
- Incidence:
  - ~6% previously uncomplicated 3rd trimester MC/DA twins vs. 13% after laser therapy
- Usually diagnosed ≥ 26 weeks
- DX: MCA-PSV dopplers:
  - MCA PSV > 1.5 MoM in donor and < 0.8 MoM in recipient
Diagnosis and TAPS Staging System

<table>
<thead>
<tr>
<th>Stage</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>MCAPS &gt; 1.5 MOM and &lt; 1.0 MOM, no compromise</td>
</tr>
<tr>
<td>II</td>
<td>MCAPS &gt; 1.7 MOM and &lt; 0.8 MOM, no compromise</td>
</tr>
<tr>
<td>III</td>
<td>Stage I or II + cardiac compromise (severely abnormal Dopplers)</td>
</tr>
<tr>
<td>IV</td>
<td>Hydrops of donor</td>
</tr>
<tr>
<td>V</td>
<td>Demise of 1 or both fetuses after diagnosis of TAPS</td>
</tr>
</tbody>
</table>

Myth 3: there is an unclear treatment protocol for TAPS

Table 4. Treatment algorithm proposed by Tollenaar et al.29

<table>
<thead>
<tr>
<th>Treatment modality</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expectant management</td>
<td>TAPS stage 1 at any GA</td>
</tr>
<tr>
<td>Laser ablation therapy</td>
<td>TAPS stage 2, non-progressive TAPS and &gt;28 wGA</td>
</tr>
<tr>
<td>UTE with PET</td>
<td>TAPS stage &gt;2 or stage 2 with progression and 28 to 32 wGA</td>
</tr>
<tr>
<td>Delivery</td>
<td>TAPS stage &gt;3 or stage 2 with progression and &gt;32 wGA</td>
</tr>
</tbody>
</table>

Perinatal outcomes for sTAPS

- Multivariable analysis indicated that donor status, antenatal TAPS stage and GA birth were independent risk factors for sPNM
- And TAPS stage 4 and GA birth were independently associated with severe neonatal morbidity

Unequal placental sharing

- Selective fetal growth restriction (sFGR)
- Discordant fetal growth
- Suspect with discordant CRL’s in 1st trimester or discordant ACs in 2nd trimester

Monochorionic complications: sFGR

- Unproportionate placental partitioning
- Incidence: 12 - 25% MC twins
- Diagnosis:
  - sFGR < 10% in smaller twin
  - Significant growth discordancy (≥25%) even at EFW > 10% in small twin
  - Increase risk adverse outcomes
- Increase in perinatal loss and adverse neurologic complications
- 20% fetal demise (smaller twin)
- 35% neurologic morbidity (larger twin)
Classification, Outcomes and Management of sFGR

<table>
<thead>
<tr>
<th>Type</th>
<th>Umbilical artery Dopplers</th>
<th>IUFD or diastolic drop (%)</th>
<th>Neurologic complications</th>
<th>GA delivery</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Panc DF</td>
<td>2-4%</td>
<td>Explicable</td>
<td>&lt;3%</td>
<td>Rare</td>
</tr>
<tr>
<td>II</td>
<td>Persistent AEDF or REDF</td>
<td>6-30%</td>
<td>More predictable</td>
<td>14%</td>
<td>90%</td>
</tr>
<tr>
<td>III</td>
<td>Intermittent AEDF or REDF</td>
<td>10-20%</td>
<td>15-40%</td>
<td>15%</td>
<td>41-42w Dopplers</td>
</tr>
</tbody>
</table>


Management options in sFGR

- Demise of MCDA twin – 10-15% risk of death of co-twin and 20-25% risk of neurologic morbidity
- Considerations include severity, stage, gestational age, parental wishes and technical considerations
- Selective reduction by cord occlusion
  - Survival > 80% for non-reduced twin with normal neurologic outcome in >90%
- Laser
  - Technically challenging – no polyhydramnios, large AAAs
  - High risk for demise of sFGR twin (65-75%)

Intrauterine demise
- Neonatal death
- Intact survival

Type I sFGR
- Expectant: 3.1%
- Laser: 16.7%
- Selective reduction: 0%

Type II sFGR
- Expectant: 16.6%
- Laser: 44.3%
- Selective reduction: 5%

Type III sFGR
- Expectant: 13.2%
- Laser: 32.9%
- Selective reduction: 0%

TRAP (Twin Reversed Arterial Perfusion)
- Occurs in 1/100 MC twins (3/4 MCDA, ¼ MOMA)
- Early vascular disruption results in abnormal AAA between twins
- Acardiac twin depends on retrograde arterial supply of deoxygenated blood from pump twin
- Diagnosis: Doppler ultrasound of acardiac fetus’ umbilical cord shows arterial blood flowing toward the acardiac twin

Management Considerations

- Sonographic markers for poor prognosis
  - Ratio of acardiac twin to pump twin > 50%
  - Polyhydramnios > 60%
  - Cardiac failure > 30%
  - PTD > 90%
  - Pump twin with cardiac failure with abnormal Dopplers
  - Increase in size of pump twin (AC of acardiac/pump >1.0)
- How do you estimate size of acardiac twin
  - $L \times W \times H \times 0.52$ (formula for a sphere)
Management

- Expectant
  - 30% loss rate between 1st trimester diagnosis and 2nd trimester intervention
- Consider intervention
  - Acardiac/pump ratio> 50%
  - Rapid growth acardiac twin
  - Hemodynamic compromise of pump twin
- Intervention
  - Occlusion of vascular connections (RFA, laser)
  - RFA survival 80-90%

Monoamniotic (MA) twins

- 1 in 10,000 pregnancies
- 1% of all monozygotic twins
- Occurs when split occurs around days 8-13

Monoamniotic (MA) twins: management

- Consider CVS or amniocentesis
- Anatomy ultrasound and fetal echo
- Growth ultrasounds
- Consider hospital admission around 24-28 weeks when patient would intervene
- Antepartum surveillance
  - BPP
  - NSTs or continuous monitoring
- Delivery by cesarean around 32-34 weeks
- Survival in anatomically normal fetuses is > 90%

Monoamniotic (MA) twins: management

- Diagnosis
  - Lack of intertwin membrane
  - Single placenta with both cord insertions close to each other
  - Cord entanglement

Monoamniotic (MA) twins: management

- Multinational cohort study 2010-2017
  - Non-anomalous uncomplicated MO/MO twins with 2 live fetus at 26 weeks included
  - 10 centers inpatient, 12 centers outpatient
  - Primary outcome IUFD
  - 195 women (290 fetuses)
  - Results
    - Overall perinatal loss rate 10.8%
    - 4 women (5.1%) inpt and 15 women (16.3%) outpt IUFD
    - Peak fetal death rate 4.7% occurring at 25 weeks
    - From 32 – 36 weeks no fetal/neonatal deaths
    - No difference in in-patient or out-patient groups

Conjoined twins

- Very rare: 10.2/million births
- 18% prenatally-diagnosed fetuses survive
- Increase rate of structural anomalies
- Outcomes depend on which organs are shared

Ultra Obstet Gyn 2000;16(3):223,
Acta Obstet Gyn Scand 2005;84(5):432,
Ultra Obstet Gyn 2006;28:681
Prefumo et al Pren Dx 2015

Inpatient vs outpatient management and timing of delivery of uncomplicated monochorionic monoamniotic twin pregnancy: the MONOMO study.
Discordant anomalies

- Structural anomalies more common in MC twins (6-8%)
- Only 20% are concordant for anomaly
- Monozygotic twins are NOT identical
  - Post-zygotic mutation
  - Variations in gene expression
  - Asymmetric x-chromosome inactivation
  - Parental imprinting
  - Discordant gene methylation
  - Vascular accidents

Options

- Expectant
- Termination
- Umbilical cord occlusion
- Bipolar cord coagulation
- Radiofrequency ablation (RFA)

RFA outcomes – for various etiologies

- About 15% PPROM (up to 25%)
- Miscarriage survivor about 5%
- Neurologic morbidity survivor about 5%
- Live birth rate about 80%
- Mean GA delivery 33-36 weeks

Death of one twin

- Bleeding of surviving twin into demise twin
  - Hypotension, hypovolemia, anemia, hypoxia, acidosis
  - 15% risk demise of co-twin
  - 25-35% risk severe neurologic morbidity in survivor
- Management
  - Immediate deliver after unwitnessed twin death – no benefit
  - Expectant management
  - Fetal brain MRI’s of survivor

Demise of co-twin

- Retrospective observational study at UCSF
- 21 MC twins (none had laser/RFA)
- Mean GA demise: 19 6/7 w (12 4/7 – 26 6/7)
- Interval to MRI: 4 3/7 w (0-12 1/7)
- 41% associated with TTTS
- Abnormal findings in 7 cases (33%)
- Majority had normal ultrasound

Take home messages

- Establish chorionicity early
- Every 1-2 week surveillance
- Anatomy surveys and echocardiography
- Options for therapy for TTTS, TAPS, anomalies, RFA
- Deliver uncomplicated MC twins around 36 weeks
Thank you