American Pediatric Surgical Association

Prenatal Counseling Series

Twin-Twin Transfusion Syndrome

from the Fetal Diagnosis and Treatment Committee of the American Pediatric Surgical Association

Editor-in-Chief: Ahmed I. Marwan, MD

Special thanks to Niti Shahi, MD, Nicholas Behrendt, MD, and Jill Stein, MD

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Twin-Twin Transfusion Syndrome

Definition
TTTS: shift of intravascular volume between twins with a shared placenta

Etiology and Background
- Mainly diagnosed in monochorionic (1 placenta), diamniotic (2 amniotic sacs) gestations who share a common placenta
- The donor and recipient twins also share multiple vascular connections/anastomoses (1)
  - Vascular anastomoses include artery-to-artery connections (AA), vein-to-vein connections (VV), and veno-arterial connections (VA)
- Progression of disease: Unbalanced blood flow in vascular anastomoses in the shared placenta resulting in unequal volume balances between both fetuses ➞ hypervolemia in recipient twin and hypovolemia in donor twin ➞ increased mortality risk, organ failure, cardiac complications and neurodevelopmental impairment (1)
- Incidence: 10-15% of monochorionic twins (2)
  - If untreated, TTTS can result in 90% mortality of one or both twins (2)
- Donor versus recipient twin:

<table>
<thead>
<tr>
<th>Donor Twin</th>
<th>Recipient Twin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td><strong>Volume shunted away from donor twin ➞ persistent hypovolemia ➞ oligohydramnios</strong></td>
</tr>
<tr>
<td><strong>US findings</strong></td>
<td>Oligohydramnios, absent bladder, abnormal Doppler blood flow</td>
</tr>
<tr>
<td><strong>Complications</strong></td>
<td>IUGR, hydrops, death (1) Increased mortality rate in donor twin (3)</td>
</tr>
</tbody>
</table>

*Figure 1.* Schematic of Twin-Twin Transfusion Syndrome.
*Courtesy of the Colorado Fetal Care Center.*
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Figure 2: Transverse grayscale ultrasound image of the fetal pelvis in a donor twin shows lack of fluid within the urinary bladder.

Figure 3: Transverse color Doppler ultrasound image of the fetal pelvis in the same donor twin shows lack of fluid within the urinary bladder with expected location between the umbilical arteries.

Figure 4: Longitudinal ultrasound of a donor twin demonstrates lack of fluid within the urinary bladder.

Courtesy of Jill Stein, MD – Colorado Fetal Care Center

• Associated anomalies:
  o IUGR in 20% of cases (2)
  o Chromosomal abnormalities (4)
  o Congenital cardiac defects (5-10)
  o Cerebral lesions (5-10)

• Worse prognosis with the following:
  o More severe presentation when it manifests <20 weeks (1, 11)
  o Higher Quintero stage
  o Fetal growth discordance >30% (3, 10), IUGR in one or both fetuses
Differential Diagnosis (2)

1) IUGR (selective intrauterine growth restriction)
2) TAPS (twin anemia polycythemia sequence)
3) Discordant twins secondary to anomaly
4) Subjective fluid discordance
5) Dichorionic twin gestation with fluid discordance
6) Discordant twins secondary to infection

Prenatal Consideration

- **Monoamniotic Dichorionic twin monitoring:**
  - 1st trimester ultrasound assessment: chorionicity, nuchal translucency
  - Starting at 16 weeks, q2 week surveillance with ultrasound: **amniotic fluid evaluation**, middle cerebral artery (MCA) peak systolic velocity (increased frequency if abnormal)
  - If patient is diagnosed with TTTS, recommend **echocardiogram**
  - Monthly fetal growth evaluations
Diagnosis

- Based on current ultrasound surveillance and **echocardiography**
- **Current staging systems:** (12)
  - Quintero staging for TTTS: (2, 4, 11)
  - Cincinnati modification of the Quintero staging: incorporates echo findings of AV valve function, ventricular hypertrophy and ventricular function (13)
  - CHOP cardiovascular score in TTTS (14-17)
  - Cardiovascular Profile Score (CVPS) for fetal hydrops (18)

<table>
<thead>
<tr>
<th>Stage 1</th>
<th>Polyhydramnios, oligohydramnios, bladder of donor visible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 2</td>
<td>Dopplers are not critically abnormal, bladder is not visualized in donor twin</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Abnormal Doppler studies in donor or recipient twin (i.e. absent or reversal umbilical artery end diastolic flow, reversal of ductus venosus a-wave, and/or pulsatile umbilical vein flow)</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Hydrops of one or both twins</td>
</tr>
<tr>
<td>Stage 5</td>
<td>Death of one or both twins</td>
</tr>
</tbody>
</table>

*Figure 6. Normal umbilical arterial spectral Doppler waveform pattern in a donor twin with brisk systolic upstroke and positive diastolic flow. Courtesy of Jill Stein, MD – Colorado Fetal Care Center*
Figure 7. Abnormal umbilical arterial spectral Doppler waveform pattern in a recipient twin with absent diastolic flow.

Courtesy of Jill Stein, MD – Colorado Fetal Care Center

Figure 8. Demonstration of polyhydramnios in Recipient twin on Ultrasound.

Courtesy of Nicholas Behrendt, MD – Colorado Fetal Care Center
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<table>
<thead>
<tr>
<th>Variable</th>
<th>Mild (Stage 3a)</th>
<th>Moderate (Stage 3b)</th>
<th>Severe (Stage 3c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AV regurgitation</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>RV/LV thickness</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>MPI (myocardial performance index)</td>
<td>&gt;2+ Z-score</td>
<td>≥ +3 Z-score</td>
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</tr>
<tr>
<td>LV-MPI</td>
<td>&gt; 0.43 to 0.48</td>
<td>≥ +4 Z-score</td>
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<td>RV-MPI</td>
<td>&gt; 0.48 to 0.56</td>
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### CHOP Cardiovascular Score- Recipient Twin

<table>
<thead>
<tr>
<th>Score</th>
<th>Ventricular characteristics</th>
<th>Valve function</th>
<th>Venous Doppler Characteristics</th>
<th>Great Vessel Analysis</th>
<th>Arterial Doppler Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cardiac enlargement</td>
<td>Tricuspid regurgitation</td>
<td>Tricuspid valve inflow</td>
<td>Outflow tracts</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>None</td>
<td>None</td>
<td>2 peaks</td>
<td>PA&gt;Aorta</td>
<td>Decreased diastolic flow</td>
</tr>
<tr>
<td>0</td>
<td>Mild</td>
<td>Mild</td>
<td>1 peak</td>
<td>PA= aorta</td>
<td>No flow or reversal of diastolic flow</td>
</tr>
<tr>
<td>1</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Decreased atrial contraction</td>
<td>PA&lt;Aorta</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Moderate-Severe</td>
<td>Moderate-Severe</td>
<td>Reversal of flow</td>
<td>RV outflow obstruction</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Moderate-Severe</td>
<td>Moderate-Severe</td>
<td></td>
<td></td>
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### Cardiomyopathy

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**Fetal Cardiovascular Profile Score**

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<tr>
<th></th>
<th>2</th>
<th>1</th>
<th>0</th>
</tr>
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<tbody>
<tr>
<td>Hydrops</td>
<td>None</td>
<td>Ascites, pleural effusion or pericardial effusion</td>
<td>Skin edema</td>
</tr>
<tr>
<td>Cardiomegaly (cardiac area/thoracic area)</td>
<td>&gt;0.2 to 0.35</td>
<td>0.35 to 0.50</td>
<td>&lt;0.2 OR &gt;0.5</td>
</tr>
<tr>
<td>Cardiac function</td>
<td>Normal, diastolic filling</td>
<td>Holosystolic TR</td>
<td>Holosystolic MR, monophasic diastolic filling</td>
</tr>
<tr>
<td>Arterial umbilical Doppler</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
</tr>
<tr>
<td>Venous Doppler (umbilical vein and ductus venosus)</td>
<td><img src="image4.png" alt="Image" /></td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
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**Treatment**

1) **Amnioreduction**
   a. Definition: removal of excess amniotic fluid from recipient twin, can be done serially
   b. Usually not a curative procedure, potential for persistence/recurrence (19–21)
   c. Frequently used if twins >26 weeks gestation (1)
   d. Indication: often for non-complicated TTTS, potentially reverses TTTS in early Quintero stages
   e. Advantages: decreases the side effects of polyhydranmios in recipient twin, may be therapeutic
   f. Risks: **worsening of TTTS**, risk of bleeding, chorioamniotic membrane separation, premature rupture of membranes (PROM)→ prematurity, fetal loss, neurologic impairment, septostomy (rupture of amniotic membrane increased need for additional procedures), uterine bleeding, chorioamnionitis, etc. (1, 2)

2) **Septostomy**
   a. Definition: deliberate puncture into the intertwin membrane to allow for equilibration of amniotic fluid volumes (21, 22)
   b. Risks: cord entanglement, fetal loss
3) Ultrasound or fetoscopic-guided radio frequency ablation (selective fetal reductions)
   a. Definition: selective radiofrequency ablation of the cord of the diseased co-twin or co-twin with significant anomaly in effort to improve the survival of the other twin
   b. Risks: neurologic injury of surviving twin, PPROM (21)

4) Fetoscopic coagulation of vascular anastomoses (laser ablation)
   a. Considered standard of care (3), improved survival over amnioreduction
   b. Indication: Advanced Quintero stages, frequently during 16-26 weeks of gestation
   c. Methods: (24-27)
      i. **Non-selective:** Coagulation of all placental vessels that cross the intertwin membrane/membranous equator, decreased donor survival
      ii. **Selective:** Coagulation of selective connections
      iii. **Sequential:** The order of ablation is as follows: donor artery-recipient vein anastomosis, recipient artery-donor vein anastomosis, V-A, and lastly A-A.
      iv. **Solomon method:** Planned laser ablation between vascular connections along the vascular equator; decreased recurrence of TTTS and TAPS (24)
   d. Amnioreduction frequently performed at the end of the procedure
   e. Advantages: increased survival of both twins, decreased neurologic morbidities (2)
   f. Risks: PROM, premature delivery, chorionic membrane septation, treatment failure (may miss vascular anastomoses), and fetal demise (2, 3)
   g. Contraindication: PPROM (1)

*Figure 9. Before and after Fetoscopic Coagulation of Vascular anastomose.*
*Courtesy of Nicholas Behrendt, MD – Colorado Fetal Care Center*
Postnatal Considerations

- Average gestational age at delivery **31-32 weeks** (28)
- After fetoscopic photo coagulation, recommend weekly ultrasound surveillance and Doppler studies, particularly for recurrent TTTS and TAPS (1)
- **Complications:** (2)
  - Twin anemia polycythemia sequence (**TAPS**)
  - Selective fetal intrauterine growth restriction (**sIUGR**)
  - **Recurrent TTTS**
  - **Fetal demise**
    - Rate of co-twin demise 12-25% (14)
    - Higher risk of death in **donor twin**
  - Neurologic injuries and/or **neurodevelopment impairment** including cerebral palsy, quadriplegia/diplegia/hemiplegia, developmental delay, blindness and hearing impairment (5)
    - Higher risk of neurodevelopment impairment with advanced gestational age at time of laser therapy, high Quintero stage, low gestational age at birth and low birth weight (limitation: only teen mother population) in both donor and recipient twins (no difference between donor and recipients) (28)
  - **Prematurity and associated complications**
  - **Cardiac complications** from volume overload such as ventricular hypertrophy, ventricular dysfunction, valvular defects and heart failure (6, 17, 29, 30)
  - **Respiratory complications**
  - **Renal failure**
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References


