Fetal Provider Information Sheet
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Twin to Twin Transfusion Syndrome (TTTS)

Incidence and Cause

TTTS occurs in ~10-20% of all monochorionic-diamniotic twin pregnancies and rarely in monochorionic-monoamniotic pregnancies and is likely a result of abnormality of the shared placenta and vasoactive mediator release that resolves with laser dichorionization. It is thus suggested that unbalanced vascular "connections" between the fetuses is necessary but not sufficient, as most monochorionic placentas have such physiologic connections. The donor becomes oliguric with renal changes evidenced via activation of the the renin-angiotensin systems. Conversely, the recipient twin exhibits evidence of increased vascular resistance and is polyuric. The recipient is also exposed to vasoconstrictive mediators such as endothelin-1, furthering a maladaptive process that can lead to a hypertensive cardiomyopathy and secondary valvar dysplasias. OB/MFMs usually monitor for development of TTTS or related phenomena every two weeks from 16 weeks onward, with more frequent follow up if there are concerns or other complications associated with monochorionic twinning.

TTTS Diagnosis and Staging:

Diagnosis

- Oligohydramnios (Oli) in the donor (<2cm maximum vertical pocket) AND
- Polyhydramnios (Poly) in the recipient (> 8cm maximum vertical pocket if less than 20 weeks gestation, > 10 cm if > than 20 weeks).
  Note: Growth discordance (>20% difference by estimated fetal weight [EFW]) or intra-uterine growth restriction (EFW <10% for gestational age) occur frequently but are not diagnostic criteria.

Quintero Staging Most frequently used schema

- Stage I Poli-Oli present; the donor's bladder remains visible
- Stage II Poly-Oli with absence of a visible donor bladder
- Stage III Poly-Oli with abnormal fetal vessel Doppler patterns (stage 3D and/or stage 3R): absent/reverse end-diastolic velocity in the umbilical artery (UA), reverse flow in the ductus venosus (DV), or pulsatile flow in the umbilical vein (UV)
  Note: bladder may or may not be seen with stage III; re-appearance of donor bladder may be a later finding.
- Stage IV Poly-oli with hydrops in either fetus
- Stage V Demise of either fetus with evidence of preceding TTTS

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Related Monochorionic Pregnancy Phenomena

- **Selective Intrauterine Growth Restriction** (**sIUGR):** Affecting one twin, in which the estimated fetal weight is <10th%ile for gestational age, while the other twin is normally grown. Distinguished from TTTS by the lack of poly/oli and lack of evidence of cardiac volume or pressure overload; can occur concomitantly with TTTS, however.
- **Twin Anemia Polycythemia Sequence** (**TAPS):** No poly/oli, but there is evidence of anemia in one twin with MCA peak systolic velocity (PSV) ≥ 1.5 times greater than the median for gestational age (perinatology.com/calculators/MCA). MCA PSV of the other twin should be ≤ 0.8 times the median. The anemic twin typically exhibits cardiac consequences of high cardiac output. More often seen post-laser, but can occur spontaneously throughout the 2nd and 3rd trimesters.

Role of Fetal Cardiac Imager Pre-intervention

- Evaluate for structural heart disease in both twins (baseline incidence is higher than for singletons, ~5-9%, higher if TTTS develops).
- Assess the fetal hemodynamic and cardiac status on donor and recipient to help in determining prognosis, need and timing of intervention, and response to therapy.
- Severity of cardiac findings do not always match severity of TTTS by Quintero staging.
- Ideally, first cardiac evaluation is done prior to any intervention, but in cases of very urgent intervention, the first fetal echocardiogram may be subsequent to the intervention. Serial evaluation may be necessary in some instances to assess for progression if initially normal.

TTTS Fetal Echocardiographic Findings

Monochorionic twins with TTTS have ~ increased risk of CHD up to 9% including VSDs, anomalies of outflows and great vessel anomalies; recipient twins with TTTS have a 10-15% incidence of pulmonary stenosis and coarctation may be increased in donors.

Donor Findings: The smaller twin, typically "stuck" against the uterine wall with little movement. Look for:

- Presence or absence of a bladder.
- Absence of end diastolic flow in the UA (likely secondary to circulating vasoconstrictors).

- Ventricular hypertrophy: significantly less common than in the recipient, but can be seen in severe cases and likely reflective of placental insufficiency
- Indexed combined cardiac output

Recipient Findings: The larger, very mobile twin is more severely affected, facing volume and pressure loading. Look for:

- Indexed combined cardiac output
- Ventricular dilation and hypertrophy
- Assessment of RV and LV systolic function
- Assessment of diastolic dysfunction
    1. Fusion of the E and A waves on tricuspid valve inflow
    2. Shortened filling time as a percentage of the R-R interval (<35%)
    3. Abnormal fetal vessel flow: DV "a" wave reversal and UV pulsations indicative of poor RV compliance
    4. Abnormally elevated RV MPIs (>0.45).
    5. Abnormal RV or LV Tissue Doppler studies consistent with diastolic impairment
- Cardiomegaly: CT area and circumference ratios. Typically, cardiomegaly reflects more hypertrophy than dilation, consistent with pressure loading
- Presence and severity of TR/MR. TR present in at least 40% of cases, MR <20%. Measure peak velocities of regurgitant jets. TR velocities of up to 2.5 times expected for gestational age can be seen, given pressure loading
- Presence and severity of pulmonary insufficiency
- Aortic-pulmonary valve size discrepancy (aortic valve larger)
- Subvalvar/valvar/supravalvar pulmonary stenosis or atresia (functional or anatomic) can develop in 5-10%.
- PDA flow reversal if inadequate RV outflow to supply pulmonary flow ("functional pulmonary atresia")
- Hydrops: pleural or pericardial effusions, ascites, skin/scalp edema. Related to venous hypertension with functional lymphatic obstruction resulting in shift of intravascular fluid into the interstitial spaces.

***Cardiovascular Scoring for descriptive purposes (not proven valuable for risk stratification at present)**

CHOP TTTS Cardiovascular Score: Assesses 5 aspects of cardiovascular function (4 for recipient, 1 for donor) to more adequately classify cardiovascular burden. There are discrepancies in cardiac disease severity when compared to Quintero staging.

- Ventricular characteristics: hypertrophy, dilation, dysfunction
- Presence and degree of atrioventricular valvar regurgitation.
- Venous Doppler patterns: AV valve inflow patterns, ductus venosus flow, and presence of umbilical venous pulsation.
- Pulmonary artery size relative to the aorta, and pulmonary valvar function (stenosis and/or insufficiency)
- Umbilical arterial flow in the donor.
- Maximum score of 20, divided into 4 severity quartiles.

Fetal Interventions and Outcomes

In the absence of intervention, severe TTTS with onset prior to 24 weeks has <10% survival of both twins

1. **Fetoscopic Laser Photocoagulation of the Communicating Vessels**: First line therapy for Stages II-IV diagnosed by 26 weeks.
   - Survival: 60-70% survival of both twins and 80-90% survival of 1 twin.
     - If recurs (5-10%, usually within a few weeks) mortality is up to 40-50%.
     - **If Reverse TTTS** occurs survival < 50%.
   - Risk factors for donor demise: >30% difference in growth of twins, UA end diastolic flow reversal.
   - Risk factors for recipient demise: hydrops, DV A wave reversal, MCA PSV >1.5 times the median.
   - Premature rupture of membranes (PROM) in 10% of mothers within 4 weeks of intervention; 20-30% before 34 weeks gestation.
   - Neurodevelopmental: severe neurologic sequelae in 8%, mild brain abnormalities in 8.ignificant neurodevelopmental abnormalities in 10-18%. Increased risk of impairment with earlier gestational age at laser treatment, Quintero stages III and IV, and low birth weight.
   - Pseudo-amniotic bands occur in 4%, with inadvertent septostomy between the sacs: associated with limb constriction, cord compression, and fetal death.
   - Failure to achieve interruption of all anastomoses occurs in 4%

2. **Amnioreduction**: Drainage of polyhydramnios. Typically done if deepest vertical pocket > 40cm or patient symptomatic.
   - Done at time of laser procedure to lower risk of PROM or premature delivery by improving placental and uterine perfusion by decreasing intrauterine pressure.
   - As isolated therapy for TTTS, typically limited to late presentations > 26 weeks. Requires serial procedures

- If TTTS diagnosed at < 26 weeks and treated only with amnioreduction: 57% survival (range of 15-85% in various series)

3. **Selective reduction** by thermal occlusion of the umbilical vessels, limited to cases where survival of one of the co-twins is very unlikely.
   - Survival of co-twin in range of 80 -93%, with long term developmental delay evident in approximately 8%.

Fetal Cardiac Imager Role and Counseling Post-Laser procedure

- Assess for PDA constriction-given that indomethacin is commonly employed to reduce risk of preterm labor post procedure
- Reassess indexed combined cardiac output.
- Severity of MR/TR: Some improvement can be seen on post op study, and can normalize over time.
- Ventricular function, particularly RV. Function usually improves within 48 hours, and normalizes frequently but not universally by 4-8 weeks post procedure
- LVH/RVH often resolves but can takes weeks/months depending on severity
- PV disease: Associated with worse TTTS, younger age of diagnosis, pericardial effusion. Flow reversal in DV. Functional PS/atresia can improve but about 1/3 persist post-delivery. Of those with persistent PS/PA, 50-73% may require balloon dilation or surgical palliation. Presence of PS/PA correlated with lower survival of at least one twin (68% vs.84%) and lower overall survival (57% vs.73%) in prospective series of 260 cases (Ortiz et al)
- Fetal vessel assessment- look for changes compared to pre-op. Elevation or discordance in MCA PSV concerning for anemia and possibly evolving TAPS
- Consider if findings consistent with rare reverse TTTS
- Cardiac Counseling: Close and timely communication with OB/MFM and Fetal Intervention team is always essential
- Postnatal increased risk for hypertension, particularly if premature or low birth weight; persistent cardiovascular implications have been suggested but clinical significance at present is unclear.

References

1. Djaafri F, Stirnemann J, Mediouni I, et al. Twin-twin transfusion syndrome –what we have learned from clinical trials. Seminars in Fetal & Neonatal Medicine 2017 (22): 367-375.
2. Van Mieghem T, Klaritsch P, Done E, et al. Assessment of fetal cardiac function before and after therapy for twin-twin transfusion syndrome. Am J Obstet Gynecol 2009.
3. Papanna R, Johnson A. Twin-twin transfusion syndrome and twin anemia polycythemia sequence: Pathogenesis and diagnosis. Uptodate.com. 2018.
4. Papanna R, Johnson A. Twin-twin transfusion syndrome: Management and outcome Uptodate.com. 2018.
5. Society for Maternal Fetal Medicine. Simpson LL. TTTS. Am J Obstet Gynecol. Wohlmuth C. Cardiac pathophysiology in TTTS: new insights into its evolution. Ultrasound Obstet Gynecol 2017. Mach 31. Epub ahead of print.
6. Ortiz et al. Rate and Outcomes of Pulmonary Stenosis and Functional Pulmonary Atresia in Recipient Twins with TTTS. Fetal Diagn Ther 2017;41(3):191-196
7. Eschbach S et al. RVOTO in complicated monochorionic twin pregnancy. Ultrasound Obstet Gynecol 2017;49:737-743
8. Gardiner et al. Ultrasound Obstet Gynecol 2014;43:652-7
9. Van Mieghem TKP et al. Assessment of fetal cardiac function beforehand after therapy for TTTS. Am J Obstet Gynecol 2009 (4):427-33
10. Spring S et al. CHD in monochorionic twins with and without TTTs. Prenat Diagn 2014 Oct;34(10): 994-9
11. Emery SP, et al. North American Fetal Therapy Network: intervention vs. expectant management for stage 1 twin-twin transfusion syndrome. Am J Obstet Gynecol 2016 Sep; 215(3): e1-7.
12. Bahtiyar MO, et al. North American Fetal Therapy Network consensus statement: prenatal surveillance of uncomplicated monochorionic gestations. Obstet Gynecol 2015 Jan; 125(1); 118-23.
13. Rychik J, et al. The twin-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease. Am J Obstet Gynecol 2007 Oct; 197(4): 392.e1-8.
14. Moon-Grady AJ. Fetal echocardiography in twin-twin transfusion syndrome. Am J Perinatol 2014 Sep;31 suppl 1:S31-38.

15. Senat MV, et al. Endoscopiic laser surgery versus serial amnioreduction for severe twin-to-twin transfusion syndrome. N Engl J Med 2004 Jul; 351(2): 136-44.
16. Crombleholme TM, et al. A prospective randomized multicenter trial of amnioreduction versus selective fetoscopic laser photocoagulation for the treatment of severe twin-twin transfusion syndrome. Am J Obstet Gynecol 2007 Oct; 197 (4):e1-396.e9.