Twin-twin transfusion syndrome

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OBJECTIVE: We sought to review the natural history, pathophysiology, diagnosis, and treatment options for twin-twin transfusion syndrome (TTTS).

METHODS: A systematic review was performed using MEDLINE database, PubMed, EMBASE, and Cochrane Library. The search was restricted to English-language articles published from 1966 through July 2012. Priority was given to articles reporting original research, in particular randomized controlled trials, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Evidence reports and guidelines published by organizations or institutions such as the National Institutes of Health, Agency for Health Research and Quality, American College of Obstetricians and Gynecologists, and Society for Maternal-Fetal Medicine were also reviewed, and additional studies were located by reviewing bibliographies of identified articles. Consistent with US Preventive Task Force guidelines, references were evaluated for quality based on the highest level of evidence, and recommendations were graded accordingly.

RESULTS AND RECOMMENDATIONS: TTTS is a serious condition that can complicate 8-10% of twin pregnancies with monochorionic diamniotic (MCDA) placentation. The diagnosis of TTTS requires 2 criteria: (1) the presence of a MCDA pregnancy; and (2) the presence of oligohydramnios (defined as a maximal vertical pocket of <2 cm) in one sac, and of polyhydramnios (a maximal vertical pocket of >8 cm) in the other sac. The Quintero staging system appears to be a useful tool for describing the severity of TTTS in a standardized fashion. Serial sonographic evaluation should be considered for all twins with MCDA placentation, usually beginning at around 16 weeks and continuing about every 2 weeks until delivery. Screening for congenital heart disease is warranted in all monochorionic twins, in particular those complicated by TTTS. Extensive counseling should be provided to patients with pregnancies complicated by TTTS including natural history of the disease, as well as management options and their risks and benefits. The natural history of stage I TTTS is that more than three-fourths of cases remain stable or regress without invasive intervention, with perinatal survival of about 86%. Therefore, many patients with stage I TTTS may often be managed expectantly. The natural history of advanced (eg, stage ≥III) TTTS is bleak, with a reported perinatal loss rate of 70-100%, particularly when it presents <26 weeks. Fetoscopic laser photocoagulation of placental anastomoses is considered by most experts to be the best available approach for stages II, III, and IV TTTS in continuing pregnancies at <26 weeks, but the metaanalysis data show no significant survival benefit, and the long-term neurologic outcomes in the Eurofetus trial were not different than in nonlaser-treated controls. Even laser-treated TTTS is associated with a perinatal mortality rate of 30-50%, and a 5-20% chance of long-term neurologic handicap. Steroids for fetal maturation should be considered at 24 0/7 to 33 6/7 weeks, particularly in pregnancies complicated by stage ≥III TTTS, and those undergoing invasive interventions.

Key words: amnioreduction, fetoscopy, laser photocoagulation, monochorionic twins, twin-twin transfusion syndrome

Question 1. How is the diagnosis of twin-twin transfusion syndrome made and how is it staged? (Levels II and III)

Twin-twin transfusion syndrome (TTTS) is diagnosed prenatally by ultrasound. The diagnosis requires 2 criteria: (1) the presence of a monochorionic diamniotic (MCDA) pregnancy; and (2) the presence of oligohydramnios (defined as a maximal vertical pocket [MVP] of <2 cm) in one sac, and of polyhydramnios (a MVP of >8 cm) in the other sac (Figure 1).[1] MVP of 2 cm and 8 cm represent the 5th and 95th percentiles for amniotic fluid measurements, respectively, and the presence of both is used to define stage I TTTS.[2] If there is a subjective difference in amniotic fluid in the 2 sacs that fails to meet these criteria, progression to TTTS occurs in <15% of cases.[3] Although growth discordance (usually defined as >20%) and intrauterine growth restriction (IUGR) (estimated fetal weight <10% for gestational age) often complicate TTTS, growth discordance itself or IUGR itself are not diagnostic criteria.[4] The differential diagnosis may include selective IUGR, or possibly an anomaly in 1 twin causing amniotic fluid abnormality.[5] Twin anemia-polycythemia sequence (TAPS) has been recently described in MCDA gestations, and is defined as the presence of anemia in the donor and polycythemia in the recipient, diagnosed antenatally by middle cerebral artery (MCA)–peak systolic velocity (PSV) >1.5 multiples of median in the donor and MCA PSV <1.0 multiples of median in the recipient, in the absence of oligohydramnios-polyhydramnios.[6] Further studies are required to determine the natural history and possible management of TAPS. TTTS can occur in a MCDA twin pair in triplet or higher-order pregnancies.

The most commonly used TTTS staging system was developed by Quintero et al[2] in 1999, and is based on sonographic findings. The TTTS Quintero staging

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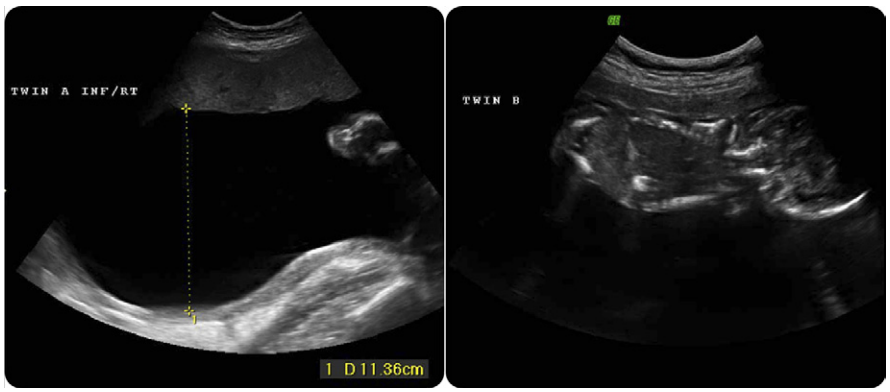
FIGURE 1
Polyhydramnios-oligohydramnios sequence



Monochorionic diamniotic twins with twin-twin transfusion syndrome demonstrating polyhydramnios in recipient's sac (twin A) while donor (twin B) was stuck to anterior uterine wall due to marked oligohydramnios.

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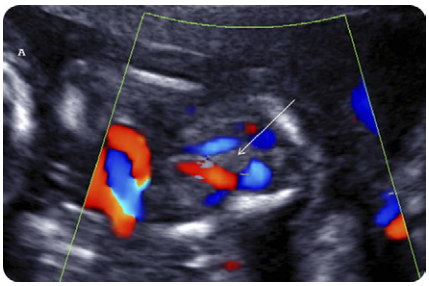
SMFM. Twin-twin transfusion syndrome. Am J Obstet Gynecol 2013.

FIGURE 2
Stage II twin-twin transfusion syndrome



Nonvisualization of fetal bladder (*arrow*) between umbilical arteries in donor twin.

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system includes 5 stages, ranging from mild disease with isolated discordant amniotic fluid volume to severe disease with demise of one or both twins (Table 1 and Figures 2 and 3). This system has some prognostic significance and provides a method to compare outcome data using different therapeutic interventions.[2] Although the stages do not correlate perfectly with perinatal survival,[7] it is relatively straightforward to apply, may improve communication between patients and providers, and identifies the subset of cases most likely to benefit from treatment.[8,9]

Since the development of the Quintero staging system, much has been learned about the changes in fetal cardiovascular physiology that accompany disease progression (discussed below). Myocardial performance abnormalities have been described, particularly in recipient twins, including those with only stage I or II TTTS.[10] Several groups of investigators have attempted to use assessment of fetal cardiac function to either modify the Quintero TTTS stage[11] or develop a new scoring system.[12] While this approach has some benefits, the models have not yet been prospectively validated. As a result, a recent expert panel concluded that there were insufficient data to recommend modifying the Quintero staging system or adopting a new system.[8] Thus, despite debate over the merits of the Quintero system, at this time it appears to be a useful tool for the diagnosis of TTTS, as well as for describing its severity, in a standardized fashion.

TABLE 1
Staging of twin-twin transfusion syndrome[2]

Stage	Ultrasound parameter	Categorical criteria
I	MVP of amniotic fluid	MVP <2 cm in donor sac; MVP >8 cm in recipient sac
II	Fetal bladder	Nonvisualization of fetal bladder in donor twin over 60 min of observation (Figure 2)
III	Umbilical artery, ductus venosus, and umbilical vein Doppler waveforms	Absent or reversed umbilical artery diastolic flow, reversed ductus venosus a-wave flow, pulsatile umbilical vein flow (Figure 3)
IV	Fetal hydrops	Hydrops in one or both twins
V	Absent fetal cardiac activity	Fetal demise in one or both twins

MVP, maximal vertical pocket.

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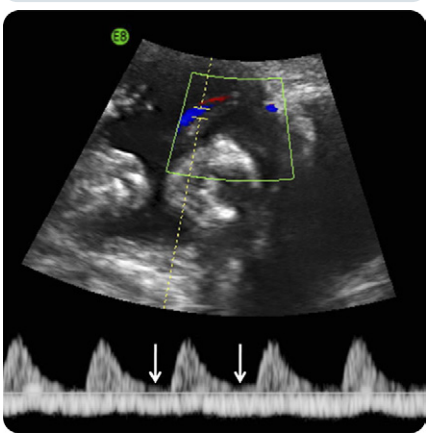
Question 2. How often does TTTS complicate monochorionic twins and what is its natural history? (Levels II and III)

Approximately one-third of twins are monozygotic (MZ), and three-fourths of MZ twins are MCDA. In general, only

FIGURE 3
Stage III twin-twin transfusion syndrome



Absent end-diastolic flow (*arrows*) in umbilical artery of donor twin.

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