Twin-twin transfusion syndrome: Management and outcome

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Literature review current through: Nov 2020. | **This topic last updated:** Oct 20, 2020.

INTRODUCTION

Monochorionic twin pregnancies are monitored for development of twin-twin transfusion syndrome (TTTS) with ultrasound examination every two weeks, beginning at 16 weeks of gestation and continuing until the mid-third trimester. Most cases of TTTS present in the early second trimester and are staged according to the Quintero system (table 1). The stage may remain stable, regress, or progress over time, and progression can occur rapidly. (See "Twin-twin transfusion syndrome and twin anemia polycythemia sequence: Screening, prevalence, pathophysiology, and diagnosis", section on 'Monitoring monochorionic pregnancies for development of TTTS and TAPS'.)

The three primary approaches to management of TTTS are expectant management, fetoscopic laser ablation of anastomotic vessels, and amnioreduction. Selective fetal reduction is another option, but is rarely performed in the absence of discordant malformations or severe selective fetal growth restriction. The choice of approach depends on the Quintero stage, maternal symptoms and signs, gestational age, and availability of requisite technical expertise.

This topic will review the management and outcome of TTTS. The pathogenesis, clinical manifestations, diagnosis, and monitoring for TTTS are discussed separately. (See "Twin-twin transfusion syndrome and twin anemia polycythemia sequence: Screening, prevalence, pathophysiology, and diagnosis".)

MANAGEMENT OF QUINTERO STAGE I

The choice of therapy for Quintero stage I TTTS is based primarily on severity of maternal discomfort from uterine distention and on cervical length. No randomized trials have compared treatment approaches for stage I TTTS. A 2016 systematic review concluded that the optimal initial management of stage I TTTS "remains in equipoise" [1].

Women with no or tolerable symptoms and a normal cervical length

Choice of therapy — For women with Quintero stage I (table 1) TTTS and no maternal symptoms or tolerable symptoms and transvaginal cervical length >25 mm, we avoid intervention and monitor TTTS status with weekly ultrasound examinations to detect progression to more severe disease. In addition to the morbidity associated with any intervention, unnecessary intervention can affect therapeutic options later in pregnancy if intervention becomes indicated because of progressive disease. For example, amnioreduction performed as a first-line treatment of minimally symptomatic stage I disease can result in an inadvertent septostomy or bloody amniotic fluid, which would make subsequent laser treatment difficult to undertake when indicated because of worsening TTTS.

This approach is based on limited but reassuring data of the outcome of well-defined stage I disease in the absence of any intervention. In a 2016 systematic review of 18 observational studies, the pooled incidence of progression in these pregnancies was 27 percent (95% CI 16-39) and overall survival was 79 percent (95% CI 62-92) with expectant management [1]. Overall survival with amnioreduction, laser therapy if progression occurs, and laser therapy as first-line therapy was 77, 68, and 84 percent, respectively. Although these findings suggest laser surgery as a first-line treatment might have a small benefit, they are limited by the biases inherent in observational data. An international

randomized trial comparing expectant management with laser ablation in management of stage I TTTS is underway and should provide better data on which to base recommendations regarding the appropriate role of early intervention at the onset of TTTS [2].

Prenatal follow-up and care — We monitor pregnancies with stage I TTTS and no maternal symptoms or tolerable symptoms and transvaginal cervical length >30 mm for disease progression with ultrasound:

- Amniotic fluid volume is assessed weekly. The North American Fetal Therapy Network reported that the mean duration from diagnosis of stage I TTTS to a change in status was 11.1 days; in those cases that progressed, the mean duration was 9 days [3].
- Fetal growth is assessed every three to four weeks. If selective fetal growth lag is identified (ie, one fetus with estimated fetal weight <10th percentile), Doppler blood flow studies of the umbilical artery and ductus venous are obtained weekly.
- Beginning at 18 weeks, Doppler blood flow studies to assess middle cerebral artery peak systolic velocities (MCA-PSV) are incorporated into the screening protocol of monochorionic multifetal pregnancies, along with Doppler blood flow studies of the umbilical artery (UA) and vein (UV) and ductus venosus (DV) [4]. Discordant values are indicative of twin anemia polycythemia sequence (TAPS), a milder form of TTTS that occurs spontaneously in 5 percent of monochorionic twins. Discordancy is defined as MCA-PSV >1.5 multiples of the median (MoM) in one fetus in conjunction with a value of <1.0 MoM in the other. TAPS is discussed in more detail below. (See 'Twin anemia polycythemia sequence' below.)
- Beginning at 30 weeks, biophysical profile scores are obtained weekly.

If TTTS stage and symptoms remain stable, the American College of Obstetricians and Gynecologists and the International Society for Ultrasound in Obstetrics and Gynecology suggest scheduling delivery at 34 to 37 weeks of gestation, in the absence of complications necessitating earlier delivery [5]. In our practice, uncomplicated monochorionic diamniotic twins are delivered by 37+0 weeks [6]. (See "Twin pregnancy: Labor and delivery", section on 'Monochorionic/diamniotic'.)

Women with debilitating symptoms or short cervical length at 16 to 26 weeks of gestation

Choice of therapy — For women with Quintero stage I TTTS at 16 to 26 weeks of gestation with debilitating symptoms (eg, significant respiratory distress and/or preterm contractions) or short cervix (≤25 mm) due to severe polyhydramnios, we recommend fetoscopic laser ablation, in agreement with most experts in the international medical community [7-9]. Cervical length <28 or 30 mm before laser surgery was predictive of preterm birth in two studies [10,11].

Fetoscopic laser ablation of placental anastomoses is an effective treatment of TTTS and, in contrast to amnioreduction alone, unlikely to require repetitive procedures. In a systematic review that assessed progression of stage I TTTS with various interventions, no pregnancy treated with laser ablation progressed to a more advanced Quintero stage, whereas 30 percent of pregnancies treated with amnioreduction progressed [12].

The procedure is described below. (See 'Fetoscopic laser ablation of anastomotic vessels' below.)

Prenatal follow-up and care after laser therapy — There are few data on which to base specific recommendations for prenatal follow-up and care after laser therapy. We have adopted the following protocol for routine post-laser fetal surveillance:

- Weekly ultrasounds are performed for the first two weeks and then every other week after laser therapy until 30 weeks of gestation, to evaluate for complications and response to therapy [13] (see 'Complications' below):
  - The amniotic fluid and fetal membranes are assessed to detect signs of membrane separation, inadvertent septostomy, membrane rupture, unexpected changes in amniotic fluid volume, and evidence of a therapeutic response. Normalization of the amniotic fluid volume occurs by week 5 in the donor amniotic

sac and by week 8 in the recipient amniotic sac in more than 95 percent of cases [14]. (See 'Persistent or recurrent TTTS' below.)

- MCA-PSV is measured to detect TAPS due to residual placental anastomoses TAPS usually occurs in the first six weeks after laser therapy. As discussed above, TAPS is diagnosed when MCA-PSV is >1.5 MoM in one fetus in conjunction with a value of <1.0 MoM in the other. (See 'Twin anemia polycythemia sequence' below.)

- Fetal weight is estimated every three to four weeks to identify severe growth lag (ie, one fetus with estimated fetal weight <10th percentile), which is typically seen in the ex-donor twin. Doppler blood flow studies of the umbilical artery in the growth-restricted fetus are obtained weekly once viability is reached. If absent or reversed diastolic flow is observed in the umbilical artery, Doppler flow studies of the ductus venosus are added to the monitoring paradigm.

  Growth-restricted donor twins often exhibit catch-up growth after laser ablation. One study reported the proportion of donor twins with growth restriction fell from 65 to 29 percent after the procedure [15]. However, if preterm delivery because of growth restriction seems likely, a course of antenatal glucocorticoids is administered. (See "Antenatal corticosteroid therapy for reduction of neonatal respiratory morbidity and mortality from preterm delivery".)

- Beginning at 30 weeks of gestation, biophysical profile scores are obtained weekly.

We do not routinely order post-laser fetal magnetic resonance imaging (MRI). Although 2 to 6 percent of fetuses will have an ischemic hemorrhagic lesion on MRI at 30 to 32 weeks of gestation following laser therapy, one study noted that 82 percent of these cases were detected by ultrasound prior to MRI [16]. In addition, monochorionic twins are known to have white matter injury, even those without known diagnosis of TTTS, so if an injury is seen, it will not be known whether it is due to the procedure. Lastly, few centers have qualified individuals on-site to read/interpret a fetal MRI.

However, MRI may be informative in cases with a co-twin demise post-laser. In theory, all vascular communications between the twins should be closed so the surviving co-twin should not be at risk of hypotension/emboli at the time of the demise, but since recurrent TTTS is possible, International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) guidelines suggest consideration of imaging (MRI) 4 to 6 weeks after a demise is detected [13].

We schedule delivery by 37+0 weeks of gestation, in the absence of complications necessitating earlier delivery. Preterm delivery is indicated due to the risk of unexplained fetal death at term. Although the ISUOG suggests delivery as early as 34 weeks, there is no evidence of an increased risk of fetal demise after 34 weeks in pregnancies treated with laser surgery.

Women with debilitating symptoms >26 weeks of gestation

Choice of therapy — For women with Quintero stage I TTTS at >26 weeks of gestation with debilitating symptoms (eg, significant respiratory distress and/or preterm contractions) or short cervix (≤25 mm) due to severe polyhydramnios, we perform amnioreduction to reduce uterine overdistention and thereby relieve maternal symptoms [7,8]. Amnioreduction may also improve TTTS. (See 'Amnioreduction' below.)

The US Food and Drug Administration investigational device exemption for fetoscopes limits their use to the treatment of TTTS from 16 to 26 weeks of gestation. Practically, laser ablation at more advanced gestational ages would be subject to several technical limitations: Fetal vernix in the amniotic fluid reduces optimal visualization, placental vessels are larger in caliber and more difficult to successfully coagulate, and current fetoscopes may not easily traverse greater in utero distances. However, some centers outside the United States offer laser ablation after 26 weeks of gestation, and there is increasing evidence that procedures performed at later gestational ages can result in outcomes comparable to those performed in the traditional 16- to 26-week period [17-20].

Prenatal follow-up and care — We have adopted the following protocol for routine post-amnioreduction fetal surveillance:

- Following amnioreduction, fetal ultrasound examination is performed weekly to evaluate for complications, progression to more advanced stage of TTTS, and response to therapy. The amniotic fluid and fetal membranes are assessed to detect signs of membrane separation, inadvertent septostomy, membrane rupture, unexpected changes in amniotic fluid volume, and evidence of a therapeutic response.

  Amnioreduction is repeated if the patient becomes symptomatic (contractions or respiratory compromise) due to uterine overdistention from recurrent polyhydramnios.

- Fetal growth is assessed every three to four weeks. If selective fetal growth lag is identified (ie, one fetus with estimated fetal weight <10th percentile), Doppler blood flow studies of the umbilical artery in the growth restricted fetus are obtained weekly. If absent or reversed diastolic flow is noted, Doppler flow studies of the ductus venosus are added to the monitoring paradigm. If fetal growth discordance is detected and preterm delivery is likely, a course of antenatal glucocorticoids is administered.

- Beginning at 28 weeks, Doppler blood flow studies to assess MCA-PSVs are obtained weekly. As discussed above, discordant values are indicative of TAPS, a milder form of TTTS that occurs spontaneously in 5 percent of monochorionic twins. TAPS is diagnosed when MCA-PSV is >1.5 MoM in one fetus in conjunction with a value of <1.0 MoM in the other. (See 'Twin anemia polycythemia sequence' below.)

- Beginning at 30 weeks of gestation, biophysical profile scores are obtained weekly.

Delivery is scheduled by 37+0 weeks of gestation, in the absence of complications necessitating earlier delivery. Early delivery is indicated due to the risk of unexplained fetal death at term.

MANAGEMENT OF QUINTERO STAGE II TO IV

Intervention for pregnancies at Quintero stage II to IV is indicated because reports suggest a poor prognosis with expectant management alone. Overall perinatal survival with Quintero stage II or more was only approximately 30 percent in a literature review of 28 studies involving a total of 68 pregnancies with untreated TTTS between 1966 and 1991 [21]. By comparison, perinatal survival was approximately 60 percent in two large series with therapeutic intervention [22,23].

Choice of therapy at 16 to 26 weeks of gestation — Fetoscopic laser ablation of placental anastomoses is the preferred procedure for definitive treatment of Quintero stage II to IV TTTS between 16 and 26 weeks of gestation [24].

Although a 2014 meta-analysis of randomized trials comparing laser ablation with amnioreduction did not find a statistically significant improvement in survival with laser therapy, the two trials had discordant results (Eurofetus reported improved survival with laser ablation [25]; the United States trial did not [22]) and in both trials the laser ablation group was more likely to be alive without neurologic complications at six years of age [26]. However, there were several limitations to these data: <200 pregnancies were studied; approximately 90 percent of pregnancies in both trials had stage II or III disease, but the proportions of stage I and stage IV disease randomized were insufficient to answer the question regarding benefit. The Eurofetus trial enrolled patients at all stages of TTTS; of the 142 randomized cases, 11 were stage I (6 randomized to laser and 5 to amnioreduction) and 2 were stage IV cases (1 randomized to laser and 1 to amnioreduction). In the United States trial, stage I cases were excluded; of the 42 randomized cases, 4 were stage IV (3 randomized to laser and 1 to amnioreduction). Thus pregnancies in the United States trial were at the more severe end of the disease spectrum. Both trials were stopped early: Eurofetus was stopped early because a planned interim analysis demonstrated a significant benefit in the laser group. The United States trial was stopped early because referring clinicians were no longer willing to refer patients to the participating centers for randomization after the publication of the Eurofetus report. The reduced enrollment along

with the finding of a statistical trend in adverse outcomes in recipient twins undergoing laser resulted in the decision to stop the trial.

Additional support for the effectiveness of laser therapy was provided by a 2013 meta-analysis of cerebral injury following laser therapy versus amnioreduction, which included four observational studies involving 357 children in the amnioreduction group and 269 children in the laser group [27]. Cerebral injury in live born infants in the amnioreduction group was more than sevenfold higher than in live borns in the laser group (95% CI 2.8-20.0). After excluding neonatal deaths from the analysis, infants from pregnancies treated with amnioreduction still had a marked increase in neurologic injury (relative risk 3.23, 95% CI 1.45-7.14) compared with the laser group. The gestational age at the time of intervention was comparable, 20 to 22 weeks; however, the median gestational age at delivery was lower in the amnioreduction group compared with the laser group, 28 to 31 versus 32 to 34. The authors speculated that the increased risk of cerebral injury in the amnioreduction group was due to the higher rate of prematurity.

Prenatal follow-up and care — Prenatal follow-up and care are identical to that in stage I TTTS patients treated with laser ablation. (See 'Prenatal follow-up and care after laser therapy' above.)

Choice of therapy at >26 weeks of gestation — Amnioreduction is the preferred intervention for treatment of Quintero stage II to IV TTTS at >26 weeks of gestation in the United States. As discussed above, the US Food and Drug Administration investigational device exemption for fetoscopes limits their use to treatment of TTTS at 16 to 26 weeks of gestation. Practically, laser ablation at more advanced gestational ages would be subject to several technical limitations: fetal vernix in the amniotic fluid reduces optimal visualization, placental vessels are larger in caliber and more difficult to successfully coagulate, and greater in utero distances may not be easily traversed by current fetoscopes. However, some centers offer laser ablation after 26 weeks of gestation, and there is increasing evidence that procedures performed at later gestational ages can result in outcomes comparable to those performed in the traditional 16 to 26 week period [17-20]. (See 'Amnioreduction' below.)

Prenatal follow-up and timing of delivery — Prenatal follow-up and delivery timing are identical to that in Stage I TTTS patients treated with amnioreduction. (See 'Prenatal follow-up and care' above.)

MANAGEMENT OF QUINTERO STAGE V

If one fetus has died, the major concerns for the co-twin are death (10 percent risk) or neurologic impairment (10 to 30 percent risk) due to their shared circulation [24]. Management is the same as in monochorionic twin pregnancies without TTTS. (See "Twin pregnancy: Prenatal issues", section on 'Death of one twin'.)

In these cases, neither laser therapy nor amnioreduction can prevent cerebral damage in the surviving twin as the insult occurs at the time of the death of the co-twin. The goal is to optimize the outcome for the surviving co-twin and avoid complications of iatrogenic prematurity. A thorough ultrasound survey of the surviving co-twin should be performed including Doppler blood flows studies of the middle cerebral artery peak systolic velocity (MCA-PSV). Excluding fetal anemia (MCA-PSV) in the setting of an acute fetal co-twin demise essentially eliminates the possibility that major exsanguination occurred and most likely has a favorable prognosis [28]. In the preterm fetus, expectant observation with serial fetal ultrasound examinations every three to four weeks is performed to follow fetal growth and central nervous development. Magnetic resonance imaging examination three to four weeks following the fetal demise is indicated to detect intracranial injury. Emergency delivery in the preterm setting does not improve co-twin outcome.

In utero transfusion to correct fetal anemia within 24 hours of intrauterine fetal death has been offered at some centers, but the benefit of this intervention has not been established [29]. We perform in utero transfusion after an acute demise when fetal anemia is documented by MCA-PSV >1.5 multiples of the median. A fetal blood sample is drawn for hemoglobin/hematocrit and a slow transfusion is started while awaiting the results, which are used to determine the volume of transfusion. (See "Intrauterine fetal transfusion of red cells".)

FETOSCOPIC LASER ABLATION OF ANASTOMOTIC VESSELS

Fetoscopic laser ablation is a procedure in which a laser is inserted through a fetoscope and used to ablate superficial blood vessels on the surface of the placenta that cross the inter-twin membrane. Although anastomoses exist deep in the placenta, their afferent and efferent branches are superficial. Theoretically, coagulation of the superficial vessels should eliminate unbalanced twin-twin transfusion.

The procedure is available at several tertiary obstetric centers in the United States and worldwide. It should only be performed by clinicians with extensive training and expertise performing the procedure.

Contraindications are center specific and may include preterm prelabor rupture of membranes, preterm labor, suspected abruption, significant membrane separation, fetal demise of one twin, fetal chromosomal or congenital abnormalities, and previous amnioreduction [18,30,31].

Patient preparation — Fetoscopic laser coagulation is generally performed as an outpatient procedure under local anesthesia with intravenous sedation, although some centers use regional anesthesia. General anesthesia with endotracheal intubation may be required in select cases because of maternal respiratory distress from extreme polyhydramnios. We administer a first-generation cephalosporin within one hour of starting the procedure; nifedipine 10 mg orally is given just prior to the procedure to suppress uterine contractions. After 24 weeks of gestation, a course of antenatal corticosteroids is administered in case of preterm delivery. Although some centers administer indomethacin rather than nifedipine, we do not use indomethacin because of reports of an increased risk of renal compromise in the donor twin when multiple doses of this agent were used to treat hydramnios in the recipient twin.

A thorough obstetric ultrasound examination is performed, including determination of the distance between the two placental umbilical cord insertion sites. If the sites are too close together (defined as <2 cm), the vascular anastomoses can be difficult to visualize and coagulate [32,33] and an alternative intervention or expectant management may be necessary. However, proximate cord insertions are uncommon, occurring in only 1 to 2 percent of cases of TTTS.

Procedure — The suspected inter-twin vascular equator is located in the region between the two placental umbilical cord insertion sites. The lie of the "stuck" donor twin typically parallels this equator. A site for entry into the recipient sac is selected at 90 degrees to the equator. Power Doppler is used to locate an avascular area in the uterine wall.

The skin is prepped with hexachlorophene and anesthetized with a local anesthetic (we use 0.25 percent bupivacaine). Percutaneous entry may be via the Seldinger technique or by sharp trocar. For the Seldinger technique, an 18-gauge diamond point needle is inserted followed by insertion of a J wire through the needle and then removal of the needle. A 9 to 12 French intravenous catheter is then placed percutaneously over the guide wire under ultrasound guidance. Alternatively, a sharp metal trocar can be placed in the cannula and used for entry into the uterus.

A 2 to 3 mm diameter fetoscope is then inserted through the cannula. If the placenta is anterior and centrally located, entry into the uterus from an extreme lateral approach can result in puncture of the placental edge or the dilated adnexal vascular complex. Specialized fetoscopes with 30 and 70 degree lens have been developed that allow better visualization of the anterior placenta in these cases. In rare cases where percutaneous access is not possible due to the adnexal vasculature, a laparoscopic-assisted approach can be utilized. This method directs the fetoscope through the posterior-lateral uterine wall under direct visualization [34].

We try to visualize all four distal extremities of both fetuses. This is especially important in cases of TTTS complicated by twin anemia polycythemia sequence (TAPS) where the plethoric twin may show signs of thrombosis of extremities (eg, skin bullae and blanching of the affected limb) [35].

We prefer the equatorial dichorionization (Solomon) technique, which has three components:

- **Identify the vascular equator and map the anastomoses** – The inter-twin membrane on the placental surface is located as a landmark. The vascular equator is then identified and the types of anastomoses mapped. The type of anastomosis is determined based on several features as they are visualized through the fetoscope.

  Arteriovenous (AV) or venoarterial (VA) connections appear as a single vessel originating from the donor or recipient; this vessel disappears into the placental mass and a second vessel in immediate proximity of the disappearing vessel can be traced leading back to the co-twin. The arterial component of the anastomosis is dark red-blue (deoxygenated blood), while the venous component is bright red (oxygenated blood). If color differentiation cannot be easily discerned, a vessel can be traced back to its origin from the cord insertion into the placenta. Placental arteries are noted to cross over placental veins.

  Arterio-arterial (AA) anastomoses appear as dark tortuous vessels that connect the twin circulations on the surface of the placenta. Often, pulsating color changes can be seen by fetoscopy as the blood components of the two twins oscillate in the vessel.

  Veno-venous (VV) anastomoses are rare. When present, they appear as relatively straight vessels that course between the two fetal circulations on the placental surface.

  In most cases, the vascular equator can be located in the recipient sac; however, occasionally it is irregular with some component located in the donor sac. The uterine wall at either end of the placenta is examined carefully to ensure that an eccentric communicating vessel is not coursing outside of the placental mass.

- **Coagulate all visible anastomoses** – Laser energy (20 to 40 watts from a diode or YAG laser) is applied through a 400 to 600 micron quartz fiber introduced through an operating channel in the fetoscope. A second channel allows for continuous irrigation to promote visualization. The anastomotic vessels are then coagulated in a specific sequential sequence (called sequential selective laser photocoagulation): Arteriovenous (AV, donor artery to recipient vein), then venous-arterial (VA, donor vein to recipient artery), and lastly arterial-arterial (AA) and venous-venous (VV) anastomoses. As an example, ablation of an AV anastomosis is shown in the video (movie 1) and in the following series of photographs (picture 1 and picture 2 and picture 3).

  Sequential selective ablation has been associated with a 40 to 50 percent reduction in risk of intrauterine demise of the donor or recipient twin compared with selective ablation, the older standard technique. The sequential selective technique requires a specific order of ablation of the type of anastomoses as stated above, whereas ablations of the anastomoses with the selective technique are done in no specific order [23,36]. It has also been associated with an almost doubling of the rate of dual perinatal survival. However, these results should be interpreted cautiously because pregnancies that underwent the standard procedure in these studies did so because of technical difficulties that prevented them from receiving the full sequential selective treatment, potentially biasing the results [23].

- **Coagulate the vascular equator (equatorial dichorionization)** – After coagulation of all visible anastomoses, a thin line of placental surface at the vascular equator is coagulated. This line extends from one edge of the placenta to the other and connects the white areas that resulted from coagulation of the individual anastomoses. The two parts of the chorionic surface of the placenta become completely separated.

  In a multicenter randomized trial comparing this Solomon technique with standard laser coagulation (ie, without coagulation of the vascular equator) in 274 patients with Quintero stage II, III, or IV TTTS, equatorial dichorionization resulted in lower rates of TAPS (3 versus 16 percent, odds ratio [OR] 0.16, 95% CI 0.05-0.49) and recurrence of TTTS (1 versus 7 percent, OR 0.21, 95% CI 0.04-0.98) [37]. When placentas were injected after delivery to look for residual anastomoses, fewer residual anastomoses were found when equatorial coagulation was performed [38]. However, equatorial coagulation did not lead to significant differences in perinatal mortality or severe neonatal morbidity, and neurodevelopment outcomes at two years of age were similar for both approaches [37,39].

The fetoscope is then removed and an amnioreduction is performed until the amniotic fluid volume appears normal in the recipient sac (maximum vertical pocket <8 cm). No more than 3 liters is removed due to the potentially increased risk of abruption. (See 'Amnioreduction' below.)

Complications — Preterm prelabor rupture of membranes (PPROM), TAPS, and inter-twin membrane rupture are the most common complications of fetoscopic laser ablation procedures. Intraamniotic bleeding may also occur and prevent completion of the procedure because of poor visualization. These complications are discussed below.

In a 2019 systematic review including 6746 fetoscopic laser photo-coagulation procedures, severe maternal complications occurred in 1.51 percent (95% CI 0.01-2.25), and placental abruption accounted for 130 of the 141 events [40]. The frequency of minor maternal complications was 4.03 percent (95% CI 2.73-5.56); bleeding during the procedure and chorioamnionitis were the two most common minor complications, accounting for 148 and 68, respectively, of the 241 minor events. In this review, obstetric complications such as PPROM, chorionic membrane separation, preterm labor, and preterm delivery were not considered maternal complications.

Other infrequent complications that have been reported include recurrent TTTS and amniotic fluid leakage into the maternal peritoneal cavity [41]. Intraperitoneal leaking is self-limited but often causes maternal discomfort, which can be controlled with analgesics.

Preterm birth — The average gestational age at delivery after fetoscopic laser surgery is approximately 31 to 33 weeks of gestation [42]. The major risk factors include preterm prelabor rupture of membranes (PPROM), short cervix, amnioinfusion during the laser procedure, and increased number of anastomoses [43].

The most common etiology for preterm birth is spontaneous preterm labor, which occurs in 48 percent of patients, followed by indicated preterm birth, which occurs in 32 percent, and scheduled deliveries in 20 percent [44].

We do not place a cerclage to reduce the risk of preterm birth, even in women with a short cervix. Preventive measures such as cervical cerclage did not prolong pregnancy or improve survival in a retrospective cohort study including 163 patients, 48 percent of whom had cerclage placement for preoperative cervical length <25 mm [45]. In another smaller retrospective study of 14 patients, the cerclage improved pregnancy duration and perinatal survival for preoperative cervical length <15 mm [46].

Preterm prelabor rupture of membranes — The most common serious complication of fetoscopic intervention is PPROM, which occurred within one and three weeks postprocedure in 7 and 17 percent of cases, respectively, in one series [41] and in up to 40 percent of cases in two other series [47,48]. PPROM is associated with a two-week mean reduction in the gestational age at birth [49]. Diagnosis and management are the same as in any pregnancy. (See "Preterm prelabor rupture of membranes: Clinical manifestations and diagnosis" and "Prelabor rupture of membranes before and at the limit of viability".)

Iatrogenic PPROM has been attributed to a persistent fetal membrane defect at the trocar entry site. Use of a small operative cannula (9 or 10 French versus 12 French) decreases the risk of PPROM but prevents use of large diameter fetoscopes and fetoscopes with angled lenses, which increase the likelihood of successful laser ablation [43].

Instillation of platelets, maternal blood, absorbable gelatin, or a collagen plug has been tried to plug the defect, but none of these approaches has been effective [50].

Membrane separation — Membrane separation can usually be seen at the site of trocar entry and is often evident on ultrasound by 24 hours after the laser procedure. It can progress on subsequent ultrasound examinations to completely encircle the uterine cavity, and no therapeutic interventions are available to prevent or correct this complication. Membrane separation is reported after 8 to 20 percent of fetoscopic laser procedures for TTTS [51-53]. It is associated with an increased risk of spontaneous and indicated preterm birth. Increasing severity of chorioamnion separation, particularly ≥10 mm, is associated with worsening pregnancy outcomes [53,54].

Rupture of the inter-twin membranes — Rupture of the inter-twin membranes creating iatrogenic monoamniotic twins occurs in up to 20 percent of cases following laser therapy [55]. It should be suspected when

the amniotic fluid in the donor sac normalizes rapidly, within 24 hours of the laser procedure.

Complications include cord entanglement and limb constriction defects, so-called pseudoamniotic band syndrome (PABS) formation resulting in compromise of blood flow to the cord or fetal extremities [56,57]. In a series of 672 consecutive TTTS cases treated with fetoscopic laser surgery, PABS occurred in 15 (2.2 percent): 10 of 15 recipient and 5 of 15 donor twins [58]. Consequences included amputation of toes in five cases and fetal demise because of constriction of the umbilical cord in one case. Risk factors for PABS were lower gestational age at laser surgery (OR per week 1.43, 95% CI 1.12-1.79) and the presence of postprocedural chorioamniotic membrane separation (OR 42, 95% CI 5-319).

Prenatal intervention is not indicated for PABS. We manage these pregnancies similarly to naturally occurring monoamniotic twins. (See "Monoamniotic twin pregnancy (including conjoined twins)".)

Intraamniotic bleeding during the procedure — Intraamniotic bleeding may obscure visualization and thus prevent completion of the procedure. In these cases, amnioinfusion of crystalloid using the rapid infuser pump utilized by trauma services can be very useful to clear the operative field. We have this equipment available and set it up at all procedures.

Lactated Ringer's solution with 1 g/L of nafcillin is administered (clindamycin 400 mg/L if the patient is penicillin allergic). The remaining portion of the procedure should be completed as rapidly as possible; often a nonselective coagulation method is used (ie, coagulating all vessels along the inter-twin membrane). Depending on the severity of the bleeding, coagulation of the vascular equator (ie, Solomon technique) may not be possible.

Fetal demise — Procedure-related fetal loss (donor or recipient) has been reported in 10 to 30 percent of cases [24]. Risk factors for fetal demise include [59-63]:

- Severe growth discordance or severe growth restriction of one twin
- Reversed end diastolic flow in the umbilical artery
- Reversed a wave in the ductus venosus
- Hydrops fetalis
- Middle cerebral artery peak systolic velocity (MCA-PSV) >1.5 multiples of the median (MoM)

Major risk factors for donor demise, which occurs in 13 percent, after laser ablation include inter-twin growth discordance >30 percent and reversed end diastolic flow (REDF) of the donor umbilical artery [59]. In a series of 466 patients from eight North American treatment centers, stepwise logistic regression showed that REDF in the umbilical artery after laser ablation was predictive of fetal death in the donor twin (OR 4.0, 95% CI 1.54-10.20), while fetal death in the recipient twin after laser therapy was predicted by hydrops (OR 3.7, 95% CI 1.1-12.7) and a reversed "a" wave in the ductus venosus (OR 2.39, 95% CI 1.27-4.51) [60]. In a smaller study (n = 215 consecutive cases), MCA-PSV >1.5 MoM was observed in 5 of 139 recipients (3.6 percent) post-laser ablation and was predictive of fetal death (odds of fetal death: OR 22, 95% CI 1.8-267); two deaths occurred among these five recipients [61].

These pregnancies are at increased risk of preterm prelabor rupture of membranes [64].

Twin anemia polycythemia sequence — TAPS is a mild variant of TTTS characterized by a large inter-twin hemoglobin difference without amniotic fluid discordance. Post-laser TAPS occurs in 2 to 13 percent of TTTS pregnancies treated with laser ablation up to six weeks after the procedure [65]. Risk factors include TTTS with few anastomoses and no artery-to-artery communications before laser ablation [66]. TAPS may also occur spontaneously. The pathogenesis, diagnosis, and classification of TAPS are reviewed separately. (See "Twin-twin transfusion syndrome and twin anemia polycythemia sequence: Screening, prevalence, pathophysiology, and diagnosis", section on 'Twin anemia polycythemia sequence'.)

- **Treatment** – Consideration for treatment is based on progression of the discordance between the MCA-PSVs of the twins. We reserve treatment for pregnancies with >stage II TAPS (ie, MCA-PSV of >1.7 MoM in one fetus and <0.8 MoM in the other fetus). TAPS after laser ablation has been treated with repeat laser therapy, in utero fetal

transfusion, selective feticide, expectant management, and early delivery. There is no consensus regarding the optimal treatment [65,67-69]. We make the decision regarding the best approach on a case-by-case basis based on gestational age and the acuity of the TAPS. If there is a significant disparity in the MCA velocities of the twins soon after the procedure, we offer selective fetal reduction or an attempt at repeat laser ablation. However, a repeat laser procedure can often be difficult due to bloody amniotic fluid as a result of the previous procedure. If termination of pregnancy is an option, it should be considered; otherwise, a repeat laser procedure is offered.

In more chronic cases of TAPS, intrauterine transfusion of red cells to the anemic fetus can be undertaken. This is best accomplished with an intraperitoneal approach to allow for the slow absorption of red cells (see "Intrauterine fetal transfusion of red cells"). Some centers will undertake a partial exchange of the plethoric twin at the same setting to potentially reduce the complications associated with hyperviscosity. In these cases, aliquots of blood are removed and replaced with equal volumes of sterile saline. Repeat procedures are based on subsequent MCA-PSVs. after 32+0 weeks of gestation. We continue expectant observation for Stage I TAPS with delivery by 37+0 weeks of gestation in the absence of progression to a more advanced stage of TAPS.

- **Outcome** – In the absence of fetal treatment, the outcome spectrum of spontaneous and post fetal laser ablation cases includes delivery of two healthy neonates, need for neonatal blood transfusion or partial exchange transfusion, and death of one or both twins. In a retrospective study of 49 twin pregnancies complicated by spontaneous TAPS, the perinatal survival rate was 83 percent (81/98) of twins, neurodevelopmental impairment occurred in 30 percent (22/74) of survivors, and was more frequent in donors (44 versus 18 percent, OR 4.1, 95% CI 1.8-9.1) [70]. Severe neurodevelopmental impairment was detected in 9 percent of survivors and was also more frequent in donors than recipients (18 versus 3 percent), although the difference did not reach statistical significance. On multivariate analysis, independent risk factors for neurodevelopmental impairment were gestational age at delivery and severe anemia.

  The only study that specifically evaluated long-term neurodevelopmental outcome of fetuses who developed TAPS after fetoscopic laser ablation for TTTS reported mild to moderate cognitive delay (score <85) in 8 of 47 children (17 percent) and severe cognitive delay (score <70) in 2 of 47 children (4 percent) assessed at 24 to 96 months of age [71]. Overall, severe neurodevelopmental impairment occurred in 4 of 47 children (9 percent): cerebral palsy (n = 1), severe motor delay (n = 1), severe cognitive delay (n = 2); these four children were delivered at 28, 29, 29, and 32 weeks of age, which may account for at least some of these impairments. The small sample size and variety of tests used for neurodevelopmental evaluation limit interpretation of these findings.

Persistent or recurrent TTTS — A 2012 systematic review reported the incidence of recurrent TTTS ranged from 0 to 16 percent [72]. Residual anastomoses can lead to persistent or recurrent TTTS. They may have been missed at the time of laser ablation or revascularized after the procedure. Measures for reducing the risk of residual anastomoses include more careful scrutiny of the placental margins (where the majority of residual anastomoses have been found) and use of the Solomon technique. (See 'Procedure' above.)

Persistent or recurrent TTTS can be managed with expectant management, repeat fetoscopic laser ablation, or amnioreduction, depending on the Quintero stage and gestational age.

Reverse TTTS — Reverse TTTS is a rare occurrence post-laser in which each twin assumes the former phenotype of the co-twin (eg, the former donor develops hydramnios and the former recipient develops oligohydramnios). It is unclear how the apparent reversal of the transfusional gradient occurs, but when present, the outcomes are compromised with overall survival rates <50 percent [73,74].

Outcome

Perinatal survival — In a 2013 literature review, overall perinatal survival after laser therapy of stage I to IV TTTS was 65 percent (1306/2016) [24]. Approximately 33 percent of pregnancies had one survivor and 50 percent had two survivors. Survival is higher with stage I and II disease and lower with stage III and IV disease. A contemporary study

reported similar results and also noted that the frequency of respiratory complications was higher in TTTS compared with uncomplicated twins largely due to the early gestational age at delivery in TTTS [75].

Neurodevelopmental impairment — In a 2011 systematic review of studies evaluating neurodevelopmental outcome in pregnancies complicated by TTTS and treated with laser [76]:

- The incidence of neurologic morbidity at birth was 6.1 percent (55/895), with no significant differences between donors and recipients.
- The incidence of any degree of neurologic impairment at follow-up at 6 to 48 months of age was 11.1 percent (140/1255), with no significant differences between donors and recipients or pregnancies with one versus two survivors.
- Cerebral palsy accounted for 39.7 percent (60/151) of long-term abnormal neurologic outcomes.

The overall risk of neurologic impairment post-laser therapy is not significantly different from the baseline risk in monochorionic twins without TTTS or in dichorionic twins matched for gestational age at delivery [77-79]. Almost all of the risk of neurologic impairment in survivors is due to complications related to preterm birth, rather than a direct result of TTTS or laser therapy [76,79-81]. In the largest study of long-term pediatric outcomes in twins treated with fetoscopic laser therapy for TTTS (n = 417), the incidence of behavioral problems was not greater than among children in the general population at two years of age [82]. Presence of behavioral problems appeared to be mostly associated with severe neurodevelopmental impairment. Perioperative fetal hemodynamic changes, such as elevated MCA-PSV >1.5 MoM and change from normal umbilical artery pulsatility index, appear to be associated with an increased risk for severe cerebral injury [83].

Renal effects — Chronic hypovolemia in the donor may result in vascular remodeling and chronic kidney disease [84], which may be prevented by laser ablation [85]. One series reported kidney failure in 7 percent of 101 newborns who received fetoscopic laser ablation compared with 20 percent who received amnioreduction [86]. Another series reported short-term neonatal renal dysfunction (creatinine level of >100 micromol/L) in 7 percent of the laser group versus 38 percent of the nonlaser group [87]. In a study of the long-term renal effects of TTTS treated with laser, all 18 surviving twin pairs had normal serum and urinary markers of renal function and no significant differences were noted between donors and recipients at a median age of three years [88].

Cardiovascular effects — Fetoscopic laser photocoagulation usually improves cardiovascular function in both twins. Optimal initiation of this therapy has shortened disease duration compared with past decades, which appears to provide time for cardiac remodeling before delivery [89]. However, congenital heart disease, particularly mild to severe right ventricular outflow tract obstruction, is detected postnatally in 8 to 16 percent of cases and may require postnatal intervention [90-94]. One series of 51 recipient survivors of laser therapy observed that 8 percent had pulmonary stenosis at the time of birth, a 200-fold increase over the rate in the general population [91]. One-half of the cases required valvular balloon dilation for treatment. Nevertheless, when assessed at a mean age of 10 years, childhood cardiac function was normal in the majority of surviving donors and recipients [95].

Long-term maternal effects — No adverse long-term maternal effects with respect to subsequent fertility, obstetric, and gynecologic outcomes have been observed after fetoscopic laser therapy [96].

AMNIOREDUCTION

Amnioreduction reduces uterine overdistention, which is a risk factor for preterm labor and preterm prelabor rupture of membranes (PPROM). It also decreases pressure inside the amniotic cavity and may thus improve uteroplacental perfusion [97,98].

Procedure — A variety of amnioreduction techniques have been described; no randomized trials have evaluated whether one is safer and more effective than another. There is no consensus regarding how much fluid to remove,

how rapidly to remove the fluid, use of tocolytic medications, or use of antibiotics.

A reasonable approach is to anesthetize the skin with a long-acting local anesthetic (eg, bupivacaine). Under ultrasound guidance, a long 18-gauge spinal needle is introduced into the amniotic sac with polyhydramnios, avoiding the placental edge, if possible. The placenta may be markedly thinned on ultrasound imaging because of uterine distension from the excessive amniotic fluid.

The needle is placed as close to the midline of the uterus as possible with a slight angulation toward the maternal xiphoid to reduce the risk of needle displacement as the uterine size diminishes with drainage of amniotic fluid. The needle can be connected to one end of the specialized tubing included in a disposable thoracocentesis tray (male to male ends) while the other end of the tubing is connected to a short 18-gauge needle that is spiked into a disposable vacuum bottle. This set-up maintains a closed system, avoids excessive needle manipulation, and allows the rate of flow to be controlled with the rollerball valve in the line.

Some authors recommend removing fluid until polyhydramnios is no longer present (maximum vertical pocket <8 cm); others suggest removing no more than 5 liters of amniotic fluid over approximately an hour [99]. Decompression of the uterus with rapid removal of a large volume of fluid may cause placental abruption or fetal bradycardia; therefore, we suggest removing no more than 3 liters of fluid in severe TTTS.

Outcome — The International Amnioreduction Registry reported outcomes from the largest series of TTTS patients undergoing amnioreduction [100]. A total of 223 twin pregnancies from 20 fetal medicine units were diagnosed with TTTS prior to 28 weeks of gestation and treated with 760 amnioreductions. The major findings from this series were:

- Complications associated with the procedure included PPROM within 48 hours of the procedure (6 percent), spontaneous delivery (3 percent), fetal distress (2 percent), fetal death (2 percent), placental abruption (1.3 percent), and chorioamnionitis (1 percent).
- Both twins were live born in 55 percent of pregnancies, one twin was live born in 31 percent, and both twins were stillborn in the remaining 14 percent. During the first four weeks of neonatal life, an additional 30 percent of live born twins succumbed.
- Intracranial abnormalities were observed on neonatal cranial ultrasound in 24 percent of recipient twins and 25 percent of donor twins that survived to four weeks of age.

SELECTIVE FETAL REDUCTION

Selective reduction of one twin is an option that may improve the prognosis of the co-twin if a technique is used that does not impact its circulation. While perinatal outcomes are comparable among the various procedures (bipolar cord coagulation, laser cord coagulation, and radiofrequency ablation [RFA]), RFA is our preferred technique for selective reduction of monochorionic twins because the smaller device reduces maternal morbidity [101].

The fetus predicted to have the least chance for survival is usually selected for the reduction procedure. For example, a recipient with advanced cardiac findings or hydrops or a donor that is growth restricted with discordant fetal weight >30 percent and abnormal umbilical artery Doppler [59].

- **TTTS** – The available data do not show a difference in survival according to whether the donor or recipient twin is targeted [102]. If bipolar cautery is used, reduction of the recipient twin is technically easier since its cord is easily visualized floating amid the excess amniotic fluid. Oligohydramnios around the donor makes this twin a more difficult target, although the donor cord can be grasped through the inter-twin membrane after entry into the recipient's amniotic cavity. This can result in a septostomy and the risk of subsequent cord entanglement. However, if the donor twin is the primary target, amnioinfusion can be performed to improve access for the bipolar forceps. Radiofrequency ablation does not require amnioinfusion [103].

Experience with selective reduction for TTTS is limited. One study including 15 cases of TTTS treated with bipolar coagulation of the umbilical cord reported an overall survival of 87 percent in the co-twin, but preterm prelabor rupture of membranes occurred in 20 percent of pregnancies within three weeks of the procedure [104]. Another study including 22 cases of TTTS treated with bipolar cautery reported an overall survival of 77 percent [105]. One infant had developmental delay at 16 months of age. In a third series of 24 cases of TTTS, the overall survival was 92 percent (one fetal death and three neonatal deaths) [102]. One infant exhibited mild motor delay at 18 months.

- **Selective fetal growth restriction** – Selective reduction is also considered in monochorionic twins with selective fetal growth restriction when fetal demise of the smaller twin is likely remote from term (eg, before 26 weeks) [13]. The goal is to reduce the risk of morbidity and mortality in the surviving co-twin.

SPECIAL POPULATIONS

Dichorionic triamniotic triplets — Fetoscopic laser ablation for treatment of TTTS in dichorionic triamniotic triplets appears to result in similar rates of perinatal and neonatal survival as compared with those in monochorionic diamniotic twins.

A systematic review of perinatal outcome after fetoscopic laser surgery for TTTS in triplet pregnancies reported the following major findings (126 triplet pregnancies, 104 dichorionic-triamniotic [DCTA] and 22 monochorionic-triamniotic [MCTA]) [106]:

- **Fetal loss** – DCTA 19.9 percent, MCTA 28.9 percent.
- **Perinatal loss** – DCTA 23.6 percent, MCTA 75.0 percent.
- **Preterm birth <28 weeks** – DCTA 16.9 percent, MCTA 37.1 percent.
- **Preterm birth <32 weeks** – DCTA 50.0 percent, MCTA 69.5 percent.
- **Survival** – In the DCTA group, all three fetuses survived in 56 percent of pregnancies, two fetuses survived in 27 percent of pregnancies, and only one fetus survived in 17 percent of pregnancies. In the MCTA group, the comparable survival rates were 56, 19 and 25 percent, respectively.
- **Abnormal neurologic outcome** – DCTA 0 to 37 percent, MCTA 0 to 50 percent.

Life-threatening abnormality of one fetus — Selective reduction has been performed for treatment of TTTS when one fetus has a very poor prognosis (eg, life-threatening malformation, severe growth restriction, severe cardiac failure, evidence of brain injury).

Stuck twin overlying the vascular equator — Laser ablation may not be possible when a stuck twin overlies the site of the placental anastomoses. Selective reduction is an option in these cases.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Multiple gestation".)

SUMMARY AND RECOMMENDATIONS

- For women with Quintero stage I twin-twin transfusion syndrome (TTTS) with no or tolerable symptoms and cervical length >25 mm, we suggest expectant management rather than invasive therapy (**Grade 2C**). We perform weekly ultrasound examinations to detect progression to more severe disease. We also follow these

pregnancies with weekly Doppler blood flow studies to assess middle cerebral artery peak systolic velocities (MCA-PSV) and biophysical profile scoring, beginning at 18 and 30 weeks of gestation, respectively. Delivery is scheduled at 36 to 37 weeks if TTTS stage and symptoms remain stable. (See 'Women with no or tolerable symptoms and a normal cervical length' above.)

- For women with Quintero stage I TTTS at 16 to 26 weeks of gestation with debilitating symptoms (eg, significant respiratory distress and/or preterm contractions) or short cervix (≤25 mm) due to severe polyhydramnios, we recommend fetoscopic laser ablation rather than amnioreduction (**Grade 1B**). Amnioreduction performed as a first-line treatment can result in an inadvertent septostomy or bloody amniotic fluid, which would make subsequent laser treatment difficult to undertake when indicated because of worsening TTTS. Amnioreduction is also more likely to require serial procedures. (See 'Women with debilitating symptoms or short cervical length at 16 to 26 weeks of gestation' above.)
    - Post-laser therapy, normalization of the amniotic fluid volume occurs by week 5 in the donor amniotic sac and by week 8 in the recipient amniotic sac in more than 95 percent of cases.
    - These pregnancies are followed closely with ultrasound and Doppler to detect abnormalities of amniotic fluid volume, abnormalities of the inter-twin membrane, and discordance in MCA-PSV or fetal growth. Biophysical profile scoring is performed weekly as of 30 weeks of gestation. Delivery is scheduled at 36 to 37 weeks of gestation, in the absence of complications necessitating earlier delivery. (See 'Prenatal follow-up and care after laser therapy' above.)
- For women with Quintero stage I TTTS at >26 weeks of gestation with debilitating symptoms or short cervix (≤25 mm) due to severe polyhydramnios, we suggest amnioreduction rather than laser ablation (**Grade 2C**). The US Food and Drug Administration investigational device exemption for fetoscopes limits their use to treatment of TTTS at 16 to 26 weeks of gestation, and practically, laser ablation at more advanced gestational ages would be subject to several technical limitations. (See 'Women with debilitating symptoms >26 weeks of gestation' above.)
    - These pregnancies are followed closely with ultrasound and Doppler to detect abnormalities of amniotic fluid volume, abnormalities of the inter-twin membranes, and discordance in MCA-PSV or fetal growth. Amnioreduction is repeated if symptomatic polyhydramnios recurs (ie, contractions or respiratory compromise). Biophysical profile scoring is performed weekly as of 30 weeks of gestation. Delivery is scheduled at 36 to 37 weeks of gestation in the absence of complications necessitating earlier delivery. (See 'Prenatal follow-up and care' above.)
- For women with Quintero stage II to IV TTTS at 16 to 26 weeks of gestation, we recommend laser ablation of placental anastomoses rather than serial amnioreduction (**Grade 2B**). Laser ablation results in greater prolongation of gestational age, higher neonatal survival, and improved long-term neurologic outcome. We use a sequential selective technique followed by the "Solomon" method to assure complete dichorionization of the placenta. (See 'Choice of therapy at 16 to 26 weeks of gestation' above.)
- For women with Quintero stage II to IV TTTS after 26 weeks of gestation, we suggest serial amnioreduction rather than laser ablation (**Grade 2C**). Use of laser therapy after 26 weeks is limited in the United States due to US Food and Drug Administration restrictions on the use of current fetoscopes as well as technical issues that make laser therapy difficult in the third trimester. (See 'Choice of therapy at >26 weeks of gestation' above.)
- Selective feticide may be the best option when TTTS is complicated by a life-threatening anomaly in one of the fetuses, after failed laser ablation, or when TAPS or recurrent TTTS occurs soon after laser therapy. (See 'Life-threatening abnormality of one fetus' above.)
- Approximately 11 percent of survivors of laser therapy have some degree of long-term neurodevelopment abnormality. Neurologic follow-up of apparently healthy neonates after laser therapy is warranted. (See 'Neurodevelopmental impairment' above.)

ACKNOWLEDGMENT

The editorial staff at UpToDate would like to acknowledge Kenneth J Moise, Jr, MD, who contributed to an earlier version of this topic review.

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Topic 6793 Version 71.0

GRAPHICS

Quintero stages for classification of twin-twin transfusion syndrome

Stage I	Oligohydramnios and polyhydramnios sequence*, and the bladder of the donor twin is visible. Dopplers in both twins are normal.
Stage II	Oligohydramnios and polyhydramnios sequence, but the bladder of the donor is not visualized. Dopplers in both twins are normal.
Stage III	Oligohydramnios and polyhydramnios sequence, nonvisualized bladder, and abnormal Dopplers. There is absent/reversed end diastolic velocity in the umbilical artery, reversed flow in a-wave of the ductus venosus, or pulsatile flow in the umbilical vein in either fetus.
Stage IV	One or both fetuses show signs of hydrops.
Stage V	One or both fetuses have died.

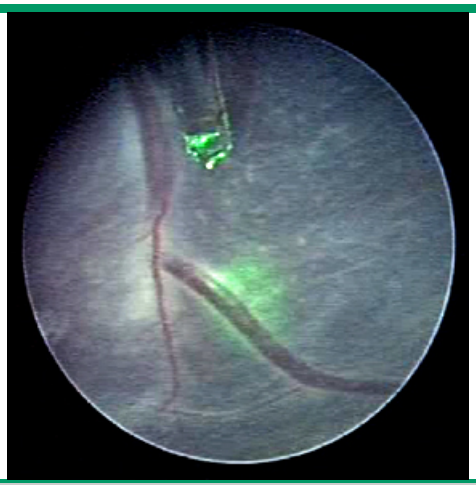
Although Quintero staging represents one method of standardization, there are several important limitations. Atypical presentations can occur; for example, the donor twin may have both a persistent bladder and abnormal umbilical Doppler flow. In addition, although higher stages are generally associated with a worsening perinatal prognosis, the clinical presentation of a particular case does not always follow an orderly progression of stages. For example, a stage I case may progress rapidly in several days to stage III and regression of disease can occur in as many as 15 percent of stage I cases and 60 percent of stage II disease.

* Before 20 weeks of gestation, the maximum vertical amniotic fluid pockets for oligohydramnios and polyhydramnios are usually defined as <2 cm and >8 cm, respectively. After 20 weeks, the maximum vertical pocket for polyhydramnios is defined as >10 cm.

Data from: Quintero RA, Morales WJ, Allen MH, et al. Staging of twin-twin transfusion syndrome. J Perinatol 1999; 19:550.

Graphic 107708 Version 4.0

Arteriovenous anastomosis preablation

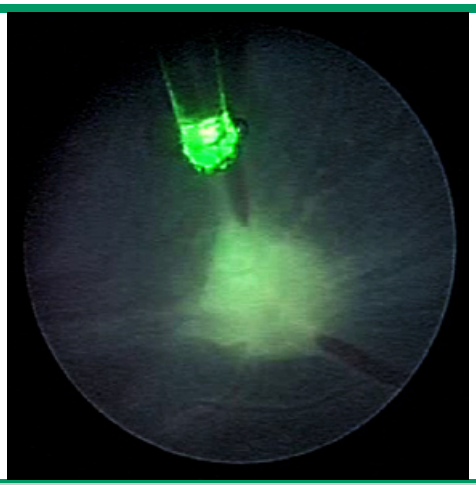


The vessel at 11 o'clock is the recipient's vein, the vessel coming in at 5 o'clock is the donor artery, the "green" targeting light is focused on the donor vessel.

Courtesy of Kenneth J Moise, Jr, MD and Anthony Johnson, DO.

Graphic 67539 Version 4.0

Arteriovenous anastomosis postablation



The ablated area between the recipient vein and donor artery. The laser fiber is at 12 o'clock.

Courtesy of Kenneth J Moise, Jr, MD and Anthony Johnson, DO.

Graphic 80616 Version 4.0

Arteriovenous anastomosis postablation

Ablated (blanched) area between the recipient vein at 12 o'clock and the donor artery at 5 o'clock.

Courtesy of Kenneth J Moise, Jr, MD and Anthony Johnson, DO.

Graphic 56339 Version 5.0

Contributor Disclosures

Ramesha Papanna, MD, MPH Nothing to disclose **Eric Bergh, MD** Nothing to disclose **Deborah Levine, MD** Nothing to disclose **Lynn L Simpson, MD** Nothing to disclose **Vanessa A Barss, MD, FACOG** Nothing to disclose

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

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