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Society for Maternal-Fetal Medicine Consult Series #72: Twin-twin transfusion syndrome and twin anemia-polycythemia sequence

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Replaces SMFM Clinical Guideline #5: Twin-twin transfusion syndrome and SMFM Consult Series #24: The importance of determining chorionicity in twin gestations.
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Thirty percent of spontaneously occurring twins are monozygotic, of which two-thirds are monochorionic, possessing a single placenta. A common placental mass with shared intertwin placental circulation is key to the development and management of complications unique to monochorionic gestations. In this Consult, we review general considerations and a contemporary approach to twin-twin transfusion syndrome and twin anemia-polycythemia sequence, providing management recommendations based on the available evidence. The following are the Society for Maternal-Fetal Medicine recommendations: (1) we recommend routine first-trimester sonographic determination of chorionicity and amnionicity (GRADE 1B); (2) we recommend that ultrasound surveillance for twin-twin transfusion syndrome begin at 16 weeks of gestation for all monochorionic-diamniotic twin pregnancies and continue at least every 2 weeks until delivery, with more frequent monitoring indicated with clinical concern (GRADE 1C); (3) we recommend that routine sonographic surveillance for twin-twin transfusion syndrome minimally include assessment of amniotic fluid volumes on both sides of the intertwin membrane and evaluation for the presence or absence of urine-filled fetal bladders, and ideally incorporate Doppler study of the umbilical arteries (GRADE 1C); (4) we recommend fetoscopic laser surgery as the standard treatment for stage II through stage IV twin-twin transfusion syndrome presenting between 16 and 26 weeks of gestation (GRADE 1A); (5) we recommend expectant management with at least weekly fetal surveillance for asymptomatic patients continuing pregnancies complicated by stage I twin-twin transfusion syndrome, and consideration for fetoscopic laser surgery for stage I twin-twin transfusion syndrome presentations between 16 and 26 weeks of gestation complicated by additional factors such as maternal polyhydramnios-associated symptomatology (GRADE 1B); (6) we recommend an individualized approach to laser surgery for early- and late-presenting twin-twin transfusion syndrome (GRADE 1C); (7) we recommend that all patients with twin-twin transfusion syndrome qualifying for laser therapy be referred to a fetal intervention center for further evaluation, consultation, and care (Best Practice); (8) after laser therapy, we suggest weekly surveillance for 6 weeks followed by resumption of every-other-week surveillance thereafter, unless concern exists for post-laser twin-twin transfusion syndrome, post-laser twin anemia-polycythemia sequence, or fetal growth restriction (GRADE 2C); (9) following the resolution of twin-twin transfusion syndrome after fetoscopic laser surgery, and without other indications for earlier delivery, we recommend delivery of dual-surviving monochorionic-diamniotic twins at 34 to 36 weeks of gestation (GRADE 1C); (10) in twin-twin transfusion syndrome pregnancies complicated by posttreatment single fetal demise, we recommend full-term delivery (39 weeks) of the surviving co-twin to avoid complications of prematurity unless indications for earlier delivery exist (GRADE 1C); (11) we recommend that fetoscopic laser surgery not influence the mode of delivery (Best Practice); (12) we recommend that prenatal diagnosis of twin anemia-polycythemia sequence minimally require either middle cerebral artery Doppler peak systolic velocity values >1.5 and <1.0 multiples of the median in donor and recipient twins, respectively, or an intertwin Δ middle cerebral artery peak systolic velocity >0.5 multiples of the median (GRADE 1C); (13) we recommend that providers consider incorporating middle cerebral artery Doppler peak systolic velocity determinations into all monochorionic twin ultrasound surveillance beginning at 16 weeks of gestation (GRADE 1C); and (14) consultation with a specialized fetal care center is recommended when twin anemia-polycythemia sequence progresses to a more advanced disease stage (stage $\geq$II) before 32 weeks of gestation or when concern arises for coexisting complications such as twin-twin transfusion syndrome (Best Practice).

Key words: chorionicity, fetal transfusion therapy, fetoscopic laser surgery, monochorionic-diamniotic twins, monochorionic twins, screening, staging, surveillance, twin anemia-polycythemia sequence, twin-twin transfusion syndrome, ultrasound

Introduction

Monozygotic twins account for 30% of spontaneously occurring twins, and two-thirds of monozygotic twins are monochorionic (MC), possessing a single placenta.[1] The presence of a common placental mass with shared intertwin placental circulation is key to the development and management of complications unique to MC gestations, such as twin-twin transfusion syndrome (TTTS) and twin anemia-polycythemia sequence (TAPS). In nearly all monochorionic-diamniotic (MCDA) pairs, vascular communications within the single placenta link the twin circulations.[2] These intertwin anastomoses are implicated in TTTS and TAPS pathophysiology. They serve as the basis for injury of the MC co-twin after a single fetal demise and influence management decisions when complications unique to MC gestations arise. This document focuses on twin chorionicity determination and the MC multiple gestation-specific diseases of TTTS and TAPS. Other complications of MC twins, including selective fetal growth restriction (FGR) and monoamniotic twins, will be presented in a separate document.

Chorionicity

Chorionicity refers to the type of placentation in multiple gestations, which partly depends on zygosity.[3] Dizygotic twins result from the fertilization of 2 oocytes by 2 sperm. Such nonidentical or "fraternal" twin pregnancies nearly always have dichorionic-diamniotic placentation, with 2 separate placental masses and amniotic sacs. Monozygotic twin pregnancies result from the fertilization of 1 oocyte by 1 sperm, forming a single zygote that splits into genetically "identical" twins. The chorionicity of monozygotic twins depends on when cleavage occurs relative to fertilization. In approximately one-third of monozygotic twin gestations, cleavage of the morula within 4 days of fertilization will result in dichorionic (DC) placentation. In most of the remaining two-thirds of monozygotic twin gestations, cleavage of the more advanced blastocyst occurs between 4 and 8 days after fertilization, resulting in MCDA twins with a single placental mass and 2 amniotic sacs. Cleavage between 8 and 12 days after fertilization occurs in $<1\%$ of twins, resulting in a monochorionic-monoamniotic gestation. Cleavage rarely occurs beyond this time, but cleavage that occurs >12 days after fertilization results in conjoined twins. Traditionally, monochorionicity has been considered diagnostic of monozygosity, which is usually true. However, rare cases of monochorionic-dizygotic twins have been reported, although the exact mechanism for this is unclear.[4]

Why is chorionicity important?

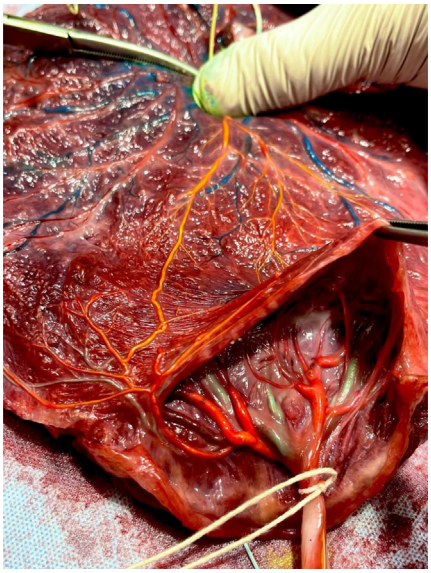
MC twins share a single placenta with intertwin vascular anastomoses connecting fetal circulations (Figure 1). Vascular anastomoses are observed in over 95% of MC placentas and do not occur in DC placentas.[5–7] A shared placenta with vascular anastomoses is implicated in certain complications of MC twins that contribute to increased morbidity and mortality, such as TTTS and TAPS.

MC twin pregnancies are at higher risk for perinatal complications than DC twin pregnancies. In 1 large twin cohort study, the perinatal mortality rate was >2-fold higher among MC twins compared with DC twins.[5] This was predominantly influenced by the marked increase in rates of fetal demise in MC twins (7.6%) vs DC twins (1.6%). Overall, neonatal morbidity, largely influenced by rates of necrotizing enterocolitis, was also increased in MC twins compared with DC controls.[5]

When is the optimal gestational age to determine chorionicity?

Evidence of 2 distinct gestational sacs on transvaginal ultrasound performed before 10 weeks of gestation indicates dichorionicity (Figure 2). However, in early MC twin gestations

FIGURE 1
Monochorionic-diamniotic twin placental dye study demonstrating intertwin vascular anastomoses



The placental surface is visualized, with forceps (image right) retracting the intertwin membrane. A thumb overlies 1 placental cord insertion, with yellow (arterial) and blue (venous) dyes injected into the superiorly located placental territory. Near the image bottom, a placental cord insertion is observed into the inferiorly located placental territory, with red (arterial) and green (venous) dyes injected into that circulation. Toward the left side of the image, near the location where the dividing membrane and placenta meet, intertwin anastomoses are demonstrated by a mixing of the colored dyes.

[Image courtesy E. Bergh, MD].

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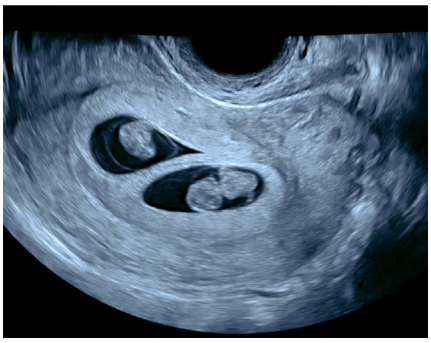
FIGURE 2
Eight-week dichorionic twin pregnancy



Two distinct gestational sacs are visualized.
[Image courtesy R. Miller, MD].

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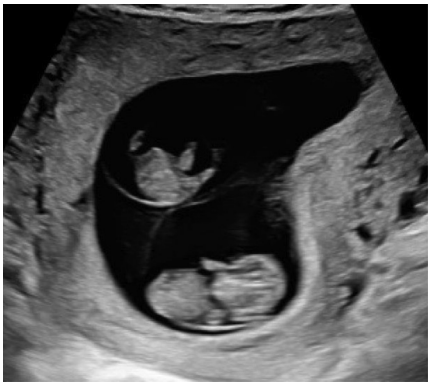
(Figure 3), the determination of amnionicity is thought to be less accurate before 10 weeks of gestation because of a delay in the sonographic appearance of the thin diamniotic membrane that is often not yet appreciated. In such cases, reassessment for the presence of an intervening membrane should be undertaken at a later ultrasound to confirm MC twin amnionicity (Figure 4).

Between 10 and 14 weeks of gestation, visualization of the interface between the placenta and the intervening twin membrane is an important determinant of chorionicity.[8] A "lambda" sign (also known as a "twin peak" sign) is the triangular projection of placental tissue into the base of the intertwin membrane (Figure 5). It represents chorionic villi

FIGURE 3
Nine-week monochorionic-diamniotic twin pregnancy



A single gestational sac is visualized, with each twin occupying a distinct amniotic space.
[Image courtesy R. Miller, MD].

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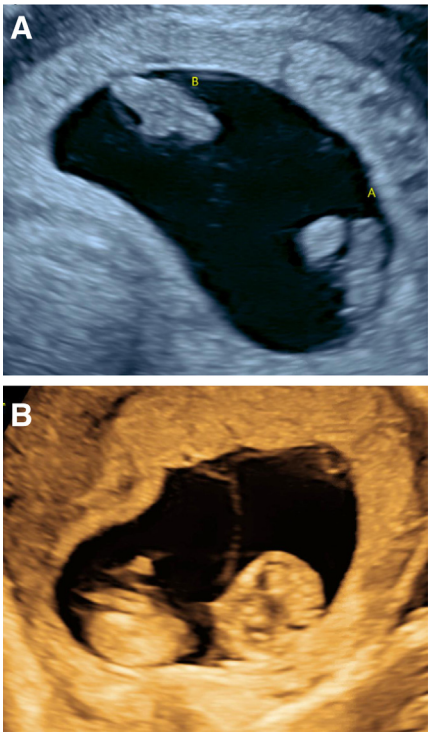
FIGURE 4
First-trimester determination of amnionicity in a monochorionic twin gestation



A, 7-week monochorionic twin pregnancy; no dividing membrane is visible. **B,** Same monochorionic twin pregnancy at 11 weeks of gestation; a dividing membrane and "T" sign are now visible.
[Image courtesy R. Miller, MD].

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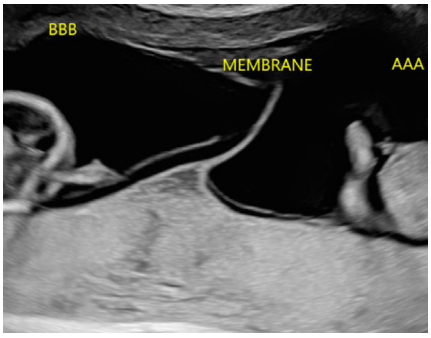
FIGURE 5
Twelve-week dichorionic twin pregnancy with "twin peak" sign



Labels "AAA" and "BBB" refer to twins A and B, respectively, and "MEMBRANE" demonstrates the dividing membrane. The "twin peak" sign is the triangular projection of placental tissue in the base of the inter-twin membrane.
[Image courtesy R. Miller, MD].

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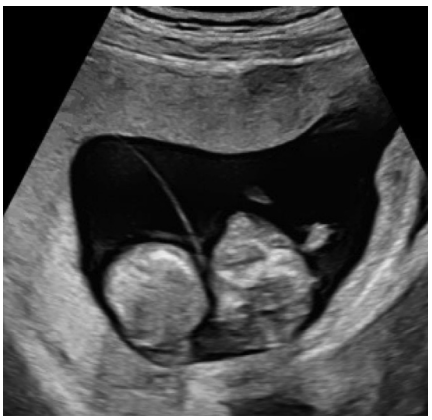
occupying space between the 2 layers of the chorion at its origin from the placenta. The presence of either a lambda sign or 2 separate placentas indicates DC placentation, with a reported sensitivity of 97% to 99% and specificity of 95% to 100%.[8,9] The lambda sign tends to disappear with advancing gestational age because of regression of the chorion frondosum to form the chorion laeve; therefore, it becomes less reliable beyond the first trimester.[8]

A "T" sign describes the ultrasound visualization of the perpendicular attachment of the intervening twin membrane to the placenta in MCDA gestations (Figure 6). The presence of a "T" sign means the absence of the "lambda" sign or the absence of the chorionic villi extending between the layers of the intertwin membrane. In 1 study, when observed in the first trimester along with a single placental mass, the "T" sign had a sensitivity of nearly 100% and specificity of 98% for identifying MCDA twin gestations.[8] However, another study showed less optimal performance of sonographic classification of chorionicity; among all twins (N=545) and specifically among MC twins (n=90), 6.4% and 19% were misclassified, respectively.[10]

After 14 weeks of gestation, ultrasound discordance of fetal sex has a positive predictive value that approaches 100% for establishing dichorionicity, although rare cases of sex-discordant MC twins have been reported.[11,12] Visualization of 2 separate placental masses can also be used to confirm dichorionicity. However, this finding is present in only about one-third of twin gestations. Both the presence of a thin bridge of placental tissue between 2 dominant placental masses and the presence of a succenturiate placental lobe can occur in MC gestations, thereby limiting this parameter as a useful diagnostic tool.[13]

FIGURE 6
Twelve-week monochorionic-diamniotic twin pregnancy



A common anterior placental mass, thin dividing membrane, and perpendicular "T" sign are visualized.
[Image courtesy R. Miller, MD].

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It has been suggested that the thickness of the intertwin membrane may help determine chorionicity in midgestation. In a study by Senat et al,[14] a threshold of 2 mm had 90% sensitivity and 76% specificity for determining MCDA membranes using standard 2-dimensional sonography at 20 to 35 weeks of gestation, and sensitivity was further improved using 3-dimensional sonography. However, membrane thickness is not sufficiently reliable to make consistently accurate determinations of chorionicity in clinical practice, and should not be used as a stand-alone measurement.

A cell-free DNA platform that analyzes single-nucleotide polymorphisms to determine chromosome copy number has been marketed to screen for aneuploidy in twin pregnancies, with the added ability to provide zygosity information. Although a recent study observed accurate zygosity prediction in 100% of cases for which testing yielded results, zygosity is not a substitute for chorionicity given that a subset of monozygotic twins will be DC.[15] **We recommend routine first-trimester sonographic determination of chorionicity and amnionicity (GRADE 1B).**[16,17]

Twin-twin transfusion syndrome

How common is twin-twin transfusion syndrome?

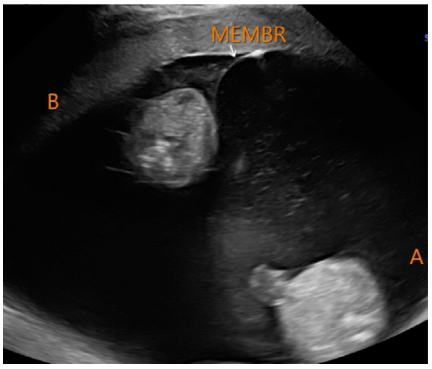
TTTS is a serious complication that impacts 8% to 12% of MCDA twin pregnancies, and is a major contributor to MC twin morbidity and mortality.[18–21] Although TTTS predominantly affects MCDA twin pregnancies, other MC multiple gestations are also at risk. Disease pathophysiology involves an imbalanced sharing of blood and vasoactive substances across a common placental circulation through vascular anastomoses.[1]

What are the diagnostic features of twin-twin transfusion syndrome, and how is it staged?

TTTS is characterized by a hypovolemic donor twin with oliguria and related oligohydramnios and a hypervolemic, hypertensive recipient twin at risk for heart failure with polyuria and polyhydramnios (Figure 7). Although either twin may be growth-restricted, selective FGR or discordant growth are not diagnostic features of TTTS. The essential requirement for an antenatal TTTS diagnosis is the presence of the oligohydramnios–polyhydramnios sequence, identified by a maximal vertical pocket of fluid $<$2 cm in the donor sac and $>$8 cm in the recipient sac, which meets the criteria for stage I TTTS (Table 1).[22]

A widely accepted TTTS staging system first described by Quintero et al[22] is regularly used in clinical practice to gauge disease severity. Additional features of TTTS associated with more advanced disease and higher stage include persistent nonvisualization of the donor twin bladder (stage II) (Figure 8), severe abnormalities upon Doppler interrogation of the umbilical artery, ductus venosus, or umbilical vein (stage III) (Figure 9, A, B, and C, respectively); presence of ascites or hydrops (stage IV) (Figure 10), and fetal demise of

FIGURE 7
Polyhydramnios-oligohydramnios sequence in a 19-week monochorionic-diamniotic twin pregnancy with stage I twin-twin transfusion syndrome



Twin A is the recipient twin with polyhydramnios and twin B is the donor twin with oligohydramnios. "MEMBR" indicates the dividing membrane, which is closely draped over twin B.
[Image courtesy R. Miller, MD].

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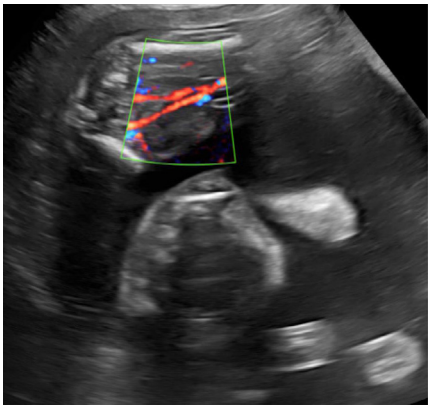
FIGURE 8
Stage II twin-twin transfusion syndrome presenting at 23 weeks of gestation



Using color Doppler study, umbilical arteries are noted to course around a sonographically empty donor twin urinary bladder.
[Image courtesy R. Miller, MD].

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1 or both twins (stage V). Although classic TTTS staging is imperfect in predicting outcomes on a case-by-case basis,[23] more advanced presentations (stage III and IV disease) generally have a less favorable outlook when compared to stage I and II cases. At all stages of TTTS, progression, regression, and stability are possible; however, the probability of progression tends to increase, and regression becomes less likely with advancing stage.[23]

TABLE 1
Quintero staging of twin-twin transfusion syndrome[22]

Stage	Ultrasound assessment	Criteria
I	Amniotic fluid	Maximal vertical pocket <2 cm in donor sac and maximal vertical pocket >8 cm in recipient sac
II	Fetal bladder	Nonvisualization of fetal bladder in donor twin over 60 minutes of observation
III	Doppler studies	Absent or reversed umbilical artery end-diastolic velocity, reversed ductus venosus a-wave flow, pulsatile umbilical vein flow
IV	Fetal ascites or hydrops	Ascites or hydrops in 1 or both twins
V	Fetal cardiac activity	Fetal demise in 1 or both twins

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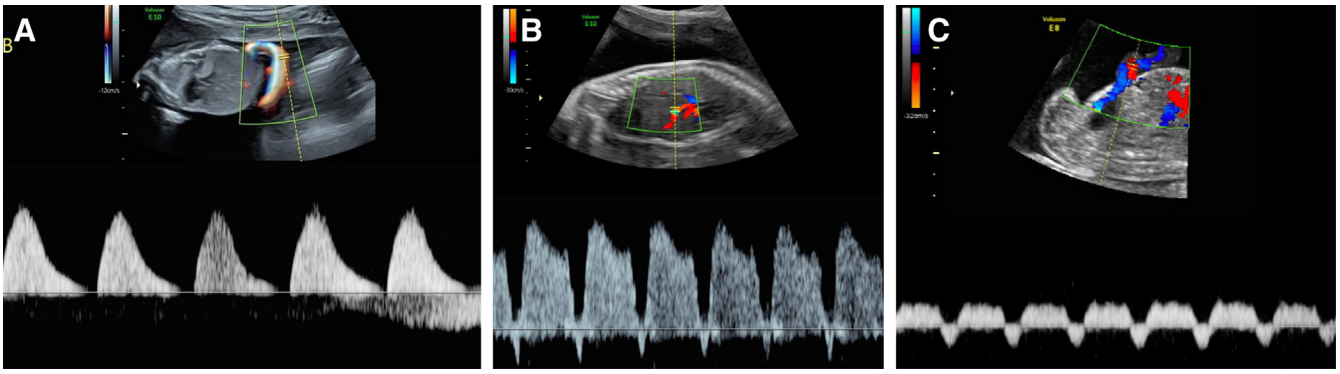
Despite these limitations, classic TTTS staging has practical benefits for evaluating candidacy for therapy, standardizing findings among providers, and facilitating research comparisons.

How and when should a patient be screened for twin-twin transfusion syndrome?

Obstetrical ultrasound is the primary tool to monitor MC twin pregnancies for TTTS. The presentation of TTTS is highly variable. Although most cases are diagnosed in the mid-trimester, TTTS can manifest at any time in gestation. For this reason, serial ultrasound surveillance is recommended for all multiple gestations with MC placentation. Although high-quality data do not exist to validate an optimal screening strategy, retrospective cohort studies evaluating a fortnightly (every-other-week) approach to surveillance beginning at 16 weeks of gestation have demonstrated effectiveness for timely TTTS diagnosis and low rates of stage V TTTS (disease involving fetal demise of 1 or both twins) with this strategy.[24,25] **We recommend that ultrasound surveillance for TTTS begin at 16 weeks of gestation for all MCDA twin pregnancies and continue at least every 2 weeks until delivery, with more frequent monitoring indicated for clinical concern (GRADE 1C).**[16,17,26–29] Concerns that should prompt more frequent monitoring include sonographic suspicion for developing or overt pathology (such as the identification of isolated polyhydramnios, subjective oligohydramnios, obvious discordance in amniotic fluid volumes, or Doppler abnormalities) and change in maternal symptomatology (such as shortness of breath, increasing abdominal girth, contractions, or pelvic pressure that might suggest the presence or worsening of polyhydramnios).

FIGURE 9
Doppler velocimetry abnormalities in stage III twin-twin transfusion syndrome



A, Donor twin umbilical artery absent end-diastolic velocity upon Doppler study in a case of stage III twin-twin transfusion syndrome at 21 weeks of gestation. **B,** Recipient twin ductus venosus a-wave reversal upon Doppler study in a case of stage III twin-twin transfusion syndrome at 26 weeks of gestation. **C,** Recipient twin umbilical vein pulsations upon Doppler study in a case of stage III twin-twin transfusion syndrome at 23 weeks of gestation. *[Image courtesy J. Miller, MD and R. Miller, MD].*

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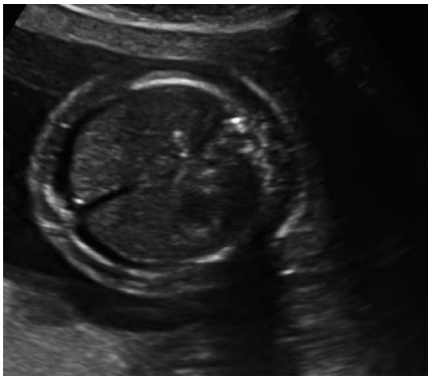
We recommend that routine sonographic surveillance for TTTS minimally include assessment of amniotic fluid volumes on both sides of the intertwin membrane and evaluation for the presence or absence of urine-filled fetal bladders, and ideally incorporate Doppler study of the umbilical arteries (GRADE 1C). Although middle cerebral artery (MCA) Doppler studies do not have a role in screening for TTTS per se, they are used to screen for TAPS (discussed later in this document), and should therefore be considered with routine surveillance sonograms for MC twins.[16,22,30–33] Fetal weight assessments are also recommended at least every 4 weeks to evaluate for FGR or intertwin growth discordance.

FIGURE 10
Recipient twin ascites in a case of stage IV twin-twin transfusion syndrome at 22 weeks of gestation



[Image courtesy R. Miller, MD].

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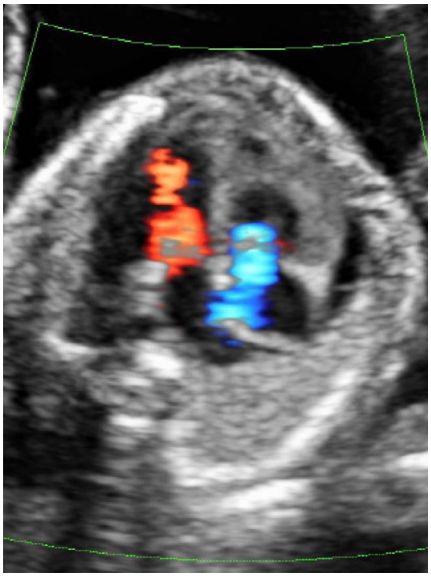
Although data evaluating the independent contribution of Doppler studies to routine MC twin surveillance are limited, isolated Doppler abnormalities may help to identify pregnancies with evolving pathology that may benefit from more frequent monitoring. In 1 retrospective cohort study involving 675 MCDA twin pairs undergoing every-other-week surveillance, including routine Doppler evaluations, 84% (16/19) of stage III or IV TTTS cases that underwent serial surveillance had abnormal Doppler findings identified before the visit in which TTTS was diagnosed.[24] Numerous international MC twin surveillance guidelines support the incorporation of umbilical artery and MCA Doppler studies into routine MC twin surveillance beginning at 16 to 20 weeks of gestation.[16,30–33] Nevertheless, absent further data proving the added value of Doppler surveillance, it is reasonable for providers and institutions to consider additional factors such as local resources and patient access to care when determining whether to include umbilical artery and MCA Doppler studies in routine MC twin surveillance strategies. Although some published monitoring strategies additionally include ductus venosus Doppler surveillance, ductus venosus studies are of unclear value as a component of routine MC twin surveillance.

Regardless of the routine surveillance strategy followed, Doppler studies of the umbilical artery, ductus venosus, and MCA are recommended following the identification of any atypical finding, such as overt TTTS, isolated polyhydramnios, subjective amniotic fluid volume discrepancy, discordant placental echogenicity or thickness, coexisting FGR, or concern for twin structural or functional cardiac abnormality. Furthermore, once a diagnosis of TTTS is established, Doppler studies of the umbilical artery and ductus venosus are necessary for staging and clinical management decision-making.

Given the well-established increased risk of congenital heart disease,[34] all MC twins should undergo fetal echocardiography.[35] MC twins affected by TTTS also commonly experience cardiovascular changes given their pathophysiology, and fetal echocardiography should be considered after the diagnosis of TTTS, even if echocardiography was previously performed. Because of hypertensive volume overload, recipient twins are at particular risk for biventricular hypertrophy, diastolic dysfunction, diminished right ventricular systolic function, and acquired right ventricular outflow tract obstruction (Figure 11).[34,36–39] A criticism of classic TTTS staging is that recipient cardiovascular changes, which may already be present in early-stage TTTS, may not be recognized with ductus venosus Doppler abnormalities, ascites, or hydrops until more advanced-stage disease manifests.[39] In response, some fetal care centers have developed and applied staging modifications that consider recipient twin cardiomyopathy.[36,39] When present, this finding may be used to effectively "up-stage" early-stage presentations and thus may influence management decisions. However, some studies have suggested that although fetal echocardiography may provide a more nuanced description of TTTS pathophysiology, cardiovascular profiling may not provide prognostic value for pregnancy outcomes or recipient survival.[40,41]

FIGURE 11
Recipient twin right ventricular hypertrophy and tricuspid regurgitation in a case of stage III twin-twin transfusion syndrome at 23 weeks of gestation



[Image courtesy R. Miller, MD].

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How should twin-twin transfusion syndrome be managed?

Management options for a given TTTS presentation depend on several factors, including disease severity and gestational age. When possible, cases in which prenatal intervention is indicated should be referred to a fetal care center. For patients with suspected or confirmed TTTS in which uncertainty exists regarding the need for therapy, clinicians should partner with a fetal care center to determine if and when a referral is advisable.

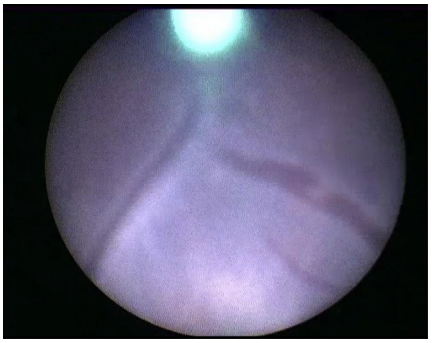
Patient counseling regarding prognosis, available management options, and their associated risks and benefits should be initiated at the time of diagnosis, further discussed upon consultation at a fetal care center (should an in-person consultation occur), and readdressed throughout pregnancy.[42] Some patients may opt for termination of the entire pregnancy based on the potential obstetrical and long-term pediatric risks associated with TTTS and its treatment. In clinical scenarios in which 1 twin is disproportionately impacted, such as coexisting severe FGR or major fetal anomaly, patients may alternatively opt to pursue selective termination of the affected twin via targeted cord occlusion therapy. The risks of such a procedure, including premature rupture of membranes and loss of the entire pregnancy, should be discussed. For patients opting to continue with pregnancy with the goal of optimizing twin outcomes, specific recommendations are provided below.

What is the treatment for advanced-stage twin-twin transfusion syndrome?

Fetoscopic laser surgery provides superior survival rates compared with expectant management or serial amnioreduction, which was the mainstay of TTTS management before the emergence of laser surgery.[43] Fetoscopic laser surgery uses laser energy to photocoagulate intertwin placental anastomoses and thus functionally "dichorionize" placental circulation, eliminating the root cause of TTTS (Figure 12). The contemporary approach uses a percutaneous access technique.[44] Fetoscopic laser surgery may be safely performed with maternal intravenous sedation and local anesthesia or under regional anesthesia, depending on the clinical circumstances.[45,46] General anesthesia is rarely necessary.

Overall, experienced fetal care centers now report dual survivors in 50% to 70% of laser cases, 1 survivor in 20% to 30% of cases, and no survivors in 10% to 20% of cases.[47–49] Although most pediatric survivors after laser surgery for TTTS will have normal neurologic outcomes, major neurologic morbidity occurs in 4% to 18% of pediatric survivors at ≥2 years of age.[50–56] Many factors likely contribute to this risk, including prematurity and the underlying TTTS pathophysiology that initially prompted therapy. **We recommend fetoscopic laser surgery as the standard treatment for stage II through stage IV TTTS presenting between 16 and 26 weeks of gestation (GRADE 1A).**[16,57]

FIGURE 12
Fetoscopic view of a single arteriovenous anastomosis



A thick-walled artery (left) containing relatively deoxygenated (visibly darker) blood is observed to communicate with a thinner-walled vein (right) containing relatively oxygenated blood immediately before laser photocoagulation. The tip of the laser fiber is in view at 12 o'clock.
[Image courtesy R. Miller, MD].

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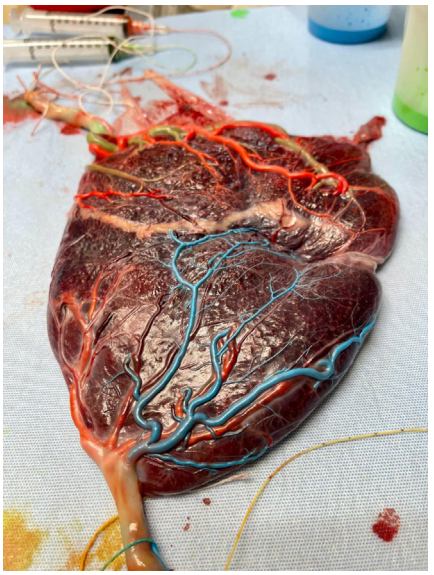
FIGURE 13
Placental dye study of a monochorionic-diamniotic twin placenta following laser photocoagulation with adjunct Solomon equatorial dichorionization



A horizontal hypoechoic line extending from edge to edge across the placental surface is observed, representing photocoagulation across the intertwin vascular equator. Colored dye has been injected into each twin's umbilical vessels, and no dye is observed to communicate between twin placental territories.
[Image courtesy E. Bergh, MD].

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What complications can occur after fetoscopic laser surgery?

The most common complication after fetoscopic laser surgery is preterm premature rupture of membranes (PPROM), which occurs in approximately a quarter of cases.[58] The development of fetofetal transfusion conditions after laser surgery, such as recurrent or reversed TTTS or TAPS, may complicate over 10% of pregnancies and serves as the rationale for the Solomon technique for equatorial "dichorionization" (Figure 13). The Solomon technique is an adjunct to standard laser surgery in which linear photocoagulation is conducted along the intertwin vascular equator (the approximate line upon which intertwin anastomoses exist) following usual laser photocoagulation of visible anastomoses.[59] This technique decreases the risk of untreated small or nonvisualized intertwin anastomoses and related post-laser TAPS and TTTS.[60,61] Although literature supporting the Solomon technique is encouraging, high-quality data are limited, and long-term pediatric neurodevelopmental benefits are unproven.[62]

Other complications associated with laser surgery include preterm labor, preterm delivery, placental abruption, infection, intertwin septostomy, direct or indirect fetal injury, and fetal death. Reports of severe maternal morbidity are rare,[63] but abdominal pain from extravasation of amniotic fluid into the peritoneal cavity or bleeding sufficient to necessitate transfusion or surgical exploration can occur.[57,64]

What is the treatment for stage I twin-twin transfusion syndrome?

Fetoscopic laser surgery for the management of stage I TTTS is controversial. Given previous reports of stage I TTTS stabilizing or regressing in 70% of cases, conventional wisdom held that, with close monitoring, a substantial subset of patients could avoid the risks of laser surgery altogether.[65] However, pooled contemporary data from the North American Fetal Therapy Network (NAFTNet) suggest that stage I disease may have a less favorable natural course than previously appreciated.[66] In this retrospective study, 70% of stage I cases had either disease progression to a more advanced stage or spontaneous preterm birth while pursuing expectant management.[66] A multicenter trial was recently published involving 117 patients with pregnancies complicated by stage I TTTS randomly assigned to immediate laser surgery or expectant management.[67] Although the study was prematurely discontinued because of slow recruitment, there was no difference in intact survival (78% vs 77%; $P=.88$) or severe neurologic morbidity (2.6% vs 4.6%; $P=.49$) between the laser and expectant management groups, respectively. Among participants randomly assigned to expectant management, 59% subsequently progressed and received laser surgery, with a 71% intact survival rate.[67]

Given the uncertainty over the natural history of stage I TTTS and limited data evaluating clinical management, it is not surprising that practice varies across fetal care centers in

the United States. The available evidence indicates that expectant management with close fetal surveillance may be appropriate for asymptomatic stage I TTTS presentations. However, when considering stage I TTTS presentations for fetoscopic laser surgery, some centers use factors such as maternal symptomatology, short cervix, patient distance from the treatment center, and fetal echocardiographic changes to determine procedural eligibility. **We recommend expectant management with at least weekly fetal surveillance for asymptomatic patients continuing pregnancies complicated by stage I TTTS and consideration of fetoscopic laser surgery for stage I TTTS presentations between 16 and 26 weeks of gestation complicated by additional factors such as maternal polyhydramnios-associated symptomatology (GRADE 1B).**[16,57]

What is the treatment for twin-twin transfusion syndrome diagnosed in early (<17 weeks) or late (>26 weeks) gestation?

Comparisons of laser surgery performed "early" (before 17 weeks) or "late" (after 26 weeks) with procedures done between 17 and 26 weeks of gestation report similar survival rates and gestational age at delivery.[68,69] One study reported an increased risk of PPROM within 7 days of surgery in cases undergoing laser surgery before 17 weeks compared with those performed between 17 and 26 weeks of gestation (25% vs 6.4%, respectively).[68] However, there were no cases of PPROM within 7 days of surgery reported in a separate cohort of 40 "early" (<17 weeks of gestation) fetoscopic laser operations, and overall rates of PPROM were not significantly different between "early" and "conventional" timing of fetoscopic laser surgery in this report.[70]

Regarding "late" procedures, a small series comparing laser surgery performed between 26 and 28 weeks of gestation with laser surgery at usual gestational ages revealed no differences in operative time, surgical complications, gestational age at delivery, or survival of at least 1 neonate.[69] Because these studies are limited by size and design, **we recommend an individualized approach to laser surgery for early- and late-presenting TTTS (GRADE 1C)**. For example, fetoscopic laser therapy may be the best option in advanced-stage presentations at early gestational ages in which pregnancy termination is not a consideration and expectant management is predicted to have a high risk of fetal demise(s) or otherwise deemed unlikely to achieve meaningful prolongation of pregnancy. For TTTS presenting beyond 26 weeks (gestational ages for which amnioreduction, expectant management, or medically indicated delivery are usually considered), laser surgery may be a viable option for select cases of severe disease presenting up to the very early third trimester to reduce risks of fetal and perinatal death or severe prematurity. When possible, fetal care center consultation and referral are recommended to help individualize care in these cases.

When should a patient be referred to a fetal care center?

Without therapy, advanced-stage TTTS presenting before 26 weeks of gestation has an extremely poor prognosis, with perinatal loss rates of at least 70% and a substantial risk for neurologic disability among survivors.[71] Therefore, **we recommend that all patients with TTTS qualifying for laser therapy be referred to a fetal intervention center for further evaluation, consultation, and care (Best Practice).**[16,17] When uncertainty exists regarding the need for therapy, clinicians should partner with a fetal care center to determine if and when a referral is advisable. A plan for an in-person consultation at a fetal care center and the timing of such a visit should be individualized on a case-by-case basis after considering case specifics, distance from the fetal care center, and patient resources and availability.

Consultation should include a detailed review of all reasonable management options, including a discussion of the fetal, maternal, and obstetrical risks and benefits of fetoscopic laser surgery. Therapeutic amnioreduction before consultation at the fetal care center is generally not recommended because registry data indicate a 15% complication rate within 48 hours of amnioreduction for TTTS.[72] Amniocentesis-associated procedural complications such as PPROM, amnion-chorion separation, bleeding, or labor may preclude interested and eligible patients from undergoing fetoscopic laser surgery.

In some instances, there may be geographic, financial, or patient-driven delays to timely fetal care center referral. In these situations, an individualized approach is advised, and therapeutic amnioreduction may be deemed necessary as a temporizing measure because of severe maternal symptomatology from polyhydramnios. Otherwise, amnioreduction for the management of TTTS is largely restricted to late disease presentations that do not qualify for fetoscopic laser surgery or delivery.

How should pregnancies be monitored after laser therapy?

There is insufficient evidence to support a specific surveillance strategy after laser treatment for TTTS.[16,57] Despite this paucity of data, many centers recommend weekly ultrasound monitoring after laser surgery to screen for recurrent or reversed TTTS or the development of TAPS. This surveillance typically includes Doppler velocimetry studies of the umbilical artery, ductus venosus, and MCA for each twin. **After laser therapy, we suggest weekly surveillance for 6 weeks followed by resumption of every-other-week surveillance thereafter, unless concern exists for post-laser TTTS, post-laser TAPS, or FGR (GRADE 2C).** Some fetal care centers offer magnetic resonance imaging after laser surgery to evaluate the fetal neuroanatomy, with limited data to support this practice.[73]

Sonographic evidence of recovery after laser surgery is usually not immediate, and normalization of ultrasound

findings, including amniotic fluid volumes, can take weeks. In cases where a donor twin bladder was nonvisualized before intervention, the reappearance of a urine-filled bladder in the early days after surgery is an encouraging sign that correlates with an increase in umbilical venous volume flow to that twin.[74] In a study that evaluated fetal hemodynamic findings after laser surgery, improvements in Doppler studies of the recipient twin ductus venosus and donor twin umbilical artery were commonly observed by day 5 after therapy, although longer times to recovery are possible.[75] Alternatively, sustained or worsening Doppler abnormalities can be observed after laser surgery in cases complicated by various types of posttherapy fetofetal transfusion or cases with coexisting FGR. Improvements in recipient twin echocardiographic findings can be gradual after laser surgery, and full recovery may take months.

Especially for the donor twin, acute worsening can be observed before improvement, which is believed to reflect twin hemodynamic adaptations resulting from abrupt laser-induced changes within a shared placental circulation. These changes may trigger what has been termed a "relative hypervolemia" for the donor twin. In this setting, the donor twin may demonstrate evidence of transient skin edema or hydrops, temporary worsening of Doppler findings (involving the ductus venosus or other vessels), or evidence of right heart overload.[75,76] Although most cases of transient donor hydrops will spontaneously resolve within days of laser surgery, some will result in fetal demise. Providers managing patients after laser surgery for TTTS should remain in contact with the treating fetal care center, especially for abnormal findings upon surveillance.

When and how should delivery of monochorionic twin pregnancies complicated by twin-twin transfusion syndrome occur?

Given limited data to support a specific gestational age for delivery of pregnancies complicated by TTTS, delivery decisions should be individualized. Factors that might influence delivery timing include disease stage, response to therapy if performed, evidence of progression, PPROM, nonreassuring status of either twin, and maternal status.[77–80] In affected pregnancies undergoing expectant management for TTTS, those with late TTTS diagnoses, or those with ongoing fetofetal transfusion despite amnioreduction or laser surgery, delivery should be considered by 32 to 34 weeks of gestation (or thereafter upon diagnosis), although earlier delivery may be indicated. If not previously administered, antenatal corticosteroids are recommended before delivery.

Premature delivery is common among patients undergoing fetoscopic laser surgery. In a NAFTNet multicenter retrospective review that included nearly 850 TTTS pregnancies, the mean gestational age at delivery after laser was 30 to 31 weeks, with the leading causes for delivery being preterm labor, PPROM, and placental abruption.[80] **Following the resolution of TTTS after fetoscopic laser surgery and without other indications for earlier delivery, we recommend delivery of dual-surviving MCDA twins at 34 to 36 weeks of gestation (GRADE 1C).**[57] **In TTTS pregnancies complicated by posttreatment single fetal demise, we recommend full-term delivery (39 weeks) of the surviving co-twin to avoid complications of prematurity unless indications for earlier delivery exist (GRADE 1C).**[57,81–83]

We recommend that fetoscopic laser surgery not influence the mode of delivery (Best Practice). Nevertheless, cesarean delivery rates are high in pregnancies complicated by TTTS, with or without prenatal treatment. In the aforementioned large NAFTNet review, approximately 70% of patients undergoing fetoscopic laser surgery subsequently had cesarean delivery.[80]

Twin anemia-polycythemia sequence

What is twin anemia-polycythemia sequence, and which fetuses are at risk?

TAPS is a chronic, insidious form of fetofetal transfusion that can impact MC multiple gestations in which an imbalanced red blood cell transfusion leads to an anemic donor twin and a polycythemic recipient twin. Pathogenesis has been linked to the presence of very small, submillimeter intertwin arteriovenous anastomoses commonly located near the placental edge.[6,84] The rate of blood flow through these minuscule anastomoses has been estimated to be approximately 5 to 15 mL per day, allowing for some degree of fetal compensation, at least in earlier disease stages.[85–88] Perhaps for this reason, twin amniotic fluid volume discordance is not a usual component of this presentation.

TAPS can develop naturally in the absence of fetal intervention or present following fetoscopic laser surgery. Naturally occurring TAPS is believed to impact approximately 2% to 5% of MCDA twin gestations, although high-quality data are lacking to support a precise incidence.[19,89–91] The disease can occur anytime in the second or third trimester. In an international registry cohort that collected 249 cases of spontaneous TAPS, an antenatal diagnosis was secured at a median gestational age of 23.7 weeks, with a range from 15.1 to 35.3 weeks.[92]

After laser surgery, TAPS seems to occur more frequently, and these presentations can progress rapidly. Within an open-label randomized controlled trial evaluating the Solomon technique for equatorial dichorionization, post-laser TAPS occurred in 15.6% of 135 participants in the control (standard, non-Solomon laser surgery) arm.[61] Observational cohorts have revealed rates of post-laser TAPS spanning from 2% to 13%, and this range may be attributable to factors including differing diagnostic standards, variation in screening strategies, and technical differences in surgical technique and surveillance.[60,93] Notably, the Solomon technique has been demonstrated to reduce the risk for post-laser TAPS. In the aforementioned randomized trial, post-laser TAPS occurred in 2.9%

of 137 participants who underwent equatorial dichorionization as an adjunct to standard laser surgery.[61] When post-laser TAPS does occur, the former TTTS recipient and donor twins may switch roles, becoming TAPS donors and recipients, respectively.[60,85]

How is the diagnosis of twin anemia-polycythemia sequence made?

TAPS can be identified either before or after delivery. The postnatal diagnosis is usually readily apparent upon visual inspection, with a pale donor twin and ruddy, plethoric-appearing recipient twin presenting in stark contrast to one another. The postnatal diagnosis is confirmed by an intertwin birth hemoglobin difference of ≥8 g/dL and either (1) a reticulocyte ratio of >1.7 between donor and recipient, supporting hematologic compensation for gradual transfusion or (2) the identification of exclusively small-vessel anastomoses (<1 mm) upon placental pathology examination.[85,94]

Unlike postnatal TAPS identification, antenatal diagnosis of the condition is often not obvious and requires a high index of clinical suspicion, especially given that it commonly presents without growth or amniotic fluid abnormalities. The requisite finding upon screening involves MCA Doppler peak systolic velocity (MCA-PSV) abnormalities suggestive of donor twin anemia and recipient twin polycythemia (Figure 14).[57] As originally described, the prenatal diagnosis of TAPS requires an MCA-PSV of >1.5 multiples of the median (MoM) for the presumed anemic donor twin and an accompanying MCA-PSV of <1.0 MoM for the presumed polycythemic recipient twin. In 1 retrospective study involving 45 uncomplicated MC twin pregnancies and 35 with TAPS, these criteria possessed 46% sensitivity, 100% specificity, 100% positive predictive value, and 70% negative predictive value.[95] Notably, although the correlation of elevated MCA-PSV with fetal anemia is well-established, the relationship between decreased MCA-PSV and polycythemia is unproven, and the optimal MCA-PSV cutoff for the recipient twin is unknown.[96] This likely impacts diagnostic accuracy for prenatal TAPS determinations.

Other criteria have been proposed to improve the accuracy of prenatal TAPS diagnosis; however, limited evidence exists to support the superiority of any particular detection strategy. Some advocate MCA-PSV cutoffs of >1.5 MoM and <0.8 MoM for the identification of donor and recipient twins, respectively. Alternatively, others recommend Δ MCA-PSV (the difference between donor and recipient MCA-PSV MoM values) for TAPS screening, with cutoffs >0.5 MoM and >1.0 MoM having been described. In the aforementioned retrospective cohort of 80 MC twin pairs with or without TAPS, Δ MCA-PSV >0.5 had 83% sensitivity, 100% specificity, 100% positive predictive value, and 88% negative predictive value.[95] A small prospective cohort study of MCDA twins with MCA-PSV measurements within 1 week of delivery and confirmed postnatal TAPS diagnoses demonstrated that Δ MCA-PSV positively correlated with neonatal hematocrit differences, whereas MCA-PSV was not reliably decreased in polycythemic twins.[96] A recent Delphi consensus of international experts endorsed the use of either absolute MCA-PSV cutoffs of ≥1.5 MoM and ≤0.8 MoM for donor and recipient twins, respectively, or a Δ MCA-PSV of ≥1.0 MoM.[97] Notably, the number of participating experts in this process was low, with only 33 completing the entire Delphi procedure. To maximize screen sensitivity of MC twin evaluations, and considering the limited accuracy of MCA-PSV values for the prediction of recipient twin polycythemia, **we recommend that prenatal diagnosis of TAPS minimally require either Doppler MCA-PSV values >1.5 MoM and <1.0 MoM in donor and recipient twins, respectively, or an intertwin Δ MCA-PSV >0.5 MoM (GRADE 1C).**

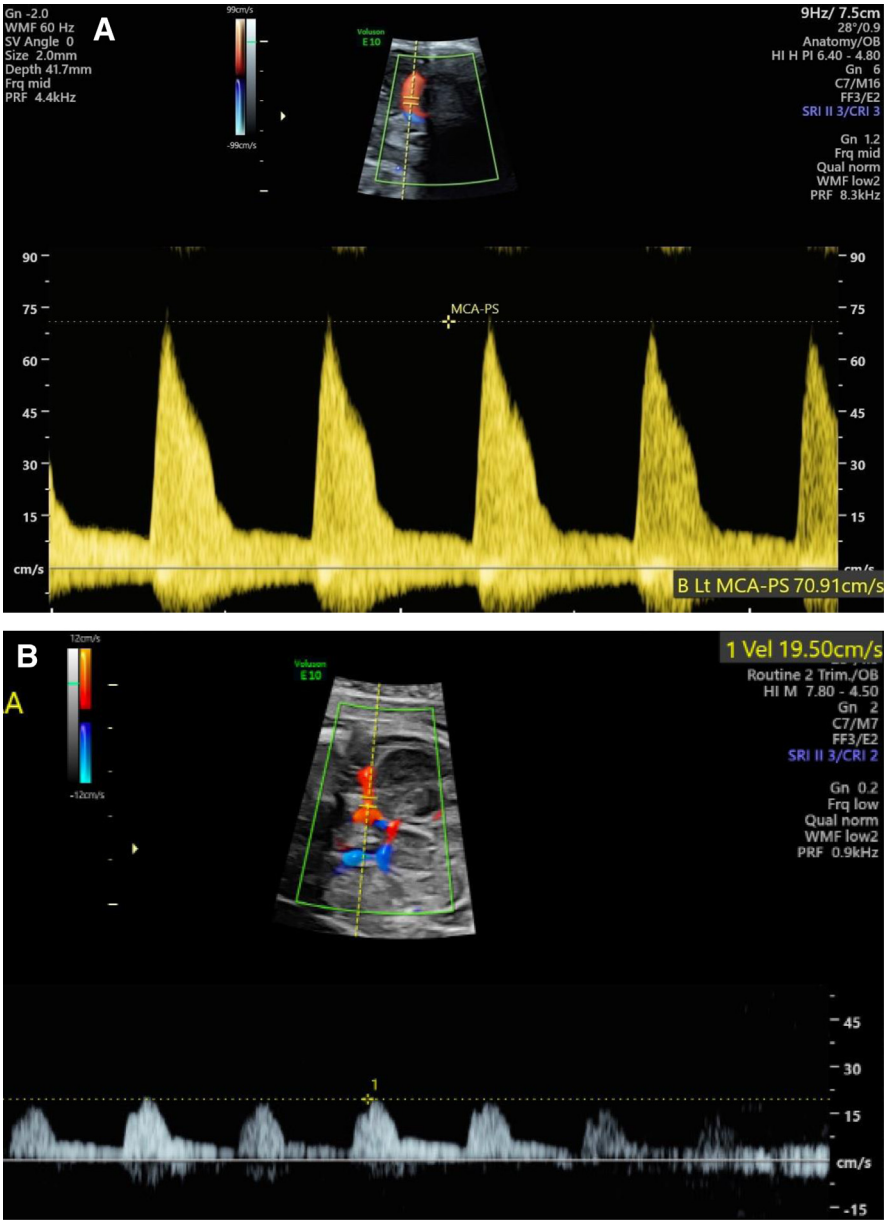
Accompanying ultrasound findings are observed in up to 86% of TAPS cases, including (1) discordant placental echogenicity, with the donor twin territory appearing thick and hyperechoic and the recipient twin territory appearing hypoechoic or normal (Figure 15); (2) recipient twin cardiomegaly, commonly with tricuspid regurgitation; or (3) a "starry sky" appearance of the recipient liver (scattered echogenic foci set against a diffusely hypoechoic liver) suggestive of hepatic congestion (Figure 16).[98,99] When some or all are detected in the presence of qualifying MCA-PSV abnormalities, these findings further support a TAPS diagnosis. Conversely, false positive diagnoses can occur with exclusive reliance upon MCA-PSV values in the absence of supporting ultrasound findings. An example of a clinical scenario that can present similarly to TAPS involves MCA-PSV abnormalities attributable to fetal hemodynamic adaptation following laser surgery.[100] Fetal anemia due to iatrogenic placental hematoma formation has also been reported to cause MCA-PSV atypia mimicking a TAPS presentation.[101]

TAPS may additionally present with critical Doppler velocimetry findings in the umbilical artery, umbilical vein, or ductus venosus, or with fetal ascites or hydrops. These findings typically manifest in the donor twin and indicate a severe form of disease. An antenatal TAPS staging system has been proposed (Table 2) that considers the degree of MCA-PSV abnormality, Doppler abnormalities in selected other vessels, and the presence of ascites or hydrops when classifying disease severity.[85] We support this TAPS staging, with the suggestion that Δ MCA-PSV >0.5 MoM be considered comparable to a stage I diagnosis.

What is the prognosis for twin anemia-polycythemia sequence?

The natural history of TAPS is incompletely understood. Outcomes appear to vary widely, from a low morbidity rate among twins born late preterm to double fetal demise in severe cases presenting early in gestation. The available evidence is limited by sample size, retrospective nature, and

FIGURE 14
Middle cerebral artery Doppler peak systolic velocity abnormalities in twin anemia-polycythemia sequence



A, Donor twin elevated middle cerebral artery Doppler peak systolic velocity (1.8 multiples of the median) in a case of stage II twin anemia-polycythemia sequence at 29 weeks of gestation. **B,** Recipient twin decreased middle cerebral artery peak systolic velocity (<0.7 multiples of the median) in a case of stage III twin anemia-polycythemia sequence at 23 weeks of gestation.
[Images courtesy J. Miller, MD and R. Miller, MD, respectively.].

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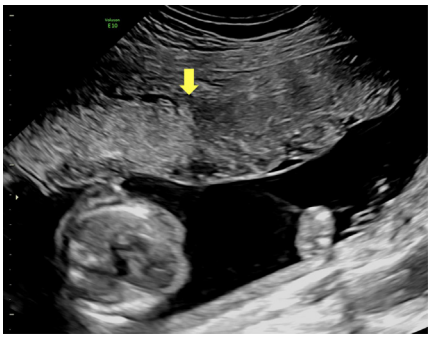
varied antenatal management approaches. Among 249 cases in a spontaneous TAPS registry, 88% were diagnosed prenatally, and 23% of these underwent expectant management.[92] The perinatal mortality rate was 15% for the entire cohort and was more likely to occur in donors (22%) than recipients (7%). Severe neonatal morbidity occurred in 33% of affected twins, without differences in incidence between donors and recipients. Independent risk factors for severe neonatal morbidity included advanced antenatal TAPS stage and gestational age at delivery.

In a meta-analysis including 506 pregnancies (38 studies), including data from the TAPS registry, fetal demise occurred in 5.2% of twins with spontaneous TAPS and 10.2% of those with post-laser TAPS, and neonatal demise occurred

FIGURE 15
Discordant placental echotexture in a monochorionic-diamniotic twin pregnancy with twin anemia-polycythemia sequence at 19 weeks of gestation



A distinction in placental echotextures exists (*arrow*), with a hyperechoic donor placental territory on the left and a hypoechoic recipient placental territory on the right.
[Image courtesy R. Miller, MD].

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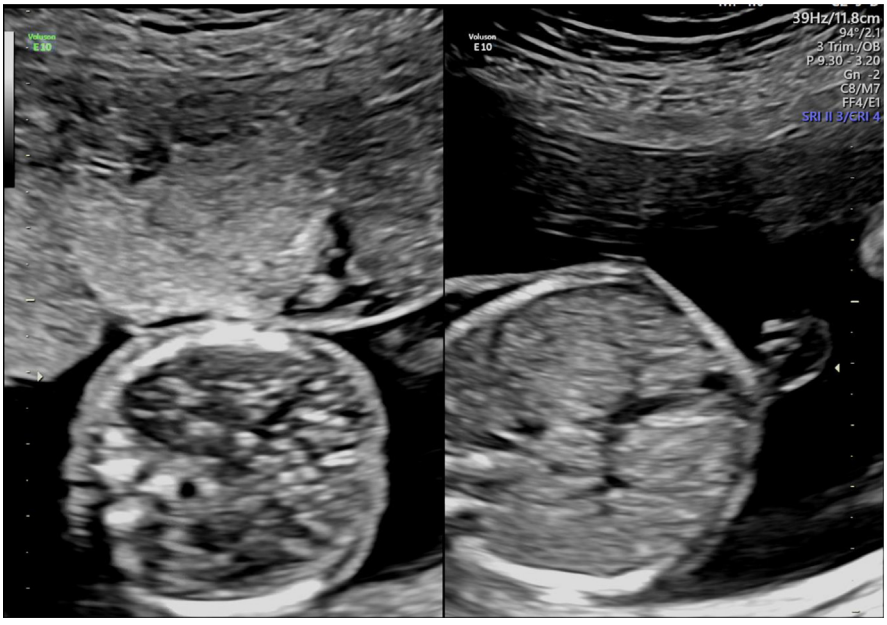
in 4.0% and 9.2%, respectively.[102] Although severe neonatal morbidity was similar between spontaneous TAPS (29.3%) and post-laser TAPS (33.3%) groups, rates of severe neurologic morbidity were 4.0% for spontaneous TAPS and 11.1% for post-laser TAPS. Among the subset of TAPS cases that were expectantly managed, fetal demise occurred in 9.8%, and severe neonatal morbidity affected 27.3%. No differences in morbidity and mortality were observed when comparing TAPS management options, including expectant management and various forms of prenatal intervention. However, the authors cautioned that the nature of the included studies limits the strength of any such comparisons.

Among newborns with TAPS, mild short-term sequelae can include the need for postnatal transfusion for the donor twin or exchange transfusion for the recipient.[103] Donor twins have been observed to have a higher rate of leukopenia and early-onset neonatal sepsis.[104] Recipient twin cardiomegaly and liver congestion tend to resolve gradually after birth. Cerebral lesions, skin necrosis, and distal limb ischemia have been reported in recipient twins, presumably due to polycythemia-related hyperviscosity.[60,105] Although robust data are lacking, pediatric studies of TAPS survivors indicate a risk for neurologic morbidity roughly comparable to the rate expected among TTTS survivors. Cases of fetal brain lesions associated with TAPS have been reported, suggesting an antenatal origin for some presentations.[106,107] Donor twins may possess a particularly increased risk for neurodevelopmental impairment (NDI), and the risk of deafness is reported to be as high as

FIGURE 16
Twin anemia-polycythemia sequence presentation in a 19-week monochorionic-diamniotic twin pregnancy



On the left, axial view of recipient twin liver with "starry sky" appearance. On the right, axial view of donor liver with normal echotexture.
[Image courtesy R. Miller, MD].

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TABLE 2
Prenatal staging of twin anemia-polycythemia sequence[85,95]

Stage	Criteria	Intertwin criteria
1	MCA-PSV >1.5 MoM in donor and MCA-PSV <1.0 MoM in recipient	Δ MCA-PSV >0.5 MoM without cardiac compromise of donor[a]
2	MCA-PSV >1.7 MoM in donor and MCA-PSV <0.8 MoM in recipient	
3	Stage 1 or 2 with cardiac compromise of donor[a]	
4	Ascites or hydrops of donor	
5	Single or double fetal demise	

MCA-PSV, middle cerebral artery Doppler peak systolic velocity; *MoM*, multiples of the median.

Adapted from Slaghekke et al,[85] 2010 and Tollenaar et al,[95] 2019.

[a] Cardiac compromise defined as absent or reversed end-diastolic flow in umbilical artery, pulsatile flow in umbilical vein, or reversed a-wave in the ductus venosus.

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15%.[103,108,109] In a retrospective series involving 49 pregnancies complicated by spontaneous TAPS, overall NDI occurred in 30% of survivors.[109] Although not significantly different within this small cohort, NDI appeared to be more common among donors (44%) than recipients (18%). Bilateral deafness was observed in 5 of 34 (15%) TAPS donors, with all cases involving auditory neuropathy spectrum disorder. This potential association and its etiology warrant further investigation.

It is possible that the existing literature overrepresents TAPS risks because of underreporting or underrecognition of mild disease presentations. Conversely, it is entirely plausible that some unexpected MC twin fetal demises are, in fact, attributable to TAPS, especially absent any universal antenatal screening strategy. If true, this would further increase mortality estimates. Ultimately, the best available data are of limited quality and suggest a disease with substantial twin morbidity and mortality risk.

When should monitoring for twin anemia-polycythemia sequence be performed?

TAPS is a serious complication of MC multiple gestations that is unlikely to be prenatally detected, especially at earlier stages, without MCA-PSV evaluation. It can present at any time in the second or third trimesters, and outcomes appear to correlate with disease severity. Detection of TAPS during pregnancy should prompt care escalation that may include heightened surveillance, fetal care center referral, fetal therapy, or delivery, with management recommendations tailored to the specifics of each case presentation.

Varying published formal guidance exists for TAPS screening, ranging from MCA-PSV assessments beginning in the midtrimester during routine ultrasound surveillance to recommendations that do not advocate any universal screening.[30,31,49,110] Critics of universal screening cite a lack of data supporting any single optimal strategy for TAPS management. However, this does not mean that treatments are wholly ineffective for managing severe TAPS presentations, with expert opinion suggesting otherwise. In addition, the widespread adoption of a universal monitoring strategy will facilitate an improved understanding of TAPS incidence and natural history. For these reasons, **we recommend that providers consider incorporating Doppler MCA-PSV determinations into all MC twin ultrasound surveillance beginning at 16 weeks of gestation (GRADE 1C).**[111] However, as previously noted, providers and institutions may consider the above information, along with local resources and patient access to care, when determining whether to include MCA Doppler studies in routine MC twin surveillance strategies. Irrespective of whether MCA-PSV assessments are included in routine screening, MCA-PSV determinations are a recommended component of all post–laser surgery surveillance, given the substantial risk for iatrogenic TAPS after TTTS treatment and the potential need for another intervention.[16,57]

How should twin anemia-polycythemia sequence be managed?

Antenatal management decisions for pregnancies complicated by TAPS should consider factors including gestational age, disease severity, the presence of coexisting twin complications such as FGR, and maternal and obstetrical factors. For stage I TAPS presenting before 32 to 34 weeks of gestation, close monitoring is generally a preferred strategy. Delivery should be considered for TAPS presentations at 32 to 34 weeks of gestation or upon diagnosis if identified later in pregnancy, with antenatal corticosteroid administration recommended as appropriate before delivery. Specific delivery timing should be individualized to consider the entire obstetrical presentation, including disease stage.

Patients with advanced-stage TAPS (stage ≥II) identified in the second or early third trimester are potential candidates for fetal therapy, and fetal care center referral is recommended in these situations. The optimal management strategy for early-onset, severe TAPS is unknown and ultimately should be individualized, with available options including expectant management, fetoscopic laser surgery,

UNNUMBERED TABLE

Summary of recommendations

Number	Recommendation	GRADE
1	We recommend routine first-trimester sonographic determination of chorionicity and amnionicity.	1B
2	We recommend that ultrasound surveillance for TTTS begin at 16 weeks of gestation for all MCDA twin pregnancies and continue at least every 2 weeks until delivery, with more frequent monitoring indicated with clinical concern.	1C
3	We recommend that routine sonographic surveillance for TTTS minimally include assessment of amniotic fluid volumes on both sides of the intertwin membrane and evaluation for the presence or absence of urine-filled fetal bladders, and ideally incorporate Doppler study of the umbilical arteries.	1C
4	We recommend fetoscopic laser surgery as the standard treatment for stage II through stage IV TTTS presenting between 16 and 26 weeks of gestation.	1A
5	We recommend expectant management with at least weekly fetal surveillance for asymptomatic patients continuing pregnancies complicated by stage I TTTS and consideration for fetoscopic laser surgery for stage I TTTS presentations between 16 and 26 weeks of gestation complicated by additional factors such as maternal polyhydramnios-associated symptomatology.	1B
6	We recommend an individualized approach to laser surgery for early- and late-presenting TTTS.	1C
7	We recommend that all patients with TTTS qualifying for laser therapy be referred to a fetal intervention center for further evaluation, consultation, and care.	Best Practice
8	After laser therapy, we suggest weekly surveillance for 6 weeks followed by resumption of every-other-week surveillance thereafter, unless concern exists for post-laser TTTS, post-laser TAPS, or FGR.	2C
9	Following the resolution of TTTS after fetoscopic laser surgery and without other indications for earlier delivery, we recommend delivery of dual-surviving MCDA twins at 34 to 36 weeks of gestation.	1C
10	In TTTS pregnancies complicated by posttreatment single fetal demise, we recommend full-term delivery (39 weeks) of the surviving co-twin to avoid complications of prematurity unless indications for earlier delivery exist.	1C
11	We recommend that fetoscopic laser surgery not influence the mode of delivery.	Best Practice
12	We recommend that prenatal diagnosis of TAPS minimally require either Doppler MCA-PSV values >1.5 MoM and <1.0 MoM in donor and recipient twins, respectively, or an intertwin Δ MCA-PSV >0.5 MoM.	1C
13	We recommend that providers consider incorporating Doppler MCA-PSV determinations into all MC twin ultrasound surveillance beginning at 16 weeks of gestation.	1C
14	Consultation with a specialized fetal care center is recommended when TAPS progresses to a more advanced disease stage ($\geq$II) before 32 weeks of gestation or when concern arises for coexisting complications such as TTTS.	Best Practice

Δ MCA-PSV, difference between donor and recipient MCA-PSV MoM values; *FGR*, fetal growth restriction; *MC*, monochorionic; *MCDA*, monochorionic-diamniotic; *MCA-PSV*, middle cerebral artery Doppler peak systolic velocity; *MoM*, multiples of the median; *TAPS*, twin anemia-polycythemia sequence; *TTTS*, twin–twin transfusion syndrome.

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UNNUMBERED TABLE

Society for Maternal-Fetal Medicine grading system: GRADE (Grading of Recommendations Assessment, Development and Evaluation) recommendations[118a]

GRADE of recommendation	Clarity of risk and benefit	Quality of supporting evidence	Implications
1A. Strong recommendation, high-quality evidence	Benefits clearly outweigh risks and burdens, or vice versa	Consistent evidence from well-performed, randomized controlled trials, or overwhelming evidence of some other form Further research is unlikely to change confidence in the estimate of benefit and risk	Strong recommendation that can apply to most patients in most circumstances without reservation Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present
1B. Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risks and burdens, or vice versa	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate	Strong recommendation that applies to most patients Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present
1C. Strong recommendation, low-quality evidence	Benefits appear to outweigh risks and burdens, or vice versa	Evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws Any estimate of effect is uncertain	Strong recommendation that applies to most patients Some of the evidence base supporting the recommendation is, however, of low quality
2A. Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burdens	Consistent evidence from well-performed randomized controlled trials or overwhelming evidence of some other form Further research is unlikely to change confidence in the estimate of benefit and risk	Weak recommendation; best action may differ depending on circumstances or patients or societal values
2B. Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burdens; some uncertainty in the estimates of benefits, risks, and burdens	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design Further research (if performed) is likely to have an effect on confidence in the estimate of benefit and risk and may change the estimate	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances
2C. Weak recommendation, low-quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens	Evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws Any estimate of effect is uncertain	Very weak recommendation; alternatives may be equally reasonable
Best practice	Recommendation in which either (1) there is an enormous amount of indirect evidence that clearly justifies strong recommendation (direct evidence would be challenging, and inefficient use of time and resources, to bring together and carefully summarize), or (2) recommendation to the contrary would be unethical		

[a] Adapted from Guyatt et al,[119] 2008.

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UNNUMBERED TABLE

Guidelines

The content of this document reflects the national and international guidelines related to twin-twin transfusion syndrome and twin anemia-polycythemia sequence

Organization	Title	Year of publication
American College of Obstetricians and Gynecologists	ACOG Practice Bulletin No 231: Multifetal gestations: Twin, triplet, and higher-order multifetal pregnancies[29]	2021
American Institute of Ultrasound in Medicine	AIUM practice parameter for the performance of fetal echocardiography[35]	2020
Expert Panel	Consensus diagnostic criteria and monitoring of twin anemia-polycythemia sequence: Delphi procedure[97]	2019
International Federation of Gynecology and Obstetrics	FIGO Good clinical practice advice: Management of twin pregnancy[32]	2019
International Society of Ultrasound in Obstetrics and Gynecology	ISUOG Practice Guidelines: role of ultrasound in twin pregnancy[31]	2016
National Institute for Health and Care Excellence	Twin and triplet pregnancy[17]	2019
North American Fetal Therapy Network	Consensus Statement: Management of complicated monochorionic gestations[57]	2015
North American Fetal Therapy Network	Consensus Statement: Prenatal management of uncomplicated monochorionic gestations[26]	2015
North American Fetal Therapy Network	Consensus statement: Prenatal surveillance of uncomplicated monochorionic gestations[1]	2015
Royal Australian and New Zealand College of Obstetricians and Gynaecologists	Best Practice Statement: Management of monochorionic twin pregnancy[33]	2011
Royal College of Obstetricians and Gynaecologists	Green-top Guideline No. 51: Management of monochorionic twin pregnancy[16]	2017
Society of Obstetricians and Gynaecologists of Canada	Guideline No. 440: Management of monochorionic twin pregnancies[30]	2023

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fetal transfusion therapy, and delivery. Selective fetal demise via targeted cord occlusion and termination of the entire pregnancy have also been described.

As with its role in the management of TTTS, the appeal of laser surgery for severe midtrimester TAPS presentations is its ability to interrupt the underlying fetofetal transfusion pathway. However, technical considerations such as placental location and lack of polyhydramnios-oligohydramnios may severely challenge or altogether preclude procedural completion. In cases where laser surgery is deemed inadvisable and for severe presentations in the early third trimester, fetal transfusion therapy may be considered. Various approaches to TAPS transfusion therapy have been described, although all involve some form of donor–twin intrauterine transfusion (IUT). A concern with any donor IUT is that it may worsen recipient twin polycythemia, which, when sufficiently severe, could trigger fetal ischemic insult or infarction of the distal extremities or brain. Although some proceduralists use an entirely intravascular approach to donor IUT, others use intraperitoneal transfusions, attempting to slow the absorption of red blood cells into the fetal circulation and theoretically decreasing the rate of blood transfer between twins.[105] In addition, some proceduralists advocate for accompanying recipient twin partial exchange transfusion (PET), in which the recipient blood is hemodiluted by gradual exchange of an equal volume of sterile isotonic crystalloid solution.[112,113] However, IUT with or without PET is ultimately considered a temporizing measure, and repeated transfusions may be indicated before delivery.

No published randomized controlled trial data exist comparing laser surgery or fetal transfusion therapy with expectant management, and the existing studies are retrospective and limited for such comparisons. An open-label randomized controlled trial is currently underway comparing laser surgery with expectant management, IUT±PET, and preterm delivery.[114] When evaluating the existing literature, it is important to consider that fetal therapy—whether laser or transfusion therapy—is generally reserved for more severe TAPS manifestations. Therefore,

comparisons based largely on case reports and series are subject to selection bias due to nonrandom treatment group allocations.

A retrospective study described 52 cases from 2 fetal care centers managed with either laser surgery (n=8), fetal transfusion therapy (n=17), or expectant observation (n=27). There was no statistically significant difference in perinatal survival rates when comparing the 3 approaches (laser 94%, transfusion 85%, expectant management 83%; $P=.30$).[115] Severe neonatal morbidity rates among live-born neonates were 7% for laser, 38% for transfusion therapy, and 24% for expectant management, yet this was also not significantly different between groups. However, no severe postnatal hematologic complications (defined as the donor requiring blood transfusion or the recipient requiring PET on the first postnatal day) were detected after laser surgery, as opposed to rates of 72% after transfusion therapy and 52% after expectant management. Laser surgery was also associated with a significantly ($P<.01$) prolonged latency from diagnosis to delivery and decreased risk for respiratory distress syndrome. A systematic review consisting of case reports and series, as well as the above study, collected 105 TAPS cases.[116] The authors found no difference in perinatal mortality between groups but a lower rate of adverse perinatal outcomes for those treated with laser or transfusion therapy compared with expectantly managed cases. In a TAPS registry-based study, 370 prenatally diagnosed TAPS cases were reported by 17 fetal care centers between 2014 and 2019.[117] Considerable heterogeneity of management approaches was observed between and even within fetal care centers. Perinatal mortality rates were 17%, 18%, 18%, 10%, and 7% for expectant management, laser, IUT±PET, delivery, and selective termination (nontargeted twin only) groups, respectively, without a significant difference among management approaches. The rates of severe neonatal morbidity were similar among the groups, ranging from 25% to 49% for all treatment modalities.

When should patients be referred to a fetal care center for twin anemia-polycythemia sequence?

Although screening aims to identify TAPS presentations that might benefit from prenatal intervention, not all suspected cases require a fetal care center referral. Specifically, cases of stage I TAPS can be safely managed with more frequent local surveillance (on an at-least-weekly basis), regardless of whether the diagnosis represents a false-positive presentation or overt early-stage TAPS. **Consultation with a specialized fetal care center is recommended when TAPS progresses to a more advanced disease stage (stage ≥II) before 32 weeks of gestation or when concern arises for coexisting complications such as TTTS (Best Practice)**. TAPS presentations (of any stage) at 32 to 34 weeks—or upon diagnosis if identified at later gestational ages—may be considered for delivery and do not necessarily require outside referral.

Conclusion

MC twins are at increased risk for perinatal morbidity and mortality, much of which is attributable to specific issues involving their shared placenta and intertwin placental circulation. TTTS and TAPS represent 2 types of fetofetal transfusion syndromes in which there is imbalanced blood flow across intertwin placental anastomoses. Frequent sonographic monitoring beginning early in the midtrimester can identify these conditions and provide opportunities for individualized management plans. ■

REFERENCES

1. Bahtiyar MO, Emery SP, Dashe JS, et al. The North American Fetal Therapy Network consensus statement: prenatal surveillance of uncomplicated monochorionic gestations. Obstet Gynecol 2015;125:118–23. https://doi.org/10.1097/aog.0000000000000599.

2. Denbow ML, Cox P, Taylor M, Hammal DM, Fisk NM. Placental angioarchitecture in monochorionic twin pregnancies: relationship to fetal growth, fetofetal transfusion syndrome, and pregnancy outcome. Am J Obstet Gynecol 2000;182:417–26. https://doi.org/10.1016/s0002-9378(00)70233-x.

3. De Paepe ME. Examination of the twin placenta. Semin Perinatol 2015;39:27–35. https://doi.org/10.1053/j.semperi.2014.10.005.

4. Chen K, Chmait RH, Vanderbilt D, Wu S, Randolph L. Chimerism in monochorionic dizygotic twins: case study and review. Am J Med Genet A 2013;161A:1817–24. https://doi.org/10.1002/ajmg.a.35957.

5. Hack KE, Derks JB, Elias SG, et al. Increased perinatal mortality and morbidity in monochorionic versus dichorionic twin pregnancies: clinical implications of a large Dutch cohort study. BJOG 2008;115:58–67. https://doi.org/10.1111/j.1471-0528.2007.01556.x.

6. Zhao DP, de Villiers SF, Slaghekke F, et al. Prevalence, size, number and localization of vascular anastomoses in monochorionic placentas. Placenta 2013;34:589–93. https://doi.org/10.1016/j.placenta.2013.04.005.

7. Lewi L, Deprest J, Hecher K. The vascular anastomoses in monochorionic twin pregnancies and their clinical consequences. Am J Obstet Gynecol 2013;208:19–30. https://doi.org/10.1016/j.ajog.2012.09.025.

8. Carroll SGM, Soothill PW, Abdel-Fattah SA, Porter H, Montague I, Kyle PM. Prediction of chorionicity in twin pregnancies at 10−14 weeks of gestation. BJOG 2002;109:182–6. https://doi.org/10.1111/j.1471-0528.2002.01172.x.

9. Maruotti GM, Saccone G, Morlando M, Martinelli P. First-trimester ultrasound determination of chorionicity in twin gestations using the lambda sign: a systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol 2016;202:66–70. https://doi.org/10.1016/j.ejogrb.2016.04.023.

10. Blumenfeld YJ, Momirova V, Rouse DJ, et al. Accuracy of sonographic chorionicity classification in twin gestations. J Ultrasound Med 2014;33:2187–92. https://doi.org/10.7863/ultra.33.12.2187.

11. Chen K, Kuhlmann R, Bell A, et al. Twin anemia-polycythemia sequence in sex-discordant monochorionic dizygotic twins. Ultrasound Obstet Gynecol 2020;56:461–2. https://doi.org/10.1002/uog.22073.

12. Suzuki T, Kagami K, Mitani Y, Yamazaki R, Ono M, Fujiwara H. Twin anemia-polycythemia sequence with blood chimerism in monochorionic dizygotic opposite-sex twins. J Obstet Gynaecol Res 2019;45:1201–4. https://doi.org/10.1111/jog.13949.

13. Lopriore E, Sueters M, Middeldorp JM, Klumper F, Oepkes D, Vandenbussche FPHA. Twin pregnancies with two separate placental masses can still be monochorionic and have vascular anastomoses. Am J Obstet Gynecol 2006;194:804–8. https://doi.org/10.1016/j.ajog.2005.09.015.

14. Senat MV, Quarello E, Levaillant JM, Buonumano A, Boulvain M, Frydman R. Determining chorionicity in twin gestations: three-dimensional (3D) multiplanar sonographic measurement of intra-amniotic membrane

thickness. Ultrasound Obstet Gynecol 2006;28:665–9. https://doi.org/10.1002/uog.2835.
15. Norwitz ER, McNeill G, Kalyan A, et al. Validation of a single-nucleotide polymorphism-based non-invasive prenatal test in twin gestations: determination of zygosity, individual fetal sex, and fetal aneuploidy. J Clin Med 2019;8:937. https://doi.org/10.3390/jcm8070937.
16. Management of monochorionic twin pregnancy: Green-top guideline no. 51. BJOG 2017;124:e1–45. https://doi.org/10.1111/1471-0528.14188.
17. Twin and triplet pregnancy. National Institute for Health Care Excellence. Available at: https://www.nice.org.uk/guidance/ng137/chapter/Recommendations. Accessed April 22, 2021.
18. Acosta-Rojas R, Becker J, Munoz-Abellana B, et al. Twin chorionicity and the risk of adverse perinatal outcome. Int J Gynaecol Obstet 2007;96:98–102. https://doi.org/10.1016/j.ijgo.2006.11.002.
19. Lewi L, Jani J, Blickstein I, et al. The outcome of monochorionic diamniotic twin gestations in the era of invasive fetal therapy: a prospective cohort study. Am J Obstet Gynecol 2008;199:514.e1–8. https://doi.org/10.1016/j.ajog.2008.03.050.
20. Lutfi S, Allen VM, Fahey J, O'Connell CM, Vincer MJ. Twin-twin transfusion syndrome: a population-based study. Obstet Gynecol 2004;104:1289–97. https://doi.org/10.1097/01.AOG.0000143828.41271.6c.
21. Ortibus E, Lopriore E, Deprest J, et al. The pregnancy and long-term neurodevelopmental outcome of monochorionic diamniotic twin gestations: a multicenter prospective cohort study from the first trimester onward. Am J Obstet Gynecol 2009;200:494.e1–8. https://doi.org/10.1016/j.ajog.2009.01.048.
22. Quintero RA, Morales WJ, Allen MH, Bornick PW, Johnson PK, Kruger M. Staging of twin-twin transfusion syndrome. J Perinatol 1999;19:550–5. https://doi.org/10.1038/sj.jp.7200292.
23. Taylor MJ, Govender L, Jolly M, Wee L, Fisk NM. Validation of the Quintero staging system for twin-twin transfusion syndrome. Obstet Gynecol 2002;100:1257–65. https://doi.org/10.1016/s0029-7844(02)02392-x.
24. Couck I, Ponnet S, Thewissen L, et al. The detection, outcome, and presentation of twin-twin transfusion syndrome in monochorionic diamniotic twin pregnancies followed with a protocol of fortnightly ultrasound examination. Fetal Diagn Ther 2021;48:353–60. https://doi.org/10.1159/000514575.
25. Brock CO, Sibai BM, Soto EE, et al. Fortnightly surveillance of monochorionic diamniotic twins for twin to twin transfusion syndrome: compliance and effectiveness. Prenat Diagn 2020;40:1598–605. https://doi.org/10.1002/pd.5810.
26. Emery SP, Bahtiyar MO, Dashe JS, et al. The North American Fetal Therapy Network Consensus Statement: prenatal management of uncomplicated monochorionic gestations. Obstet Gynecol 2015;125:1236–43. https://doi.org/10.1097/aog.0000000000000723.
27. Sueters M, Middeldorp JM, Lopriore E, Oepkes D, Kanhai HH, Vandenbussche FP. Timely diagnosis of twin-to-twin transfusion syndrome in monochorionic twin pregnancies by biweekly sonography combined with patient instruction to report onset of symptoms. Ultrasound Obstet Gynecol 2006;28:659–64. https://doi.org/10.1002/uog.3819.
28. Thorson HL, Ramaeker DM, Emery SP. Optimal interval for ultrasound surveillance in monochorionic twin gestations. Obstet Gynecol 2011;117:131–5. https://doi.org/10.1097/AOG.0b013e31820292ec.
29. Multifetal gestations: twin, triplet, and higher-order multifetal pregnancies: ACOG practice bulletin, number 231. Obstet Gynecol 2021;137:e145–62. https://doi.org/10.1097/aog.0000000000004397.
30. Lee HS, Abbasi N, Van Mieghem T, et al. Guideline no. 440: management of monochorionic twin pregnancies. J Obstet Gynaecol Can 2023;45:587–606.e8. https://doi.org/10.1016/j.jogc.2023.05.018.
31. Khalil A, Rodgers M, Baschat A, et al. ISUOG Practice Guidelines: role of ultrasound in twin pregnancy. Ultrasound Obstet Gynecol 2016;47:247–63. https://doi.org/10.1002/uog.15821.
32. FIGO Working Group on Good Clinical Practice in Maternal-Fetal Medicine. Good clinical practice advice: role of ultrasound in the management of twin pregnancy. Int J Gynaecol Obstet 2019;144:338–9. https://doi.org/10.1002/ijgo.12743.
33. Management of monochorionic twin pregnancy. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Available at: https://ranzcog.edu.au/wp-content/uploads/2022/05/Management-of-Monochorionic-Twin-Pregnancy.pdf. Accessed March 19, 2024.
34. Bahtiyar MO, Dulay AT, Weeks BP, Friedman AH, Copel JA. Prevalence of congenital heart defects in monochorionic/diamniotic twin gestations: a systematic literature review. J Ultrasound Med 2007;26:1491–8. https://doi.org/10.7863/jum.2007.26.11.1491.
35. AIUM practice parameter for the performance of fetal echocardiography. J Ultrasound Med 2020;39:E5–16. https://doi.org/10.1002/jum.15188.
36. Habli M, Michelfelder E, Cnota J, et al. Prevalence and progression of recipient-twin cardiomyopathy in early-stage twin-twin transfusion syndrome. Ultrasound Obstet Gynecol 2012;39:63–8. https://doi.org/10.1002/uog.10117.
37. Karatza AA, Wolfenden JL, Taylor MJ, Wee L, Fisk NM, Gardiner HM. Influence of twin-twin transfusion syndrome on fetal cardiovascular structure and function: prospective case-control study of 136 monochorionic twin pregnancies. Heart 2002;88:271–7. https://doi.org/10.1136/heart.88.3.271.
38. Lopriore E, Bökenkamp R, Rijlaarsdam M, Sueters M, Vandenbussche FP, Walther FJ. Congenital heart disease in twin-to-twin transfusion syndrome treated with fetoscopic laser surgery. Congenit Heart Dis 2007;2:38–43. https://doi.org/10.1111/j.1747-0803.2007.00070.x.
39. Rychik J, Tian Z, Bebbington M, 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;197:392.e1–8. https://doi.org/10.1016/j.ajog.2007.06.055.
40. Stirnemann JJ, Mougeot M, Proulx F, et al. Profiling fetal cardiac function in twin-twin transfusion syndrome. Ultrasound Obstet Gynecol 2010;35:19–27. https://doi.org/10.1002/uog.7488.
41. Stirnemann JJ, Nasr B, Proulx F, Essaoui M, Ville Y. Evaluation of the CHOP cardiovascular score as a prognostic predictor of outcome in twin-twin transfusion syndrome after laser coagulation of placental vessels in a prospective cohort. Ultrasound Obstet Gynecol 2010;36:52–7. https://doi.org/10.1002/uog.7713.
42. Krispin E, Javinani A, Odibo A, et al. Consensus protocol for management of early and late twin-twin transfusion syndrome: Delphi study. Ultrasound Obstet Gynecol 2024;63:371–7. https://doi.org/10.1002/uog.27446.
43. Roberts D, Neilson JP, Kilby MD, Gates S. Interventions for the treatment of twin-twin transfusion syndrome. Cochrane Database Syst Rev 2014;2014:CD002073. https://doi.org/10.1002/14651858.CD002073.pub3.
44. De Lia JE, Cruikshank DP, Keye WR Jr. Fetoscopic neodymium:YAG laser occlusion of placental vessels in severe twin-twin transfusion syndrome. Obstet Gynecol 1990;75:1046–53.
45. Ferschl MB, Feiner J, Vu L, Smith D, Rollins MD. A comparison of spinal anesthesia versus monitored anesthesia care with local anesthesia in minimally invasive fetal surgery. Anesth Analg 2020;130:409–15. https://doi.org/10.1213/ane.0000000000003947.
46. Hoagland MA, Chatterjee D. Anesthesia for fetal surgery. Paediatr Anaesth 2017;27:346–57. https://doi.org/10.1111/pan.13109.
47. Bamberg C, Hecher K. Update on twin-to-twin transfusion syndrome. Best Pract Res Clin Obstet Gynaecol 2019;58:55–65. https://doi.org/10.1016/j.bpobgyn.2018.12.011.
48. Miller R. Minimally invasive fetal therapy and open fetal surgery. In: Fleischer AC, Abramowicz J, Goncalves LF, et al, eds. Fleischer's sonography in obstetrics and gynecology: textbook and teaching cases, 8th ed. New York, NY: McGraw-Hill Education; 2018:847–64.

49. Society for Maternal-Fetal Medicine, Simpson LL. Twin-twin transfusion syndrome. Am J Obstet Gynecol 2013;208:3–18.

50. Banek CS, Hecher K, Hackeloer BJ, Bartmann P. Long-term neurodevelopmental outcome after intrauterine laser treatment for severe twin-twin transfusion syndrome. Am J Obstet Gynecol 2003;188:876–80. https://doi.org/10.1067/mob.2003.202.

51. Graef C, Ellenrieder B, Hecher K, Hackeloer BJ, Huber A, Bartmann P. Long-term neurodevelopmental outcome of 167 children after intrauterine laser treatment for severe twin-twin transfusion syndrome. Am J Obstet Gynecol 2006;194:303–8. https://doi.org/10.1016/j.ajog.2005.07.040.

52. Gray PH, Poulsen L, Gilshenan K, Soong B, Cincotta RB, Gardener G. Neurodevelopmental outcome and risk factors for disability for twin-twin transfusion syndrome treated with laser surgery. Am J Obstet Gynecol 2011;204:159.e1–6. https://doi.org/10.1016/j.ajog.2010.08.041.

53. Lenclen R, Ciarlo G, Paupe A, Bussieres L, Ville Y. Neurodevelopmental outcome at 2 years in children born preterm treated by amnioreduction or fetoscopic laser surgery for twin-to-twin transfusion syndrome: comparison with dichorionic twins. Am J Obstet Gynecol 2009;201:291.e1–5. https://doi.org/10.1016/j.ajog.2009.05.036.

54. Lopriore E, Ortibus E, Acosta-Rojas R, et al. Risk factors for neurodevelopment impairment in twin-twin transfusion syndrome treated with fetoscopic laser surgery. Obstet Gynecol 2009;113:361–6. https://doi.org/10.1097/AOG.0b013e318195873e.

55. Salomon LJ, Ortqvist L, Aegerter P, et al. Long-term developmental follow-up of infants who participated in a randomized clinical trial of amniocentesis vs laser photocoagulation for the treatment of twin-to-twin transfusion syndrome. Am J Obstet Gynecol 2010;203:444.e1–7. https://doi.org/10.1016/j.ajog.2010.08.054.

56. Vanderbilt DL, Schrager SM, Llanes A, Hamilton A, Seri I, Chmait RH. Predictors of 2-year cognitive performance after laser surgery for twin-twin transfusion syndrome. Am J Obstet Gynecol 2014;211:388.e1–7. https://doi.org/10.1016/j.ajog.2014.03.050.

57. Emery SP, Bahtiyar MO, Moise KJ; North American Fetal Therapy Network. The North American fetal therapy network consensus statement: management of complicated monochorionic gestations. Obstet Gynecol 2015;126:575–84. https://doi.org/10.1097/aog.0000000000000994.

58. Beck V, Lewi P, Gucciardo L, Devlieger R. Preterm prelabor rupture of membranes and fetal survival after minimally invasive fetal surgery: a systematic review of the literature. Fetal Diagn Ther 2012;31:1–9. https://doi.org/10.1159/000331165.

59. Slaghekke F, Oepkes D. Solomon technique versus selective coagulation for twin-twin transfusion syndrome. Twin Res Hum Genet 2016;19:217–21. https://doi.org/10.1017/thg.2016.25.

60. Robyr R, Lewi L, Salomon LJ, et al. Prevalence and management of late fetal complications following successful selective laser coagulation of chorionic plate anastomoses in twin-to-twin transfusion syndrome. Am J Obstet Gynecol 2006;194:796–803. https://doi.org/10.1016/j.ajog.2005.08.069.

61. Slaghekke F, Lopriore E, Lewi L, et al. Fetoscopic laser coagulation of the vascular equator versus selective coagulation for twin-to-twin transfusion syndrome: an open-label randomised controlled trial. Lancet 2014;383:2144–51. https://doi.org/10.1016/s0140-6736(13)62419-8.

62. van Klink JMM, Slaghekke F, Balestriero MA, et al. Neurodevelopmental outcome at 2 years in twin-twin transfusion syndrome survivors randomized for the Solomon trial. Am J Obstet Gynecol 2016;214:113.e1–7. https://doi.org/10.1016/j.ajog.2015.08.033.

63. Sacco A, Van der Veeken L, Bagshaw E, et al. Maternal complications following open and fetoscopic fetal surgery: a systematic review and meta-analysis. Prenat Diagn 2019;39:251–68. https://doi.org/10.1002/pd.5421.

64. Peralta CFA, Sbragia L, Corrêa-Silva EPB, et al. [Maternal complications following endoscopic surgeries in fetal Medicine]. Rev Bras Ginecol Obstet 2010;32:260–6.

65. O'Donoghue K, Cartwright E, Galea P, Fisk NM. Stage I twin-twin transfusion syndrome: rates of progression and regression in relation to outcome. Ultrasound Obstet Gynecol 2007;30:958–64. https://doi.org/10.1002/uog.5189.

66. Emery SP, Hasley SK, Catov JM, et al. North American Fetal Therapy Network: intervention vs expectant management for stage I twin-twin transfusion syndrome. Am J Obstet Gynecol 2016;215:346.e1–7. https://doi.org/10.1016/j.ajog.2016.04.024.

67. Stirnemann J, Slaghekke F, Khalek N, et al. Intrauterine fetoscopic laser surgery versus expectant management in stage 1 twin-to-twin transfusion syndrome: an international randomized trial. Am J Obstet Gynecol 2021;224(528):e1–12. https://doi.org/10.1016/j.ajog.2020.11.031.

68. Baud D, Windrim R, Keunen J, et al. Fetoscopic laser therapy for twin-twin transfusion syndrome before 17 and after 26 weeks' gestation. Am J Obstet Gynecol 2013;208:197.e1–7. https://doi.org/10.1016/j.ajog.2012.11.027.

69. Valsky DV, Eixarch E, Martinez-Crespo JM, et al. Fetoscopic laser surgery for twin-to-twin transfusion syndrome after 26 weeks of gestation. Fetal Diagn Ther 2012;31:30–4. https://doi.org/10.1159/000330369.

70. Lecointre L, Sananes N, Weingertner AS, et al. Fetoscopic laser coagulation for twin-twin transfusion syndrome before 17 weeks' gestation: laser data, complications and neonatal outcome. Ultrasound Obstet Gynecol 2014;44:299–303. https://doi.org/10.1002/uog.13375.

71. Berghella V, Kaufmann M. Natural history of twin-twin transfusion syndrome. J Reprod Med 2001;46:480–4.

72. Mari G, Roberts A, Detti L, et al. Perinatal morbidity and mortality rates in severe twin-twin transfusion syndrome: results of the International amnioreduction Registry. Am J Obstet Gynecol 2001;185:708–15. https://doi.org/10.1067/mob.2001.117188.

73. Stirnemann J, Chalouhi G, Essaoui M, et al. Fetal brain imaging following laser surgery in twin-to-twin surgery. BJOG 2018;125:1186–91. https://doi.org/10.1111/1471-0528.14162.

74. Baschat AA, Gungor S, Glosemeyer P, Huber A, Hecher K. Changes in umbilical venous volume flow after fetoscopic laser occlusion of placental vascular anastomoses in twin-to-twin transfusion syndrome. Am J Obstet Gynecol 2010;203(479):e1–6. https://doi.org/10.1016/j.ajog.2009.11.013.

75. Gratacós E, Van Schoubroeck D, Carreras E, et al. Impact of laser coagulation in severe twin-twin transfusion syndrome on fetal Doppler indices and venous blood flow volume. Ultrasound Obstet Gynecol 2002;20:125–30. https://doi.org/10.1046/j.1469-0705.2002.00749.x.

76. Gratacós E, Van Schoubroeck D, Carreras E, et al. Transient hydropic signs in the donor fetus after fetoscopic laser coagulation in severe twin-twin transfusion syndrome: incidence and clinical relevance. Ultrasound Obstet Gynecol 2002;19:449–53. https://doi.org/10.1046/j.1469-0705.2002.00642.x.

77. Borse V, Shanks AL. Twin-to-twin transfusion syndrome. In: StatPearls. Treasure Island. StatPearls Publishing. 2021. Available at: https://www.ncbi.nlm.nih.gov/books/NBK563133/. Accessed July 29, 2024.

78. Chon AH, Chang MR, Chmait HR, Korst LM, Friedlich PS, Chmait RH. Delivery timing after laser surgery for twin-twin transfusion syndrome. J Perinatol 2020;40:248–55. https://doi.org/10.1038/s41372-019-0532-5.

79. Stirnemann JJ, Quibel T, Essaoui M, Salomon LJ, Bussieres L, Ville Y. Timing of delivery following selective laser photocoagulation for twin-to-twin transfusion syndrome. Am J Obstet Gynecol 2012;207:127.e1–6. https://doi.org/10.1016/j.ajog.2012.06.042.

80. Zaretsky MV, Tong S, Lagueux M, et al. North American Fetal Therapy Network: timing of and indications for delivery following laser ablation for twin-twin transfusion syndrome. Am J Obstet Gynecol MFM 2019;1:74–81. https://doi.org/10.1016/j.ajogmf.2019.02.001.

81. Fang YMV, Guirguis P, Borgida A, Feldman D, Ingardia C, Herson V. Increased neonatal morbidity despite pulmonary maturity for deliveries occurring before 39 weeks. J Matern Fetal Neonatal Med 2013;26:79–82. https://doi.org/10.3109/14767058.2012.728647.

82. Tita ATN, Landon MB, Spong CY, et al. Timing of elective repeat cesarean delivery at term and neonatal outcomes. N Engl J Med 2009;360:111–20. https://doi.org/10.1056/NEJMoa0803267.

83. Zanardo V, Simbi AK, Franzoi M, Soldà G, Salvadori A, Trevisanuto D. Neonatal respiratory morbidity risk and mode of delivery at term: influence

of timing of elective caesarean delivery. Acta Paediatr 2004;93:643–7. https://doi.org/10.1111/j.1651-2227.2004.tb02990.x.

84. de Villiers SF, Slaghekke F, Middeldorp JM, Walther FJ, Oepkes D, Lopriore E. Placental characteristics in monochorionic twins with spontaneous versus post-laser twin anemia-polycythemia sequence. Placenta 2013;34:456–9. https://doi.org/10.1016/j.placenta.2013.02.005.

85. Slaghekke F, Kist WJ, Oepkes D, et al. Twin anemia-polycythemia sequence: diagnostic criteria, classification, perinatal management and outcome. Fetal Diagn Ther 2010;27:181–90. https://doi.org/10.1159/000304512.

86. van den Wijngaard JPHM, Lewi L, Lopriore E, et al. Modeling severely discordant hematocrits and normal amniotic fluids after incomplete laser therapy in twin-to-twin transfusion syndrome. Placenta 2007;28:611–5. https://doi.org/10.1016/j.placenta.2006.10.002.

87. Lopriore E, van den Wijngaard JP, Middeldorp JM, et al. Assessment of feto-fetal transfusion flow through placental arterio-venous anastomoses in a unique case of twin-to-twin transfusion syndrome. Placenta 2007;28:209–11. https://doi.org/10.1016/j.placenta.2006.03.006.

88. Lopriore E, Van den Wijngaard JP, Pasman SA, et al. Quantification of feto-fetal transfusion rate through a single placental arterio-venous anastomosis in a monochorionic twin pregnancy. Placenta 2009;30:223–5. https://doi.org/10.1016/j.placenta.2008.11.012.

89. Veujoz M, Sananès N, Severac F, et al. Evaluation of prenatal and postnatal diagnostic criteria for twin anemia-polycythemia sequence. Prenat Diagn 2015;35:281–8. https://doi.org/10.1002/pd.4545.

90. Nakayama S, Ishii K, Kawaguchi H, et al. Perinatal outcome of monochorionic diamniotic twin pregnancies managed from early gestation at a single center. J Obstet Gynaecol Res 2012;38:692–7. https://doi.org/10.1111/j.1447-0756.2011.01759.x.

91. Gucciardo L, Lewi L, Vaast P, et al. Twin anemia polycythemia sequence from a prenatal perspective. Prenat Diagn 2010;30:438–42. https://doi.org/10.1002/pd.2491.

92. Tollenaar LSA, Slaghekke F, Lewi L, et al. Spontaneous twin anemia polycythemia sequence: diagnosis, management, and outcome in an international cohort of 249 cases. Am J Obstet Gynecol 2021;224(213):e1–11. https://doi.org/10.1016/j.ajog.2020.07.041.

93. Habli M, Bombrys A, Lewis D, et al. Incidence of complications in twin-twin transfusion syndrome after selective fetoscopic laser photocoagulation: a single-center experience. Am J Obstet Gynecol 2009;201(417):e1–7. https://doi.org/10.1016/j.ajog.2009.07.046.

94. Lopriore E, Slaghekke F, Oepkes D, Middeldorp JM, Vandenbussche FP, Walther FJ. Hematological characteristics in neonates with twin anemia-polycythemia sequence (TAPS). Prenat Diagn 2010;30:251–5. https://doi.org/10.1002/pd.2453.

95. Tollenaar LSA, Lopriore E, Middeldorp JM, et al. Improved prediction of twin anemia-polycythemia sequence by delta middle cerebral artery peak systolic velocity: new antenatal classification system. Ultrasound Obstet Gynecol 2019;53:788–93. https://doi.org/10.1002/uog.20096.

96. Fishel-Bartal M, Weisz B, Mazaki-Tovi S, et al. Can middle cerebral artery peak systolic velocity predict polycythemia in monochorionic-diamniotic twins? Evidence from a prospective cohort study. Ultrasound Obstet Gynecol 2016;48:470–5. https://doi.org/10.1002/uog.15838.

97. Khalil A, Gordijn S, Ganzevoort W, et al. Consensus diagnostic criteria and monitoring of twin anemia-polycythemia sequence: Delphi procedure. Ultrasound Obstet Gynecol 2020;56:388–94. https://doi.org/10.1002/uog.21882.

98. Bamberg C, Diemert A, Glosemeyer P, Hecher K. Quantified discordant placental echogenicity in twin anemia-polycythemia sequence (TAPS) and middle cerebral artery peak systolic velocity. Ultrasound Obstet Gynecol 2018;52:373–7. https://doi.org/10.1002/uog.17535.

99. Tollenaar LSA, Lopriore E, Middeldorp JM, et al. Prevalence of placental dichotomy, fetal cardiomegaly and starry-sky liver in twin anemia-polycythemia sequence. Ultrasound Obstet Gynecol 2020;56:395–9. https://doi.org/10.1002/uog.21948.

100. Ishii K, Murakoshi T, Matsushita M, Sinno T, Naruse H, Torii Y. Transitory increase in middle cerebral artery peak systolic velocity of recipient twins after fetoscopic laser photocoagulation for twin-twin transfusion syndrome. Fetal Diagn Ther 2008;24:470–3. https://doi.org/10.1159/000178531.

101. Sela HY, Miller R, Abellar RG, Simpson LL. Placental hematoma mimicking twin anemia-polycythemia sequence following selective laser photocoagulation for twin-twin transfusion syndrome. Prenat Diagn 2014;34:1123–5. https://doi.org/10.1002/pd.4457.

102. Giorgione V, D'Antonio F, Manji A, Reed K, Khalil A. Perinatal outcome of pregnancy complicated by twin anemia-polycythemia sequence: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2021;58:813–23. https://doi.org/10.1002/uog.23585.

103. Lopriore E, Slaghekke F, Oepkes D, Middeldorp JM, Vandenbussche FP, Walther FJ. Clinical outcome in neonates with twin anemia-polycythemia sequence. Am J Obstet Gynecol 2010;203(54):e1–5. https://doi.org/10.1016/j.ajog.2010.02.032.

104. Visser GL, Tollenaar LSA, Bekker V, et al. Leukocyte counts and other hematological values in twin-twin transfusion syndrome and twin anemia-polycythemia sequence. Fetal Diagn Ther 2020;47:123–8. https://doi.org/10.1159/000500859.

105. Herway C, Johnson A, Moise K, Moise KJ Jr. Fetal intraperitoneal transfusion for iatrogenic twin anemia-polycythemia sequence after laser therapy. Ultrasound Obstet Gynecol 2009;33:592–4. https://doi.org/10.1002/uog.6334.

106. Lopriore E, Slaghekke F, Kersbergen KJ, et al. Severe cerebral injury in a recipient with twin anemia-polycythemia sequence. Ultrasound Obstet Gynecol 2013;41:702–6. https://doi.org/10.1002/uog.12337.

107. Luminoso D, Figueira CO, Marins M, Peralta CF. Fetal brain lesion associated with spontaneous twin anemia-polycythemia sequence. Ultrasound Obstet Gynecol 2013;42:721–2. https://doi.org/10.1002/uog.12574.

108. Slaghekke F, van Klink JM, Koopman HM, Middeldorp JM, Oepkes D, Lopriore E. Neurodevelopmental outcome in twin anemia-polycythemia sequence after laser surgery for twin-twin transfusion syndrome. Ultrasound Obstet Gynecol 2014;44:316–21. https://doi.org/10.1002/uog.13387.

109. Tollenaar LSA, Lopriore E, Slaghekke F, et al. High risk of long-term neurodevelopmental impairment in donor twins with spontaneous twin anemia-polycythemia sequence. Ultrasound Obstet Gynecol 2020;55:39–46. https://doi.org/10.1002/uog.20846.

110. Oliver E, Navaratnam K, Gent J, Khalil A, Sharp A. Comparison of international guidelines on the management of twin pregnancy. Eur J Obstet Gynecol Reprod Biol 2023;285:97–104. https://doi.org/10.1016/j.ejogrb.2023.04.002.

111. Tongsong T, Wanapirak C, Sirichotiyakul S, Tongprasert F, Srisupundit K. Middle cerebral artery peak systolic velocity of healthy fetuses in the first half of pregnancy. J Ultrasound Med 2007;26:1013–7. https://doi.org/10.7863/jum.2007.26.8.1013.

112. Genova L, Slaghekke F, Klumper FJ, et al. Management of twin anemia-polycythemia sequence using intrauterine blood transfusion for the donor and partial exchange transfusion for the recipient. Fetal Diagn Ther 2013;34:121–6. https://doi.org/10.1159/000346413.

113. Slaghekke F, van den Wijngaard JP, Akkermans J, et al. Intrauterine transfusion combined with partial exchange transfusion for twin anemia polycythemia sequence: modeling a novel technique. Placenta 2015;36:599–602. https://doi.org/10.1016/j.placenta.2015.01.194.

114. Trial NL6879 (NTR7057). Netherlands Trial Register. Available at: https://onderzoekmetmensen.nl/en/trial/26505. Accessed August 7, 2024.

115. Slaghekke F, Favre R, Peeters SH, et al. Laser surgery as a management option for twin anemia-polycythemia sequence. Ultrasound Obstet Gynecol 2014;44:304–10. https://doi.org/10.1002/uog.13382.

116. Hill KM, Masoudian P, Fung-Kee-Fung K, El Demellawy D. Intrauterine interventions for the treatment of twin anemia-polycythemia sequence: a systematic review. J Obstet Gynaecol Can 2019;41:981–91. https://doi.org/10.1016/j.jogc.2018.04.005.

117. Tollenaar LSA, Slaghekke F, Lewi L, et al. Treatment and outcome of 370 cases with spontaneous or post-laser twin anemia-polycythemia

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sequence managed in 17 fetal therapy centers. Ultrasound Obstet Gynecol 2020;56:378–87. https://doi.org/10.1002/uog.22042.

118. Society for Maternal-Fetal Medicine (SMFM), Norton ME, Kuller JA, Metz TD. Society for Maternal-Fetal Medicine special statement: Grading of Recommendations Assessment, Development, and Evaluation (GRADE) update. Am J Obstet Gynecol 2021;224:B24–8. https://doi.org/10.1016/j.ajog.2020.12.1200.

119. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924–6. https://doi.org/10.1136/bmj.39489.470347.AD.

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