

Ultrasound Assessment and Surgical Treatment of Twin-Twin Transfusion Syndrome

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ABSTRACT

The ultrasound diagnosis, management and treatment of twin-twin transfusion syndrome (TTTS) have had a remarkable number of positive developments in the last 20 years. Together, they have resulted in TTTS being the most common condition seen and treated in fetal therapy centers today. This chapter discusses the basic ultrasound assessment of TTTS patients in a step-by-step fashion, to provide a structure to the sonographic examination. This includes review of the diagnostic criteria, the sonographic assessment of disease severity and preoperative ultrasound assessment. The chapter also reviews the rationale for, as well as the fundamental laser technique and its variations, including the nonselective technique, selective laser photocoagulation of communicating vessels (SLPCV), sequential selective laser photocoagulation of the communicating vessels (SQLPCV) and the 'Solomon' technique, and provides potential explanations for the outcome differences of each technique. Future developments in terms of surgical technique and long-term outcome studies are also discussed.

Keywords: Twin-twin transfusion syndrome, Ultrasound, Fetal therapy, Laser surgery.

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INTRODUCTION

Twin-twin transfusion syndrome (TTTS) occurs in approximately 5 to 10% of monochorionic twins.¹ Monochorionic twins themselves occur in approximately 0.7% of all pregnancies.² Therefore, TTTS occurs in approximately 0.07% of all pregnancies. This amounts to approximately 2,800 pregnancies in United States per year affected with TTTS.³ The disease is thought to occur from an unbalanced transfer of blood between two monochorionic twins through placental vascular anastomoses.⁴ Although proof of this etiology has proven somewhat elusive, a wealth of indirect evidence does suggest this to be the fundamental mechanism for the development of this condition.⁵⁻⁷ The unbalanced exchange of blood between two monochorionic fetuses results in a set of hemodynamic alterations that ultimately place the pregnancy at risk of being lost.^{8,9} The recipient twin develops polyuria and polyhydramnios, and is presumed to be hypertensive. The donor twin develops anuria and oligohydramnios, and is presumed to be hypotensive. Loss of the pregnancy may result either from

preterm delivery or miscarriage or demise of one or both fetuses. Untreated, TTTS results in pregnancy loss rate is of approximately 95%.¹⁰

Significant achievements have been made in both the understanding as well as in the evaluation and treatment of patients with TTTS. Included in those achievements are standardization of the diagnostic criteria, the development of a staging system to assess the severity of the disease, the development of an effective laser surgical technique to eliminate the vascular anastomoses, the scientific demonstration of the superiority of laser therapy over serial amniocentesis and continuous improvements in the actual performance of the laser surgery.

ULTRASOUND ASSESSMENT

Step I: Sonographic Definition of TTTS

TTTS is an entity defined by ultrasound.¹¹ In and of itself, this represents a remarkable milestone in the diagnosis of the disease, nowadays. Prior to establishing ultrasound as the tool to diagnose TTTS, other criteria such as difference in the hemoglobin concentration of each twin or surgical pathology had been used and were ultimately rejected.¹²⁻¹⁵ Within ultrasound, a better understanding of the different sonographic findings was necessary to distinguish essential elements of the condition versus variations in the presentation of the condition.^{16,17} For example, estimated fetal weight discordance between the two fetuses may or may not be present in all cases of TTTS.^{18,19} Similarly, abnormal Doppler findings could also be present in a varying percentage of patients with TTTS.²⁰ Therefore, unification of the ultrasound criteria to define the disease required the designation of unique ultrasound parameters that would define the condition in general, after which, the role of additional sonographic findings could be better established.

The definition of TTTS by ultrasound requires the demonstration of a single placenta, ideally demonstration of same external genitalia, and significant amniotic fluid volume discordance between the two fetuses. A value of a maximum vertical pocket (MVP) of 8 cm or more in the sac of the recipient twin and 2 cm or less in the sac of the donor twin constitute cutoffs that are significantly above and below the 95th and the 5th percentile for MVP in a normal pregnancy.²¹⁻²⁸ While some groups have suggested that the

maximum vertical pocket of 8 cm should be changed to 10 cm above 20 weeks,²⁹ our group has shown that this recommendation results in an underestimation of the incidence of bona fide TTTS of 27%.^{11,30} The diagnosis of monochorionicity requires the sonographic demonstration of a single placenta a thin dividing membrane and the absence of a 'twin peak' sign.^{14,31-35} This diagnosis is made best in the first trimester such that the sensitivity and specificity decrease with advanced gestational age.^{34,35} One aspect of the ultrasound diagnosis of chorionicity that has not been highlighted enough is the hindrance represented by oligohydramnios in the diagnosis of the presence or absence of a twin peak sign. Indeed, the demonstration of a twin peak sign or a T-sign requires the presence of fluid on both sides of the membrane. Patients that present with oligohydramnios or anhydramnios in one sac, by definition, may not have enough fluid on both sides of the membrane to accurately assess these signs. As a corollary, the diagnosis of chorionicity should be made with caution or not at all if the twin peak sign or its absence cannot be definitively established.³⁶⁻³⁹

Although TTTS usually occurs in patients with a monochorionic placenta, the physician should be aware of important variations in this regard. Monochorionic placentas may not necessarily have a single disk, but instead be bilobed.^{40,41} In such cases, the inability to document a twin-peak sign from the presence of oligohydramnios in one sac may be compounded by the apparent presence two placentas. Vascular anastomoses between the two disks are obviously present to allow the development of the syndrome.⁴² Placental vascular anastomoses have been described by us and others in patients with dichorionic monozygotic twins.⁴³ These patients may also develop TTTS as any other monochorionic diamniotic twin pair.^{42,44,45} Monochorionic dizygotic twin pregnancies can also occur, presumably through the fusion of the morula of two dizygotic fetuses during the implantation process.⁴⁶ They too can develop vascular anastomoses and TTTS.⁴⁷ Lastly, placental vascular anastomoses may also occur in dichorionic dizygotic twins.⁴⁸ Such anastomoses were only thought to occur in certain species including bovines, but have now been reported more and more in human pregnancies.⁴⁸ These patients may also develop TTTS. Therefore, while the demonstration of a single placenta and an absent 'twin-peak sign' is characteristic of most TTTS cases, rare variations occur. These variations serve to confirm that placental vascular anastomoses are a sine qua non for the condition to develop.

Similar to the limitations or hindrances in demonstrating the chorionicity, the sonographic demonstration of similar

external genitalia may be difficult with the presence of oligohydramnios in one of the sacs. As mentioned above, fetuses may also be dizygotic and still present with TTTS.⁴⁷ Therefore, although ideally the demonstration of similar external genitalia in the fetuses would aid in establishing the diagnosis, this diagnosis can often not be made.

The ultrasound assessment of the maximum vertical pocket in the sac of the recipient twin requires that the measurement be taken in an area free of fetus or cord. Furthermore, the measurement should be done perpendicular to the skin while the patient is lying in a dorsal position. The assessment of the maximum vertical pocket in the sac of the donor twin may be limited as mentioned above. Furthermore, although most donor twins are tightly apposed to the walls of the uterus, in approximately 15% of cases the donor twin can move freely within the amniotic cavity although it may lack amniotic fluid entirely. This results from folding of the dividing membrane around the body of the fetus and back to the wall of the uterus. On ultrasound, this folding of the membrane appears as a sling with which the fetus is attached to the uterus. If unrecognized, the maximum vertical pocket in the sac of this fetus could be mistakenly assessed as within the sac of the recipient twin. We have called this sonographic sign the 'cocoon sign',⁴⁹ which represents a potential pitfall in the assessment of the amniotic fluid volume in the sac of the donor twin.

Step II: Staging of TTTS

The heterogeneous ultrasound presentation of TTTS had been recognized by numerous investigators.⁵⁰⁻⁵⁹ This included the presence or absence of hydrops, the presence or absence of abnormal arterial or venous Dopplers and varying levels of amniotic fluid volume discordance. An important step in the understanding of the ultrasound presentation of TTTS came with the realization that the disease could present with various degrees of severity as opposed to with different risk factors. This led to the original development of the Quintero staging system.¹¹ The Quintero staging system was based on the empiric observation of the different sonographic presentations of the disease in the absence of modifications introduced by treatment. Thus, the Quintero staging system was based on an unbiased sonographic description of the presentation and natural history of the disease.

For the purposes of the staging system, categorical variables were identified and preferably used. This avoided resorting to nomograms that could hinder the practical nature of the staging system. The staging system was also based on the natural assumption that the different sonographic presentations would represent different degrees of severity.

Thus, demise was a worse presentation than hydrops, which was a worse presentation than abnormal Dopplers, which was a worse presentation than lack of visualization of the bladder of the donor, which was worse than visualization of the bladder of the donor. Thus, stage I was defined as visualization of the bladder of the donor twin. Stage II was lack of visualization of the bladder of the donor twin in at least 60 minutes of continuous ultrasound examination. Stage III was defined as the presence of critically abnormal Dopplers including absent or reverse end-diastolic velocity in the umbilical artery, reverse flow in the ductus venosus, or pulsatile umbilical venous flow. Stage IV was defined as hydrops. Stage V was defined as demise of one or both fetuses. Stage III and IV patients could present with a visible bladder or a nonvisible bladder of the donor. In the classic presentation, the bladder of the donor twin would not be visible. In the 'atypical' presentation of stage III or stage IV, the bladder of the donor twin is visible.¹¹ Although some authors have suggested modifying the Quintero staging system to include the presence or absence of superficial anastomoses,⁶⁰ or different echocardiographic findings,⁶¹⁻⁶³ there is no evidence to suggest that it would need to be modified or changed.⁶⁴ That is not to say that echocardiographic information may not be useful, particularly as it pertains to preoperative and postoperative assessment, since the Quintero staging system pertains only to the preoperative evaluation. Therefore, the Quintero staging system continues to be practical, reproducible and used universally in the preoperative assessment and management of TTTS.

Step III: Cervical Assessment by Ultrasound

In general, a short cervical length, as assessed by ultrasound, has been associated with an increased risk for pregnancy loss and premature delivery.⁶⁵⁻⁶⁹ A short cervix has also been identified as a risk factor for preterm labor and miscarriage in twins⁷⁰ and in patients with TTTS.⁷¹ Therefore, ultrasound assessment of the cervical length is a fundamental step in the evaluation of patients with TTTS. In our laboratory, assessment of the cervical length is in fact the first step in the evaluation of patients with TTTS. Assessment of the cervical length is best performed using a transvaginal ultrasound, particularly since transabdominal assessment of the cervical length has been shown to miss a significant proportion of patients with a short cervix.⁷² Prior to performing the transvaginal ultrasound assessment, the sonographer or physician must first assess whether the patient has complained of leakage of fluid which could represent premature rupture of membranes. If a question exists as to whether the membranes are intact or not, the exam is then performed via a transperineal approach.⁷³

Approximately 6 to 7% of patients with TTTS will present with a short cervix.⁷⁴ Although a cervical cerclage has not been conclusively shown to benefit patients with a short cervix in singleton pregnancies and may even be considered detrimental in twin gestations,^{75,76} our group and others have shown that the outcome of patients with a short cervix treated with a cervical cerclage is similar to that of patients with a cervix of normal length.⁷⁷ Thus, patients that present with a cervical length of 2.5 cm or less at our laboratory are offered a cervical cerclage. The timing of the placement of the cerclage may vary. The cerclage may be performed at the time of the laser surgery, or the day after the surgery.⁷⁸ Occasionally, ultrasound may show a separation of the amniotic membrane from the periphery of the uterus at the level of the lower uterine segment. This sonographic finding has been dubbed 'moon sign'.⁷⁹ It is unclear why such sign would developed in patients with polyhydramnios. Presumably, the increase in size of the uterine walls may outdo the stretching capability of the amniotic membrane. The presence of a moon sign may or may not represent an increase risk for gross rupture of the membranes or miscarriage after laser therapy.^{78,79}

Step IV: Ultrasound Mapping

The previous three steps in the ultrasound assessment of patients with TTTS can be performed in centers that do not necessarily offer surgery. If the patient is to be assessed at a surgical center, the next step in the evaluation consists of preoperative mapping. The goal of preoperative ultrasound mapping is to predict the location of the anastomoses as well as the location of the dividing membrane to decide the surgical approach. First the location an extension of the placenta is noted. For example, it is important to know to which degree the placenta extends inferiorly or superiorly. Similarly, it is important to determine how much it extends to each of the lateral walls. Second, the location of the insertion of the umbilical cords is also noted using color Doppler.⁸⁰ Naturally, the anastomoses are expected to be present between the two umbilical cords. Although a critical short distance between the two umbilical cords⁸¹ may seem like an obvious impediment for the performance of the laser therapy,⁸² an actual value for this measurement has not been established. Notwithstanding, the further apart the umbilical cords are, the less likely they are to have either numerous or significantly large anastomoses. The actual location of the umbilical cords may also herald the degree of difficulty that may be encountered during surgery. For example, if a velamentous insertion is identified, the operator must be careful not to use this area for the insertion of the trocar, as it may result in unintentional injury to velamentous vessels

with resulting exsanguination and demise of one or both fetuses. Ultrasound documentation of the location of the umbilical cords is best done by using the icons provided by the ultrasound software. Third, the position of the donor twin may also aid and the prediction of the location of the vascular anastomoses. Indeed, most donor twins are apposed to the walls of the uterus. As such, the dividing membrane follows the location of the donor twin in most cases. For example, if the donor twin is lying longitudinally, one can anticipate that the vascular anastomoses will run transversely. Conversely, if the donor twin is lying transversely, one can anticipate that the vascular anastomoses will run in an up and down direction. The position of the donor twin relative to the placental mass is also important to note. Ideally, the donor twin is outside of the placental mass so that the anastomoses are not obscured by its presence. Alternatively, if the donor twin is lying over the placental mass, this may hinder significantly the identification of the vascular anastomoses, particularly if the degree of anhydramnios is such that displacement of the donor twin during surgery is minimal or impossible. Lastly, the position of the donor twin relative to the placenta-free area in patients with an anterior placenta is also important to note. In most cases, the placenta-free area is on the side of the recipient twin. However, if the donor twin is lying beneath the placenta-free area of the uterus this may increase the likelihood of unintentional disruption of the dividing membrane during trocar entry. The location of the donor twin in the placenta free area and the corresponding unintentional septostomy during trocar entry occurs in approximately 15% of patients. At the end of the ultrasound mapping, it is recommended to depict these findings graphically on the patient's abdomen by the use of a marker. The location of the umbilical cords is noted with a circle containing the letters 'D' and 'R.' The position of the donor twin is also drawn on the patient's abdomen. Lastly, the anticipated entry site for the surgery is marked with an 'X'.

LASER TREATMENT OF TTTS

Nonselective Technique

The treatment of TTTS has evolved through the years and has included expectant-medical management⁸³ to *sectio parva*,⁸⁴ to serial amniocentesis,⁸⁵⁻⁸⁷ to the current treatment using laser photocoagulation of the placental vascular anastomoses.⁸⁸⁻⁹³ The rationale for the use of laser photocoagulation in TTTS stems from the fact that (a) TTTS does not occur in dichorionic twins, where there are no placental vascular anastomoses (see exceptions above of cases of dichorionic twins with vascular anastomoses); (b) TTTS occurs via placental vascular anastomoses; (c) TTTS should disappear if the anastomoses are ablated.

The use of laser energy to obliterate the placental vascular anastomoses was first proposed in 1990.⁸⁸ Unfortunately, the original reports did not describe how to identify the vessels that were responsible for blood exchange between the fetuses. The next approach described by Yves Ville et al, consisted in the identification and obliteration of vessels that would cross the dividing membrane.⁹¹ Although this technique was nonselective, i.e. it did not differentiate anastomotic vs nonanastomotic placental vessels crossing the dividing membrane, it was a significant improvement over the previous approach. The nonselective approach relies on the assumption that the dividing membrane would lie parallel to the so-called vascular equator. The fact is, however, that actual location of the dividing membrane may bear very little relationship with the vascular equator. Therefore, a better way of identifying the actual anastomoses was needed.

The Selective Technique

In 1998, Quintero et al described the selective laser photocoagulation of communicating vessels (SLPCV) technique.⁹² This technique required a systematic assessment of the vascular equator to identify placental vascular anastomoses and differentiate them from nonanastomotic vessels. The technique also assumed that, once identified, the anastomoses could be photocoagulated (a two-step process). This technique was dubbed 'SLPCV'. Clinical studies demonstrated that the use of a nonselective technique would unnecessarily target vessels that were not involved in blood exchange between the fetuses.⁹⁴ Targeting nonanastomotic vessels could result in the loss of significant placental territory for one or both fetuses, with the associated increased risk for demise of one or both twins.⁹¹ By definition, performance of the SLPCV technique requires an adequate and precise identification of the vascular anastomoses followed by their laser obliteration. A gap between theory and practice may develop if these steps cannot be followed due to training or technological limitations. In our laboratory, we had been able to perform the SLPCV in approximately 98% of the cases in which we have attempted the surgery.⁷⁴ In the remaining 2%, the anastomoses cannot be traced entirely to their site of origin. In those cases, the vessels are lasered as close to their terminal end as possible, even though the actual final location of the anastomosis cannot be seen.

The acronym used for the selective technique, i.e. SLPCV defines the systematic approach that needs to take place to identify and photocoagulate all of the vascular anastomoses. Other acronyms used to describe the performance of the laser surgery may or may not be similar

to the SLPCV technique. For example, while performing SLPCV, the dividing membrane is always respected. Purposeful injury to the dividing membrane, or so-called 'septostomy', is not part of the SLPCV technique.⁹⁵ Though not implicit, the performance of a laparotomy to access the amniotic cavity is also not part of the SLPCV technique. While general anesthesia was originally used in our cases,⁹⁶ surgery can be best performed under local anesthesia.⁹⁷ Therefore, the acronym SLPCV, should apply only to those surgeries in which access to the amniotic cavity is performed under local anesthesia, percutaneously and following a systematic and thorough identification and obliteration of the placental vascular anastomoses.^{18,92,98}

Joining the Dots: The 'Solomon' Technique

The incidence of patent vascular anastomoses on surgical pathology analysis of the placentas, as well as the incidence of failed surgery with resulting persistent or reverse TTTS has varied significantly between centers. In a study by Robyr et al, the incidence of failure to obliterate all vessels in failed surgery was 22%.⁹⁹ Resulting fetal anemia from any of these complications was also 22%. Anemia after demise of one of the fetuses was also noted as a complication. Lopriore et al reported an incidence of 33% of residual patent placental vascular anastomoses in 52 TTTS patients treated with laser at their institution.¹⁰⁰ In comparison, our groups have consistently shown an incidence of patent anastomoses of approximately 1.8 to 4%, and an incidence of suspected fetal anemia of only 2.7% as surmised by an elevated middle cerebral artery peak systolic velocity, and no anemia after demise of the cotwin.⁷⁴ The reason behind such discrepant results may lie in the rate of performance of the SLPCV technique. Indeed, in an article by Stirnemann, the researchers reported performing the SLPCV technique in only 34% of the patients, and suggest that most surgeries involve lasering both anastomotic and nonanastomotic vessels.^{29,101} Of note, the proposed 'selectivity index', a log ratio of anastomotic vs nonanastomotic lasered vessels, is mathematically inaccurate and should not be used to assess the adequacy of the laser surgery.¹⁰² To compensate for the high rate of failed surgeries, some groups proposed 'joining the dots' between photocoagulated areas on the surface of the placenta.²⁹ This is based on the assumption that placental anastomoses could still exist between identified vascular anastomoses that would somehow escape endoscopic detection.¹⁰³ This surgical technique has been dubbed 'the Solomon technique',²⁹ in reference to the biblical passage where, in order to resolve a dispute between two alleging mothers of a child, King Solomon proposed to cut the baby in half (1 Kings 3:16-28, NIV). The analogy, therefore, is

that by lasering the areas of the placenta between endoscopically-identified and lasered vascular anastomoses, the placenta would be 'cut in half.' Recent studies suggest that indeed, relative to the author's prior experience with selective laser surgery, the use of the Solomon technique may be associated with improved perinatal outcomes.^{104,105} Interestingly, the perinatal outcomes reported in these studies using a 'selective technique' are not as favorable as those reported by us with the use of SLPCV.¹⁰⁶ For example, in the study by Ruano et al, the incidence of failed surgery, [defined as recurrent TTTS or twin-anemia-polycythemia syndrome (TAPS)] was 13% (10/76), compared to 3.5% (2/56) with the Solomon technique or compared to 1.5% (3/193) in patients treated by us with a selective or a sequential-selective technique ($p = 0.02$ and 0.000 , respectively).¹⁰⁶ Similarly, in the article by Baschat et al, the incidence of failed surgery, defined as recurrent TTTS or TAPS was 21% (15/71) in the 'selective laser' group, with an 8.5% (6/71) rate of recurrent TTTS. This is also statistically higher than our 1.5% incidence as described above ($p = 0.01$).¹⁰⁶ Therefore, the apparent improved perinatal outcomes from the use of the 'Solomon technique' may simply represent a step forward in the learning curve in the performance of the SLPCV technique, rather than a true advantage over the SLPCV technique. On the other hand, it is conceivable that lasering innocent placental areas between anastomotic vessels could result in unnecessary complications, such as accidental lasering of nonanastomotic vessels. A randomized clinical trial is being conducted in Europe comparing SLPCV with the Solomon technique (www.trialregister.nl, trial ID: NTR1245). For now, as in the biblical passage, it may not be all that wise to suggest 'cutting the placenta in half'. Instead, what is required, is that the surgeon be able to adequately identify and ablate the placental vascular anastomoses in the placenta. This amounts perhaps to better training and better technology.

Sequential SLPCV: The Sequential Technique

The development of the selective technique represented an important step in the surgical treatment of TTTS. SLPCV is indeed an anatomical surgical technique, which identifies and obliterates only the placental vascular anastomoses. Intrauterine fetal demise of one of the two fetuses however, would occur in approximately 9 to 29% of cases.^{92,94} Because TTTS presumably occurs from an excessive transfer of blood from the donor twin to the recipient twin, the sequence with which the anastomoses are obliterated during surgery could have prognostic implications. Indeed, if the anastomoses from the donor to the recipient are obliterated first, that would stop immediately the transfer

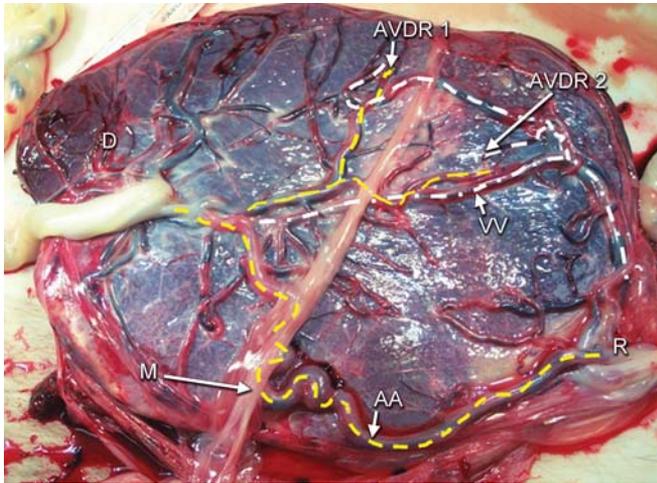


Fig. 1: Assessment of the vascular anastomoses in an untreated monochorionic–diamniotic placenta in a case of TTTS. An arteriovenous anastomosis from donor-to-recipient (AVDR1) can be seen superiorly. Note that this anastomosis is within the sac of the donor twin. A second arteriovenous anastomosis from donor to recipient (AVDR2) is seen below. Additionally, a large vein-to-vein (VV) and very large artery-to-artery (AA) anastomoses are also present. Several other vessels cross the dividing membrane (M) from the donor sac into the recipient’s sac, but do not represent vascular anastomoses (nonanastomotic vessels). Yellow dashed line: artery; White dashed line: vein; D: donor; R: recipient

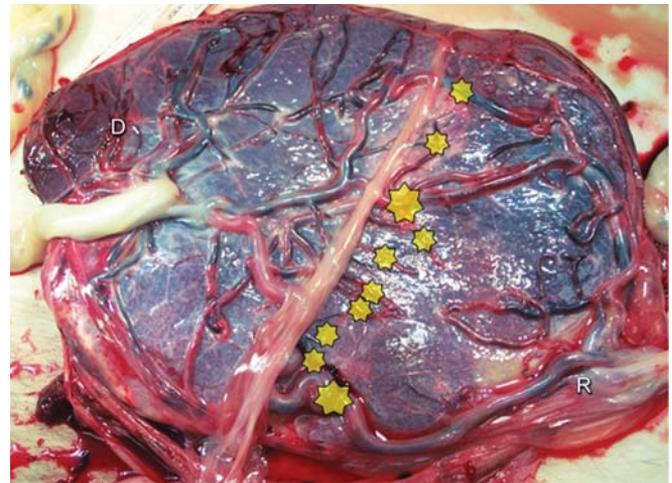


Fig. 2: Non-SLPCV. This surgical technique would target all vessels crossing the dividing membrane, regardless of their anastomotic or nonanastomotic nature. Using as an example the same placenta as in Figure 1, a total of approximately 10 laser shots would be necessary to ablate all of the vessels crossing the dividing membrane. D: donor; R: recipient

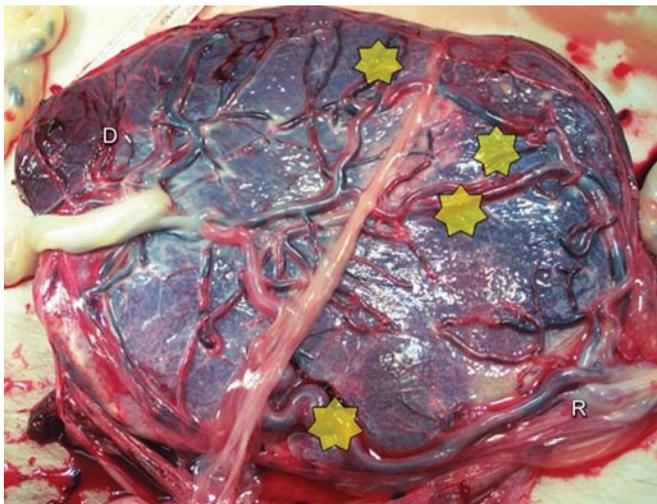


Fig. 3: SLPCV: using this technique, the anastomotic vessels are targeted, while preserving nonanastomotic vessels. Only 4 laser shots are required to entirely separate the circulation between the two fetuses. The rest of the vessels crossing the dividing membrane belong to the territory of the donor twin. Of interest, the donor twin in this case would end up with more placental territory than the recipient twin (as it occurs in 33% of cases in our series). D: donor; R: recipient

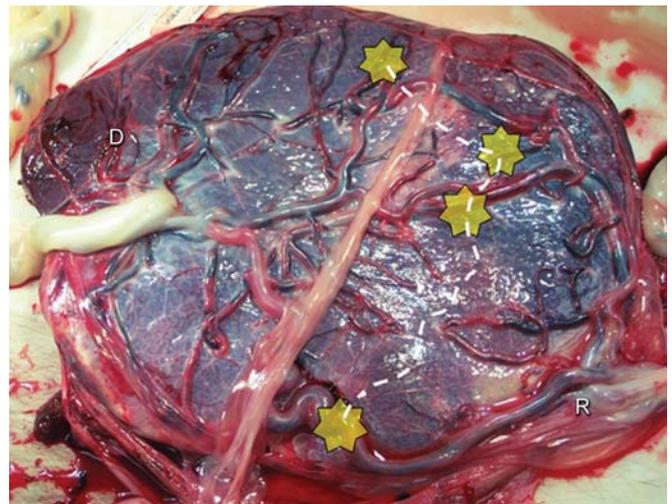


Fig. 4: Solomon technique: the laser shots have been joined by lasering areas of the placenta (dashed white line) presumably containing anastomoses that cannot be identified endoscopically. The potential for injuring nonanastomotic vessels in that irregularly curved path is apparent. If all anastomoses are correctly identified during the selective technique, the Solomon technique should not reduce the rate of patent vascular anastomoses or failed surgery, but instead could increase the risk for complications similar to the nonselective technique. D: donor; R: recipient

of blood from this twin to the recipient. Furthermore, during this interval, however brief, the recipient twin would be transfusing the donor twin back. As a result, the donor twin, which is presumably hypotensive, would stop losing blood as soon as the laser process starts while at the same time would start receiving additional blood back from the recipient twin. The photocoagulation of the vascular

anastomoses from-donor-to-recipient first, followed by from-recipient-to-donor second was called the ‘sequential technique’ or SQLPCV. Using a sequential technique, our group showed a reduction in the rate of intrauterine fetal demise of the donor twin from 21 to 7%, and an increase in the double survival rate from 56 to 75%.¹⁰⁶ Our group is currently assessing the merits of the SQLPCV technique

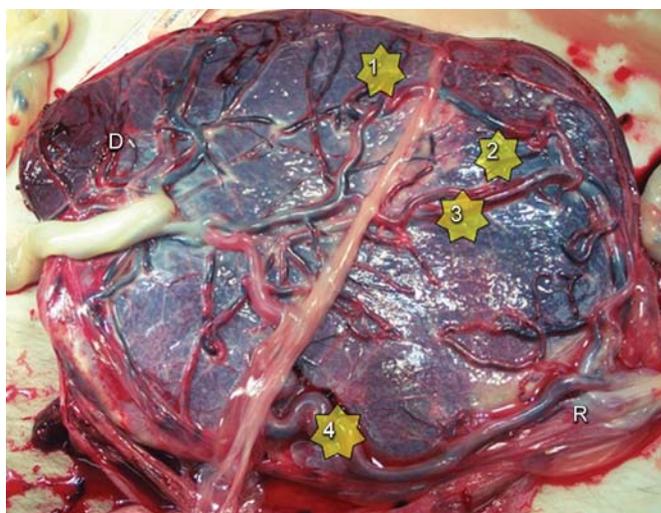


Fig. 5: Sequential SLPCV. In this technique, the vascular anastomoses are lasered in sequence: AVDRs (arteriovenous anastomoses from donor to recipient) first (shots 1 and 2), followed by AVDRs (arteriovenous anastomoses from recipient to donor). If superficial anastomoses are also present (20% of all TTTS cases), it is unclear whether they should be lasered before or after the AV anastomoses.^{106,108} The sequence of shots in this case ablates the two AVDRs (shots 1 and 2) first, followed by the VV and AA anastomoses (shots 3 and 4, respectively). In this particular placenta, there are no arteriovenous anastomoses from recipient to donor (AVDRs). D: donor; R: recipient

through a randomized clinical trial of the USFetus group. While a sequential technique may not necessarily be required in all cases, it could have an indication in patients where the condition of the donor twin would be most compromised. Figures 1 to 5 show how the different laser techniques discussed above would be performed, using as a theoretical example a nontreated monochorionic–diamniotic placenta of a patient with TTTS.

Umbilical Cord Occlusion

Interruption of the blood exchange between the fetuses can also be accomplished by occluding one of the two umbilical cords. This procedure should be contemplated only as a last resort to treat the syndrome. Unfortunately, the availability of bipolar photocoagulation and radiofrequency ablation has resulted in an unwarranted number of selective feticide in patients that otherwise could have perhaps been treated best with laser surgery.^{29,107} Umbilical cord occlusion should not be offered as an alternative to laser because of limitations of the surgeon or the center, unless the patient cannot be referred to another center capable of offering laser. Umbilical cord occlusion should be offered to patients with TTTS in which additional complicating circumstances may exist. This may be the case in patients with a severe congenital anomaly of one of the twins, or a moribund hypoxic fetus. Since such cases are rare, the

performance of selective feticide the umbilical cord occlusion in TTTS should be an exception, rather than the rule. In our laboratory, while we offer umbilical cord occlusion to all stage III and IV patients as a management option, other than in the above examples, such option is never chosen. Indeed, the counseling to our patient involves mentioning a survival rate of approximately 90% with a 5% risk of neurological damage if laser therapy is chosen, compared to 90% survival and a 5% risk of neurological damage to the surviving cotwin if umbilical cord occlusion is chosen. Therefore, since both survival and morbidity statistics are similar between the two procedures, but with umbilical cord occlusion one of the fetuses is denied the chance to survive, the justification isn't there to offer feticide to an otherwise anatomically normal fetus.

CONCLUSION

The ultrasound diagnosis, management and treatment of TTTS have had a remarkable number of positive developments in the last 20 years. By far, TTTS is indeed the most common condition seen in fetal therapy centers worldwide. Although most centers agree on the sonographic definition, debate still exists as to whether the cutoff of the maximum vertical pocket of the recipient twin should be 8 or 10 after 20 weeks. Our data has shown that using a cutoff of 10 cm after 20 weeks would disqualify at least 25% of stage III to IV TTTS patients. Despite the remarkable progress in therapy, significant differences in perinatal outcomes between treating centers remain. It is clear that the condition can be effectively treated by ablating all vascular anastomoses between the fetuses. Differences of opinion exist as to whether all such anastomoses can be identified endoscopically or not. Furthermore, once identified, differences in the ability to effectively obliterate such anastomoses have also been reported. Our data suggests that proper identification and photocoagulation of all vascular anastomoses is possible in upwards of 98.5% of cases using the SLPCV technique. Therefore, it would not seem warranted to suggest the existence of hidden parenchymal anastomoses to explain incomplete identification of the anastomoses, or lasering of uninvolved placental areas to avoid failed surgeries. Our group is interested in establishing the scientific merit of the sequential technique, and its use in the different surgical scenarios. Results of this study should clarify the role of performing both an anatomical and a functional surgical ablation of the placental vascular anastomoses. Further follow-up data should shed even further light on long-term outcomes.

REFERENCES

1. Lutfi S, Allen VM, Fahey J, O'Connell CM, Vincer MJ. Twin-twin transfusion syndrome: A population-based study. *Obstet Gynecol* 2004 Dec;104(6):1289-1297.
2. Wenstrom KD, Gall SA. Incidence, morbidity and mortality, and diagnosis of twin gestations. *Clin Perinatol* 1988 Mar;15(1):1-11.
3. Mathews TJ, MacDorman MF. Infant mortality statistics from the 2007 period linked birth/infant death data set. National vital statistics reports: from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System. 2011 Jun 29;59(6):1-30.
4. Quintero R, Quintero L, Pivatelli A, Bornick P, Allen M, Johnson P. The donor-recipient (D-R) score: in vivo endoscopic evidence to support the hypothesis of a net transfer of blood from donor to recipient in twin-twin transfusion syndrome. *Prenat Neonat Med* 2000;5:84-91.
5. Ishii K, Chmait RH, Martinez JM, Nakata M, Quintero RA. Ultrasound assessment of venous blood flow before and after laser therapy: approach to understanding the pathophysiology of twin-twin transfusion syndrome. *Ultrasound Obstet Gynecol* 2004 Aug;24(2):164-168.
6. van Gemert MJ, Scherjon SA, Major AL, Borst C. Twin-twin transfusion syndrome. Three possible pathophysiologic mechanisms. *J Reprod Med* 1997 Nov;42(11):708-714.
7. Wieacker P, Wilhelm C, Prompeler H, Petersen KG, Schillinger H, Breckwoldt M. Pathophysiology of polyhydramnios in twin transfusion syndrome. *Fetal Diagn Ther* 1992;7(2):87-92.
8. Mahieu-Caputo D, Dommergues M, Delezoide AL, Lacoste M, Cai Y, Narcy F, Jolly D, Gonzales M, Dumez Y, Gubler MC. Twin-to-twin transfusion syndrome. Role of the fetal renin-angiotensin system. *Am J Pathol* 2000 Feb;156(2):629-636.
9. Mahieu-Caputo D, Meulemans A, Martinovic J, Gubler MC, Delezoide AL, Muller F, Madelenat P, Fisk NM, Dommergues M. Paradoxical activation of the renin-angiotensin system in twin-twin transfusion syndrome: an explanation for cardiovascular disturbances in the recipient. *Pediatr Res* 2005 Oct;58(4):685-688.
10. Kontopoulos EV, Quintero RA. Treatment of twin-twin transfusion syndrome: an evidence-based analysis. In: Quintero RA, editor. *Twin-twin transfusion syndrome*. London: Informa; 2007. p 127-137.
11. Quintero RA, Morales WJ, Allen MH, Bornick PW, Johnson PK, Kruger M. Staging of twin-twin transfusion syndrome. *J Perinatol* 1999 Dec;19(8 Pt 1):550-555.
12. Danskin FH, Neilson JP. Twin-to-twin transfusion syndrome: what are appropriate diagnostic criteria? *Am J Obstet Gynecol* 1989 Aug;161(2):365-369.
13. Berry SM, Puder KS, Bottoms SF, Uckele JE, Romero R, Cotton DB. Comparison of intrauterine hematologic and biochemical values between twin pairs with and without stuck twin syndrome. *Am J Obstet Gynecol* 1995 May;172(5):1403-1410.
14. Saunders N, Snijders R, Nicolaides K. Twin-twin transfusion syndrome during the 2nd trimester is associated with small intertwin hemoglobin differences. *Fetal Diagn Ther* 1991;6(1-2):34-36.
15. Fisk NM, Borrell A, Hubinont C, Tannirandorn Y, Nicolini U, Rodeck CH. Fetofetal transfusion syndrome: do the neonatal criteria apply in utero? *Arch Dis Child* 1990 Jul;65(7 Spec No):657-661.
16. Blickstein I. The twin-twin transfusion syndrome. *Obstet Gynecol* 1990;76(4):714-722.
17. Mari G, Roberts A, Detti L, Kovanci E, Stefos T, Bahado-Singh RO, Deter RL, Fisk NM. Perinatal morbidity and mortality rates in severe twin-twin transfusion syndrome: results of the International Amnioreduction Registry. *Am J Obstet Gynecol* 2001 Sep;185(3):708-715.
18. Chmait RH, Kontopoulos EV, Korst LM, Llanes A, Petisco I, Quintero RA. Stage-based outcomes of 682 consecutive cases of twin-twin transfusion syndrome treated with laser surgery: the USFetus experience. *Am J Obstet Gynecol* 2011 May;204(5):393 e1-6.
19. Chmait RH, Korst LM, Bornick PW, Allen MH, Quintero RA. Fetal growth after laser therapy for twin-twin transfusion syndrome. *Am J Obstet Gynecol* 2008 Jul;199(1):47 e1-6.
20. Rizzo G, Arduini D, Romanin C. Uterine artery doppler velocity waveforms in twin pregnancies. *Obstet Gynecol* 1993 Dec;82(6):978-983.
21. Magann EF, Bass JD, Chauhan SP, Young RA, Whitworth NS, Morrison JC. Amniotic fluid volume in normal singleton pregnancies. *Obstet Gynecol* 1997 Oct;90(4 Pt 1):524-528.
22. Magann EF, Chauhan SP, Barrilleaux PS, Whitworth NS, Martin JN. Amniotic fluid index and single deepest pocket: weak indicators of abnormal amniotic volumes. *Obstet Gynecol* 2000 Nov;96(5 Pt 1):737-740.
23. Magann EF, Chauhan SP, Bofill JA, Martin JN Jr. Comparability of the amniotic fluid index and single deepest pocket measurements in clinical practice. *Aust N Z J Obstet Gynaecol* 2003 Feb;43(1):75-77.
24. Magann EF, Chauhan SP, Martin JN Jr, Whitworth NS, Morrison JC. Ultrasonic assessment of the amniotic fluid volume in diamniotic twins. *J Soc Gynecol Investig* 1995 Jul-Aug;2(4):609-613.
25. Magann EF, Chauhan SP, Whitworth NS, Anfanger P, Rinehart BK, Morrison JC. Determination of amniotic fluid volume in twin pregnancies: ultrasonographic evaluation versus operator estimation. *Am J Obstet Gynecol* 2000 Jun;182(6):1606-1609.
26. Magann EF, Doherty DA, Chauhan SP, Busch FW, Mecacci F, Morrison JC. How well do the amniotic fluid index and single deepest pocket indices (below the 3rd and 5th and above the 95th and 97th percentiles) predict oligohydramnios and hydramnios? *Am J Obstet Gynecol* 2004 Jan;190(1):164-169.
27. Magann EF, Martin JN Jr. Amniotic fluid volume assessment in singleton and twin pregnancies. *Obstet Gynecol Clin North Am* 1999 Dec;26(4):579-593.
28. Magann EF, Whitworth NS, Bass JD, Chauhan SP, Martin JN Jr, Morrison JC. Amniotic fluid volume of third-trimester diamniotic twin pregnancies. *Obstet Gynecol* 1995 Jun;85(6):957-960.
29. Chalouhi GE, Essaoui M, Stirnemann J, Quibel T, Deloison B, Salomon L, Ville Y. Laser therapy for twin-to-twin transfusion syndrome (TTTS). *Prenat Diagn* 2011 Jul;31(7):637-646.
30. Quintero RA. Twin-twin transfusion syndrome. *Clin Perinatol* 2003 Sep;30(3):591-600.
31. Quintero R, Morales W, Allen M, Bornick P, Johnson P, Krueger M. Staging of twin-twin transfusion syndrome. *Journal of perinatology: official journal of the California Perinatal Association* 1999;19:550-555.
32. Monteagudo A, Timor-Tritsch IE, Sharma S. Early and simple determination of chorionic and amniotic type in multifetal gestations in the first fourteen weeks by high-frequency transvaginal ultrasonography. *Am J Obstet Gynecol* 1994 Mar;170(3):824-829.

33. Monteagudo A, Timor-Tritsch IE. Second- and third-trimester ultrasound evaluation of chorionicity and amnionicity in twin pregnancy. A simple algorithm. *J Reprod Med* 2000 Jun; 45(6):476-480.
34. Sepulveda W, Sebire NJ, Hughes K, Kalogeropoulos A, Nicolaides KH. Evolution of the lambda or twin-chorionic peak sign in dichorionic twin pregnancies. *Obstet Gynecol* 1997 Mar;89(3):439-441.
35. Sepulveda W, Sebire NJ, Hughes K, Odibo A, Nicolaides KH. The lambda sign at 10-14 weeks of gestation as a predictor of chorionicity in twin pregnancies. *Ultrasound Obstet Gynecol* 1996 Jun;7(6):421-423.
36. Bajoria R, Kingdom J. The case for routine determination of chorionicity and zygosity in multiple pregnancy. *Prenat Diagn* 1997 Dec;17(13):1207-1225.
37. Finberg HJ. The 'twin peak' sign: reliable evidence of dichorionic twinning. *J Ultrasound Med* 1992 Nov;11(11): 571-577.
38. Rode ME, Jackson M. Sonographic considerations with multiple gestation. *Semin Roentgenol* 1999 Jan;34(1):29-34.
39. Wood SL, St Onge R, Connors G, Elliot PD. Evaluation of the twin peak or lambda sign in determining chorionicity in multiple pregnancy. *Obstet Gynecol* 1996 Jul;88(1):6-9.
40. Benirschke K, Masliah E. The placenta in multiple pregnancy: outstanding issues. *Reprod Fertil Dev* 2001;13(7-8):615-622.
41. Machin G. Placentation in multiple births. *Twin Res* 2001 Jun;4(3):150-155.
42. Lopriore E, Sueters M, Middeldorp JM, Klumper F, Oepkes D, Vandebussche FP. Twin pregnancies with two separate placental masses can still be monochorionic and have vascular anastomoses. *Am J Obstet Gynecol* 2006 Mar;194(3):804-808.
43. Foschini MP, Gabrielli L, Dorji T, Kos M, Lazzarotto T, Lanari M, Landini MP. Vascular anastomoses in dichorionic diamniotic-fused placentas. *Int J Gynecol Pathol* 2003 Oct;22(4):359-361.
44. Lage JM, Vanmarter LJ, Mikhail E. Vascular anastomoses in fused, dichorionic twin placentas resulting in twin transfusion syndrome. *Placenta* 1989 Jan-Feb;10(1):55-59.
45. Quintero R, Kontopoulos EV, Barness E, Steffensen TS, Hilbelink D, Chmait R, Benirschke K, Bornick PW. Twin-twin transfusion syndrome in a dichorionic-monozygotic twin pregnancy: the end of a paradigm? *Fetal Pediatr Pathol* 2010 Jan;29(2):81-88.
46. Ekelund CK, Skibsted L, Sogaard K, Main KM, Dziegiel MH, Schwartz M, Moeller N, Roos L, Tabor A. Dizygotic monochorionic twin pregnancy conceived following intracytoplasmic sperm injection treatment and complicated by twin-twin transfusion syndrome and blood chimerism. *Ultrasound Obstet Gynecol* 2008 Nov;32(6):832-834.
47. Quintero RA, Mueller OT, Martinez JM, Arroyo J, Gilbert-Barness E, Hilbelink D, Papenhausen P, Sutcliffe M. Twin-twin transfusion syndrome in a dizygotic monochorionic-diamniotic twin pregnancy. *J Matern Fetal Neonatal Med* 2003 Oct; 14(4):279-281.
48. Biran V, Bornes M, Aboura A, Masmoudi S, Drunat S, Baumann C, Osimani S, Dalle JH, Sterkers G, Verloes A, et al. A long-term competent chimeric immune system in a dizygotic dichorionic twin. *Pediatrics* 2011 Aug;128(2):e458-463.
49. Quintero RA, Chmait RH. The cocoon sign: a potential sonographic pitfall in the diagnosis of twin-twin transfusion syndrome. *Ultrasound Obstet Gynecol* 2004 Jan;23(1):38-41.
50. Yamada A, Kasugai M, Ohno Y, Ishizuka T, Mizutani S, Tomoda Y. Antenatal diagnosis of twin-twin transfusion syndrome by Doppler ultrasound. *Obstet Gynecol* 1991 Dec;78(6):1058-1061.
51. Bromley B, Frigoletto FD Jr, Estroff JA, Benacerraf BR. The natural history of oligohydramnios/polyhydramnios sequence in monochorionic diamniotic twins. *Ultrasound Obstet Gynecol* 1992 Sep 1;2(5):317-320.
52. Ishimatsu J, Yoshimura O, Manabe A, Matsuzaki T, Tanabe R, Hamada T. Ultrasonography and Doppler studies in twin-to-twin transfusion syndrome. *Asia Oceania J Obstet Gynaecol* 1992 Dec;18(4):325-331.
53. Pretorius DH, Budorick NE, Scioscia AL, Krabbe JK, Ko S, Myhre CM. Twin pregnancies in the second trimester in women in an alpha-fetoprotein screening program: sonographic evaluation and outcome. *AJR Am J Roentgenol* 1993 Nov;161(5):1007-1013.
54. Reisner DP, Mahony BS, Petty CN, Nyberg DA, Porter TF, Zingheim RW, Williams MA, Luthy DA. Stuck twin syndrome: outcome in thirty-seven consecutive cases. *Am J Obstet Gynecol* 1993 Oct;169(4):991-995.
55. Ohno Y, Ando H, Tanamura A, Kurauchi O, Mizutani S, Tomoda Y. The value of Doppler ultrasound in the diagnosis and management of twin-to-twin transfusion syndrome. *Arch Gynecol Obstet* 1994;255(1):37-42.
56. Weiner CP, Ludomirski A. Diagnosis, pathophysiology, and treatment of chronic twin-to-twin transfusion syndrome. *Fetal Diagn Ther* 1994 Sep-Oct;9(5):283-290.
57. Lachapelle MF, Leduc L, Cote JM, Grignon A, Fournon JC. Potential value of fetal echocardiography in the differential diagnosis of twin pregnancy with presence of polyhydramnios-oligohydramnios syndrome. *Am J Obstet Gynecol* 1997; 177(2):388-394.
58. Lees CC, Schwarzler P, Ville Y, Campbell S. Stuck twin syndrome without signs of twin-to-twin transfusion. *Ultrasound Obstet Gynecol* 1998 Sep;12(3):211-214.
59. Mari G, Detti L, Levi-D'Ancona R, Kern L. "Pseudo" twin-to-twin transfusion syndrome and fetal outcome. *J Perinatol* 1998 Sep-Oct;18(5):399-403.
60. Taylor MJ, Govender L, Jolly M, Wee L, Fisk NM. Validation of the Quintero staging system for twin-twin transfusion syndrome. *Obstet Gynecol* 2002 Dec;100(6):1257-1265.
61. Michelfelder E, Gottliebson W, Border W, Kinsel M, Polzin W, Livingston J, Khoury P, Crombleholme T. Early manifestations and spectrum of recipient twin cardiomyopathy in twin-twin transfusion syndrome: relation to Quintero stage. *Ultrasound Obstet Gynecol* 2007 Dec;30(7):965-971.
62. Rychik J, Tian Z, Bebbington M, Xu F, McCann M, Mann S, Wilson RD, Johnson MP. The twin-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease. *Am J Obstet Gynecol* 2007 Oct;197(4):392 e1-8.
63. Stirnemann JJ, Mougeot M, Proulx F, Nasr B, Essaoui M, Fournon JC, Ville Y. Profiling fetal cardiac function in twin-twin transfusion syndrome. *Ultrasound Obstet Gynecol* 2010 Jan;35(1):19-27.
64. Stamilio DM, Fraser WD, Moore TR. Twin-twin transfusion syndrome: an ethics-based and evidence-based argument for clinical research. *Am J Obstet Gynecol* 2010 Jul;203(1):3-16.
65. Cook CM, Ellwood DA. The cervix as a predictor of preterm delivery in 'at-risk' women. *Ultrasound Obstet Gynecol* 2000 Feb;15(2):109-113.

66. Owen J. Evaluation of the cervix by ultrasound for the prediction of preterm birth. *Clin Perinatol* 2003 Dec;30(4):735-755.
67. Rozenberg P, Gillet A, Ville Y. Transvaginal sonographic examination of the cervix in asymptomatic pregnant women: review of the literature. *Ultrasound Obstet Gynecol* 2002 Mar;19(3):302-311.
68. Shennan A, Jones B. The cervix and prematurity: aetiology, prediction and prevention. *Semin Fetal Neonatal Med* 2004 Dec;9(6):471-479.
69. Slager J, Lynne S. Assessment of cervical length and the relationship between short cervix and preterm birth. *J Midwifery Womens Health* 2012 Jul;57 Suppl 1:S4-11.
70. Conde-Agudelo A, Romero R, Hassan SS, Yeo L. Transvaginal sonographic cervical length for the prediction of spontaneous preterm birth in twin pregnancies: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2010 Aug;203(2):128 e1-12.
71. Taylor MJ, Denbow ML, Duncan KR, Overton TG, Fisk NM. Antenatal factors at diagnosis that predict outcome in twin-twin transfusion syndrome. *Am J Obstet Gynecol* 2000 Oct;183(4):1023-1028.
72. Hernandez-Andrade E, Romero R, Ahn H, Hussein Y, Yeo L, Korzeniewski SJ, Chaiworapongsa T, Hassan SS. Transabdominal evaluation of uterine cervical length during pregnancy fails to identify a substantial number of women with a short cervix. *J Matern Fetal Neonatal Med* 2012 Sep;25(9):1682-1689.
73. Jeanty P, d'Alton M, Romero R, Hobbins JC. Perineal scanning. *Am J Perinatol* 1986 Oct;3(4):289-295.
74. Quintero, RA, 2007. Ultrasound assessment in twin-twin transfusion syndrome. In RA Quintero (ed), *Twin-Twin Transfusion Syndrome* (pp71-90). London: InformaHealth.
75. Berghella V, Odibo AO, To MS, Rust OA, Althuisius SM. Cerclage for short cervix on ultrasonography: meta-analysis of trials using individual patient-level data. *Obstet Gynecol* 2005 Jul;106(1):181-189.
76. Hassan SS, Romero R, Maymon E, Berry SM, Blackwell SC, Treadwell MC, Tomlinson M. Does cervical cerclage prevent preterm delivery in patients with a short cervix? *Am J Obstet Gynecol* 2001 Jun;184(7):1325-1329; discussion 9-31.
77. Chavira ER, Khan A, Korst LM, Miller D, Goodwin TM, Chmait RH. Are patients with twin-twin transfusion syndrome and a very short cervix candidates for laser surgery? *J Ultrasound Med* 2009 May;28(5):633-639.
78. Chmait RH, Korst LM, Llanes A, Mullin P, Lee RH, Ouzounian JG. Perioperative characteristics associated with preterm birth in twin-twin transfusion syndrome treated by laser surgery. *Am J Obstet Gynecol* 2013 Jun 7. [Epub ahead of print]
79. Devlieger R, Scherjon SA, Oepkes D, Meerman R, Timmerman D, Vandenbussche FP. Ultrasound visualization of fetal membrane detachment at the uterine cervix: the 'moon sign'. *Ultrasound Obstet Gynecol* 2003 Oct;22(4):431-432.
80. Di Salvo DN, Benson CB, Laing FC, Brown DL, Frates MC, Doubilet PM. Sonographic evaluation of the placental cord insertion site. *Am J Roentgenol* 1998 May;170(5):1295-1298.
81. Hack KE, Nikkels PG, Koopman-Esseboom C, Derks JB, Elias SG, van Gemert MJ, Visser GH. Placental characteristics of mono chorionic diamniotic twin pregnancies in relation to perinatal outcome. *Placenta* 2008 Nov;29(11):976-981.
82. Bajoria R. Abundant vascular anastomoses in monoamniotic versus diamniotic mono chorionic placentas. *Am J Obstet Gynecol* 1998 Sep;179(3 Pt 1):788-793.
83. Jones J, Sbarra A, Dilillo L, Cetrulo CL, D'Alton ME. Indomethacin in severe twin-to-twin transfusion syndrome. *Am J Perinatol* 1993 Jan;10(1):24.
84. Urig MA, Simpson GF, Elliott JP, Clewell WH. Twin-twin transfusion syndrome: the surgical removal of one twin as a treatment option. *Fetal Ther* 1988;3(4):185-188.
85. Wax JR, Blakemore KJ, Blohm P, Callan NA. Stuck twin with cotwin nonimmune hydrops: successful treatment by amniocentesis. *Fetal Diagn Ther* 1991;6(3-4):126-131.
86. Saunders NJ, Snijders RJ, Nicolaides KH. Therapeutic amniocentesis in twin-twin transfusion syndrome appearing in the second trimester of pregnancy. *Am J Obstet Gynecol* 1992 Mar;166(3):820-824.
87. Dennis LG, Winkler CL. Twin-to-twin transfusion syndrome: aggressive therapeutic amniocentesis. *Am J Obstet Gynecol* 1997 Aug;177(2):342-347; discussion 347-349.
88. 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 Jun;75(6):1046-1053.
89. Ville Y, Hecher K, Ogg D, Warren R, Nicolaides K. Successful outcome after Nd:YAG laser separation of chorioangiopagus-twins under sonoendoscopic control. *Ultrasound Obstet Gynecol* 1992 Nov 1;2(6):429-431.
90. De Lia JE, Kuhlmann RS, Harstad TW, Cruikshank DP. Fetoscopic laser ablation of placental vessels in severe previable twin-twin transfusion syndrome. *Am J Obstet Gynecol* 1995 Apr;172(4 Pt 1):1202-1208; discussion 1208-1211.
91. Ville Y, Hyett J, Hecher K, Nicolaides K. Preliminary experience with endoscopic laser surgery for severe twin-twin transfusion syndrome. *N Engl J Med* 1995 Jan;332:224-227.
92. Quintero R, Morales W, Mendoza G, Allen M, Kalter C, Giannina G, Angel JL. Selective photocoagulation of placental vessels in twin-twin transfusion syndrome: evolution of a surgical technique. *Obstet Gynecol Surv* 1998 Dec;53(12):s97-s103.
93. Hecher K, Diehl W, Zikulnig L, Vetter M, Hackeloer BJ. Endoscopic laser coagulation of placental anastomoses in 200 pregnancies with severe mid-trimester twin-to-twin transfusion syndrome. *Eur J Obstet Gynecol Reprod Biol* 2000 Sep;92(1):135-139.
94. Quintero RA, Comas C, Bornick PW, Allen MH, Kruger M. Selective versus non-selective laser photocoagulation of placental vessels in twin-twin transfusion syndrome. *Ultrasound Obstet Gynecol* 2000 Sep;16(3):230-236.
95. Harkness UF, Crombleholme TM. Twin-twin transfusion syndrome: where do we go from here? *Semin Perinatol* 2005 Oct;29(5):296-304.
96. Rossi AC, Kaufman MA, Bornick PW, Quintero RA. General vs local anesthesia for the percutaneous laser treatment of twin-twin transfusion syndrome. *Am J Obstet Gynecol* 2008 Aug;199(2):137.e1-7.
97. Ville Y, Hecher K, Gagnon A, Sebire N, Hyett J, Nicolaides K. Endoscopic laser coagulation in the management of severe twin-to-twin transfusion syndrome. *Br J Obstet Gynaecol* 1998 Apr;105(4):446-453.
98. Quintero R. Selective laser photocoagulation of communicating vessels in twin-twin transfusion syndrome. In: Quintero R, editor. *Diagnostic and operative fetoscopy*. New York: The Parthenon Publishing Group; 2002. p 43-54.
99. Robyr R, Lewi L, Salomon LJ, Yamamoto M, Bernard JP, Deprest J, Ville Y. 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 Mar;194(3):796-803.
100. Lopriore E, Middeldorp JM, Oepkes D, Klumper FJ, Walther FJ, Vandebussche FP. Residual anastomoses after fetoscopic laser surgery in twin-to-twin transfusion syndrome: frequency, associated risks and outcome. *Placenta* 2007 Feb-Mar; 28(2-3):204-208.
 101. Stirnemann JJ, Nasr B, Quarello E, Ortqvist L, Nassar M, Bernard JP, Ville Y. A definition of selectivity in laser coagulation of chorionic plate anastomoses in twin-to-twin transfusion syndrome and its relationship to perinatal outcome. *Am J Obstet Gynecol* 2008 Jan;198(1):62 e1-6.
 102. Crisan LS, Kontopoulos EV, Quintero RA. Appraisal of the selectivity index in a cohort of patients treated with laser surgery for twin-twin transfusion syndrome. *Am J Obstet Gynecol* 2010 Feb;202(2):157 e1-5.
 103. Lewi L, Jani J, Cannie M, Robyr R, Ville Y, Hecher K, Gratacos E, Vandecruys H, Vandecaveye V, Dymarkowski S, et al. Intertwin anastomoses in monochorionic placentas after fetoscopic laser coagulation for twin-to-twin transfusion syndrome: is there more than meets the eye? *Am J Obstet Gynecol* 2006 Mar;194(3):790-795.
 104. Ruano R, Rodo C, Peiro JL, Shamshirsaz A, Haeri S, Nomura ML, Salustiano EM, de Andrade KK, Sangi-Haghpeykar H, Carreras E, et al. Fetoscopic laser ablation of the placental anastomoses in twin-twin transfusion syndrome using the 'Solomon technique'. *Ultrasound Obstet Gynecol* 2013 Apr 24. [Epub ahead of print]
 105. Baschat AA, Barber J, Pedersen N, Turan OM, Harman CR. Outcome after fetoscopic selective laser ablation of placental anastomoses vs equatorial laser dichorionization for the treatment of twin-to-twin transfusion syndrome. *Am J Obstet Gynecol* 2013 May 22. [Epub ahead of print]
 106. Quintero RA, Ishii K, Chmait RH, Bornick PW, Allen MH, Kontopoulos EV. Sequential selective laser photocoagulation of communicating vessels in twin-twin transfusion syndrome. *J Matern Fetal Neonatal Med* 2007 Oct;20(10):763-768.
 107. Chalouhi GE, Stirnemann JJ, Salomon LJ, Essaoui M, Quibel T, Ville Y. Specific complications of monochorionic twin pregnancies: twin-twin transfusion syndrome and twin reversed arterial perfusion sequence. *Semin Fetal Neonatal Med* 2010 Dec;15(6):349-356.
 108. Nakata M, Murakoshi T, Sago H, Ishii K, Takahashi Y, Hayashi S, Murata S, Miwa I, Sumie M, Sugino N. Modified sequential laser photocoagulation of placental communicating vessels for twin-twin transfusion syndrome to prevent fetal demise of the donor twin. *J Obstet Gynaecol Res* 2009 Aug;35(4):640-647.

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