MONOCHORIONIC TWIN PREGNANCY: TWIN-TO-TWIN TRANSFUSION SYNDROME (TTTS)

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1. INTRODUCTION

Twin-to-twin transfusion syndrome (TTTS) is defined as the presence of a polyhydramnios-oligohydramnios sequence in a monochorionic twin (MC) pregnancy. TTTS affects about 10-15% of monochorionic pregnancies, usually between 16-26 weeks. Monochorionic pregnancy prevalence is estimated around 1/250, so this situation can appear in at least 1/2000 pregnancies.

TTTS results from a chronic unbalanced blood flow exchange between both twins through the placental vascular communications existing in all monochorionic placentas. Some factors favour the development of TTTS, but the triggers of the syndrome in individual cases may be difficult to understand because there is a great variability in each specific case. In general, MC complicated with TTTS have relatively few vascular communications in comparison with uncomplicated pregnancies, and there is a predominance of arteriovenous anastomoses from donor to recipient. There is a predominance of fetal growth restriction and marginal/velamentous cord insertion in the donor. Mathematical models support that these factors, as well as the existence of cardiac malformations in one twin, may facilitate the development of TTTS.

TTTS is characterised by hypervolemia in the recipient fetus, resulting in compensatory polyuria, enlarged urinary bladder and polyhydramnios. The donor twin has hypovolemia, resulting in oliguria, with reduced or absent visualisation of the urinary bladder, and oligoanhydramnios, which gives a characteristic ultrasound appearance, defined as stuck twin syndrome. These haemodynamic changes promote a compensatory activation of the renin-angiotensin system and other vasoactive systems, which presents hypertension and can develop tubular dysplasia due to persistent oliguria. The recipient receives these vasoactive factors and, despite suppressing their renin-angiotensin system, develops hypertension, which in combination with hypervolemia, induces hypertrophic cardiomyopathy. In a high proportion of cases the donor is smaller, and even presents selective fetal growth restriction criteria (sFGR), but it is only in a small proportion (<5%) of cases that the recipient is smaller.

Without treatment, TTTS before 26 weeks is associated with a dire prognosis, with 90-100% mortality and 50-90% of severe sequelae in survivors.

There are no good predictive markers of TTTS. The best strategy is fortnightly ultrasound follow-up of all MC, which allows early detection and therapy in most cases.

2. DIAGNOSIS AND STAGING OF TTTS

2.1 Diagnostic criteria

TTTS diagnosis is based on the presence of a severe polyhydramnios-oligohydramnios sequence and urinary bladder discordance in a monochorionic pregnancy.

- Recipient with polyhydramnios (Deepest-Vertical-Pocket (DVP) > 8 cm if ≤ 20 weeks, > 10 cm if > 20 weeks) and enlarged urinary bladder. In cases of early onset (< 16.0 weeks), TTTS can be considered even with a DVP < 8 cm if all other criteria are met.
- Donor with oligohydramnios (DVP < 2 cm) with very reduced or absent fetal bladder.

Other ultrasound signs may be found but <u>are not diagnostic criteria</u>:

- sFGR is present in 40-50% of TTTS cases, commonly, but not always, affecting the donor.
- Doppler abnormalities are very common and used to classify severity.

2.2 TTTS staging

TTTS severity is classified into 5 stages, according to the Quintero staging system:

- Stage I: the urinary bladder is still visible in the donor twin.
- Stage II: the urinary bladder in the donor is not visualized at any moment during the examination.
- Stage III: severe or critical Doppler abnormalities:
    - Absent or reversed end-diastolic flow in umbilical artery (UA), in any of the twins (usually the donor).
    - Reversed a-wave flow in ductus venosus (DV) and/or presence of pulsations in umbilical vein (UV) in any of the twins (usually the recipient).
- Stage IV: Fetal hydrops in any of the twins (usually the recipient).
- Stage V: Demise of one or both twins.

STAGE	I	II	III	IV	V
Donor urinary bladder	Present	Absent	Absent	Absent	Absent
Doppler abnormality	-	-	+	+	+/-
Hydrops	-	-	-	+	+/-
Fetal demise	-	-	-	-	+

The progression of the TTTS stage may be very variable and some cases have a slow, while others have a an abrupt progression to more severe stages. However, with proper follow-up every 2 weeks, most cases will be detected in stage I or II.

While most cases follow the sequence defined by the staging system above, atypical forms can occasionally be seen. The most characteristic among these is the so-defined "atypical stage III", where Doppler abnormalities are present, but donor bladder is still visible. These cases are frequently associated with sFGR and the presence of large artery-to-artery anastomoses, and occasionally with intermittent UA flow in the donor twin.

3. DIFFERENTIAL DIAGNOSIS

Differential diagnosis must be considered with sFGR and amniotic fluid discordance.

Selective fetal growth restriction

A considerable proportion of TTTS (50%) are associated with sFGR. If TTTS criteria are met, the association with sFGR determines a poorer prognosis for the donor, but it does not change the indication for fetoscopic therapy.

If the TTTS criteria are not met, the case is classified as isolated sFGR, and this must be clearly differentiated from TTTS to avoid unnecessary treatments.

	TTTS	**sFGR**
EFW* and discordance	Variable	<10th and ≥25%
AGA/recipient fetus** Amniotic fluid Urinary bladder Ductus venosus	 > 8 cm before 20 weeks/ > 10 cm after 20 weeks Enlarged Variable (elevated PI)	 Normal or slightly increased Normal Normal

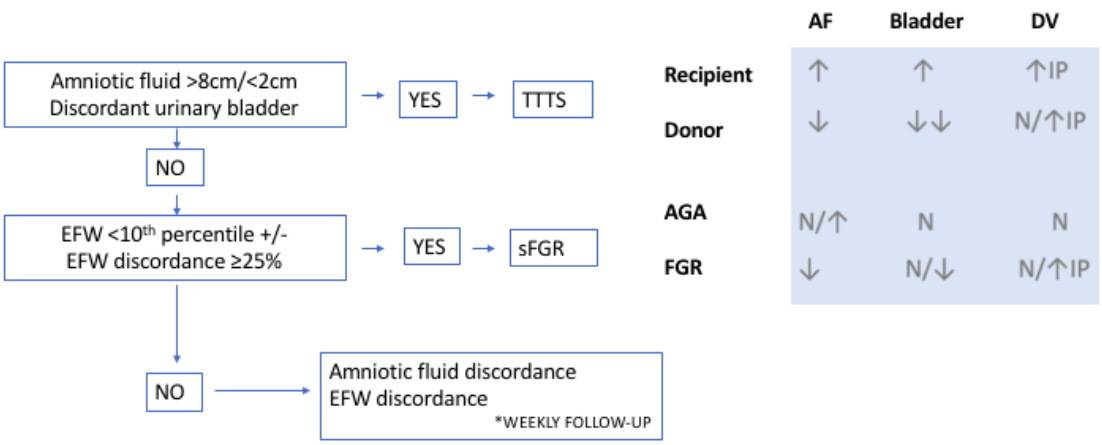
FGR/donor fetus		
Amniotic fluid	< 2 cm	Normal or slightly reduced
Urinary bladder	Very reduced/Not visible	Normal or slightly reduced

* Estimated fetal weight (EFW) ** Appropriate for gestational age (AGA)

Amniotic fluid or biometric discordance

Amniotic fluid discordance can be relatively common, and it is essential to differentiate this situation from TTTS, to avoid unnecessary treatment. The diagnosis of amniotic fluid discordance is normally made when ≥ 3 cm and is made by exclusion of the criteria of TTTS. Amniotic fluid discordance is associated with a 40-50% risk of TTTS or sFGR and must be monitored weekly.

Amniotic fluid discordance may also be associated with discordant fetal sizes (> 20%) without meeting sFGR criteria. In those cases, weekly follow-up is also performed.



4. DIAGNOSTIC CONFIRMATION AND PRE-OPERATIVE EVALUATION

4.1 Diagnostic confirmation, staging and preoperative planning

Evaluation of DVP of each sac, size of both fetal urinary bladders, fetal biometry and Doppler of UA and DV for staging. Comprehensive examination of the location and margins of the placenta

and intertwin membrane, and identification of umbilical cord insertions. The most likely situation of the placental equator is estimated based on umbilical cord insertions.

4.2 Cervical length assessment

TTTS increases the risk of preterm delivery or early gestational loss. A short cervix (< 15 mm) is one of the strongest risk factors for preterm delivery in TTTS, and consequently it is associated with poorer survival. However, it is not a contraindication for laser therapy. The efficacy of cervical cerclage at the time of fetal surgery is controversial, and in some cases cervical length increases remarkably after the amniodrainage performed as part of fetal therapy. The decision to perform a cerclage must be individualised and discussed with the parents.

4.3 Evaluation of the fetal anatomy, brain and heart

MC twins are associated with a 2- to 3-fold increase in the risk of malformations as compared with singletons and dichorionic twins, most of which are discordant, i.e. present in only one twin. Fetal anatomy must be reassessed before therapy.

Specifically, while they are not part of the diagnostic criteria, fetal brain and cardiac assessment are mandatory and can provide information that influences counselling and management:

- TTTS is associated with an increased risk of brain damage. A thorough neurosonographic evaluation is mandatory to rule out the presence of findings that suggest hypoxic-ischaemic damage (mainly ventriculomegaly, periventricular hyperechogenicity or porencephalic lesions) and adjust counselling and decisions as appropriate.
- There is a higher prevalence of congenital cardiac defects, which should be identified before deciding the type of therapy and counselling the parents.
- TTTS is associated with pulmonary stenosis/atresia in up to 10-15% of cases, normally in stage III onwards but sometimes in earlier stages. Part of these cases will reverse during pregnancy or after birth, but up to 30% may persist postnatally. It may be very difficult or impossible to ascertain whether pulmonary stenosis/atresia is purely functional or anatomic, and this can only be seen with follow-up.
- Tricuspid regurgitation is a common finding in the recipient, but it does not modify prognosis when the severity staging is used, and therefore it is not used as a severity criterion.

In the presence of a discordant fetal anomaly, the possibility of selective termination may be discussed with the parents.

In the absence of remarkable findings, a quantitative fluorescent PCR (QF-PCR) for trisomy 21 will be performed in amniotic fluid obtained during surgery. In the presence of signs suggesting a potential anomaly, comparative genomic hybridisation (CGH-Array) genetic test will be performed.

4.4 Predictors of fetal demise and poor outcome

Fetal demise fetoscopy can occur in 3-6% of recipients and 8-10% of donors, mostly within the first days post-procedure. Factors associated to a higher risk are:

- Donor: gestational age < 18.0 weeks, reverse end-diastolic flow in the UA and intertwin fetal biometry discordance > 30%.
- Recipient: middle cerebral artery peak systolic velocity (MCA-PSV) value > 1.5 MoMs.

Premature rupture of membranes is the main obstetrical complication after fetoscopic therapy, responsible for a substantial proportion of adverse outcomes. There are no good predictors of PPROM excepting for a very short cervix.

5. TREATMENT OF TTTS

5.1 Therapeutic options

<u>Fetoscopic laser coagulation of placental anastomoses</u>

Fetoscopic laser coagulation of vascular anastomoses is the first choice and the only aetiological treatment. It aims for the survival of both fetuses and, in the event of the intrauterine demise of one, has a protective effect on the survivor. In experienced centres, the survival rate is > 90% for at least one fetus, and 75-80% for both fetuses, with a risk of neurological damage at 30 weeks of 1-2%.

Considerations and comments:

- Once TTTS is diagnosed, fetoscopic laser should be performed as soon as possible, normally within 24-48 hours of diagnosis. Delays in therapy should only be due to logistic reasons (normal means of travel).

- Invasive procedures and/or amnioreduction prior to fetoscopy are contraindicated. They worsen the prognosis, as they are associated with a higher risk of premature rupture of membranes, intracavitary bleeding, septostomy or membrane detachment, that may render fetoscopy impossible or very difficult.
- Stage I TTTS: results of a recent randomised clinical trial show a progression rate of 60% in cases with expectant management, with no significant differences in perinatal outcomes in laser versus expectant management, and a similar overall survival without neurological morbidity in both groups. Expectant management of stage I entails important difficulties in patients who live far away, and anxiety in many parents due to uncertainty (which includes not only rapid progression but also unexpected fetal death). In our centre, fetoscopy laser is offered to all patients with stage I TTTS. However, if the parents are willing, expectant management with strict follow-up (every 1-3 days) can be considered in very selected situations: asymptomatic and cervical length > 30 mm. Expectant management can also be contemplated in cases > 28 weeks.

- Laser therapy is normally indicated between 16+0 and 28+6 weeks, but extension of these limits can be considered in selected cases:
    - Early laser (< 17 weeks) is associated with a higher risk of premature rupture of membranes (up to 40% before 32 weeks), pregnancy loss (10-15% increase), prematurity < 32 weeks (10-15% increase) and lower neonatal survival at 28 days compared to procedures performed ≥ 17 weeks. For this reason, in early cases with strictly normal Doppler and slow progression, expectant management with close follow-up (1-3 times/week) may be attempted until ≥ 17 weeks. On the contrary, and exceptionally, laser can be performed from 15+0 if very aggressive progression and particularly stage III+ is present.
    - Late TTTS > 26 weeks: up to 28+6 weeks laser has shown similar results as compared with cases performed < 26+0 weeks. In selected cases and after discussion with parents, laser can be considered in cases ≥ 29 weeks, bearing in mind that at advanced gestational ages it is often technically more difficult.

- In the presence of discordant anomaly or signs of brain damage in one fetus, umbilical cord laser occlusion/ablation of the affected fetus should be considered and discussed with the parents.

- Whilst PPROM in women with a short cervical length, even if only subclinical leakage, should be considered a contraindication for laser therapy.

Amniodrainage

Amniodrainage, or amnioreduction, is a symptomatic and non-aetiological treatment, with the aim of reducing the polyhydramnios, the consequent risk of prematurity, and improving maternal symptomatology. Amniodrainage is part of and performed during laser therapy. However, amniodrainage alone is a palliative technique, and requires serial procedures because polyhydramnios recurs within days and is associated with significant neurological morbidity and maternal complications (including PPROM and placental abruption).

Management of late TTTS with amniodrainage: beyond the gestational age ranges where laser is offered, amniodrainage reduces the polyhydramnios, improves maternal discomfort, and in many cases, prolongs pregnancy, allowing fetal lung maturation. Severe polyhydramnios normally reappears within days. In some cases, the signs of TTTS seem to improve or even disappear. In any event, strict monitoring is mandatory and elective delivery should be indicated as soon as the gestational age allows it, normally between 32 and 34 weeks. Late TTTS can be a rapidly progressing and devastating complication. It may reappear abruptly and progress within hours, with very poor outcomes despite advanced gestational age.

Amnioreduction can also be offered in TTTS with PPROM to relieve maternal symptoms, but normally the outcomes are very poor.

See Polyhydramnios protocol for a technical description of the amniodrainage procedure. The main specific consideration for TTTS is that the puncture should always be made as far as possible from the donor, and ideally, if possible, in a diametrically-opposed location in the uterus, to avoid the risk of septostomy.

5.2 Fetoscopic laser procedure

Fetoscopic treatment consists of coagulation with diode or Nd:YAG laser of all placental inter-twin vascular anastomoses along the vascular equator. The modification known as Solomon technique consists of coagulating the entire placental vascular equator, creating a “line” of coagulation that joins all coagulated spots where the anastomoses existed. The objective is to avoid missing very small calibre vessels and consequently reduce the risk of recurrent TTTS and

twin anaemia-polycythaemia sequence (TAPS). However, the Solomon technique may increase the risk of premature rupture of membranes and placental abruption. Thus, the technique will be adapted to the characteristic of each specific placenta. Selective coagulation is performed and where there are areas of poorer visualization or access (i.e. anterior placenta), the Solomon technique may be used in specific portions of the vascular equator. After laser coagulation, amnioreduction of the recipient sac is performed until the DVP of amniotic fluid is normalised (< 6 cm).

Complications

- Maternal: The incidence of severe maternal complications is low (<1%) and these include intrauterine bleeding, dilutional anaemia and ascites due to amniotic fluid leakage. Other rarer complications include Mirror Syndrome (usually associated with the presence of hydrops or large volume amnioreduction), chorioamnionitis (<1%) and very rarely placental abruption.
- Fetal-perinatal: The main complications occurring due to, or despite, the laser are extreme preterm labour (8-10%), preterm prelabour rupture of membranes (20-30%) and intrauterine demise of one or both twins (5-10%). Less frequent are TAPS (1-2%) and amniotic band syndrome, especially in cases complicated with septostomy (<2%).

  Other fetal complications of TTTS may be observed, but they should not be attributed to laser, but rather to the course of the disease:

  - Central Nervous System (CNS) lesions: classically, TTTS is associated with poorer neurodevelopment, ranging from 10-20%. Most of these complications are associated with severe or extreme prematurity, but in a small proportion there are CNS abnormalities already detectable in utero. For this reason, a systematic examination at 30-32 weeks with neurosonography and/or MRI is essential. This will detect 1-3% of severe lesions, usually hypoxic-ischaemic injuries (porencephaly or cortical development malformations).
  - Thrombotic-ischaemic phenomena (intestinal, renal or even limbs). Normally in the recipient, they are manifested as intestinal or renal hyperechogenicity or limb amputation and can appear before surgery or some weeks later.

6. FOLLOW-UP AND DELIVERY AFTER TTTS TREATMENT

Immediate postoperative period

The patient will remain admitted with bed rest and under thromboembolic prophylaxis until ultrasound assessment after 24 hours. In the absence of complications, the patient may start relative rest and can be discharged.

Initial (2-4 weeks) ultrasound follow-up

-Weekly follow-up-

Evaluation of fetal vitality, cervical length, signs of chorioamniotic detachment, amniotic fluid DVP, fetal bladders and Doppler evaluation (UA, DV and MCA-PSV Doppler).

Doppler abnormalities and amniotic fluid normalise within days, but they may take longer, particularly in advanced stages and in the recipient fetus:

- Donor: progressive recovery of amniotic fluid levels and visualisation of urinary bladder. Transient signs of haemodynamic overload can be observed, especially in stage III+, and they are supposed to reflect rapid normalisation of blood volume while oliguria persist. The most common signs of overload are:
    - Increased post-op pulsatility in DV (including DV with absent or reversed a-wave).
    - Tricuspid insufficiency and, more rarely, acceleration in pulmonary artery flow, including ductus arteriosus with reversed flow.
    - Mild hydropic signs are subcutaneous oedema of the upper body, ascites or hydrothorax.

    These signs indicate an effective therapy, they usually disappear within days and are rarely seen after 1-2 weeks.

- Recipient: Normalisation of amniotic fluid and decrease in urinary bladder size. Improvement of volume overload signs, including DV flow and tricuspid regurgitation, may take 1-2 weeks to normalise. In case of severe cardiac involvement (usually pulmonary atresia), in 30% of cases alterations may persist during pregnancy and postnatal life, making postnatal therapy necessary.

**Postoperative discordance in MCA-PSV:* this may be seen in the immediate postoperative period, and most commonly the ex-recipient is the fetus with high PSV. This observation is

usually explained by the order of coagulation of placental vessels, which may leave open a large VA (or AV) while the other vessels have been coagulated, allowing acute unidirectional transfusion for seconds or minutes. For this reason, it is advisable to follow an order in the coagulation (i.e. one AV followed by one VA of similar size) and try to coagulate anastomoses as quickly as possible. If it is due to intraoperative phenomena, the discordance will be a transient finding that improves rapidly and disappears over days after surgical treatment. In case of persistent signs of TAPS, refer to the specific section.

Later (>2-4 weeks) ultrasound follow-up

In the absence of complications, ultrasound monitoring can be performed every 15 days. These controls will include:

- Amniotic fluid and bladder monitoring: the risk of TTTS recurrence in experienced hands is very low (<1%).
- Fetal biometry monitoring.
- Doppler assessment of both twins, including evaluation of UA and DV and especially MCA-PSV to rule out the presence of TAPS (1-2% in experienced centres). TAPS may appear shortly after or many weeks after an apparently successful surgery.
- Cervical length.
- Detailed assessment of placenta and membranes is to rule out chorioamniotic detachment and/or septostomy, which may occur in 15-20% of cases and are associated with an increased risk of preterm rupture of membranes and preterm delivery < 32 weeks, and with an increased risk of pseudo-amniotic bands (see below)
- Cardiac evaluation: In addition to a basic cardiac evaluation, at least one complete echocardiography is recommended, especially if either fetus (usually the recipient) had signs of cardiac dysfunction prior to surgery due to hypertensive status. Resolution of these signs may take up to 4 weeks. The most frequent findings in the recipient are cardiomegaly due to biventricular hypertrophy and right ventricular outflow tract obstruction (up to 10% of cases) leading to stenosis and even functional pulmonary atresia, which may persist and require postnatal surgical treatment in up to 30% of cases.
- Neurological evaluation: The risk of neurological injury at 30-32 weeks is below 2%. Neurosonography will be routinely performed, generally at 30-32 weeks or 4-6 weeks afterwards in TTTS stage V cases, to rule out the presence of acquired CNS lesions. If CNS abnormality is suspected, it will be performed at the time of suspicion. In cases of high risk

of neurological injury (TTTS stage IV or V), pathological or inconclusive neurosonography, the CNS study should be complemented by MRI.

**Fetal demise of one fetus:* While most cases will happen within the first days after surgery, it may occur unexpectedly at any time after a successful surgery. Aside from the inevitable stress for parents, fetal death after a successful surgery entails no additional risks for the other twin and should not be a reason to change monitoring or follow-up.

**Signs of pseudo-amniotic band:* If septostomy or detachment are seen, weekly follow-up is mandatory to assess for such signs, consisting of a focal ring-like constriction at any point of the affected limb, with distal swelling of the hand/foot/limb. Early identification of such signs allows for timely intervention (normally elective delivery) and prevents severe damage of the affected limb.

Obstetric follow-up and Delivery

Relative rest, avoiding efforts and standing for long periods, is recommended until the end of pregnancy. If there are no complications, elective delivery is recommended between 36-37 weeks.

In the absence of laser complications (TAPS, sFGR, Doppler abnormalities), there is insufficient evidence to systematically recommend the mode of delivery by elective caesarean section. However, the probability of caesarean section is much higher in twins, and given the history of fetal surgery, the mode of delivery should always be discussed individually.

In case of septostomy, due to the risks of monoamniotic pregnancy, elective delivery will be scheduled at 32 weeks by elective caesarean section and after fetal pulmonary maturation and fetal neuroprotection.

7. TWIN ANAEMIA POLYCYTHAEMIA SEQUENCE

7.1 Definition and physiopathology

Twin Anaemia Polycythaemia Sequence (TAPS) represents a feto-fetal transfusion where one twin is anaemic (donor), whereas the other twin presents polycythaemia (recipient). It occurs spontaneously in 3-5% of uncomplicated monochorionic pregnancies, and in 1-2% after laser treatment for TTTS. The main difference with TTTS is the magnitude of the inter-twin transfusion. TAPS is characterised by a chronic, very slow inter-twin transfusion through a few vascular anastomoses of small diameter (< 1 mm), causing a haematologic but not a haemodynamic disorder, as in TTTS.

7.2 Prenatal diagnosis and staging

Prenatal diagnosis is based on the Doppler assessment of the middle cerebral artery peak systolic velocity (MCA-PSV) in both twins, and defined as either:

- Donor > 1.5 MoM and recipient < 1.0 MoM;

- MoM delta value (MoM donor – MoM recipient) > 0.5 irrespective of MCA-PSV values.

Associated non-diagnostic ultrasound signs:

- Amniotic fluid discordance may be present, but the criteria for TTTS are not met. However, exceptionally, TAPS may evolve to TTTS, and in this case should be managed accordingly.
- 'Starry sky' liver: Congestive liver in the polycythemic fetus (40-60%) with increased echogenicity of the portal system walls and decreased echogenicity of the parenchyma.
- Signs of heart failure (cardiomegaly, tricuspid insufficiency) in the donor, normally associated with, but may precede, hydrops.
- Differences in echogenicity and placental thickness (40-50%): the placental portion of the anaemic/donor fetus is more echogenic and thickened, while the placental portion of the polycythemic/recipient fetus is less echogenic and thinner.

<u>Severity staging:</u>

The staging system initially included the MoM values of the MCA, but a later modification proposed the evaluation of the MoM delta value (MoM donor – MoM recipient) as a better predictor of the severity of the disease. Both criteria can be used.

- I: [Donor MoM >1.5 MoM + Recipient MoM <1.0] OR [Delta value >0.5]
- II: [Donor MoM >1.5 MoM + Recipient MoM <0.8] OR [Delta value >0.7]
- III: Stage I or II with haemodynamic involvement: signs of cardiac dysfunction (absent or reversed end-diastolic flow in UA, reverse DV, pulsatile VU) in the donor.
- IV: Fetal hydrops in the donor.
- V: Death of one or both fetuses

7.3 Postnatal diagnosis and staging

- TAPS can be diagnosed postnatally by a haemoglobin discordance > 8 g/dL and reticulocyte count ratio (reticulocytes of anaemic fetus/polycythaemic fetus) > 1.7 (to differentiate it from acute peripartum transfusion, in which there is no increase in reticulocyte production in the anaemic twin).

A staging system based on postnatal haemoglobin discordance has been proposed:

TAPS stage	Haemoglobin discordance (g/dL)
I	>8
II	>11
III	>14
IV	>17
V	>20

7.3 Management

Spontaneous TAPS is usually a mild, late-onset complication that often does not require active management or is not even detected until neonatal life. Less frequently, spontaneous TAPS can be more severe, and treatment should be considered.

TAPS after fetoscopic laser is usually severe and requires treatment.

TAPS management requiring an active treatment is controversial. No treatment has shown significant differences in perinatal survival or neurological damage between the different therapeutic strategies. Awaiting the results of an ongoing randomised clinical trial (TAPS Trial) the following therapeutic options have been proposed:

- Expectant management until delivery: Mild and/or spontaneous TAPS, especially in stages I-II, without hydrops.
- Fetoscopic laser: laser in TAPS may be considerably more difficult than in TTTS, due to the presence of fluid in the donor's sac and the poorer visualisation of the placental surface, which is not flattened by the polyhydramnios as in TTTS. There is greater need for amnioinfusion. The risk of obstetrical complications may be higher, but there are no high-quality series documenting that. In TAPS, vascular anastomoses are expected to be smaller than in TTTS, and their visualisation may be more challenging. Particularly, post-laser TAPS may be particularly challenging since the amniotic fluid is often stained, and the replacement of amniotic fluid is required.
- Intrauterine transfusion to the donor fetus. As a stand-alone treatment, this approach was suggested but has been virtually abandoned in most centres. It can be considered as an adjunct to laser therapy to treat severe anaemia in the donor (normally stage IV) in an attempt to reduce mortality, but there are no series supporting the effectiveness of this approach.
- Selective reduction by cord occlusion can be considered in the presence of a severe anomaly or signs suggesting brain injury in one of the fetuses (usually the anaemic one).
- Delivery: Elective delivery by caesarean section will be considered from 32-34 weeks onwards, after previous fetal lung maturation and fetal neuroprotection. Earlier delivery may be considered depending on the severity of TAPS and if fetoscopy is not technically feasible.

Subsequent follow-up will be adapted to the therapeutic strategy and clinical severity.

Normally, unless there is a clear resolution after laser therapy, ultrasound surveillance is recommended twice a week, including Doppler evaluation and assessment of hydrops and/or cardiac dysfunction signs. In all cases, neurosonography +/- MRI is recommended to rule out neurological involvement, especially of the anaemic fetus.

8. ACARDIAC TWIN OR TWIN REVERSED ARTERIAL PERFUSION (TRAP)

8.1 Definition and physiopathology

This is a very rare complication, with an incidence of 1% in monochorionic pregnancies, being somewhat more frequent in triplet and monoamniotic pregnancies. It is defined by the presence of an acardiac fetus that has no connection with the placental villous circulation. The acardiac fetus is connected to and receives oxygenated blood from its co-twin, which is anatomically normal and defined as the "pump" fetus, through direct arterio-arterial (AA) and veno-venous (VV) anastomoses (usually one of each). The poorly oxygenated arterial blood of the normal twin flows reversely through the umbilical artery of the acardiac twin from early pregnancy. For this reason, the acardiac fetus is poorly developed and presents multiple severe anomalies (acardiac, acephalus, incomplete development of the upper limbs, generalised oedema). An acardiac twin is a lethal anomaly incompatible with life in 100% of cases. The "pump" fetus is morphologically normal but faces high risk of perinatal mortality due to the hyperdynamic and cardiac failure situation, as well as an increased risk of preterm birth related with polyhydramnios.

The risk of fetal loss for the "pump" fetus during the first trimester is 30-80%. In addition to haemodynamic overload, there is an increased risk of fetal brain injury. Episodes of hypovolemia-hypervolemia can occur intermittently, leading to acute and unpredictable ischaemic-thrombotic events, which explain the adverse outcomes for the pump twin. While there is great variability in the evolution of apparently similar cases, certain factors have been described to carry a higher risk of fetal loss during the first of second trimester:

- Acardiac fetus size >50% greater than pump fetus.
- Signs of hyperdynamic/cardiac overload (cardiomegaly, tricuspid insufficiency, hydrops) in the "pump" fetus.
- Monoamniotic pregnancy

8.2 Management

Although there are no clinical trials supporting this option, TRAP is often managed actively due to the risks described above and the relatively high uncertainty and unpredictability of clinical evolution and prognosis. Active management consists of selective termination of the acardiac fetus by cord occlusion or intrafetal coagulation. In monoamniotic cases, this should be accompanied by umbilical cord section.

In this centre, the treatment of choice is laser or bipolar cord coagulation from 16-17 weeks onward. Intra-fetal radiofrequency ablation has also been described with similar results.

Early (i.e. 12 weeks) intrafetal laser ablation has been described by some authors, but it must be performed very early and represents a challenging technique due to the difficulty of achieving effective coagulation while avoiding haemorrhagic events and death of the co-twin.

Pre-surgical monitoring

Weekly monitoring is recommended to assess signs of overload and polyhydramnios in the "pump" fetus, which can be considered as further indication for active management.

- Doppler evaluation (AU, DV and MCA-PSV) of the "pump" fetus.
- Weekly echocardiographic assessment: tricuspid insufficiency, pulmonary artery flow.
- Amniotic fluid assessment of both sacs

Post-surgical monitoring

Immediate follow-up: Echocardiographic assessment and evaluation of signs of fetal anaemia in the "pump" fetus.

After the intervention, weekly monitoring during the first month and, once or twice a month thereafter.

Neurosonography +/- MRI is recommended between 30-32 weeks. If no complications are detected, elective delivery is recommended between 36-37 weeks.