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Specific complications of monochorionic twin pregnancies: twin–twin transfusion syndrome and twin reversed arterial perfusion sequence

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S U M M A R Y

Monochorionic twins are subjected to specific complications which originate in either imbalance or abnormality of the single placenta serving two twins. This unequal placental sharing can cause complications including twin–twin transfusion syndrome (TTTS), twin anemia–polycythemia sequence (TAPS), selective intrauterine growth restriction or twin reversed arterial perfusion sequence (TRAP). Monochorionicity also makes the management of these specific complications as well as that of a severe malformation in one twin hazardous since the spontaneous death of one twin exposes the co-twin to a risk of exsanguination into the dead twin and its placenta. The latter is responsible for the death of the co-twin in up to 20% of the cases and in ischemic sequelae in about the same proportions in the survivors. Although the symptoms of all these complications are very different, the keystone of their management comes down to either surgical destruction of the inter-twin anastomoses on the chorionic plate when aiming at dual survival or selective and permanent occlusion of the cord of a severely affected twin aiming at protecting the normal co-twin. This can be best achieved by fetoscopic selective laser coagulation and bipolar forceps cord coagulation respectively.

1. Introduction

Monochorionic (MC) twins are characterized by their interdependency through a shared placental mass and fetoplacental circulation. All complications of MC twins are based on inter-twin discordance, encompassing fetal size, amniotic fluid volume, fetoplacental hemodynamics as well as structural defects. In all of these high risk situations, the death of the most affected twin can trigger exsanguination of the survivor into the dead twin and its placenta, thus threatening the survivor with death in around 20% of cases, or with the development of ischemic lesions in various organs – mainly the brain – in around 20% of cases also. Therefore the management of all specific complications in MC pregnancies exposed to the risk of losing one twin in utero justifies considering the interruption of the inter-twin anastomoses with the aim of addressing the cause of the disease, such as in twin–twin transfusion syndrome (TTTS) or twin reversed arterial perfusion sequence (TRAP) sequence, in order to prevent the consequences of the death of one twin for the survivor. The most severe and spectacular specific complications in MC twin pregancies are TTTS and TRAP.

2. Twin–twin transfusion syndrome

2.1. Prenatal diagnosis of TTTS

TTTS occurs during mid-trimester in most cases, mainly around 20–21 weeks, although the diagnosis can also be suspected in first and third trimesters of pregnancy. The diagnosis may sometimes be suspected by acute clinical symptoms related to polyhydramnios such as uterine distension, contractions or dyspnea, although it is generally recognized during ultrasound follow-up of asymptomatic MC pregnancies by the association of oliguric oligohydramnios in one twin and polyuric polyhydramnios in the co-twin.

The diagnosis of TTTS is easy in most cases but relies upon strict ultrasound criteria. Whereas most teams use a 2 cm cut-off for the deepest vertical pool (DVP) to characterize oligohydramnios, the diagnosis of polyhydramnios is controversial. In the Eurofetus trial[1] an 8 cm cut-off before 20 weeks and 10 cm thereafter were adopted and are now widely used in Europe. Others consider an 8 cm cut-off throughout pregnancy. The oliguric twin is named the donor twin and the polyuric twin the recipient. Cases presenting with severe oligohydramnios in the donor are sometimes named ‘stuck twin’ since this fetus appears wrapped in its membranes as in a cocoon. These cases may be mistakenly diagnosed as monoamniotic since the inter-twin membrane may not be visible. Because of the underlying hypervolemia and its cardiac effects, the recipient twin

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may exhibit a wide spectrum of echocardiographic findings describing the syndrome-related cardiomyopathy.[2–12] Such findings include cardiac hypertrophy and cardiomegaly, atrio-ventricular regurgitation, ductus venosus Doppler abnormalities as well as decreased systolic function in the most severe cases. The most striking feature is the right ventricle outflow tract (RVOT) stenosis that develops in around 5% of cases.[8,13] However, studies describing the range of cardiac involvement in the recipient twin have failed to find any prognostic relationship following percutaneous laser coagulation.[3,4] This also applies to hydropic recipients that usually respond well to appropriate surgical management.

Since TTTS develops acutely in most cases, a close follow-up of MC twins is required. In our experience a bimonthly regimen is sufficient for the early recognition of the disease.

In an optimal setting, once the diagnosis is suspected, referral should be made within 24 h in order to confirm the diagnosis and plan surgery. Initial ultrasound assessment includes a detailed anomaly scan together with Doppler studies of both twins as well as endovaginal measurement of cervical length (Table 1). The most widely used classification is the Quintero staging system[14] (Table 2) but its prognostic value is debated.[15,16] Although it should not impact on the treatment strategy and counseling, fetal echocardiography may be added to this initial assessment to evaluate cardiac function in the recipient twin.

Counseling before surgery is optimally based upon gestational age, fetal status and cervical length at presentation. The choice of the appropriate treatment strategy is a strong determinant of prognosis in TTTS. Surgical technique itself has been shown to be an important factor of perinatal mortality and neurological morbidity. The evolution of surgical techniques has resulted in improved outcome over the past 20 years together with increasing complexity of prenatal care in these cases.

In most developed countries, prenatal care for TTTS is managed by a small number of specialized centers that can offer training and experience for diagnosis and counseling as well as surgical skills and specialized perinatal management. Ideally, referral to specialized centers should be organized through a specific network, thus reducing the time interval between diagnosis and treatment. Since percutaneous laser coagulation of placental vessels has been shown to be the best first-line treatment for overall TTTS in an international randomized trial, this network should be articulated around centers that can offer such treatment. Conversely, referral to a non-specialized center with suboptimal first-line treatment such as amniodrainage may strongly impede the prognosis by making a second-line fetoscopy impossible or technically challenging in cases with intra-amniotic bleeding or membrane tenting following amniodrainage. The development of such networks was made possible by the increasing awareness and early recognition of MC twins' specific complications as well as improvement in treatment options.

Table 1
Initial assessment

Diagnosis	Chorionicity known. DVP >8 cm (<20 weeks), DVP >10 cm (>20 weeks) + distended bladder DVP <2 cm + small or no visible bladder
Biometry	IUGR in the donor twin
Anatomy scan	Pre-existent brain damage Pleural, pericardial effusion, ascitis, overt hydrops Malformations
Doppler	UA: PI and diastolic flow DV: PI and 'a'-wave MCA: PSV
Echocardiography	Specific cardiomyopathy in the recipient.
Cervical length	Short cervix <15 mm Funneling

DVP, deepest vertical pool; IUGR, intrauterine growth restriction; UA, umbilical artery; PI, pulsatile index; DV, ductus venosus; MCA, middle cerebral artery; PSV, peak systolic velocity.

Table 2
Quintero staging system

Stage I	Both bladders are still visible No Doppler anomalies
Stage II	The bladder is invisible in the donor twin No Doppler anomalies
Stage III	Doppler anomalies in either twin: AREDF in the UA Absent or negative 'a' wave in the DV Pulsatile flow in the UV
Stage IV	Pleural effusion, pericardial effusion, ascitis or hydrops in either twin
Stage V	Death of one twin

AREDF, absent/reversed end diastolic flow; UA, uterine artery; DV,; UV,.

2.2. Treatment options in TTTS

Therapeutic options include specific and non-specific treatments. Non-specific strategies include expectant management, amniodrainage and septostomy. The only specific treatment is selective laser coagulation of placental vessels (SLCPV) since it targets the placental anastomoses that underlie the pathogenesis of the syndrome. Depending on gestational age at diagnosis and fetal status, cord coagulation and elective preterm delivery can also be considered whenever appropriate.

2.3. Fetoscopic laser coagulation of placental anastomoses

The rationale for fetoscopic laser coagulation is to interrupt the chorionic anastomoses between the twins' circulations, thus stopping the hemodynamic imbalance that defines the syndrome. Therefore, the goal of SLPCV is to virtually 'dichorionize' an initially MC placenta.

Initially performed by laparotomy,[17] the technique was greatly simplified by a minimally invasive percutaneous approach under local or epidural anesthesia that has transformed the prognosis of the disease.[18–22] Although SLPCV requires specific training and equipment, it is now widely used as first-line treatment in overall TTTS. Amnioreduction concludes the procedure in order to relieve most of the intrauterine pressure. Cerclage seems indicated and can be performed whenever the cervix is found short <15 mm (5th centile) following surgery. These are the only cases that benefit from epidural analgesia allowing for the two procedures to be performed in the same operative time.[23]

Survival rates of at least one twin following SLPCV range between 65% and 85%, whereas survival of both twins ranges between 35% and 50%.[1,18,19,21,22,24,25] Although several retrospective studies have shown improved outcome following SLPCV compared to amnioreduction, only one completed randomized trial has compared both strategies at between 16 and 26 weeks, showing the overall superiority of SLPCV both in terms of survival and neurological morbidity but also gestational age at delivery.[1]

Maternal morbidity following SLPCV is minimal.[1,26] The risk of placental abruption is no higher than that following amnioreduction and occurs in about 1% of the cases, mostly for drained volumes exceeding 4 L. The most frequent obstetrical complication is preterm premature rupture of membranes (PPROM) <34 weeks which occurs in 28% of cases and mostly during the 3–4 weeks following the procedure.[26] Miscarriage, defined by a delivery <24 weeks, occurs in 5–23% of cases.[18,26–28]

The optimal treatment strategy for Quintero stage I cases remains controversial, since few data exist regarding the

superiority of SLPCV in this subgroup. Three retrospective studies have shown that the disease is progressive in only 30–45% of these cases, meaning that the remaining would probably not require an invasive procedure.[29–31] Therefore in these cases, expectant follow-up might be considered an alternative to SLPCV. An international randomized trial (TTTS1) specifically addressing this question will soon commence.

2.4. Amnioreduction

Amnioreduction was long considered the reference treatment for TTTS. The rationale is to serially relieve the intrauterine pressure by draining the excess of fluid from the polyhydramniotic sac and thus prevent miscarriage and prolong the pregnancy. The underlying mechanisms of the syndrome persist, and, depending on the severity of the condition, multiple procedures are usually required until the pregnancy reaches an acceptable gestational age for elective preterm delivery to be performed. In our experience, a 1–2 week interval between procedures is generally sufficient.[1]

Despite its apparent simplicity, this procedure carries a high rate of complications such as PPROM, placental abruption and chorioamnionitis. The overall prognosis displays a wide variability across studies with twin survival rates ranging from 40% to 80% together with a 5–50% rate of neurological morbidity in the survivors and a mean gestational age at birth of 28 weeks.[32–37]

2.5. Septostomy

The rationale for septostomy is to artificially relieve the pressure in the polyhydramniotic sac by needle-opening the inter-twin membrane, therefore letting the amniotic fluid flow freely from one sac into the other. Although two randomized trials yelded similar survival rates with amnioreduction and septostomy[38,39] the latter is at risk of severe complications related to iatrogenic pseudo-monoamniocity, such as cord entanglement, although this has not been specifically addressed in published work. Furthermore, as in amnioreduction, the procedure needs sometimes to be repeated. Overall, septostomy has been abandoned by most teams.

2.6. Cord coagulation

Spontaneous intrauterine fetal death occurring in MC pregnancy carries a 40% to 50% risk of adverse outcome in the surviving twin, based upon small retrospective studies.[40,41] Acute anemia secondary to massive blood transfer from the survivor into its dead co-twin and placenta may result either in fetal death or in neurological damage. Therefore, selective termination in MC twins mandates complete and permanent interruption of blood flow in the cord to prevent acute exsanguination in the survivor. Cord coagulation may be considered a form of therapy in TTTS whenever the prognosis of one twin is considered dismal with a high risk of spontaneous intrauterine death, thus making laser dichorionization hazardous. Indeed placental injection studies have shown that coagulation is incomplete after FSLC in up to 20% the cases.[42] Indications may comprise malformation, neurological damage and extreme intrauterine growth restriction (IUGR) of one twin.

Several techniques have been suggested, including cord ligation, intrahepatic radiofrequency occlusion, monopolar or bipolar forceps coagulation. In a recent systematic review, bipolar forceps appeared to be the safest option.[43] Survival rates are generally above 80% in most series[43–45] together with a normal neurological outcome in 90% of these cases.[44] However, the prognosis seems strongly related to gestational age at surgery with strikingly lower survival rates for procedures performed before 18 weeks.[43,44] As for SLCPV, cord coagulation carries a 23% risk of PPROM <34 weeks.[43,44]

Aside from ethical considerations, three reasons strongly suggest that cord coagulation should not be considered a first-line treatment in overall TTTS cases and should only be considered in specific indications:

1. It is impossible to predict which one of the twins would die if intrauterine fetal demise (IUFD) should follow SLCPV.
2. Gestational age at delivery is identical in cord coagulation and SLCPV.
3. Cord coagulation is technically challenging even in experienced hands.

2.7. Specificities of TTTS >26 weeks

Although most cases are diagnosed at around 20–21 weeks, TTTS can occur in late pregnancy, meaning that close follow-up should be maintained up until delivery. Because of iatrogenic risks and technical difficulties, most centers generally agree on a 26 week upper limit to perform SLCPV. However, improvement in the technique and outcome legitimately raises the possibility of extending this limit. A small retrospective work comparing amnioreduction and SLCPV after 26 weeks has shown a 100% survival rate with similar gestational ages at delivery but with a lower neurological morbidity in the group treated by SLCPV.[46] However, SLCPV is challenging after 26 weeks, mostly because of technical reasons including difficult visualization of the whole placental surface and the size of the vessels. Technical feasibility should therefore be carefully assessed prior to deciding upon surgical management, and in most cases, planned delivery following amnioreduction and steroid administration for lung maturation appears the most reasonable option for TTTS occurring >26 weeks.

2.8. Strategies, follow-up and complications

Despite improved prognosis, patients treated by SLCPV are still at risk of complications until delivery and should be monitored closely. In our unit, once the early postoperative period has been reached, patients are monitored on a weekly basis. This follow-up aims to detect anemia–polycythemia sequence, recurrence of TTTS, growth restriction and subsequent brain damage of one or both twins.

2.9. Surgical failure

Surgical failure is defined by postoperative symptomatic patent anastomoses. Two situations may occur as a consequence of patent anastomoses: recurrence of TTTS and fetal anemia. Although patent anastomoses may be found in one-third of cases on placental studies following SLCPV,[47] surgical failure occurs in up to 18% of cases,[21] the rest leading to otherwise uncomplicated pregnancies.

2.10. Anemia

The Doppler measurement of peak systolic velocity in the middle cerebral artery (PSV-MCA) is an easy, non-invasive and reliable method to assess the risk of postoperative fetal anemia following surgical treatment of TTTS.[48] Two mechanisms can result in postoperative fetal anemia:

1. Twin anemia–polycythemia sequence (TAPS). A paradoxical transfusion may occur following SLCPV as a consequence of one or few small persistent anastomoses with a unidirectional net

blood shift from one twin to the other, usually from the ex-recipient to the ex-donor. The diagnosis is suspected whenever PSV-MCA >1.5 multiple of the mean) MoM in one twin defining anemia and PSV-MCA <0.8 MoM in the co-twin assumed to be polycythemic.[49]
2. Postoperative fetal demise with concurrent exsanguination of the survivor into the dead twin and its placenta. The diagnosis is suspected if the PSV-MCA >1.5 MoM in the survivor.

In both cases, FBS can confirm the diagnosis and a fetal transfusion can be given concurrently. In our experience, postoperative anemia occurs in 9% of cases.[21]

In cases complicated by TAPS, several iterative transfusions are sometimes necessary since the anastomosis remains patent. In some cases, repeat laser may help if the surgeon is able to identify the responsible anastomosis. In other cases, cord coagulation may appear as the only option. Overall survival in these cases approximates 80%.[49]

In a small retrospective study on survival following rescue intrauterine transfusion after IUFD of one twin, the outcome was favorable in 7/11 (64%) cases.[41] However, the rationale for transfusion is ill-defined: it may prevent demise, but it probably does not prevent cerebral damage.

2.11. Recurrence of TTTS

Recurrence occurs in the same proportions as TAPS, sometimes weeks after the first procedure. The diagnosis is based on ultrasound as described before but often disclosing early signs with recurrent/persistent anuria in the donor, often preceding recurrence of polyhydramnios. Difficult primary procedures appear to be a risk factor for subsequent recurrence.[21] Depending on technical conditions and anticipated surgical difficulties, gestational age and fetal status, treatment options include repeat laser, amniodrainage and cord coagulation with an overall perinatal survival rate of 40%.[49]

2.12. Neurological damage

Because of the underlying angioarchitecture of their placenta, MC pregnancies are at risk of brain damage, especially following acute hemodynamic insults. The spectrum of brain lesions is not specific for MC twins nor for TTTS, they rather belong to the wide spectrum of disruptive vascular injury for which TTTS is one of many causes. Prenatal imaging can reliably diagnose brain damage in 5–14% of cases following SLCPV, in either the donor or the recipient.[50,51] Sonographic findings cover the whole spectrum of ischemic–hemorrhagic damage. Following postoperative fetal demise of one twin, neurological damage occurs in about 10% of cases.[52] In most cases brain damage becomes visible on ultrasound only 1 month to 6 weeks after the insult.[41]

Compared to SLCPV, amnioreduction carries a significantly higher neurological morbidity that is probably related to ongoing acute transfers through the anastomoses left uncoagulated in these cases.[1]

Fetal MRI performed at around 31 weeks may be a useful adjunct to ultrasound for postoperative screening of brain injury in high risk situations.[53]

2.13. Other complications

Aside from syndrome-related cardiac manifestations in the recipient twin and brain damage, numerous vascular manifestations have been described as a result of either MC twinning itself, TTTS or its treatment, including aplasia cutis, limb ischemia, and bowel atresia. Pseudoamniotic bands have been reported as a consequence of membrane laceration following invasive procedures in TTTS.[54] These occur in about 1–2% of cases and may lead to limb ischemia or amputation.

2.14. Long term follow-up

The Eurofoetus multicentre randomized trial has shown that in severe TTTS treated before 26 weeks of gestation, laser therapy resulted in higher survival rates and better neurologic outcomes than did amnioreduction, both in the perinatal period and during the first 6 months of life.[1] More recently, these results have been confirmed by a Cochrane systematic review which stated that 'Endoscopic laser coagulation of anastomotic vessels should be considered in the treatment of all stages of TTTS to improve perinatal and neonatal outcome.'[1,55] However, the current level of evidence did not determine whether treatment with laser coagulation increases or reduces the risk of neurodevelopmental delay or intellectual impairment in childhood compared with other therapies. Indeed, uncertainty about long term neurological outcome remains a major concern for both parents and physicians.[56,57]

Cognitive and motor developmental delay are relatively common and have been related to both fetoscopic selective laser coagulation (FSLC) and AD.[34,58–62] Long term follow-up studies report abnormal neurodevelopment in up to 6% to 17% of the cases at 2 years of age. Lopriore et al.[51] reported the highest rate in 82 cases, including cerebral palsy (7%), severe mental delay (8%) and deafness (1%), using the Bayley Scales of Infant Development (BSID-II). De Lia et al.[63] reported a 6% rate of a composite abnormal neurological development at 14 months of age.[17] Banek et al.[59] and Graef et al.[58] reported 11% (10/89) and 6% (6/111) rates of abnormal neurodevelopment considering only severe abnormalities; [58,59] these authors did not find any difference between former donors and former recipients, as confirmed in the meta-analysis by Rossi et al.[64]

We have addressed this issue in the prospective long-term follow-up of the 128 cases that were delivered in France within the randomized Controlled Eurofetus Trial,[1] for neurological and neurodevelopmental evaluation at up to 6 years of age.[65] Primary outcome was a composite of death and major neurological impairment.

There were no additional deaths up to the end of follow-up for the 120 infants who were alive at the age of 6 months. At the end of the 6-year follow-up, 60 (82%) and 33 (70%) of the children had a normal neurological evaluation in the FSLC and AD treatment groups respectively ($P = 0.12$). The overall rate of major neurological abnormalities was 12% and was consistent with rates reported in the literature.[51,58–62] In multivariate analysis, treatment group and Quintero stage at diagnosis remained significant predictors of a poor outcome [hazard ratio (95% confidence interval): 0.61 (0.41; 0.90), $P = 0.01$; 3.23 (2.19; 4.76), $P < 0.001$ respectively]. Infants treated in the laser group had higher ASQ scores at the age of 5 years (60 months): 261.3 ± 53.7 vs 228.6 ± 79.1, $P = 0.04$. This study demonstrates that at the time of decision-making, FSLC therapy is associated with an almost 40% reduction in the risk of fetal death or long-term major neurological impairment and that infants treated in the FSLC group have higher ASQ scores at the age of 5 years (60 months).

Long-term follow-up of TTTS survivors following FLSC has also assessed cardiological and endocrine functions. Although these fetuses are genetically identical they were subjected to opposite hemodynamic and metabolic conditions during fetal life. Long-term cardiological follow-up of 89 fetuses born alive after intrauterine treatment of TTTS by FSLC laser at a mean age of 21 months showed that 10 (11%) of the former recipient twins presented abnormal

Table 3
Methods used for cord coagulation of the acardiac mass in TRAP sequence

Reference	Method	No. of cases operated	GA (weeks) at treatment	Treatment delivery interval (weeks)	Pump twin survival	Remarks
Ville et al.[20]	Laser coagulation	4	22.75	11	100%	Two failed coagulations and an intrauterine transfusion in one of these two cases
Quintero et al.[94]	Percutaneous umbilical cord ligation	10	21.6	4.1	50%	Two failed ligation among the survivors
Deprest et al.[95,96]	Laser coagulation and ligation	3	22	6	66.7%	One case required two ligations as first one was incomplete
Rodeck et al.[82]	Thermocoagulation with a wire electrode	4	17.5	18.75	100%	
Arias et al.[77]	Various invasive procedures	22	21.8	N/A	86.3%	Two births at 25 weeks
Sepulveda et al.[97,98]	Absolute alcohol injection into the intra-abdominal umbilical artery l	3	25.3	6.2	100%	0ne birth at 25 weeks
Deprest et al.[93]	Bipolar coagulation	5	19.8	13.6	80%	Dislodgment of membranes at port insertion and PPROm 2 days after surgery (19weeks)
Holmes et al.[99]	Monopolar thermoocoagulation	11	20.4	17.2	73%	
Soothill et al.[100]	Intra-abdominlal laser	2	17.5	20.5	100%	One incomplete occlusion for at least 2 weeks
Tsao et al.[83]	Radiofrequency ablation	13	20.7	15.5	92.3%	One neonatal death after birth at 24.4 weeks
Tan et al.[89]	Various techniques	71	20	15	76%	25.3% failure rate
Robyr et al.[44]	Bipolar cord coagulation	17	18.6	13.2	64.7%	Two surgical failures And two neonatal death (birth at 26 and 28 weeks)
Hecher et al.[101]	Laser coagulation of placental anastomoses or the umbilical cord	60	18.3	19.1	80%	Two neonates developed periventricular leukomalacia. One case of ventricular septal defect
Lewi et al.[45]	Laser and bipolar cord coagulation	22	~21	~14.4	74%	One intra-operative cord perforation
Quintero et al.[102]	Various techniques for umbilical cord occlusion	51	21.2	8.6	65%	Author insists on the influence of surgical access on PROM
Lee et al.[103]	Radiofrequency ablation	29	Between 18 and 24	Mean gestational age at delivery 34.6	86%	Two thermal injuries at the site of the grounding pads
Livingston et al.[78]	Radiofrequency ablation	17	21	16	94%	Four undelivered at the time of report
O'Donoghue et al.[104]	Interstitial laser therapy	10	16.6	12.7	60%	One failed surgery at 12 weeks
He et al.[105]	Bipolar cord coagulation	4	22.8	10.6	50%	One failed cord occlusion

TRAP, twin reversed arterial perfusion; GA, gestational age.

pulmonary artery and valve dysfunction including pulmonary stenosis in 8% (95% confidence interval: 2.2–18.9).[66] Masche et al. is the only one who studied pre- and postnatal growth after intrauterine laser therapy.[67] Moreira et al.[68] and Chmait et al.[69] had already noted that laser therapy can prevent donor twins from further growth restriction by stopping the chronic blood loss towards the recipient twin, and leads to maintenance of the donor's growth. Masche confirmed that the growth restriction of the donor and the accelerated growth of the recipient are stopped after laser therapy and that at a median age of 4 years, the difference in weight and height between donors and recipients seems to be overcome, although Duncombe et al.[70] showed that a significant growth discordance between donors and recipients persists in cases managed with serial amnioreduction. The next issue to be addressed in the long term relates to the well-established observation that children born small for gestational age have an increased risk of developing high blood pressure, metabolic disease and diabetes later in life.[71,72] This could therefore also apply to former donor twins in TTTS. Follow-up studies are currently being conducted.

2.15. Conclusion

Since most of the suggested classifications of the disease have failed in providing accurate preoperative prognostic stratification, the best remaining is the treatment strategy itself. Percutaneous fetoscopic laser coagulation is now widely used as first-line treatment. Although this statement is true in the overall population of TTTS, alternative options should be considered in specific indications. Before 26 weeks, amniodrainage should be considered only if referral to a laser-equiped specialized center is impossible because it will strongly impede the chances of rescue laser. This should also discourage a test amniocentesis before referral even if the intention is to lower the level of emergency in symptomatic patients. After 26 weeks, amniodrainage, steroids and planned delivery is the most reasonable option although SLCPV may be considered in selected cases.

Because of a high risk of subsequent complications remaining after SLCPV, close monitoring is warranted until delivery, focusing on Doppler studies and potential brain damage. Magnetic resonance imaging planned at around 31 weeks may screen these high risk patients for neurological injury.

Secondary surgical failure defined by TAPS or recurrence impacts the prognosis markedly. In these cases, the treatment strategy depends upon the fetal and obstetrical status as well as technical factors that influence surgery.

3. Twin reversed arterial perfusion (TRAP) sequence

TRAP sequence or acardiac twining occurs in 1% of MC pregnancies. Two conditions are necessary for its development.[73] Circulatory failure should occur in one of the two twins of a MC pregnancy, at around between 8 and 12 weeks of gestation. This

embryologically twin mass is usually abnormal[74] and the TRAP sequence is characterized by a specific angioarchitecture defined by an arterio-arterial and a veno-venous inter-twin anastomosis that supports the development of an abnormal twin (acardiac twin) that would not have developed further on its own. Heterokaryotypic monozygotism, such as aneuploidy, has been discussed as a possible aetiological factor of TRAP, most likely when this karyotype abnormality arises after splitting of the fertilized ovum.[75] The acardiac twin often presents with other severe malformations[73] to such an extent that it seems appropriate to call this a mass or a tumor rather than a fetus, especially when counseling the pregnant woman.

The acardiac twin is hemodynamically dependent on his healthy co-twin supporting the hemodynamic burden of this parasite twin. The growth of the acardiac twin threatens the survival of the pump twin by increasing the risk of congestive cardiac failure, IUFD, polyhydramnios, PPROM, preterm labor, and premature delivery. Perinatal mortality rates for the pump twin have been reported to be around 35–55%.[74,76,77] Surgical management significantly improves survival, with survival rates of around 74–94%.[45,78]

However, the optimal management strategy remains ill-defined. Expectant management presents high risk of heart failure in the pump twin.[74,76,79] The rationale of surgical procedures is the interruption of the vascularization of the acardiac twin for which several techniques have been described: ultrasound-guided fetal cord ligation or compression,[80] bipolar coagulation, laser coagulation, transsection with harmonic ultrasound scalpel,[81] thermocoagulation[82] and radiofrequency ablation[83] (Table 3). Although prognostic ultrasound markers have been reported,[84–86] data regarding the optimal gestational age for selective reduction are still limited. Cord coagulation using a bipolar forceps is a reliable technique with 74% survival of the normal co-twin for Lewi et al.,[45] 70% for Robyr et al.,[44] 77% for Diehl et al.,[87] 76% for Nicolini et al.,[88] 80% for Hecher et al.[79] as well as the 76% survival rate of the literature review of Tan et al.[89] 76%. Recently, some authors[78,83,89] suggested the superiority of intrafetal ablation (radiofrequency mainly) when compared to extrafetal coagulation (laser, bipolar etc.). Their main argument does not concern the survival rate, as it remains comparable between these techniques (76% and 71.4%). The main argument[89] was a 23% prematurity rate for radiofrequency which is significantly less than the 58% rate reported with other techniques ($P = 0.003$).

Two studies[86,87] evaluating the surviving pump twins reported that interventions at an advanced gestational age, following the development of signs of cardiac decompensation, carry a higher risk of cardiac complications[90] and unfavorable neurological outcome.[86,87,91] These complications may be related to the prolongation of the underlying pathology, the consequences or relative failure of the surgical procedure or else to the related prematurity.[86] In TRAP sequence, early diagnosis may therefore allow early intervention in order to protect and save the normal twin.[83] In a recent retrospective review, Lewi et al.[92] report the natural history of TRAP sequence from diagnosis, between 11 and 13 weeks' gestation, to planned intervention at 16–18 weeks, as the policy in most centers involved in fetal surgery is to perform prophylactic intervention at 16–18 weeks after obliteration of the coelomic cavity.

They followed 24 cases of TRAP sequence diagnosed in the first trimester, which opted for prophylactic surgery at 16–18 weeks to arrest the reversed flow. Spontaneous death of the pump twin occurred between diagnosis and planned intervention in 33% of the cases while 21% manifested with spontaneous arrest of flow to the acardiac twin. Prophylactic surgery was performed in 46% ($n = 11$) of the cases with persistent flow towards the acardiac mass at 16–18 weeks. The technique used was intrafetal coagulation of the abdominal area next to the cord insertion by introducing a Nd:YAG laser fiber through an 18-gauge needle under ultrasound guidance. They report a 90% survival rate in these cases with 90% of the deliveries occurring after 32 weeks.

Further evaluation of less invasive techniques should be pursued. At the present time we support the use of bipolar forceps for cord coagulation to be performed electively, before viability and before signs of decompensation or compromise of the pump twin arise.[83,86] Although this procedure can be performed from 16 weeks onwards,[20] we recommend 18 weeks as a threshold unless the progression of the disease indicates otherwise since we hypothesize that surgery after 18 weeks, as in TTTS, could minimize the trauma made to the uterus and the membranes.

3.1. Conclusion

The use of bipolar forceps for cord coagulation in TRAP sequence can still be viewed as the gold standard for cord coagulation when performed from 18 weeks onwards,[93] ensuring controllable, complete and permanent cord obstruction. It is relatively simple and widely available.[93] Larger series exploring earlier and less invasive techniques are needed before these can be viewed as validated alternatives.

Practice points

- Monochorionic twins cannot be managed independently from each other.
- Spontaneous death of one MC twins poses a significant risk to its co-twin.
- Selective coagulation of chorionic plate anastomoses is best achieved by fetoscopy guided laser surgery.
- Selective cord coagulation is best achieved using ultrasound-guided cord coagulation.

Research directions

- Pathophysiology of twin-to-twin transfusion syndrome is incompletely understood and may hinder other forms of less invasive management.
- The management of isolated oligo-poly-hydramnios sequence, or stage I TTTS, the superiority of laser surgery over expectant management is currently under investigation in an international RCT.
- Alternative techniques to bipolar coagulation for selective fetocide in MC twins should be explored in order to offer first or early second trimester interventions.

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None declared.

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