Placental surgery in complicated monochorionic pregnancies. Handling maternal-fetal conflict of interest

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Monochorionic (MC) twins account for 20% of spontaneous twin pregnancies and almost 5% occur as a result of medically assisted reproduction [6]. In view of the rising rate of pregnancies in older women and the frequent recourse to assisted reproduction techniques, the incidence of MC twin pregnancies is increasing [1].

Monochorionic (MC) twins are characterized by their interdependency through a shared placental mass and fetoplacental circulation [11]. They are therefore subjected to specific and serious complications responsible for severe perinatal complications [17]. 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

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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 1/ addressing the cause of the disease, such as in twin to twin transfusion syndrome (TTTS) or twin reversed arterial perfusion sequence (TRAP) sequence, or 2/ in order to prevent the consequences of the death of one twin for the survivor, such as in selective severe growth restriction or lethal abnormality in one MC twin [3].

I. FETOSCOPY AND ULTRASOUND GUIDED PROCEDURES USED IN PLACENTAL SURGERY FOR COMPLICATED MONOCHORIONIC PREGNANCIES

Placental surgery is either one of two types:

1. fetoscopic selective laser coagulation of placental vessels (FSLCPV) aiming at separating the two placental territories as fairly as possible and aiming for the survival of both twins, or at least decreasing the risk of damage to the survivor in case one twin dies after the procedure;
2. selective umbilical cord permanent occlusion, aiming at terminating one MC twin while protecting the co-twin the direct consequences of a single IUFD in MC twins.

Both types of surgery can be performed under local anesthesia (1% xyocaine or 1% lignocaine) is injected from skin to myometrium, a small skin incision is performed. A cannula is inserted percutaneously under ultrasound guidance, preferably in an area devoid of placenta. Instruments either laser-loaded fetoscope or bipolar forceps can then be passed down the operative canula, using only one port. Irrespective of the strategy chosen, the prognosis seems strongly related to gestational age at surgery with strikingly lower survival rates for procedures performed before 18 weeks [16, 20].

I.1. Fetoscopic selective laser coagulation of placental vessels

The goal of surgical intervention is to ablate all intertwin anastomoses [19]. Theoretically, the latter run on the surface of the chorionic

plate and can be identified as arterio-venous, arterio-arterial or venovenous anastomoses by following them towards both end insertions, although this may be difficult or impossible towards the donor. They should be left intact when the examination confirms that they belong to just one twin. This requires appropriate visualization as well as a reasonable angle of the laser fiber to the vessels. The above are a function of placental location, fetal position and the transparency of the amniotic fluid and of the membranes. When the placenta is anterior, access through anterior abdominal wall becomes more difficult. There is also continuing debate on the selection of chorionic plate vessels to be coagulated. We initially overcame this problem by coagulating all vessels crossing the dividing membrane [21]. Although the reproducibility of this technique was clear, we learned that as a result of the polyhydramnios in the recipient's sac, the location of the dividing membrane is pushed towards the placental territory of the donor twin and its anatomical location bears little relationship to the actual distribution of the vascular territories of the two fetuses. Whilst this technique effectively interrupts vascular communications between the two fetuses, many donor vessels visible on the recipient's side of the membrane will be unnecessarily coagulated reducing the vascular territory of the donor, and exposing this twin to a potentially higher risk of fetal death. Identification of the anastomoses led to a more selective approach to coagulate only the vessels involved in blood exchange between the fetuses. We introduced an index of selectivity (S) as the ratio of selective over NSCs (adding one to the numerator and to the denominator to prevent having zero). This index was designed to describe both the proportion as well as the total number of each type of coagulation. In terms of survival of at least 1 twin and survival of both twins at 28 days postnatal, our results showed a clear benefit of selective surgery, especially for the donors whose survival was significantly higher. Although a cutoff value of $S = -0.25$ was justified for high selectivity by a clear-cut difference in perinatal outcome, further studies are still needed before considering this particular cutoff as a prognostic factor in itself [20].

I.2. Selective and permanent occlusion of the umbilical cord of one twin

The goal is to occlude at once and permanently all vessels of the umbilical cord of one MC twin or an acardiac mass. Several techniques have been suggested, including cord ligation, intrahepatic radio-

frequency occlusion, monopolar or bipolar forceps coagulation. In a recent systematic review, bipolar forceps appeared to be the safest option (Rossi *et al.* 2009) [16]. Survival rates are generally above 80% in most series together with a normal neurological outcome in 90% of these cases [14].

II. SPECIFIC CONSIDERATIONS BY INDICATION FOR SURGERY

II.1. Twin-to-twin transfusion syndrome

Most of the suggested classifications of the TTTS disease have failed in providing accurate preoperative prognostic stratification, and therefore 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 the overall severity of the disease as well as the uncertainty over the outcome of a pregnancy diagnosed with severe TTTS, one could also listen to the request for termination either selective cord occlusion of the most severely affected twin or of the whole pregnancy.

A high risk of subsequent complications remaining after successful SLCPV, and 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.

Recurrence of TTTS can occur up to several weeks after the first procedure, emphasizing the need for continuous ultrasound surveillance until delivery. In our experience, the recurrence rate is 8.9% of which 11% were stage 1, 43% stage 2, 45% stage 3, and 1% stage 4. This

is compatible with the 0-14% recurrence rate reported in the literature [4]. As would be expected, recurrence of TTTS (10.1%) was significantly more frequent in the low-selectivity group [20]. Recurring TTTS is a very complex problem whose therapeutic approach is not yet defined. Repeat laser procedure for recurrent TTTS is commonly quoted to be difficult [4]. Depending on technical conditions, gestational age, placental position and fetal status, with an overall perinatal survival rate of 50% [4].

Placental anastomoses may still be present even in successfully treated cases in up to 20% of the placentae examined after delivery [10].

Twin-Anemia-Polycythemia Sequence (TAPS) results from a unidirectional blood shift from one twin to the other, usually from the ex-recipient to the ex-donor, and is suspected when a discordance is found in the measurement of the peak systolic velocity in the middle cerebral artery (PSV-MCA): PSV-MCA >1.5 multiple of the mean (MoM) in one twin (anemic) and PSV-MCA <0.8 MoM in the co-twin (polycythemic) [15]. Fetofetal exsanguination following post-operative fetal demise results in exsanguination of the survivor into the dead twin. The diagnosis is suspected if the PSV-MCA >1.5 MoM in the survivor [18]. The resulting anemia in either one of these complications (9% of cases) can be confirmed by fetal blood sampling, and then be treated by a single or multiple intrauterine blood transfusions. In some TAPS cases, a repeat laser is performed to target the responsible anastomosis. However, although transfusion might improve survival in single survivors, it is uncertain whether it prevents cerebral damage [13].

In these cases, the treatment strategy depends upon the fetal and obstetrical status as well as technical factors that influence surgery, inasmuch as upon the women's appraisal of the likely outcome and surrounding uncertainties.

II.2. Selective intrauterine growth restriction

Monochiorionic diamniotic twin pregnancies complicated with severe intra-uterine growth restriction (IUGR) of one twin before 24 weeks with continuous or intermittent absent- or reversed-end-diastolic-flow (AREDF) in the umbilical artery, pose a double challenge: survival of the affected twin is very compromised and the consequences of its spontaneous death in utero is a major threat to its co-twin.

Active management of these cases seems therefore justified either with the aim of a fair separation of placental territories using SLCPV

or selective coagulation of the umbilical cord (CC) of the severely growth retarded twin.

Active management of severe IUGR with AREDF in the umbilical artery seems beneficial [5]. Survival rates with SLPCV are similar in selective-IUGR and TTTS3D. However, there is a trend for higher survival rates in the AGA-twin for CC. The choice of the technique should be driven by objective counselling on survival of both IUGR and AGA-twins and therefore utility values expressed by the pregnant woman.

II.3. Primary Twin Anemia Polycythemia Sequence (TAPS)

TAPS occurs primarily in 1-3% of all otherwise seemingly uncomplicated monochorionic pregnancies [8]. As described in post-operative cases Doppler measurement of peak systolic velocity in the middle cerebral artery (PSV-MCA) is an easy, non-invasive and reliable method to assess fetal anemia / polycythemia sequence.

Depending upon gestational age at diagnosis, technical conditions, and potential irreversible damage suspected in one or both twins, management options encompass SLCPV, intrauterine blood transfusion(s), elective preterm delivery of both twins, selective cord coagulation or termination of the whole pregnancy.

II.4. Twin-Reversed-Arterial Perfusion (TRAP) Sequence

TRAP sequence or acardiac twining occurs in 1% of MC pregnancies. The angioarchitecture of the placenta in these MC pregnancies is characterized by the perfusion of a partially developed twin-mass by a normally formed fetus (pump-twin) through an artery-to-artery anastomosis. This could occur either as the result of an early cardiac malformation and prolonged retrograde perfusion of one of two twins or the maintenance of a heterokaryotypic embryonic mass made possible only by the monochorionic structure of the placenta [2].

The healthy co-twin supports 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%. Surgical management significantly improves survival, with survival rates of around 74-94% [3]. The rationale of

surgical procedures is also the occlusion of the umbilical vascularization of the acardiac mass.

When prenatal diagnosis is made in the first or early second trimester prior to cardiac decompensation of the pump-twin, a dilemma is early intervention *versus* heightened surveillance with a theoretical chance of around 50% for no intervention being necessary either because the acardiac mass would lose its vascular supply spontaneously or before an elective delivery in the third trimester. Interventions at an advanced gestational age, following the development of signs of cardiac decompensation, carry a higher risk of cardiac complications and unfavorable neurological outcome [3]. Early diagnosis followed by serial examination with the aim to plan an elective procedure from 18 weeks' onwards would probably see around 1/3 of the pump twins to die in the interval while the blood flow to the acardiac mass would have stopped by then in up to 1/5 cases, leaving about 50% of the cases diagnosed up for fetal intervention which is usually associated with an 80-90 % survival rate [11].

II.5. Severe malformation in one monochorionic twin

Despite MC twins are monozygotic, the co-twin of malformed MC twin is structurally normal in around 80% of the cases.

When the malformation is either lethal *in utero* or is amenable to selective termination of pregnancy under the relevant law, selective fetocide can be performed using cord occlusion techniques as described above in other indications.

Although the overall survival for the normal twin is around 80% when the procedure is performed in the second trimester, selective termination performed in the third trimester would avoid most losses related to late miscarriage, leading to preterm delivery instead [9, 14].

III. MATERNAL COMPLICATIONS OF INTRAUTERINE SURGERY

General anesthesia could be avoided in the procedures described in this paper, local or at most regional anaesthesia being sufficient at a lower risk to the woman [7, 23]. In our experience, procedure-related complications include painful amniotic fluid leakage into the maternal

peritoneal cavity in the immediate postoperative period and post-operative pain at the point of entry (7-9%) requiring supplemental analgesia with opioids, vaginal bleeding leading to miscarriage (4-7%) preterm premature rupture of the membranes in up to 17% of the within 3 weeks of the procedure and including clinical chorio-amnionitis in 2-3% of the cases. However the most severe direct complication reported seems to be placental abruption (1-2%) [12]. Merz *et al.* (2012) attempted to collect all maternal complications following FSLCPV and not surprisingly found that these were under-reported and could reach a 17% rate in papers using a systematic reporting system with up to 2% severe complications. These included placental abruption, severe chorioamnionitis, mirror hydrops and amniotic fluid embolism which could potentially be fatal.

Although maternal complications following fetoscopy or ultra-sound guided intrauterine surgery are fewer than reported with open fetal surgery, and although there is no literature available to compare these complications to those expected following second trimester termination of pregnancy in these indications, women should be made aware as part of their counseling.

DISCUSSION

Monochorionic pregnancies present with a prospective risk of developing a specific complication, potentially lethal for one or both twins of 10-25% [17]. The diagnosis of either one of these complications is usually made in the second trimester. Effective surgical management has been developed and is likely to be indicated in over half of these cases. Although the prognosis can only be tailored to individual cases and mostly following surgery, overall survival is broadly around 50% which justifies discussing the options of selective termination or termination of the whole pregnancy. Both maternal and fetal interests might be challenged further in countries limiting termination for medical indication up to the second trimester, since the prognosis of these pregnancies can only best assessed in the third trimester. This is likely to lead to an excess in TOP in cases which could have led to a favorable outcome in as much as to force women to continue their pregnancy with one or two severely affected fetuses [22].

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