Placental characteristics and complications in monochorionic twin pregnancies

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Chapter 7

Laser surgery in twin-twin transfusion syndrome with proximate cord insertions

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Abstract

Objective: To estimate the prevalence of proximate cord insertions in twin-twin transfusion syndrome (TTTS) and evaluate the outcome after fetoscopic laser coagulation surgery.

Methods: We included all TTTS cases treated with laser at our center between 2002 and 2013. Placentas were examined after birth and injected with colored dye. TTTS cases without complete placental injection study were excluded. We recorded the presence of proximate cord insertions (distance < 5cm) after birth and the presence and types of residual anastomoses. We compared the clinical outcome and placental findings in cases with and without proximate cord insertions.

Results: The prevalence of proximate cord insertions in TTTS placentas was 2% (4/252). Perinatal mortality in the TTTS group with and without proximate cord insertions was 13% (1/8) and 12% (61/496), respectively (P=1.0). Residual anastomoses were detected in all placentas with proximate cord insertions (100%, 4/4) compared to 27% (66/248)(P<.01) in TTTS placentas without proximate cord insertions.

Conclusion: Fetoscopic laser coagulation in TTTS cases with proximate cord insertions is challenging due to technical difficulties in visualizing the vascular equator and results in an increased risk of incomplete laser treatment.

Keywords: proximate umbilical cord insertions, twin-twin transfusion syndrome, fetoscopic laser coagulation surgery

Introduction

The omnipresent vascular anastomoses are the anatomic prerequisite for twin-twin transfusion syndrome (TTTS).[1] Fetoscopic laser coagulation of the vascular anastomoses is considered to be the most effective treatment for TTTS.[2] On pre-operative ultrasound, and again at the start of the fetoscopy, the cord insertion sites and the location of the vascular equator between both cord insertions are evaluated. When the distance between cord insertions is very close, so-called proximate cord insertions, technical difficulties in identifying the vascular equator may occur. In addition, the anastomoses in these cases may have a larger diameter than usual. Fetoscopic laser coagulation surgery may then either not be considered as the first treatment of choice or may fail due to technical limitations in identifying anastomoses.[3]

To date, the prevalence and clinical consequences of proximate cord insertions in TTTS placentas have not been studied. The aim of the present study was to compare the outcome after laser surgery in TTTS cases with and without proximate cord insertions.

Materials and methods

All TTTS pregnancies treated with fetoscopic laser coagulation surgery at Leiden University Medical Center between April 2002 and March 2013 were eligible. The technique used for fetoscopic laser coagulation was either the standard selective laser technique or, more recently, the Solomon technique.[4] According to our guideline, laser surgery is performed in TTTS stage II, III or IV and in cases with stage I with clinical symptoms of polyhydramnios.[5] Diagnosis of TTTS was based on the

internationally accepted criteria: polyhydramnios (deepest vertical pocket ≥ 8cm before 20 weeks or 10cm after 20 weeks of gestation) in the recipient sac and oligohydramnios (deepest vertical pocket ≤ 2cm) in the donor sac.[2] We included in the present study only TTTS cases with complete placenta examination after birth including colored dye injection to identify residual anastomoses. Injection with colored dye was performed according to our previously published protocol.[6] Severely damaged placentas were excluded from the postnatal placenta injection study. We also excluded placentas in case of single or double intrauterine fetal demise (IUFD) when delivery occurred more than a week later after demise and the corresponding placenta-sharing was macerated. Pictures of the injected placenta were taken using a high-resolution digital camera. A measuring-tape was placed on the placenta to allow post-hoc measurements on the digital picture. We recorded the presence of proximate cord insertions, defined as a distance between both cords insertion sites < 5 cm, prenatally detected by ultrasound and measured at postnatal placental examination. We recorded the presence, number and types of residual anastomoses. All measurements were performed using Image J 1.45s (Image J, National Institute of Health, USA). Part of placental data reported in this study was reported in previous publications.[7-9]

The following perinatal data were recorded: TTTS stage, gestational age at laser, recurrence/reversal of TTTS, post-laser twin anemia-polycythemia sequence (TAPS), gestational age at birth and perinatal death (either fetal demise or neonatal death). Treatment failure in fetoscopic laser coagulation surgery was defined as the presence of residual anastomoses after color dye injection.

The primary aim of this study was to estimate the prevalence of proximate cord insertions and compare the clinical outcome and placental characteristics in TTTS cases with and without proximate cord insertions.

Statistics

Mann-Whitney U test was used to compare continuous variables and Fisher's exact test was used to analyze categorical variables. Statistical significance was considered when a P-value <.05. SPSS Statistics v20.0 (SPSS Inc., Chicago, IL, USA) was applied to perform statistical analysis.

Results

During the study period, 432 TTTS twin pregnancies were consecutively managed with fetoscopic laser coagulation surgery at our center. A total of 148 (35%) placentas were not delivered at our center or not shipped back to our center. Of the remaining 284 placentas, we excluded 11 placentas due to remote (> 1week) single or double fetal demise and 21 cases due to severe damage to the cord insertions or placenta, or fixation in formalin. Complete placental data, including colored dye injection studies, were available for 252 placentas and included in the present study. Proximate cord insertions were detected in 4 TTTS cases, yielding overall prevalence of 2% (4/252). No TTTS cases with proximate cord insertions were treated with other intervention (such as umbilical cord clamping) during the study period. Examples of placentas with and without proximate cord insertions after color dye injection were shown in Figure 1 and 2, respectively. Baseline characteristics of TTTS cases with and without proximate cord insertions are summarized in Table 1.

Table 1 Baseline characteristics

	PCI (n=4)	No PCI (n=248)
GA at laser - weeks[a]	19 (16-23)	20 (18-23)
Quintero stage - n (%)		
Stage 1	0	21 (8)
Stage 2	2 (50)	86 (35)
Stage 3	2 (50)	126 (51)
Stage 4	0	15 (6)
Anterior placenta- n (%)	1 (25)	78 (31)

[a]Denotes median (IQR). PCI: proximate cord insertions.

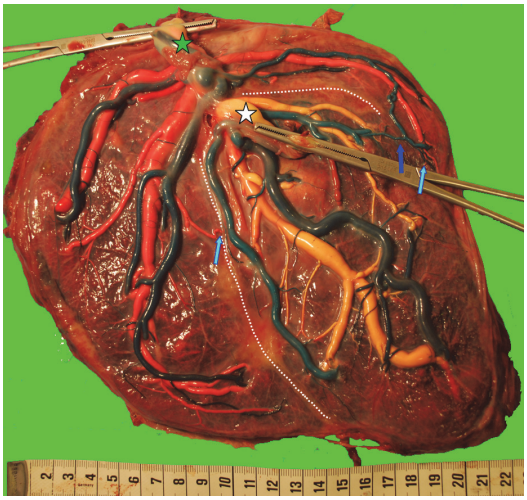

Figure 2 TTTS placenta with proximate cord insertion (delivery at 30 weeks) after colored dye injection: AA and VV residual anastomoses are indicated with blue stars and yellow arrows, respectively. Light-blue arrows indicate several residual AV anastomoses The white dotted lines show the laser coagulation demarcation line.

Figure 1 TTTS placenta without proximate cord insertion (delivery at 32 weeks) after colored dye injection: Solomon technique was used to coagulate the whole vascular equator (white dotted line). No residual anastomoses are found.

Clinical outcome data: Post-laser TAPS in the group with and without proximate cord insertions was 25% (1/4) and 14% (35/248), (P=.46). No cases of recurrent TTTS were detected in the proximate cord insertions group, compared to 2% (5/248)(P=1.00) in the group without proximate cord insertions. In the case of post-laser TAPS in the group with proximate cord insertions, laser surgery was performed at 25 weeks' gestation but failed because of difficulty in identifying the vascular equator and severe bleeding. At 27 weeks' gestation, evidence of severe fetal anemia in the

donor and polycythemia in the recipient were detected on Doppler ultrasound examination, confirming the diagnosis of TAPS. An emergency caesarean section was performed at 27 weeks' gestation due to signs of fetal distress in the donor. Hemoglobin level at birth in the donor was 2.6 g/dL (reticulocyte count 172‰) versus hemoglobin level of 18.7 g/dL in the recipient (reticulocyte count 72 ‰), confirming the diagnosis of TAPS. The anemic donor died after 4 weeks of intensive care treatment due to severe cerebral injury (intraventricular hemorrhage grade 4) and severe respiratory distress syndrome. Overall perinatal survival in the TTTS group with and without proximate cord insertions was 87% (7/8) and 88% (435/496), respectively (P=1.00). Further details on the clinical outcome of all TTTS pregnancies are shown in Table 2.

Table 2 Pregnancy outcome in TTTS twins with and without proximate cord insertion

	PCI (n=4)	No PCI (n=248)	P value
Recurrent TTTS – n (%)	0 (0)	5 (2)	1.00
Post-laser TAPS– n (%)	1 (25)	35 (14)	.46
GA at birth – weeks[a]	32 (27-34)	32 (29-35)	.89
Perinatal mortality– n (%)[b]	1 (13)	61 (12)	1.00

[a] Denotes median (IQR). [b] Means the number of fetus.

Placental outcome data: Residual anastomoses were detected after colored dye injection in each TTTS placentas with proximate cord insertions (100%, 4/4) compared to 27% (66/248)(P<.01) in TTTS placentas without proximate cord insertions. The median number of residual anastomoses in TTTS placentas with and without proximate cord insertions was 13 (interquartile range (IQR): 7-24) and 0

(IQR: 0-1), respectively (P<.01) The overall prevalence of residual arterio-arterial (AA) and veno-venous (VV) anastomoses in TTTS placentas with proximate cord insertions was significantly higher compared to placentas without proximate cord insertions, 100% (4/4) versus 5% (13/248)(P<.01) and 50% (2/4) versus 4% (9/248)(P<.01), respectively. In the case with proximate cord insertions and post-laser TAPS, the diameter of the residual AA anastomosis was very small (< 1 mm). Further details on the injected placentas with and without proximate cord insertions are shown in Table 3.

Table 3 Characteristics of placenta with and without proximate cord insertions

	PCI (n=4)	No PCI (n=248)	P value
Presence of RA – n (%)	4 (100)	66 (27)	.01
No. of overall RA [a]	13 (7-24)	0 (0-1)	<.01
Residual AV -n (%)	13 (7-23)	0 (0-0)	<.01
Residual AA -n (%)	4 (100)	13 (5)	<.01
Residual VV -n (%)	2 (50)	9 (4)	.01

RA: residual anastomoses a Denotes median (IQR).

Discussion

In this study, we evaluated the prevalence and clinical consequences of proximate umbilical cord insertions in TTTS twins treated with fetoscopic laser coagulation surgery. We found that proximate cord insertions are rare in TTTS cases (2%, 4/252). Residual anastomoses were detected in each case with proximate cord insertions

and TAPS developed in one of these cases, emphasizing the difficulty in achieving dichorionization in these rare cases. Our study suggests that TTTS pregnancies with proximate cord insertions may pose a technical challenge for fetal surgeons due to problems related to the identification of the vascular equator, impeding complete laser photocoagulation of all potential anastomoses.

This important technical limitation of laser surgery in these specific TTTS cases was first reported in another small case series (n=6) by Gandhi et al in 2011.[3] The authors reported an overall perinatal mortality of 42% (5/12) in TTTS cases with proximate cord insertions, and in one case treated with laser surgery, both fetuses died due to residual anastomoses located between the close cord insertions. Based on their experience, Gandhi et al suggest that other fetal interventions (such as selective feticide or amnioreduction) should be considered in these cases.[3] Interestingly, we found that the rate of perinatal survival in the 4 cases with proximate cord insertions was similar to the control group. One of the possible explanation for the lack of association between proximate cord insertions, residual anastomoses and adverse outcome could be related to the nature of these anastomoses. As shown after placental injection, each case with proximate cord insertions had an AA anastomosis. As previously shown, AA anastomoses are known to prevent the development of TTTS or TAPS (provided the AA anastomosis is sufficiently large).[8-10] In one case, however, post-laser TAPS occurred despite the presence of an AA anastomosis, but the size of the anastomosis was very small. This is in agreement with one of our case reports.[10]

This peculiar placental angio-architecture in TTTS placentas with proximate cord insertions appears to be similar to monoamniotic placentas. Monoamniotic

placentas are also characterized with proximate cord insertions and a high prevalence of AA and VV anastomoses.[11] Concomitantly, monoamniotic twin pregnancies have also a reduced risk of developing TTTS due to the presence of AA anastomoses.[11, 12]

Several studies have investigated the relation between cord insertion distance and perinatal outcome in monochorionic twin pregnancies.[3, 13, 14] Importantly, international consensus agreement on the definition of proximate cord insertions is lacking. The optimal method to determine the clinically most useful cord distance, by using cord distance as continuous variable, and asses its correlation with outcome parameters, would require a dataset too large to be practical. We therefore propose the empirically chosen 5 cm cut-off for use in future studies at least until better evidence for another cut-off becomes available. In one study by Nikkels et al, a higher perinatal mortality rate was found in placentas with short cord insertion distance.[13] However, a wider cut-off value (<14 cm) for proximate cord insertions was chosen.[13] In another study by Hack et al, using a lower cut-off value(<5cm), no clear relationship between clinical outcome and distance between cord insertions in monochorionic and monoamniotic pregnancies was found.[11, 14] In accordance with Hack et al, we also found no difference in perinatal outcome between TTTS pregnancies with and without proximate cord insertions in this study adopting <5cm as the cut-off value as well.

Our data should be interpreted with care due to the retrospective nature of the study and the small number of cases with proximate cord insertions, preventing accurate statistical analysis. Larger (multicenter studies) are required to evaluate the perinatal morbidity and mortality in TTTS cases with proximate cord insertions and

determine if fetoscopic laser surgery is the most effective treatment in such cases. Another potential limitation of our study lies in the fact that we excluded cases if placental injection was not performed, including macerated placentas with TTTS. Excluding cases with IUFD may have introduced a potential, but unavoidable selection bias.

In conclusion, although proximate cord insertions are rare in TTTS placentas, they create a great technical challenge for fetal surgeons due to the difficulty in determining the vascular equator. More studies are required to confirm these findings and determine the best treatment in TTTS cases with proximate cord insertions. In addition, determination of a uniform cut-off value to define "proximate cord insertions" would be useful to allow accurate comparisons between different cohorts in the near-future. For future studies, we propose the uniform use of "5 cm" as cut-off to define proximate cord insertions, either detected antenatally (during pre-operative ultrasound scan) or measured postnatally at placental examination.

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