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American Journal of Obstetrics & Gynecology 2009;201:66.e1-4.

# Chapter 2

## Residual anastomoses in twin-to-twin transfusion syndrome treated with selective fetoscopic laser surgery: localization, size, and consequences

# Abstract

## *Objective:*

To study the localization and size of residual anastomoses in twin-to-twin transfusion syndrome treated with fetoscopic laser surgery and correlate the findings with outcome.

## *Study design:*

Placental injection in twin-to-twin transfusion syndrome placentas treated with laser was performed by using colored dye.

## *Results:*

A total of 77 twin-to-twin transfusion syndrome placentas were included in the study. Residual anastomoses (n=48) were found in 32% (25/77) of lasered placentas. Most residual anastomoses were localized near the margin of the placenta. The majority of residual anastomoses (67%; 32/48) were very small (diameter, < 1 mm). Eleven of the 25 cases (44%) in the residual anastomoses group developed twin anemia-polycythemia sequence.

## *Conclusion:*

Most residual anastomoses in twin-to-twin transfusion syndrome placentas treated with laser are very small and localized near the placental margin. Almost half of cases with residual anastomoses developed twin anemia-polycythemia sequence after laser surgery.

# Introduction

Twin-to-twin transfusion syndrome (TTTS) affects approximately 15% of monochorionic twin pregnancies and results from unbalanced intertwin blood flow between the donor and the recipient twin through placental vascular anastomoses. Untreated, TTTS is associated with high perinatal mortality and morbidity.[1] Fetoscopic laser occlusion of the vascular anastomoses is currently the best treatment option for TTTS.[2] The aim of laser surgery is to separate completely both fetal circulations by occluding all placental vascular anastomoses. However, several studies have shown that residual anastomoses (RA) may still be present after laser surgery and can be detected in up to 33% of lasered placentas.[3,4] RA may lead to recurrence of TTTS in 14% of cases and twin anemia polycythemia sequence (TAPS) in 13% of cases.[5]

The aim of this study was to measure the size of the RA and determine the localization of the RA in relation to the margin of the placenta. A secondary aim of this study was to determine the association between RA and hematologic complications at birth.

# Materials and methods

TTTS placentas treated with laser at the Leiden University Medical Center and consecutively examined at our center between June 1, 2002, and Aug. 1, 2008, were included in this study. Leiden University Medical Center is the national referral center for in utero management of TTTS in The Netherlands. Part of the placental data in this study was included in a previous report on RA.[4] We excluded TTTS cases with intrauterine fetal demise (because of placental maceration) and TTTS cases treated with an alternative laser technique that comprises coagulation of the placental surface along the entire vascular equator. Damaged placentas were excluded if deterioration was too extensive to allow adequate and complete injection study. Furthermore, TTTS cases in which laser surgery was interrupted because of poor visibility or other reasons, were also excluded. Diagnosis of TTTS was based on internationally accepted standardized antenatal ultrasound criteria.[6]

Placental injection with colored dye was performed to determine the localization, size, type, and number of RA. Details on the technique used for placental injection have been described previously.[4] Digital pictures of the placentas were taken perpendicularly to the placenta. We measured the length of the vascular equator on the digital picture of the placenta using Image Tool for Windows version 3.0 (Image Tool, San Antonio, TX). We measured the

distance between each RA and the margin of the placenta and expressed this distance as a percentage of the distance between margin and center of the vascular equator. We divided the distance between margin and center of the vascular equator into 5 equal segments (of 20%).

The following obstetric and neonatal data were retrieved from our databases, including gestational age at laser surgery and at birth, localization of the placenta on the uterine wall (anterior or posterior), recurrence of TTTS, TAPS, hemoglobin levels and reticulocyte count at birth, need for blood transfusion or partial exchange transfusion at birth. For the purpose of this study, diagnosis of TAPS was based on postnatal criteria.7 Postnatal criteria were chronic anemia in the donor (hemoglobin, < 2 standard deviations [SD])[8,9] and polycythemia in the recipient (hematocrit, > 65%) on day 1. Chronic anemia was differentiated from acute anemia based on the presence of a reticulocyte count > 2 SD.[9]

Results of categorical variables were compared with the $x^2$ test. Continuous variables were analyzed with the independent samples *t* test. A P value less than .05 was considered to indicate statistical significance. Analysis was performed by using SPSS version 14 (SPSS Inc, Chicago, IL).

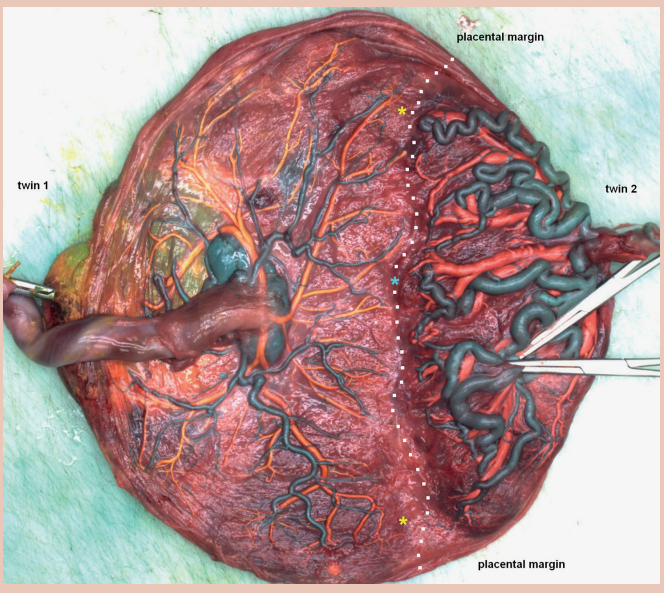


**Figure 1.** TTTS placenta treated with laser surgery at 17 weeks' gestation and delivered at 33 weeks' gestation. The white dots show the vascular equator and the light-blue star indicates the center of the vascular equator. The yellow stars indicate 2 small RA near the margins of the placenta: 1 arteriovenous anastomosis (top of the picture) at 27% distance from the placental margin (in relation to the placental center) and 1 venovenous anastomosis (bottom of the picture) at 17% distance from the placental margin.

## Results

A total of 123 TTTS placentas treated with laser were consecutively examined at our center. Forty-one placentas were excluded because of intrauterine fetal demise (n=22), laser coagulation of the entire vascular equator (n=14), or damaged placenta (n=6). Four TTTS cases were excluded because laser surgery was incomplete because of a "stucktwin" on the vascular equator

(n=2) or blurred vision (n=2). In 1 case, a large arterioarterial anastomosis was detected during fetoscopy but could not be coagulated because of its size. This placenta was included in the analysis but the arterioarterial anastomosis was excluded from the calculations.

A total of 77 placentas were thus analyzed. RA were found in 25 (32%) placentas.
These 25 placentas showed 48 anastomoses, a mean number of 2 RA per placenta (range,



| | RA group (n=25) | No RA group (n=52) | p value |
|---|---|---|---|
| Gestational age at laser (wk) [a] | 20.3±3.7 | 20.6±3.1 | 0.62 |
| Gestational age at birth (wk) [a] | 31.9±3.1 | 32.9±3.7 | 0.26 |
| Anterior placenta, n(%) | 10 (40%) | 19 (37%) | 0.77 |
| TAPS after laser surgery, n(%) | 11 (44%) | 0 (0%) | <0.001 |
| Intertwin hemoglobin difference at birth (g/dL) [a] | 10.0±5.5 | 2.1±2.5 | <0.001 |
| Intertwin reticulocyte count difference at birth (‰) [a] | 68.3±74.1 | 8.9±10.5 | <0.001 |
| Neonates requiring a blood transfusion at birth, n(%) | 16 (64%) | 5 (10%) | <0.001 |
| Neonates requiring a partial exchange transfusion, n(%) | 11 (44%) | 0 (0%) | <0.001 |

RA, residual anastomoses; SD, standard deviation; TAPS, twin anemia-polycythemia sequence.
[a] Values given as mean ± SD.

**Table 1:** Differences between the group with and without residual anastomoses

1-5). Most RA were arteriovenous anastomoses (85%; 41/48), of which 41% (17/41) were from donor to recipient and 59% (24/41) from recipient to donor. Residual arterioarterial anastomoses were found in 10% (4/48) of cases and venovenous anastomoses in 7% (3/48). The majority of RA (67%, 32/48) were very small (diameter, < 1 mm). An example of RA detected near the placental margin is shown in Figure 1. The localization of RA on the vascular equator is shown in Figure 2. Most RA were localized close to the placental margin.

Differences in perinatal outcome between the group with and without RA are

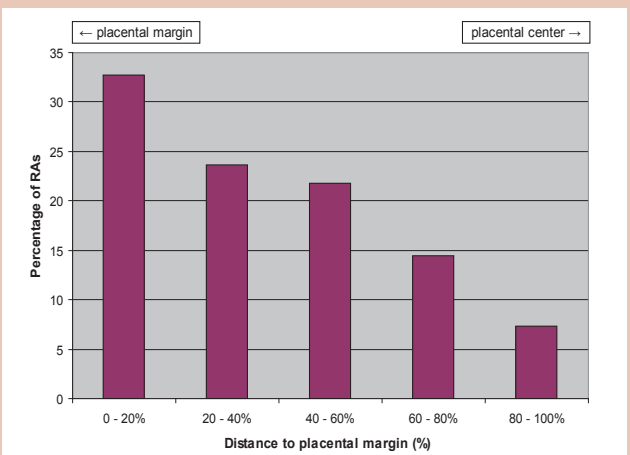


**Figure 2.** Localization of residual anastomoses in relation to the placental margin

shown in table 1. Presence of RA was associated with a higher incidence of TAPS. Recurrent TTTS after laser was not found in this cohort. Twins in the RA group were more often anemic or polycythemic at birth requiring a blood transfusion (64%) or a partial exchange transfusion (44%) compared with infants in the no-RA group (10% and 0%, respectively).

# Comment

This study shows that RA after laser are a common finding and that most RA are situated near the margin of the placenta. This finding is in accordance with a previous study from Lewi et al.[3] in which they found that most missed anastomoses (56%) were within 2 cm of the placental margin.

The reason for the clustering of RA near the placental margins is not clear. Two explanations may be envisaged: first, placental margins may be more difficult to visualize during fetoscopic surgery because of technical reasons associated with the position and the angle of the fetoscope. Ideally, the fetoscope should be inserted perpendicularly to the vascular equator to allow a clear view of the whole vascular equator. However, this is not always possible, particularly when the placenta is placed on the anterior uterine wall. A suboptimal angle of the fetoscope may prevent a complete view of the vascular equator, and in particular of the placental margin. A second possible explanation may that placental margins may be less well scrutinized during fetoscopic laser surgery, even in the absence of previously mentioned technical problems related to the angle of the fetoscope.

Second, as shown in this and other studies, RA are clearly associated with TAPS or recurrent TTTS after laser surgery.[3-5] Whether more careful scrutinization of the placental margins can lead to reduction of RA and its associated complications needs further study.

A third important result of this study is that most RA are very small (diameter, < 1 mm). This finding is in agreement with previous reports.[3,4] Various reasons may explain the high rate of these hair-thin anastomoses. First, anastomoses that are barely visible on placental examination without colored dye may obviously be even more difficult to detect during fetoscopy that took place several weeks/months before. Second, placental vessels of the donor twin may have been collapsed at the time of fetoscopy because of hypovolemia and vasoconstriction.

Further research to find a way to reduce the rate of RA and associated complications is

warranted. A possible solution for this problem could be to draw a laser coagulation line across the entire vascular equator from one placental margin to the other, instead of coagulating only the visible anastomoses. Hypothetically, this technique may be more effective in coagulating all vascular anastomoses, in particular the very small anastomoses that may be difficult to identify during fetoscopy. We have recently started a randomized control trial (named Solomon trial; www.trialregister.nl, trial ID: NTR1245) to determine whether this alternative laser technique (so-called Solomon technique) reduces the incidence of RA and consequently the incidence of TAPS and recurrent TTTS.



The incidence of RA (32%) found in this study was similar to our previous report.[4] Lewi et al.[3] also reported a 32% (16/50) incidence of RA by using a similar placenta injection technique with colored dye. In contrast, Quintero et al.[10,11] report a much lower incidence of RA (4%; 3/75 and 6%; 4/62) in their series of lasered placentas by using air injection. Differences in incidence of RA could theoretically be explained by differences in surgical techniques and expertise. However, care should be taken when interpreting the various results. Difference in incidence of RA could also be related to methodologic differences, including the injection technique used (colored dye injection vs air injection) and selection bias. We were not able to examine a consecutive series of all placenta injected at our center as not all placentas delivered elsewhere are shipped back to our department. A selection bias is thus introduced because uncomplicated cases are more likely to deliver elsewhere and this could explain the higher incidence of RA reported in our studies. We have shown in a previous study that complicated TTTS-cases after laser surgery were more commonly delivered at our tertiary care center.[12]

An important limitation of the measurements performed in this study warrants further attention. In vitro examination of the placenta on a table/flat surface is a simplification of the more complex in vivo situation in which the placenta is attached on a concave uterus. Care should thus be taken when extrapolating our in vitro measurements to the in vivo situation.

Although laser surgery has been shown to be the best available treatment for TTTS, results are still suboptimal, leaving room for improvement. This study shows that, as most RA are situated near the placental margin, fetal surgeons may need to inspect the margins of the vascular equator more carefully. Whether this knowledge can lead to reduction of RA by more careful surgical technique needs further study.

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