Fetoscopic laser therapy for twin-twin transfusion syndrome before 17 and after 26 weeks’ gestation

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OBJECTIVE: The purpose of this study was to compare perinatal outcomes of pregnancies that underwent “early” (<17 weeks’ gestation) or “late” (>26 weeks’ gestation) fetoscopic laser ablation of placental vascular anastomoses for twin-twin transfusion syndrome (TTTS) with “conventional” cases that were treated at 17-26 weeks’ gestation.

STUDY DESIGN: We conducted a single center, retrospective analysis of 325 consecutive pregnancies that underwent fetoscopic laser therapy for severe TTTS.

RESULTS: Twenty-four “early,” 18 “late,” and 283 “conventional” pregnancies with severe TTTS underwent laser therapy. Fetoscopy during pregnancy, gestation at delivery, survival rate, and complications were comparable among groups, except for preterm premature rupture of membranes at <7 days after laser therapy, which was more common in the “early” group than in either of the other 2 groups.

CONCLUSION: Laser therapy for TTTS at <17 or >26 weeks’ gestation has similar outcomes to procedures done at 17-26 weeks’ gestation. We suggest that conventional gestational age guidelines of 16-26 weeks for laser therapy for TTTS should be reevaluated.

Key words: laser therapy, fetoscopy, monochorionic twins, neonatal death, twin-twin transfusion syndrome, TTTS


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Editors’ Choice

In 2004, a randomized controlled trial demonstrated that fetoscopic laser ablation of placental anastomoses in TTTS resulted in better perinatal outcomes than serial amnioreduction. Only pregnancies at 16-26 weeks’ gestation were included in this trial. Part of the rationale for these gestational age limits was that fetoscopic laser ablation at <16 weeks may be more challenging, because the amnion and chorion may not have yet fused. After 26 weeks’ gestation, it was felt that more traditional approaches (such as expectant management, serial amnioreduction, or preterm delivery) were preferred. As is common practice in the first randomized trial that evaluates any new therapy, stringent inclusion and exclusion criteria were set. These trial criteria have been adopted by the Food and Drug Administration (FDA) in the United States, which, under the Humanitarian Device Exemption Program, permits fetoscopic equipment to “be used for the treatment of TTTS for fetuses whose gestational age is between 16 and 26 weeks.” In the United States, any fetoscopic procedure outside of these limits can proceed only by special exemption from the FDA.

Extremely premature birth is associated with major long-term handicaps that include cerebral palsy, mental retardation, and/or hearing, visual, and respiratory impairment. Because these fettuses also experience morbidity that is related to TTTS per se (abnormal Doppler results, hydrops, anemia, polycythemia, and renal and cardiac dysfunction), preterm delivery carries a high risk of significant neonatal morbidity.
and death, compared with age-matched control subjects, especially at <29 weeks’
gestation.13

Although TTTS most commonly oc-
curs during the second trimester of preg-
nancy, it can develop at <16 and >26
weeks’ gestation.14 Reports of perinatal
outcomes after early and late laser pro-
cedures are sparse.15,16 The aim of our
study was to report on pre- and postnatal
characteristics and perinatal outcome of
early and late laser procedures and to
compare these with procedures that were
performed within the more conven-
tional range of 17–26 weeks’ gestation.

MATERIALS AND METHODS

We conducted a retrospective chart re-
view of all consecutive monochorionic/
diamniotic twin pregnancies that were
complicated by severe TTTS and had been
managed with fetoscopic laser abla-
tion of vascular anastomoses at Mount
Sinai Hospital, Toronto, Ontario, Can-
da (a regional/national referral center
for fetoscopy) between January 1999 and
April 2012. Exclusion criteria were tri-
plets, fetal death at first presentation, and
fetal chromosomal or congenital abnor-
malities. The study was approved by the
Research Ethics Board of the hospital
(MSH REB #12-0190-C).

TTTS was diagnosed with standard ul-
trasound criteria,17 that included oligo-
hydranmios (deepest vertical pool, <2
cm) in the donor and polyhydramnios
(deepest vertical pool, >8 cm at <20
weeks’ gestation or >10 cm at >20
weeks’ gestation) in the recipient twin.
Staging was performed according to
Quintero et al18 (in stage III, the suffix
“R” is used when the recipient is affected,
and “D” when the donor is affected).
Cases were divided into 3 groups based
on the timing of the laser procedure: (1)
“early,” <17 weeks’ gestation, (2) “con-
ventional,” 17–26 weeks’ gestation; or (3)
“late,” >26 weeks’ gestation. For the
early group, a cutoff of 17 weeks was
chosen to allow sufficient power for
statistical analysis. Eight cases at <16
weeks’ gestation will be described sepa-
rate.

Selective laser ablation of placental
anastomoses was performed as previ-
ously described.6,12 Most procedures
were performed with local maternal an-
esthesia (Xylocaine; AstraZeneca, Lon-
don, UK) with intravenous sedation
(remifentanil ± propofol; n = 292 cas-
es); a few cases, during our initial expe-
rience, were performed with general
(n = 16 cases) or regional (n = 17 cases)
anesthesia. A 2-mm 0-degree fetoscope
and 3.7-mm (11F) operating sheath
(Karl Storz GmbH, Tüttlingen, Ger-
many) and a 600 μ Nd:YAG laser fiber
(Surgical Laser Technologies Inc, Mont-
gomeryville, PA) were introduced
through a 12F operating sheath (Cook
Medical Inc, Bloomington, IN) that had
been inserted directly with the use of a
trocar under continuous ultrasound
guidance. Thirty- and 70-degree feto-
scopes and a curved operating sheath
were used, as necessary, for the visualiza-
tion of anterior placentas. In 1 case of
TTTS at 16.1 weeks’ gestation with a
completely anterior placenta, 900 mL of
warmed NaCl 0.9% were first infused
into the recipient’s sac through a 20-G
needles. This amnioinfusion created a
safe “window” so that transplacental tro-
char passage could be avoided.

Intertwin placental vascular anasto-
moses were identified, and all were abl-
ated selectively along the vascular equa-
tor. Amnioinfusion was used as necessary,
and, at the end of the procedure, amniore-
duction was performed to leave the deep-
est amniotic fluid pool in the normal
range. Prophylactic tocolytics (indometh-
acin [rectally] and nifedipine [orally]) and
antibiotics (cefazolin [intravenously])
were administered routinely.

After the laser procedures, patients
were kept for 1 night in the hospital and
discharged the next morning; follow-up
evaluation was performed at Mount Si-
mai, or the patient was referred back to
their local regional perinatal center for
follow-up evaluation. Details regarding
pregnancy and neonatal outcomes were
obtained from hospital records, patients,
and/or referring physicians.

Demographics, TTTS stage, perioper-
ative characteristics, complications, and
maternal and neonatal outcomes were
recorded. “Major” maternal compli-
cations were defined as (1) intensive care
unit admission, (2) pulmonary edema,
(3) “mirror” syndrome, or (4) hemor-
riage (per vagina or intraperitoneally)
that required blood transfusion.

Categoric variables were compared
among the 3 groups by the Pearson χ²
test (or the Fisher exact test as indicated).
For continuous variables, medians were
compared by the Wilcoxon-Mann-Whit-
ney test. A probability value of <.05 was
considered statistically significant. Statis-
tical analyses were performed with STATA
software (version 11; Stata Corporation,
College Station, TX).

RESULTS

In the 13-year study period, 325 cases of
severe TTTS were treated with fetoscopy
selective laser ablation of the placental
anastomoses. Twenty-four cases (7.4%) underwented “early” laser therapy; 283 cases
(87.1%) underwent “conventional” laser
therapy, and 18 cases (5.5%) underwent
“late” laser therapy. Demographics, laser
therapy data and complications, TTTS
stage, and neonatal outcomes are shown in
Table 1. Maternal characteristics, year of
laser procedure, and placental location
were similar in all groups.

Early vs conventional laser therapy

TTTS stage, duration of surgery, and
need for cerclage were similar in both
groups. Although the rate of preterm
premature rupture of the membranes
(PPROM) at <32 weeks’ gestation was
similar between groups, there were more
cases of PPROM within 7 days of laser
surgery in the early group; there were,
however, no differences in the rate of
preterm delivery within 7 days, <28
weeks’ gestation, or <32 weeks’ gesta-
tion. Laser therapy to delivery interval
was longer in early, compared with con-
ventional, cases; the gestational age at
delivery was similar in both groups. There
were no significant differences in survival
at either 7 or 30 days of life for 1 or both
fetuses, in neonatal deaths within 7 days
of birth, in mode of delivery, or in birth-
weight between early and conventional
cases. There were no differences in mater-
nal complications between the groups
(8.3% vs 5%; P = .361).

Table 2 summarizes the 8 cases that were
treated with laser therapy at <16 weeks
gestation (range, 14.6–15.6 weeks’ gesta-
### TABLE 1
Demographics, laser data, complications, stage, and neonatal outcomes among groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Laser therapy timing</th>
<th>“Conventional”</th>
<th>“Early”</th>
<th>“Late”</th>
<th>P value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td>31 (18–47)</td>
<td>31 (20–41)</td>
<td>30 (22–38)</td>
<td>.988</td>
<td>.398</td>
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<tr>
<td>Nulliparity, n (%)</td>
<td></td>
<td>109 (41.3%)</td>
<td>9 (45%)</td>
<td>5 (31.3%)</td>
<td>.816</td>
<td>.602</td>
</tr>
<tr>
<td>Laser therapy characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior placenta</td>
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<td>126 (44.5)</td>
<td>9 (37.5)</td>
<td>7 (38.9)</td>
<td>.53</td>
<td>.808</td>
</tr>
<tr>
<td>Gestational age at surgery, wk&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td>21 (17.1–25.6)</td>
<td>16 (14.6–17.0)</td>
<td>27.1 (26.1–30.3)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cervical length, mm&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td>36 ± 10</td>
<td>37 ± 7</td>
<td>31 ± 12</td>
<td>.334</td>
<td>.09</td>
</tr>
<tr>
<td>Cerclage, n (%)</td>
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<td>24 (8.5)</td>
<td>1 (4.2)</td>
<td>2 (11.1)</td>
<td>.706</td>
<td>.661</td>
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<tr>
<td>Length of surgery, min&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td>57 (19–180)</td>
<td>53 (25–145)</td>
<td>58 (30–142)</td>
<td>.505</td>
<td>.845</td>
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<td>Twin-twin transfusion syndrome stage, n (%)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td></td>
<td>13 (4.6)</td>
<td>—</td>
<td>1 (5.6)</td>
<td>.034</td>
<td>.686</td>
</tr>
<tr>
<td>II</td>
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<td>92 (32.5)</td>
<td>6 (25.0)</td>
<td>4 (22.2)</td>
<td>.034</td>
<td>.686</td>
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<td>III</td>
<td></td>
<td>151 (53.4)</td>
<td>16 (66.7)</td>
<td>7 (38.9)</td>
<td>.034</td>
<td>.686</td>
</tr>
<tr>
<td>IV</td>
<td></td>
<td>27 (9.5)</td>
<td>2 (8.3)</td>
<td>6 (33.3)</td>
<td>.034</td>
<td>.686</td>
</tr>
<tr>
<td>III and IV</td>
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<td>178 (62.9)</td>
<td>18 (75.0)</td>
<td>13 (72.2)</td>
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<td>.615</td>
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<td>Laser therapy complication, n (%)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preterm premature rupture of membranes after laser therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7 d</td>
<td></td>
<td>18 (6.4)</td>
<td>6 (25.0)</td>
<td>1 (5.6)</td>
<td>.006</td>
<td>1</td>
</tr>
<tr>
<td>&lt;32 wk</td>
<td></td>
<td>180 (63.7)</td>
<td>14 (58.3)</td>
<td>10 (55.5)</td>
<td>.661</td>
<td>.327</td>
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<tr>
<td>Preterm labor after laser therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7 d</td>
<td></td>
<td>32 (11.3)</td>
<td>1 (4.2)</td>
<td>2 (11.1)</td>
<td>.491</td>
<td>1</td>
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<tr>
<td>&lt;28 d</td>
<td></td>
<td>56 (19.8)</td>
<td>1 (4.2)</td>
<td>5 (27.8)</td>
<td>.059</td>
<td>.378</td>
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<td>Major maternal complication</td>
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<td>14 (5.0)</td>
<td>2 (8.3)</td>
<td>—</td>
<td>.361</td>
<td>1</td>
</tr>
<tr>
<td>Any maternal complication</td>
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<td>25 (8.8)</td>
<td>3 (12.5)</td>
<td>2 (11.1)</td>
<td>.469</td>
<td>.669</td>
</tr>
<tr>
<td>Mode of delivery, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal/vaginal</td>
<td></td>
<td>152 (53.7)</td>
<td>13 (54.2)</td>
<td>8 (44.4)</td>
<td>.66</td>
<td>.12</td>
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<tr>
<td>Vaginal/cesarean</td>
<td></td>
<td>3 (1.1)</td>
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<td>1 (5.6)</td>
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<tr>
<td>Cesarean</td>
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<td>108 (38.2)</td>
<td>8 (6.9)</td>
<td>6 (33.3)</td>
<td></td>
<td></td>
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<td>Unknown</td>
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<td>20 (7.1)</td>
<td>3 (12.5)</td>
<td>3 (16.7)</td>
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<td></td>
</tr>
<tr>
<td>Obstetric outcome</td>
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<tr>
<td>Preterm labor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;32 wk gestation, n (%)</td>
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<td>142 (50.2)</td>
<td>14 (58.3)</td>
<td>5 (27.8)</td>
<td>.526</td>
<td>.088</td>
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<tr>
<td>&lt;28 wk gestation, n (%)</td>
<td></td>
<td>78 (27.6)</td>
<td>7 (29.2)</td>
<td>3 (16.7)</td>
<td>.817</td>
<td>.417</td>
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<tr>
<td>Gestational age at delivery, wk&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td>31 ± 5</td>
<td>30 ± 4</td>
<td>33 ± 3</td>
<td>.482</td>
<td>.076</td>
</tr>
<tr>
<td>Laser-delivery interval, wk&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td>10 (0–22)</td>
<td>14 (0.4–19)</td>
<td>6 (0.1–10)</td>
<td>&lt;.001</td>
<td>.005</td>
</tr>
<tr>
<td>Neonatal outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At least 1 survivor, n (%)</td>
<td></td>
<td>246 (86.9)</td>
<td>20 (83.8)</td>
<td>17 (94.4)</td>
<td>.542</td>
<td>.711</td>
</tr>
<tr>
<td>Dual survivors, n (%)</td>
<td></td>
<td>160 (56.6)</td>
<td>13 (56.5)</td>
<td>14 (77.8)</td>
<td>1</td>
<td>.089</td>
</tr>
</tbody>
</table>

tion). All but 1 case were stage III; 1 case had needed a previous amniinfusion to create an amniotic fluid "window" to allow safe trochar insertion to avoid the placenta. Three of 8 cases (38%) were complicated by PPROM within 7 days of the laser therapy. Of 16 fetuses, 11 (69%) were born alive and thrived. Two donors, both with absent end-diastolic velocity in the umbilical artery, and 1 donor with reverse A waves in the ductus venosus died within 24 hours of the laser therapy. In 1 case of postoperative twin-anemia-polycythemia syndrome, the recipient who was transfused in utero (hemoglobin level, 36 g/L) at 20 weeks' gestation died 2 days later; when the patient went into spontaneous labor at 24 weeks' gestation, the donor was noted to be dead on admission (birthweight, 485 g). Finally, one patient (Table 2; case 7) had an emergency cesarean section for preterm labor at 26.3 weeks' gestation; the birthweights were 810 g and 490 g, respectively, for recipient and donor. The donor died

<table>
<thead>
<tr>
<th>Case</th>
<th>Gestational age at laser therapy, wk</th>
<th>Twin-twin transfusion syndrome stage</th>
<th>Placental position</th>
<th>Length of surgery, min</th>
<th>Preterm premature rupture of membranes within 7 d</th>
<th>Gestational age at delivery, wk</th>
<th>Adverse outcome</th>
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<tr>
<td>1</td>
<td>15.6</td>
<td>III R</td>
<td>Anterior</td>
<td>48</td>
<td>No</td>
<td>32.6</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>15.6</td>
<td>III R + D</td>
<td>Anterior</td>
<td>41</td>
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<td>32.3</td>
<td>—</td>
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<tr>
<td>3</td>
<td>15.1</td>
<td>III R</td>
<td>Posterior</td>
<td>28</td>
<td>No</td>
<td>24.1</td>
<td>Intrauterine fetal death at 20 weeks' gestation</td>
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<tr>
<td>4</td>
<td>15.1</td>
<td>III R + D</td>
<td>Anterior</td>
<td>38</td>
<td>Yes</td>
<td>28.1</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>15.5</td>
<td>III D</td>
<td>Posterior</td>
<td>38</td>
<td>Yes</td>
<td>30.1</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>15.5</td>
<td>III R</td>
<td>Anterior</td>
<td>30</td>
<td>No</td>
<td>33.1</td>
<td>—</td>
</tr>
<tr>
<td>7</td>
<td>15.6</td>
<td>III D</td>
<td>Posterior</td>
<td>38</td>
<td>No</td>
<td>26.3</td>
<td>—</td>
</tr>
<tr>
<td>8</td>
<td>15.6</td>
<td>II</td>
<td>Posterior</td>
<td>38</td>
<td>No</td>
<td>32.6</td>
<td>—</td>
</tr>
</tbody>
</table>

from complications of extreme prematurity and low birthweight; the recipient survived.

**Late vs conventional laser therapy**

TTTS stage was significantly higher in late cases compared with conventional cases (Table 1). Indeed, one-third of the recipients were hydropic (stage IV) in the late group, compared with 9.5% in the conventional group ($P = .034$). There were no differences in either the duration or technical difficulty of laser surgery or in the rate of postoperative complications. Women in the late group delivered later than those in the conventional group; however, the laser therapy-to-delivery interval was significantly shorter in late cases compared with conventional cases, although the mean interval in the late group was 6 weeks.

Despite late cases presenting at a more advanced stage of TTTS, survival of at least 1 fetus and dual survival were higher in the late group compared with the conventional group. There were no significant differences in birthweight between late and conventional cases. There were no significant maternal complications in the late laser therapy group.

The 18 patients in the late group are detailed in Table 3. PPROM within 7 days of laser therapy occurred only once. One neonate from the late group died in its first week of life. Two donors (both with stage IV TTTS) died in utero within 24 hours of the laser therapy. In case 4, the prolonged duration of the procedure (142 minutes) was related to closely approximated placental cord insertions and intraamniotic bleeding that necessitated an amnio exchange of 20 L. The recipient died within 24 hours of the procedure, probably of acute severe anemia. A massive grade IV intraventricular hemorrhage was detected in the donor. Labor was induced 6 days after laser therapy with a plan for palliative care, and the neonate died shortly after birth. Finally, in 1 case who underwent surgery at 26.6 weeks gestation for stage IV TTTS, the recipient died unexpectedly 7 weeks after

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**TABLE 3**

Details of 18 pregnancies treated with laser therapy at >26 weeks’ gestation

<table>
<thead>
<tr>
<th>Case</th>
<th>Gestational age at laser treatment, wk</th>
<th>Twin-twin transfusion syndrome stage</th>
<th>Placental location</th>
<th>Length of surgery, min</th>
<th>At preterm premature rupture of membranes</th>
<th>At delivery</th>
<th>Recipient</th>
<th>Donor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>26.0</td>
<td>III D</td>
<td>Posterior</td>
<td>61</td>
<td>—</td>
<td>35.5</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>26.1</td>
<td>II</td>
<td>Anterior</td>
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<td>36.6</td>
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<td>—</td>
</tr>
<tr>
<td>3</td>
<td>26.1</td>
<td>III R</td>
<td>Posterior</td>
<td>34</td>
<td>—</td>
<td>31.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>26.4</td>
<td>III D</td>
<td>Anterior</td>
<td>142</td>
<td>—</td>
<td>27.3</td>
<td>Neonatal death$^a$</td>
<td>Intrauterine fetal death$^b$</td>
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$^a$ At < 1 week; $^b$ Within 24 hours of laser therapy; $^c$ At 34 weeks’ gestation.
COMMENT
In this study, we found that fetoscopic laser therapy for TTTS before either 16 or 17 weeks’ gestation and >26 weeks’ gestation was feasible and safe and yielded similar outcomes to cases who were treated between 17–26 weeks. Our data from control group of cases who were treated between 17 and 26 weeks’ gestation was similar to previously published studies in terms of gestational age at therapy, perinatal outcome, and complication rates.6,19,20

To our knowledge, this is the first study to evaluate the potential role of fetoscopic laser therapy for severe TTTS at <16 weeks’ gestation. Early TTTS is a rare complication of monochorionic/diamniotic twins; only 8 of 325 cases (2.5%) of our cohort came to our center at <16 weeks’ gestation. Early development of TTTS can pose a diagnostic and therapeutic challenge. The diagnostic criteria may indeed need to be modified slightly; for example, the recipient’s bladder may cycle rapidly rather than being persistently distended, and an 8-cm definition for “polyhydramnios” may be too generous at this gestation because fetal blood volume and urine output are less. The volume of amniotic fluid in the recipient’s sac may preclude easy trochar insertion; in our experience, previous amnioinfusion by a separate needle, especially with a completely anterior placenta, creates an amniotic fluid “window” that enables safe trochar insertion without traversing the placenta.

Our results demonstrate that laser therapy is a feasible option even at this early stage of pregnancy. Indeed, the duration of fetoscopy, preterm labor rate, and neonatal outcomes in this early laser therapy group were comparable with conventional control subjects. The rate of PPROM within 1 week after laser therapy was increased in the early group; however, this did not translate into an increased rate of premature delivery. This PPROM may be the result of iatrogenic distension of the uterine cavity (amnioinfusion to optimize placental visualization) or the creation of a surgical defect in the membranes and is not the result of an inflammatory or infectious process, which is known to trigger preterm labor.21 Moreover, recent studies showed that cases of early PPROM22 and twin pregnancies complicated by PPROM23 are less likely to be complicated by chorioamnionitis when compared with late PPROM or PPROM in a singleton pregnancy. The rate of PPROM was related inversely to gestational age at laser therapy (<16 weeks’ gestation, 38%; 16–17 weeks’ gestation, 19%; >17 weeks gestation, 6%), which perhaps reflects the degree of chorioamnion fusion with advancing gestation. Despite documented PPROM and occasional transient oligohydramnios, anhydramnios was never observed on ultrasound follow-up evaluation of these cases. Potential strategies to reduce this rate of PPROM might be either the use of a smaller cannula (eg, 10F) or to delay laser procedures until >17 weeks’ gestation; however, the latter option must be weighed carefully against the potential adverse sequelae from progressive TTTS per se. To illustrate this, all but one of our early cases at <16 weeks’ gestation were stage III severe TTTS. Without intervention, early onset severe TTTS is associated with a high perinatal loss rate.2,14,24 Conversely, amnioreduction may compromise later fetoscopic interventions because of intraamniotic bleeding or membrane separation. Some fetal interventions in early pregnancy have been reported to be associated with an increased risk of fetal loss or mechanical fetal anomalies25,26; however, our results demonstrate the feasibility and safety of laser therapy, even at this early stage of pregnancy. We suggest that, once TTTS is diagnosed in early gestation, all management options, which include selective pregnancy termination, expectant management, amnioreduction, and fetoscopic laser ablation, should be discussed with parents.

When TTTS occurs at >26 weeks’ gestation, management options consist of either serial amnioreduction or preterm delivery, both of which carry a significant risk of neonatal death or major long-term handicap. Indeed, amnioreduction is associated with a 23% rate of neurologic sequelae in survivors,4,5,15,27,28 and preterm delivery from 26–28 weeks carries similar neurologic risks in the 70–80% of survivors29,30. Moreover, in our study, in one-third of the TTTS cases who underwent laser therapy at >26 weeks gestation, the recipient was hydropic (stage IV). At our institution, preterm delivery of a hydropic fetus at <29 weeks gestation is associated with an almost 100% mortality rate; therefore, in consultation with our neonatal colleagues, we elected to offer laser therapy as an option in these cases. Technical considerations (more turbid amniotic fluid, larger placental vessels, a bigger uterine cavity, and larger fetuses), restrictions by regulatory agencies (eg, FDA), potential maternal risks, and an anecdotally more benign evolution of TTTS after 26 weeks31 have discouraged many units from offering laser therapy at >26 weeks’ gestation. Late laser therapy, however, may allow time for both fetuses to recover in utero from the cardiac,11,12 renal, and other complications of TTTS and should enable the birth of more stable babies at a later gestational age. Even a relatively short period to allow the equilibration of hydropic changes can facilitate resuscitation and improve neonatal outcome.32

The duration of laser procedure and the complication rates were similar to those cases who were treated from 17–26 weeks’ gestation. Moreover, although this did not reach statistical significance, neonatal survival in the late laser therapy group was better than the survival rate in cases who underwent surgery at 17–26 weeks’ gestation. There were no major adverse complications related to the laser procedure.

To our knowledge, no studies have been published regarding laser therapy for TTTS at <16 weeks gestation. Our experience supports the results of 2 previous European studies that reported on fetoscopic laser therapy for TTTS at >26 weeks’ gestation.15,16 Middeldorp et al15 compared 10 cases treated with laser with 11 cases treated with amnioreduction at >26 weeks’ gestation. Despite the small sample size, neonatal morbidity
and mortality rates were worse in the amnioreduction group compared with the laser therapy group. In another study, 28 cases of TTTS who were treated with laser therapy at >26 weeks’ gestation were compared with 324 cases treated between 16-26 weeks’ gestation. There were no differences in the duration of surgery, complication rates, gestational age at delivery, or neonatal survival of at least 1 fetus.

The main limitations of our study were its retrospective design and the relatively small number of cases that were available for study, especially in the early group. The latter mainly is due to the relative rarity of early and late cases. From a practical perspective, it is unlikely that a randomized controlled trial for early or late TTTS will be conducted because the benefit demonstrated between 16 and 26 weeks’ gestation will preclude ethical equipoise. In this situation, a possible source of gathering evidence would be a prospective or retrospective cohort study. We suggest that our study contributes significantly in this field and highlights the need for a large prospective multicenter registry, with detailed neonatal and childhood outcome evaluation.

In our experience, fetoscopic laser therapy at <17 or >26 weeks’ gestation had similar outcomes compared with laser therapy from 17-26 weeks’ gestation. In light of these and other emerging data, we suggest that the current gestational age restrictions for laser therapy of 16-26 weeks should be reevaluated.

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REFERENCES