

PRELIMINARY EXPERIENCE WITH ENDOSCOPIC LASER SURGERY FOR SEVERE TWIN-TWIN TRANSFUSION SYNDROME

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Abstract *Background.* In monozygotic twin pregnancies, there are placental vascular communications between the two fetuses. In 15 percent of such pregnancies there is an imbalance in net blood flow between the twins, resulting in the twin-twin transfusion syndrome. The recipient twin may have severe hydramnios during the second trimester of pregnancy, and there is a high risk of perinatal death and cerebral palsy in survivors. This condition can now be treated by endoscopic coagulation of the vascular anastomoses responsible for fetofetal transfusion with a neodymium:yttrium-aluminum-garnet (Nd:YAG) laser.

Methods. We performed intrauterine surgery in 45 pregnant women carrying twins at 15 to 28 weeks of gestation (median, 21); in each case there was severe hydramnios in one fetus due to the twin-twin transfusion syndrome. With the use of local anesthesia and continuous ultrasound visualization, a rigid fetoscope 2 mm in diameter, housed in a 2.7-mm cannula, was introduced transabdominally into the amniotic cavity of the recipient

twin. A systematic search was made for all vessels approaching or crossing the membrane between the twins, and these were coagulated with an Nd:YAG laser by means of a fiber in the side arm of the cannula.

Results. Coagulation of the communicating vessels was successful in all cases. The total number of fetuses who survived to delivery was 48 (53 percent), and the number of pregnancies with at least 1 survivor was 32 (71 percent). Among the live-born infants, the median gestational age at delivery was 35 weeks (range, 25 to 40), and the median birth weight was 2098 g (range, 550 to 4252). The median interval between the endoscopic laser procedure and delivery was 14 weeks (range, 0 to 21). All the survivors were developing normally at a median age of 12 months (range, 2 to 24).

Conclusions. Our preliminary experience suggests that the twin-twin transfusion syndrome can be treated effectively by endoscopic laser coagulation of the communicating placental vessels. (N Engl J Med 1995;332:224-7.)

IN monozygotic twin pregnancies, embryonic splitting occurs within three days after fertilization in approximately one third of cases, resulting in two separate fetuses with independent placental circulations.^{1,2} Splitting after the third day is associated with vascular communications between the placentas; when cleavage is delayed beyond day 12, the fetuses are conjoined. An imbalance in the net flow of blood across the placental vascular communications from one fetus (the donor) to the other (the recipient) results in the twin-twin transfusion syndrome, which occurs in approximately 15 percent of monozygotic twin pregnancies.^{3,4}

It has been hypothesized that primary maldevelopment of the placenta of the donor twin causes increased peripheral resistance in the placental circulation, which promotes shunting of blood to the recipient; the donor suffers from both hypovolemia due to blood loss and hypoxia due to placental insufficiency.^{5,6} The recipient fetus compensates for its expanded blood volume with polyuria, but since protein and cellular components remain in its circulation, the consequent increase in oncotic pressure draws water from the maternal compartment across the placenta. A vicious cycle of hypervolemia, polyuria, and hyperosmolality is established, leading to high-output heart failure and hydramnios, with consequent spontaneous miscarriage or very premature delivery. In severe cases of hydramnios during the second trimester of pregnancy, there is a high risk of perinatal death and brain damage due to a combination of factors, including intrauterine hypoxia and preterm delivery.^{6,7} In addition, the death of one fetus, usually the donor twin, precipitates severe he-

modynamic changes in the circulation of the other and leads to death or hypoxic-ischemic sequelae.⁸

Improved survival has been reported after treatment with serial amniocentesis and drainage of large volumes of amniotic fluid.^{6,9-11} We have previously used this treatment strategy in the management of 25 monozygotic twin pregnancies in which one fetus had severe second-trimester hydramnios due to the twin-twin transfusion syndrome. The data on our first 19 cases have already been reported.⁶ The low survival rate among these fetuses (32 percent) prompted us to seek an alternative therapeutic option. De Lia et al. used laser coagulation to interrupt the communication of placental vessels.¹² General or regional anesthesia was given, and an endoscope was introduced into the uterus after laparotomy and hysterotomy. Despite the theoretical advantage of this approach, the technique has not gained widespread acceptance because of its invasive nature. More recently, we described a percutaneous technique for laser coagulation with the patient under local anesthesia.¹³ We report herein our preliminary experience with endoscopic laser coagulation in the management of 45 consecutive pregnancies complicated by the twin-twin transfusion syndrome.

METHODS

During a two-year period (1992 to 1994), we performed endoscopic laser coagulation of the vascular placental anastomoses in 45 monozygotic twin pregnancies. The mothers were referred to our center because one fetus had severe hydramnios due to the twin-twin transfusion syndrome at 15 to 28 weeks of gestation (median, 21). In all cases the women gave written consent, and the study was approved by the hospital ethics committee.

In each case, ultrasound examination showed monochorionic, diamniotic twin fetuses that were discordant in size. The larger twin (the presumed recipient) had a distended bladder and was surrounded by an abnormally large quantity of amniotic fluid (hydramnios), whereas in the smaller twin (the presumed donor) the bladder was

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always empty and the fetus appeared to be fixed to the placenta or the uterine wall because of oligohydramnios. The difference between the twins in estimated fetal weight,¹⁴ expressed as a percentage of the weight of the recipient twin, was 14 to 64 percent (median, 29 percent). The degree of hydramnios, as assessed by measurement of the deepest vertical pool of amniotic fluid, was 8 to 18 cm (median, 13).

In carrying out the laser coagulation, we first performed a detailed ultrasound examination, including color flow mapping, to localize the placenta, the intertwin amniotic membrane, the placental insertion of the umbilical cords, and the communicating blood vessels on the chorionic plate. The site of entry on the mother's abdomen was chosen to avoid injury to the placenta or the fetuses and to allow access to the suspected area of vascular communication. Local anesthetic (2 percent lidocaine) was injected down to the myometrium. Under continuous ultrasound visualization, a rigid 2-mm-diameter fetoscope (field of vision, 75 degrees) housed in a 2.7-mm cannula (KeyMed, Southend, United Kingdom, or Storz, Tuttlingen, Germany) was introduced transabdominally into the amniotic cavity of the recipient twin. A 400- μ m neodymium:yttrium-aluminum-garnet (Nd:YAG) laser fiber (MBB, Munich, Germany) was passed down the side arm of the cannula to 1 cm beyond the tip of the fetoscope.

A combination of ultrasonographic and direct vision was used to examine the chorionic plate systematically along the whole length of the intertwin membrane and to identify the crossing vessels, which were coagulated by the administration of a total of 1000 to 4500 J (239 to 956 kcal) of heat delivered by 3-second pulses with an output of 30 to 50 W at a distance of 1 cm. Subsequently, amniotic fluid was drained (median, 2760 ml; range, 400 to 6500) through the cannula of the fetoscope for 10 to 20 minutes to obtain normalization of the amniotic-fluid volume, judged subjectively, on ultrasonographic examination. The procedure took 30 to 90 minutes to complete, and the women were allowed to go home after a few hours, after the administration of prophylactic antibiotics and tocolytic agents.

RESULTS

Good visualization of the intertwin membrane and coagulation of the crossing vessels was achieved in all cases by the procedure, but it was more difficult to achieve in the 18 cases in which the placentas were located anteriorly. In one case laser coagulation was performed successfully at 17 weeks but was repeated at 22 weeks because there was a recurrence of the twin-twin transfusion syndrome.

The total number of fetuses who survived to delivery was 48 (53 percent), and the number of pregnancies with at least one survivor was 32 (71 percent). Among the live-born infants, the median gestational age at delivery was 35 weeks (range, 25 to 40), and the median birth weight was 2098 g (range, 550 to 4252). The median interval between the endoscopic laser procedure and delivery was 14 weeks (range, 0 to 21). Two babies had clinical signs of hypertrophic cardiomyopathy at birth; one died during cardiac surgery, but the other responded well to medical therapy and the ventricular hypertrophy resolved by the age of three months. All the survivors were developing normally at the median age of 12 months (range, 2 to 24).

In 16 pregnancies both babies were born alive, in 16 one baby was born alive, and in 13 none survived to delivery. (In two of the cases in which no babies were born alive, selective feticide was performed after laser coagulation because of ventriculomegaly in the donor twin, and the second twin was spontaneously aborted one week later. In one additional case of selective feticide a healthy baby was born.) The gestational ages at laser coagulation and delivery in each case are shown in Figure 1. There was no significant difference between the three outcome groups in gestational age at presentation, the degree of difference in estimated fetal weight between the twins, or the degree of hydramnios, expressed either in terms of the deepest vertical pool of amniotic fluid or in terms of the volume of amniotic fluid that was drained at fetoscopy. The incidence of anterior placentas was similar in the three groups (8 of 16 pregnancies in which both babies were born alive, 6 of 16 in which one baby was born alive, and 4 of 13 in which neither fetus survived).

In 16 pregnancies both babies were born alive. Laser coagulation was performed at 17 to 28 weeks (median, 21), and delivery occurred at 27 to 37 weeks (median, 35). In 13 of these 16 cases both babies survived, but in the other 3 cases one of the babies died in the neonatal period. In the first case delivery was at 36 weeks' gestation, and the former recipient twin died during cardiac surgery for right ventricular muscle hypertrophy. In the second case there was spontaneous rupture of the membranes at 27 weeks, and the former donor twin died of respiratory distress syndrome. In the third case delivery was at 37 weeks, and the former donor twin died of pulmonary hypoplasia associated

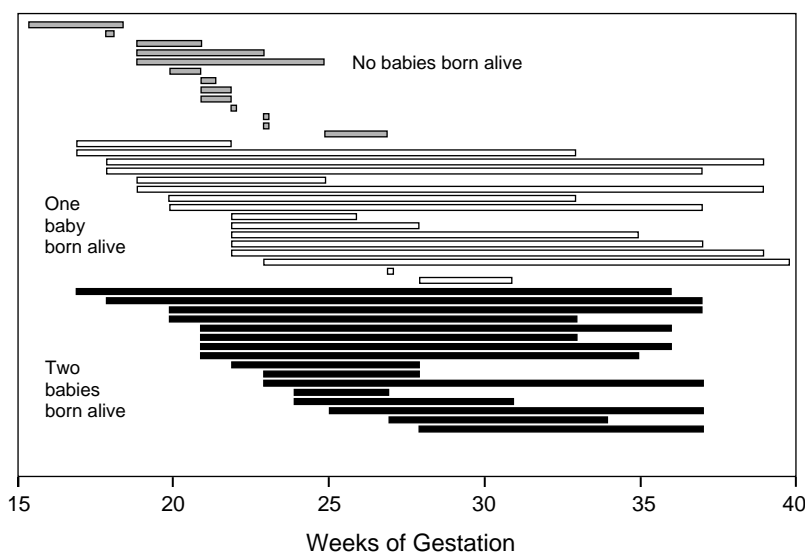


Figure 1. Outcome of Endoscopic Laser Coagulation for the Twin-Twin Transfusion Syndrome.

The lines represent the length of time between the laser-coagulation procedure and delivery in each of the 45 pregnancies with the twin-twin transfusion syndrome. In 13 pregnancies the fetuses did not survive to delivery (□), in 16 one baby in each pair of twins was born alive (▨), and in 16 both babies in each pair were born alive (■).

with bilateral renal agenesis, whereas the recipient twin, who had unilateral renal agenesis, survived.

In 15 pregnancies one of the fetuses died in utero after laser coagulation and the other survived. In this group laser coagulation was performed at 17 to 28 weeks (median, 20), and delivery was at 25 to 39 weeks (median, 33). In 12 of the 15 cases the donor fetus died; death occurred within 24 hours after laser coagulation in 11 of these cases, and 8 weeks later in 1 case. In three cases the hydropic recipient fetus died; in two of these, death occurred within 24 hours of laser coagulation, and in the third it occurred 3 weeks later. The donor fetuses in these three cases survived, but in one of them mild ventriculomegaly was noted three weeks after laser coagulation. After delivery at 34 weeks, obstructive hydrocephalus was diagnosed and was successfully treated by ventriculoperitoneal shunting; the child, who was 14 months old at this writing, was developing normally.

In three cases the donor fetus had ventriculomegaly at presentation, and selective feticide was performed after laser coagulation at 20, 21, and 23 weeks. In the first two cases there was spontaneous abortion 1 week later, but in the third a normal baby was delivered at 40 weeks.

There were another 11 pregnancies with no survivors. In this group laser coagulation was performed at 15 to 25 weeks (median, 21) and delivery occurred at 18 to 27 weeks (median, 22). In six pregnancies both fetuses died in utero; in four of the six, death occurred within 24 hours of laser coagulation, and in the other two, deaths occurred 2 to 3 weeks after an apparently successful procedure. In the remaining five cases in which no fetus survived to delivery, the mothers presented with vaginal bleeding and contractions. In one case there was spontaneous miscarriage 3 days later, and in four the donor fetus died within 24 hours of laser coagulation and spontaneous abortion occurred 1 to 6 weeks later, although the recipient twin had survived the laser procedure. In two of these last four cases the amniotic fluid at the time of fetoscopy was black from a previous intraamniotic hemorrhage, and exchange of fluid with Hartman solution was necessary before the communicating placental vessels could be visualized for coagulation.

DISCUSSION

This study demonstrates the feasibility of an endoscopic technique for the coagulation of placental vessels and interruption of the twin-twin transfusion syndrome. Furthermore, the data suggest that this treatment may be associated with a higher survival rate and a lower risk of cerebral palsy than treatment with serial drainage of amniotic fluid.

The goal of the systematic coagulation of all superficial placental vessels that cross or are adjacent to the intertwin amniotic membrane is to interrupt the vascular communication between the circulations of the two fetuses. Arteriovenous anastomoses are thought to have an important role in the hemodynamic disturbance un-

derlying fetofetal transfusion. These anastomoses are found deep in common cotyledons (subunits of the placenta), but the afferent and efferent branches are superficial.¹ Although the intertwin membrane does not necessarily overlie these common cotyledons, the coagulation of all crossing vessels will inevitably include the afferent and efferent branches of these anastomoses.

In 19 (42 percent) of the 45 pregnancies we studied, the donor fetus died within 24 hours of endoscopy. We have previously suggested that in the twin-twin transfusion syndrome the donor fetus is subjected not only to chronic hemorrhage and hypovolemia, but also to severe placental insufficiency.^{5,6} In monochorionic twin pregnancies there are many vascular communications between the circulations of the two fetuses, and although the donor twin has an overall loss of blood, this twin may be dependent for oxygenation on blood from the recipient. It could be postulated that the laser coagulation of all communicating vessels deprived the donor twin of this source of oxygen and hastened its death. Alternatively, coagulation of all placental vessels that cross the intertwin membrane may have interrupted the vascular supply to more than the common cotyledons, thus destroying whatever little reserve previously existed in an already compromised placenta. Nevertheless, coagulation of the communicating vessels appears to have a protective effect on the recipient fetus when the donor fetus dies. In our experience with the drainage of amniotic fluid, the death of one fetus was associated with the death of the other in 5 of 7 cases,⁶ whereas among the twins treated with laser coagulation, the death of the second twin occurred in only 6 of 22 pregnancies in which at least one twin died.

Cerebral palsy with periventricular leukomalacia is a well-recognized complication in monochorionic twins and is usually attributed to vascular accidents after the intrauterine death of one of the twins.¹⁵⁻¹⁷ We observed this complication in 25 percent of the fetuses that survived the drainage procedure. Suggested mechanisms include a severe hypotensive episode due to hemorrhage from the survivor into the placenta of the dead fetus or disseminated intravascular coagulation after the release of thromboplastin from the dead fetus. Laser coagulation of communicating vessels should prevent these complications and may explain the absence of cerebral palsy among the live-born infants and the high rate of survival among the second twins after the intrauterine death of one twin. However, brain damage observed in association with the twin-twin transfusion syndrome does not necessitate the death of one of the fetuses and may be the consequence of intrauterine ischemic-hypoxic brain injury.¹⁸ Three of the fetuses in our study had ventriculomegaly at presentation, and in these cases selective feticide was performed after laser coagulation of the placental vessels. In the donor fetus hypoxia may be the consequence of hypovolemia, anemia, and uteroplacental insufficiency, whereas in the recipient fetus hypoxia may be due to increased blood viscosity and congestive heart failure related to hypervolemia.

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