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Review article

Fetoscopic guide laser therapy for twin–twin transfusion syndrome

Yao-Lung Chang [a,b,*]

[a] Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital, Taiwan, ROC
[b] Chang Gung University College of Medicine, Taiwan, ROC

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ABSTRACT

Twin-twin transfusion syndrome (TTTS) affects 1 in 10 monochorionic (MC) twin pregnancies, and is the most important cause of death and neurological injuries in live-born fetuses in MC twins. Since one randomized trial demonstrated that fetoscopic laser photocoagulation achieved better outcomes than serial amniodrainage for all stages of TTTS before 26 weeks, centers of fetoscopic laser therapy for TTTS are currently being initiated worldwide. This review discusses the history, instruments and techniques of fetoscopic laser photocoagulation for TTTS. Finally, we report our current outcomes of TTTS treated by fetoscopic laser photocoagulation in a single center in Taiwan.

Introduction

In the 1970s, a fetoscope was used mainly for diagnostic purposes, or for small procedures such as biopsies, due to the limitation of the visual field and the nature of invasiveness. In Chang Gung Memorial Hospital, we also introduced fetoscope instruments into practice in the 1980s (Fig. 1), but due to the emergence of high resolution ultrasound, the diagnostic role of the fetoscope will soon be replaced by sonography, and shall eventually be abandoned.

Until the 1980s, the diameter of the scope was decreased, due to the advance of technology (small diameter of scope available) and availability of video endoscopy[1] (Fig. 2), and the role of fetoscopic guide laser therapy for the management of specific complications of monochorionic (MC) twins, such as twin-twin transfusion syndrome (TTTS) and twin reversed artery perfusion (TRAP), was established.[1] Since then, fetoscopy has gained an established place in fetal medicine.

Why is the fetoscope suitable for the management of TTTS? This is because there are several advantages of fetoscopic therapy for TTTS: (1) both fetuses usually are of a normal structure: parents accept the surgery to save the pregnancy; (2) the key pathophysiological basis of TTTS is communicating vessels at the placenta, which does not need an operation on the fetuses; and (3) polyhydramnios in the recipient sac – there is a good operation field for the fetal surgeon.

There is a relatively higher incidence of TTTS in patients needing fetal therapy (15% in MC twins[2] and diagnosed before 26 gestational weeks) compared to other fetal anomalies, such as cases of congenital diaphragmatic hernia, needing fetal intervention (approximately 1 in 2200 live births,[3] if flung-to-head ratio <1.0).[4] There were approximately 8.8 TTTS fetoscope surgeries and one fetoscope surgery for congenital diaphragmatic hernia.[5] Therefore, fetoscopic guide laser therapy (FLP) for TTTS became the most popular fetoscopic surgery.

If TTTS is of early onset (before gestational age of 26 weeks) and untreated, it is associated with a dismal prognosis, with perinatal mortality rates exceeding 90%.[6] Traditionally, serial amnioreduction and laser therapy are the most effect treatment methods for TTTS.[7] Serial amnioreduction is effective in prolonging a pregnancy, due to a reduced amount of amniotic fluid to prevent premature rupture of the membranes (PROM) and preterm labor; laser therapy directly coagulates the intertwin anastomotic vessels, in order to divide the placenta into a functional dichorionic placenta.[8] Since the first randomized trial on interventions for TTTS was published, [9] it has been recognized that the first-line treatment for all stages of TTTS diagnosed before 26 weeks, is laser treatment. The purpose of this review article is to describe the update of FLP for TTTS.

History of FLP for TTTS

The rationale for using laser treatment for TTTS, is to interrupt the vascular anastomoses that allow blood exchange between the fetuses, thus eliminating the pathophysiology of TTTS. The

* Chang Gung Memorial Hospital, Linkou Medical Center, 5, Fu-Shin Street, Kweishan, Taoyuan 333, Taiwan, ROC.
E-mail address: j12054@cgmh.org.tw.

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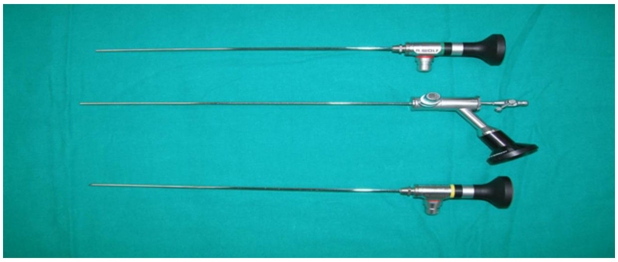

Fig. 1. Fetoscope in the 1980s, of a relatively large size, and without a working channel, mainly for the purpose of diagnosis.

pioneers, who developed the basic technique of such a surgery, are De Lia and associates. In 1983, De Lia saw a case of TTTS with one fetus hydrops at 23 weeks' gestation and gave the mother digoxin, in order to treat the heart failure of the hydropic fetus.[10] Both fetuses eventually survived, but the hydropic recipient twin was later found to be affected with cerebral palsy. After examining the placenta, De Lia found that only a single arteriovenous anastomosis existed between the two involved fetuses, on the placenta. At that time, he came up with the idea that, if he could block the single arteriovenous anastomosis, he might treat the disease. Eventually, his group performed the first laser treatment in 1988.[11] However, De Lia et al did not describe how to identify the communicating vessels for laser photocoagulation under a fetoscope. In 1955, Ville et al reported their preliminary experience with laser treatment for TTTS.[12] They used the dividing membrane as the landmark, and all vessels crossing the dividing membrane were to be coagulated. Importantly, Ville et al also replaced the technique from laparotomy (initially described by De Lia et al) to percutaneous insertion of the scope into the uterine cavity. FLP for TTTS then came into the minimal invasive era.

Ville et al are the first to describe how the operation can be performed and reproduced, however, many non-anastomotic vessels could cross the dividing membrane (Fig. 3) and thus be occluded by the method described. Until now, the non-selective method is not totally abandoned; when the distal end or the origin of the vessels cannot be indentified as an anastomosis or normal vessels, then non-selective coagulation of the crossing vessels can still be done.[13]

In 1998, Quintero et al described a surgical technique named 'selective laser photocoagulation of communicating vessels (SLPCV).[8] SLPCV selectively coagulates the communicating vessels and preserves the non-communicating vessels, even though they

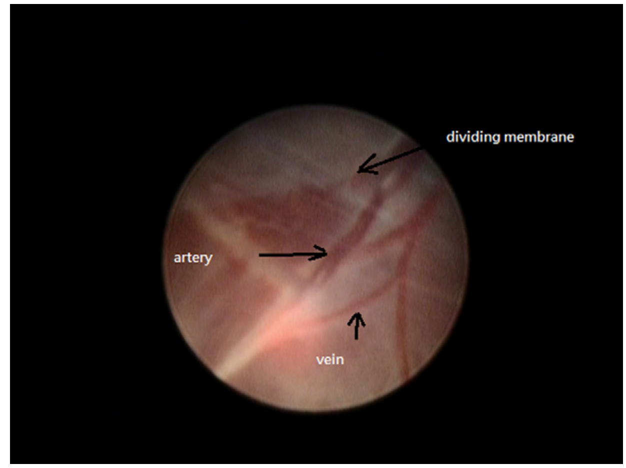

Fig. 3. One artery and one vein cross the dividing membrane.

cross the dividing membrane. In Quintero's description of SLPCV, each placental artery is followed to its terminal end in the placenta (arteries cross over veins) and a returning vein from that cotyledon should be traced draining back to the same twin. If blood is drained to the other twin, a deep arteriovenous anastomosis (AV) is present (Fig. 4). Arterio-arterial or veno-venous anastomoses are easily identified by noting the lack of a terminal end for an artery or a vein. SLPCV compares favorably with the previous nonselective technique, resulting in a lower rate of dual fetal demise (5.6% vs. 22%).[14] Now, in most centers, SLPCV has become the technique of choice for FLP. Quintero et al further described the sequential method of selective laser photocoagulation (SQLPCV) and found that it was associated with a decreased likelihood of intrauterine fetal death (IUFD) of the donor twin and an increased rate of dual survivors compared to SLPCV.[15] However, this technique needs to map the placenta vessels first, before laser coagulation, and needs a little longer operation time.

Fetoscope

Several manufacturers have developed equipment specifically designed for fetal surgery. Currently, the experience gathered with any type of fetoscope is limited, and no evidence shows that one particular brand of endoscope performs better than another.[16] The Eurofoetus group cooperated with the manufacturer of endoscopic

Fig. 2. Current fetoscope, with a relatively small diameter and a working channel.

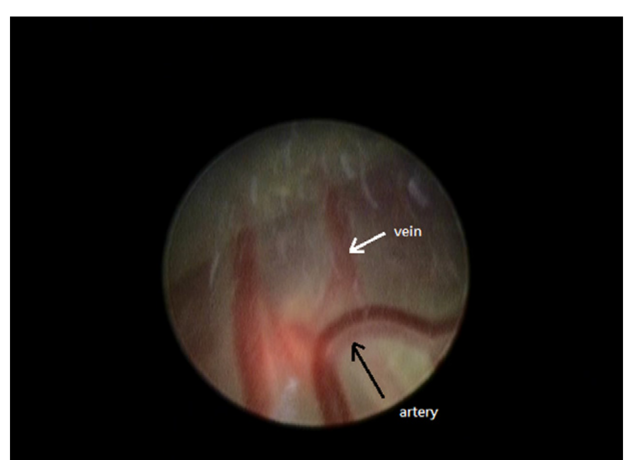

Fig. 4. Recipient artery to donor vein anastomotic vessels.

instruments (Karl Storz, Tuttlingen, Germany) and Karl Storz's fetoscope gained FDA approval. This is the only fetoscope available in Taiwan, due to government regulation. In Storz's designation, the laser fiber can, through a special design, be curved, but at the cost of fitting a larger sheath (3.7 mm) as compared with a smaller one (2.2 mm) for the posterior placenta, plus a limited angle of 30 degrees. Quintero designed the fetoscope, which is like a laparoscope; the scope and sheath can be separated under operation. With this kind of design, not only can they laser the vessels through the trocar while exerting a gentle pressure on the vessel to decrease blood flow during the coagulation[2] but it can also be applied to TTTS, with an anterior placenta in which the anastomoses were inaccessible with the standard technique (inaccessible anterior placentas). In Quintero's description, the anastomoses were first identified using a 25 or 70 degree rigid diagnostic endoscope. The anastomoses were then targeted with a zero degree operating rigid endoscope, by withdrawing it within the sheath a short distance, and using the sheath to gently indent the placenta (trocar assistance).[17] However, with the fetoscope, the scope and cannulas cannot be separated during the operation like in Storz's design; the trocar assistant technique cannot be performed. Another disadvantage of Storz's design is that it is not possible to change the fetoscope to a different angle (0 degree or 30 degree), due to the different cannulas between 0 and 30 degrees. If the zero degree scope is chosen initially, not all anastomoses can be coagulated; another puncture to the uterine cavity is required to insert the 30 degree scope.

In our experience, Storz's fetoscope has the advantage of a small diameter in cases with a mainly posterior placenta. However, in cases of an anterior placenta, although the design of the angle scope with a forward oblique 30 degree view and a deflecting mechanism for the laser fiber could fire vessels at difficult angles, as the scope and cannulas were fitted together, unlike in the design of Quintero et al, the cannulas can prevent the amniotic fluid leakage from the uterus due to the sheath not sliding through the myometrium during the operation. Therefore, the leakage of amniotic fluid becomes a problem if the fetoscope needs to be moved to a larger angle to hit the vessels, usually in the anterior placenta, and the operation needs to be done in a relatively short time, or the surgery would become difficult. A 400 μm laser fiber has been suggested to be applied to the 30 degree scope, but as our experience the 600 μm laser fiber also can be applied to the 30 degree scope with higher coagulation efficiency.

Laser machine

The working environment in FLP for TTTS is within the amniotic fluid. A CO2 laser is highly absorbed by water, so it cannot be used in FLP. The Nd:YAG and diode lasers can be used in FLP. They are named by reference to their acting medium. The diode laser has been recognized as having several advantages, both theoretical and practical, over the Nd:YAG laser, with a more appropriate wavelength for blood vessel coagulation, a smaller size, and a significantly lower cost.[2] In our experience, although the diode laser was small and less costly, there was a need to replace the key element every 5 years, which was costly. The price of the diode and Nd:YAG lasers are not very different in the Taiwanese market, so the advantage of the diode laser over the Nd:YAG laser is not so obvious. We tried both the Nd:YAG and diode lasers initially; the efficiency of the two lasers is comparable, however, we chose to use the Nd-YAG laser.

Anesthesia

Many centers today use local anesthesia for FLP[18,19]; local anesthesia is performed using a 27-gauge needle and 5–8 mL of 1% lidocaine with epinephrine 1:100,000.[19]

The needle was inserted deep into the uterine serosa under continuous ultrasound monitoring.[19] In our center, we used epidural anesthesia for most surgery, due to the lack of adequate experience with local anesthesia. We also prefer to use local anesthesia for performing FLP, especially in cases of posterior placenta. In some cases of a short cervix, due to the need for cervical cerclage, epidural anesthesia was chosen so that the two operations could be performed simultaneously.

Technique for FLP

Trocar entry

Identify the possible vessels at the uterine wall and abdominal wall by the sonographic color Doppler mode; choose the placenta free area. In cases of posterior placenta, because of polyhydramnios, it is usually easier to find a free space to insert the trocar. However, if the placenta is mainly anterior, sometimes due to the placenta position, the entry space is limited and the risk of septotomy and transplacental insertion of the trocar is high. According to the statement of Yamamoto et al, transplacental entry of the fetoscope has no significant effect on clinical outcomes, despite the fact that that insertion through the placenta may carry a higher risk of intraamniotic bleeding.[20] The risk of inadvertent septotomy has been estimated as 7% after fetoscopic laser therapy, and was associated with a substantially increased risk of adverse perinatal outcomes and pseudoamniotic band syndrome.[21]

Anterior placenta

In order to overcome the poor visual field for indentifying and coagulating the intertwin anastomotic vessels, deflecting mechanisms by Storz's design, side-firing fibers,[22] posterior uterine access under laparoscopic assistance[23] or through a periumbilical maternal laparotomy[24] have been proposed. In Chang Gung Memorial Hospital, a 30 degree scope by Storz's design, with deflecting mechanisms, was applied for anterior placenta. Because of our limited experience, in cases where the donor twin occupied the space of trocar entry, mini-laparotomy, in order to access the intertwin anastomoses from the fundal trocar entry, may be a better choice.

Differentiate the communicating and non-communicating vessels

As SLPCV is a widely accepted method for FLP, we introduced the procedure of SLPCV in Chang Gung Memorial Hospital. The rationale of detecting the communicating vessels between the two involved fetuses was described by Quintero et al.[8] A deep A-V communication from donor to recipient, or recipient to donor, is identified if the artery originates from one cord and ends in a cotyledon from which the emerging vein runs towards the other twin's cord. (Fig. 4) Arteries appear darker due to the deoxygenated blood and veins appear lighter due to the nature of oxygenated blood in the placenta. (Figs. 3 and 4) In the condition of TTTS, the donor twin is usually hypotensive and hypovolemic. In theory, lasering of the vein still allows for blood to be lost into the cotyledon, and may further increase the degree of donor anemia. Therefore, if it is possible, laser the donor artery to the recipient vein first, then laser the recipient artery to the donor twin; this may decrease the risk of donor anemia, even in case of IUFD of the donor.

Superficial artery-to-artery or vein-to-vein anastomoses are also coagulated and are identified as vessels which do not have a terminal end in the placenta, but rather continue their course from one umbilical cord to the other. All vessels are followed systematically from the point they cross the intertwining membrane. Under the fetoscope, those vessels that cross over the dividing membrane, but through tracing their course appear as normal vessels, should be preserved.

Laser photocoagulation

The laser power usually starts with 15–20 watts. If the gestational age is advanced, or the communicating vessels are large, it may be necessary to increase the power of laser to 25–30 watts with a continuous mode. In our experience, the laser source is a diode laser; the energy to coagulate the vessels may be slightly lower.

Amnioreduction

After laser photocoagulation, the amniotic fluid is drained. Due to placental abruption having been reported as a potential complication of large volume amnioreduction,[25] we usually drained the amniotic fluid in order to leave the maximum vertical pocket (MVP) <8 cm. We normally perform amniodrainage from the sheath of the scope; removing the scope and keeping the sheath in the uterus makes the drainage more effective than keeping the scope in the sheath.

Surgical failure

Symptomatic surgical failure, characterized by persistent TTTS, reverse TTTS and twin anemia-polycythemia sequence in TTTS treated by FLP, has been reported as 18%.[26] This may occur weeks after the operation, and there is a need for continuous ultrasound surveillance until delivery. Repeat FLP for surgical failure is usually difficult, hence amnioreduction or selective termination may be chosen.

Complications

FLP has evolved as the treatment of choice in TTTS. Certainly, the procedure is not free of complications. In our series, 11.36% of cases experienced premature rupture of membrane (PROM) within 3 weeks, 6.5% of mothers experienced pulmonary edema, 4.3% of cases experienced uterine bleeding during the operation and 2.2% of cases experienced chorioamnionitis needing termination.

Learning curve

In the review report by Ahmed et al, they emphasized that a learning curve certainly exists, although they failed to show a significant impact of high case loads (experience) on the fetal outcomes.[27] Morris et al found that they needed the experience of 61 and 111 procedures to reach a 85% and 90% survival rate, respectively, for at least one of the twins.[28] In our own experience, we also found that the fetal survival rate could be improved with increasing experience in using FLP for TTTS.[19]

Fetal outcomes

The overall survival of TTTS treated by a fetoscope, has been estimated as ranging from 45% to 70%, and survival of at least one twin from 60% to 85%, higher in a meta-analysis report by Rossi and D'Addario.[29] The incidence of severe neurodevelopmental delay is still considerable in survivors of TTTS treated by FLP and had been reported as ranging from 6% to 18%.[30–36] Low gestational age at delivery has been found as the significant factor associated with neurological impairment in TTTS treated by FLP in other reports.[33,35]

In our series, in severe TTTS treated by FLP in Chang Gung Memorial Hospital, the severe neurological deficit by neurological evaluation at a corrected age of 1 year was 6%,[37]; two survival rated was 50.0% and at least survival rate was 79.5%.[19]

Fetal growth after FLP

According to the study by Chmait et al, more than half of the donor fetuses with intrauterine growth restriction (IUGR) at the time of laser surgery showed a subsequent *in utero* catch-up growth, such that their birth weights were within the normal range.[38] Therefore, twin weight discordance and donor fetus IUGR, may partly be due to intertwin imbalance in anastomoses and appear to improve after laser therapy for TTTS.

Conclusion

Currently, FLP is the first choice of treatment for severe TTTS onset before 26 weeks. The outcomes of TTTS treated by FLP improve after a learning period. Procedure related complications decrease as the number of cases performed increases. Thus, it makes sense to limit the number of centers, to optimize the technical expertise.[39]

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