Perinatal Outcomes With Laser Surgery for Twin–Twin Transfusion Syndrome

Peter H. Gray,[1] Robert Cincotta,[2] Fung Yee Chan,[2] and Barbara Soong[2]

[1] *Division of Neonatology, Mater Mothers' Hospital, University of Queensland, Brisbane, Queensland, Australia*
[2] *Centre for Maternal Fetal Medicine, University of Queensland, Mater Mothers' Hospital, South Brisbane, Queensland, Australia*

The aim of this tertiary hospital–based cohort study was to determine and compare perinatal outcome and neonatal morbidities of pregnancies with twin–twin transfusion syndrome (TTTS) before and after the introduction of a treatment program with laser ablation of placental communicating vessels. Twenty-seven pregnancies with Stage II–IV TTTS treated with amnioreduction were identified (amnioreduction group). The data were compared with that obtained from the first 31 pregnancies with Stage II–IV TTTS managed with laser ablation of placental communicating vessels (laser group). Comparisons were made for perinatal survival and neonatal morbidities including abnormalities on brain imaging. The median gestation at therapy was similar between the two groups (20 vs. 21 weeks, $p = .24$), while the median gestation at delivery was significantly greater in the laser treated group (34 vs. 28 weeks, $p = .002$). The perinatal survival rate was higher in the laser group (77.4% vs. 59.3%, $p = .03$). Neonatal morbidities including acute respiratory distress, chronic lung disease, requirement for ventilatory assistance, patent ductus arteriosus, hypotension, and oliguric renal failure had a lower incidence in the laser group. On brain imaging, ischemic brain injury was seen in 12% of the amnioreduction group and none of the laser group of infants ($p = .01$). In conclusion, these findings indicate that perinatal outcomes are improved with less neonatal morbidity for monochorionic pregnancies with severe TTTS treated by laser ablation of communicating placental vessels when compared to treatment by amnioreduction.

Twin–twin transfusion syndrome (TTTS) is the most common major complication of monochorionic twin pregnancy with up to 15% having the polyhydramnios/oligohydramnios sequence. Untreated, the literature indicates that less than 20% survive when delivery occurs at less than 28 weeks' gestation (Gul et al., 2003). Amnioreduction for TTTS has been employed for some years with survival rates of 50% to 70% being most commonly reported (Cincotta et al., 2000; Dickinson & Evans, 2000; Johnsen et al., 2004; Lopriore et al., 2003). More recently laser ablation of the placental communicating vessels has been advocated as the preferred treatment for this condition, though overall survival rates have not been shown to be markedly improved (De Lia et al., 1995; Hecher et al., 2000; Quintero et al., 2003; Senat et al., 2004; Ville et al., 1995).

Amnioreduction has the potential to prolong a pregnancy by decreasing the risk of extreme prematurity, but the underlying twin–twin transfusion continues, with possible perturbations in cerebral blood flow continuing. With laser ablation the underlying process of blood flow between the fetuses through placental communicating channels is interrupted with the potential to result in improved outcomes.

Cardiac complications are well documented in survivors of TTTS after amnioreduction, especially in recipient twins. These include ventricular hypertrophy, and pulmonary outflow tract obstruction (Fesslova et al., 1998; Zosmer et al., 1994) A high incidence of other neonatal complications has also been described following TTTS pregnancies in which amnioreduction was the principle intervention (Duncombe et al., 2003; Lopriore et al., 2003). Despite some reports of abnormal brain ultrasonography following the advent of laser ablation of communicating placental vessels for the management of TTTS (Hecher et al., 1999; Quintero et al., 2003; Senat et al., 2004), minimal data are available on neonatal morbidities.

Accordingly the aim of the present study is to compare perinatal outcomes and neonatal morbidities before and after the introduction of a laser therapy program for severe TTTS in a single tertiary referral center.

Methods

This observational study consisted of TTTS pregnancies managed in the Maternal Fetal Medicine Unit at the Mater Mothers' Hospital, Brisbane. As the study was a quality assurance activity, according to the guidelines of the Mater Health Services' Human Research Ethics Committee, it was exempt from

Received 10 October, 2005; accepted 8 February, 2006.

Address for correspondence: Dr P. H. Gray, Division of Neonatology, Mater Mothers' Hospital, Raymond Tce, South Brisbane, Queensland 4101, Australia. E-mail: Peter.Gray@mater.org.au

formal review and approval. TTTS was diagnosed by ultrasound with the features of polyhydramnios in one twin sac (the deepest vertical pool of amniotic fluid being greater than or equal to 8 cms) and oligohydramnios (the deepest vertical pool being less than or equal to 2 cms) in the co-twin of a monochorionic pregnancy. A thin dividing membrane between the two sacs without the 'twin peak' sign was identified by ultrasonography. The pregnancies were staged according to the criteria of Quintero et al. (1999). For those pregnancies managed prior to the introduction of the program of laser ablation of placental communicating vessels, the staging was carried out retrospectively, with prospective staging being performed with commencement of the laser program.

Laser therapy was introduced in March 2002 with serial amnioreduction being the standard treatment prior to this time. Therapeutic amnioreduction was performed with an 18G needle under local anaesthetic. A median of two (range one to four) procedures were undertaken per pregnancy with the total volume of amniotic fluid drained per procedure ranging from 0.4 to 4.0 litres (median 1.8 litres). Laser ablation was performed under general anaesthetic. A 3.5 mm trochar was inserted under ultrasound guidance into the uterine cavity percutaneously. A viewing fetoscope (Wolff) was then inserted, with the vasculature on the surface of the monochorionic placenta being mapped and the anastomoses between the twins' circulations identified. An operating fetoscope (Wolff) was then inserted with a laser fibre being inserted down the side port. A Dornier diode laser was used to ablate the anastomoses along the vascular equator using the selective technique (Quintero et al., 2000). The criteria for laser therapy were Stage II TTTS of early onset with severe polyhydramnios and all cases of Stage III and IV TTTS.

Forty-nine consecutive cases of TTTS were identified from January 1994 until the commencement of the laser program. Two pregnancies were treated with cord occlusion of the recipient twin and nine were assessed as Stage I. These were excluded from further analysis. There were 38 Stage II–IV pregnancies of which 27 were treated with amnioreduction. In 11 cases amnioreduction was not performed because of delivery shortly after presentation or intrauterine death. From March 2002 to December 2003, 45 pregnancies with TTTS were identified. Four cases were assessed as Stage I and were not analyzed further. Forty-one pregnancies were considered for laser ablation of the communicating vessels. Laser therapy was not undertaken in two Stage II pregnancies (one delivered before laser treatment could be performed, while the parents of the other declined treatment because of fetal ventriculomegaly), six Stage III pregnancies (three delivered before laser treatment, one was found to have premature rupture of membranes and two cases of parental refusal — one because of a twin having an intraparenchymal intracranial hemorrhage) and two Stage IV pregnancies (one had cervical incompetence and the other had premature rupture of membranes). Laser therapy was thus undertaken in 31 pregnancies. Accordingly comparisons were made between the 31 pregnancies managed with laser therapy (laser group) and the 27 pregnancies in which amnioreduction were performed (amnioreduction group).

Perinatal mortality (intrauterine and neonatal death) was compared between the TTTS cases between the two groups. Neonatal morbidities between the two groups were also compared. Standard neonatal intensive care practices were employed with mechanical ventilation as deemed appropriate. Respiratory complications were documented with chronic lung disease of prematurity diagnosed on the basis of a need for supplemental oxygen at 28 days (Bancalari et al., 1979) and 36 weeks' gestation corrected for prematurity (Shennan et al., 1988). For the purposes of the study, hypotension was defined as a mean blood pressure below that appropriate for gestational age and deemed to require treatment with colloid or crystalloid. Inotropes were only used for hypotension unresponsive to treatment with fluids. Renal failure was defined as a urine output of less than 1 ml/kg/h during the first 3 days of life. Cranial ultrasonography was performed during the first week of life and thereafter when indicated on clinical grounds.

For statistical analysis, Student's t test was used for continuous normally distributed variables with the Mann-Whitney test for nonparametric data. Results of categorical variables were compared using the chi-squared test. A p value of less than .05 was considered to be significant. Analysis was performed using Statistix 8. No prospective power analysis was performed.

Results

The 27 pregnancies with Stage II–IV TTTS in the amnioreduction group were evaluated. The median (IQ range) gestation at therapy was 20 (19–22) weeks, range 18 to 28 weeks. Delivery occurred at a median (IQ range) gestational age of 28 (26–31) weeks, range 19 to 36 weeks. The mean (*SD*) interval from diagnosis to delivery was 7.3 (4.7) weeks. There were 19 pregnancies resulting in both twins being born alive. The median birthweight for the donors was 940 g in comparison to 1312 g for the recipients (p = .11).

There were 31 pregnancies with Stage II–IV TTTS that underwent laser ablation of the communicating placental vessels. In one instance, laser therapy could not be completed due to hemorrhage into the amniotic cavity making visualization of the placental vessels difficult. In another case, insertion of the fetoscope was followed by persistent fetal bradycardia, so laser ablation was not attempted. The pregnancy was subsequently managed by amnioreduction. Laser surgery was successful for the remaining pregnancies. All 31 pregnancies have been included in the laser group, however, on an intention-to-treat basis. The median (IQ range) of therapy was 21 (19–23) weeks, similar to the gestational age for the amnioreduction group (p = .24). Delivery occurred at a median (IQ

https://doi.org/10.1375/twin.9.3.438 Published online by Cambridge University Press

Table 1

Perinatal Outcome per Total Number of Fetuses According to Stage of Twin–Twin Transfusion Syndrome

	Amnioreduction group (n = 54)		Laser group (n = 62)		
Stage	Alive	Dead	Alive	Dead	p value
II	9 (56.3%)	7 (43.7%)	3 (30%)	7 (70%)	.19
III	19 (59.4%)	13 (40.6%)	28 (82.3%)	6 (17.7%)	.04
IV	4 (66.7%)	2 (33.3%)	17 (94.4%)	1 (5.6%)	.07
Total	32 (59.3%)	22 (40.7%)	48 (77.4%)	14 (22.6%)	.03

range) gestational age of 34 (29.5–36) weeks, range 20 to 38 weeks, significantly greater than in the amnioreduction group (p = .002). The mean (*SD*) interval from therapy to delivery was 10.3 (5.5) weeks, significantly longer than in the amnioreduction group (p = .03). There were 22 pregnancies with both twins being born alive in the laser group. The median birthweight for the donors was 1780 g in comparison to 1870 g for the recipients (p = .58). When the birthweights of the live-born twins were compared between the two groups, the laser twins — both donor and recipients — were of greater birthweight, though statistical significance was only reached for the donors.

Table 1 shows the survival rate by stage per total number of fetuses in the two groups with the overall perinatal survival rate being significantly better in the laser group (77.4% vs. 59.3%, p = .03). While there was a substantial improvement in outcome for the Stage IV cases, statistical significance was not reached.

Table 2 shows the pregnancy outcome by stage of TTTS in terms of whether there were no survivors, at least one survivor or two survivors. Overall the patients in the laser group were more likely to have a pregnancy with one survivor than patients in the amnioreduction group (87.1% vs. 66.7 %) though this failed to achieve statistical significance (p = .06). Additionally, pregnancies in the laser group were more likely to result in two survivors than in the amnioreduction group (67.7% vs. 51.9%), though again statistical significance was not achieved (p = 0.21).

Pregnancy losses in terms of fetal and neonatal death and in donors and recipients are shown in Table 3.

Table 3

Pregnancy Losses in Twin–Twin Transfusion Pregnancies in the Amnioreduction and Laser Groups

	Amnioreduction group (n = 54)	Laser group (n = 62)	p value
Fetal death of donor	7 (25.9%)	8 (25.8%)	.99
Fetal death of recipient	6 (22.2%)	3 (9.7%)	.18
Fetal deaths	13 (24.0%)	11 (17.7%)	.40
Neonatal death of donor	4 (14.8%)	1 (3.2%)	.12
Neonatal death of recipient	5 (18.5%)	2 (6.4%)	.16
Neonatal deaths	9 (16.7%)	3 (4.8%)	.037
Donor deaths	11 (40.7%)	9 (29.0%)	.35
Recipient deaths	11 (40.7%)	5 (16.1%)	.036

There was no difference in fetal deaths between the groups, but there were fewer neonatal deaths in the laser group (p = .037). Analysis did not reveal a difference overall in deaths of donor twins between the groups, but there were significantly fewer recipient deaths in the laser group (p = .036). In the amnioreduction group there was no difference in the outcome in terms of fetal deaths between donor and recipient twins. In the laser group, more fetal donor deaths were found in comparison to fetal recipient deaths, though this was not statistically significant (p = .09).

Table 4 shows the neonatal characteristics of the TTTS twins in the two groups. Acute respiratory morbidity occurred more frequently in the amnioreduction group with respiratory assistance being required for a significantly greater duration. While more infants in the amnioreduction group required supplemental oxygen at 36 weeks' postmenstrual age compared to the laser era, this was not statistically significant.

The incidence of patent ductus arteriosus (PDA) requiring treatment with indomethacin was greater in the amnioreduction group as was the incidence of hypotension and the requirement for inotropic support. Oliguric renal failure during the first days of life was more common in the amnioreduction group though no infant developed chronic renal disease.

Neurologic morbidities are shown in Table 5. There was no difference in the incidence of hemorrhagic brain

Table 2

Pregnancy Outcome by Stage of Twin–Twin Transfusion Syndrome

	Amnioreduction group				Laser group			
		No survivors	At least 1 survivor	Two survivors		No survivors	At least 1 survivor	Two survivors
Stage		n (%)	n (%)	n (%)		n (%)	n (%)	n (%)
II	n = 8	3 (37.5)	5 (62.5)	3 (37.5)	n = 5	3 (60)	2 (40)	1 (20)
III	n = 16	5 (31.2)	11 (68.8)	9 (56.3)	n = 17	1 (5.9)	16 (94.1)	12 (70.6)
IV	n = 3	1 (33.3)	2 (66.7)	2 (66.7)	n = 9	0	9 (100)	8 (88.9)
Total	n = 27	9 (33.3)	18 (66.7)	14 (51.9)	n = 31	4 (12.9)	27 (87.1)	12 (67.7)

https://doi.org/10.1375/twin.9.3.438 Published online by Cambridge University Press

Table 4

Neonatal Morbidities in Live-Born Neonates in the Amnioreduction and Laser Groups

	Amnioreduction group (n = 41)	Laser group (n = 51)	p value
Respiratory distress			
Nil	8 (13.8%)	24 (47.1%)	.0001
Respiratory distress syndrome	33 (56.9%)	11 (21.6%)	
Transient tachypnoea of newborn	27 (46.6%)	16 (31.4%)	
PIE/Pneumothorax	3 (7.3%)	0	.049
Oxygen (days) median (IQ range)	3 (0–22)	1 (0–1)	.001
IPPV	24 (58.5%)	10 (19.6%)	.0001
days – median (IQ range)	2 (0–8)	0 (0–0)	.0001
Ventilatory assistance	28 (68.3%)	23 (45.1%)	.026
days – median (IQ range)	2 (0–23)	1 (0–2)	.003
Chronic lung disease — 28 d	7 (17.1%)	2 (3.9%)	.034
— 36 wk	4 (9.8%)	2 (3.9%)	.26
Patent ductus arteriosus	9 (22.0%)	3 (5.6%)	.023
Hypotension	19 (46.3%)	4 (7.8%)	.0001
Dopamine administration	15 (36.6%)	3 (5.6%)	.0002
Oliguric renal failure	12 (29.3%)	2 (3.9%)	.0007
Sepsis	13 (31.7%)	4 (7.8%)	.003

Note: PIE, pulmonary interstitial emphysema; IPPV, intermittent positive pressure ventilation.

lesions diagnosed by cranial ultrasound between the groups with no infant having a grade 3–4 periventricular hemorrhage (PVH). In the amnioreduction group cystic periventricular leukomalacia (PVL) was diagnosed in three infants. An additional two infants had evidence of cerebral atrophy on brain imaging despite having had no prior cystic changes visualized on ultrasound. None of the infants during the laser era had evidence of ischemic brain injury, this being statistically significant compared to the amnioreduction group of infants (p = .01).

In general, morbidities in the neonatal period were significantly reduced for the laser treated group of infants. The mean length of hospital stay was 32.8 days (SD = 28.9 days) in the laser group significantly less in comparison to the mean of 48.0 days (SD = 41.8 days) in the amnioreduction group (p = .042).

Discussion

The present study examined the outcomes of TTTS pregnancies managed by fetoscopic laser ablation of the placental anastomoses compared to serial amnioreduction in a single perinatal center. The results indicate that the survival rate improved significantly from 59.3% to 77.4%. This was associated with a prolongation of the pregnancies from a median of 28 weeks' gestation to a median of 34 weeks, with a corresponding reduction in neonatal morbidity. The survival rate in the amnioreduction group was somewhat lower than some previous reports (Dickinson & Evans, 2000; Lopriore et al., 2003). This is probably because the outcomes from the less severe Stage I TTTS pregnancies were not included in the current study as preliminary observational data suggest no benefit for laser surgery for these pregnancies (Quintero et al., 2003). With exclusion of Stage I pregnancies, Duncombe et al. (2003) reported a survival rate of 55.1%, very similar to the 59.3% in our series.

The laser program for ablation of placental communicating vessels for severe TTTS at the Mater Mothers' Hospital only commenced following extensive training of the maternal fetal medicine specialists (Chan et al., 2003). The overall survival rate of 77.4% and the pregnancy outcome of having at least one twin survive to hospital discharge of 87.1% is better than many previous reports (Hecher et al., 2000; Quintero et al., 2003). In the recently reported randomized control trial of endoscopic laser surgery versus serial amnioreduction for severe TTTS, the overall survival rate was 56% with 76% of pregnancies having at least one survivor (Senat et al., 2004). It would thus seem that overall, with appropriate training resulting in the necessary skills prior to embarking on a laser program, the 'learning curve'

Table 5

Neurologic Morbidities in the Amnioreduction and Laser Groups of Infants

	Amnioreduction group (n = 41)	Laser group (n = 51)	p value
PVH (grade 1–2)	3 (7.3%)	4 (7.8%)	.92
PVH (grade 3–4)	0	0	
Cystic PVL	3 (7.3%)	0	.049
Cerebral atrophy	2 (4.9%)	0	.11
Ischemic brain injury	5 (12.2%)	0	.01

Note: PVH, periventricular hemorrhage; PVL, periventricular leukomalacia.

https://doi.org/10.1375/twin.9.3.438 Published online by Cambridge University Press

reported by others (De Lia et al., 1995; Hecher et al., 2000) need not occur or can be minimized.

We have reported the outcomes in terms of at least one twin surviving to hospital discharge (in addition to perinatal survival of all fetuses) as has been the practice of other authors. This may imply that the outcome of such a pregnancy would be seen as a success. However, we counsel families according to the overall survival rate of fetuses as most families want both twins to survive and be well. We have observed that most families are highly motivated to undertake laser surgery as this treatment offers a chance that both twins may survive rather than consider treatment options such as cord occlusion. While most mothers are grateful to take one baby home, the grief associated with the loss of a twin is substantial (Swanson et al., 2002) and thus this needs to be managed with appropriate support and sensitivity.

Analysis of the outcome according to the staging of TTTS as proposed by Quintero et al. (1999) indicated that in the amnioreduction group the worst outcomes were for the Stage IV pregnancies, similar to other series (Duncombe et al., 2003; Quintero et al., 2003). There was a marked improvement in outcome for the Stage IV TTTS pregnancies following laser therapy which was related to the resolution of hydrops which occurred in all cases. The outcome for the Stage III pregnancies also improved following the introduction of the laser program, consistent with the findings of Quintero et al. (2003).

An early study revealed that the rate of intrauterine fetal death for donor fetuses was 42% following laser therapy (De Lia et al., 1999), probably related to unequal placental sharing between the two fetuses. Selective laser ablation of placental vessels as undertaken in the present group has reduced the donor fetal loss to 26%, similar to the 27% reported by Quintero et al. (2003). The marked reduction in the incidence of 'recipient' deaths was largely related to the improved outcome for the hydropic fetuses who survived *in utero* following laser surgery, with neonatal death also being avoided. Thus it would seem that laser therapy has the greatest potential in offering benefits to Stage III and IV TTTS pregnancies especially in relation to recipient fetuses.

The gestational age at delivery was significantly greater in the laser group. This was associated with a lower incidence of neonatal complications. Whereas there is some information on neonatal morbidity when amnioreduction was the principal therapy for TTTS, minimal data are available following laser therapy. Sutcliffe et al. (2001) reported that 38% of surviving infants who delivered at a mean of 31 to 33 weeks' gestation were mechanically ventilated compared to the 20% in our cohort. Importantly, chronic lung disease which has been found to be associated with neurodevelopmental impairment occurred less frequently following introduction of the laser program.

In the present series, a significantly greater incidence of ischemic brain injury was found in the amnioreduction compared to the laser group of infants. In accordance with our findings, cystic PVL (Dickinson & Evans, 2000) and cerebral atrophy (Lopriore et al., 2003; Trespidi et al., 1997) have been described when amnioreduction has been the main therapeutic intervention employed for TTTS. The majority of studies on the outcomes of pregnancies following laser therapy have reported little or no neonatal data regarding cranial ultrasonographic findings, though Hecher et al. (1999) found that the incidence of abnormal ultrasonographic findings in the brain was significantly lower among surviving infants after laser surgery than after amniocentesis. In the randomized controlled trial of Senat et al. (2004), cystic PVL was described in the laser group, though it occurred significantly less often than in the amnioreduction group. None of the infants in our series had evidence of ischemic brain injury on ultrasound which is encouraging. A brain scan without significant hemorrhagic or ischemic injury, however, does not necessarily equate with a normal neurodevelopmental outcome (Tran et al., 2005). This can only be ascertained by follow-up of the children to infancy and beyond so that outcome in terms of cerebral palsy and cognitive deficits can be determined.

As far as we know, this is the first observational cohort study in which twin pregnancies complicated by TTTS managed in the same perinatal center before and after the introduction of a laser program have been reported. Thus while the management of the pregnancies was undertaken by the same team of maternal fetal medicine specialists throughout the study period, the study has the potential for bias as the treatment was not undertaken contemporaneously. Nevertheless the gestational age for therapy was similar for the two groups of patients, with a highly significant difference seen between the groups for gestation at delivery, perinatal outcomes and neonatal complications. It should also be noted that even though similar numbers of TTTS pregnancies were assessed in the amnioreduction and laser groups, the amnioreduction group was gathered over an 8-year period, with most of the mothers being resident in Queensland, as the study hospital is a tertiary referral center for the State. The laser group was treated over a little less than 2 years. Over 50% of the mothers were referred from centers outside of Queensland (including international referrals from New Zealand), thus explaining the shorter duration of recruitment for this group.

Overall we would agree with the findings of Fox et al. (2005) in their systematic review, that fetoscopic laser ablation of placental anastomoses seems to be more effective than serial amnioreduction in the treatment of TTTS with less perinatal mortality and neonatal morbidity. Until results from additional randomized controlled trials are available, we believe that laser therapy has an important role to play in the management of severe TTTS when undertaken by appropriately trained specialists.

https://doi.org/10.1375/twin.9.3.438 Published online by Cambridge University Press

References

Bancalari, E., Abdenour, G. E., & Feller, R. (1979). Bronchopulmonary dysplasia: Clinical presentation. *Journal of Pediatrics*, *79,* 819–823.

Chan, F. Y., Soong, B., Taylor, A., Bornick, P., Allen, M., Cincotta, R., & Quintero, R. (2003). Fetal endoscopic telesurgery using an internet protocol connection: Clinical and technical challenges. *Journal of Telemedicine and Telecare*, *9*(Suppl. 2), S12–14.

Cincotta, R. B., Gray, P. H., Phythian, G., Rogers, Y. M., & Chan, F. Y. (2000). Long-term outcome of twin-twin transfusion syndrome. *Archives of Disease in Childhood Fetal and Neonatal Edition, 83,* F171–176.

De Lia, J. E., Kuhlmann, R. S., Harstad, T. W., & Cruikshank, D. P. (1995). Fetoscopic laser ablation of placental vessels in severe previable twin–twin transfusion syndrome. *American Journal of Obstetrics and Gynecology*, *172,* 1202-1211.

De Lia, J. E., Kuhlmann, R. S., & Lopez, K. P. (1999). Treating previable twin-twin transfusion syndrome with fetoscopic laser surgery: Outcomes following a learning curve. *Journal of Perinatal Medicine*, *27*, 61–67.

Dickinson, J. E., & Evans, S. F. (2000). Obstetric and perinatal outcomes from the Australian and New Zealand Twin–Twin Transfusion Syndrome Registry. *American Journal of Obstetrics and Gynecology*, *182,* 706–712.

Duncombe, G. J., Dickinson, J. E., & Evans, S. F. (2003). Perinatal characteristics and outcomes of pregnancies complicated by twin-twin transfusion syndrome. *Obstetrics and Gynecology, 101,* 1190–1196.

Fesslova, V., Villa, L., Nava, S., Mosca, F., & Nicolini, U. (1998). Fetal and neonatal echocardiographic findings in twin–twin transfusion syndrome. *American Journal of Obstetrics and Gynecology*, *179,* 1056–1062.

Fox, C., Kilby, M. D., & Khan, K. S. (2005). Contemporary treatments for twin-twin transfusion syndrome. *Obstetrics and Gynecology*, *105,* 1469–1477.

Gul, A., Aslan, H., Polat, I., Cebeci, A., Bulut, H., Sahin, O., & Yavuz, C. (2003). Natural history of 11 cases of twin-twin transfusion syndrome without intervention. *Twin Research*, *6,* 263–266.

Hecher, K., Plath, H., Bregenzer, T., Hansmann, M., & Hackelöer, B. J. (1999). Endoscopic laser surgery versus serial amniocentesis in the treatment of severe twin–twin transfusion syndrome. *American Journal of Obstetrics and Gynecology*, *180,* 717–724.

Hecher, K., Diehl, W., Zikulnig, L., Vetter, M., & Hackelöer, B. J. (2000). Endoscopic laser coagulation of placental anastomoses in 200 pregnancies with severe mid-trimester twin-to-twin transfusion syndrome. *European Journal of Obstetrics, Gynecology and Reproductive Biology, 92,* 135–139.

Johnsen, S. L., Albrechtsen, S. A., & Pirohen, J. (2004). Twin-twin transfusion syndrome treated with serial amniocenteses. *Acta Obstetricia et Gynecologica Scandinavica, 83,* 326–329.

Lopriore, E., Nagel, H. T. C., Vandenbussche, F. P. H. A., & Walther, F. J. (2003). Long-term neurodevelopmental outcome in twin-to-twin transfusion syndrome. *American Journal of Obstetrics and Gynecology*, *189,* 1314–1319.

Quintero, R. A., Comas, C., Bornick, P. W., Allen, M. H., & Kruger, M. (2000). Selective versus non-selective laser photocoagulation of placental vessels in twin-to-twin transfusion syndrome. *Ultrasound in Obstetrics and Gynecology*, *16,* 230–236.

Quintero, R. A., Dickinson, J. E, Morales, W. J. Bornick, P. W., Bermudez, C., Cincotta, R., Chan, F. Y., & Allen, M. H. (2003). Stage based treatment of twin–twin transfusion syndrome. *American Journal of Obstetrics and Gynecology*, *188*, 1333–1340.

Quintero, R. A., Morales, W. J., Allen, M. H., Bornick, P. W., Johnson, P. K., & Kruger, M. (1999). Staging of twin-twin transfusion syndrome. *Journal of Perinatology*, *19,* 550–555.

Senat, M. V., Deprest, J., Boulvain, M., Paupe, A., Wioner, N., & Ville, Y. (2004). Endoscopic laser surgery versus serial amnioreduction for severe twin-to-twin transfusion syndrome. *New England Journal of Medicine*, *351,* 136–144.

Shennan, A. T., Dunn, M. S., Ohlsson, A., Lennox, K., & Hoskins, E. M. (1988). Abnormal pulmonary outcomes in premature infants: Prediction from oxygen requirement in the neonatal period. *Pediatrics, 82,* 527–532.

Sutcliffe, A. G., Sebire, N. J., Pigott, A. J., Taylor, B., Edwards, P. R., & Nicolaides, K. H. (2001). Outcome for children born after in utero laser therapy for severe twin-twin transfusion syndrome. *British Journal of Obstetrics and Gynaecology*, *108,* 1246–1250.

Swanson, P. B., Pearsall-Jones, J. C., & Hay, D. A. (2002). How mothers cope with the death of a twin or higher multiple. *Twin Research*, *5,* 156–164.

Tran, U., Gray, P. H., & O'Callaghan, M. J. (2005). Neonatal antecedents for cerebral palsy in extremely preterm babies and interaction with maternal factors. *Early Human Development*, *81, 555–561.*

Trespidi, L., Boschetto, C., Caravelli, E., Villa, L., Kustermann, A., & Nicolini, U. (1997). Serial amniocenteses in the management of twin-twin transfusion syndrome: When is it valuable? *Fetal Diagnosis and Therapy*, *12,* 15–20.

Ville, Y., Hyett, J., Hecher, K., & Nicolaides, K. (1995). Preliminary experience with endoscopic laser surgery for severe twin-twin transfusion syndrome. *New England Journal of Medicine*, *332*, 224–227.

Zosmer, N., Bajoria, R., Weiner, E., Rigby, M., Vaughan, J., & Fisk, N. M. (1994). Clinical and echographic features of in utero cardiac dysfunction in the recipient twin in twin-twin transfusion syndrome. *British Heart Journal*, *72,* 74–79.

https://doi.org/10.1375/twin.9.3.438 Published online by Cambridge University Press