

Fetoscopic laser ablation for twin-to-twin transfusion syndrome in Malaysia: A 15-month retrospective cohort review from an emerging centre in South East Asia

Lee Na Tan, MRCOG^{1,2,3}, Glenn J Gardener, FRANZCOG⁴, J Ravichandran R Jeganathan, M.Med(O&G)⁵, Aruku Naidu Apana, FRCOG¹, Ghani Hassan Perumal, Dip (Medical Assistant)¹, Rohanita Ahmad Zainuddin, Dip Nursing (Midwifery)¹, Mark David Kilby, FRCOG^{6,7}

¹Hospital Raja Permaisuri Bainun, Ministry of Health, Ipoh, Malaysia, ²Hospital Umum Sarawak, Kuching, Malaysia, ³Hospital Tunku Azizah, Ministry of Health, Kuala Lumpur, Malaysia, ⁴Mater Centre for Maternal Fetal Medicine, Brisbane, Qld., Australia, ⁵Hospital Sultanah Aminah, Ministry of Health, Johor Bahru, Malaysia, ⁶Fetal Medicine Centre, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, United Kingdom, ⁷Institute of Metabolism and System Research, College of Medical and Dental Sciences, University of Birmingham, Edgbaston, United Kingdom

ABSTRACT

Introduction: The authors aim to review the early outcomes of fetoscopic laser ablation (FLA) to improve outcomes for twin-to-twin transfusion syndrome (TTTS) in an emerging national centre in Malaysia.

Materials and Methods: This is a retrospective cohort study of 17 monochorionic diamniotic (MCDA) twin pregnancies with severe TTTS treated by FLA over 15 months in a single centre by a single operator after performing simulations.

Result: The overall survival rate at day 28 after birth for at least one twin was 76% while the dual-twin survival was 64%. The survival rates at day 28 after birth for at least one twin for stages II, III and IV were 90% vs 40% vs 100% ($p=0.054$) while dual survival rates were 80% vs 0% vs 100% ($p=0.05$), respectively. The rate of miscarriage was higher with anterior placentation compared to posterior placentation (33% vs 18%, $p=0.660$). There was one case of recurrent TTTS and no twin anaemia-polycythaemia sequence post-FLA. The fetal medicine unit in Ipoh is the national centre in Malaysia which covers the whole country, including the western coast of the Borneo Island (Sabah, Sarawak and Labuan) accessible only by air travel. All three cases from Borneo Island had resolved TTTS after FLA and dual neonatal survival at day 28 after birth.

Conclusion: This data from an emerging new fetoscopic laser centre in Malaysia indicates results consistent with the published international learning curve and within the limits of good clinical governance.

KEYWORDS:

Solomon technique; fetoscopic laser ablation; placenta vascular anastomoses; twin-to-twin transfusion syndrome; fetoscopic laser ablation simulation; Malaysia

INTRODUCTION

The incidence of multiple pregnancies, particularly twins, in Malaysia is increasing with the universal use of assisted

reproductive therapy in healthcare systems and increased maternal age at conception, because of delayed fecundity.¹ Monochorionicity is present in approximately 20% of all twin pregnancies and results from the cleavage of a single zygote, with subsequent sharing of the placenta between the fetuses.^{2,3} Twin-to-twin transfusion syndrome (TTTS), selective fetal growth restriction (sFGR), twin reversed arterial perfusion sequence (TRAPs) and twin anaemia-polycythaemia sequence (TAPS) are some examples of complications specific to monochorionic (MC) pregnancies.

TTTS specifically is the consequence of "unbalanced" net flow of blood between the two fetuses through placental vascular anastomoses (arterioarterial, venovenous and arteriovenous) as well as unequal sharing of placental territory between these fetuses.^{4,5} Djaafri et al.⁶ and Berghella et al.⁷ reported that TTTS complicates up to 15% of MC pregnancies and has a fetal mortality rate of up to 90% without treatment.

Fetoscopic laser ablation (FLA) of shared placental vascular anastomoses has been demonstrated to improve survival outcomes in TTTS.^{8,9} The single and dual twin survival rates for TTTS following FLA have been quoted to be as high as 91% and 61%, respectively, and is superior therapy in comparison with other treatment options such as serial amniocentesis, septostomy or selective fetal reduction.^{10,11} Neurodevelopmental outcomes of infants with TTTS are more favourable after FLA compared to amniocentesis, for both short-term (3-16% vs 5-38% for cerebral injury, respectively) and long-term outcomes (3-12% cerebral palsy (CP) and 7-18% neurodevelopmental impairment (NDI) vs 5-23% CP and 14-26% NDI, respectively).^{12,13}

The current fetal medicine team in Raja Permaisuri Bainun Hospital (HRPB), Ipoh is the national centre in Malaysia providing FLA services since the beginning of 2019. This is a retrospective cohort study to present the outcomes of FLA in the first consecutive 17 MC pregnancies complicated by severe TTTS between March 2019 until May 2020. The authors aim to review the early outcomes of FLA in this emerging national centre in which FLA service was started

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Corresponding Author: Tan Lee Na

Email: tanleena2021@gmail.com

after performing simulations and offered to all TTTS patients nationwide including the states of Sabah and Sarawak on Borneo Island, accessible only by air travel.

MATERIALS AND METHODS

Study Population

The authors retrospectively reviewed the prenatal and neonatal outcomes (up to 28 days) in all monochorionic diamniotic (MCDA) twin pregnancies in which FLA was performed over a 15-month period. The prospective ultrasound diagnosis of TTTS was made using accepted international criteria and staged using the Quintero staging system.¹⁴ TAPS was diagnosed antenatally based on discrepancies of middle cerebral artery peak systolic velocity (MCA-PSV) measurement using a Multiple of Median (MoM) (delta MCA-PSV of more than 0.5). FLA was performed on all MCDA cases with TTTS Quintero stages II, III and IV between gestational ages ranging from 17⁰ to 27⁶, within 48 hours of diagnosis.

Procedure

Prior to performing FLA on the first patient with TTTS, the team (a surgeon, a senior medical assistant and a nursing sister) underwent simulated training to replicate the actual clinical scenario to improve the performance of FLA in real patients.¹⁵ Actual postpartum monochorionic placentas were fixed onto the floor of a container and submerged in water. The container was subsequently covered and fetoscope was inserted through a hole made in the lid of the container, following which FLA was performed on the placental vascular anastomoses. The placentas were examined post-procedure to evaluate the completeness of laser ablation using color dye injection. All human cases of FLA were performed by a single operator (one of the authors, LNT), who had undergone a 1-year clinical fellowship at Birmingham Women's Foundation trust (observed and participated in FLA for TTTS with more than 60 cases per annum).

In cases of monochorionic twin pregnancies complicated by TTTS, transabdominal ultrasound scan including placental site documentation with the mapping of umbilical cord insertions was performed by the operating team prior to surgery, and written consent was obtained from all subjects. All patients received a single dose of pre-operative intravenous Cefuroxime 1.5 grams, 6 hours before operation. All surgeries were performed in the operation theatre, using a 'minimal touch technique' with local analgesia only (10 ml 2% lignocaine hydrochloride and 10 ml 0.5% Marcaine of the skin, subcutaneous tissues and uterine muscle of the portal entry site), with additional maternal sedation with intravenous midazolam and fentanyl if required.

A vascular access trocar (Terumo Radifocus) and cannula were inserted under ultrasound guidance into the amniotic sac of the recipient twin, followed by insertion of a straight-forward (2mm, 0o, Karl Storz) fetoscope.^{16,17} In cases with anterior placentation, the subjects were positioned in either lithotomy or lateral positions to improve visualisation and ablation of placental vascular anastomoses. In all cases, direct visualisation and mapping of the placental vascular anastomoses were performed, followed by FLA of the anastomoses (30W, diode laser, Dornier Medilas D

Multibeam) using a selective, sequential technique and then the "Solomon modification".^{9,18} Amnioreduction was performed after FLA to achieve a deepest vertical amniotic pool depth of between 6 and 8 cm, and in cases where there were still significantly high amniotic fluid volume despite amnioreduction of between 2 and 3 litres, amnioreduction was performed only until the uterus was less distended and the mother felt comfortable lying supine. If the cervical length prior to delivery was less than 25mm from transvaginal scan, a cervical cerclage (McDonald) was inserted after FLA and amnioreduction.

Clinical assessment of all women and fetuses was performed immediately after surgery and they were reviewed again at 24 hours post-surgery for fetal viability, MCA-PSV Doppler measurements and sonographic evidence of inadvertent septostomy. Cases were subsequently followed up by weekly ultrasound scans in their respective referral centers and delivery outcomes were collected through telephone communication with both doctors and patients.

Outcome Measures

Intra-operative, immediate (within 24 hours) and post-operative outcomes, along with live birth rate and neonatal survival at day 28 were analysed. The primary outcomes were survival of the fetuses at day 28 after birth, intraoperative and immediate (within 48 hours) complications. Intraoperative outcomes included non-completion of surgery, bleeding, uterine rupture and escalation of analgesia, whereas immediate post-operative outcomes included miscarriage (loss of pregnancy at less than 24 weeks' gestation), preterm pre-labour rupture of membranes (PPROM), preterm labour, placental abruption, in-utero fetal demise and septostomy. Secondary outcomes were diagnoses during antenatal follow-up and at delivery, such as TAPS, resolution or recurrence of TTTS, PPRM, interval from procedure to delivery and survival of baby at birth.

Statistical Analysis

Statistical analysis was conducted with the SPSS software (IBM SPSS Statistics, version 25 MacOS) and qualitative data were compared using χ^2 test or Fisher exact test as appropriate. Continuous variables were tested for normality. Mann-Whitney U test was used to compare between groups for the continuous variables and Kaplan-Meier test for survival. A probability value of less than 0.05 was considered statistically significant. Interquartile range calculation was used in this study to account for extreme outliers in this dataset.

RESULTS

Over the period of 15 months, there was a total of 18 cases of FLA done for severe TTTS identified from the hospital records. Of these cases, 17 (94%) were MCDA and 1 (6%) dichorionic triamniotic which was excluded from this study. During the study period, none of the patients diagnosed with TTTS referred to HRPB declined FLA or opted for other treatment options. The subjects were all Malaysians with the exception of one Thailand national residing in Malaysia, and the ethnic origins were 10 Malays, 3 Chinese, 1 Indian, 1 Dayak and 1 Kadazandusun.

Table I: Background and case characteristics (n=?)

	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17
Quintero staging	II	IIID	II	II	IV	III	II	II	II	IIIR	IIIR	II	IIID	IV	II	II	II
Gestation at diagnosis	26	25	21	19	25	21	22	25	21	19	22	24	17	23	18	24	20
Growth discrepancy	36%	30%	19%	40%	47%	64%	9%	7%	4%	19%	38%	41%	53%	21%	25%	39%	35%
Placental location	Pos	Ant	Ant	Pos	Pos	Ant	Pos	Pos	Pos	Pos	Ant	Pos	Pos	Pos	Pos	Ant	Ant

C: case; D: donor; R: recipient; Ant: anterior; Pos: posterior

Table II: Duration of surgery, intra-operative, immediate post-operative and pregnancy outcomes (n=?)

Outcomes	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17
Intra-operative																	
Duration of surgery (min)	64	80	50	58	50	60	50	51	32	50	50	68	48	55	35	60	60
Non completion	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Bleeding	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Uterine rupture	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Escalation of analgesia	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Immediate post-operative																	
Miscarriage	N	N	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N
PPROM	N	N	N	N	N	Y	N	N	N	Y	N	N	N	N	N	N	N
Preterm labour	N	N	N	N	N	-	N	N	N	N	N	N	N	N	N	N	N
Placental abruption	N	N	N	N	N	-	N	N	N	N	N	N	N	N	N	N	N
IUFD	N	N	N	N	N	-	N	N	N	N	N	N	N	N	N	N	N
Septostomy	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pregnancy Outcomes																	
TAPS	N	N	N	N	N	-	-	N	N	N	-	N	-	N	N	N	N
Resolved TTTS	Y	N	Y	Y	Y	-	-	Y	Y	Y	-	Y	-	Y	Y	Y	Y
Recurrent TTTS	N	Y	N	N	N	-	-	N	N	N	-	N	-	N	N	N	N
PPROM (w, d)	N	N	N	N	N	Y (d1)	N	N	Y (d5)	Y (d1)	N	N	Y (w4)	N	N	N	N
Donor survival in-utero	Y	Y	Y	Y	Y	-	-	Y	Y	Y	-	Y	-	Y	Y	Y	Y
Recipient survival in-utero	Y	Y	Y	Y	Y	-	-	Y	Y	Y	-	Y	-	Y	Y	Y	Y
Donor survival and weight at birth (g)	1800	600	1500	750	900	N/A	N, N, 350	1450	1980	580	570	1295	N/A	1510	1500	800	1500
Recipient survival and weight at birth (g)	1800	900	1700	900	1000	N/A	N, N, 380	2100	2500	580	590	1320	N/A	1715	1700	1100	1700
Donor neonatal survival (d28)	Y	N	Y	Y	Y	-	-	Y	Y	N	-	Y	-	Y	Y	N	Y
Recipient neonatal survival (d28)	Y	Y	Y	Y	Y	-	-	Y	Y	Y	-	Y	-	Y	Y	Y	Y
Gestation at delivery (w)	37	28	35	27	29	21	23	34	33	25	23	31	22	33	33	26	33
Procedure to delivery interval (w)	11	3	14	8	4	0	1	9	12	6	1	7	5	10	15	2	13
Mode of delivery	C-sec	C-sec	Vag	C-sec	Vag	Vag	Vag	C-sec	C-sec	Vag	Vag	C-sec	Vag	C-sec	C-sec	Vag	C-sec

C: case; N: No; Y: Yes; PPRM: preterm pre-labour rupture of membrane; IUFD: intrauterine fetal demise of either one or both twins; TAPS: twin anaemia-polycythaemia sequence; TTTS: twin-to-twin transfusion syndrome; PPRM: preterm prelabour rupture of membrane; w: week; d: day; g: gram; FLA: fetoscopic laser ablation; C-sec: caesarean section; Vag: vaginal delivery

Table III: Perinatal data for TTTS post-FLA (n=?)

Median (IQR)	Quintero stage n(%)			
	Overall	II	III	IV
Gestational age at procedure (weeks) - Median (IQR)	22 (5)	21.5 (4)	21 (5.5)	24 (2)
Gestational age at delivery (weeks) - Median (IQR)	29 (9)	33 (7)	23 (5)	31 (4)
Procedure to delivery interval (weeks) - Median (IQR)	7 (9)	10 (6)	3 (5)	7 (6)
At least 1 survivor	13/17 (76)	9/10 (90)	2/5 (40)	2/2 (100)
1 survivor	2/17 (11)	1/10 (10)	2/5 (40)	0/2
2 survivors	11/17 (64)	8/10 (80)	0/5 (0)	2/2 (100)
Donor death (in-utero)	0/17 (0)	0	0	0
Recipient death (in-utero)	0/17 (0)	0	0	0
Donor neonatal survivor	11/17 (64)	8/10 (80)	0/5 (0)	2/2 (100)
Recipient neonatal survivor	13/17 (76)	9/10 (90)	2/5 (40)	2/2 (100)

IQR: interquartile range; Survivor: measured up to 28 days of life

Table I shows the characteristics of the cases at the time of diagnosis, with 10 cases diagnosed with Quintero stage II, 5 stage III, and 2 stage IV TTTS. The median gestation at diagnosis was 22 weeks (IQR: 5 weeks). None of the cases had concurrent TAPs prior to FLA. The growth discrepancy ranged from 4% to 64% with a median of 35% (IQR: 21.5%). Anteriorly located placenta was diagnosed in 6 out of 17 (35%) cases while the remaining 11 (65%) had posterior placentation.

The median surgery time was 50 minutes (IQR: 10 minutes). Table II demonstrates the intra-operative and immediate post-operative outcomes of FLA. There were no intraoperative complications (intra-abdominal bleeding or uterine rupture) and all cases were performed to completion; however, 1 case required escalation of analgesia (Case 3) with intravenous midazolam and fentanyl from initially only having local analgesia. In the immediate post-operative period, case 6 had amniorrhesis and miscarried 6 hours after FLA. There were three other cases with amniorrhesis; case 9 had preterm prelabour rupture of membrane (PPROM) 5 days after FLA and delivered 12 weeks later with dual twin survival; case 10 had amniorrhesis at 1 hour after FLA and induction of labour was commenced for chorioamnionitis 6 weeks later with single baby survival; case 13 had PPROM at week 4 and miscarried 1 week after. All fetuses were viable in-utero after FLA and there were no cases with placental abruption or septostomy. All cases required amnioreduction from the recipient sac and one case (case 7) had cervical cerclage for cervical length of 13 mm diagnosed pre procedure.

Table II also shows the outcomes during pregnancy and after delivery. For pregnancies with anteriorly located placenta, two out of six cases ended with miscarriage, whereas the rate was lower in cases with posteriorly located placenta (2 out of 11 cases) (33% vs. 18%, $p=0.660$). Case 2 had recurrent TTTS and had amnioreduction subsequently. There was no TAPS after FLA in this study. Of the 13 cases who did not miscarry, 4 (30%) delivered vaginally while 9 cases (64%) underwent caesarean section.

The perinatal outcomes of severe TTTS post-FLA are summarised in Table III. The overall survival rate for at least one twin was 76% while dual twin survival was 64% at day 28 after birth. The survival rates at day 28 after birth for at least one twin for stages II, III and IV were 90% vs 40% vs 100% ($p=0.054$), respectively, and dual twin survival for stages II, III and IV were 80% vs 0% vs 100% ($p=0.005$),

respectively. The median procedure-to-delivery time was 7 weeks (IQR: 9 weeks).

DISCUSSION

The 15-month review of the outcomes for FLA cases performed has shown a positive trend with overall survival rates of 76% and 64% for at least one infant survival and dual infant survival, respectively, which is comparable with internationally published success rates. This study reveals a low rate of intra- and post-operative complications, which further supports the safety of timely intervention with FLA for the treatment of TTTS to improve the outcomes of these pregnancies. The outcomes of FLA were least favourable in stage III TTTS, with only 40% survival of at least one twin, and 0% dual survival at day 28 after delivery. Although the survival rates in this study were best for cases with stage IV at diagnosis, there were only two cases in this group and the result did not reach statistical significance. Until further studies are done to confirm these findings, the authors would recommend early detection of TTTS to improve FLA outcomes in these patients.

In this series, three cases had miscarriage within 2 weeks of FLA. Case 6 had amniorrhesis after FLA was completed and delivered 6 hours after procedure. Case 7 had cervical shortening prior to FLA, and cervical cerclage was inserted vaginally (McDonald cerclage) after FLA and amnioreduction. However, she had contractions a week later and the cervical suture was removed when the contractions failed to subside despite tocolysis. The third case (case 11) is described below. The proportion of concomitant sFGR of growth discrepancy of more than 25% with TTTS in this study is consistent with that published by Van Winden et al (2015) at 67%.¹⁹ There were no cases of in-utero fetal demise in our cohort, although in the literature this ranges between 10 and 30%.²⁰⁻²²

Anterior placentation has been associated with additional technical challenges in visualising and ablating all vessels successfully with a higher rate of miscarriage. One particularly challenging case faced in the early phase of performing FLA was case 2, which took 80 minutes to complete due to difficulty in ablating a vessel located anteriorly. Follow-up ultrasonography revealed recurrent TTTS with worsening polyhydramnios in the recipient, with amnioreduction done once. The patient delivered at 28 weeks with single baby survival (recipient) at day 28 after birth.

Case 11 was referred at 22 weeks' gestation with stage III TTTS and severe polyhydramnios with deepest vertical pool (DVP) measuring 20 cm. Despite amnioreduction of 3 litres after FLA, the DVP measured 15 cm; however, no further amnioreduction was done because the patient's abdomen was soft and sudden massive amnioreduction might increase the risk of preterm labour or placental abruption. She miscarried 5 days after the procedure.

This study supports the use of only straight-forward scope for all FLA regardless of placental localisation instead of using different scopes (curved/angulated) for anterior placentation, which may result in lower overall cost of equipment. The technical difficulties of ablating vessel anastomoses in these subjects can be overcome with several measures. If vessels could not be visualised clearly due to placental 'folding' when polyhydramnios was not profound, amnioinfusion was performed to stretch and flatten the placenta surface to aid visualisation of vessel anastomoses. On the other hand, for cases with severe polyhydramnios and the length of scope was not enough to reach the placental surface, amnioreduction was performed. Cloudy amniotic fluid was resolved by performing amnio-exchange using warm normal saline infusion. Excess amniotic fluid was drained after completion of FLA to achieve a DVP of between 6 and 8 cm. Access for subjects with anterior placentation was improved by tilting patients on lateral positions and performing meticulous sonography by utilising both grey-scale and colour Doppler scans prior to trochar insertion to minimise the risk of bleeding and viscus injuries. This data also shows that most women tolerate the procedure well under local analgesia, which potentially results in lower risks associated with regional/general anaesthesia as well as encouraging earlier mobilisation post-procedure.

The strength of our team is that as the national referral centre for FLA, all cases are performed by the same dedicated team members. Each additional case enhanced the learning curve exponentially when team members worked increasingly in tandem. The learning experience is further reinforced by a comprehensive pre-operative planning for each case as well as a post-procedural discussion involving the whole team in spite of the relatively lower volume. Studies by Peeters et al. (2014) and Morris et al. (2010) regarding the learning curve for fetoscopic laser surgery have shown that operators reach a level of competence after at least 25 cases and outcomes are improved after about 61 cases and 3.4 years of experience.^{15,23} Although more cases are required before we reach this number, the initiation of FLA services was deemed to be of priority to improve outcomes of TTTS in the country. However, due to the high cost of training for the whole team at an established training centres, repeated simulations were done locally instead to increase familiarity and improve troubleshooting amongst team members. After performing five simulations as a team, the first case of FLA was done in March 2019. Although the simulation model was not as realistic as an advanced simulator, the cost of our simulator was low and easy to assemble.

Another interesting point to note in this study is the safety of patient transfer using flights to access FLA treatment. Cases 4 (stage II), 5 (stage IV) and 17 (stage II) travelled 2 hours from Sabah and Sarawak via commercial flights and then 4 hours

on land to reach HRPB. All mothers travelled home within 1 week after the procedure with 1 to 2 weekly follow-ups by the maternal-fetal medicine consultants at their primary care centres. All three had resolution of TTTS after FLA with live babies at day 28 after birth. To our knowledge, at the time of writing, the fetal medicine unit in HRPB which is located in the northern region of Peninsular Malaysia, is the single national referral centre for treatment of severe TTTS with FLA. Malaysia is formed by Peninsular Malaysia and East Malaysia (Sabah, Sarawak and Labuan on Borneo island), which is 132,091 km² and 198,444 km², respectively.²⁴ Geographically, East Malaysia is separated from Peninsular Malaysia by the South China Sea, and the only mode of transport is by air travel. The major safety concerns arising from these transfers are the risks of preterm delivery, PPRM, miscarriage and antepartum haemorrhage during the journey, which may deter referrals for FLA and deprive patients of life-saving procedure. The findings offer reassurance that distance should not be a reason to dismiss FLA as a treatment option for TTTS to patients from remote areas, after careful assessment of risks such as the presence of contractions and cervical shortening. This service can also be expanded to Malaysia's neighbouring countries in South East Asia where FLA is not available locally yet by increasing awareness about TTTS and the use of laser coagulation as the preferred treatment.²⁶

The main limitation of this study is the small number of subjects resulting in non-statistically significant findings. The other limitation is the lack of direct placental evidence to demonstrate the completeness of occlusion of vessel anastomoses. Most patients travelled back to their respective hospitals for post-operative reviews and delivery, and due to financial constraints and distance, majority could not travel to HRPB for follow-up after the primary surgery. Most hospitals did not have expertise to perform complex ultrasound surveillance of placenta in the antenatal period to support regression of TTTS and postpartum examination of placenta using color dye injection was not done in most cases. The 'success' of FLA therefore relied mainly on simpler and less specialised sonographic measurements indicating resolution of TTTS during the antenatal period which are easier to perform, including normalisation of liquor volume, presence of urine in bladder and improvement in Doppler studies and fetal hydrops. In this region where subspecialised care by Fetal Medicine Consultants is not widely available, further training of obstetricians in future should incorporate the evaluation of placenta both sonographically as well as by colour dye injection after birth to improve the accuracy of diagnosis.

Further studies looking into larger numbers and long-term outcomes, including single and dual survival outcomes and morbidities for our cases treated with FLA, are required. It is also important to note that the survival of fetuses above the threshold of viability in Malaysia is also influenced by post-delivery care, taking into consideration the resources and availability of neonatology care in different delivery centres where the babies are born. Decision regarding mode of delivery is made at the time of delivery by individual obstetricians caring for these women post-FLA, although the majority of cases were delivered via caesarean section.

CONCLUSION

In summary, the early outcomes of FLA done in the emerging national centre in Malaysia are encouraging and are consistent with the internationally published learning curve within the limits of good clinical governance. Early diagnosis and timely intervention are crucial to improve outcomes for cases of monochorionic pregnancies complicated by TTTS. Long-term follow-up of these babies are required to establish the sequelae as well as delayed morbidity. It is also vital to have a dedicated core team who are adequately trained to perform FLA in order to achieve optimal results with minimal complications. Distance from treatment centre and air travel should not discourage referrals for FLA as a life-saving measure to treat severe TTTS.

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