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Management of monochorionic diamniotic twin gestation affected by Type-II selective fetal growth restriction: cost-effectiveness analysis

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KEYWORDS: fetal; growth restriction; intervention; laser; monochorionic diamniotic; multifetal; photocoagulation; radiofrequency

ABSTRACT

Objective *Monochorionic twin gestations affected by Type-II selective fetal growth restriction (sFGR) are at increased risk of intrauterine fetal demise, extreme preterm birth, severe neurodevelopmental impairment (NDI) and neonatal death of one or both twins. In the absence of a consensus on the optimal management strategy, we chose to evaluate which strategy was cost-effective in the setting of Type-II sFGR.*

Methods *A decision-analytic model was used to compare expectant management (EM), bipolar cord occlusion (BCO), radiofrequency ablation (RFA) and fetoscopic laser photocoagulation (FLP) for a hypothetical cohort of 10 000 people with a monochorionic diamniotic twin pregnancy affected by Type-II sFGR. Probabilities and utilities were derived from the literature. Costs were derived from the Healthcare Cost and Utilization Project and adjusted to 2023 USD. The analytic horizon, taken from the perspective of the pregnant patient, extended throughout the life of the child or children. An incremental cost-effectiveness ratio of 50 000 USD per quality-adjusted life year defined the willingness-to-pay threshold. One-way and probabilistic sensitivity analysis was also performed.*

Results *For base-case estimates, RFA was the most cost-effective strategy compared with all of the other interventions included, with an incremental cost-effectiveness ratio of 14 243 USD per quality-adjusted life year. One-way sensitivity analysis demonstrated that the utilities assigned to fetal demise and severe NDI, as well as the costs of preterm birth before 32 weeks, most strongly impacted the model outcomes. On probabilistic sensitivity analysis, RFA was the most cost-effective strategy in 78% of runs, followed by BCO at 20%, EM at 2% and FLP in 0% of runs. When compared with EM, RFA led to 58 fewer births before 28 weeks' gestation, 273 fewer cases of severe NDI and 22 more deliveries after 32 weeks. When compared with FLP, RFA resulted in 259 fewer cases of severe NDI and 3177 more births after 32 weeks. When compared with BCO, RFA resulted in 1786 more neurologically intact neonates and 34 fewer cases of severe NDI.*

Conclusions *On base-case analysis, RFA was found to be the most cost-effective strategy in the management of monochorionic diamniotic twin pregnancies affected by Type-II sFGR. However, these findings were not robust on sensitivity analysis, indicating the potential benefit of BCO and EM. In the absence of large clinical trials, these data should not be taken to guide management. Future studies should evaluate management strategies for Type-II sFGR related to long-term neonatal outcomes, inclusive of quality-of-life indicators, in a prospective multicenter cohort. © 2024 The Author(s). Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

Selective fetal growth restriction (sFGR) impacts 10–15% of all monochorionic twin pregnancies[1]. This diagnosis carries significant risks throughout pregnancy, including fetal demise of one or both twins, preterm delivery, fetal

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distress, neonatal death and long-term neurodevelopmental impairment (NDI). There are multiple management options for sFGR including expectant management (EM), radiofrequency ablation (RFA), fetoscopic laser photocoagulation (FLP) and bipolar cord occlusion (BCO). Two of these management strategies, namely RFA and BCO, result in the obligatory loss of one fetus. All of these strategies carry significant risks and the overall prognosis of the pregnancy can still remain guarded, even after a successful procedural intervention[1,2].

The diagnosis of sFGR can be further categorized into Type-I, -II and -III. According to the Gratacós classification system[3], in Type-I sFGR there is positive end-diastolic flow in the umbilical artery, in Type-II there is persistent absent or reversed end-diastolic flow and in Type-III there is intermittent absence or reversal of flow. Type-II sFGR carries the highest risk of perinatal complications[3–5]. Meta-analyses have shown that pregnancies affected by Type-II sFGR have higher rates of abnormal postnatal brain imaging, intraventricular hemorrhage, intrauterine fetal demise (IUFD), co-twin demise and neonatal death of one or both twins[6]. Owing to the poor prognosis in these cases, there has been ongoing research into the best way to manage these pregnancies, specifically comparing EM with FLP[3–6].

Conducting a potential clinical trial comparing these various interventions presents ethical issues. Critically, RFA and BCO result in the selective termination of one fetus, which is neither morally acceptable to all patients nor universally permitted legally. Furthermore, randomizing management strategies in such a high-risk clinical scenario removes patient autonomy when it remains unknown whether one, if any, of the interventions is more beneficial to the pregnancy[1].

In the absence of a clinical trial, we elected to perform a cost-effectiveness analysis comparing all four management strategies for Type-II sFGR in monochorionic diamniotic (MCDA) twin pregnancies.

METHODS

A decision-analytic model, constructed from a healthcare payor perspective, was created using TreeAge Pro (Healthcare Version 2023; Tree Age Inc., Williamstown, MA, USA) to simulate a theoretical cohort of 10 000 pregnant women. This sample size was chosen owing to the number of twin births in the USA (i.e. 110 000 births per annum)[7]. Considering that 10–15% of these are monochorionic twin pregnancies, we estimated that 10 000 MCDA pregnancies occur per annum[1,7]. Approval was sought from the Institutional Review Board at the University of Chicago, which deemed this study as exempt from review (IRB23-1545).

Per person costs pertained to procedures, antenatal surveillance, delivery costs and neonatal intensive care unit costs. Probabilities were related to the pregnancy outcomes as well as NDI after delivery.

A schematic of a portion of the decision tree is displayed in Figure 1. The decision tree was designed with input from a multidisciplinary team of experts in maternal–fetal medicine, maternal–fetal surgery and healthcare economics. Studies included in our analysis represent data from multidisciplinary care centers. Furthermore, data informing our model inputs were derived from studies that specifically reported on outcomes related to Type-II sFGR (Table 1).

All theoretical patients entered the model with a known diagnosis of MCDA twin pregnancy affected by Type-II sFGR at a median gestational age of 20 weeks[4]. This gestational age was chosen owing to evidence suggesting 20 weeks as the average time of diagnosis of sFGR[3]. After this, patients would undergo EM, RFA, BCO or FLP. Outcomes following each of these interventions included preterm prelabor rupture of membranes, fetal loss of one or both twins, preterm delivery (before 28 weeks, 28–32 weeks, after 32 weeks), neonatal death of one or both twins or the diagnosis of postnatal NDI, defined as none, mild or severe (Table 1).

We assumed that 60% of deliveries occurring before 28 weeks' gestation would have some degree of NDI[41], although this probability was assumed to be lower in the setting of BCO because of data demonstrating a lower frequency of NDI after BCO[41]. For EM, the frequency of NDI was assumed based on gestational age, which was again derived from general data and expert opinion of the authors, using an outcome of cerebral palsy. The probability of preterm birth was also assumed at a general rate of 70%.

Focus was placed on selecting data from articles concentrating on sFGR as a complication of MCDA twin pregnancy, and carefully deselecting probabilities and other variables that evaluated other complications, such as twin–twin transfusion syndrome or twin anemia–polycythemia sequence.

We assumed the gestational age at delivery would be between 34 and 37 weeks, depending on the branch of the model. Guidelines suggest that MCDA pregnancies be delivered between 34 + 0 and 37 + 6 weeks, and earlier than 34 weeks if there are complications, although there are no specific guidelines regarding the timing of delivery of Type-II sFGR neonates[42,43]. With our delivery timing range assumed at a maximum gestational age of 34–37 weeks, we calculated the average number of ultrasound examinations required for fetal surveillance, biophysical profile and umbilical artery and middle cerebral artery (MCA) Doppler ultrasound. Depending on the timing of delivery for two living twins, the following estimations were made regarding the number of surveillance ultrasound scans carried out: delivery before 28 weeks' gestation, an average of three (range, 1–5) scans; delivery between 28 and 32 weeks, an average of six (range, 5–7) scans; and delivery after 34 weeks, an average of eight (range, 7–9) scans. For a singleton pregnancy resulting from RFA, BCO or spontaneous IUFD, the mean (range) numbers of surveillance ultrasound scans were the same. Details of the costs for the surveillance scans for singleton or twin pregnancy, and the range of costs based on timing of delivery, are shown in Table 1.

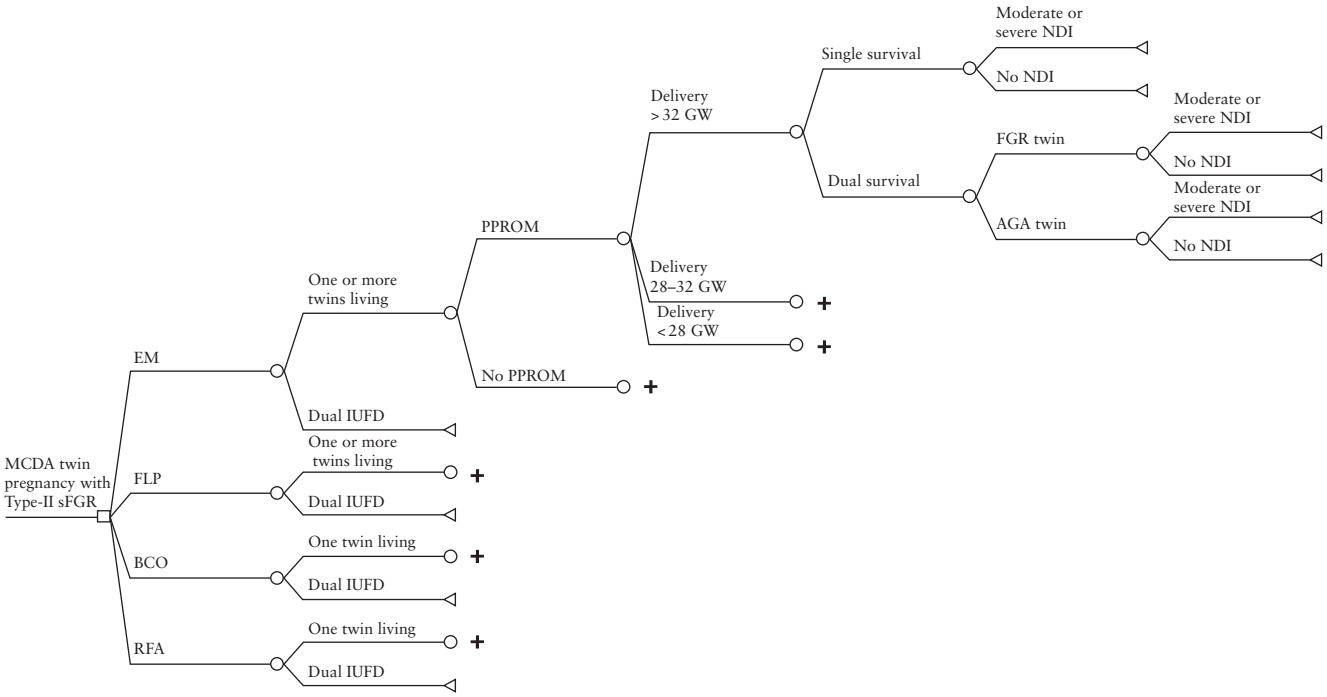

Figure 1 Abbreviated decision-tree diagram comparing four management strategies for monochorionic diamniotic (MCDA) twin pregnancy impacted by Type-II selective fetal growth restriction (sFGR). It is not representative of full decision model or entire breadth of probability pathways. Branches hidden to facilitate display are indicated (+) and are similar to those displayed. AGA, appropriate-for-gestational age; BCO, bipolar cord occlusion; EM, expectant management; FGR, fetal growth restriction; FLP, fetoscopic laser photocoagulation; GW, gestational weeks; IUFD, intrauterine fetal demise; NDI, neurodevelopmental impairment; PPROM, preterm prelabor rupture of membranes; RFA, radiofrequency ablation.

Costs in the model were derived from the Healthcare Cost and Utilization Project and were converted to 2023 USD. We chose to model utilities based on the pregnant person's perspective, rather than the neonate's perspective, to avoid shifting bias away from selective fetal reduction. This choice is in line with other studies that model termination of pregnancy[13,44,45].

Utilities were evaluated from the pregnant person's perspective, and the horizon was the remainder of the pregnant patient's life after delivery. Based on available data, we modeled the average age at first delivery as 27.3 years, with an average life expectancy of 79.3 years in the USA[7,46]. Therefore, our time horizon for the remaining life after pregnancy was 52 years, allowing us to capture the total number of years that quality-adjusted life years (QALYs), a measure of improvement or decrements in overall health, could be affected. All utilities were derived from the literature, or, if lacking, by consensus of the authors. We assumed that IUFD, procedure-related pregnancy loss, neonatal death or raising a child with NDI would reduce the quality of life for the pregnant person for the remainder of their lives. Given the length of our analytic horizon as the entire lifetime of the pregnant patient after delivery, we discounted utilities at a rate of 3% per annum[44,47]. This horizon was chosen because, although many of the model inputs only apply to the duration of the pregnancy itself, raising a child with potential NDI is a lifelong endeavor. The utility estimate for the pregnant person raising a child with any degree of NDI was lower than for those experiencing a pregnancy loss of any type. This is in line with other decision analyses focused on raising a child or children with lifelong conditions[44,47].

We assumed that the willingness-to-pay (WTP) threshold would be defined as an incremental cost-effectiveness ratio of 50 000 USD/QALY[44]. We report strategies as cost-effective, meaning the strategy does not exceed the WTP, and as dominant, meaning that the strategy is both cost-saving and more effective than the strategy with which it is being compared.

We performed one-way sensitivity analysis for all inputs to identify if any were influencing the outcomes of the model. We also chose to perform prespecified two-way sensitivity analyses focused on NDI and perinatal mortality to identify if there was any specific model input that drove the outcomes of the analysis. Monte Carlo probabilistic sensitivity analysis was performed wherein all inputs to the model were varied simultaneously over 1000 runs. Beta distributions were used for probability and utility inputs, and gamma distribution was used for cost inputs. Probabilities that were assumed and did not have estimates in the literature were varied in our sensitivity analyses by 50% above and below the base estimate to provide a confidence range. As an additional sensitivity analysis, we performed a threshold analysis by varying all inputs beyond their prespecified ranges to assess if the findings of the decision analysis changed. Further, we performed another sensitivity analysis, raising the WTP to 100 000 USD to account for varied perspectives on healthcare expenditure[44]. All

Table 1 Cost estimates, outcome probabilities and utilities for base-case model comparing management strategies for Type-II selective fetal growth restriction in diamniotic twin pregnancy

Variable	*Base value*	*Range*	*Reference*
Cost (2023 USD)			
Antepartum admission 28–32 w	11 421.54	8136.44–14 706.64	8
Antepartum admission > 32 w	11 754.30	7895.35–15 613.24	8
Antepartum admission < 28 w	9092.28	7139.43–11 045.13	8
Total BPP for singleton gestation 28–32 w	1011.06	842.55–1179.57	9
Total BPP for singleton gestation < 28 w	505.53	168.51–842.55	9
Total BPP for singleton gestation > 32 w	1516.59	1348.08–1685.10	9
Total BPP for twin gestation 28–32 w	2022.12	1685.10–2359.14	9
Total BPP for twin gestation < 28 w	1011.06	337.02–1685.10	9
Total BPP for twin gestation > 32 w	2696.16	2359.14–3033.18	9
Umbilical BCO	6567.20	5223.69–7910.71	9
Twin delivery 28–32 w	469 657.81	401 158.43–538 157.19	10,11
Singleton delivery > 32 w	75 508.05	63 462.88–87 553.22	10,11
Twin delivery > 32 w	94 205.52	78 784.89–109 626.14	10,11
Singleton delivery < 28 w	453 979.72	416 180.07–491 779.37	10,11
Twin delivery < 28 w	639 379.20	590 549.97–688 208.43	10,11
Singleton delivery 28–32 w	196 770.60	163 288.74–230 252.46	10,11
Dual IUFD	7687.76	0–7687.76	12
Single IUFD	3843.88	0–3843.88	12
FLP	6567.20	5223.69–7910.71	9
Total MCA Doppler for singleton delivering 28–32 w	1236.06	1030.05–1442.07	9
Total MCA Doppler for singleton delivering < 28 w	618.03	206.01–1030.05	9
Total MCA Doppler for singleton delivering > 32 w	1854.09	1648.08–2060.10	9
Total MCA Doppler for twins delivering 28–32 w	2472.12	2060.10–2884.14	9
Total MCA Doppler for twins delivering < 28 w	1236.06	412.02–2060.10	9
Total MCA Doppler for twins delivering > 32 w	1854.09	2472.00–3296.00	9
Total US monitoring for singletons delivering 28–32 w	893.22	744.35–1042.09	9
Total US monitoring for twins delivering 28–32 w	2051.82	1709.85–2393.79	9
Total US monitoring for singletons delivering > 32 w	1339.83	1190.96–1488.70	9
Total US monitoring for twins delivering > 32 w	2735.76	2393.79–3077.73	9
Total US monitoring for singletons delivering < 28 w	446.61	148.87–744.35	9
Total US monitoring for twins delivering < 28 w	1025.91	341.97–1709.85	9
Mild NDI	62 789.62	31 394.81–94 183.24	12
Neonatal death	117 598.00	67 204.00–167 992.00	13
RFA	6567.20	5223.69–7910.71	9
Severe NDI	229 546.61	0–229 546.61	12
Total UA Doppler for singletons delivering 28–32 w	710.34	591.95–828.73	9
Total UA Doppler for singletons delivering > 32 w	1065.51	947.12–1183.90	9
Total UA Doppler for singletons delivering < 28 w	355.17	118.39–591.95	9
Total UA Doppler for twins delivering 28–32 w	1420.68	1183.90–1657.46	9
Total UA Doppler for twins delivering > 32 w	1894.24	1657.46–2131.02	9
Total UA Doppler for twins delivering < 28 w	710.34	236.78–1183.90	9
Probability			
Fetal outcome			
Cotwin IUFD after BCO	0.13	0.093–0.17	2,5,14–20
Cotwin IUFD after RFA	0.14	0.11–0.17	2
Twin pregnancy continuing after FLP	0.59	0.56–0.62	4,21,22
Twin pregnancy continuing after EM	0.69	0.59–0.78	4,21,22
Dual IUFD after EM	0.087	0.058–0.12	4,22,23
Dual IUFD after laser	0.034	0.025–0.045	4,21,22
Single neonatal survival after FLP	0.25	0.22–0.27	21,22,24
One or more surviving fetus after RFA	0.81	0.76–0.86	25
One or more surviving fetus after EM	0.71	0.59–0.82	4,21,24
Twin delivery			
> 32 w after EM	0.30	0.22–0.39	3,24,26
< 28 w after EM	0.13	0.07–0.19	3,24,26
> 32 w after FLP	0.54	0.40–0.68	3,8,21
28–32 w after FLP	0.38	0.14–0.61	3,8,21
Neonatal death			
Delivery < 28 w after BCO	0.093	0.06–0.13	14,16–19,27,28
Delivery < 28 w after EM	0.20	0.04–0.36	3,29
Delivery < 28 w after FLP	0.25	0.19–0.32	3,29
Delivery < 28 w after RFA	0.25	0.13–0.37	2,25

Continued over.

Table 1 *Continued*

Variable	*Base value*	*Range*	*Reference*
No NDI			
Delivery > 32 w after BCO	0.71	0.57–0.85	14,16–19,27,28
Delivery > 32 w after EM	0.79	0.67–0.90	26,27,30,31
Delivery > 32 w after FLP	0.50	0.37–0.63	26,32,33
Delivery > 32 w after RFA	0.80	0.62–0.98	25
PPROM			
After BCO	0.21	0.11–0.30	34
After EM	0.03	−0.03 to 0.09	24
After FLP	0.33	0.25–0.41	35,36
After RFA	0.33	0.11–0.56	2
Severe NDI			
Delivery 28–32 w after BCO	0.003	−0.016 to 0.023	5
Delivery 28–32 w after EM	0.05	0.004–0.13	26,27,30,31
Delivery 28–32 w after FLP	0.07	0.004–0.14	29
Delivery 28–32 w after RFA	0.05	−0.015 to 0.099	25
Delivery < 28 w after BCO	0.045	−0.0047 to 0.096	30
Delivery < 28 w after EM	0.004	0.002–0.006	15,26,31,33
Delivery < 28 w after FLP	0.067	0.04–0.091	26,32,33
Delivery < 28 w after RFA	0.085	−0.015 to 0.09	25
Singleton delivery			
28–32 w after RFA	0.13	0.08–0.18	25
> 32 w after RFA	0.67	0.61–0.72	25
< 28 w after RFA	0.17	0.11–0.23	25
< 28 w after EM	0.17	0.03–0.31	21
28–32 w after EM	0.70	0–0.70	21
Utility (3% discount rate)			
Impact of fetal demise on pregnant patient	0.92	0.6–0.99	37
Impact of severe CP on pregnant patient	0.59	0–0.59	37
Impact of mild CP on pregnant patient	0.79	0–0.84	37
Impact of neonatal death on pregnant patient	0.92	0.6–0.99	38–40
Preterm birth	0.80	0.6–0.99	Assumed

BCO, bipolar cord occlusion; BPP, biophysical profile; CP, cerebral palsy; EM, expectant management; FLP, fetoscopic laser photocoagulation; IUFD, intrauterine fetal demise; MCA, middle cerebral artery; NDI, neurodevelopmental impairment; PPROM, preterm prelabor rupture of membranes; RFA, radiofrequency ablation; UA, umbilical artery; US, ultrasound; w, weeks of gestation.

portions of this decision analysis adhered to Consolidated Health Economic Evaluation Reporting Standards and good practices as elucidated by The Professional Society for Health Economics and Outcomes Research.

RESULTS

In our theoretical cohort, RFA was found to be the most cost-effective strategy in base-case analysis (Tables 1 and 2), with a cost saving of over 14 000 USD and the highest overall QALY of all strategies analyzed. In this analysis, RFA resulted in fewer cases of severe NDI and a higher frequency of a cotwin without any diagnosis of NDI, and these benefits were consistent over 1000 iterations of the model in a theoretical cohort of 10 000 patients with MCDA gestation.

On one-way sensitivity analysis, the model inputs most strongly influencing the outcomes of the model were the presence and severity of NDI, the utility assigned to NDI and the costs of preterm birth before 32 weeks. When compared with EM, RFA led to 58 fewer births before 28 weeks, 273 fewer cases of severe NDI and 22 more deliveries after 32 weeks. When compared with FLP, RFA resulted in 259 fewer cases of severe NDI and 3177 more births after 32 weeks. When compared with BCO, RFA resulted in 1786 more neurologically intact neonates and 34 fewer cases of severe NDI (Table 3).

Monte Carlo probabilistic sensitivity analysis was performed to model the real world more closely, acknowledging that some probabilities are more or less likely to occur, and was performed in 1000 runs of various iterations of model inputs. On probabilistic sensitivity analysis, RFA was the most cost-effective strategy in 78% of runs, followed by BCO at 20%, EM at 2% and FLP in 0% of runs.

The WTP was set at 50 000 USD/QALY, and RFA was notably more cost-effective than the other strategies at this WTP and continued to be cost-effective as the WTP increased to 100 000 USD. At a lower WTP of 10 000 to 20 000 USD, BCO was more cost-effective than RFA, but quickly dropped in cost-effectiveness as the WTP increased. Both EM and FLP were below the cost-effectiveness threshold regardless of the WTP setting (Figure 2).

DISCUSSION

Under base-case assumptions, we found that RFA for the management of Type-II sFGR in MCDA twin pregnancies

Table 2 Base-case analysis evaluating cost-effectiveness of management strategies for Type-II selective fetal growth restriction in monochorionic diamniotic twin pregnancy

Strategy	*Cost per person (2023 USD)*	*Effectiveness per person (QALY)*	*Incremental cost-effectiveness (USD)*
Expectant management	400 896	43	−15 086
Bipolar cord occlusion	278 802	44	—
Radiofrequency ablation	328 912	47	+14 243
Fetoscopic laser photocoagulation	351 938	29	−1188

Data unchanged after adjusting for bipolar cord occlusion cost (Table 1). QALY, quality-adjusted life year.

Table 3 Selected fetal and obstetric outcomes in theoretical cohort of 10 000 monochorionic diamniotic twin pregnancies with Type-II selective fetal growth restriction, according to management strategy

Strategy	*Cotwin IUFD*	*Single IUFD*	*Neonatal death**	*Severe NDI*	*No NDI*	*PPROM*	*Delivery < 28 weeks*	*Delivery > 32 weeks*
EM	875	6672	1989	689	7872	307	1724	6647
BCO	1317	NA	929	450	6214	2087	1277	6807
RFA	1394	NA	2495	416	8000	3338	1666	6669
FLP	353	3446	2546	675	5910	3303	635	3492
Strategy favored	FLP	FLP	BCO	RFA	RFA	EM	FLP	BCO

Data are given as *n*. Data unchanged after adjusting for bipolar cord exclusion (BCO) cost (Table 1). *Of one twin. EM, expectant management; FLP, fetoscopic laser photocoagulation; IUFD, intrauterine fetal demise; NA, not applicable; NDI, neurodevelopmental impairment; PPROM, preterm prelabor rupture of membranes; RFA, radiofrequency ablation.

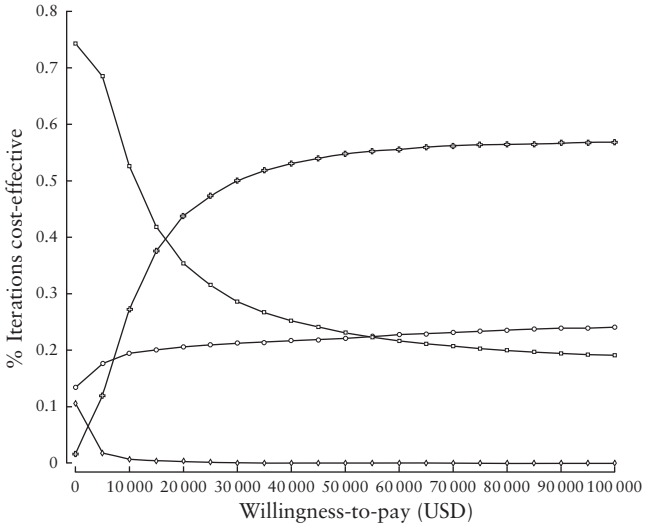

Figure 2 Cost-effectiveness acceptability curves showing probability that intervention (bipolar cord occlusion (▫), expectant management (○), fetoscopic laser photocoagulation (◊) or radiofrequency ablation (RFA) (⌖)) is cost-effective compared with alternatives for range of values of maximum willingness-to-pay (WTP) and incremental cost-effectiveness ratio. At lower WTP, three of four strategies are not cost-effective, but as WTP increases, RFA becomes increasingly cost-effective compared with other strategies.

was most likely to be cost-effective compared with BCO, FLP and EM. When performing probabilistic sensitivity analysis, RFA remained cost-effective in 78% of model iterations. BCO was cost-effective in 20% of iterations of the model, suggesting that the dominance of RFA is not clear-cut. EM was less cost-effective than both selective reduction strategies, and notably, FLP was never the preferred strategy. At this time, further research is needed to elucidate when and why certain strategies may be best for specific pregnancies.

At present, there is no clear standard of care when it comes to managing Type-II sFGR in monochorionic twin pregnancies[1,2]. This is partly because sFGR has only been classified over the past two decades[2,3]. There is also variation in the way in which sFGR is reported in terms of its severity, and this remained consistent in our review of the literature[34]. When reviewing the literature to extract probabilities for various outcomes, we were also careful to establish which outcomes were of the utmost importance for the patient and the pregnancy. Outcomes reported in our analysis were determined by a consensus paper from 2020 that established a group of core outcomes for pregnancies impacted by sFGR, including: live birth, gestational age at delivery and birth weight, and pregnancy or infant loss, among others[14]. We modeled a surrogate of parental stress with a decrement in QALY for the birthing parent who experienced a perinatal loss or those who gave birth to a child with NDI. The key finding that NDI is a major driving factor of cost-effectiveness is related very closely to gestational age at delivery, birthweight and intertwin birth-weight discordance[34,48].

Research surrounding the optimal management for sFGR is limited to single-center studies, retrospective observational studies, case series or meta-analyses[14,29,49–51]. However, these data are susceptible to unmeasured confounding, institutional bias towards a particular treatment option and juridico-legal restrictions on selective fetal reduction. These factors may play a role in the results obtained from observational cohort studies.

Studies commonly include all classifications of sFGR, which can make the data challenging to interpret. It is

known that Type-II sFGR portends the worst clinical prognosis and, therefore, the greatest opportunity for optimizing management. Many studies available for review also investigate two strategies head-to-head, or examine outcomes after only one strategy[4,14,29,49–51]. While our decision analysis suggested that RFA is the most cost-effective strategy, this should not be interpreted as dogma to guide management. Our findings highlight the need for further cohort studies investigating each fetal intervention strategy[1].

Our decision analysis was unable to model patient perspective and preference owing to the lack of data available in the literature. RFA and BCO both result in the selective termination of a fetus, which is unacceptable to many patients and illegal or inaccessible in many areas of the world[1]. We chose to model RFA and BCO separately because, although they both involve fetal reduction to a singleton pregnancy, they require different expertise and resources and carry their own disparate procedural risks. Patient-centered perspectives about willingness to undergo any or all of these procedures are not only relevant, but vital, in providing adequate care and counseling to families impacted by a diagnosis of sFGR.

To our knowledge, this is the first decision analysis comparing four management strategies for Type-II sFGR, and provides initial insights into optimal management strategies. However, this study is not without limitations.

Our model assumes patients are candidates and willing participants for all four strategies without considering resource allocation, which does not fully align with the real world[1]. Our assumptions for this model carry weight in terms of the output of the decision analysis, with factors such as gestational age at delivery and probability of NDI having a major impact on which strategy is favored. We also used an average gestational age at diagnosis of sFGR based on the literature[3] and made assumptions regarding the frequency and number of ultrasound examinations that would be performed. Perinatal centers have internal protocols that impact on the mode and frequency of fetal surveillance, which we accounted for in the model by varying the costs over a large range. A limitation of these assumptions is that they may not be applicable to every patient and healthcare setting. Another limitation of this study is that our data were obtained from papers that did not always compare each strategy, raising the possibility of selection bias in the original studies cited.

Furthermore, recent data suggest that abnormalities in the MCA and ductus venosus Doppler ultrasound portend a worse prognosis and could be used for risk stratification to determine which pregnancies may be better suited for EM or for intervention[15,23]. Owing to limitations in the reported literature, specifically very small sample sizes, we were unable to perform a subgroup analysis focused on different management strategies in the setting of abnormal Doppler findings.

Finally, improvements in the management of the premature neonate have occurred over the last three decades and have an impact not only on the incidence and severity of NDI, but also on the lifetime costs for the parents and QALYs measured in this study. Our conversion of the costs related to preterm birth and raising a child with significant healthcare needs were derived from literature from both the 1990s and the 2010s, which may represent some variation in accuracy related to the costs calculated because of advances in neonatal care[5,10,23].

In conclusion, our base-case and probabilistic sensitivity analyses suggest that RFA is the most cost-effective strategy in a theoretical cohort of 10 000 people with a MCDA twin pregnancy affected by Type-II sFGR. Interestingly, FLP was by far the least cost-effective strategy, which is compelling considering the previous data available on outcomes after FLP including prolonged gestation compared with EM[4]. As this study is the first decision analysis to compare four fetal interventions for Type-II sFGR, our findings are not intended to guide clinical management, but to generate hypotheses for future vital research in this area.

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