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Original Research

Comparison of Pregnancy Outcomes of Previable and Periviable Rupture of Membranes After Laser Photocoagulation for Twin–Twin Transfusion Syndrome

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OBJECTIVE: To describe the pregnancy outcomes of patients who experienced previable and periviable prelabor rupture of membranes (PROM) after the treatment of twin–twin transfusion syndrome.

METHODS: We conducted a retrospective cohort study of patients whose pregnancies were complicated by twin–twin transfusion syndrome who were treated with fetoscopic laser photocoagulation at a single fetal center and subsequently experienced PROM from April 2010 to June 2019. Outcomes were infant survival and latency from PROM to delivery. Patients were grouped by gestational age at PROM (before 26 weeks of gestation and 26 weeks or later). The group with PROM before 26 weeks of gestation was stratified by gestational age at PROM for further description of outcomes.

RESULTS: Two-hundred fifty of 653 patients (38%) developed PROM, 81 before 26 weeks of gestation and 169 after 26 weeks of gestation. In the setting of PROM before 26 weeks of gestation, the rate of survival of both twins to neonatal intensive care unit (NICU) discharge was 46.3%, compared with 76.9% in the setting of PROM at 26 weeks of gestation or later ($P<.001$); the survival rate of at least one twin was 61.2% and 98.5%, respectively ($P<.001$). Fourteen, 22, and 45 patients experienced PROM at 16–19 6/7, 20–22 6/7, and 23–25 6/7 weeks of gestation, respectively. Survival of both twins and at least one twin to NICU discharge was 25.0%, 47.4%, 52.8% (for two) and 33.3%, 47.4%, and 77.8% (for at least one), respectively, among those groups. Fifty-seven of the 81 patients with PROM before 26 weeks of gestation experienced a latency longer than 48 hours. In the setting of PROM before 26 weeks of gestation, when latency lasted longer than 48 hours, overall survival was improved (69.6% vs 53.7%, respectively, $P=.017$). With latency longer than 48 hours and PROM at 16–19 6/7, 20–22 6/7, and 23–25 6/7 weeks of gestation, survival of both twins to NICU discharge was 60.0%, 61.5%, and 60.7%, respectively, and survival of at least one twin was 80.0%, 61.5%, and 85.7%, respectively.

CONCLUSION: Earlier gestational age at PROM after laser photocoagulation is associated with longer latency but lower rates of survival. When PROM occurs before 26 weeks of gestation and latency exceeds 48 hours, rates of neonatal survival are significantly improved.

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Twin–twin transfusion syndrome complicates approximately 8–15% of monozygotic twin pregnancies.[1,2] The diagnosis is based on amniotic fluid discordance between twins, with oligohydramnios in the "donor" fetus and polyhydramnios in the "recipient" fetus.[2,3] Clinical management is based on staging, described by Quintero et al,[3] with progressive shunting of blood volume from the donor to the recipient, leading first to oligohydramnios in the donor and polyhydramnios in the recipient, then absence of the donor bladder, then Doppler abnormalities in the donor or recipient, with final progression to hydrops and, finally, death of one or both fetuses. When twin–twin transfusion syndrome presents in the second trimester and progresses beyond stage I disease, there is as high as a 90% mortality rate and an 18% risk of neurodevelopmental complications in pregnancies managed expectantly.[4,5] Selective fetoscopic laser photocoagulation of these shared placental vascular connections (with or without Solomon) is sometimes offered as early as stage 1 disease,[6] and selective fetoscopic laser photocoagulation becomes standard of care treatment for stage 2 and above.[7,8]

Though intervention has greatly improved outcomes, with survival of at least one twin in 76–88%,[7,9] complications persist. A major driver of postoperative complications is prelabor rupture of membranes (PROM).[10] Studies have evaluated rates of chorionamnion separation, rupture of membranes, risk of recurrence of twin–twin transfusion syndrome, development of fetal twin-anemia-polycythemia sequence, and placental abruption.[9,11–13] Prelabor rupture of membranes is the most frequent complication, affecting roughly one third of all fetoscopic laser procedures.[10,14] Although studies have evaluated postoperative PROM,[10,11,14] there is a paucity of data examining outcomes after selective fetoscopic laser photocoagulation specifically in the setting of previable and periviable rupture of membranes.[11,14] Thus, we sought to describe the outcomes of pregnancies complicated by twin–twin transfusion syndrome in individuals treated with selective fetoscopic laser photocoagulation who subsequently experienced PROM before 26 weeks of gestation and compare their pregnancy characteristics and outcomes with those of a referent group of pregnancies complicated by twin–twin transfusion syndrome in individuals treated with selective fetoscopic laser photocoagulation who subsequently experienced PROM after 26 weeks of gestation.

METHODS

This was a retrospective cohort study of patients who received treatment for twin–twin transfusion syndrome at the Cincinnati Children's Fetal Care Center from April 2010 to June 2019, underwent selective fetoscopic laser photocoagulation and subsequently experienced PROM. This study was approved by the IRB of Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio (IRB# 2020-0476). Data were collected by members of the medical and perinatal research team. Validation of data collection was performed using a random medical record audit by authors S.T. and M.H. of 5% of the patients in the study database. Kappa for agreement reached above 0.9 for all fields before statistical analysis. Previable PROM refers to rupture of membranes before 20 weeks of gestation and periviable PROM refers to rupture of membranes from 20–25 6/7 weeks of gestation.[15–17] Because patients were cared for in multiple institutions, there were minor variations in management; however, the general management of PROM at University of Cincinnati Hospital is included here. In the setting of PROM before 22 weeks of gestation, in accordance with Ohio law at the time, patients were counseled regarding the risks and benefits of termination. Otherwise, patients were offered expectant management unless there were signs of maternal compromise or labor; consideration of latency antibiotics at the time of diagnosis was at the discretion of the managing practitioner and the patient, with subsequent inpatient fetal monitoring at the time at which a patient would desire neonatal resuscitation.[16,17] Betamethasone for fetal benefit was typically administered at the time when the patient desired full intervention including neonatal resuscitation. The earliest betamethasone and neonatal resuscitation were offered at our institution was 22 0/7 weeks of gestation; however, this gestational age limit may have varied at other included centers.

The diagnosis of twin–twin transfusion syndrome was based on a monochorionic-diamniotic twin pregnancy complicated by, at a minimum, polyhydramnios in the recipient (more than 8 cm depth of amniotic fluid) and oligohydramnios in the donor (less than 2 cm depth of amniotic fluid), with the exclusion of other causes for fluid discrepancy. Staging was assigned using the Quintero staging.[2,3] All cases in which selective fetoscopic laser photocoagulation was completed for twin–twin transfusion syndrome and the patient experienced rupture of membranes before 37 weeks of gestation were included. Patients who required a second procedure remained in the cohort (n=2). Exclusion criteria were higher order multiple gestation, diagnosis of aneuploidy or fetal anomaly expected to drastically affect neonatal survival, and patients who elected pregnancy termination

after previable rupture of membranes. Patients in whom diagnostic fetoscopy was performed but laser photocoagulation was not technically possible were excluded. Patients who were noted to have an abruption were included in the final analysis, because this could be a result of the PROM or the surgery. Patients who experienced a postoperative fetal death after laser photocoagulation were also included in the final analysis.

All referred patients underwent evaluation with a comprehensive fetal anatomic ultrasonogram and fetal echocardiogram.[18] Doppler evaluation of the ductus venous, middle cerebral artery, umbilical vein, and umbilical artery were performed.[19] *Abnormal Doppler results* were defined as absent or reverse end diastolic flow in the mid-cord of the umbilical artery, reversal of flow in the A-wave of the ductus venous, or pulsatile umbilical venous flow. *Concomitant selective fetal growth restriction* was defined as estimated fetal weight (EFW) of one twin that was less than the third percentile or the combination of two or more of: EFW of one twin less than the 10th percentile, abdominal circumference of one twin less than the 10th percentile, EFW discordance of 25% or greater, and umbilical artery Doppler abnormalities of the smaller twin.[18,19] Surgery for twin–twin transfusion syndrome was recommended for stage II and greater disease. Risks and benefits of surgery compared with observation were reviewed with patients in the setting of stage I with recipient cardiomyopathy. Data collected included patient demographic characteristic, maternal, neonatal, and pregnancy outcomes. Record of diagnosis of PROM and gestational age at time of PROM were ascertained by medical record review. Patients were diagnosed with PROM by generally accepted clinical criteria, with at least two of the following: evidence of ruptured membranes on speculum examination, positive ferning on microscopy, or positive AmniSure.[16,20] In the rare case of uncertain diagnosis, amnio-dye test was offered at the discretion of the admitting physician (n=1 confirmed PROM in the cohort).

The primary outcome was infant survival to neonatal intensive care unit (NICU) discharge. Secondary outcomes were gestational age at delivery and latency from PROM to delivery. To assess the immediate risk of PROM after surgery, a secondary analysis of outcomes when PROM occurred within 1 week of surgery was planned. Gestational age was extracted from the medical record and was based on the best obstetric estimate of gestational age.[21] Patients who experienced PROM were grouped by gestational age at PROM for comparison (before 26 weeks of gestation vs 26 weeks of gestation or later). Baseline characteristics and outcomes were analyzed. Patients who experienced PROM were further stratified as follows: PROM at 16 0/7–19 6/7 weeks of gestation, 20 0/7–22 6/7 weeks, 23 0/7–25 6/7 weeks, and 26 weeks or later. In a further attempt to eliminate bias of outcomes from preterm labor compared with PROM, a secondary analysis was planned of patients who had at least 48 hours of latency, with evaluation of the primary and secondary outcomes in this subgroup of patients.

Statistical analysis using χ^2 or Fisher exact test for categorical data and Kruskal-Wallis or two-sample *t* test for continuous variables was performed as appropriate. *Significant differences* were defined as comparisons with $P<.05$ and 95% CIs not inclusive of the null value of 1.0. Linear regression was performed to evaluate the relationship between gestational age at the time of PROM and latency from PROM to delivery. Given possible changes and advancements in obstetric neonatal care from 2010 to 2019, linear regression was adjusted for year of delivery and linear regression evaluating the year of birth and overall neonatal survival was performed. Missing data were characterized as missing in our analysis and are denoted in footnotes of tables. Statistical analyses were performed using STATA 15.1.

RESULTS

A total of 653 pregnancies met inclusion criteria (Fig. 1). More than one third (250/653, 38.3%) of patients experienced PROM at some point in the pregnancy after selective fetoscopic laser photocoagulation. Twelve percent (81/653) experienced PROM before 26 weeks of gestation. No patients elected for termination. Of the 250 pregnancies in which the patient experienced PROM, the average latency from selective fetoscopic laser photocoagulation to PROM was 7.5 weeks (95% CI 6.9–8.1), with an average gestational age at PROM of 27.8±4.5 weeks and an average gestational age at delivery of 29.6±4.1 weeks.

Baseline characteristics were similar between groups (Table 1), with the exception that patients who experienced PROM before 26 weeks of gestation were more likely to have undergone surgery for twin–twin transfusion syndrome at an earlier gestational age (Table 1). The rates of PROM were 14 of 653 (2.1%), 22 of 653 (3.4%), and 45 of 653 (6.9%) at 16–19 6/7, 20–22 6/7, and 23–25 6/7 weeks of gestation, respectively. Regarding the primary outcome, in the setting of PROM before 26 weeks of gestation, the rate of survival of both twins to NICU discharge was 46.3%, compared with 76.9% in the setting of PROM at 26

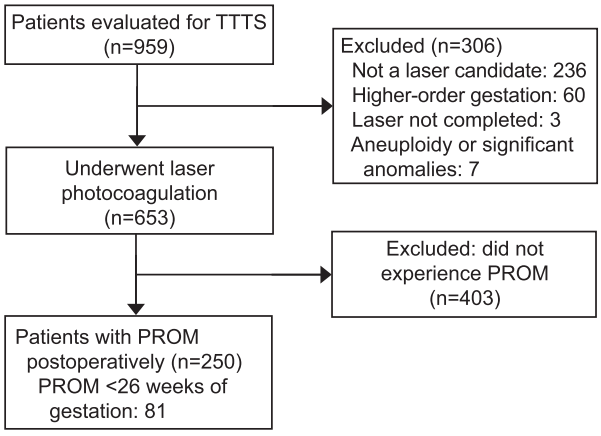

Fig. 1. Study flow diagram. TTTS, twin–twin transfusion syndrome; PROM, prelabor rupture of membranes.

Forde. Postoperative PROM after TTTS Surgery. Obstet Gynecol 2022.

weeks of gestation or later ($P<.001$), and survival rates for at least one twin were 61.2% and 98.5%, respectively ($P<.001$). Regarding the survival rate per infant, these findings equate to an overall survival of 53.7% if PROM occurs before 26 weeks of gestation and 87.8% if PROM occurs after 26 weeks of gestation ($P<.001$). Placental abruption was noted at the time of delivery in 9 of 81 (11.1%) patients who experienced PROM before 26 weeks of gestation compared with 11 of 169 (6.5%) patients who experienced PROM at 26 weeks of gestation or later ($P=.209$). Eighteen of the 653 patients (2.8%) experienced PROM within 7 days of surgery, with a mean gestational age at delivery of 23.4 weeks (95% CI 21.4–25.4 weeks). The average latency from PROM to delivery was longer in patients who experienced PROM in less than 7 days (n=18) compared with 7 days (n=232) or longer postoperatively (3.1 weeks vs 1.6 weeks, $P=.025$).

Linear regression demonstrated an inverse correlation between gestational age at PROM and latency ($R^2=0.26$, $aR^2=0.25$), with earlier gestational age at PROM correlated with a longer latency to delivery (Table 2). Year of delivery was not associated with rates of neonatal survival ($aR^2<0.01$, $P=.661$). Despite this longer latency, earlier gestational age at PROM was associated with earlier delivery and lower rates of neonatal survival. For patients who experienced PROM at 16–19 6/7 weeks of gestation, 20–22 6/7 weeks, 23–25 6/7 weeks, and 26 weeks or later, the mean gestational ages at delivery were 22.5±5.2 weeks, 24.9±3.7 weeks, 26.9±2.5 weeks, and 31.4±2.0 weeks, respectively ($P<.001$). Rates of survival of both twins to NICU discharge were 25.0%, 47.4%, 52.8%, and 76.9%, respectively ($P<.001$). Rates of survival of one or more twins to NICU

Table 1. Baseline Characteristics of the Study Population

Characteristic	PROM (Weeks of Gestation)		P
	Before 26 (n=81)	26 or Later (n=169)	
Age (y)	28.9±6.1 (27.6–30.2)	30±5.6 (29.2–30.8)	.177
BMI (kg/m^2)	28.5±5.0 (27.4–29.6)	29.9±6.4 (28.9–30.9)	.081
Infertility treatment	9 (11.1) (5–20)	13 (7.7) (4–13)	.766
History of spontaneous preterm birth	7/52 (13.5) (6.7–25.3)	11/93 (11.8) (6.7–19.9)	.778
Gestational age at evaluation (wk)	18.9±2.0 (18.5–19.3)	20.2±2.8 (19.8–20.6)	< .001
Gestational age at surgery (wk)	19.2±2.0 (18.8–19.6)	20.6±2.8 (20.2–21)	< .001
Quintero stage at SFLP*			.323
I	5 (6.3)	18 (10.8)	
II	20 (25.3)	29 (17.5)	
III	47 (59.5)	98 (59.0)	
IV	7 (8.9)	21 (12.7)	
Selective fetal growth restriction†	25 (31) (21–42)	65 (38) (31–46)	.228
Laser energy (joules)	11,581.0±10,352.9 (9,330–13,800)	9,676.5±6,251.6 (8,730–10,600)	.095
Cervical length postprocedure (cm)	3.7±1.2 (3.4–4.0)	3.9±1.0 (3.8–4.1)	.070

PROM, prelabor rupture of membranes; BMI, body mass index; SFLP, selective fetoscopic ablation of placental anastomoses.
Data are mean±SD (95% CI), n (%) (95% CI), n/N (%) (95% CI), or n (%) unless otherwise specified.

* There were two discrepant data points for preoperative Quintero stage in the group of patients who experienced PROM before 26 weeks of gestation (incongruent value from operative report and preoperative ultrasonogram); these were categorized as missing. There were three discrepant data points for preoperative Quintero stage in the group of patients who experienced PROM at 26 weeks of gestation or later (incongruent value from operative report and preoperative ultrasonogram); these were categorized as missing.

† Defined as estimated fetal weight (EFW) of one twin less than the third percentile or the combination of at least two of four parameters: EFW of one twin less than the 10th percentile, abdominal circumference of one twin less than the 10th percentile, EFW discordance of 25% or greater, umbilical artery Doppler abnormalities of the smaller twin.

Table 2. Outcomes of Pregnancies in the Setting of Prelabor Rupture of Membranes at Various Gestational Age Ranges

Outcome	PROM (Weeks of Gestation) 16 0/7–19 6/7 (n=14)	20 0/7–22 6/7 (n=22)	23 0/7–25 6/7 (n=45)	26 or Later (n=169)	P*
Quintero stage at time of surgery†					.624
I	0	1 (4.8)	4 (9.1)	18 (10.8)	
II	3 (21.4)	6 (28.6)	11 (25.0)	29 (17.5)	
III	9 (64.3)	12 (57.1)	26 (57.8)	98 (59.0)	
IV	2 (14.3)	2 (9.5)	3 (6.7)	21 (12.7)	
Gestational age at PROM (wk)	18.5±1.0 (18.0–19.0)	21.3±0.9 (20.9–21.7)	24.3±1.0 (24.0–24.6)	30.4±2.6 (30.0–30.8)	
Gestational age at delivery (wk)	22.5±5.2 (19.8–25.2)	24.9±3.7 (23.3–26.4)	26.9±2.5 (26.2–27.6)	31.5±2.4 (31.1–31.9)	< .001
Latency (wk)‡	4.0±5.4 (1.2–6.8)	3.5±3.7 (2.0–5.1)	2.6±2.7 (1.8–3.4)	1.1±1.6 (0.9–1.3)	< .001
Fetal death before onset of labor	6/28 (21.4) (10.2–39.5)	4/44 (9.1) (3.6–21.2)	8/90 (8.9) (4.6–16.6)	36/338 (10.7) (7.8–14.4)	.248
Survival to NICU discharge§					
Both twins	3/12 (25.0) (8.9–53.2)	9/19 (47.4) (27.3–68.3)	19/36 (52.8) (37.0–68.0)	103/134 (76.9) (69.0–83.2)	< .001
At least 1 twin	4/12 (33.3) (13.8–60.9)	9/19 (47.4) (27.3–68.3)	28/36 (77.8) (61.9–88.3)	132/134 (98.5) (94.7–99.6)	< .001
Outcomes for those with latency longer than 48 h after PROM	n=7	n=16	n=34	n=82	
Gestational age at delivery (wk)	26.2±5.0 (22.5–29.9)	26.1±3.5 (24.4–27.8)	27.6±2.4 (26.8–28.4)	31.4±2.0 (31–31.8)	.182
Latency (wk)	8.0±5.2 (4.2–11.8)	4.8±3.6 (3.0–6.6)	3.4±2.6 (2.5–4.3)	2.2±1.7 (1.8–2.6)	< .001
Survival to NICU discharge§					
Both twins	3/5 (60.0) (23.1–88.2)	8/13 (61.5) (35.5–82.3)	17/28 (60.7) (42.4–76.4)	52/70 (74.3) (63.0–83.1)	.470
At least 1 twin	4/5 (80.0) (37.6–96.4)	8/13 (61.5) (35.5–82.3)	24/28 (85.7) (68.5–94.3)	69/70 (98.6) (92.3–99.7)	< .001

PROM, prelabor rupture of membranes; NICU, neonatal intensive care unit.
Data are n (%), mean±SD (95% CI), or n/N (%) (95% CI), or unless otherwise specified.
* Regarding gestational ages, latency, and survival to NICU discharge, *P* values listed are referring to the significance of the data's being nonrandom, not the significance of the data trend. For evaluation of the trend, please refer to the linear regression in the Results section.
† There were two discrepant data points for preoperative Quintero stage in the group of patients who experienced PROM before 26 weeks of gestation (incongruent value from operative report and preoperative ultrasonogram); these were categorized as missing. There were three discrepant data points for preoperative Quintero stage in the group of patients who experienced PROM at 26 weeks of gestation or later (incongruent value from operative report and preoperative ultrasonogram); these were categorized as missing.
‡ Time from rupture of membranes to delivery, in weeks.
§ Reported only for twins for whom neonatal medical records were available for review and entry into the REDCap database. Although birth data were available on every patient in the column, full neonatal data were available only for the numbers shown in the denominators; thus, only those are included in the survival outcome data.

discharge were 33.3%, 47.4%, 77.8%, and 98.5%, respectively ($P<.001$). Additional rates of neonatal morbidity with PROM at 16–19 6/7 weeks of gestation, 20–22 6/7 weeks, and 23–25 6/7 weeks are summarized in Appendix 1, http://links.lww.com/AOG/C897. Due to prematurity in the setting of PROM before 26 weeks of gestation, risk of respiratory distress syndrome at birth was extremely high (92.6%). Risks of intraventricular hemorrhage grade III–IV, necrotizing enterocolitis, and sepsis were 7.3%, 4.9%, and 9.8% respectively.

In attempt to minimize confounding from PROM that occurred secondary to preterm labor, a secondary analysis of pregnant patients with latency longer than 48 hours after PROM was performed (Table 2). Fifty-seven of the 81 patients with PROM before 26 weeks of gestation experienced a latency longer than 48 hours, and 82 of the 169 patients with PROM at 26 weeks of gestation or later experienced a latency longer than 48 hours. Among patients who remained pregnant for more than 48 hours after PROM, mean latency from

PROM to delivery also decreased as gestational age at the time of PROM increased (Table 2). The average gestational ages at delivery were not significantly different in the patients who remained pregnant more than 48 hours after PROM at 16–19 6/7 weeks of gestation, 20–22 6/7 weeks, and 23–25 6/7 weeks (Table 2, P=.182). In the setting of PROM before 26 weeks of gestation, when latency lasted longer than 48 hours, the overall survival rate per fetus was improved (69.6%, 95% CI 61.0–78.0% vs 53.7%, 95% CI 44.9–60.8%, respectively, P=.017). In pregnant patients with latency longer than 48 hours and PROM at 16–19 6/7 weeks of gestation, 20–22 6/7 weeks, 23–25 6/7 weeks, and 26 weeks or later, survival rates of both twins to NICU discharge were 60.0%, 61.5%, 60.7%, 74.3% respectively (Table 2, P=.470). Survival rates of at least one twin to NICU discharge were significantly different among groups, with survival of 80.0%, 61.5%, 85.7%, and 98.6% (Table 2, P<.001), respectively. These outcomes are summarized in Figures 2 and 3. In this subset, linear regression again identified an inverse relationship between gestational age at the time of PROM, with earlier gestational age at PROM correlated with longer latency to delivery (R^2=0.24, aR^2=0.24).

DISCUSSION

Prelabor rupture of membranes before 26 weeks of gestation complicated 12.4% of all selective fetoscopic laser photocoagulation procedures for twin–twin transfusion syndrome. Prelabor rupture of membranes before 26 weeks of gestation was associated with lower rates of neonatal survival despite longer latency, compared with PROM at 26 weeks of gestation or later. Preterm labor may occur as a complication of selective fetoscopic laser photocoagulation in the early postoperative period, resulting in delivery less than 48 hours after PROM[9,22]; thus, to discern between true PROM cases after selective fetoscopic laser photocoagulation and ruptured membranes that occurred during preterm labor, a secondary analysis was performed for pregnant patients with latency longer than 48 hours, as has previously been described in the literature.[23] If latency lasted longer than 48 hours, the rate of survival of at least one twin to NICU discharge was at least 61.5% in every group examined.

Although previous studies have reported PROM rates after fetal interventions,[10,11,14] there are limited data regarding PROM before 26 weeks of gestation. Beck et al[10] examined rates of PROM and pregnancy outcomes in the setting of selective fetoscopic laser photocoagulation and bladder shunting for fetal lower urinary tract obstruction and identified an increased risk of perinatal death with increased PROM rates. Papanna et al[22] examined selective fetoscopic laser photocoagulation cases to identify characteristics associated with preterm delivery at 32 weeks of gestation or less. Rupture of membranes was associated with gestational age at delivery, but periviable PROM was not specifically evaluated. A

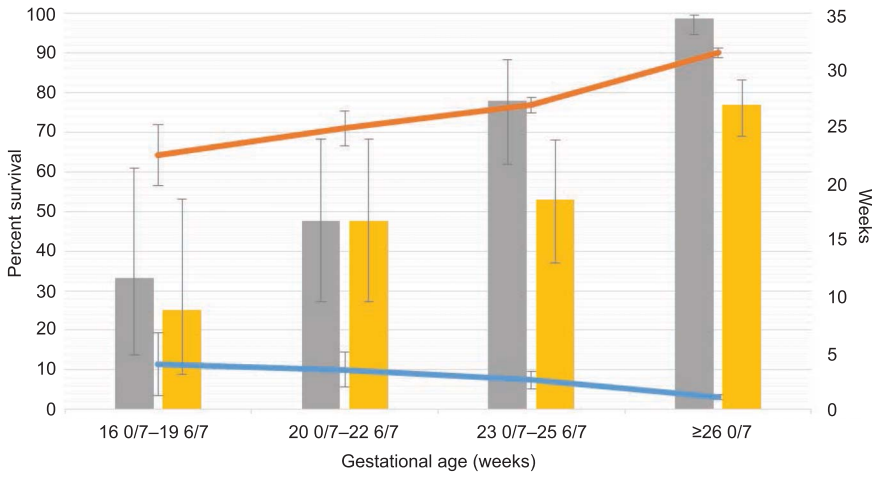

Fig. 2. Survival to neonatal intensive care unit discharge, latency from prelabor rupture of membranes (PROM) to delivery, and gestational age at delivery when PROM occurs at various gestational age categories. The left y-axis represents the percent survival of one or more twins (*gray bars*) or both twins (*yellow bars*) at each of the gestational age categories listed on the x-axis. The right y-axis represents the number, in weeks, of both gestational age at delivery (*orange line*) and latency from PROM to delivery (*blue line*) at each of the gestational age categories listed on the x-axis. Latency is inversely correlated with gestational age at PROM; however, increasing gestational at delivery and neonatal survival is correlated with later onset of PROM after selective fetoscopic ablation of placental anastomoses. See Table 2 for numeric details.

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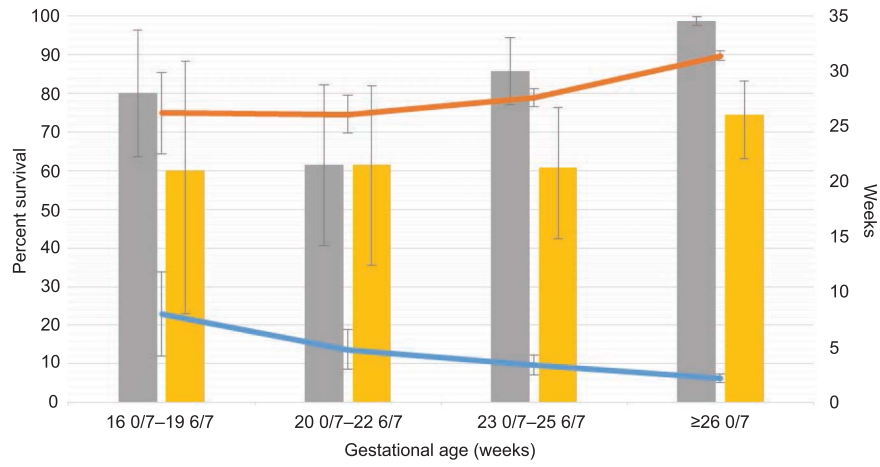

Fig. 3. Survival to neonatal intensive care unit (NICU) discharge, latency, and gestational age at delivery when prelabor rupture of membranes (PROM) occurs at various gestational age categories in a subanalysis of pregnant patients with latency longer than 48 hours from PROM to delivery. The left y-axis represents the percent survival of or one or more twin (*gray bars*) or both twins (*yellow bars*) at each of the gestational age categories listed on the x-axis. The right y-axis represents the number, in weeks, of both gestational age at delivery (*orange line*) and latency from PROM to delivery (*blue line*) at each of the gestational age categories listed on the x-axis. Latency remains inversely correlated with gestational age at PROM; however, there is no longer a statistically significant association between gestational age at PROM and neonatal survival to NICU discharge. See Table 2 for numeric details.

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MEDLINE, EMBASE, and Scopus search (publication range 2000–2022) using the search terms ("fetoscopic laser photocoagulation" OR "fetoscopic laser" OR "laser photocoagulation") AND ("previable rupture of membranes" OR "periviable rupture of membranes") yielded no publications. This study is the first to evaluate previable and periviable postoperative PROM after selective fetoscopic laser photocoagulation and indicates that survival is possible even with previable PROM after selective fetoscopic laser photocoagulation.

Before this study, much of the counseling provided to patients in the setting of PROM after selective fetoscopic laser photocoagulation was based on spontaneous PROM;[23,24] however, it is unclear how applicable these data are to the population experiencing PROM after a laser procedure. In a retrospective study, Wong et al[25] previously evaluated spontaneous PROM before 26 weeks of gestation in the setting of monochorionic and dichorionic twins. Overall neonatal survival at NICU discharge was 43%, and only 17% survived without significant neonatal morbidity. In our study, survival for both twins was 46.3% and survival of at least one twin was 61.2%, equating to an overall survival rate per infant of 53.7%. Overall survival increased further to 69.5% if latency lasted longer than 48 hours. Similarly to the findings of Wong et al, there was neither a survival nor gestational age benefit with PROM at 20–22 6/7 weeks of gestation compared with PROM before 20 weeks of gestation. Whether or not this trend persists among larger cohorts is an interesting question of future study.

The mechanisms that lead to some patients to experiencing PROM earlier than others, and for prolonged latency, remain unknown. There was no difference in preoperative Quintero staging among groups; however, if a pregnancy develops stage III or IV disease at 16 weeks of gestation, compared with 20 weeks of gestation, that pregnancy is inherently at higher risk of earlier rupture just due to the timing of surgery alone. For this reason, the latency data were examined, and, interestingly, earlier surgery is associated with longer latency yet still lower survival. Previously, it has been shown that in twin–twin transfusion syndrome there are higher levels of inflammatory markers in the amniotic fluid[26] than in maternal serum, and likely in a physiologic protective mechanism, an increase in tissue inhibitor of metalloproteinases.[27] Perhaps an imbalance in the in-utero environment results in PROM, and further evaluation of the levels of inflammatory markers, matrix metalloproteinases, and their inhibitors at the time of surgery is warranted as these markers may provide insight into a patient's risk of postoperative PROM and may better elucidate the mechanism by which postoperative PROM occurs.

A key strength of this study is the size of the study population, with more than 650 fetoscopic surgeries and 250 patients with PROM. Data were obtained from a single fetal surgical center, with uniformity in surgical care and postoperative management recommendations.

Our study is limited by the inability to account for physician or patient intent regarding management of

the pregnancy after rupture of membranes, though some insight is inferred by the fact that no patients elected for termination after PROM and all patients, by nature of their inclusion in this study, were willing to undergo fetal surgery. It is important to note that all patients involved in this study had polyhydramnios secondary to twin–twin transfusion syndrome, and these results may not be applicable to patients with PROM in the setting of other fetal interventions. Furthermore, it is possible that PROM may have occurred in some of the included patients even in the absence of twin–twin transfusion syndrome or selective fetoscopic laser photocoagulation. Although there were birth data for every patient who experienced PROM in our study, there were not NICU data for every patient; thus, there is a small percentage of patients lost to follow-up, which could influence our conclusions. Furthermore, although we had sufficient data to examine survival to NICU discharge, due to incomplete longer-term neonatal outcome data among patients who delivered outside of the study institution's health care network, we were unable to analyze what may also be meaningful outcomes, such as survival rates at 1 year of life. Additionally, although this study evaluated survival, long-term physical and neurologic outcomes were not examined. Especially in the setting of previable and periviable PROM with the possibility of periviable birth, an understanding of long-term morbidity and neurologic prognosis is key in decision-making.

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