OBSTETRICS

Management of short cervix in twin-to-twin transfusion syndrome: a role for pessary placement following fetoscopic laser surgery?

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BACKGROUND: Preterm labor and delivery is a major concern for patients with twin-to-twin transfusion syndrome undergoing fetoscopic laser surgery. A preoperative short cervix is a risk factor for preterm labor. Pessary placement is a short-acting intervention that may be useful to reduce this adverse event.

OBJECTIVE: This study aimed to investigate the relationship between pessary placement and preterm delivery in monochorionic twin pregnancies with twin-to-twin transfusion syndrome and a short cervix before fetoscopic laser surgery.

STUDY DESIGN: This was a retrospective study in 2 centers, including all pregnancies affected by twin-to-twin transfusion syndrome that underwent fetoscopic laser surgery with the Solomon technique between 2013 and 2022 (center A) and 2014 and 2022 (center B) with a preoperative cervical length below 25 mm. This study explored the correlation between cervical length and fetoscopic laser surgery—to—delivery interval following active or expectant management and compared perinatal outcomes between patients managed expectantly and patients managed with pessary placement, using multivariate analysis to control for potential confounders. Patients with a cervical length below 5 mm were not included in the comparative analysis.

RESULTS: Of 685 patients, 134 met the inclusion criteria. Moreover, 21 patients were treated with a cervical cerclage and excluded from the analysis, leaving 113 patients for the final analysis. There was a significant negative correlation between cervical length at fetoscopic laser surgery and the risk of early delivery (adjusted odds ratio, 0.66; 95% confidence interval, 0.49—0.81; $P<.001$). The use of a pessary correlated with fewer patients delivering before 28 weeks of gestation (adjusted odds ratio, 0.28; 95% confidence interval, 0.09—0.75), fewer double neonatal demise (adjusted odds ratio, 0.2; 95% confidence interval, 0.05—0.75). Posthoc subgroup analysis suggested that these improvements were essentially noticeable for cervical lengths between 5 and 18 mm, where pessary placement was associated with an increased fetoscopic laser surgery—to—delivery interval (+24 days; 95% confidence interval, 0.86—42; $P=.042$) and later gestational age at delivery (+3.3 weeks; 95% confidence interval, 0.86—42; $P=.035$).

CONCLUSION: Patients with a moderately shortened cervix, between 5 and 18 mm, may benefit from pessary placement after fetoscopic surgery for twin-to-twin transfusion syndrome, resulting in a reduction of adverse neonatal outcomes, double neonatal demise, and severe preterm delivery.

Key words: Arabin pessary, fetoscopic laser surgery, preterm delivery, short cervix, Solomon technique, twin-to-twin transfusion syndrome

Introduction

Twin-to-twin transfusion syndrome (TTTS) affects 10% to 15% of monochorionic twin pregnancies and is a major cause of perinatal morbidity and mortality.[1—5] Fetoscopic laser occlusion of placental anastomoses has proven to be the most effective first-line treatment of stages II to IV TTTS and of symptomatic stage I TTTS.[6—8] Despite continuous improvements in the surgical technique and perinatal survival, morbidity and mortality remain significant.[9—11] Prematurity, either spontaneous or elective, accounts for the largest part of adverse perinatal and long-term outcomes. Preoperative cervical length (CL) of <15 mm is found in approximately 5% of TTTS cases[10] and is a major risk factor for pregnancy loss and preterm delivery for patients with TTTS undergoing fetoscopic surgery.[12—14] Hence, there is a need for effective interventions to prevent preterm delivery. The active management of a short cervix in twin pregnancies at midgestation remains controversial.[15] In TTTS, a randomized controlled trial (RCT) is unlikely to be successfully conducted owing to the low prevalence and the number and heterogeneity of additional potential confounders affecting the outcome. Although the use of cervical cerclage remains the main rescue therapy in extremely short or dilated cervices,[16] its benefits in twin pregnancies with moderately shortened cervices are unproven. Although the pathway leading to preterm delivery in twins is multifactorial,[17] some studies suggested that the Arabin pessary may reduce the incidence of severe preterm delivery in those cases, especially in monochorionic pregnancies.[18,19] By relieving pressure on the cervix, its mechanical effect might be even stronger in TTTS, where the cervix may be weakened by the initial polyhydramnios in the recipient's sac and by the invasiveness of the fetoscopic surgery, leading to a particularly high incidence of preterm delivery before 34 weeks of gestation.

Thus, this study aimed to investigate the effect of a short preoperative CL and the potential benefits of pessary placement on perinatal outcomes in patients presenting with a TTTS operated by fetoscopic laser surgery (FLS).

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AJOG at a Glance

Why was this study conducted?

This study aimed to investigate the potential benefits of pessary placement on preterm delivery for patients with twin-to-twin transfusion syndrome (TTTS) undergoing fetoscopic laser surgery (FLS) with a preoperative short cervix.

Key findings

Pessary placement was associated with an increased interval between FLS and delivery and gestational age at delivery. This resulted in a decrease in double neonatal demise. Subgroup analysis suggested an increased efficacy of pessary placement in patients with a preoperative cervical length below 18 mm.

What does this add to what is known?

Patients undergoing FLS for TTTS with a preoperative short cervix may benefit from pessary placement.

Material and Methods

Study population

We conducted a multicentric study and reviewed all cases of monochorionic diamniotic twin pregnancies referred for TTTS and treated by FLS, presenting with a preoperative CL of <25 mm confirmed by transvaginal ultrasound. Measurements were performed by credentialled providers according to the International Society of Ultrasound in Obstetrics and Gynecology guidelines.[20] Cases treated in 2 centers between 2013 and 2022 (center A: Department of Obstetrics and Fetal Medicine, Necker—Enfants Malades Hospital, Assistance Publique — Hôpitaux de Paris, Paris, France) and 2014 and 2022 (center B: Heart Hospital Research Institute and the Fetal Medicine and Surgery Center (Gestar), São Paulo, Brazil) were pooled. TTTS was diagnosed as follows: presence of oligohydramnios (maximal vertical pool [MVP] of <2 cm) in the donor's sac, polyhydramnios in the recipient's sac (defined as an MVP of >8 cm before 20 weeks of gestation and >10 cm after 20 weeks of gestation), and discordant bladder size between both fetuses, and all cases were staged preoperatively.[21] Triplet pregnancies, monoamniotic pregnancies, congenital malformations or chromosomal ano malies, preterm premature rupture of membranes (PPROM) before surgery, and fetal death at referral were excluded.

Procedures

Percutaneous surgeries were performed with the same technique. An 8F to 10F trocar (Cook Medical, Bloomington, IN) is inserted in the polyhydramnios cavity under ultrasound guidance, using the Seldinger method. Placental vessel coagulations are performed using a 1.3-or 2-mm semirigid fetoscope or a 3.3-mm rigid 3-channel fetoscope (Karl Storz SE & Co KG, Tuttlingen, Germany) and a diode laser fiber (Dornier MedTech GmbH, Wessling, Germany). Coagulations were all performed with the "Solomon" technique where intertwin anastomoses are identified, coagulated, and connected by a thin continuous line of coagulation on the chorionic plate across the entire distance between placental edges.[7] An amnioreduction is performed at the end of the procedure. In addition, procedures are performed under local or locoregional anesthesia, tocolysis (indomethacin or atosiban depending on the gestational age [GA] for center A and nifedipine with or without terbutaline for center B), antibiotic prophylaxis (cefazolin), and maternal sedation (remifentanil) in center A.

Cervical management

The management of the short cervix was decided and initiated within 24 hours after fetoscopic intervention. As there is no consensual approach in the management of TTTS with a preoperative short cervix, the choice of the modality was left to the decision of the attending surgeon. Patients were divided into 3 groups:

- Expectant management FLS without any cervical intervention.
- Pessary placement: An Arabin pessary (Dr Arabin GmbH & Co KG, Witten, Germany) was placed within the first 24 hours after fetoscopic surgery.
- Cervical cerclage: This was performed using the McDonald technique immediately after the fetoscopic procedure under regional anesthesia.

Postoperative management

After laser surgery, patients were hospitalized between 24 and 72 hours. Tocolysis was discontinued after 24 hours. Evaluation of the twins' viability, the Doppler measurements, the bladder, the amniotic fluid volume, and the integrity of the intertwin membranes were performed before discharge. Patients were discharged with a weekly follow-up that could be performed at the fetoscopy centers or by the referring maternal-fetal medicine specialist. In case of complete recovery, delivery was either spontaneous or elective (cesarean or vaginal), according to local protocols from 34 weeks of gestation onward.[22]

Preoperative characteristics

Preoperative data included maternal age, parity, GA at laser surgery, TTTS stage according to the Quintero staging system, maximum vertical pocket (MVP) in the recipient sac, placental location, and preoperative CL measured in millimeters.

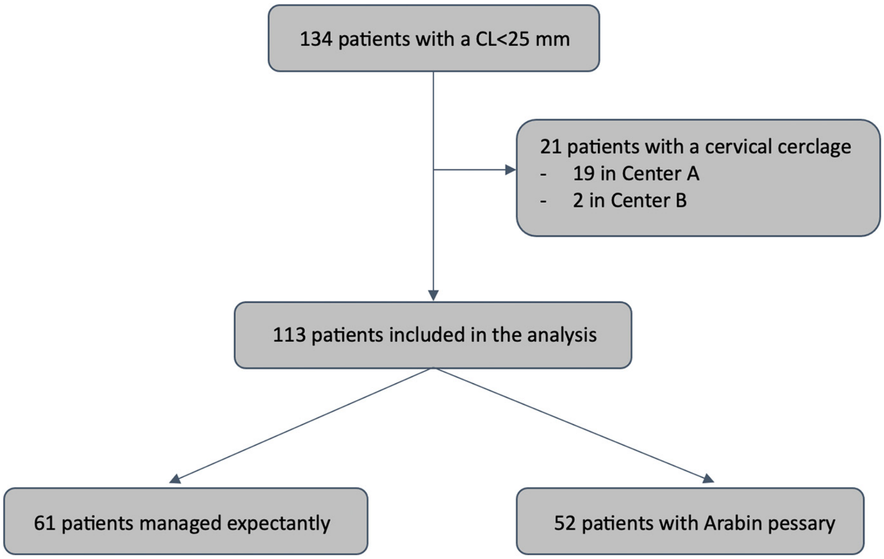
Outcomes

Postoperative outcomes reported were PPROM along with GA and GA at delivery, which was divided into 3 groups: <24, 24 to 28, and 28 to 32 weeks of gestation. The interval between FLS and delivery (in days) and probabilities of delivery within 2 weeks and within 1 month after FLS were calculated. Moreover, survival at birth and neonatal survival (at 28 days or at discharge) were reported.

Statistical analysis

Continuous variables are presented as median and interquartile range (IQR), and

FIGURE 1
Flowchart



CL, cervical length.

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they were compared using the Wilcoxon-Mann-Whitney test. Frequencies and percentages were used for categorical variables and compared using the chi-square test or Fisher exact test, as appropriate. CL was modeled as a linear continuous variable in millimeters. The probabilities of early delivery after fetoscopy as a function of preoperative CL were predicted using logistic regression. Parity (nulliparous vs multiparous), GA at laser surgery (in weeks), center, Quintero stage (stages III–IV vs stages I–II), CL (as a continuous variable in millimeters) at surgery, and number of survivors at delivery (1 vs 2) were incorporated in a multivariate logistic regression model to estimate adjusted odds ratios (aORs) and to compare binary outcomes between groups. Continuous variables (FLS-to-delivery interval and GA at delivery) were compared using a multiple linear regression, adjusted on potential confounding factors. A *P* value of <.05 was considered significant. All analyses were performed using R (http://www.r-project.org; R Foundation, Vienna, Austria).

Ethical statement
The study protocol was approved by our institutional review board (Comité d'éthique de la recherche de l'Assistance Publique des Hôpitaux de Paris; approval number: 00011928; reference number: 2021-07-14).

Results
Study population
Between 2013 and 2022, 134 of 685 monochorionic diamniotic twin pregnancies (20%) with a preoperative cervix length of <25 mm underwent FLS for TTTS: 67 patients (50%) were treated in each center. An emergency cerclage was performed in 21 of 134 patients (16%), who were excluded, leaving 113 patients for the comparative analysis (Figure 1). Details of both preoperative characteristics and perinatal outcomes of the 21 patients treated with cerclage are available in Supplemental Table 1. Of 113 patients, 61 (45%) were managed expectantly, and 52 (39%) were managed with pessary placement. Detailed characteristics are presented in Table 1. Patients with pessary placement had a significantly shorter cervix at presentation (median: 18.5 mm [IQR, 14–20] vs 21 mm [IQR, 17–22] for patients managed expectantly; *P*<.001). Both groups had similar GA at FLS (median: 22.6 weeks [IQR, 21.00–24.14] vs 22.86 weeks [IQR, 20.71–24.46] for patients managed expectantly and with pessary placement; *P*>.9). We found no difference between the groups concerning placental location, parity, distribution of Quintero stages, and MVP.

Correlation between preoperative cervical length and fetoscopic laser surgery–to–delivery interval
Figure 2 displays the evolution of the mean FLS-to-delivery interval (in days) according to CL at presentation in patients managed expectantly and actively (pessary or cerclage). In both groups, there was a correlation between FLS-to-delivery interval and preoperative CL and the difference between groups decreased with increasing CLs.

Correlation between cervical length and probabilities of early delivery
Predicted probabilities of early delivery accordingly to CL at surgery were estimated by logistic regression. As shown in Figure 3, the probability of early delivery after FLS significantly correlated with preoperative cervical shortness in patients managed expectantly, both within 28 days (aOR, 0.66; 95% confidence interval [CI], 0.49–0.81; *P*<.001) and within 14 days (aOR, 0.6; 95% CI, 0.37–0.78; *P*=.005). Although a similar trend was found in patients treated with a pessary, the correlation between preoperative CL and probabilities of early delivery did not reach significance (aOR: 0.9 [95% CI, 0.76–1.04; *P*=0.2] for delivery within 1 month and 0.89 [95% CI, 0.73–1.06; *P*=.2] for 2 weeks). In addition, the probabilities of early delivery after FLS were higher in cases managed expectantly than in cases treated with a pessary.

Comparison of perinatal outcomes between pessary-based and expectant management groups
The raw outcomes in both groups are presented in Table 2. Univariate analysis yielded no significant difference in perinatal outcomes. The rate of early delivery tended to be higher in patients managed expectantly, although not significantly (25% of patients managed expectantly delivering within 28 days

TABLE 1
Population characteristics according to the management modality

Characteristic	Expectant (n=61)[a]	Pessary (n=52)[a]	Overall (N=113)[a]	*P* value[b]
Center				.004
A	34 (56)	14 (27)	48 (42)	
B	27 (44)	38 (73)	65 (58)	
GA at laser	22.60 (21.00–24.14)	22.86 (20.71–24.46)	22.71 (20.71–24.29)	>.9
Anterior placenta	33 (54)	25 (48)	58 (51)	.7
Nulliparous	36 (59)	34 (65)	70 (62)	.6
Quintero stage				.14
1	14 (23)	13 (25)	27 (24)	
2	19 (31)	8 (15)	27 (24)	
3	27 (44)	27 (52)	54 (48)	
4	1 (1.6)	4 (7.7)	5 (4.4)	
MVP (cm)	13.00 (10.50–14.00)	12.00 (10.80–14.00)	12.00 (10.50–14.00)	.6
CL (mm)	21.0 (17.0–22.0)	18.5 (14.0–20.0)	20.0 (15.0–22.0)	<.001

CL, cervical length; *GA*, gestational age; *MVP*, maximum vertical pool.

[a] Statistics presented: number (percentage) or median (interquartile range); [b] Statistical tests performed: the chi-square test of independence, the Wilcoxon rank-sum test, and the Fisher exact test.

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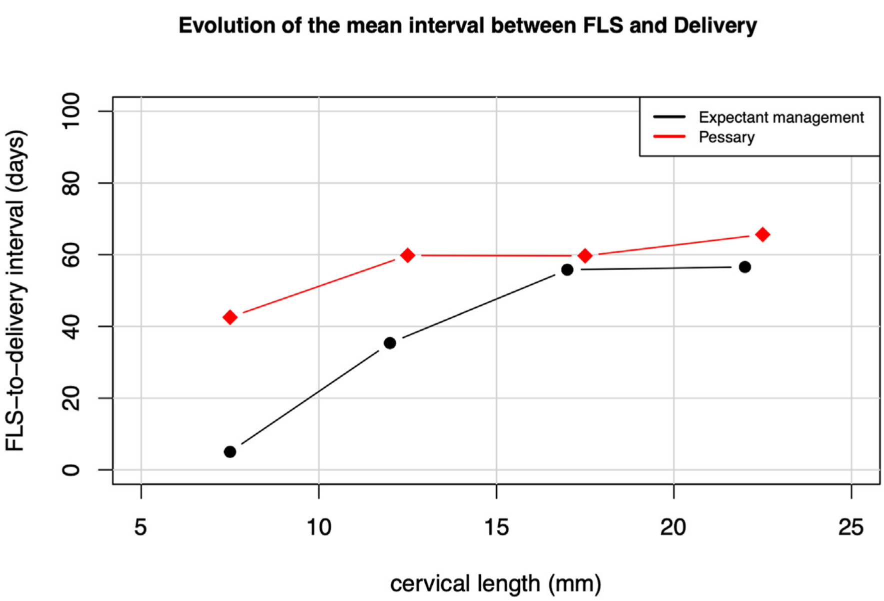
vs 16% in case of pessary placement; *P*=.4). Similarly, 34% of patients managed expectantly delivered before 28 weeks of gestation vs 23% of patients managed with pessary placement (*P*=.3).

FIGURE 2
Evolution of the mean interval between FLS and delivery according to CL



The CL was divided in blocks of 5 mm, and the mean FLS-to-delivery interval (*dots*) was computed for each block.

CL, cervical length; *FLS*, fetoscopic laser surgery.

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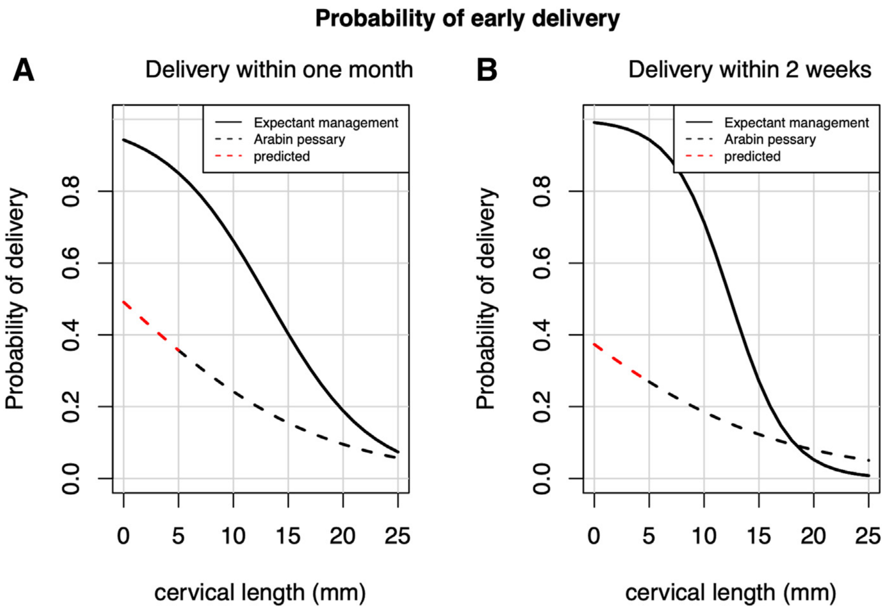
The results of the multivariate logistic regression model are shown in Figure 4. After controlling for confounding factors, the placement of a pessary was associated with a marked reduction in the rates of delivery before 24 weeks of gestation (aOR, 0.2; 95% CI, 0.03–0.97) and before 28 weeks of gestation (aOR, 0.28; 95% CI, 0.09–0.75) compared with expectant management. Moreover, this was associated with a similar reduction in the rates of delivery within a month after FLS (aOR, 0.17; 95% CI, 0.04–0.58). In addition, the use of a pessary seemed to increase the FLS-to-delivery interval by 13 days (95% CI, 1.5–25.0) compared with expectant management (*P*=.028). Similar trends were found in the rates of delivery before 32 weeks of gestation, although nonsignificant (aOR, 0.54; 95% CI, 0.22–1.28), and delivery within 2 weeks after FLS (aOR, 0.36; 95% CI, 0.09–1.30). No significant correlation between the incidence of PPROM and the management modality was found.

Overall, after adjustment, the use of an Arabin pessary was associated with fewer double neonatal demise (aOR, 0.2; 95% CI, 0.05–0.68) and a trend toward increased overall neonatal survival (aOR,

FIGURE 3
Probability of early delivery after FLS according to preoperative CL



The *solid line* represents patients managed expectantly, and the *dashed line* represents patients treated with pessary. The *red dashed line* represents the prediction based on the equation on the interval (5 to 25 mm), as no pessary was placed when patients presented with an initial CL of <5 mm.

CL, cervical length; *FLS*, fetoscopic laser surgery.

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2.05; 95% CI, 0.934−4.48), although nonsignificant.

Subgroup analysis based on preoperative cervical length (<18 mm and >18 mm)

The observation of the data shown in Figure 3 suggested a possible threshold effect at 18 mm of preoperative CL. Therefore, we performed a posthoc subgroup analysis accordingly. The results of the multivariate log-binomial regression model and subsequent aORs are shown in Table 3. In 41 patients with a CL of <18 mm (17 patients were managed expectantly, and 24 patients were managed with a pessary), the efficacy of pessary placement was confirmed and associated with a significant reduction in the rates of delivery before 28 weeks of gestation (aOR, 0.09; 95% CI, 0.01−0.57) compared with expectant management. In addition, it was associated with a significant reduction in delivery within 2 weeks and within a month after FLS (aOR: 0.06 [95% CI, 0.00−0.48] and 0.04 [95% CI, 0.00−0.37], respectively). This translated into a significant reduction in double neonatal demises (aOR, 0.05; 95% CI, 0.00−0.47). Moreover, the use of a pessary increased the FLS-to-delivery interval by 24 days (95% CI, 0.86−42.00; *P*=.042) compared with expectant management (*P*=.042), resulting in a significantly delayed delivery (+3.3 weeks; 95% CI, 0.25−6.30; *P*=.035).

Conversely, in patients with a CL of >18 mm, none of the aforementioned associations were significantly affected by pessary placement (Table 2 and Figure 3): early delivery (aOR: 1.99 [95% CI, 0.25−19.6] for delivery within 2 weeks and 0.37 [95% CI, 0.06−1.85] for delivery within 1 month); double neonatal demise (aOR: 0.38; 95% CI, 0.06−1.86); FLS-to-delivery interval (+6.3 days; 95% CI, −8.9 to 22.0; *P*=.4), or GA at delivery (+1.3 week; 95% CI, −0.74 to 3.40; *P*=.2) for patients treated with a pessary and managed expectantly.

Comment

Preterm delivery remains a major concern in TTTS, occurring in up to 45% of pregnancies treated with FLS before 32 weeks of gestation.[10,14] This outcome follows multifactorial mechanisms,[17] of which some are particularly relevant to twin pregnancies, including acute uterine distension and cervical weakness. These 2 are particularly challenged by acute polyhydramnios in TTTS and by the invasiveness of intrauterine surgery. Adding to the multifactorial causes of prematurity in twins, the wide adoption of the Solomon technique significantly improved neonatal survival but came along with increased PPROM and early preterm delivery as a drawback, particularly when performed early in pregnancy.[10,11] As a short cervix is likely to be the only preoperative visible part of the iceberg of risk factors for spontaneous delivery in TTTS,[23] acting on it could be a valid option to prevent this adverse outcome.

Principal findings

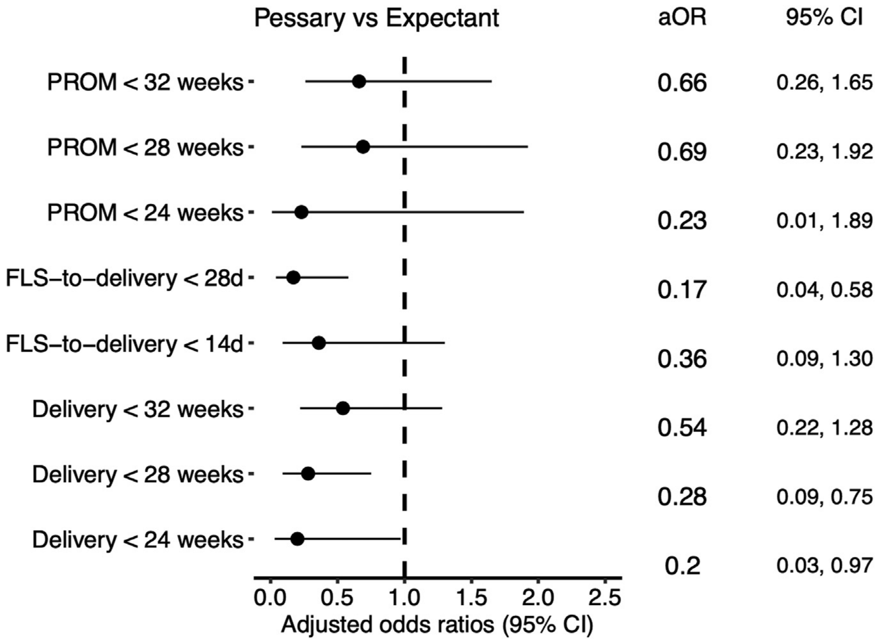
Here, we observed a significant relationship between CL at FLS and perinatal outcomes in monochorionic diamniotic pregnancies affected by TTTS. Although preoperative CL was shorter in this group, pessary placement was associated with a more favorable perinatal outcome, including fewer patients delivering within a month after FLS and before 24 or 28 weeks of gestation and increased interval between surgery and delivery. Overall, this resulted in fewer double neonatal demise at discharge. Posthoc subgroup analysis suggested that these improvements were essentially noticeable for a CL below 18 mm.

Results in the context of what is known

The literature shows conflicting results about the efficacy of pessary placement to prevent preterm birth (PTB) in otherwise uncomplicated multiple pregnancies. Although a first RCT

FIGURE 4

Forest plot displaying the results of multivariate logistic regression and aORs, comparing patients managed expectantly with those treated with pessary for a CL of <25 mm



The odds ratios were computed after adjusting on parity (nulliparous vs multiparous), GA at FLS, center, Quintero stages (stages III—IV vs stages I—II), preoperative CL (as continuous variable, in mm), and the number of fetus alive at delivery (1 vs 2).

aOR, adjusted odds ratio; *CI*, confidence interval; *CL*, cervical length; *FLS*, fetoscopic laser surgery; PROM, premature rupture of membranes.

Bartin. Pessary placement for twin-to-twin transfusion with short cervix undergoing laser surgery. Am J Obstet Gynecol 2024.

reported a significant reduction in PTB before 34 weeks of gestation in twin pregnancies complicated by a short cervix, this observation was not confirmed by a larger RCT or in the meta-analysis of these 2 trials.[19,24,25] Nonetheless, extending these conclusions to our population of abnormal twin pregnancies challenged by acute uterine distension and uterine surgery is debatable, given its systematic exclusion from these studies and adding to the multifactorial mechanisms potentially responsible for prematurity.[17]

The exact mechanism through which a pessary acts is unclear. Among the hypotheses put forward, it is thought to act mechanically by supporting the cervix and readdressing the intrauterine pressure toward the vaginal floor, uterine walls, and surrounding structures. This mechanical constraint is theoretically enhanced in TTTS, owing to the recipient's polyhydramnios in a uterus already distended and stretched by a twin pregnancy, which is a well-known risk factor for cervical shortening and preterm delivery.[15,26–28] Nonetheless, in TTTS, the relationship between ultrasound assessment of polyhydramnios, intra-amniotic pressure, and cervical shortening remains unclear. The absence of cervical recovery after amnioreduction goes against the idea of a purely mechanical effect of polyhydramnios on CL.[29,30] In a recent study, Berg et al[31] focused on the effect of intra-amniotic fluid pressure from polyhydramnios on CL and perinatal outcomes. Although the recipient's MVP significantly correlated with intra-amniotic pressure and CL, they found no correlation between intra-amniotic pressure and cervical shortening or perinatal outcomes. All these observations suggest that the relationship between CL and amniotic volume may result from an interaction between increased pressure from mild polyhydramnios and intrinsic cervical fragility and sensitivity to modifications of mechanical conditions. Therefore, the shortest cervices, allegedly the weakest ones, may particularly benefit from a pessary, which would be consistent with our observations.

The efficacy of pessary placement on the occurrence of PPROM is debated. A pessary may change the cervical inclination, thus reducing the exposure of membranes to the outer environment. However, in our series, we found no significant benefit of a pessary on PPROM rates. Multiple reasons may explain this observation. First, the membrane exposure hypothesis is more plausible with a dilated cervix, at least minimally, which is inconsistent with our management protocol as these patients are mainly treated with cervical cerclage. Second, in TTTS treated by FLS, PPROM could be favored by the surgery, because of a combined effect of a degree of membrane tearing by the introduction of the fetoscope and the high level of energy delivered on the chorionic plate by laser coagulation, particularly when using the Solomon technique and at an earlier GA.[10,32] However, double survival is also more frequent with this technique; thus, subsequent uterine distension with the growth of 2 survivors could also act mechanically on the cascade of events weighing on cervical competence and PPROM.[9–11]

In a recent retrospective study, Buskmiller et al[33] similarly compared cervical interventions to prevent preterm delivery in TTTS with a short cervix at FLS. In contrast with our series, they found no evidence of the efficacy of any management method, particularly a pessary, despite having a large group of patients managed expectantly, which allowed them to use a propensity score method to account for confounding factors. However, they included all patients with a preoperative CL of <30 mm, which may have had a dilutional effect on the effect of the cervical intervention: based on our observation, cervices of >20 mm seemed to be more frequent than shorter ones

TABLE 2
Pregnancy outcome according to the management modality

Outcomes	Expectant (n=61)[a]	Pessary (n=52)[a]	Overall (N=113)[a]	*P* value[b]
GA at delivery	30.1 (27.1–33.3)	31.1 (28.2–33.2)	31.0 (27.3–33.3)	.2
Preterm delivery (wk)				
<24	9 (15.0)	5 (9.6)	14 (12.0)	.6
<28	21 (34.0)	12 (23.0)	33 (29.0)	.3
<32	37 (61.0)	27 (52.0)	64 (57.0)	.5
Alive at delivery				.8
None	9 (15.0)	6 (12.0)	15 (14.0)	
1	10 (16.0)	7 (14.0)	17 (15.0)	
Both	42 (69.0)	37 (74.0	79 (71.0)	
PPROM				
<24 wk	4 (6.6)	1 (1.9)	5 (4.4)	.4
<28 wk	14 (23.0)	9 (17.0)	23 (20.0)	.6
<32 wk	23 (38.0)	12 (23.0)	35 (31.0)	.14
FLS to delivery (d)	51 (30–74)	54 (38–81)	53 (34–76)	.4
<14	9 (15.0)	6 (12.0)	15 (14.0)	.9
<28	15 (25.0)	8 (16.0)	23 (21.0)	.4
TAPS or recurrent TTTS	2 (4.2)	2 (3.1)	4 (3.5)	>.9

FLS, fetoscopic laser surgery; *GA*, gestational age; *PPROM*, preterm premature rupture of membranes; *TAPS*, twin anemia polycythemia sequence; *TTTS*, twin-to-twin transfusion syndrome.

[a] Statistics presented: number (percentage) or median (interquartile range); [b] Statistical tests performed: the chi-square test of independence, the Wilcoxon rank-sum test, and the Fisher exact test.

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(Supplemental Figure). In addition, they separated the combined treatments with approximately 30 patients included in each group, and this may have also limited the statistical power in the overall population analysis and even more so in a subgroup analysis, favoring the absence of statistical significance. Our results are consistent with the observation of Carreras et al,[34] who evaluated the use of a pessary in TTTS with a preoperative cervix of <25 mm. Despite a relatively small cohort, spontaneous preterm delivery and, subsequently, related perinatal morbidity were significantly higher in patients managed expectantly.

Clinical implications

Given the risks of PTB related to both TTTS and a short cervix and their subsequent perinatal complications, interventions for a short cervix could be considered in high-risk patients. Although cervical cerclage could not be properly compared with pessary placement, mainly because of differences in preoperative characteristics, it may be considered a rescue therapy.[16] The combined experience of 6 centers within the North American Fetal Therapy Network suggested that a cervical cerclage for preoperative CLs of <25 mm did not affect the outcomes. However, in the subgroup analysis of 57 cases with a moderately shortened cervix (16–20 mm), cerclage was associated with a prolonged interval of 3 weeks between surgery and delivery.[35] Patients with moderate cervical shortening (between 5 and 18–20 mm) may benefit the most from pessary placement. In patients with a CL of above 18 to 20 mm, the effect of any cervical intervention, including a pessary, remains uncertain, as these services may be intrinsically more resilient to mechanical pressure. Following the basic principle of "first do no harm," the use of the Arabin pessary seems tolerable even for a relative efficacy, as no increase in significant adverse effect was reported with this device and because the additional cost to that of the overall management of TTTS seems negligible. Nonetheless, more prospective data, if not randomized trials, would be informative to properly assess the efficacy of each method for the management of a shortened cervix in TTTS.

Strengths and limitations

The strengths of this work include 2 large-volume fetal centers that have a long-time experience in FLS for TTTS and a coherent and comparable management of TTTS. Surgery was performed using the same technique (ie, the Solomon technique), providing homogeneity in specific postoperative complications (recurrence or twin anemia polycytemia sequence).

Several limitations are to be acknowledged. First, the retrospective nature of this study, along with a degree of heterogeneity in population characteristics, may have affected the outcomes (Supplemental Table 3). In addition, the

TABLE 3
Results of subgroup analysis according to the initial CL

	CL<18 mm (n=41)		CL≥18 mm (n=72)	
Outcomes	aOR	*P* value	aOR	*P* value
Delivery within 2 wk	0.06 (0.00—0.48)	.023	1.99 (0.25—19.60)	.5
Delivery within 1 mo	0.04 (0.00—0.37)	.012	0.37 (0.06—1.85)	.2
GA at delivery of <28 wk	0.09 (0.01—0.57)	.022	0.44 (0.11—1.57)	.2
Double demise at discharge	0.05 (0.00—0.47)	.023	0.38 (0.06—1.86)	.3

The data show the results of the multivariate analysis in the subpopulations. Confounding factors included in the model were CL (in millimeter), center (A vs B), gestational age at laser surgery (in weeks), Quintero stage, and number of surviving fetuses at the time of delivery.

aOR, adjusted odds ratio; *CL*, cervical length; *GA*, gestational age.

Bartin. Pessary placement for twin-to-twin transfusion with short cervix undergoing laser surgery. Am J Obstet Gynecol 2024.

differences in perioperative management between centers, tocolysis protocols, and laws regulating the termination of pregnancy provided heterogeneity, although we intended to address this issue by incorporating the center in a multivariate analysis. Second, we did not incorporate the additional use of vaginal progesterone in multivariate analysis, which may constitute a potentially significant bias. Progesterone has been largely evaluated in both singleton and multiple pregnancies and showed some efficacy in preventing spontaneous preterm delivery, particularly in high-risk asymptomatic twin pregnancies complicated by a short cervix.[15,36,37] In a recent RCT, Rehal et al[37] evaluated the use of vaginal progesterone in a population of twin pregnancies. Although progesterone was not associated with a reduction in PTB in the overall population, their subgroup analysis suggested a potential benefit in the case of a CL of <30 mm. These results are in contradiction with the results of Klein et al[38] who did not observe a similar reduction. Nonetheless, in acute TTTS with polyhydramnios, shortening of the cervix and its subsequent resilience to surgery may be different from those with an initial short cervix and overall asymptomatic twin pregnancies. In our study, progesterone was only used liberally and mainly by center B, in 17 patients who also had pessary placement. Although progesterone itself was not incorporated in multivariate analysis, we did incorporate the center, which might partly reduce this bias. In addition, these patients were compared with 26 patients in center B who had pessary placement alone (details shown in Supplemental Table 2) and had similar outcomes.

Finally, another limitation of our study is the absence of exhaustive data on a previous history of PTB. There was 1 patient in center A who benefited from cerclage and was not included in the analysis. The proportions of primigravidas were 65% in the pessary group and 59% in the expectant group. Assuming that a history of PTB would be a significant event among patients from center B, we included the center as a potential confounding variable, and this may, in part, compensate for this potential bias.

Conclusion

Preterm delivery is a major concern for patients with TTTS undergoing FLS. Cervical shortening plays a central role in spontaneous prematurity after FLS for TTTS, which constitutes a large part of pregnancies delivered early. Cervical interventions should be considered to address this complication. Patients with a moderately short cervix between 5 and 18 mm may benefit the most from pessary placement. Nonetheless, more prospective data are required to precisely assess the efficacy of management methods. ■

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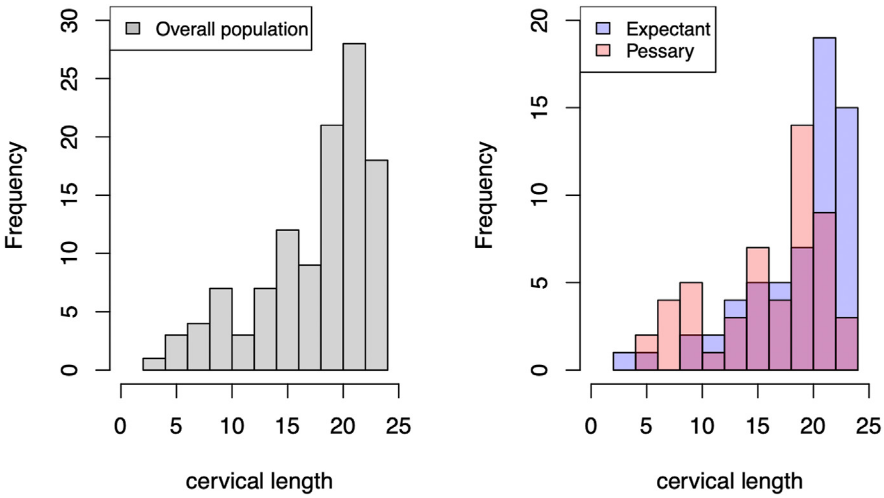
SUPPLEMENTAL FIGURE
Distribution of cervical length in our population



Bartin. Pessary placement for twin-to-twin transfusion with short cervix undergoing laser surgery. Am J Obstet Gynecol 2024.

SUPPLEMENTAL TABLE 1
Characteristics and outcomes of patients treated with cervical cerclage

Characteristic	n=21[a]
GA at FLS	20.90 (18.71—23.00)
Anterior placenta	9 (43.0)
Nulliparous	18 (86.0)
Quintero stage	
1	9 (43.0)
2	6 (29.0)
3	5 (24.0)
4	1 (4.8)
MVP (cm)	10.00 (9.00—12.00)
Cervical length (mm)	12.0 (5.0—17.0)
Outcomes	
Preterm delivery	
<24 wk	8 (38.0)
<28 wk	12 (57.0)
<32 wk	17 (81.0)
Alive at delivery	
None	7 (33.0)
1	3 (14.0)
Both	11 (52.0)
FLS to delivery (d)	
<14 d	9 (43.0)
<28 d	11 (52.0)

CL, cervical length; *GA*, gestational age; *FLS*, fetoscopic laser surgery; *MVP*, maximum vertical pool.

[a] Statistics presented: median (interquartile range) or number (percentage).

Bartin. Pessary placement for twin-to-twin transfusion with short cervix undergoing laser surgery. Am J Obstet Gynecol 2024.

SUPPLEMENTAL TABLE 2
Compared characteristics and outcomes of patients treated with pessary alone or with pessary and progesterone in center B

Characteristic	Pessary alone (n=26)[a]	Pessary + progesterone (n=17)[a]	P value[b]
CL (mm)	20.0 (10.2—21.8)	20.0 (14.0—20.0)	>.9
GA at surgery	22.86 (21.18—23.25)	22.71 (20.57—24.43)	.6
GA at delivery (wk)	30.9 (27.5—33.2)	32.6 (27.1—34.1)	.8
<24	4 (15)	2 (12)	>.9
<28	7 (27)	5 (29)	>.9
FLS to delivery (d)	58 (34—84)	48 (31—75)	.6
<28	4 (15)	4 (24)	.7
<14	4 (15)	3 (18)	>.9

CL, cervical length; *FLS*, fetoscopic laser surgery; *GA*, gestational age.

[a] Statistics presented: median (interquartile range) or number (percentage); [b] Statistical tests performed: the Wilcoxon rank-sum test and the Fisher exact test.

Bartin. Pessary placement for twin-to-twin transfusion with short cervix undergoing laser surgery. Am J Obstet Gynecol 2024.

SUPPLEMENTAL TABLE 3
Population characteristics by center

Characteristic	Center A (n=67)[a]	Center B (n=67)a	P value[b]
GA at laser (wk)	22.71 (20.21—24.64)	22.29 (20.71—24.00)	.4
Placental location (anterior)	31 (46.0)	36 (54.0)	.5
Nulliparous	47 (70.0)	41 (61.0)	.4
Quintero stage			<.001
1	28 (42.0)	8 (12.0)	
2	19 (28.0)	14 (21.0)	
3	20 (30.0)	39 (58.0)	
4	0 (0)	6 (9.0)	
MVP (cm)	11.00 (10.00—13.35)	12.00 (11.00—14.00)	.018
Management			<.001
Expectant	34 (51.0)	27 (40.0)	
Cervical cerclage	19 (28.0)	2 (3.0.0)	
Arabin pessary	14 (21.0)	38 (57.0)	
Cervical length	18.0 (14.0—21.0)	20.0 (14.0—22.0)	.3

GA, gestational age; *MVP*, maximum vertical pool.

[a] Statistics presented: number (percentage) or median (interquartile range); [b] Statistical tests performed: the chi-square test of independence, the Kruskal-Wallis test, and the Fisher exact test.

Bartin. Pessary placement for twin-to-twin transfusion with short cervix undergoing laser surgery. Am J Obstet Gynecol 2024.