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# Cervical cerclage for preterm birth prevention in twin gestation with short cervix: a retrospective cohort study

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**KEYWORDS:** cerclage; cervical ultrasound; cervix; prematurity; twins

## ABSTRACT

***Objective*** *To determine if cervical cerclage reduces the rate of spontaneous early preterm birth in cases of dichorionic–diamniotic (DCDA) twin gestation with an ultrasound-detected short cervix.*

***Methods*** *This was a retrospective cohort study of 40 consecutive DCDA twin gestations at Saint Peter's University Hospital from November 2006 to November 2014 in which cervical cerclage was performed for an ultrasound-determined cervical length of 1–24 mm at 16–24 weeks' gestation. The cases were matched with 40 controls without cerclage for cervical length and gestational age at cervical assessment. The primary outcome measure was spontaneous birth < 32 weeks.*

***Results*** *There was no difference between the two groups in maternal age, body mass index (BMI), cigarette smoking, use of* in-vitro *fertilization (IVF), parity and prior spontaneous preterm birth. There were more Caucasian women among the controls compared with cases. In the cases, compared with controls, spontaneous delivery < 32 weeks was significantly less frequent (20.0%* vs *50.0%; relative risk, 0.40 (95% CI, 0.20–0.80)). In the prediction of spontaneous delivery < 32 weeks, logistic regression analysis demonstrated that the risk was reduced with the insertion of cervical cerclage (odds ratio, 0.22 (95% CI, 0.058–0.835);* $P = 0.026$*), corrected for maternal age, BMI, racial origin, cigarette smoking, IVF, parity and previous preterm birth.*

***Conclusion*** *In DCDA twin gestation with a short cervix, treatment with cervical cerclage may reduce the rate of early preterm birth. The findings suggest the need for adequate randomized controlled trials on cerclage in twin gestations with a short cervix.* *Copyright © 2016 ISUOG. Published by John Wiley & Sons Ltd.*

## INTRODUCTION

With a prevalence of less than 2% of all pregnancies, twin pregnancies account for more than 25% of spontaneous early preterm births[1,2]. Strategies for prevention of preterm birth include the use of vaginal progesterone, cervical pessary and cervical cerclage. Individual patient data meta-analyses (IPDMAs) from randomized controlled trials (RCTs) reported that vaginal progesterone in twin gestation with a sonographic short cervix did not significantly reduce the rate of preterm birth < 33 weeks, but it reduced the risk of composite neonatal morbidity and mortality[3,4]. The Arabin pessary has been shown to be effective in reducing early preterm birth in singleton gestations with short cervix and has generated interest in its use in twin gestations[5]. A RCT in twin gestations found that prophylactic use of the Arabin pessary reduced the rate of early preterm birth, but only in the subgroup with a short cervix[6]. However, a large multicenter RCT on the use of the Arabin pessary in unselected twin gestations, administered either prophylactically or for those with cervical length ≤ 25 mm, had no effect on spontaneous birth < 34 weeks or neonatal outcome[7]. An IPDMA of RCTs primarily on singletons that included 49 sets of twins found that, in twin gestation with a short cervix, the use of cervical cerclage may double the rate of spontaneous early preterm birth[8]. These results led to recommendations in the 'Choosing Wisely' program (an initiative of the American Board of Internal Medicine aimed at advancing a dialogue on avoiding wasteful or unnecessary medical tests, treatments and procedures) to warn patients against physicians' recommendations to perform cerclage for a short cervix in twin gestation[9]. The IPDMA was subsequently repeated, controlling for confounders, and concluded that cerclage did not reduce the incidence of delivery < 34 weeks' gestation, and its use was associated

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with an increase in respiratory distress syndrome and a birth weight < 1500 g[8,10]. However, a recent retrospective cohort study reported that cerclage in twin gestation with short cervix reduced the rate of early preterm birth ($n = 57$ cerclage *vs* 83 expectant)[11].

Our group has routinely screened twin gestations and offered cerclage for a short cervix since the 1990s with encouraging results[12]. Consequently, we have continued to perform cervical ultrasound screening and offered cervical cerclage for a progressively shortening cervix. The purpose of this retrospective cohort study was to determine whether cerclage in DCDA twin gestations with short cervix reduces the rate of spontaneous preterm birth < 32 weeks' gestation.

## PATIENTS AND METHODS

This was a retrospective cohort study of DCDA twin gestations with serial vaginal cervical sonography performed in women who were asymptomatic. Excluded cases were monoamniotic and monochorionic–diamniotic twin gestations, those with major fetal defects and women who had placenta previa or complained of contractions or vaginal bleeding, or were found to have signs or symptoms of intra-amniotic infection. Approval was obtained from the institutional review boards of the institutions involved.

The study cases included 49 consecutive asymptomatic DCDA twin gestations that were routinely screened with vaginal sonographic cervical length assessments every 2 weeks from 16 to 24 weeks' gestation at Saint Peter's University Hospital, New Brunswick, NJ, USA, between November 2006 and November 2014. Nine of these cases with cervical length of 0 mm, a dilated external cervical os and visible membranes were excluded from subsequent case–control matching and statistical analysis. The 40 cases included in the analysis were treated with cervical cerclage for short cervix at 16–24 weeks' gestation.

Cerclage placement was considered when the cervical length was < 25 mm. Cervical lengths of 16–25 mm were considered as intermediately short and additional factors utilized to offer a cerclage included rate of cervical shortening, progressive shortening within this range, history of prior spontaneous preterm birth or mid-trimester loss and gestational age at onset of cervical shortening. A cervical length of ≤ 15 mm was a definitive indicator for offering cerclage. The sonographic cervical length was not used by itself to determine whether to place the cerclage. The technical difficulty is the same regardless of cervical length on ultrasound, including those with zero length, since these cervices are equally thick and long and simply dilate from within.

The preoperative evaluation assessed for vaginal bleeding, vaginal discharge, cervical lacerations, intra-amniotic infection and uterine contractions. Speculum examinations were performed with the use of Q-tips to evert the exocervix to look for vaginal–cervical discharge, cervical lacerations and appearance and location of the membranes, if visible. All patients had an evaluation of serum white blood cell (WBC) count and differential. The patient was observed for a period of up to 48 h before surgery if there was any concern of infection, presence of contractions and/or labor. An isolated finding of vaginal discharge was evaluated for a definitive diagnosis and treated for at least 2 days. Evaluation of vaginal discharge included a wet mount microscopic evaluation without cultures. Amniocentesis was considered if there was a clinical/laboratory suspicion of infection or the cervix was dilated with membranes at, or past, the external os. If amniocentesis was indicated it was the last step of the evaluation process and performed within several hours of the cerclage procedure so that the amniocentesis results were a true assessment of intra-amniotic infection at the time of cerclage placement. Evidence of intra-amniotic infection was defined as WBC count > 50, glucose level < 15 mg/dL and positive Gram staining for WBCs or bacteria. Cultures were taken but results were not used in decisions regarding cerclage placement. Evidence of intra-amniotic infection was a contraindication for cerclage. During this period of observation, repeat vaginal sonography was sometimes performed to identify any unfavorable change in cervical status. If membranes were beyond the exocervix, membrane tension, ability to reduce membranes digitally and cervical thickness/effacement were assessed by digital examination to determine technical feasibility of cerclage placement. An effaced cervix was considered evidence of labor and a contraindication to cerclage. Those that did not satisfy the criteria for cerclage placement during the period of preoperative evaluation were not offered the procedure. Preoperative prophylactic antibiotics, initially clindamycin and then ceftriaxone, and perioperative indomethacin were administered.

The modified McDonald cervical cerclage procedure was performed by one of two operators (C.H. and E.R.G.). In the operating room, a sponge stick was placed in the endocervical canal to determine the location of the membranes and the anterior lip of the cervix was grasped with the sponge stick. A Foley catheter was passed within the endocervical canal and its balloon was inflated with 30 mL of fluid to displace the membranes from the operative site and avoid inadvertent membrane puncture during suture placement. Two pieces of 0 Prolene (Ethicon, Somerville, NJ, USA) were used with a CT needle, with placement begun at the first to second cervical–vaginal rugal folds at 12 o'clock. At our institution, we use Prolene because (1) it is non-reactive and monofilamentous and therefore may be associated with less inflammation and microbial growth within the suture in comparison with other suture materials, and (2) the needles attached to this suture material are of a size that allows the operator better access to the upper areas of the vagina and cervix leading to consistent high cerclage placement. If a cervical laceration was present the sutures had to be placed beyond the apex of the laceration with or without dissection of the cervical–vaginal mucosa. We placed two sutures for added reinforcement and the second suture was placed above the first by 3–10 mm. Before tying the sutures,

we performed a digital examination to identify whether the sutures had entered the endocervical canal. If this occurs the sutures tear from within the cervix and lead to cerclage failure. If this was identified, the suture was removed and replaced. We then catheterized the bladder and allowed the urine to drip onto a clean gauze pad and observed for evidence of hematuria signifying suture entry into the bladder. When the sutures were tied, we created approximately 12 alternating knots. This was to assist in its removal when appropriate. Postoperatively, the suture knots migrate into the cervical stroma. The multiple knots help to guide the scissors during cerclage removal. At the time of suture removal the scissors were kept parallel to the knots in order to guarantee cutting the circular portion rather than the 'suture tails'. The patients were discharged within 24 h of surgery without medication.

Approximately 1 week after surgery, we perform sonography to identify the height of the cerclage. This is to give feedback on cerclage placement, which is used to train on placement of the suture material as high as feasible and to reduce interoperator variability. This information is not used to determine whether to reoperate. Sutures at our institution are generally placed within 5 mm of the base of the bladder or approximately 2 cm from the external cervical os.

Controls were selected from DCDA twin pregnancies participating in one of three European multicenter studies of sonographic screening for preterm birth by cervical length at 19 + 0 to 24 + 6 weeks' gestation[7,13,14]. All ultrasound scans were carried out by sonographers who had received the appropriate Certificate of Competence of The Fetal Medicine Foundation (www.fetalmedicine.com). Each transvaginal scan was performed over a period of about 3 min and the shortest of three measurements was recorded. The databases were searched for 40 asymptomatic controls with no cerclage who were managed expectantly, and matched to the cases treated with cerclage for the following characteristics: cervical length and gestational age at cervical assessment (within ± 7 days). In one study, women underwent cervical length assessment as part of an observational study and women with cervical length ≤ 19 mm were referred to their obstetrician for expectant management but in some cases they had cervical cerclage or the administration of progesterone vaginal pessaries[13]. In another study, women with cervical length < 15 mm were randomized to vaginal progesterone or expectant management[14]. In the third study, women were randomized to Arabin cervical pessary or expectant management[7].

The outcome measure was spontaneous preterm birth < 32 weeks' gestation. Data on pregnancy outcome were collected from hospital maternity records or the general practitioners of the women. The obstetric records of all patients delivered < 32 weeks (< 223 days) were examined to determine if the preterm birth was iatrogenic or spontaneous. The latter included those with spontaneous onset of labor and those with preterm prelabor rupture of membranes.

### Statistical analysis

Continuous variables were summarized as the median and interquartile range (IQR) and categorical variables were presented as numbers and percentages. Comparisons between the outcome groups was by chi-square or Fisher's exact test for categorical variables and Mann–Whitney *U*-test for continuous variables. Logistic regression analysis was used to demonstrate whether the risk for spontaneous delivery < 32 weeks was reduced with the insertion of cervical cerclage, corrected for maternal age, body mass index (BMI), racial origin, cigarette smoking, *in-vitro* fertilization (IVF), parity and prior preterm delivery. The risk of spontaneous preterm birth from time of insertion of cervical cerclage or start of expectant management until 32 weeks' gestation was assessed using Kaplan–Meier analysis[15], in which gestational age was the time scale, spontaneous delivery was the event and elective deliveries were treated as censored. Significance was set as a *P*-value of < 0.05, two-tailed. Using the primary outcome measure of spontaneous preterm birth < 32 weeks' gestation, with the effect size of 60% at the error level of $\alpha = 0.05$, a sample size of 40 women in each of the cervical cerclage and expectant management groups (total of 80 women) achieved a power of 82%. The statistical software package SPSS Statistics 22.0 (IBM Corp., Armonk, NY, USA) and MedCalc (Medcalc Software, Ostend, Belgium) were used for data analyses.

## RESULTS

Maternal characteristics of cases and controls are compared in Table 1. They were matched for cervical length and gestational age at cervical assessment. In both the cerclage and control groups the distribution of the preoperative cervical length was as follows: no case with < 5 mm; nine cases with 5–9 mm; 24 cases with 10–14 mm; five cases with 15–19 mm; and two cases with 20–24 mm. One case had cerclage placement at a cervical length of 23 mm because it was identified at 16 weeks and there was a history of prior spontaneous preterm birth.

Perinatal outcomes in the cases and controls are described in Table 2. In both cerclage and control groups, all babies survived. In the cerclage group, compared with controls, there was a significantly lower rate of spontaneous birth < 32 weeks and higher gestational age at birth and birth weight of both twins. In addition, there were significantly lower rates of spontaneous birth < 34, < 30 and < 28 weeks' gestation in the cerclage group. There were no differences between the groups for rates of spontaneous labor/preterm prelabor rupture of the membranes and no onset of labor. The difference in rate of birth at 32 weeks' gestation represented a 60% reduction in the cerclage group (relative risk, 0.40 (95% CI, 0.20–0.80)).

In the prediction of spontaneous delivery <32 weeks' gestation, logistic regression analysis demonstrated that the risk was reduced by the placement of cervical cerclage (odds ratio, 0.22 (95% CI, 0.058–0.835); $P = 0.026$),

**Table 1** Maternal characteristics in 40 twin gestations with cervical cerclage for short cervix and 40 matched controls without cerclage

| *Characteristic* | *Cerclage (n = 40)* | *No cerclage (n = 40)* | P |
|---|---|---|---|
| Maternal age (years) | 31.0 (28.0–34.8) | 34.9 (31.4–37.4) | 0.940 |
| Maternal BMI (kg/m$^2$) | 27.0 (24.0–31.0) | 25.1 (22.1–28.2) | 0.467 |
| Racial origin | | | |
| Caucasian | 17 (42.5) | 28 (70.0) | 0.024 |
| Black | 13 (32.5) | 7 (17.5) | 0.196 |
| Asian | 10 (25.0) | 5 (12.5) | 0.252 |
| Cigarette smoker | 2 (5.0) | 1 (2.5) | > 0.999 |
| *In-vitro* fertilization | 13 (32.5) | 14 (35.0) | > 0.999 |
| Parity | | | |
| Nulliparous | 24 (60.0) | 30 (75.0) | 0.232 |
| Previous SPTB | 9 (22.5) | 9 (22.5) | > 0.999 |
| No previous SPTB | 7 (17.5) | 1 (2.5) | 0.057 |
| Cervical length (mm) | 12 (5–23) | 12 (5–24) | 0.985 |
| GA at cervical assessment (weeks) | 21.9 (16.1–24.9) | 22.9 (16.6–24.9) | 0.013 |

Data are given as median (interquartile range) or *n* (%). BMI, body mass index; GA, gestational age; SPTB, spontaneous preterm birth.

**Table 2** Perinatal outcomes in 40 twin gestations with cervical cerclage for short cervix and 40 controls without cerclage

| *Perinatal outcome* | *Cerclage (n = 40)* | *No cerclage (n = 40)* | P |
|---|---|---|---|
| GA at birth (weeks) | 36.0 (32.9–37.4) | 31.6 (27.1–36.7) | < 0.0001 |
| Spontaneous birth | | | |
| < 34 weeks | 12 (30.0) | 25 (62.5) | 0.007 |
| < 32 weeks | 8 (20.0) | 20 (50.0) | 0.009 |
| < 30 weeks | 3 (7.5) | 14 (35.0) | 0.005 |
| < 28 weeks | 3 (7.5) | 12 (30.0) | 0.020 |
| Onset of labor | | | |
| Spontaneous/PPROM | 31 (77.5) | 32 (80.0) | > 0.999 |
| No labor | 9 (22.5) | 8 (20.0) | > 0.999 |
| Mode of delivery | | | |
| Vaginal for both twins | 6 (15.0) | 17 (42.5) | 0.013 |
| Vaginal/Cesarean section | 2 (5.0) | 0 (0.0) | 0.494 |
| Cesarean section for both twins | 32 (80.0) | 23 (57.5) | 0.053 |
| Birth weight, Twin A (g) | 2357 (1870–2643) | 1600 (850–2435) | < 0.0001 |
| Birth weight, Twin B (g) | 2338 (1960–2673) | 1687 (923–2277) | < 0.0001 |

Data are given as median (interquartile range) or *n* (%). GA, gestational age; PPROM, preterm prelabor rupture of membranes.

corrected for maternal age, BMI, racial origin, cigarette smoking, IVF, parity and prior preterm delivery.

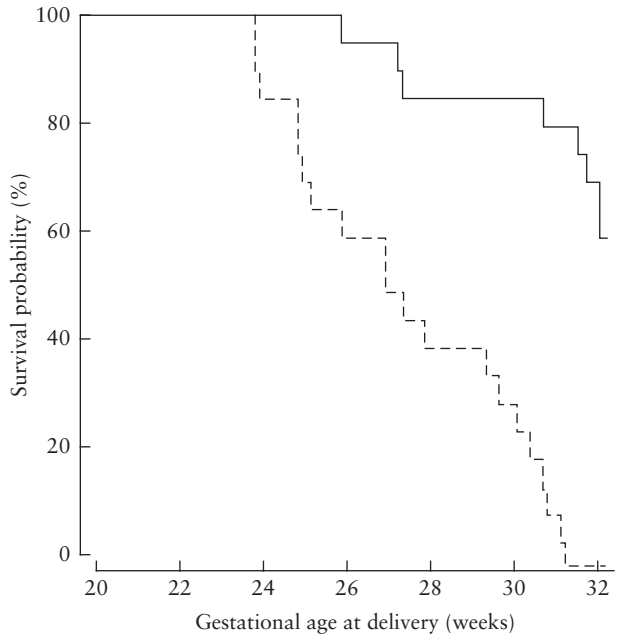
On Kaplan–Meier analysis (Figure 1), the cumulative percentage of patients who did not give birth spontaneously before 32 weeks' gestation was significantly higher in the cerclage group than in the control group (hazard ratio, 0.300 (95% CI, 0.142–0.633); $P = 0.002$).

## DISCUSSION

This retrospective cohort study in DCDA twin gestations with short cervix has shown that cervical cerclage was associated with a 60% reduction in the rate of spontaneous birth < 32 weeks' gestation. These results are consistent with those of a recent retrospective cohort study in twin gestations with cervical length ≤ 15 mm at 16–24 weeks' gestation that also showed benefit from cerclage placement, with a reduction in the rate of spontaneous birth < 34 weeks by 49%[11]. These findings are in marked contrast to the findings of the IPDMA of three RCTs on the use of cervical cerclage for short cervix in twin pregnancies, which reported no impact on the rate of spontaneous birth < 34 weeks[10].

The strengths of the study include, first, the relatively large cohort of consecutive DCDA twin gestations with short cervix treated with cerclage by two physicians at one center who used a standardized preoperative protocol and cerclage procedure, good matching with a group of controls that were managed expectantly and standardized methodology for cervical-length measurement.

The main limitation of the study arises from its retrospective nature and that it was not a randomized trial. Controls were selected from three European studies, two of which were RCTs, and we attempted to reduce potential bias by ensuring similar demographic characteristics between cases and controls. There may have been differences in the care of cases compared with controls, other than the use of cerclage, which could have affected perinatal outcome. However, there was no known effective therapy to reduce spontaneous early preterm birth in twins during the study period. Despite the matching process, there were dissimilarities in maternal characteristics between the cases and controls.




| Number at risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| No cervical cerclage | | | | | | | |
| *n* | 40 | 40 | 38 | 32 | 28 | 25 | 20 |
| Cervical cerclage | | | | | | | |
| *n* | 40 | 40 | 40 | 39 | 37 | 37 | 32 |

**Figure 1** Kaplan–Meier plot of probability of continued pregnancy without delivery among patients treated with cervical cerclage as compared with expectant management. Cervical cerclage reduces risk of spontaneous birth < 32 weeks' gestation by 70% (hazard ratio, 0.300 (95% CI, 0.142–0.633); $P = 0.002$). ——, cases with short cervix treated with cerclage; – – –, untreated controls. Numbers at risk with and without cerclage are indicated below the graph.

We have addressed this limitation by performing a logistic regression analysis to determine whether the risk for spontaneous delivery < 32 weeks was reduced by the insertion of cervical cerclage, corrected for maternal age, BMI, racial origin, cigarette smoking, IVF, parity and prior preterm delivery. Finally, we did not report on neonatal morbidity and therefore could not assess the impact of cerclage on these perinatal outcome measures.

We presented a clinical and surgical approach associated with a better perinatal outcome than the control. As a result, twin gestations with a short cervix that responded favorably to cerclage placement were identified. It is our hope that the approach described can help in the design of RCTs. We suggest that women randomized to the cerclage group should undergo the described clinical approach and, if the results are not satisfactory, they should not be offered the procedure. Deviation from this approach may actually conceal cerclage benefit. If the proportion of appropriately chosen cases is less than the proportion that should not be surgically treated it could give the impression that cerclage is of no benefit or harmful. This may explain the difference in outcomes between this study and the meta-analysis report of the RCTs on the use of cerclage in twin gestation[8].

Our study findings, along with of those of Roman *et al.*[11], provide evidence that the use of cervical cerclage for twin gestations with short cervix can potentially reduce spontaneous early preterm birth. Ultimately, the results require confirmation in RCTs. We have provided information on cervical-length assessment, preoperative assessment and decision-making, and cerclage technique to assist in the development of such a trial.

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