

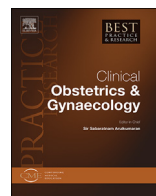


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Cervical cerclage in twin pregnancy

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A B S T R A C T

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Cervical cerclage in women with twin pregnancy is not routinely indicated but appears to be beneficial in subjects with a history of preterm birth or very short cervix or dilated cervix. There is a paucity of literature data regarding transabdominal or laparoscopic cervical cerclage (LCC) in twin pregnancy. It is uncertain whether LCC is more effective than transvaginal cerclage. Our own experience of 24 cases of LCC in twin pregnancy showed encouraging results. Further, well-planned studies are required to answer whether, when, and how cervical cerclage should be performed in women with twin pregnancy.

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Twins have a 50% rate of preterm birth (PTB) and 5 times higher risk of neonatal death than those with singletons. The proposed pathophysiological mechanisms responsible for spontaneous PTB in twin pregnancies include intrauterine infection, cervical incompetence, and additional uterine stretch/distension [1]. There is also increased secretion of mediators such as corticotrophin-releasing hormone from the larger placental mass and factors produced by the maturing fetal lung, such as surfactant protein-A, which stimulates myometrial contractility and may contribute to preterm parturition [2].

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Numerous interventions have been attempted to delay the time of delivery and, subsequently, prevent PTBs in twin gestation.

It has been shown that cervical cerclage in women with singleton pregnancy and cervical incompetence improves their perinatal outcomes; however, the value of cervical cerclage in twin pregnancy is less certain. This manuscript reviews the role of cervical cerclage in the prevention of PTB in women with twin pregnancy.

Routine cervical cerclage for women with twin pregnancy

Cervical cerclage placement indications are very specifically outlined for singleton pregnancies. It is generally accepted that routine cervical cerclage in women with twin pregnancy is not indicated, as it has not been shown to reduce PTB rate. The guidelines issued by the American College of Obstetricians and Gynecologists (ACOG), Society of Obstetricians and Gynaecologists of Canada (SOGC), and Royal College of Obstetricians and Gynaecologists (RCOG) do not currently recommend the routine use of cervical cerclage in the prevention of PTB in twin pregnancies [3–5].

Cervical cerclage in women with twin pregnancy and a history of PTB

Facco et al. retrospectively compared between 1995 and 2005 the gestational age at delivery for pregnant subjects carrying twins and with ($n = 23$) or without ($n = 270$) a history of PTB in a previous singleton pregnancy. Women with a history of PTB had an increased risk of PTB in both univariate [73.9% versus 44.4%; odds ratio (OR): 3.5; 95% CI: 1.4–9.37] and multivariate analyses (OR: 3.3; 95% CI: 1.3–8.7) [6].

Another retrospective study based on an American birth registry between 1995 and 2000 found similar results. The risk of PTB before 35 weeks was 32.9%, 23.0%, and 37.7% ($P < 0.001$) for nulliparous women ($n = 635$), multiparous women without a history of PTB ($n = 418$), and multiparous women with a history of PTB ($n = 215$), respectively ($P = .023$) [7].

In an RCT involving 50 twin pregnancy, which compared the use of cervical cerclage or not in women with or without a history of PTB, it was found that cerclage did not appear to reduce the incidence of PTB [8].

In a multicenter randomized controlled trial that included 1292 pregnant women whose obstetricians were uncertain whether to recommend cervical cerclage, most of whom had a history of early delivery or cervical surgery, there were fewer deliveries before 33 weeks in the cerclage group (83, 13%) than that in the noncerclage group (110, 17%) ($P = 0.03$). This trial suggests that, on balance, cervical cerclage should be offered to women with twin pregnancy and in whom there was a history of PTB in a previous pregnancy. However, it was noted that the use of cervical cerclage was associated with a doubling of the risk of puerperal pyrexia [9].

Cervical cerclage for short cervical length in twin pregnancy

Short cervical length is a recognized indication for singleton pregnancies but does not entirely apply in twin pregnancies, presumably due to different mechanisms that lead to cervical shortening. In twin pregnancies, the median cervical length at the time of the anomaly scan (22–24 weeks) is similar to that of singletons, but a higher proportion of twins have cervical length less than 25 mm (12.9% versus 8.4% in singletons) and less than 15 mm (4.5% versus 1.5%) [10,11].

Cervical length less than 25 mm is associated with 10% risk for birth before 33 weeks, while cervical length less than 15 mm is associated with 30% risk for birth before 33 weeks [10].

According to a patient-level meta-analysis of 3 RCTs that included twin gestations with a short CL, defined as cervical length of 25 mm before 24 weeks, a total of 49 twin gestations with a short cervical length were identified [12], with 24 in the cerclage group and 25 in the control group. There was no difference in the rates of PTB before 34 weeks of gestation (primary outcome) and PTB <37 weeks, <35 weeks, <32 weeks, <28 weeks, and <24 weeks (secondary outcome). However, it is accepted that the negative finding is almost entirely due to the small sample size. The authors concluded that large trials were necessary.

A Cochrane review published in 2014 [13] also concluded that there was no evidence that cervical cerclage is effective in reducing the risk of PTB in twin pregnancy even when ultrasound examination showed a short cervix and that more research was needed because of the paucity of literature data. It seems, therefore, that the value of cervical cerclage in women with a short cervix (<25 mm) and twin pregnancy remains uncertain.

Nevertheless, in a more recent study, in a sub-group analysis of patients with cervical length <1.5 cm, there was a significantly decreased risk of PTB <35 weeks [37% versus 71.4%; adjusted RR 0.49 (0.26–0.93)] in women who underwent cervical cerclage [14].

A recent meta-analysis also suggested that cerclage placement is beneficial for the reduction of PTB and the prolongation of pregnancy in twin pregnancies with a cervical length of <15 mm [15].

Cervical cerclage for dilated cervix in twin pregnancy

There is currently no consensus on the use of emergency cerclage when dilated cervix and exposed membranes were found by physical exam in twin pregnancies. Emergency cervical cerclage for dilated cervix with exposed membranes is known to be effective in singleton pregnancies. In twin pregnancies, studies in literature also suggest a beneficial effect of emergency cervical cerclage in pregnancy prolongation and neonatal survival as summarized in Table 1 [16–24]. Nevertheless, in twin pregnancies with advanced cervical dilatation and protruding membranes, emergency cervical cerclage should be an option only for carefully selected patients after counselling about the possible complications and low success rate [16].

Following an emergency cerclage for cervical dilatation, the obstetrical outcomes appeared similar between twin pregnancy and singleton pregnancy. One study including 43 patients (12 twin and 31 singleton pregnancies) who underwent emergency/physical exam-indicated cerclage placement, the median time from cerclage placement to delivery, the median gestational age at delivery, and the likelihood of delivery at >32 weeks were all similar between the 2 groups [17]. Two retrospective studies also suggested that emergency cerclage inserted in mid-trimester in women with twin pregnancy and dilated cervix is beneficial [18,19].

Table 1

Cervical cerclage for dilated cervix in twin pregnancy—effects on pregnancy prolongation and neonatal survival.

Author, year	Indication for cerclage	Twin pregnancies	GA at cerclage (weeks)	Time interval to delivery (weeks)	Perinatal survival
Cilingir et al., 2018 [16]	More than 50% effacement or cervical dilatation	10	27.3 (21–34) ^c	6.4 (4.1–11) ^c	60.0%
Rebarber et al., 2014 [17]	Dilated cervix or exposed membranes	12	19.9 ^e	13.1 (3.7–15) ^c	83.3%
Levin et al., 2012 [18]	More than 50% effacement or cervical dilatation	14	20.1 ± 2.5 ^a	10.2 ± 6.4 ^a	75.0%
Aguilera et al., 2013 [19]	Exposed membranes	10	20.6 ± 2.5 ^a	8.1 ± 4.5 ^a	70.0%
Miller et al., 2014 [20]	Dilated cervix	104	16–24 ^b	9.9 (3–14.1) ^c	66.3%
Park et al., 2018 [21]	Cervical dilation 4.0 (1.5–5.0) cm	17	20.7 (19.4–21.7) ^c	4.4 (3.2–5.2) ^c	79.0%
Chun et al., 2018 [22]	Painless dilated cervix >1.0 cm and visible prolapsed membranes	32	22.3 ± 1.8 ^a	6.8 ± 3.9 ^a	50.0%
Roman et al., 2016 [23]	Dilated cervix 1.0–4.5 cm	38	16–24 ^b	10.5 ± 5.6 ^a	73.4%
Abbasi et al., 2018 [24]	Cervical dilatation 2.6 ± 1.3 cm	27	21.5 ± 2.6	7.3 ± 5.5 ^a	70.4%
					69.7% ^d

GA: gestational age;

^a Mean ± standard deviation;

^b Range of weeks;

^c Mean in days (range of days);

^d Mean live birth rate.

^e Standard deviation not reported.

In a single-institution retrospective cohort study of 442 women who underwent a cerclage during the study period, 104 (23.5%) had twins. The mean gestational age and digital cervical length at placement did not differ by plurality. Although twins were more likely to deliver at a slightly earlier median gestation (31.9 weeks; interquartile range, 24.9–35.1 weeks) than singletons (32.7 weeks; interquartile range, 24.6–38.3 weeks) ($P = .015$), the frequency of delivery before 28 weeks did not differ between these 2 groups (33.7% versus 35.8%, $P = .69$).

Another retrospective cohort study by Park drew similar conclusion that obstetric and neonatal outcomes of physical examination-indicated cerclage in twin pregnancies were comparable to those in singleton pregnancy [21].

Roman compared perinatal outcomes in twin pregnancies complicated by premature asymptomatic cervical dilatation treated with rescue cerclage with expectant management. The results showed that women in the cerclage group gave birth at a more advanced gestational age (31.2 versus 24.3 weeks); had a longer interval to delivery (10.5 versus 3.7 weeks); a lower rate of PTB at <34 weeks (52.6 versus 94.7%), <32 weeks (44.7% versus 89.4%), <28 weeks (31.6% versus 89.4%), and <24 weeks (13.1% versus 47.3%); and reduced perinatal mortality and morbidity [23]. A retrospective cohort study by Abbasi also found that rescue cerclage can prolong pregnancy and improve perinatal outcomes in asymptomatic women with twin pregnancy and cervical dilatation before 25 weeks of gestation, when compared to expectant management [24].

Despite the lack of evidence from randomized controlled trials, emergency cervical cerclage in twin pregnancy seemed to have a positive effect in pregnancy prolongation and neonatal survival, and it should be an option for carefully selected patients after counselling the complications and low success rate.

Trans-abdominal/laparoscopic cervical cerclage

The vast majority of current literature data regarding cervical cerclage in twin pregnancy is about transvaginal cerclage (TVC). There are relatively little data on trans-abdominal cervico-isthmic cerclage or laparoscopic cervical cerclage (LCC) for women whom have had a failed TVC or a very short cervix. A recent study reported 7 patients with twin gestations undergoing abdominal cerclage (due to a history of TVC failure or short cervix not amenable to TVC) demonstrated no surgical complications and a take-home-baby rate of 7/7 (100%) albeit with a neonatal complication (such as hyaline membrane disease, chronic lung disease, and intestinal obstruction as a result of meconium ileus, transient tachypnea of the newborn, and respiratory distress syndrome) rate of 50%. In this study, a review of the literature was also performed, which identified a further 8 publications including 16 cases of twin gestations undergoing abdominal cerclage with similar favorable outcomes (live birth rate 28/32 [88.0%]) [25].

There are fewer cases of LCC among women with twin pregnancy. In general, the success rate of LCC is comparable to laparotomy cervico-isthmic cerclage but has the advantages of speedier recovery, less postoperative pain, and less blood loss [26,27]. LCC for twins is sporadically reported in the studies of LCC. When reviewing the literature, we have identified a total of 10 cases of LCC in twin pregnancy [28–31]. Thus far, nine of the 10 cases were successful in preventing PTB.

Our series of LCC in women with twin pregnancy

We have recently reported on our initial experience with preconception LCC [32]. In our center, we have now performed a total of 868 cases of LCC, where 636 cases were followed up over one year; 24 subjects of the 636 cases had twin pregnancy with LCC either inserted preconception ($n = 21$) or postconception ($n = 3$). All women underwent a simplified LCC [32]. The inclusion criteria are a diagnosis of cervical incompetence associated with (i) one or more previous mid-trimester loss(es); (ii) a previously failed TVC; or (iii) a short cervix not amenable to TVC. The study was approved by the Fuxing hospital's Institutional Review Board.

The surgical procedure was performed by one of two surgeons and has been described in detail in our previous publication [32]. In brief, a routine four-port laparoscopy was performed in the lithotomy position. A cup uterine elevator (Shikonghou, China) (Fig. 1) was inserted into the vagina after the appropriately sized cup was selected. In cases where the LCC was performed preconception, the pole of



Fig. 1. Uterine elevator and different sizes of cups.

the uterine elevator was inserted into the uterine cavity (1 cm below the fundus). In cases where the LCC was performed postconception, the cup was adjusted to the tip of the elevator and the pole was not inserted into the cervical or uterine canal at all. The uterus was then elevated so that the cup margin would correspond to the cervico–isthmic junction of the uterus. A 5-mm Mersilene tape (RS-22; Ethicon, Inc., Somerville, NJ, USA) was then used, with both needles straightened on the operating tray before insertion into the insufflated abdomen through the 5-mm left lateral port. Without dissecting the bladder of the uterus and in an anteverted position, the straightened needle was inserted in a posterior–anterior direction at the lateral edge of the vaginal cup so that it would transverse the cervix at the cervico–isthmic junction. As the needle was inserted, the uterus was moved from an anteverted position to a retroverted position so that the tip of the needle would come out at the level of the border of the uterovesical reflection. This was repeated for the contralateral side. A diagnostic hysteroscopy was then performed to confirm that the tape had not entered the cervical canal (only for the nonpregnant patients) and the Mersilene tape was then tied after cutting off the two needles, followed by four to five intracorporeal square knots, with 3–4 cm of free tape left at either edge (Fig. 2). Post-operatively, a transvaginal ultrasound was performed on days 5–7 to further confirm and visualize the position of the suture at the cervico–isthmic junction. All women were advised to be delivered by cesarean section, and the cerclage was routinely removed during delivery to avoid possible future suture migration.

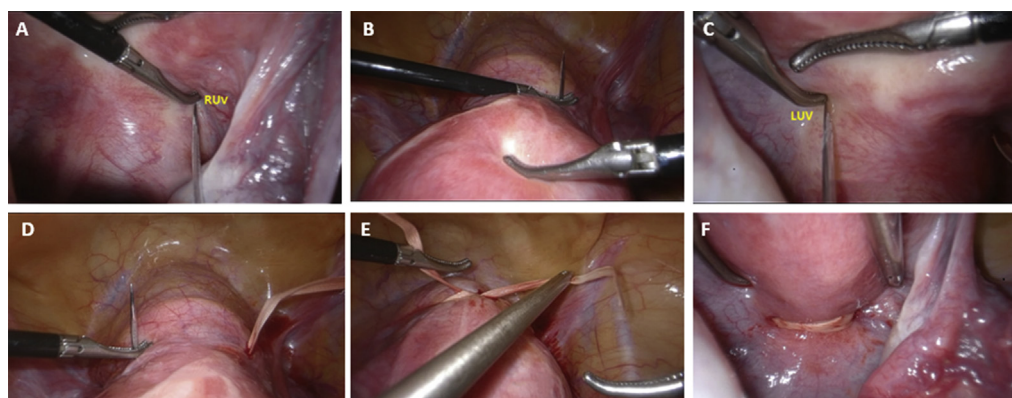


Fig. 2. Steps for simplified laparoscopic cervical cerclage (LCC). A. Without dissecting the bladder of the uterus and in an anteverted position, the straightened needle was inserted in a posterior–anterior direction at the lateral edge of the vaginal cup so that it would transverse the cervix at the cervico–isthmic junction. (Right uterine vessel, RUV). B. The needle can now be seen coming out anteriorly in the utero-vesicle pouch. C–D The procedure was repeated on the left side. (Left uterine vessel, LUV). E. The Mersilene tape was then tied after cutting off the two needles, followed by four to five intracorporeal square knots with 3–4 cm of free tape left at either edge. F. The tape over the posterior aspect of the uterus at the end of the procedure.

The study included a total of 24 women with a mean age of 31.5 ± 4.1 years (range 23–39 years). The indication for LCC was: previously failed TVC 8/24 (33.3%), previous mid-trimester loss 10/24 (41.7%), previous cervical surgery 1/24 (4.2%), and combined (cervical surgery with previous mid-trimester loss) 5/24 (20.8%). All cases were performed successfully with no surgical or anesthetic complications. The mean $\pm$ SD operation time was 39.2 ± 13.1 (range 20–60) min, and the mean blood loss was 8.7 ± 3.8 (range 5–20) ml. The demographic details are summarized in Table 2.

Regarding the method of conception, 5/24 (20.8%) women conceived naturally, 4/24 (16.7%) conceived following ovulation induction, and 15/24 (62.5%) conceived with IVF. There were 3/24 (12.5%) second-trimester miscarriages and no stillbirths. The live birth rate was 21/24 (87.5%). Cesarean section was performed in all live birth cases. The median gestation at delivery was 35 (range 23–38) weeks; 16/24 (66.7%) women delivered after 34 weeks, all with babies alive and well. One woman delivered at 23 weeks, and another woman at 24 weeks, both with painless cervical dilatation despite an LCC; a third woman delivered at 26 weeks due to uncontrolled uterine contraction. All these three cases had subsequent neonatal deaths of the twins. In terms of obstetric complications, 4/24 (16.7%) experienced preeclampsia, 2/24 (8.3%) gestational diabetes, and 1/24 (4.2%) preterm pre-labor rupture of membranes. Two of the 24 women had both gestational diabetes and preeclampsia. The reproductive outcome beyond the first trimester of all women is summarized in Table 3.

Our results suggest that LCC in women with twin gestations and cervical incompetence appeared to produce encouraging results, with 16/24 (66.7%) women delivering after 34 weeks and 21/24 (87.5%) women producing live births. In addition, in our series, 4/24 (16.7%) conceived following ovulation induction and 15/24 (62.5%) conceived with IVF; it seemed that the use of prophylactic LCC might be beneficial in improving reproductive outcomes in high-risk infertile patients with known cervical incompetence who subsequently conceived twin gestations through IVF-ET treatment.

Comparison of LCC between singleton and twin pregnancy

We recently reported our experience in a series of 100 LCC for women with singleton pregnancy who had experienced a previously failed TVC. In that series, 82/100 (82%) of women conceived, with a subsequent live birth rate of 53/55 (96.4%) for women with pregnancy progressing beyond the first trimester [32]. The results suggest that the live birth rate after LCC in twin pregnancy appears lower than that of singleton pregnancy, which is to be expected; on the other hand, given that the subjects have 2 significant risk factors for preterm delivery, namely, cervical incompetence and twin pregnancy. The observation that LCC can achieve a live birth rate of 87.5% in this group of subjects is very encouraging. The significant finding should be confirmed with larger cohort studies.

Table 2
Patient characteristics of twin pregnancy following LTC.

Age (years)	31.5 $\pm$ 4.1 (23–39)
Indication for LCC ^a	
Failed TVC	8/24 (33.3%)
Mid-trimester loss	10/24 (41.7%)
Cervical surgery	1/24 (4.2%)
Combined	5/24 (20.8%)
Insertion of LCC	
Preconception	21/24 (87.5%)
Postconception	3/24 (12.5%)
Method of conception	
Natural	5/24 (20.8%)
Ovulation induction	4/24 (16.7%)
IVF	15/24 (62.5%)

LCC = Laparoscopic cervical cerclage.
TVC = Transvaginal cerclage.
Combined = Cervical surgery and mid-trimester loss.
Presented as median (range), rate (percentage), or mean (standard deviation).
^a In addition to a finding of a short cervix <25 mm.

Table 3

Reproductive outcomes of twin pregnancy (beyond first trimester) following LCC.

Outcome	
Miscarriage	3/24 (12.5%)
Stillbirth	0/24 (0%)
Live birth	21/24 (87.5%)
Neonatal death ^a	3/24 (12.5%)
Gestation at delivery (weeks)	35 (23–38)
≥37	3/24 (12.5%)
≥34 to <37	13/24 (54.2%)
≥28 to <34	5/24 (20.8%)
<28	3/24 (12.5%)
Birth weight (grams) ^b	2316 ± 416
Obstetric complications ^c	
Preeclampsia	4/24 (16.7%)
Gestational diabetes	2/24 (8.3%)
PPROM	1/24 (4.2%)

Presented as median (range), rate (percentage).

PPROM=Preterm prelabor rupture of membranes.

^a Three gestations resulted in neonatal deaths at 23/24/26 weeks.^b Excluding the three extremely premature gestations resulting in neonatal deaths.^c Two women suffered from both GDM and preeclampsia.

Comparison of LCC and TVC in twin pregnancy

There are no formal RCT or cohort studies comparing LCC and TVC in women with twin pregnancy. Current literature data on the outcome of emergency TVC in women with cervical incompetence and twin pregnancy are summarized in Table 1, which showed a mean live birth rate of 69.7% (range 50%–83.8%). The results seem inferior to that of LCC. Nevertheless, the numbers are rather small, and there are confounding variables that need to be taken into consideration. Although preliminary data seem to suggest that LCC is more efficacious, carefully planned matched cohort studies are needed to confirm whether indeed LCC is more superior than TVC.

In conclusion, LCC appears to be a safe, simple, and minimally invasive approach, which could potentially play an important role in women with established cervical incompetence and twin gestations who have had a failed TVC or a very short cervix that is not amenable to a TVC. The encouraging results presented in this review should be considered preliminary and confirmed in a larger cohort study.

In summary, cervical cerclage in women with twin pregnancy is not routinely indicated but appears to be of benefit in subjects with a history of PTB or very short cervix or dilated cervix. It is uncertain whether LCC is more effective than TVC; further well-planned studies are required to answer whether, when, and how cervical cerclage should be performed in women with twin pregnancy.

Practice points

- Cervical cerclage in women with twin pregnancy is not routinely indicated but appears to be of benefit in subjects with a history of PTB or very short cervix or dilated cervix.
- LCC appears to be a safe, simple, and minimally invasive approach, which could potentially play an important role in women with established cervical incompetence and twin gestations, especially for women who have had a failed TVC or a cervix that is not amenable to a TVC.
- The use of prophylactic LCC might be beneficial in improving reproductive outcomes in infertile patients with known cervical incompetence who subsequently conceived twin gestations through IVF-ET treatment.

Research agenda

- The value of prophylactic LCC in women with twin pregnancy could potentially play an important role in women with established cervical incompetence and twin gestations, but the result is preliminary and should be confirmed in a larger cohort study.
- It is uncertain whether LCC is more effective than TVC; further well-planned studies are required to answer whether, when, and how cervical cerclage should be performed in women with twin pregnancy.

Conflict of interest

The authors have no conflicts of interest with regard to the present article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bpobgyn.2019.06.001>.

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