**Full Title:** Efficacy of transvaginal cervical cerclage in women at preterm risk following previous emergency cesarean section

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**Disclosure Statement:**

The authors report no conflict of interest.

**ABSTRACT**

**Introduction:**

Emergency cesarean sections (EMCS) are associated with subsequent preterm birth (PTB), particularly at full dilatation (FDCS) which are a cause of both second trimester miscarriages and early, recurrent spontaneous PTB (sPTB). The optimal management for these women in subsequent pregnancies is currently unknown. This study aims to assess efficacy of transvaginal cervical cerclage (TVC) in prevention of PTB among women who have had an EMCS followed by a subsequent late miscarriage (LM) or sPTB.

**Materials and methods:** A historical cohort study was performed assessing outcomes of women attending the Preterm Surveillance Clinic at St Thomas’ Hospital, London who received TVC, with a history of EMCS (pregnancy A) followed by a sPTB/LM (pregnancy B), and a subsequent pregnancy (pregnancy C). A historical reference group managed in the same clinic was identified comprising women with any risk factor for sPTB, who required TVC. Incidence of delivery >24 to <30 weeks was compared with relative risk (RR) and 95% confidence intervals (CI). Subgroup analysis was carried out assessing women who had a previous FDCS.

**Results:**

209 women with a previous EMCS during labor (50 with FDCS), followed by sPTB/LM were identified. 178 progressed beyond 24 weeks, of these 56 received TVC and formed the study group. 905 high risk women were identified, of these 154 received TVC and formed the reference group. Despite TVC treatment, 17/56 (30%) of the study group delivered <30 weeks’ gestation compared to 5/154 (3%) of the reference group (RR=9.4, 95%CI 3.6 – 24.2, p<0.001). In the subset of 17 women in the study group with a previous FDCS, followed by sPTB/LM, 6/17 (35%) delivered <30 weeks’ gestation, significantly higher than the reference group (p<0.001) but similar to EMCS at less than full dilatation (35% vs. 28%, p=0.596). Overall 33/72 (46%) women receiving cerclage with prior EMCS had either a midtrimester loss or delivery <30 weeks.

**Conclusions:**

TVC appears less effective among pregnant women who have had an EMCS followed by a sPTB/LM compared with other high risk women to prevent PTB. The lack of efficacy in the subgroup with a FDCS was similar.

**Key Words:**

Cervical cerclage, preterm birth, full dilatation cesarean section, FDCS

**Abbreviations:**

PTB – preterm birth

LM – Late miscarriage

sPTB – spontaneous preterm birth

EMCS – Emergency cesarean section

FDCS – full dilatation cesarean section

TVC – transvaginal cervical cerclage

**Key message:**

Vaginally placed cervical cerclages appear less efficacious in women who have previously undergone a late miscarriage or preterm delivery following an emergency cesarean section.Further prospective trials are urgently required to establish optimal management of this group of women.

**MAIN TEXT**

**INTRODUCTION:**

Preterm birth (PTB), in which delivery occurs prior to 37 weeks’ gestation, has significant long term health consequences, projected to cost health services in England and Wales £939 million per year.1 It is a substantial determinant of adverse outcome with regards to survival and quality of life.2 Morbidity is inversely correlated to gestation at delivery, and the most significant adverse outcomes are associated with very preterm birth, prior to 32+0 weeks’ gestation. In 2018, it was estimated that 0.8% of live births were before 30 weeks in England and Wales.3 More recently it has been demonstrated that second stage CS are a risk factor for a subsequent preterm delivery and late miscarriage (LM). The incidence of spontaneous PTB (sPTB) associated with CS undertaken at full dilatation is believed to be approximately 13.5%.4 There is a three-fold increased risk of recurrent sPTB or LM (between 16 and 24 weeks) compared to vaginal delivery.5 However the risk is on a continuum with regards to the extent of cervical dilatation at the time of all emergency CS, the risk increasing with advancing dilatation.6

For the year 2017-18, the overall CS rate in the United Kingdom (UK) was reported to be 28%. 16.2% of all deliveries were by emergency CS equating to >100,000 procedures every year7. Overall six percent of all EMCS are undertaken at full dilatation and the clinical problem is only likely to increase as CS rates continue to rise,6–8 particularly at advanced cervical dilatations, the latter being partly attributable to an increased incidence and higher failure rates of instrumental deliveries.9,10 It is estimated that rates of failed instrumental delivery in the UK increased from 8.4% in 1992 to 12.9% in 2001. In addition, attempts at instrumental delivery have decreased: 3.9% of all operative deliveries in 1992 had no attempt at instrumental compared to 5.3% in 2001.11

There is a paucity in the literature regarding the most appropriate treatment modalities in women who experience LM or sPTB following an EMCS, evidence currently being limited to case reports.12,13 Currently management of women with LM or sPTB following an EMCS in subsequent pregnancies is no different to that of women with a sPTB/LM history without previous EMCS. Evidence for treatments that recognize the additional risk factors posed by a previous EMCS is limited to case reports in the literature.12,13

This study therefore aims to assess the efficacy of transvaginal cervical cerclage (TVC) in women who have experienced a LM or sPTB after an EMCS to prevent preterm birth.

**MATERIALS AND METHODS:**

A historical cohort study was performed using data from the Preterm Clinical Network Database with ethical permissions (REC Ref. 16/ES/0093; IRAS project ID 180134). This database includes dedicated data from pregnant women at risk of preterm birth (www.medscinet.net/ukpcn).

The study group was selected from women who had attended the Preterm Surveillance Clinic at St Thomas’ Hospital London between September 2002 and September 2019. Women with a history of previous EMCS during labor, at any gestation (Pregnancy A) and a subsequent sPTB, (defined as delivery less than 37 weeks) or LM, (defined as delivery between 14 and 24 weeks) in a later pregnancy (Pregnancy B), followed by a subsequent singleton pregnancy (Pregnancy C) were identified. Those who received TVC during pregnancy C formed the study group. Cerclages were both history and ultrasound indicated (inserted where the cervical length was <25mm) as per standard clinical practice/protocols.14 Women were excluded if preterm delivery was medically indicated, if they received transabdominal cerclage or if outcome data was not available. Women were also excluded if 24 weeks’ gestation was not reached in Pregnancy C because our historical reference group had not recorded this data as it was from 24 weeks’ evaluating the use of fetal fibronectin. Women who were recorded to have a full dilatation caesarean section (FDCS) in the initial pregnancy formed a subgroup for secondary analysis. Figure 1 shows schematically how the study groups were derived.

The reference group was selected, comprising of women who had reached 24 weeks’ gestation with a TVC and at least one risk factor for preterm birth including: a history of previous sPTB or preterm pre-labor rupture of membranes at less than 37 weeks gestation; a previous LM, known uterine anomaly or previous invasive cervical surgery (eg large loop excision of the transformation zone; cone biopsy).

Demographic, pregnancy and delivery data was collected in women with TVC including: gravidity, body mass index (BMI kg/m2), ethnicity, age in pregnancy C, gestation at delivery, mode of delivery, whether initial pregnancy was term or preterm, and dilatation (cm) at time of initial CS if recorded.

The primary outcome was sPTB delivery between 24+0 and 29+6 weeks. This endpoint was selected due to recent NICE guidelines advocating admission, administration of tocolytics, corticosteroids and magnesium sulphate for women who are in suspected preterm labor < 30 weeks’ gestation14. Preterm delivery before 37 weeks was also analyzed.

In addition, we also compared outcomes in the two groups that the study population was derived from. This included women who did not receive cerclage.

**Statistical Analyses:**

Statistical analysis was undertaken using IBM SPSS Statistics Version 25. Demographic characteristics were analyzed using student t-tests where data was continuous and Chi-squared tests where categorical. A chi-squared test was used to compare delivery between 24 and 30 weeks between the EMCS group and the reference group along with relative risk (RR) and 95% confidence intervals (CI). Subgroup analysis comparing the FDCS group with the reference group was also performed. A chi-squared test was carried out to compare outcomes in women within the EMCS group whose initial pregnancy was term vs. those whose initial pregnancy was preterm (<37 weeks).

**RESULTS:**

209 women with a previous EMCS during labor (50 with FDCS) (pregnancy A), followed by sPTB/LM (pregnancy B) were identified. 178 progressed beyond 24 weeks, of these 56 (31%) received TVC in pregnancy C and formed the study group. 107 women received no cerclage, 15 women were excluded because they received transabdominal cerclage. 905 high risk women were identified, of these 154 (17%) received TVC and formed the reference group. 17 of the 56 women in the study group had a FDCS and were analyzed as a subgroup. Of the 31 women excluded because they did not reach 24 weeks gestation, 16 received TVC and 15 received no cerclage.

Demographic data for the study and reference groups are shown in Table 1. There were significantly more primigravid women in the reference group (11/139 (7.9%) vs. 0/56 (0%) as our study group required two previous pregnancies. There were also significantly more black women in the study group than the reference group (31/56, 55% vs. 13/154, 8%, p<0.001).

For the study group, the mean gestation for TVC insertion was 15.3 (standard deviation = 5.1). 37.5% (21/56) were history indicated, 37.5% (21/56) were ultrasound indicated and 25% (14/56) did not have the indication recorded.

Table 2 shows the outcome of pregnancies comparing the study and reference groups. Despite TVC treatment, 17/56 (30%) of the study group delivered <30 weeks’ gestation compared to 5/154 (3%) of the reference group (RR=9.4, 95%CI 3.6– 24.2, p<0.001). However, the number of women delivering prior to 30 weeks with a TVC was similar between women who had a FDCS and those who had an EMCS at less than full dilatation (6/17 (35%) vs. 11/39 (28%) respectively, p = 0.596). In addition, 16/72 (22%) women receiving TVC in the study population had a mid-trimester loss (16-24 weeks).

The mean gestation for TVC insertion among the 16 women who had a mid-trimester loss was 15.1 (standard deviation = 3.2). 25% (4/16) were history indicated, 56% (9/16) were ultrasound indicated and 19% (3/16) did not have the indication recorded.

In the women who did not receive cerclage in our two populations that the groups were derived from, there were significantly more sPTB <30 weeks in those with a previous EMCS compared to the high-risk reference population (24/107 (22%) vs. 14/751 (2%) respectively) and <37 weeks (53/107 (50%) vs. 153/751 (20%)).

16 women in the study population had a preterm delivery in pregnancy A. 7/16 delivered prior to 30 weeks in pregnancy C compared to 10/40 women who delivered at term in pregnancy A. The difference between these two groups was not statistically significant (p = 0.168).

**DISCUSSION:**

The results from this analysis have demonstrated TVC to be less effective among women with a previous EMCS followed by either a sPTB or LM, compared to all groups of women at high risk of preterm delivery. The risk of preterm delivery <30 weeks’ gestation in women with TVC and previous FDCS was 35%. The lack of efficacy of the TVC is in women with all EMCS and is not just confined to women with a previous FDCS. The lack of efficacy is even greater when taking into account mid-trimester losses. Our historical reference group had not recorded this data, as it was a study from 24 weeks’ evaluating the use of fetal fibronectin, so we were unable to make a formal comparison.

 Overall delivery <30 weeks was high, regardless of whether a cerclage was performed in women who had had a previous EMCS as an etiological factor, highlighting the fact that this is a high risk group. A direct comparison between those who received cerclage and those who did not was not valid as cerclage use may be related to a shortening cervix, i.e. those who received cerclage may have had a higher risk. When we included midtrimester losses, the “failure” rate of cerclage was even higher (46%) for all deliveries after cerclage and before 30 weeks.

It is hypothesized that the increased incidence of sPTB/LM in women with a history of EMCS may be due to an inadvertently low uterine incision which may encroach effaced cervical tissue leading to structural change. Although the exact cervical dilatation at the time of previous CS was not known for all women in this study, it has previously been documented that the greater the cervical dilatation at the time of EMCS, the greater this risk of LM/sPTB in subsequent pregnancies.6 When labor is prolonged, tissues can become edematous and anatomical boundaries less easily identified. If the incision is in cervical, as opposed to uterine, tissue a defect or scar may result in cervical insufficiency in future pregnancies. In addition, although the primary incision may not be in cervical tissue, angle extensions may contribute to cervical injury.4 This proposed structural change may also be influenced by suture material, healing process and infection.

This concept of incisions in effaced cervical tissue, has been postulated as early as 1939.15 A previous ultrasound study has demonstrated that cesarean sections performed in labor were more likely to have the cesarean scar located in cervical tissue as opposed to the lower segment of the uterus. The greater the cervical dilatation at the time of cesarean section, the more likely the scar was to be located in cervical tissue.16

We hypothesize that the higher failure rate of TVC in women with a previous EMCS compared to the reference group, may be due to the fact that vaginally placed cerclages are sited in the distal cervix, whereas cervical damage is most likely to be more proximal thus rendering them less effective, although the exact mechanism of pregnancy loss or preterm labor is not certain. We hypothesize that transabdominal cerclage may be a more effective treatment option in these women, potentially due to the fact the suture is positioned higher in the cervix, above the proposed area of previous scar tissue. This suggestion is based on speculation and is hypothesis generating only. Future studies are needed to assess this treatment modality.

This study was carried out using data from a large cohort of women with the specific combinations of risk factors (FDCS + sPTB; first stage CS + sPTB risk). All women were managed during the index pregnancy “C” at a hospital with an established and experienced specialist preterm service.

Selection bias is a possible limitation due to the retrospective nature of the study and because of the indications for the TVC. However, we have selected a study group with only one risk factor and the numbers in this study are large and therefore we do not believe it would have had a large effect. The reference group was managed by the same research team as this study population. The decision-making with regards to criteria for cerclage insertion would therefore be comparable for all groups. Cerclages were inserted according to a standard protocol for both history and ultrasound indications. At the time these women were seen in the preterm clinic, the risks of FDCS were not well established, therefore this was not the indication for cerclage. Although the two groups were not perfectly matched and there is the possibility of confounding factors such as ethnicity, we believe this is unlikely due to the high rate of failure, suggesting this is a real entity. This should be considered in future studies. The reference group and study group had similar histories, approximately 88% of the reference group had a previous preterm birth and approximately 70% had a previous late miscarriage.

The mode of delivery in the reference group was in some cases unconfirmed. It is therefore possible that some women in the reference group may have had an EMCS however if so, this would increase the significance of our findings. Prospective confirmation of our findings is needed. Some women in our study group did not have dilatation at CS recorded. Therefore, lack of differences in efficacy of cerclage between EMCS and FDCS needs confirmation.

Whether or not the caesarean section in pregnancy A was carried out at term or preterm could be a possible confounding factor for the outcomes in pregnancy C. Previous preterm birth is a risk factor for subsequent spontaneous preterm birth.17 6 out of 56 women in the study group delivered preterm in pregnancy A. The sub analysis carried out on this population did not find any significant differences in outcomes between these two groups of women.

Women may have an EMCS for diverse reasons and may suffer a range of complications. Prospective and longitudinal studies are required to investigate which elements of the EMCS (BMI, indication, uterine trauma, dilatation, chorioamnionitis, vaginal birth after cesarean, post-partum hemorrhage) are most associated with subsequent PTB outcomes and target preventative strategies. Prospective evaluation of cervical length and other predictors of preterm delivery such as fetal fibronectin in women who have had a previous EMCS are urgently required in order to predict outcome in future pregnancies. Prospective trials are also required to assess the efficacy of treatment modalities (eg transabdominal cerclage, vaginal pessaries and progesterone) in these women if they are identified as being at high risk of preterm delivery. Future studies should also include the impact on both recurrent and mid-trimester events.

Concurrently, strategies should be deployed to reduce CS rates. A recent WHO guideline provides guidance on a range of interventions designed to reduce unnecessary CS, including educational interventions; the use of clinical guidelines, audit and feedback to healthcare professionals; and the possible use of second opinions for CS where resources are adequate to support this.18 For this issue, maintaining skills for operative vaginal delivery are required.

The incidence of FDCS has been steadily increasing and it is estimated that at least 6% of all emergency CS in the UK are carried out at full dilatation.11 A prospective evaluation of risk would enhance our understanding of the problem. The reason for this rise is multifactorial, and includes an increase in failure rates of instrumental delivery accompanied by a decline in attempts at instrumental delivery.10 These may be a result of reduced exposure and opportunities for training under the supervision of more senior and experienced colleagues, in part due to rising CS rates. Furthermore, tackling the maternal obesity crisis has the potential to have a two-tiered effect at reducing the CS rate. Firstly, by directly reducing the risk of CS which is higher in obese women,20 and secondly by improving the success rate of instrumental deliveries which are more likely to be unsuccessful.21

**CONCLUSION:**

Women with a history of CS carried out in labor, regardless of dilatation at time of procedure remain high risk of early preterm birth following TVC. This study has highlighted an important clinical issue, suggesting that TVC is not as effective in women with an EMCS followed by sPTB/LM compared to other high risk groups of women. Following recent publication of the Saving Babies Lives Care Bundle v.2 in March 2019,22 in the UK, women with a history of FDCS will be offered screening (transvaginal ultrasound cervical length measurement) but the optimum management for these women is not yet established. Both the identification, preferably prior to an adverse event, and treatment of these women require further research.

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**TWEETABLE ABSTRACT:**

Transvaginal cervical cerclage appears less effective when preterm birth occurs after an emergency cesarean section.

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**Tables**

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|  | **Previous Emergency Cesarean Section and spontaneous preterm birth/late miscarriage** **(N = 56)** | **Reference group with risk factor for spontaneous preterm birth****(N=154)** | **P value** |
| Age (years)Mean (SD) | (n = 55)35.4 (7.1) | (n = 138) 31.2 (5.0) | 0.944 |
| BMIMean (SD) | (n = 49)28.3 (6.8) | (n = 111) 26.7 (5.1) | 0.201 |
| Gravidity123>3 | (n = 56)00749 | (n =139)11493544 | **<0.001** |
| Ethnicity (n, %) WhiteBlackAsianUnknown |  15, 27%31, 55% 2, 4% 8, 14% |  121, 78%13, 8%6, 4%14, 10% | **<0.001** |

**Table 1:** Maternal demographics comparing women who had transvaginal cerclage in emergency cesarean section population (EMCS) and reference population.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Previous Emergency Cesarean Section and spontaneous preterm birth/late miscarriage****(N = 56)** | **Reference group with risk factor for spontaneous preterm birth****(N=154)** | **Relative Risk [95% CI]** | **P value** |
| Gestation at delivery < 30 weeks, n (%) | 17 (30) | 5 (3) | 9.4 [3.6 – 24.2] | <0.001 |
| Gestation at delivery < 37 weeks, n (%) | 33 (59) | 37 (24) | 2.5 [1.7 – 3.5] | <0.001 |

**Table 2:** Delivery prior to 30 and 37 weeks’ in EMCS and reference populations.

**Figure Legends**

**Figure 1:** Schematic of how study and reference groups were derived

**Key:**

EMCS – emergency cesearean section; PTB – preterm birth; sPTB – spontaneous preterm birth; TVC – transvaginal cerclage.