

Cervical cerclage in the prevention of preterm birth

Rachael Simcox* MBBS, BSc

Clinical Research Fellow

Andrew Shennan MD, FRCOG

Professor of Obstetrics

*Maternal and Fetal Research Unit, Division of Reproduction and Endocrinology,
King's College London School of Medicine at Guy's, King's College and St Thomas' Hospitals,
10th Floor, North Wing, St. Thomass' Hospital, London SE1 7EH, UK*

Cervical cerclage has been used in the management of cervical insufficiency for several decades, yet the indications are uncertain and benefits marginal. It remains a controversial intervention. The diagnosis of cervical insufficiency is traditionally based on a history of recurrent second trimester miscarriages, or very preterm delivery whereby the cervix is unable to retain the pregnancy until term.

Cervical cerclage has been the subject of many observational and randomised controlled trials. This article reviews the literature regarding the effectiveness of elective or emergency transvaginal cerclage and transabdominal cerclage.

Key words: preterm birth; cervical cerclage; cervical suture; cervical insufficiency.

Preterm birth is defined as the birth of an infant prior to 37 completed weeks' gestation¹ and is the most common cause of neonatal morbidity and mortality. The incidence of preterm birth ranges from 5 to 12%², with the annual number of preterm births estimated to be 13 million worldwide. In developed countries there has been a tendency towards an increase in preterm birth. This may be due to a higher incidence of multiple pregnancies secondary to fertility treatments and iatrogenic deliveries (which constitute a third of all preterm deliveries) due to improved surveillance and earlier intervention in high risk pregnancies. More recent evidence suggests that spontaneous preterm deliveries may also be increasing.³ Despite major progress in perinatology and neonatology, few interventions have improved outcome.⁴ The

* Corresponding author. Tel.: +44 20 7188 3634; Fax: +44 20 7620 1227.
E-mail address: rach.simcox@kcl.ac.uk (R. Simcox).

consequence of preterm birth is often one of long-term physical, mental, social and financial burden. There is significant aetiological heterogeneity in preterm birth and maternal or fetal factors may be responsible. Pre-pregnancy predictors of preterm birth include historical factors such as previous second trimester miscarriage or preterm birth, demographic factors such as social class and ethnicity, or other risk factors such as smoking, alcohol and drug abuse. Maternal factors such as systemic or intra-uterine infection, uterine overdistension in the case of multifetal pregnancies, and Müllerian duct abnormalities can give rise to preterm birth. Placental insufficiency, and fetal growth restriction are also associated.

Much research has focussed on prediction of preterm birth and primary prevention, as the results with secondary prevention with tocolytic agents used to treat established preterm labour have been disappointing.⁵ Whatever the cause of the onset of parturition, the final common pathway is cervical shortening and dilatation; hence cervical cerclage may be helpful either as a preventative or therapeutic measure.

ROLE OF THE CERVIX AND INCIDENCE OF CERVICAL INSUFFICIENCY

The primary function of the cervix is to remain closed and retain the pregnancy until fetal maturation. It not only provides mechanical strength, but also acts as a barrier to ascending infection. Although preterm delivery is almost certainly multifactorial, the importance of cervical dysfunction is increasingly recognised.⁶ The multiple and potentially overlapping causes of preterm delivery, as well as the lack of a consistent definition, make the true incidence of cervical insufficiency (previously known as cervical incompetence) difficult to ascertain. It is said to occur in about 1% of the obstetric population⁷ and 8% of the population with recurrent mid trimester losses.⁸ Unfortunately there is no diagnostic test or proven criteria for cervical insufficiency. Diagnosis is usually made retrospectively based on a history of recurrent second trimester loss (or early preterm delivery) following painless cervical dilatation in the absence of contractions, bleeding or other causes of recurrent pregnancy loss.⁹ Other definitions include 'recurrent second trimester or early third trimester loss of pregnancy caused by the inability of the uterine cervix to retain a pregnancy until term'¹⁰ and 'a physical defect in the strength of the cervical tissue that is either congenital (inherited) or acquired'.¹¹ However, this is difficult to prove as successful pregnancies often occur even after multiple losses.

PATHOPHYSIOLOGY

Term labour results from the physiological activation of the components of the parturition pathway; uterine contractility, cervical dilatation and membrane activation. It is proposed that preterm labour results from pathological processes that activate one or more of these components.¹² The pathophysiology of cervical insufficiency is poorly understood. The normal function of the cervix depends on the regulation of the extracellular matrix, of which collagen is the major macromolecule (70% Type I, 30% Type III).¹³ Proteoglycans, in particular PG-S2/decorin, together with collagen fibrils are responsible for maintaining the tensile strength of the cervix. Decreases in collagen content and an increase in collagenolytic activity are associated with cervical ripening. There are also changes in the cellular component of the cervix with an influx of macrophages, neutrophils and mast cells, leading to cytokine and prostaglandin production. Nitric oxide synthase expression is upregulated. These changes in cervical ripening at

term are similar to an inflammatory response.¹⁴ However, the exact chain of events has not been fully elucidated.

A difficulty in obtaining biopsies from the human cervix before, during, and after term or preterm delivery further prevents research to improve our understanding.¹⁵ The limited data on cervical pathophysiology suggest there may be deranged biochemistry in the dysfunctional cervix. In one study, decreased collagen stability was demonstrated in the cervixes of non-pregnant women with a history of cervical insufficiency.¹⁶ Another found high collagenolytic activity in cervical biopsies taken from women in the second trimester who had a diagnosis of cervical insufficiency.¹⁷ In some women there may be a structural abnormality of the connective tissue of the cervix that is unable to sustain pregnancy, so some cases can be attributed to a 'mechanical' problem due to previous cervical surgery or congenital anomalies. However, the majority of women diagnosed with cervical insufficiency have normal anatomy, leading to the suggestion that there is a continuum of cervical integrity and it is not simply a categorical variable that is either fully functional (competent) or non-functional (incompetent).¹⁸

Cervical change can be the end result of many different processes of either maternal or fetal origin, and although the primary problem may not be the cervix, there is likely to be an association between ascending infection and a cervix that is effacing. This is the rationale for making the cervix the target of intervention.

TYPES OF CERVICAL CERCLAGE

Cervical cerclage was first proposed by Shirodkar in 1955¹⁹, but despite over half a century of use it still remains an obstetric dogma. The procedure involves making a circular incision in the cervix at the level of the internal os and dissecting the bladder free. A dilute solution of adrenaline is often used to open tissue planes and promote haemostasis. An encircling suture is placed in the region of the internal os and lower uterine segment, by passing antero-posteriorly then postero-anteriorly through the paracervical broad ligament. The knot is tied in front of the cervix in the midline, and the incisions closed with continuous 2/0 Vicryl. A modified Shirodkar technique can be used with the knot tied posteriorly and buried.

In 1957 McDonald simplified this technique.²⁰ His method does not require the bladder to be dissected free. A purse-string suture is placed around the cervix to approximate to the level of the internal os. There have been no randomised controlled trials comparing Shirodkar cerclage with McDonald cerclage, although some assume that the 'higher' the suture is placed the better, as this provides a longer functional cervix.²¹ Comparing the two by ultrasound cervical measurement does reveal a greater increase in cervical length associated with the Shirodkar suture.²² However, retrospective studies have not demonstrated a statistically significant difference in the rate of preterm birth or neonatal survival between the two methods.²²⁻²⁴ A wide non-absorbable suture, such as 5 mm Mersilene tape, or a monofilament suture is usually used, but there have been no randomised trials comparing the two. The wider tape may be more prone to infection, but less likely to 'tear' out. The type of suture material used varies depending on clinician preference.

ELECTIVE CERCLAGE

Although cerclage has been available for more than 50 years, only three randomised trials have been conducted to compare elective cerclage with expectant management

in women with an appropriate past obstetric history.^{25–27} Two further trials of elective cerclage that used different criteria are also described here.^{28,29}

Lazar et al recruited women at moderate risk based on a scoring system of risk factors.²⁵ A total of 506 women were randomised and 268 allocated to McDonald cerclage, and 238 to no cerclage. Although the groups were comparable in the number of previous preterm deliveries, women in the cerclage group had had significantly more second trimester losses. There was no significant difference in preterm delivery between the two groups, although those with cerclage were more likely to be admitted to hospital and receive tocolytics. In another study, Rush et al recruited 194 women with at least two previous preterm deliveries (or one or more prior to 34 weeks). Ninety-six patients were randomised to McDonald suture and 98 to expectant management.²⁷ There was no difference in outcome, with 34% delivering prior to 37 weeks in the cerclage group and 34% in the no cerclage group. In a third study, the Medical Research Council and Royal College of Obstetricians and Gynaecologists conducted an international multicentre trial which recruited 1292 women. The inclusion criteria was based on their obstetricians uncertainty as to whether to recommend cervical cerclage. Most women had a history of early delivery or cervical surgery.²⁶ Randomisation allocated 647 women to cerclage and 645 to no cerclage. Overall there were fewer deliveries prior to 33 weeks in the cerclage group compared with the controls (83/647 versus 110/645, $p = 0.03$). However, the reduced incidence of preterm delivery did not result in a benefit for the neonate and 25 women needed to be treated to prevent one preterm delivery. The trial has been criticised for only recruiting women with an uncertain diagnosis of cervical insufficiency and diluting the results by excluding those at highest risk. However, the overall preterm delivery rate was 28%, a rate that would be expected of a high risk population. In those women with three or more second trimester losses, a cervical suture halved the incidence of preterm delivery prior to 33 weeks, and it was concluded that it is to these women that cervical cerclage should be offered.

A fourth randomised trial, conducted in the Netherlands, recruited women based on a history suggestive of cervical insufficiency.²⁸ This trial differs from the above as women had transvaginal ultrasound assessment of cervical length. Twenty-three women were assigned to prophylactic cerclage and 44 to the observational group. In those in the observational group with ultrasound evidence of cervical shortening (<25 mm) a further random assignment of therapeutic cerclage and bed rest or bed rest alone was performed. No significant difference was found between the prophylactic cerclage group and the observational group in preterm delivery <34 weeks' gestation (3/23 vs 6/44, respectively). The results of the therapeutic cerclage are described below.

A fifth randomised study on elective cerclage recruited 50 twin pregnancies who had had ovulation induction.²⁹ No significant difference was observed between the two groups; 10 (45%) women in the suture group and 11 (48%) in the non-suture group delivered preterm.

ULTRASOUND MEASUREMENT OF CERVICAL LENGTH AND PRETERM DELIVERY

Historically cervical cerclage has been offered on a basis of suspected cervical insufficiency following previous second trimester miscarriage or preterm delivery. However, there is still a wide variation in the use of cerclage, which reflects the limited amount of evidence of efficacy. A diagnosis of cervical insufficiency is difficult to make, as

preterm labour is multifactorial in nature, and it is likely that most cervical sutures are inserted unnecessarily, i.e. they do not benefit outcome. Therefore, in order to identify those who may benefit from cerclage, transvaginal ultrasound of cervical length can be used as a predictor of preterm delivery.

Transvaginal measurement of cervical length is highly reproducible, with little inter- and intra-observer error.³⁰ A transvaginal probe is placed in the anterior fornix and a sagittal section of the cervix obtained, with the internal os, endocervical canal and external os in view. The scan is performed over 3–5 min and the shortest cervical length is recorded. Ultrasounds of a normal and a short cervix with funnelling are shown in Figure 1.

Measurement of cervical length is a sensitive predictor of preterm delivery in low^{31,32} and high risk pregnancies.^{33,34} For early preterm delivery a cervical length ≤ 15 mm has a positive predictive value of approximately 50%, and a negative predictive value of $>95\%$.³⁵ The risk of preterm delivery increases exponentially with decreasing length, from $<1\%$ at 30 mm to 80% at 5 mm.³¹

ULTRASOUND-INDICATED SUTURE

As ultrasound is an objective and reliable method of accurately measuring cervical length it can be used as a screening test to identify women at risk. A therapeutic cerclage can then be inserted based on the finding of a short cervix. However, the evidence regarding whether this reduces the risk of preterm delivery is conflicting, and there is no general consensus as to what constitutes a short cervix.

Four randomised controlled trials have compared ultrasound-indicated cerclage with conservative management.^{28,36–38} Rust et al randomised 113 patients with a short cervix (<25 mm) to receive either cerclage ($n = 55$) or expectant management ($n = 58$).³⁶ There was no significant difference in preterm delivery between the cerclage and expectant group (35% versus 36%). Berghella et al randomly assigned 61 women with a short cervix (<25 mm) to cerclage ($n = 31$) or no cerclage ($n = 30$).³⁷ The primary outcome was preterm delivery prior to 35 weeks. No difference was found in those who received a cerclage (14/31) compared with those who did not (14/30). To et al randomised 253 women with a cervical length of ≤ 15 mm to cerclage ($n = 127$) or expectant management ($n = 126$).³⁸ The majority of these women were low risk based on past obstetric history. The proportion of preterm

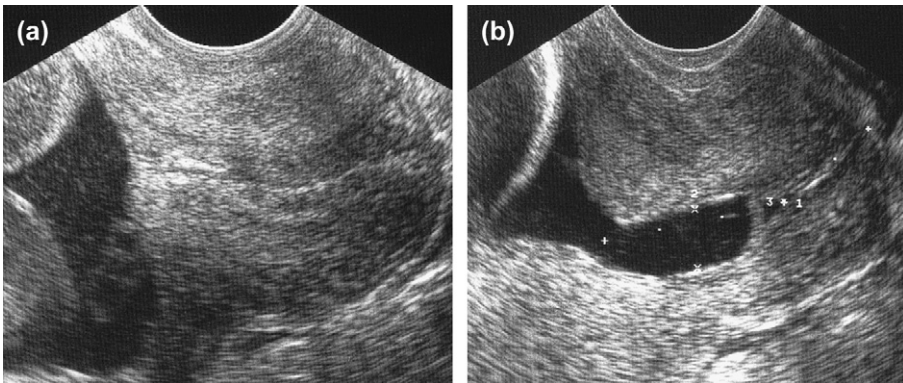


Figure 1. Ultrasound of (a) a normal cervix and (b) a short cervix with funnelling.

delivery prior to 33 weeks was similar in both groups: 28/127 in the cerclage group versus 33/126 in the control group ($p = 0.44$). The fourth randomised trial (CIPRACT) by Althusius et al recruited only women who were at high risk based on past obstetric history suggestive of cervical insufficiency.²⁸ As part of the larger study on cerclage described above, 35 women were found to have a cervix <25 mm determined by ultrasound. Of the 19 women who received a cerclage, none delivered before 34 weeks. This was significantly fewer than those on bed rest alone (7/16).

There are several aspects of the study designs that make interpretation of these trials difficult. Rust et al, Berghella et al and To et al selected both high and low risk women.^{36–38} Rust et al delayed cervical cerclage for 48–72 h in order to exclude infection by amniocentesis.³⁶ The influence of this delay on cervical ripening is unknown. There was also a greater incidence of placental abruption in this study, suggesting other causes of preterm labour. Rust et al and Berghella et al included twin pregnancies.^{36,37} However the pathophysiology of preterm labour in multifetal pregnancies and the cervical length at which to intervene may be different from singleton pregnancies. Also Rust et al and Berghella et al included women who had cervical funnelling, irrespective of cervical length. This ultrasound finding is more subjective than cervical length. Three of the studies chose to insert a suture if the cervical length was <25 mm, whilst one had a cut-off of 15 mm. The appropriate threshold for therapeutic cerclage is unknown. To et al used a cut-off of 15 mm as the risk of delivery increases exponentially below this.³⁸ However, it may be too late to intervene at this stage as a preoperative length of <15 mm is associated with visible fetal membranes at the time of suture insertion, and a poor outcome.³⁹

However, in singleton pregnancies of women who have had a previous preterm birth or second trimester loss, cerclage appears to be associated with a significant reduction in preterm birth²⁸ and a meta-analysis of this subgroup of patients from the above trials agrees with this conclusion despite the numbers being small (RR 0.61, 95% CI 0.40–0.92).⁴⁰ Further large randomised controlled trials on women at high risk of preterm birth are needed.

CERVICAL LENGTH FOLLOWING ELECTIVE CERCLAGE

Transvaginal assessment of cervical length can be useful after suture insertion in predicting preterm delivery. An increase in cervical length is often seen post cerclage⁴¹ with the best predictor of outcome being length of closed cervix above the suture. Funnelling of the membranes to the level of the suture is associated with earlier preterm delivery^{42,43} and a length of ≥ 10 mm above the suture is associated with the best prognosis.³⁹

In some instances, a short cervix occurs in women with a cerclage in situ, with membranes prolapsing through the cervical suture. Whether a second suture or a reinforcing cerclage should be offered is not known. One small retrospective study found that placement of a reinforcing cerclage was associated with earlier delivery compared to expectant management.⁴⁴ Furthermore it is not known whether a positive fetal fibronectin in the presence of a short cervix can help target those who may benefit from a reinforcing cerclage.

META-ANALYSES AND SYSTEMIC REVIEWS OF CERCLAGE

Several meta-analyses and systematic reviews on cervical cerclage have been published with differing conclusions.^{45–47} One found that cervical cerclage reduced deliveries

prior to 34 weeks (OR 0.77, 95% CI 0.59–0.99), with 20 cervical cerclages needed to prevent one case of preterm birth <34 weeks, but this did not translate into a reduction in perinatal mortality.⁴⁵ A second meta-analysis concluded that the effectiveness of prophylactic cerclage in preventing preterm delivery in women at low or medium risk for second trimester loss has not been proven.⁴⁶ Bachmann et al considered that pooling of studies in a meta-analysis was inappropriate due to considerable differences in quality, and so they opted to perform a systematic review. They suggested that cerclage had a significant effect in preventing preterm birth prior to 34 weeks, although the greatest weight was contributed by the MRC/RCOG study.⁴⁷

The results of any meta-analyses are limited due to the significant heterogeneity between studies. This is due to the use of different recruitment criteria, risk status and outcomes. Some include both elective and therapeutic cerclage as well as singleton and multiple pregnancies⁴⁵, so it is possible that benefit in a particular population is diluted.

Another systematic review and meta-analysis aimed to determine the effectiveness of cerclage in women with a sonographically measured short cervix.⁴⁸ Again, the characteristics of the studies differed and the populations were not uniform. Only two were randomised controlled trials, the remainder were prospective or retrospective observational studies. The effect of cerclage on delivery at <34 weeks was not significant (RR 0.95, CI 0.57–1.59). Subgroup analysis showed cerclage to be beneficial in some populations and detrimental in others, so results from the total population may be misleading. There was a significant reduction in preterm birth prior to 35 weeks in those women with a previous preterm birth or second trimester miscarriage (RR 0.61, 95% CI 0.40–0.92). This risk reduction (approximately 40%) is similar to that quoted for women with three or more previous preterm deliveries in the largest trial of cerclage (MRC/RCOG). It is possible that there is an important beneficial effect of cerclage in a minority of pregnant women at highest risk.

EMERGENCY CERCLAGE

Cervical effacement and dilatation is a painless phenomenon. Occasionally women present in the mid trimester with minor symptoms and on examination the fetal membranes are visible, protruding through the external os in an 'hour glass' shape. In these circumstances an emergency or 'rescue' cerclage can be done once other causes of second trimester miscarriage have been excluded. The patient is placed in the Trendelenburg position and the herniating forewaters gently reduced. Simple measures such as placing the patient in a head-down tilt, filling the bladder and applying gentle traction can help achieve membrane reduction. Often the membranes are reduced with the aid of an inflated Foley catheter.⁴⁹ Some have tried amnioreduction, although this has not been found to prolong pregnancy.⁵⁰

There have been no randomised studies evaluating emergency cerclage. One non-randomised prospective study which compared emergency cerclage with bed rest found women treated with cerclage had a significantly higher mean birth weight, but this did not translate into a difference in perinatal mortality, and the study was small.⁵¹ From the limited evidence available there are several factors associated with very preterm delivery in women treated with emergency cerclage: membranes prolapsing beyond the level of the external os, need for cerclage prior to 22 weeks' gestation and nulliparity.⁵² Subclinical infection of the fetal membranes or intrauterine space is implicated in up to 40% of cases of very preterm birth⁵³, but a much smaller proportion of

cases of chorioamnionitis are clinically obvious. For this reason, some studies have performed amniocentesis prior to cerclage to exclude infection and to try to identify biomarkers to predict outcome.⁵⁴

COMPLICATIONS

Despite being a relatively simple procedure cervical cerclage is not without risk and the potential hazards need to be weighed against the possible benefits. Reported adverse events shortly after suture insertion include abdominal pain, vaginal bleeding, bladder injury and premature pre-labour rupture of the membranes (pPROM). Rupture of the membranes is more likely during emergency cerclage when the cervix is effaced and dilated, and the fetal membranes are prolapsing into the vagina. The incidence of pPROM at the time of suture insertion in emergency cerclage is reported in 13–51% of cases.^{55–57} Late complications include subclinical or overt chorioamnionitis, possibly due to the presence of a foreign body precipitating infection. The definition of maternal infection varies between different studies as does the interval between suture insertion and infection. Infection following elective cerclage is reported in 1–8% of women^{9,57–60}, 16–33% of those with a ultrasound-indicated (therapeutic) cerclage^{11,36,57} and 9–37% of those with an emergency cerclage.^{51,57} In an effort to reduce this complication rate, some authors prescribe perioperative antibiotics, although any benefit has not been established.^{57,61} As mentioned above, in order to exclude chorioamnionitis prior to suture insertion, an amniocentesis^{36,57} can be done, although awaiting the culture results will delay the procedure as well as exposing the pregnancy to another intervention.

The cerclage procedure can be covered with tocolytics due to the increased uterine irritability caused by manipulating the cervix or the obstetrician's desire to avoid labour with a suture in place.⁶² Other complications include preterm delivery, uterine rupture or difficulty in cerclage removal (reported to be 1%).²⁶

TRANSABDOMINAL SUTURE

In those with a very poor past obstetric history, when conventional vaginal cerclage has not been successful or when extensive surgery has left very little cervical tissue, a transabdominal procedure can be attempted. Transabdominal cervical cerclage (TAC), first described in 1965, involves a laparotomy to insert a suture above the cardinal and uterosacral ligaments.⁶³ The procedure has also been done laparoscopically.⁶⁴ Theoretically, the higher placement of the suture may be better at preventing funnelling at the internal os and reduce the risk of pPROM. Most case series of TAC have reported excellent success rates (85–90%).⁶⁵ A systematic review comparing TAC with transvaginal cerclage in patients with a previous failed transvaginal cerclage found the likelihood of perinatal death or delivery prior to 24 weeks was 6% after TAC, compared with 12.5% after repeat transvaginal cerclage.⁶⁶ The morbidity associated with any open abdominal procedure needs to be considered, especially as a TAC usually requires two laparotomies — one for insertion and one for caesarean section. The possibility of other complications needs to be considered, such as intrauterine death in the second trimester requiring a hysterotomy if a dilatation and evacuation cannot be performed through the stitch. Intrauterine growth restriction from inadvertent ligation of the uterine arteries has also been reported.⁶⁵ Whether it is best to insert the suture pre-pregnancy or in the first trimester is not known.

SUMMARY

Although cervical cerclage is commonly used in clinical practice there is still limited evidence on its efficacy, and hence a wide variation in clinical application. Difficulties in defining and diagnosing cervical insufficiency and the multifactorial nature of preterm delivery make it difficult to be certain who will benefit from a suture. Those women with the highest risk of preterm delivery are most likely to benefit, and since there is usually only minor morbidity associated with suture insertion, it would seem prudent to offer cerclage. For those women with a less certain diagnosis the decision is more difficult. Ultrasound assessment of cervical length is useful in the prediction of preterm birth, and for those with a reassuringly long cervix an unnecessary procedure could be avoided. However, the evidence is still conflicting as to whether cerclage is beneficial once cervical shortening occurs and at what cervical length to intervene.

Practice points

- Historically cervical cerclage is offered on the basis of suspected cervical insufficiency. However this diagnosis is difficult to make and there is still wide variation in the use of cerclage, which reflects the limited amount of evidence of efficacy of the procedure.
- The largest trial of elective cerclage found that 25 women needed to be treated to prevent one preterm birth less than 33 weeks.
- Transvaginal ultrasound measurement of cervical length is a highly reproducible, sensitive predictor of preterm birth, although there is conflicting evidence as to whether inserting a suture into a cervix found to be short on ultrasound improves outcome.
- Emergency rescue cerclage and abdominal cerclage can be justified given the poor prognosis, although there is little evidence to support their efficacy.

Research agenda

- Further research into the physiology of cervical ripening at term will aid the understanding of pathological preterm birth.
- Large randomised trials are needed in women at high risk of preterm birth to determine whether cerclage is of benefit in those with a short cervix identified on ultrasound, and also to establish the optimum cervical length at which to intervene.
- The potential value of a reinforcing cerclage, when ultrasound demonstrates a short cervix in a woman with a cerclage in situ, needs to be further investigated.
- A large randomised trial is needed to determine whether, after a failed elective vaginal cerclage, a transabdominal cervico-isthmic suture is superior to a repeat vaginal approach in terms of both perinatal and maternal outcomes.

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