Published in final edited form as:

J Perinat Med. 2019 July 26; 47(5): 500–509. doi:10.1515/jpm-2018-0388.

Patients with acute cervical insufficiency without intra-amniotic infection/inflammation treated with cerclage have a good prognosis

Max Mönckeberg^{1,2}, Rafael Valdés³, Juan P. Kusanovic^{3,4,7}, Manuel Schepeler⁵, Jyh K. Nien⁵, Emiliano Pertossi⁴, Pablo Silva^{3,4}, Karla Silva³, Pía Venegas¹, Ulises Guajardo⁶, Roberto Romero^{7,8,9,10}, and Sebastián E. Illanes^{1,5}

¹Department of Obstetrics and Gynecology, Faculty of Medicine, Universidad de los Andes, Santiago, Chile

²Department of Public Health and Epidemiology, Faculty of Medicine, Universidad de los Andes, Santiago, Chile

³Center for Research and Innovation in Maternal-Fetal Medicine (CIMAF), Hospital Sótero del Río, Santiago, Chile

⁴Division of Obstetrics and Gynecology, School of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile

⁵Department of Obstetrics and Gynecology, Clínica Dávila, Santiago, Chile

⁶Faculty of Medicine, Universidad de los Andes, Santiago, Chile

⁷Perinatology Research Branch, NICHD/NIH/DHHS, Bethesda, MD and Detroit, MI, USA

⁸Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI, USA

⁹Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, MI, USA

¹⁰Center for Molecular Medicine and Genetics, Wayne State University, Detroit, MI, USA

Abstract

Background: The frequency of intra-amniotic infection/inflammation (IAI/I) in patients with midtrimester cervical insufficiency is up to 50%. Our purpose was to determine the perinatal outcomes of cervical cerclage in patients with acute cervical insufficiency with bulging membranes, and to compare the admission-to-delivery interval and pregnancy outcomes according to the results of amniotic fluid (AF) analysis and cerclage placement.

Methods: This was a retrospective cohort study including singleton pregnancies with cervical insufficiency between 15–26.9 weeks in two tertiary health centers. IAI/I was defined when at

Corresponding author: Max Mönckeberg, MD., Department of Obstetrics and Gynecology, Department of Public Health and Epidemiology, Faculty of Medicine, Universidad de los Andes, Santiago, Chile, San Carlos de Apoquindo 2200, Las Condes, Santiago, Phone: +56 (2) 226181381, mmonckebergz@uandes.cl.

Author contributions: All authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Disclosure: The authors report no conflicts of interest.

least one of the following criteria was present in AF: a) a WBC count >50 cells/mm³; b) glucose concentration <14 mg/dl; and/or c) a Gram stain positive for bacteria. Three different groups were compared: 1) absence of IAI/I with placement of cerclage; 2) amniocentesis not performed with placement of cerclage; and 3) IAI/I with or without cerclage.

Results: Seventy patients underwent an amniocentesis to rule-out IAI/I. The prevalence of IAI/I was 19%. Forty-seven patients underwent a cerclage. Patients with a cerclage had a longer median admission-to-delivery interval (33 days vs. 2 days; $p<0.001$) and delivered at a higher median gestational age (27.4 weeks vs. 22.6 weeks; $p=0.001$) than those without a cerclage. The neonatal survival rate in the cerclage group was 62% vs. 23% in those without cerclage ($p=0.01$). Patients without IAI/I that underwent a cerclage had a longer median admission-to-delivery interval [43 days vs. 1 day; $p<0.001$], delivered at a higher median gestational age (28 weeks vs. 22.1 weeks; $p=0.001$), and had a higher neonatal survival rate (67% vs. 8%; $p<0.001$) than those with IAI/I.

Conclusions: The pregnancy outcomes of patients with midtrimester cervical insufficiency and bulging membranes are poor since they have a high prevalence of IAI/I. Therefore, a pre-operative amniocentesis is key to identify the best candidates for the subsequent placement of a cerclage.

Keywords

amniotic fluid analysis; bulging membranes; cervical cerclage; cervical incompetence; cervical insufficiency; cervical stitch; intra-amniotic infection; intra-amniotic inflammation; MIAC; microbial invasion of the amniotic cavity

INTRODUCTION

Cervical insufficiency is defined as the inability of the uterine cervix to retain the fetus in the absence of uterine contractions in the second trimester [1–4]. This condition occurs in approximately 0.15%–1% of live births [5–7] during the second trimester of pregnancy, and it is associated with spontaneous abortion, extreme prematurity and adverse obstetrical and neonatal outcomes [7–9]. Cervical cerclage has been successfully used in the management of patients with a history of second trimester losses and progressive shortening of the cervix in the second trimester [10–32], although there is some evidence against its efficacy [33–39]. The most severe form of cervical insufficiency is the passive and painless dilatation of the uterine cervix leading to bulging membranes [40–42], and a solid body of evidence supports the benefit of placing a cerclage in those patients [43–53].

The presence of intra-amniotic infection/inflammation (IAI/I) is associated to adverse pregnancy outcomes in women with spontaneous preterm labor with intact membranes [54–60], preterm prelabor rupture of membranes (pPROM) [61–65] and cervical insufficiency. Indeed, between 13% and 51% of patients with cervical insufficiency and bulging membranes have a positive amniotic fluid culture and the presence of IAI/I has been consistently associated with poor prognosis [66–71]. It has been shown that 76% of patients with cervical insufficiency and microbial invasion of the amniotic cavity (MIAC) delivered within the first 48 hours of admission [67]. Moreover, Mays et al. [68] reported that patients without intra-amniotic infection managed with cervical cerclage delivered at a significantly higher gestational age and had better neonatal survival rates than those managed without

amniocentesis, or than patients with intra-amniotic infection but managed expectantly. Collectively, these results indicate that IAI/I strongly affect the pregnancy outcomes of patients with cervical insufficiency.

The objectives of this study were to determine the perinatal outcomes of cervical cerclage in patients with acute cervical insufficiency with bulging membranes in the second trimester, and to compare the admission-to-delivery interval and pregnancy outcomes according to the results of the amniotic fluid analysis and cervical cerclage placement.

MATERIALS AND METHODS

Study design and population. This is a retrospective cohort study including all singleton pregnancies between 15 and 26.9 weeks of gestation with the diagnosis of cervical insufficiency and bulging membranes that were admitted at the Hospital Sótero del Río and Clínica Dávila in Santiago, Chile, between January 2009 and May 2017. Exclusion criteria were: 1) patients with the diagnosis of cervical insufficiency due to an asymptomatic short cervix (<25 mm); 2) cases with cervical insufficiency that presented with cervical dilatation at digital examination, but without bulging membranes at speculum examination; 3) patients with the diagnosis of clinical chorioamnionitis at admission; 4) cases for whom there were incomplete or absent records of the results of amniotic fluid analysis (if an amniocentesis was performed) or pregnancy outcomes; 5) twin gestations; and 6) fetal congenital anomalies.

We retrospectively reviewed all the medical records with the diagnosis of “cervical insufficiency” or “cervical incompetence” at admission and/or discharge, all surgical procedures that included the terms “cervical cerclage” or “cervical stitch”, and all the laboratory records of non-genetic amniocenteses performed during the study period. Demographic and clinical characteristics of patients were recorded, as well as data from previous pregnancies, the results of maternal blood laboratory tests, as well as those of amniotic fluid analysis. Information regarding the inpatient management, pregnancy and neonatal outcomes were also collected. All data obtained from medical records were recorded on a pre-specified database. The use of demographic, clinical, laboratory and sonographic data collected from chart review was approved by the Institutional Review Boards of Hospital Sótero del Río and Clínica Dávila.

The standard management of patients with cervical insufficiency with bulging membranes in the second trimester consists of a pre-operative amniocentesis to exclude IAI/I before the placement of a cervical cerclage. Yet, the final decision of performing an amniocentesis and placing a cerclage was at the discretion of the physician. Women with the diagnosis of IAI/I are usually not considered candidates for cervical cerclage, and they have expectant management under broad spectrum antibiotic coverage including Ceftriaxone and Metronidazole, or Ceftriaxone and Clindamycin, with or without the addition of a macrolide. In patients with IAI/I, induction of labor is not routinely performed, except in cases in which maternal health is considered at risk.

Based on that, patients were classified into the following groups: 1) Group 1: absence of IAI/I and managed with cervical cerclage; 2) Group 2: amniocentesis not performed and managed with cervical cerclage; and 3) Group 3: presence of IAI/I, with or without cervical cerclage.

Definitions.

Spontaneous preterm delivery was defined by the presence of regular uterine contractions occurring at a frequency of at least two every 10 minutes associated with cervical changes before 37 completed weeks, leading to preterm delivery. Preterm PROM was diagnosed by sterile speculum examination confirming pooling of amniotic fluid in the vagina in association with ferning tests when necessary, before 37 weeks of gestation and in the absence of labor. Clinical chorioamnionitis was diagnosed according to the criteria proposed by Gibbs et al. [72] including maternal temperature of $\geq 37.8^{\circ}\text{C}$ and two or more of the following criteria: uterine tenderness, malodorous vaginal discharge, maternal leukocytosis (> 15000 cells/mm³), maternal tachycardia (>100 beats/min) and fetal tachycardia (>160 beats/min). IAI/I was defined when at least one of the following three criteria was present in amniotic fluid [73–75]: a) a white blood cell (WBC) count >50 cells/mm³; b) glucose concentration <14 mg/dl; and/or c) a Gram stain positive for bacteria.

Sample collection.

Amniotic fluid was obtained by transabdominal amniocentesis under ultrasonographic guidance. Samples of amniotic fluid were transported to the laboratory in a sterile capped syringe. Amniotic fluid WBC count, glucose concentration and Gram stain were also performed shortly after collection in all patients as previously described [73, 74]. The results of these tests were used for clinical management. Amniotic fluid cultures for aerobic, anaerobic and genital Mycoplasmas were performed at the discretion of the physician.

Statistical analyses.

Normality of distribution in numerical variables was tested using Shapiro-Wilk test. In variables fitting normal distribution, comparisons between or among groups were made by t-test or one-way analysis of variance (ANOVA), as appropriate. In numerical variables not fitting a normal distribution, comparisons were made using Mann-Whitney U-test or Kruskal-Wallis test. Comparisons between or among proportions were performed with Chi-square or Fisher's exact tests as appropriate. The statistical package used was STATA v.14.2. (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP). A two-tailed, p-value <0.05 was considered statistically significant.

RESULTS

Demographic and clinical characteristics of the study population.

Figure 1 shows disposition of patients who are part of the study. Initially, 105 cases of cervical insufficiency were identified. We excluded: a) 15 cases of cervical insufficiency in which there was cervical dilatation, but without bulging membranes at speculum evaluation; b) seven cases of twin pregnancies; c) two cases presenting <15 weeks; d) two cases

presenting >266/7 weeks; e) one patient was lost to follow-up; and f) one case for whom the results of amniotic fluid analyses were not available.

A total of 77 patients were included in the study. The demographic and clinical data, according to the results of amniotic fluid analyses, are reported in Table 1. The mean gestational age at admission was 21.8 ± 2.5 weeks. Forty-seven (61%) patients were nulliparous, 17% (13/77) had a history of previous spontaneous preterm birth and 14% of patients (11/77) had a history of second trimester pregnancy loss. Two cases (3%) had a history of cervical cerclage due to cervical insufficiency in previous pregnancies, and 13% (10/77) were under vaginal progesterone treatment because of a short cervix.

At admission, 91% (70/77) of patients underwent an amniocentesis to exclude IAI/I. According to the results of the amniotic fluid analyses, 19% (13/70) of them had IAI/I. Patients with IAI/I had a significantly greater cervical dilatation (mean: 4.3 ± 2.2 cm vs. 2.9 ± 2.0 cm, $p=0.015$), higher maternal WBC count (mean: 15.1 ± 3.5 cells $\times 10^3/\text{mm}^3$ vs. 11.6 ± 2.5 cells $\times 10^3/\text{mm}^3$, $p=0.002$), and higher maternal serum concentrations of C reactive protein (mean: 19.7 ± 23.8 mg/L vs. 4.4 ± 5.5 mg/L, $p=0.025$) than patients without IAI/I. No adverse events were observed due to the performance of the amniocenteses.

During the initial evaluation, 34% (26/77) of patients were not considered candidates for a cervical cerclage and underwent expectant management. The main contraindications for cervical cerclage were: a) presence of IAI/I (11 cases), b) onset of spontaneous preterm labor within 48 hours after admission (nine cases), c) pPROM within 48 hours of admission (two cases), d) gestational age higher than 256/7 weeks (two cases), e) current pregnancy with an intrauterine device (one case), and f) suspected clinical chorioamnionitis occurring within 48 hours of admission (one case).

On the other hand, 66% (51/77) of patients were considered candidates for cervical cerclage and underwent this procedure. In 8% (4/51) of cases, rupture of the membranes occurred during the cerclage. In these cases, the procedure was stopped, and patients were managed with antibiotic treatment. The remaining 47 patients received a cervical cerclage.

Patients managed with a cervical cerclage had a significantly longer admission-to-delivery interval [median admission-to-delivery interval: 33 days, interquartile range (IQR): 12–89 vs. 2 days, IQR: 1–20, $p<0.001$] and delivered at a significantly higher gestational age (median gestational age at delivery: 27.4 weeks, IQR: 23.4–35.9 vs. 22.6 weeks, IQR: 21.4–25.6, $p=0.001$) than those who did not have a cerclage. The neonatal survival rate in the cerclage group was 62% (29/47), compared to 23% (7/30) in those without cerclage ($p=0.01$).

Perinatal outcomes according to amniotic fluid analysis and cervical cerclage.

Table 2 displays the perinatal outcomes according to the status of the amniotic fluid and cerclage placement. Patients without IAI/I that underwent a cervical cerclage had good pregnancy outcomes. The median admission-to-delivery interval was 43 days (IQR: 15–89 days), and the median gestational age at delivery was 28 weeks (IQR: 23.7–36.3 weeks). In

this group, the neonatal survival rate was 67% (26/39). There were no significant differences regarding pregnancy outcomes between groups 1 and 2.

In contrast, patients with IAI/I (group 3) had a poor pregnancy outcome. Their median admission-to-delivery interval was 1 day (IQR: 1–10 days), and the median gestational age at delivery was 22.1 weeks (IQR: 20.7–23.4 weeks). This was significantly shorter compared to groups 1 and 2. Moreover, the proportion of patients delivering within the first 48 hours and 7 days after admission was significantly higher in group 3 compared with groups 1 and 2. Indeed, 69% of patients presenting with cervical insufficiency with bulging membranes and IAI/I delivered within the first 48 hours of admission, and the neonatal survival rate was only 8% (1/13).

There were two patients in group 3 for whom a cervical cerclage was inserted. In both cases, the amniocentesis was performed at the discretion of their physicians at the time of cerclage placement. Unfortunately, the amniotic fluid analyses were consistent with IAI/I. In both patients the cervical cerclage was not removed and underwent expectant management with broad spectrum antibiotics. The first case delivered at 23.3 weeks of gestation (11 days after admission), and the second case delivered at 23.4 weeks (one day after admission). Both neonates died shortly after delivery. The remaining 11 cases of this group were managed expectantly with broad spectrum antibiotics and without a cervical cerclage. Their median admission-to-delivery interval was 1 day (IQR: 1–10 days), and the median gestational age at delivery was 22 weeks (IQR: 20.4–23.9 weeks). Only one neonate survived; this case was admitted at 25.6 weeks of gestation and delivered at 28.6 weeks (23 days after admission).

DISCUSSION

Principal findings of the study:

1) 60% of patients with cervical insufficiency and bulging membranes in the second trimester were nulliparous; 2) patients with cerclage had a significantly longer admission-to-delivery interval, as well as significantly higher gestational age at delivery and neonatal survival rate than those who did not have a cerclage; 3) patients with cervical insufficiency and bulging membranes without IAI/I, that underwent a cervical cerclage, had a median admission-to-delivery interval of 43 days, a median gestational age at delivery of 28 weeks, and a neonatal survival rate of 67%; 4) in contrast, patients with cervical insufficiency and bulging membranes with IAI/I had a median admission-to-delivery interval of 1 day, a median gestational age at delivery of 22 weeks, and a neonatal survival rate of 8%; 5) no maternal and fetal adverse events were reported during the performance of the transabdominal amniocenteses; and 6) 8% of patients ruptured the membranes during cerclage.

The role of emergency cerclage in cervical insufficiency.

Previous studies have evaluated the effect of cervical cerclage on pregnancy outcomes in women with cervical insufficiency and bulging membranes [43–53, 76–80], reporting the benefits of this intervention. Evidence from a small randomized clinical trial [46] demonstrated that, in women with cervical insufficiency and bulging membranes, placement

of a cervical cerclage was associated with a significant longer admission-to-delivery interval, higher gestational age at delivery, and lower incidence of preterm birth <34 weeks compared to patients assigned to expectant management. In addition, Ehsanipoor et al. [53] reported a systematic review and meta-analysis including 10 studies [43–52] assessing the effects of cerclage in cases of cervical insufficiency and bulging membranes in the second trimester, showing that an emergency cervical cerclage significantly reduced the risk of preterm delivery <34 weeks, and significantly increased the interval from admission-to-delivery, gestational age at delivery, and overall neonatal survival compared to expectant management. In agreement with those reports, we observed herein that placement of a cervical cerclage was associated with a 31-day increase in the median admission-to-delivery interval compared with expectant management, and with a significant increase in the gestational age at delivery and neonatal survival rates.

Similarly, cervical cerclage has demonstrated benefits in prolongation of gestation when used in populations at high risk of preterm birth [81–83]. A systematic review and meta-analysis of randomized trials reported by Berghella et al. [84], including five trials [85–89] evaluated the effects of cervical cerclage versus no cerclage in patients with a history of preterm birth and a sonographic short cervix (<25 mm) <24 weeks of gestation. Placement of a cervical cerclage was associated with a significant reduction in the risk of preterm birth and perinatal morbidity and mortality.

Cervical insufficiency and intra-amniotic infection/inflammation.

In this study, 91% of patients with cervical insufficiency and bulging membranes in the second trimester underwent an amniocentesis to rule-out IAI/I before placement of cervical cerclage, and 34% of patients were not considered candidates for a cervical cerclage mainly due to the presence of signs of IAI/I or onset of labor shortly after admission. The role of IAI/I and its effects over the outcome of pregnancies in women with cervical insufficiency with bulging membranes is well established in the literature [67–71, 90, 91]. The incidence of subclinical intra-amniotic infection demonstrated by amniotic fluid cultures has been reported as high as 51% [67, 69]. In the present study, the prevalence of IAI/I (based on amniotic fluid Gram stain, WBC count and glucose concentration) was 19%. In a similar population, Mays et al. [68], using amniotic fluid lactate dehydrogenase and glucose concentrations, reported 38% (7/18) of amniocentesis suggesting IAI/A. Also, Diago-Almela et al. [92], using a combination of amniotic fluid level of interleukin-6, glucose, WBC count, and leucocyte esterase test reported an incidence of IAI/I of 64% (20/31). The mean gestational age at delivery in patients without IAI/I was 35.1 weeks, and the reported neonatal survival was 100%. The prevalence of IAI/I in our study was lower compared to what has been previously reported, probably due to the lower diagnostic performance of the amniotic fluid markers used for detecting cases of IAI/I. In our study, patients with IAI/I had a median admission-to-delivery interval of only one day (IQR: 1–10). Moreover, 69% of these cases had labor and delivered within 48 hours from admission. These results are consistent with previous studies. Other reports [67, 70] suggest that in patients with cervical insufficiency, bulging membranes and an amniocentesis suggesting IAI/I, the rates of delivery within 48 hours from admission were between 50% and 76%. In addition, Mays et

al. [68] reported that the mean admission-to-delivery interval in patients with IAI/I was 3.8 ± 4.6 days, which is similar to what was found in our study.

On the other hand, performing a cervical cerclage in patients without IAI/I increases the possibilities of achieving a favorable pregnancy outcome. Mays et al. [68] reported a mean gestational age of delivery of 35.2 ± 4.2 weeks in this subgroup of patients, with a mean admission-to-delivery interval of 93.4 ± 33.1 days. Similarly, Diago-Almela et al. [92] reported a mean gestational age at delivery of 35.4 weeks, with a mean admission-to-delivery interval of 89 days. These latency periods are higher than that observed in our study. This may be explained due to differences in diagnostic criteria used for establishing the diagnosis of IAI/I, and differences in the magnitude of cervical dilatation at admission (2.5 ± 0.8 cm in Mays et al. and 2.9 ± 1.9 cm in our study). In previous reports, advanced cervical dilatation with protrusion of membranes through external os has been systematically associated with adverse pregnancy outcomes [91, 93–104]. In this study, advanced cervical dilatation with bulging membranes was not considered an exclusion criterion for cervical cerclage placement.

Altogether, these findings suggest that a significant proportion of patients with cervical insufficiency are affected by IAI/I, and that delivery will occur soon after admission since the optimal management of patients with intra-amniotic infection/inflammation has not been determined. Performing a cervical cerclage in patients with IAI/I may be harmful for the mother and fetus, and also ineffective in increasing the admission-to-delivery interval.

Strength and limitations:

To our knowledge, this is the largest study reporting patients that underwent an amniocentesis before cerclage placement. The fact that patients with cervical insufficiency and bulging membranes without IAI/I, that underwent a cervical cerclage, had a neonatal survival rate of 67% is a major finding. This study has some limitations. First, its retrospective design makes it especially susceptible to selection bias, since the final decision of performing or not a preoperative amniocentesis, and subsequently a cervical cerclage, depended only on the clinical criteria of the attending physician. Second, given the sample size, it is difficult to establish with certainty whether the poor pregnancy outcome observed in patients with IAI/I is a consequence of the latter, or due to the lack of placement of cervical cerclage. Also, given the small number of patients in the group that underwent an emergency cerclage without amniocentesis, it is difficult to establish proper comparisons among groups.

CONCLUSIONS

Patients with midtrimester cervical insufficiency and bulging fetal membranes have adverse pregnancy outcomes, and placement of a cervical cerclage is an effective therapy for those cases. However, a significant number of patients with cervical insufficiency and bulging fetal membranes have IAI/I, and its presence is associated with poor prognosis. Therefore, in patients with demonstrated IAI/I, considering the potential maternal and fetal risks of placing a cervical cerclage and the lack of evidence of its benefits, we propose that this surgical procedure should not be recommended. In contrast, absence of IAI/I is associated to

a better pregnancy outcome, and placement of a cervical cerclage should be strongly recommended in these cases. Preoperative amniocentesis is crucial to exclude IAI/I and plays a major role to select patients who are best candidates for an emergency cervical cerclage.

Acknowledgments

Funding: This research was supported, in part, by the Perinatology Research Branch, Division of Obstetrics and Maternal-Fetal Medicine, Division of Intramural Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, U.S. Department of Health and Human Services (NICHD/NIH/DHHS); and, in part, with Federal funds from NICHD/NIH/DHHS under Contract No. HHSN275201300006C.

REFERENCES

- Owen J, Iams JD, Hauth JC. Vaginal sonography and cervical incompetence. *Am J Obstet Gynecol* 2003;188(2):586–96. [PubMed: 12592276]
- Romero R, Espinoza J, Erez O, Hassan S. The role of cervical cerclage in obstetric practice: can the patient who could benefit from this procedure be identified? *Am J Obstet Gynecol* 2006;194(1):1–9. [PubMed: 16389003]
- ACOG Practice Bulletin No.142: Cerclage for the management of cervical insufficiency. *Obstet Gynecol* 2014;123(2 Pt 1):372–9. [PubMed: 24451674]
- Roman A, Suhag A, Berghella V. Cerclage: Indications and Patient Counseling. *Clin Obstet Gynecol* 2016;59(2):264–9. [PubMed: 27015230]
- Lidegaard O Cervical incompetence and cerclage in Denmark 1980–1990. A register based epidemiological survey. *Acta Obstet Gynecol Scand* 1994;73(1):35–8. [PubMed: 8304022]
- Shennan A, Jones B. The cervix and prematurity: aetiology, prediction and prevention. *Semin Fetal Neonatal Med.* 2004;9(6):471–9. [PubMed: 15691785]
- Anum EA, Brown HL, Strauss JF 3rd. Health disparities in risk for cervical insufficiency. *Hum Reprod* 2010;25(11):2894–900. [PubMed: 20643692]
- McElrath TF, Hecht JL, Dammann O, Boggess K, Onderdonk A, Markenson G, et al. Pregnancy disorders that lead to delivery before the 28th week of gestation: an epidemiologic approach to classification. *Am J Epidemiol* 2008;168(9):980–9. [PubMed: 18756014]
- Robertson JE, Lisonkova S, Lee T, De Silva DA, von Dadelszen P, Synnes AR, et al. Fetal, Infant and Maternal Outcomes among Women with Prolapsed Membranes Admitted before 29 Weeks Gestation. *PLoS One.* 2016;11(12):e0168285. [PubMed: 28002467]
- Barth WH Jr., Yeomans ER, Hankins GD. Emergent cerclage. *Surg Gynecol Obstet* 1990;170(4):323–6. [PubMed: 2321124]
- Final report of the Medical Research Council/Royal College of Obstetricians and Gynaecologists multicentre randomised trial of cervical cerclage. MRC/RCOG Working Party on Cervical Cerclage. *Br J Obstet Gynaecol* 1993;100(6):516–23. [PubMed: 8334085]
- Guzman ER, Forster JK, Vintzileos AM, Ananth CV, Walters C, Gipson K. Pregnancy outcomes in women treated with elective versus ultrasound-indicated cervical cerclage. *Ultrasound Obstet Gynecol* 1998;12(5):323–7. [PubMed: 9819870]
- Althuisius SM, Dekker GA, van Geijn HP, Hummel P. The effect of therapeutic McDonald cerclage on cervical length as assessed by transvaginal ultrasonography. *Am J Obstet Gynecol* 1999;180(2 Pt 1):366–9. [PubMed: 9988802]
- Matijevic R, Olujic B, Tumbri J, Kurjak A. Cervical incompetence: the use of selective and emergency cerclage. *J Perinat Med* 2001;29(1):31–5. [PubMed: 11234614]
- Berghella V, Haas S, Chervoneva I, Hyslop T. Patients with prior second-trimester loss: prophylactic cerclage or serial transvaginal sonograms? *Am J Obstet Gynecol* 2002;187:747–51. [PubMed: 12237658]

16. Cockwell HA, Smith GN. Cervical incompetence and the role of emergency cerclage. *J Obstet Gynaecol Can.* 2005;27(2):123–9. [PubMed: 15937588]
17. Poggi SH, Vyas N, Pezzullo JC, Landy HJ, Ghidini A. Therapeutic cerclage may be more efficacious in women who develop cervical insufficiency after a term delivery. *Am J Obstet Gynecol* 2009;200(1):68.e1–3. [PubMed: 19019324]
18. Scheib S, Visintine JF, Miroshnichenko G, Harvey C, Rychlak K, Berghella V. Is cerclage height associated with the incidence of preterm birth in women with an ultrasound-indicated cerclage? *Am J Obstet Gynecol* 2009;200(5):e12–e15.
19. Berghella V, Keeler SM, To MS, Althuisius SM, Rust OA. Effectiveness of cerclage according to severity of cervical length shortening: a meta-analysis. *Ultrasound Obstet Gynecol* 2010;35(4):468–73. [PubMed: 20052661]
20. Berghella V, Mackeen AD. Cervical length screening with ultrasound-indicated cerclage compared with history-indicated cerclage for prevention of preterm birth: a meta-analysis. *Obstet Gynecol* 2011;118(1):148–55. [PubMed: 21691173]
21. Celen S, Simsek Y, Ozyer S, Sucak A, Kaymak O, Turkcpar F, et al. Effectiveness of emergency cervical cerclage in patients with cervical dilation in the second trimester. *Clin Exp Obstet Gynecol* 2011;38(2):131–3. [PubMed: 21793272]
22. Abo-Yaqoub S, Mohammed AB, Saleh H. The effect of second trimester emergency cervical cerclage on perinatal outcome. *J Matern Fetal Neonatal Med* 2012;25(9):1746–9. [PubMed: 22372642]
23. Alfirevic Z, Stampalija T, Roberts D, Jorgensen AL. Cervical stitch (cerclage) for preventing preterm birth in singleton pregnancy. *Cochrane Database Syst Rev* 2012(4):Cd008991. [PubMed: 22513970]
24. Conde-Agudelo A, Romero R, Nicolaides K, Chaiworapongsa T, O'Brien JM, Cetingoz E, et al. Vaginal progesterone vs. cervical cerclage for the prevention of preterm birth in women with a sonographic short cervix, previous preterm birth, and singleton gestation: a systematic review and indirect comparison metaanalysis. *Am J Obstet Gynecol* 2013;208(1):42.e1–e18. [PubMed: 23157855]
25. Skupski DW, Lin SN, Reiss J, Eglinton GS. Extremely short cervix in the second trimester: bed rest or modified Shirodkar cerclage? *J Perinat Med* 2014;42(1):55–9. [PubMed: 23924522]
26. Gimovsky AC, Suhag A, Roman A, Rochelson BL, Berghella V. Pessary versus cerclage versus expectant management for cervical dilation with visible membranes in the second trimester. *J Matern Fetal Neonatal Med* 2016;29(9):1363–6. [PubMed: 26067268]
27. Ozgur Akkurt M, Yavuz A, Sezik M, Okan Ozkaya M. Infant outcomes following midtrimester emergency cerclage in the presence of fully dilated cervix and prolapsing amniotic membranes into the vagina. *J Matern Fetal Neonatal Med* 2016;29(15):2438–42. [PubMed: 26414335]
28. Rius M, Cobo T, Garcia-Posadas R, Hernandez S, Teixido I, Barrau E, et al. Emergency Cerclage: Improvement of Outcomes by Standardization of Management. *Fetal Diagn Ther* 2016;39(2):134–9. [PubMed: 26202176]
29. Szychowski JM, Owen J, Hankins G, Iams JD, Sheffield JS, Perez-Delboy A, et al. Can the optimal cervical length for placing ultrasound-indicated cerclage be identified? *Ultrasound Obstet Gynecol* 2016;48(1):43–7. [PubMed: 26277877]
30. Alfirevic Z, Stampalija T, Medley N. Cervical stitch (cerclage) for preventing preterm birth in singleton pregnancy. *Cochrane Database Syst Rev* 2017;6:Cd008991. [PubMed: 28586127]
31. Bayrak M, Gul A, Goynumer G. Rescue cerclage when foetal membranes prolapse into the vagina. *J Obstet Gynaecol* 2017;37(4):471–5. [PubMed: 28141950]
32. Shivani D, Quek BH, Tan PL, Shephali T. Does rescue cerclage work? *J Perinat Med* 2018;46(8):876–80. [PubMed: 29936490]
33. Berghella V, Daly SF, Tolosa JE, DiVito MM, Chalmers R, Garg N, et al. Prediction of preterm delivery with transvaginal ultrasonography of the cervix in patients with high-risk pregnancies: does cerclage prevent prematurity? *Am J Obstet Gynecol* 1999;181(4):809–15. [PubMed: 10521734]

34. Rust OA, Atlas RO, Jones KJ, Benham BN, Balducci J. A randomized trial of cerclage versus no cerclage among patients with ultrasonographically detected second-trimester preterm dilatation of the internal os. *Am J Obstet Gynecol* 2000;183(4):830–5. [PubMed: 11035321]
35. Baxter JK, Airolidi J, Berghella V. Short cervical length after history-indicated cerclage: is a reinforcing cerclage beneficial? *Am J Obstet Gynecol* 2005;193(3 Pt 2):1204–7. [PubMed: 16157138]
36. Pelham JJ, Lewis D, Berghella V. Prior cerclage: to repeat or not to repeat? That is the question. *Am J Perinatol* 2008;25(7):417–20. [PubMed: 18546079]
37. Nelson L, Dola T, Tran T, Carter M, Luu H, Dola C. Pregnancy outcomes following placement of elective, urgent and emergent cerclage. *J Matern Fetal Neonatal Med* 2009;22(3):269–73. [PubMed: 19330713]
38. Wing DA, Szychowski J, Owen J, Hankins G, Iams JD, Sheffield JS, et al. Gestational age at previous preterm birth does not affect cerclage efficacy. *Am J Obstet Gynecol* 2010;203(4):377.e1–4. [PubMed: 20579957]
39. Kuon RJ, Hudalla H, Seitz C, Hertler S, Gawlik S, Fluhr H, et al. Impaired Neonatal Outcome after Emergency Cerclage Adds Controversy to Prolongation of Pregnancy. *PLoS One*. 2015;10(6):e0129104. [PubMed: 26121653]
40. Harger JH. Cerclage and cervical insufficiency: an evidence-based analysis. *Obstet Gynecol* 2002;100(6):1313–27. [PubMed: 12468179]
41. Makino Y, Makino I, Tsujioka H, Kawarabayashi T. Amnioreduction in patients with bulging prolapsed membranes out of the cervix and vaginal orifice in cervical cerclage. *J Perinat Med* 2004;32(2):140–8. [PubMed: 15085890]
42. Roman A, Suhag A, Berghella V. Overview of Cervical Insufficiency: Diagnosis, Etiologies, and Risk Factors. *Clin Obstet Gynecol* 2016;59(2):237–40. [PubMed: 27015229]
43. Olatunbosun OA, al-Nuaim L, Turnell RW. Emergency cerclage compared with bed rest for advanced cervical dilatation in pregnancy. *Int Surg* 1995;80(2):170–4. [PubMed: 8530237]
44. Morin L, Klam S, Hamilton EF. Emergency cerclage for prevention of second trimester loss. *Am J Obstet Gynecol* 1997;176(1 Pt 2):S147.
45. Novy MJ, Gupta A, Wothe DD, Gupta S, Kennedy KA, Gravett MG. Cervical cerclage in the second trimester of pregnancy: a historical cohort study. *Am J Obstet Gynecol* 2001;184(7):1447–54; discussion 54–6. [PubMed: 11408867]
46. Althuisius SM, Dekker GA, Hummel P, van Geijn HP. Cervical incompetence prevention randomized cerclage trial: emergency cerclage with bed rest versus bed rest alone. *Am J Obstet Gynecol* 2003;189(4):907–10. [PubMed: 14586323]
47. Daskalakis G, Papantoniou N, Mesogitis S, Antsaklis A. Management of cervical insufficiency and bulging fetal membranes. *Obstet Gynecol* 2006;107(2 Pt 1):221–6. [PubMed: 16449104]
48. Pereira L, Cotter A, Gomez R, Berghella V, Prasertcharoensuk W, Rasanen J, et al. Expectant management compared with physical examination-indicated cerclage (EM-PEC) in selected women with a dilated cervix at 14(0/7)–25(6/7) weeks: results from the EM-PEC international cohort study. *Am J Obstet Gynecol* 2007;197(5):483.e1–8. [PubMed: 17980182]
49. Stupin JH, David M, Siedentopf JP, Dudenhausen JW. Emergency cerclage versus bed rest for amniotic sac prolapse before 27 gestational weeks. A retrospective, comparative study of 161 women. *Eur J Obstet Gynecol Reprod Biol* 2008;139(1):32–7. [PubMed: 18243484]
50. Ventolini G, Genrich TJ, Roth J, Neiger R. Pregnancy outcome after placement of ‘rescue’ Shirodkar cerclage. *J Perinatol* 2009;29(4):276–9. [PubMed: 19158805]
51. Curti A, Simonazzi G, Farina A, Mehmeti H, Facchinetti F, Rizzo N. Exam-indicated cerclage in patients with fetal membranes at or beyond external os: a retrospective evaluation. *J Obstet Gynaecol Res* 2012;38(12):1352–7. [PubMed: 22640560]
52. Aoki S, Ohnuma E, Kurasawa K, Okuda M, Takahashi T, Hirahara F. Emergency cerclage versus expectant management for prolapsed fetal membranes: a retrospective, comparative study. *J Obstet Gynaecol Res* 2014;40(2):381–6. [PubMed: 24147884]
53. Ehsanipoor RM, Seligman NS, Saccone G, Szymanski LM, Wissinger C, Werner EF, et al. Physical Examination-Indicated Cerclage: A Systematic Review and Meta-analysis. *Obstet Gynecol* 2015;126(1):125–35. [PubMed: 26241265]

54. Gomez R, Ghezzi F, Romero R, Munoz H, Tolosa JE, Rojas I. Premature labor and intra-amniotic infection. Clinical aspects and role of the cytokines in diagnosis and pathophysiology. *Clin Perinatol* 1995;22(2):281–342. [PubMed: 7671540]
55. Maymon E, Romero R, Chaiworapongsa T, Berman S, Conoscenti G, Gomez R, et al. Amniotic fluid matrix metalloproteinase-8 in preterm labor with intact membranes. *Am J Obstet Gynecol* 2001;185(5):1149–55. [PubMed: 11717649]
56. Yoon BH, Romero R, Moon JB, Shim SS, Kim M, Kim G, et al. Clinical significance of intra-amniotic inflammation in patients with preterm labor and intact membranes. *Am J Obstet Gynecol* 2001;185(5):1130–6. [PubMed: 11717646]
57. Friel LA, Romero R, Edwin S, Nien JK, Gomez R, Chaiworapongsa T, et al. The calcium binding protein, S100B, is increased in the amniotic fluid of women with intra-amniotic infection/inflammation and preterm labor with intact or ruptured membranes. *J Perinat Med* 2007;35(5):385–93. [PubMed: 17624933]
58. DiGiulio DB, Romero R, Amogan HP, Kusanovic JP, Bik EM, Gotsch F, et al. Microbial prevalence, diversity and abundance in amniotic fluid during preterm labor: a molecular and culture-based investigation. *PLoS One*. 2008;3(8):e3056. [PubMed: 18725970]
59. Lee J, Oh KJ, Yang HJ, Park JS, Romero R, Yoon BH. The importance of intra-amniotic inflammation in the subsequent development of atypical chronic lung disease. *J Matern Fetal Neonatal Med* 2009;22(10):917–23. [PubMed: 19718578]
60. Romero R, Miranda J, Chaiworapongsa T, Korzeniewski SJ, Chaemsaihong P, Gotsch F, et al. Prevalence and clinical significance of sterile intra-amniotic inflammation in patients with preterm labor and intact membranes. *Am J Reprod Immunol* 2014;72(5):458–74. [PubMed: 25078709]
61. Maymon E, Romero R, Pacora P, Gervasi MT, Edwin SS, Gomez R, et al. Matrilysin (matrix metalloproteinase 7) in parturition, premature rupture of membranes, and intrauterine infection. *Am J Obstet Gynecol* 2000;182(6):1545–53. [PubMed: 10871477]
62. Maymon E, Romero R, Pacora P, Gomez R, Athayde N, Edwin S, et al. Human neutrophil collagenase (matrix metalloproteinase 8) in parturition, premature rupture of the membranes, and intrauterine infection. *Am J Obstet Gynecol* 2000;183(1):94–9. [PubMed: 10920315]
63. Shim SS, Romero R, Hong JS, Park CW, Jun JK, Kim BI, et al. Clinical significance of intra-amniotic inflammation in patients with preterm premature rupture of membranes. *Am J Obstet Gynecol* 2004;191(4):1339–45. [PubMed: 15507963]
64. DiGiulio DB, Romero R, Kusanovic JP, Gomez R, Kim CJ, Seok KS, et al. Prevalence and diversity of microbes in the amniotic fluid, the fetal inflammatory response, and pregnancy outcome in women with preterm pre-labor rupture of membranes. *Am J Reprod Immunol* 2010;64(1):38–57. [PubMed: 20331587]
65. Romero R, Miranda J, Chaemsaihong P, Chaiworapongsa T, Kusanovic JP, Dong Z, et al. Sterile and microbial-associated intra-amniotic inflammation in preterm prelabor rupture of membranes. *J Matern Fetal Neonatal Med* 2015;28(12):1394–409. [PubMed: 25190175]
66. MacDougall J, Siddle N. Emergency cervical cerclage. *Br J Obstet Gynaecol* 1991;98(12):1234–8. [PubMed: 1777455]
67. Romero R, Gonzalez R, Sepulveda W, Brandt F, Ramirez M, Sorokin Y, et al. Infection and labor. VIII. Microbial invasion of the amniotic cavity in patients with suspected cervical incompetence: prevalence and clinical significance. *Am J Obstet Gynecol* 1992;167(4 Pt 1):1086–91. [PubMed: 1415396]
68. Mays JK, Figueroa R, Shah J, Khakoo H, Kaminsky S, Tejani N. Amniocentesis for selection before rescue cerclage. *Obstet Gynecol* 2000;95(5):652–5. [PubMed: 10775723]
69. Bujold E, Morency AM, Rallu F, Ferland S, Tetu A, Duperron L, et al. Bacteriology of amniotic fluid in women with suspected cervical insufficiency. *J Obstet Gynaecol Can.* 2008;30(10):882–7. [PubMed: 19038071]
70. Lee SE, Romero R, Park CW, Jun JK, Yoon BH. The frequency and significance of intraamniotic inflammation in patients with cervical insufficiency. *Am J Obstet Gynecol* 2008;198(6):633.e1–8. [PubMed: 18342290]

71. Oh KJ, Lee SE, Jung H, Kim G, Romero R, Yoon BH. Detection of ureaplasmas by the polymerase chain reaction in the amniotic fluid of patients with cervical insufficiency. *J Perinat Med* 2010;38(3):261–8. [PubMed: 20192887]
72. Gibbs RS, Blanco JD, St Clair PJ, Castaneda YS. Quantitative bacteriology of amniotic fluid from women with clinical intraamniotic infection at term. *J Infect Dis* 1982;145(1):1–8. [PubMed: 7033397]
73. Romero R, Jimenez C, Lohda AK, Nores J, Hanaoka S, Avila C, et al. Amniotic fluid glucose concentration: a rapid and simple method for the detection of intraamniotic infection in preterm labor. *Am J Obstet Gynecol* 1990;163(3):968–74. [PubMed: 1698338]
74. Romero R, Yoon BH, Mazor M, Gomez R, Diamond MP, Kenney JS, et al. The diagnostic and prognostic value of amniotic fluid white blood cell count, glucose, interleukin-6, and gram stain in patients with preterm labor and intact membranes. *Am J Obstet Gynecol* 1993;169(4):805–16. [PubMed: 7694461]
75. Lisonkova S, Sabr Y, Joseph KS. Diagnosis of subclinical amniotic fluid infection prior to rescue cerclage using gram stain and glucose tests: an individual patient meta-analysis. *J Obstet Gynaecol Can.* 2014;36(2):116–22. [PubMed: 24518909]
76. Novy MJ, Haymond J, Nichols M. Shirodkar cerclage in a multifactorial approach to the patient with advanced cervical changes. *Am J Obstet Gynecol* 1990;162(6):1412–9; discussion 9–20. [PubMed: 2360574]
77. Ochi M, Ishikawa K, Itoh H, Miwa S, Fujimura Y, Kimura T, et al. Aggressive management of prolapsed fetal membranes earlier than 26 weeks' gestation by emergent McDonald cerclage combined with amniocentesis and bladder overfilling. *Nihon Sanka Fujinka Gakkai Zasshi* 1994;46(4):301–7. [PubMed: 8151171]
78. Caruso A, Trivellini C, De Carolis S, Paradisi G, Mancuso S, Ferrazzani S. Emergency cerclage in the presence of protruding membranes: is pregnancy outcome predictable? *Acta Obstet Gynecol Scand* 2000;79(4):265–8. [PubMed: 10746840]
79. Ciavattini A, Delli Carpini G, Boscarato V, Febi T, Di Giuseppe J, Landi B. Effectiveness of emergency cerclage in cervical insufficiency. *J Matern Fetal Neonatal Med* 2016;29(13):2088–92. [PubMed: 26365717]
80. Gluck O, Mizrahi Y, Ginath S, Bar J, Sagiv R. Obstetrical outcomes of emergency compared with elective cervical cerclage. *J Matern Fetal Neonatal Med* 2017;30(14):1650–4. [PubMed: 27491941]
81. Heath VC, Souka AP, Erasmus I, Gibb DM, Nicolaides KH. Cervical length at 23 weeks of gestation: the value of Shirodkar suture for the short cervix. *Ultrasound Obstet Gynecol* 1998;12(5):318–22. [PubMed: 9819869]
82. Berghella V, Rafael TJ, Szychowski JM, Rust OA, Owen J. Cerclage for short cervix on ultrasonography in women with singleton gestations and previous preterm birth: a meta-analysis. *Obstet Gynecol* 2011;117(3):663–71. [PubMed: 21446209]
83. Berghella V, Ciardulli A, Rust OA, To M, Otsuki K, Althuisius S, et al. Cerclage for sonographic short cervix in singleton gestations without prior spontaneous preterm birth: systematic review and meta-analysis of randomized controlled trials using individual patient-level data. *Ultrasound Obstet Gynecol* 2017;50(5):569–77. [PubMed: 28295722]
84. Berghella V, Odibo AO, To MS, Rust OA, Althuisius SM. Cerclage for short cervix on ultrasonography: meta-analysis of trials using individual patient-level data. *Obstet Gynecol* 2005;106(1):181–9. [PubMed: 15994635]
85. Althuisius SM, Dekker GA, Hummel P, Bekedam DJ, van Geijn HP. Final results of the Cervical Incompetence Prevention Randomized Cerclage Trial (CIPRACT): therapeutic cerclage with bed rest versus bed rest alone. *Am J Obstet Gynecol* 2001;185(5):1106–12. [PubMed: 11717642]
86. Rust OA, Atlas RO, Reed J, van Gaalen J, Balducci J. Revisiting the short cervix detected by transvaginal ultrasound in the second trimester: why cerclage therapy may not help. *Am J Obstet Gynecol* 2001;185(5):1098–1105. [PubMed: 11717641]
87. Berghella V, Odibo AO, Tolosa JE. Cerclage for prevention of preterm birth in women with a short cervix found on transvaginal ultrasound examination: a randomized trial. *Am J Obstet Gynecol* 2004;191(4):1311–7. [PubMed: 15507959]

88. To MS, Alfirevic Z, Heath VC, Cicero S, Cacho AM, Williamson PR, et al. Cervical cerclage for prevention of preterm delivery in women with short cervix: randomised controlled trial. *Lancet* 2004;363(9424):1849–53. [PubMed: 15183621]
89. Owen J, Hankins G, Iams JD, Berghella V, Sheffield JS, Perez-Delboy A, et al. Multicenter randomized trial of cerclage for preterm birth prevention in high-risk women with shortened midtrimester cervical length. *Am J Obstet Gynecol* 2009;201(4):375.e1–8. [PubMed: 19788970]
90. Aguin E, Aguin T, Cordoba M, Aguin V, Roberts R, Albayrak S, et al. Amniotic fluid inflammation with negative culture and outcome after cervical cerclage. *J Matern Fetal Neonatal Med* 2012;25(10):1990–4. [PubMed: 22372938]
91. Jung EY, Park KH, Lee SY, Ryu A, Joo JK, Park JW. Predicting outcomes of emergency cerclage in women with cervical insufficiency using inflammatory markers in maternal blood and amniotic fluid. *Int J Gynaecol Obstet* 2016;132(2):165–9. [PubMed: 26553528]
92. Diago Almela VJ, Martinez-Varea A, Perales-Puchalt A, Alonso-Diaz R, Perales A. Good prognosis of cerclage in cases of cervical insufficiency when intra-amniotic inflammation/infection is ruled out. *J Matern Fetal Neonatal Med* 2015;28(13):1563–8. [PubMed: 25212978]
93. Treadwell MC, Bronsteen RA, Bottoms SF. Prognostic factors and complication rates for cervical cerclage: a review of 482 cases. *Am J Obstet Gynecol* 1991;165(3):555–8. [PubMed: 1892180]
94. Lipitz S, Libshitz A, Oelsner G, Kokia E, Goldenberg M, Mashlach S, et al. Outcome of second-trimester, emergency cervical cerclage in patients with no history of cervical incompetence. *Am J Perinatol* 1996;13(7):419–22. [PubMed: 8960611]
95. Yip SK, Fung HY, Fung TY. Emergency cervical cerclage: a study between duration of cerclage in situ with gestation at cerclage, herniation of forewater, and cervical dilatation at presentation. *Eur J Obstet Gynecol Reprod Biol* 1998;78(1):63–7. [PubMed: 9605451]
96. Benham BN, Balducci J, Atlas RO, Rust OA. Risk factors for preterm delivery in patients demonstrating sonographic evidence of premature dilation of the internal os, prolapse of the membranes in the endocervical canal and shortening of the distal cervical segment by second trimester ultrasound. *Aust N Z J Obstet Gynaecol* 2002;42(1):46–50. [PubMed: 11926640]
97. Groom KM, Shennan AH, Bennett PR. Ultrasound-indicated cervical cerclage: outcome depends on preoperative cervical length and presence of visible membranes at time of cerclage. *Am J Obstet Gynecol* 2002;187(2):445–9. [PubMed: 12193941]
98. Terkildsen MF, Parilla BV, Kumar P, Grobman WA. Factors associated with success of emergent second-trimester cerclage. *Obstet Gynecol* 2003;101(3):565–9. [PubMed: 12636963]
99. Grobman WA, Terkildsen MF, Soltysik RC, Yarnold PR. Predicting outcome after emergent cerclage using classification tree analysis. *Am J Perinatol* 2008;25(7):443–8. [PubMed: 18767009]
100. Delabaere A, Velemir L, Ughetto S, Accoceberry M, Niro J, Vendittelli F, et al. Emergency cervical cerclage during mid-trimester of pregnancy: Experience of Clermont-Ferrand. *Gynecol Obstet Fertil* 2011;39(11):609–13. [PubMed: 21872520]
101. Deb P, Aftab N, Muzaffar S. Prediction of outcomes for emergency cervical cerclage in the presence of protruding membranes. *ISRN Obstet Gynecol* 2012;2012:842841. [PubMed: 22474592]
102. Fortner KB, Fitzpatrick CB, Grotegut CA, Swamy GK, Murtha AP, Heine RP, et al. Cervical dilation as a predictor of pregnancy outcome following emergency cerclage. *J Matern Fetal Neonatal Med* 2012;25(10):1884–8. [PubMed: 22385390]
103. Fuchs F, Senat MV, Fernandez H, Gervaise A, Frydman R, Bouyer J. Predictive score for early preterm birth in decisions about emergency cervical cerclage in singleton pregnancies. *Acta Obstet Gynecol Scand* 2012;91(6):744–9. [PubMed: 22375688]
104. Steenhaut P, Hubinont C, Bernard P, Debieve F. Retrospective comparison of perinatal outcomes following emergency cervical cerclage with or without prolapsed membranes. *Int J Gynaecol Obstet* 2017;137(3):260–4. [PubMed: 28281278]

Figure 1.
Disposition of patients who are part of the study.

Table 1.

Demographic and clinical characteristics of study population at admission, according to the results of amniotic fluid analyses

	No IAI/I (N=57)	Amniocentesis Not Performed (N=7)	IAI/I (N=13)	p-value
Maternal age (years)	28.4 (± 7.3)	25.0 (± 7.7)	26.8 (± 5.8)	0.429
Gestational age (weeks)	21.8 (± 2.7)	21.9 (± 1.0)	21.8 (± 2.4)	0.999
Body mass index (kg/m ²)	27.8 (± 5.6)	25.1 (± 5.3)	30.0 (± 5.4)	0.176
Nulliparity	58 (33/57)	71 (5/7)	69 (9/13)	0.675
Prior second trimester loss	18 (10/57)	14 (1/7)	0 (0/13)	0.271
Prior preterm birth	19 (11/57)	0 (0/7)	15 (2/13)	0.602
Prior cervical cerclage	4 (2/57)	0 (0/7)	0 (0/13)	1.000
Uterine malformation	2 (1/57)	14 (1/7)	0 (0/13)	0.201
Active smoking	11 (6/57)	0 (0/7)	0 (0/13)	0.770
Progesterone use before admission	14 (8/57)	0 (0/7)	15 (2/13)	0.731
Cervical dilatation (cm)	2.9 ± 1.9	3.7 ± 3.1	4.3 ± 2.1 ^(a)	0.059
Maternal heart rate (bpm)	93 ± 12	92 ± 10	101 ± 10 ^(b)	0.081
Body temperature (°C)	36.5 ± 0.3	36.3 ± 0.7	36.7 ± 0.5	0.018
White blood cells count (x10 ³ /mm ³)	11.6 ± 2.5	15.4 ± 6.8	15.1 ± 3.5 ^(c)	0.005
C-reactive protein (mg/L)	4.4 ± 5.5	24.5 ± 38.0	19.7 ± 23.8 ^(d)	0.085

Values are expressed as % (proportion) or mean (± standard deviation)

Bivariate analysis:

^aComparison between groups “No IAI/I” and “IAI/I”: P = 0.015.

^bComparison between groups “No IAI/I” and “IAI/I”: P = 0.033.

^cComparison between groups “No IAI/I” and “IAI/I”: P = 0.002.

^dComparison between groups “No IAI/I” and “IAI/I”: P = 0.025.

Table 2.

Pregnancy outcomes according to amniotic fluid analysis and cerclage

	Group 1 Cerclage + No IAI/I (N=41)	p-value ^(a)	Group 2 Cerclage + Amniocentesis not performed (N=4)	p-value ^(b)	Group 3 IAI/I (N=13)	p-value ^(c)
Admission-to-delivery interval (days)	43 (15.0 – 89.0)	0.675	21.5 (16.0 – 64.5)	0.010	1 (1.0 – 10.0)	<0.001
Gestational age at delivery (weeks)	28 (23.7 – 36.3)	0.523	25.4 (24.1 – 30.4)	0.047	22.1 (20.7 – 23.4)	0.001
Birthweight (grams)	1212 (660 – 2890)	0.531	897 (690 – 1792)	0.032	550 (435 – 625)	0.002
Delivery <48 hours from admission	2 (1/41)	0.911	0 (0/4)	0.029	69 (9/13)	<0.001
Delivery <7 days from admission	12 (5/41)	0.613	0 (0/4)	0.029	69 (9/13)	<0.001
Delivery <24 weeks	27 (11/41)	0.714	25 (1/4)	0.053	85 (11/13)	0.001
Delivery <28 weeks	49 (20/41)	0.321	75 (3/4)	0.426	92 (12/13)	0.005
Delivery <32 weeks	61 (25/41)	0.511	75 (3/4)	0.235	100 (13/13)	0.005
Neonatal survival ^(d)	67 (26/39)	0.607	75 (3/4)	0.022	8 (1/13)	<0.001

Values are expressed as % (proportion) or median (interquartile range)

^(a) p-values for comparison between groups 1 and 2.^(b) p-values for comparison between groups 2 and 3.^(c) p-values for comparison between groups 1 and 3.^(d) Two newborns in group 1 were delivered in participating centers and were posteriorly transferred to other centers for neonatal management. No information regarding neonatal survival was available for both cases.