

Original Investigation

Prevention of preterm delivery by cervical cerclage; A comparison of prophylactic and emergency procedures

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Introduction

Cervical insufficiency can be described as an inability of cervix uteri to retain the pregnancy in the absence of objective signs of labor ;

like regular uterine contractions , especially in the second trimester. It has a particular clinical importance since preterm birth and prematurity related risks are high in this group of patients . Incidence is around 1 % in general obstetric population , but this rate is 8 % within the patient groups with second trimester pregnancy loss ¹. Etiology is not clear but risk factors include antecedent cervical surgeries like conization ; repetitive dilatation and curretages ; congenital uterine anomalies ; in utero diethylstilbestrol exposition and possibly, the most important is history of cervical insufficiency in previous pregnancies ². Bed rest , activity restriction and vaginal pessaries are non-surgical treatment modalities for cervical insufficiency and the effectiveness of these modalities have been evaluated by many authors in literature. Activity restriction has been found ineffective in one study , moreover, another study showed a higher risk of preterm delivery in the activity restricted group ³⁴. In singleton pregnancies diagnosed with short cervix , expectant management was compared with vaginal pessaries.

Vaginal pessaries showed to be more effective at reducing delivery under 34 gestational weeks ⁵. However, in twin pregnancies vaginal pessary was not superior to expectant management in the respect of delivery under 34 gestational weeks in a contemporary publication ⁶. On account of conflicting results and inadequate evidences ; non surgical treatment modalities are generally discouraged ².

Cervical cerclage procedures can be performed transabdominally or transvaginally. Transabdominal approaches should be reserved for patients with cervical anatomical disturbances like trachelectomized patients and also for patients with repetitive failure of transvaginal cerclage that resulted in pregnancy loss. Mc-Donald and Schirodkar type transvaginal cervical cerclages are the most known and performed. Both are effective and noninferior to each other.

Cerclage indications can be classified as ; history based prophylactic cerclage and physical examination based emergency cerclage procedures.

American College of Obstetrician and Gynecologists (ACOG) defines prophylactic cerclage indications as ; painless cervical dilatation or requirement of cervical cerclage in a prior pregnancy. Painless cervical dilatation in the second trimester and cervical length under 25 mm. with history of preterm birth before 34 gestational weeks in a prior pregnancy constituted the emergency cerclage indications 2.

Success of these cerclage procedures on preventing preterm delivery may be effected by some clinical parameters and patient characteristics. The aim of this study is to analyze and compare outcomes of prophylactic and emergency cerclages performed in a tertiary referral center; also, to delineate factors that can effect the efficiency of cervical cerclage, like body mass index, pre cerclage cervical length and neutrophil-lymphocyte ratio .

Materials and Methods

Patient Selection

Cervical cerclage procedures performed between January 2012 – February 2019 were reviewed retrospectively by using hospital records. Pregnancy and labor information was obtained by telephone based search when needed. ACOG recommendations on cerclage indications were taken as guidelines. Prophylactic cerclage was applied between 11-14 gestational weeks, after first trimester screening tests, for patients with prior history of cervical insufficiency. Emergency cerclage was performed for patients with painless cervical dilatation at the second trimester; also, for patients with preterm birth history and diagnosis of short cervix in the current pregnancy. Cervical cerclage procedures were not performed in the presence of regular uterine contractions, active vaginal bleeding, chorioamnionitis, fetal anomaly, rupture of membranes and dilated cervix beyond 3 cm.

Intervention

Pre-cerclage cervical length is measured by transvaginal ultrasound (TVUS), with empty bladder and minimum of three measurements, then the mean value is taken. The amount of cervical dilatation is also measured by TVUS under sterile conditions. Mc-Donald cervical cerclage applied to all patients, Schirodkar type cerclage was not used in this study population. Sterilization achieved by application of povidone iodine to the vagina and cervix under sedoanalgesia. Cervix anterior part grasped with oval clamp and stitched at points 12, 9, 6 and 3. Non absorbable braided suture material (Cervix-set B.Braun) used for suturing . Prolapsed membranes relocated by placing and inflating a pediatrics foley catheter into the cervical canal in patients with dilated cervix.

Prophylactic antibiotic, intramuscular progesterone and indomethacine were given to all patients postoperatively. Postoperative complications defined as massive vaginal bleeding , chorioamnionitis and premature rupture of membranes. Operation time was taken from induction of anesthesia till end of stitch procedure; hospitalization time from operation till discharge.

Statistical Analysis

Statistical analysis was performed by using the statistical package software (Version 17.0, SPSS Inc., Chicago, IL, USA). If continuous variables were normal, they are described as the mean±standard deviation ($p>0.05$ in Kolmogorov-Smirnov test or

Shapira-Wilk ($n < 30$)), and if the continuous variables were not normal ; they are described as the median. Comparisons between groups were applied by using student-t test for normally distributed data and Mann Whitney U test is used for the data which were not normally distributed . The categorical variables between the groups was analyzed by using the Chi square test or Fisher Exc. test. Values of $p < 0.05$ were considered as statistically significant.

This study is approved by the Institutional Ethical Committee at 05/14/2019, with the project number of KA19/168 . Informed consent of patients has been obtained before cervical cerclage procedures.

Results

During the study period, 89 cervical cerclage procedures total were performed in this tertiary center. Twin pregnancies and pregnancies that ended before 21st week of gestation were excluded from the study (figure 1). As a result, 75 patients with singleton pregnancies and diagnosis of cervical insufficiency were included in the study. Twenty-seven of 75 patients were in the emergency cerclage group and 48 were in the prophylactic group. Mean BMI values; hospitalization time and gestational week of cerclage application were significantly higher in the emergency group compared to prophylactic cerclage group. Latency period, which is from cerclage week to delivery week was significantly shorter for the emergency cerclage patients ($14,2 \pm 6,5$ vs. $21,7 \pm 4,8$ $P: 0,000$). Nonetheless, there were no statistically significant differences between the two groups regarding other parameters (Table 1). The effects of BMI, preoperative cervical length and neutrophil-lymphocyte ratio on the week of delivery under and above 34 gestational weeks were evaluated. Patients who gave birth before 34 gestational weeks had significantly higher BMI values than the values of patients who gave birth after 34 gestational weeks ($28,2 \pm 4,4$ vs $25,0 \pm 4,2$ $P: 0,04$) in the prophylactic cerclage group. Although the same findings were prevailing the difference was not significant for the emergency cerclage patients ($31,8 \pm 10,6$ vs $28,0 \pm 3,4$ $P: 0,186$) (Table 2).

Mean precerclage cervical length of patients who delivered before and after at 34 gestational weeks were $30,9 \pm 5,3$ mm ve $35,1 \pm 7,9$ mm ($P: 0,117$) respectively in the prophylactic cerclage patients. Same values were $9,6 \pm 6,3$ mm ve $16,6 \pm 6,7$ mm ($P: 0,136$) respectively for the emergency group (Figure 2,3).

In the emergency cerclage group; when we consider the gestational week of patients with dilated cervix, the rate of birth before 34 weeks was 70 %. Whereas this rate was 30 % in the group without dilatation and diagnosis of short cervix only, however, the difference was still not significant ($P: 0,120$) (table 3) .

Discussion

As mentioned before, cervical cerclage procedures' main determinant of success is the capability of preventing preterm birth and related adverse outcomes. In this cohort the prophylactic cerclage group has a higher mean gestational age, higher birth rate above 34 gestational weeks , higher mean gestational weight , and lower complication rate than the emergency cerclage group, but neither of them reached statistical significance . Mean gestational week at delivery of the emergency cerclage group was $33,6 \pm 5,9$ weeks and was comparable with the prophylactic cerclage groups' mean gestational week at delivery which was $35,6 \pm 4,5$ week ($P: 0,117$).

Birth weeks and perinatal outcomes of history based and ultrasound based cervical cerclage patients were compared in previous studies⁷⁸. Gluck et al. compared the obstetric outcomes of patients admitted with cervical dilatation or shortened cervical length to history indicated cerclage patients ; gestational week at delivery and birthweights were similar for both groups⁹. Liddiard et al. also did not find any significant difference in birth weeks , birthweights , live birth rates and neonatal intensive care unit (NICU) need between the emergency and prophylactic cerclage groups. In the same study, complication rate of emergency cerclage patients was higher than the prophylactic cerclage group, but it should be taken into account that approximately half of the patients in the emergency group had twin pregnancies and at least 3 cm cervical dilatation at admittance (11). In a recently published metaanalysis, which also includes the two previously mentioned studies, birth week and birth weights were found to be significantly lower with the risk of membrane rupture higher in the emergency cerclage group¹⁰. In our cohort , age and pregnancy types were similar in both groups, but BMI values were significantly higher amongst emergency cerclage patients(29,4±7,1 vs 25,7±4,4 p: 0,006). Mean gestational week at delivery and mean birth weight were higher in the prophylactic cerclage group, whereas complication rate , delivery under 34 gestational weeks and hospitalization time were higher in the emergency cerclage group but only differences between hospitalization time could reach statistical significance. In emergent cases , there is a process that has already started and ongoing; short or dilated cervix is the sign of impending threat of cervical insufficiency . In prophylactic cases, however, there is generally a wellknown history of cervical insufficiency in a previous pregnancy, so both patient and physician are well-prepared for clinical situations and required treatment options in a current pregnancy . It makes sense that forestalling a process that has not yet started is easier than forestalling one that has already started. Differences between two groups may be partially explained this way. Nevertheless, since differences were not significant regarding delivery time , birthweight , complication rate , NICU admission we can conclude that outcomes of both cerclage types are similar and comparable . Latency period from cerclage to delivery is significantly higher in the prophylactic group, but gestational week at cerclage is higher in the emergency group as expected. Since mean cerclage week is 13,9±1,7 and 19,4±3,2 (P:0,000) in the prophylactic and emergency group respectively ; the longer latency period of the prophylactic group can be partially attributed to this difference.

Cervical cerclage procedure is recommended with evidence level IA for patients who had spontaneous preterm birth or diagnosed cervical insufficiency in previous pregnancies and cervical length under 25 mm in their current pregnancy¹ Berghella et al. published a meta-analysis including four randomized controlled trials and concluded that patients with history of cervical insufficiency can be safely followed by serial TVUS cervical length measurement¹¹: so unnecessary, history indicated prophylactic cerclage procedures can be reduced. A retrospective study of Brown et al. found approximately 50 % of patients with history did not require cerclage who were followed by serial TVUS measurements. Moreover, the obstetrical and perinatal outcomes were similar between groups⁷. The main aim of serial cervical length measurements in patients with a history of cervical insufficiency is to reduce unnecessary cerclage procedures and related complications . In this study, ACOG's criterias are followed and cervical cerclage performed between 11-14 weeks of pregnancy on patients with a history of cervical insufficiency in a previous pregnancy . Cervical lengths measured

just before the procedure by TVUS . Mean cervical length of patients delivered at and after 34 gestational weeks was $35,1 \pm 7,9$ mm and $30,9 \pm 5,3$ mm for deliveries under 34 gestational week in the prophylactic cerclage group ($P: 0,117$) . The same values were $16,6 \pm 6,7$ mm and $9,6 \pm 6,3$ mm for the emergency cerclage group respectively ($P: 0,136$). As a result, the increment of precerclage cervical length is associated with improvement of gestational week at delivery , although differences were not significant in this study . When we consider the subgroup of emergency cerclage patients who had admitted with cervical dilatation , delivery under 34 gestational week was higher than the group who did not have cervical dilatation. Difference was not significant again ; in our opinion a limited number of patients is the explanation , otherwise it is highly probable that improvement of gestational week at delivery is directly proportional with precerclage cervical length. Liberal use of cerclage may have adverse outcomes and risks, but with appropriate indications , the procedure will be effective and improve obstetrical and perinatal outcomes .

It is known , high BMI values are generally together with various adverse pregnancy and obstetric outcomes. There are publications studying the effect of BMI on cerclage procedures. Suhag et al. studied the effect of prepregnancy BMI on success of history and ultrasound indicated cerclage procedures and did not find any effect of BMI ¹². In another retrospective observational study , again there was not any relation between BMI and latency period ; from cerclage to delivery ¹³. Interestingly , Schirodkar type cerclage has been found superior to Mc-Donald type in obese patient groups when gestational week at delivery was considered ¹⁴. One study showed inverse proportion between BMI and gestational week at delivery in history indicated cerclage patients¹⁵. Mean BMI of the emergency cerclage group was significantly higher than prophylactic cerclage patients ($29,4 \pm 7,1$ vs $25,7 \pm 4,4$, $p:0,006$) in this study . This difference may originate from general adverse effects of higher BMI on obstetrical outcomes. Inverse proportion between gestational week at delivery and BMI was significant in prophylactic cerclage patients . Similar relation also observed in emergent cerclage patients, but with lack of statistical significance. In total, high BMI values seem to have a negative effect on cerclage efficiency. This may have importance especially when consulting the efficiency of procedures with patients.

Neutrophile-lymphocyte ratio is accepted as an indicator of proinflammatory processes . Role of this ratio on predicting prognosis of chronic , oncologic and acute inflammatory diseases has been studied in many publications. Also, there are studies investigating the relationship of neutrophile-lymphocyte ratio with ovarian torsion and preeclampsia. Since delivery is a proinflammatory process, one can speculate that preterm delivery is also such a process and neutrophile-lymphocyte ratio may have a predictive effect on predicting early delivery. As a result of literature search , we coincided a study , which delineated a relationship between increment of neutrophile-lymphocyte ratio and delivery under 28 gestational weeks in patients with recurrent cervical cerclages ¹⁶. In our study, neutrophile-lymphocyte ratio was similar between emergency and prophylactic cerclage patients ($3,8$ vs $3,5$ $P:0,196$). In a subgroup analysis ; neutrophile-lymphocyte ratio in emergency cerclage patients delivered before and after 34 gestational weeks was $3,5 \pm 0,9$ and $4,0 \pm 1,4$ respectively . In history indicated prophylactic cerclage patients, again neutrophile-lymphocyte ratio was higher in patients who delivered at and after 34 gestational weeks, the difference was not significant ($3,2 \pm 0,7$ vs $3,5 \pm 0,9$ $P:0,342$). Higher neutrophile-lymphocyte ratio in deliveries after 34 gestational weeks seems an unexpected finding , but since

differences are not evident and size of cohort is limited, a clear comment cannot be made on this aspect of the study.

Main limitation of this study arise from its' retrospective nature .Furthermore results are robust for this cohort , since strict criterias are used to indicate patients who are candidate for prophylactic and emergency cerclage procedures .Also number of included patients is not that insufficient when we consider the incidence of cervical incompetence.

Conclusion

Main indications of prophylactic cervical cerclage procedures are well defined in contemporary and evidence based guidelines.In this context patients with history of three or more preterm deliveries under 24 th gestational weeks and patients with one or more preterm deliveries under 24 th gestational weeks who had cervical length measurement under 25 mm in current pregnancy have indication for cervical cerclage procedure¹⁷. Results of this study showed us that ; emergency cerclage procedures may have positive effect on prolongation of gestational week at delivery. And similar to prophylactic cerclage procedures ; emergency cerclage procedures may be effective on prevention of preterm and severely preterm deliveries. This result should not be interpreted as emergency cerclage is as effective as prophylactic cerclage and it can substitute to prophylactic procedure.

In conclusion, emergency cerclage procedure seems effective like prophylactic cervical cerclage and their outcomes are comparable for this study. Precerclage cervical length correlates with gestational week at delivery in both cerclage types . Cervical dilatation at admission may be a poor prognostic factor for preterm delivery in emergency cerclage patients . Increment in BMI values also has a negative effect on gestational week at delivery . A conclusion could not be made on whether there is a relationship between neutrophile-lymphocyte ratio and cerclage outcomes . Diversity of study results in literature is hindering to make a certain conclusion, but according to these findings, results of both groups seem comparable. More detailed randomized studies may enlighten the relationship between these factors and cerclage procedure outcomes .

Conflict of Interest: The authors declare that they have no competing interests.

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| | 34 weeks > | 34 weeks ≤ | P value |
|---|----------------------|-------------------|----------------|
| Prophylactic cerclage group Mean precerclage cervical length (mm.) | 30,9±5,3 mm | 35,1±7,9 mm | 0,117 |
| Mean BMI | 28,2±4,4 | 25,0±4,2 | 0,04 |
| Neutrophil-lymphocyte ratio | 3,5±0,9 | 3,2±0,7 | 0,342 |

| | Prophylactic | Emergency | P value |
|---|---------------------|------------------|----------------|
| Age(years) | 29,9±4,4 | 31,7±4,4 | 0,104 |
| Body Mass Index (BMI) | 25,7±4,4 | 29,4±7,1 | 0,006 |
| Type of pregnancy Spontaneous | 75 % n:36 | 81.5 % n:22 | 0,438 |
| Assisted Reproductive Techniques | 25 % n:12 | 18.5 % n:5 | |
| Mean Hospitalization time (days) | 1,02 days | 5,1 days | 0,003 |
| Mean gestational week at cervical cerclage | 13,9±1,7 | 19,4±3,2 | 0,000 |
| Mean gestational week at birth | 35,6±4,5 | 33,6±5,9 | 0,117 |
| Mean time from cerclage to labor (in weeks) | 21,7±4,8 | 14,2±6,5 | 0,000 |
| Mean Precerclage Neutrophile-Lymphocyte ratio | 3,5±0,8 | 3,8±1,2 | 0,196 |
| Complication rate | 2,1 % n:1 | 7,4 % n : 2 | 0,368 |
| Gestational week at delivery 34 weeks > | 20,8 % n : 10 | 37 % n : 10 | 0,175 |
| 34 weeks ≤ | 79,2 % n: 38 | 63 % n : 17 | |
| NICU need | 37 % n : 10 | 21,3 % n : 10 | 0,178 |
| Birth weights (grams) | 2842±957 | 2475±1193 | 0,149 |

| | | | |
|----------------------------------|------------|-------------|-------|
| Emergency cerclage group | | | |
| Mean precerclage cervical length | 9,6±6,3 mm | 16,6±6,7 mm | 0,136 |
| Mean BMI | 31,8±10,6 | 28,0±3,4 | 0,186 |
| Neutrophil-lymphocyte ratio | 4,0±1,4 | 3,5±0,9 | 0,411 |

Table 3. Gestational week at delivery according to presence or absence of cervical dilatation, in emergency cerclage patients

| Birth week | No cervical dilatation | Dilatation |
|------------|------------------------|------------|
| 34 weeks > | 30 % | 70 % |
| 34 weeks ≤ | 64 % | 35 % |

p: 0,120

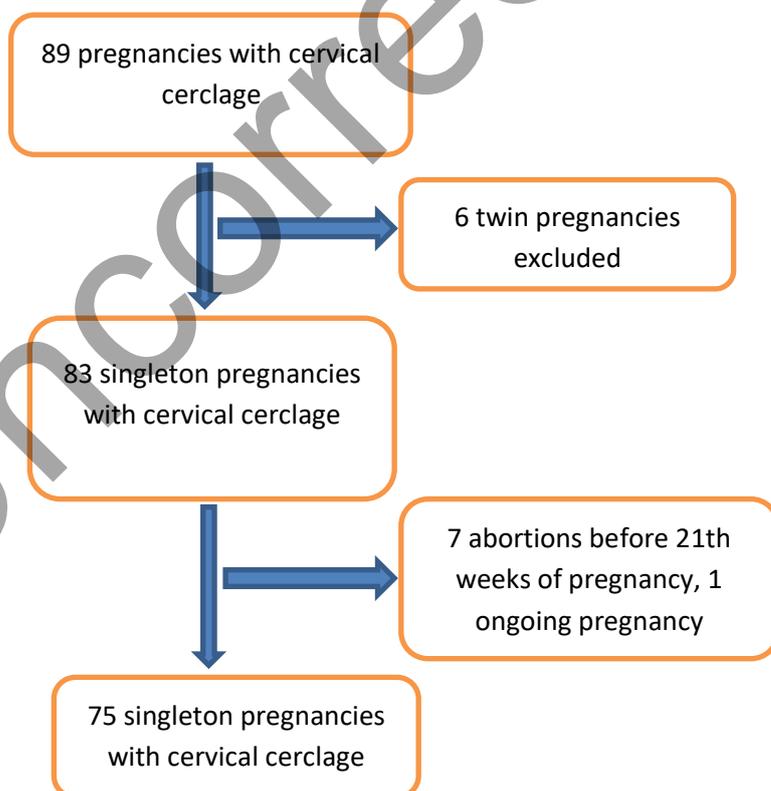


Figure 1. Flow diagram of the study



Figure 2. Precerclage cervical length and gestational week at delivery in emergency cerclage group

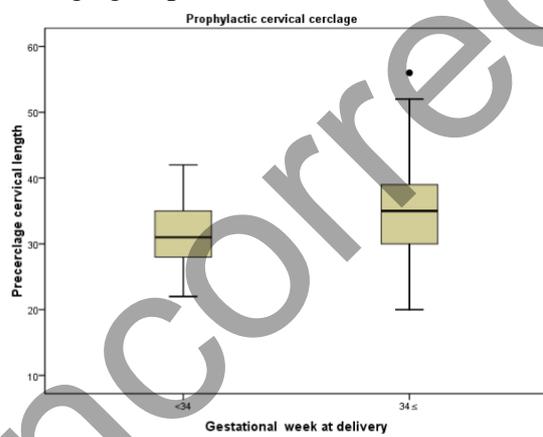


Figure 3. Precerclage cervical length and gestational week at delivery in prophylactic cerclage group

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