Pregnancy Outcomes According to Cervical Cerclage Indications and Factors Affecting Pregnancy Duration and Outcomes: A 2-Year Comparison Of Patients Who Underwent History-Based, Ultrasound-Based, or Rescue Cerclage

……Hospital Clinical Research Ethics Committee (ethics no.2023-605, date: 22.11.2023)

Study Protocol

This study retrospectively reviewed data from pregnant women who underwent cerclage from July 2021 to July 2023 in ……. Hospital, which is a perinatal medical center in Istanbul, Turkey. The local ethics committee approved the study.
All procedures followed the relevant guidelines and regulations of the institutional ethics review board and the Declaration of Helsinki.

The patients were divided into three subgroups for data analysis. Group 1 included patients with history-indicated cerclage, who had second-trimester pregnancy loss associated with painless cervical dilatation in the absence of labor or placental abruption, or previous cerclage due to painless cervical dilatation in the second trimester. Group 2 comprised patients with ultrasound-indicated cerclage, who had a history of spontaneous preterm birth before the 34th week previously and their cervical length was <25 mm before the 24th week of gestation in the current singleton pregnancy, or who had <10 mm cervical length in the current singleton pregnancy without history. Group 3 consisted of patients undergoing rescue cerclage, who had premature cervical dilatation and exposure of fetal membranes in the vagina, was detected in ultrasound or speculum examination of the cervix. All cervical cerclage procedures were performed by a senior obstetrician using the McDonald technique with Mersilene tape or No:1 proline. We collected the following data from medical records: maternal age at cervical cerclage, gravidity, parity, body mass index, history of a cervical cone biopsy, history of premature birth and cervical cerclage, procalcitonin level, C-reactive protein (CRP) level, gestational age at cerclage, pre-and post-cerclage cervical lenght (CL), week of birth, pregnancy complications (preterm premature rupture of the membranes (PPROM), abruptio placenta, chorioamnionitis). We defined successful cerclage as postponing birth until after the 28th week of gestation and a 'good outcome' was defined as delivery beyond 34 completed weeks. We reviewed the indications and the pregnancy outcomes (miscarriage, gestational age at delivery, birth weight, prolongation of pregnancy, and rate of preterm birth before 34 weeks) of cervical cerclage and analyzed the factors associated with successful cervical cerclage in our perinatal medical center.

Moreover, receiver operating characteristic (ROC) curves were used to calculate the pre-cerclage and post-cerclage CL cut-off value required to predict if birth could be postponed birth until after the 28th week of gestation in women with cervical issuficiency (CI). Thus, we

extracted significant factors for a successful cervical cerclage for long-term pregnancy sustenance in women with CI.

Statistical Analysis Plan

All data were analyzed using the statistical software package SAS version 15.2 (SAS Institute Inc.). The Kolmogorov-Smirnov test was used to test the normality assumption. The three groups of patients were compared in terms of three outcomes, successful cerclage, good outcomes, and PPROM. For categorical variables, a comparison among the three groups of patients regarding socio-demographics and clinical features was conducted using the Chi-square or Fisher's exact test, as appropriate. For continuous variables, the three groups of patients were compared using the Kruskal-Wallis test or analysis of variance (ANOVA), as appropriate. Within each group, we compared the patients in terms of successful cerclage, good outcomes, and PPROM. A p-value less than 0.05 was considered statistically significant. The predictive power of pre- and post-operation cervix length in identifying successful cerclage was evaluated using receiver operating characteristic (ROC) curves, and the area under the curve (AUC) determined the discriminative ability of the parameters. The optimal cut-off values are derived using Youden's Index.

Results

We included 129 patients with a singleton pregnancies in this study. Three membrane rupture complications occured during the cervical cerclage procedure (all three cases were in the emergency cerclage group and the pouches were prolapsed). Externally, no uncontrollable bleeding or injury to the bladder and/or rectum occurred during cerclage. The sample size was 129 patients, with 32 in the history-indicated cerclage group (G1), 62 in the ultrasound-indicated cerclage group (G2), and 35 in rescue cerclage group (G3). Only six (4.6%) pregnancies resulted in miscarriage before 20 weeks of gestation. Among these three groups, significant differences were observed in gravidity, parity, history of preterm birth, and history of CI. In group 1, the average gravidity was 4.69 (2.05), whereas in groups 2 and 3, it was much lower at 2.47 (1.83) and 2.23 (3.81), respectively. Similarly, parity was much higher in group 1 than in groups 2 and 3.

We compared the three groups in terms of factors that could affect cervical cerclage success and pregnancy outcomes of cerclage cases. Among these three groups, significant

differences were observed in cerclage week, the time elapsed from cerclage to childbirth, post-operation cervix length, complication rates, successful cerclage and good outcomes (delivery beyond 34 completed weeks).

The average cerclage week was 14.39 (1.99) in group 1, but the week of cerclage performance was later in groups 2 and 3 (21.47 (2.97) and 20.98 (4.14), respectively).

The average time elapsed from cerclage to childbirth was much longer in group 1, with an average of 143.63 (41.27) days, whereas it was relatively shorter in group 2, with an average of 94.46 (35.16) days. The shortest time elapsed from cerclage to birth was observed in group 3, with an average of 69.82 (49.35) days.

In groups 1 and 2, the percentage of patients with successful cerclage was much higher (90.6% and 88.7%, respectively) than in group 3 (66.7%). Similarly the percentage of patients with good outcomes was much higher for the patients in groups 1 and 2 in comparison with group 3. The earlier cerclage is applied after CI is identified, the longer the time from cerclage to birth.

We also evaluated the effects of preop cervical length, postop cervical length, preop procalcitonin value, preop CRP, cerclage week, and cerclage material on cerclage results for each group separately. Withing group 1, we compared the patients who had successful cerclage with the patients who did not in terms of pre-op cx, post-op cx, procalcitonin, CRP, the week of cerclage, and the material of cerclage. We found significant difference in these two groups in terms of the average procalcitonin; however, we only had three patients with unsuccessful cerclage and all three patients had the same procalcitonin values. Therefore, we did not report the p-value for this comparison. Based on this result, although we cannot clearly say that high procalcitonin values reduce cerclage success in the prophylactic cerclage group, the effects of procalcitonin need to studied on cerclage success in more detail.

In the prophylactic cerclage group, there was also a significant difference between patients with and without PPROM ($p<.0001$). The average post-operation cervix length for patients without PPROM was 34.5 (4.64) mm, whereas the average post-operation cervix length for patients with PPROM was 19.4 (0.85) mm. We concluded that the longer the postoperative cervix length, the lower the probability of PPROM in the prophylactic cerclage group.

Within group 2, there were significant differences between patients with and without successful cerclage in terms of post-cerclage cervical lenght and procalcitonin levels. The average post-op cervix length was 26.1 (7.37) mm for the patients with successful cerclage, whereas the average post-op cervix length was 18.0 (9.23) mm for patients without successful cerclage (p=.015). The average procalcitonin level was 0.06 (0.03) μg/L for patients without successful cerclage, and was 0.04 (0.02) μg/L for patients with successful cerclage.

In the ultrasound-indicated cerclage group, the mean postoperative cervix length of patients with successful cerclage was longer. In this group, we can say that as the postoperative cervical length increases, the success of the procedure increases.

When we compared the patients with and without PPROM in group 2, we found that there was a significant difference between the groups in terms of post-op cervix length (p=.010). Patients with PPROM had a shorter post-op cervix length (18.6 (9.02) mm) than patients without PPROM (26.3 (7.32) mm). We conclude that in the ultrasound-indicated cerclage group, as in the prophylactic cerclage group, the longer the postoperative cervix length, the lower the likelihood of PPROM. In this group, similar to the findings for successful cerclage, there were also significant differences between patients with and without good outcomes in terms of post-op cervix length and procalcitonin levels. The average length of post-op cervix length was 27.4 (6.56) mm for patients with good outcomes, whereas the average post-op cervix length of was 19.6 (8.60) mm for patients poor outcomes (p<.001). The average procalcitonin level was 0.05 (0.02) μg/L for patients with poor outcomes, and was 0.04 (0.02) μg/L for patients with good outcomes.

As a result of our analysis for group 3, we found no significant differences (All p-values >.05). Lastly, we used ROC curves to calculate the pre-cerclage and post-cerclage CL cut-off value required to predict if birth could be postponed until after the 28th week of gestation in women with CI. Thus, we extracted significant factors for a successful cervical cerclage for long-term pregnancy sustenance in women with CI. In group 2, we used Youden's Index to determine an optimal cut-off value for the post-operation cervix length and the pre-operation cervix length. For the post-operation cervix length, the optimal cut-off value was determined as 23.87 with sensitivity=0.83, specificity=0.72 (AUC=0.78). The area under curve

(AUC) for the analysis with the pre-operation cervix length was equal to 0.52, meaning that this parameter did not have a predictive power for identifying successful cerclage.