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A novel method for assessing the condition of the cervix before labor induction: Cervical length/thickness ratio

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Ethics Committee approval was taken from the Bursa Yüksek İhtisas Training and Research Hospital Ethics Committee, 2011-KAEK-25 2019/07-15.
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Abstract

Background/Aim: Due to the increasing cesarean rates globally, new methods for supporting vaginal delivery and induction of successful vaginal delivery are still being developed. We aimed to obtain an easy-to-use method that can predict the effectiveness of cervical ripening agents before labor induction. So, we presented the effects on labor by measuring the thickness of the cervix and the cervical length/thickness ratio ultrasonographically.

Methods: In this prospective cohort study, we evaluated 183 pregnant between 37 and 41 weeks of gestational age and will apply vaginal delivery induction. Before oxytocin induction, we applied 10 mg dinoprostone vaginally to women whose cervix was stiff. We started labor induction with oxytocin when regular uterine contractions or dilatation occurred. We used the Bishop Scoring System for favorable cervix defining. Then, we compared the groups with successful and unsuccessful cervical ripening regarding cervical length and thickness parameters.

Results: The mean cervical thickness of the pregnant women with successful cervical ripening was 34.5 (7.5) mm before treatment, while the mean values of the unsuccessful group were 29.2 (9.1) mm ($P < 0.001$). The cervical length did not differ between the two groups (31.6 [8.2] vs. 32.5 [6.8], $P = 0.44$), while the cervical length/thickness ratio was lower in the group with successful ripening (0.9 [0.38–2], $P < 0.001$). Cervical length/thickness ratio was the highest predictor of the favorable cervix with dinoprostone. Each 1 unit decrease in the length/thickness ratio of the cervix increases the preparation of the cervix for induction by 0.25 times ($P = 0.04$). A successful response to dinoprostone can be obtained if the cervical length/thickness ratio is <1.06 mm ($P < 0.001$).

Conclusion: In conclusion, assessing the cervix's condition before labor induction by measuring the cervical length/thickness ratio may be a good predictor of cervical ripening activity.

Keywords: Cervix uteri, Cervical length, Ultrasonography, Cervical thickness

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Introduction

During pregnancy, the cervix has extensive remodeling, resulting in softening, shortening, and dilation (a process referred to as ripening) to allow delivery. Sudden transformations result in preterm birth. Cervical softening, which begins soon after conception and advances throughout pregnancy, is an essential change [1, 2]. The current clinical approach for assessing the cervix involves a subjective evaluation of cervical immobility as soft, medium, and firm categories based on digital examination [1].

The cervical condition affects the induction time and the vaginal delivery process in pregnant women for whom we are planning labor induction. If the cervical condition is not favorable, a period of cervical ripening is usually expected before induction to shorten the induction time and maximize the possibility of vaginal delivery. Although cervical status at induction suggests the chance of cesarean delivery, it does not predict whether avoiding induction of labor and managing the patient with anticipation will result in a higher chance of vaginal delivery [3, 4].

The two primary methods for cervical ripening are mechanical interventions [4] (such as balloon catheterizing) and using pharmacologic agents (such as prostaglandins) [3]. A universal definition for favorable or unfavorable cervix has not yet been established. Many clinicians consider a Bishop score < 6 indicative of an unfavorable cervix and the need for a ripening agent, while others utilize a lower threshold [5].

There is no specific practice for the best agent to use for cervical ripening. Both mechanical and pharmacologic agents are acceptable. The choice should be based on clinicians' preferences and experience unless there is a contraindication for the agent or technique [6,7]. Balloon catheters have few adverse effects and are a potentially irritated vaginal procedure for catheterization. It is easier to access than prostaglandin agents. In contrast, an advantage of prostaglandins is that they promote myometrial contractility, reducing the need for oxytocin to increase or induce labor. Contrarily, a disadvantage of using prostaglandins is the possibility of excessive uterine activity, leading to fetal heart rate (FHR) abnormalities. However, neither the theoretical advantage nor the disadvantage in clinical studies resulted in differences in clinically significant outcomes (e.g., cesarean delivery, neonatal morbidity) [6-9].

Once a ripening agent starts, it generally continues until the cervix is favorable. Prostaglandins stimulate the biophysical changes that lead to cervical ripening and growth in myometrial contractility [10].

While discussions continue about the application preparations of the Dinoprostone (PGE-2) ovule, which is commonly used in cervical maturation and induction of labor induction [11, 12], articles on the future use of this agent are also published [13]. There are no clear objective criteria regarding the efficacy and use of dinoprostone, which is still universally used as a cervical ripening agent. Although the pre-treatment Bischop score is being evaluated, the evidence for efficacy remains low.

In our experience, we frequently use the Dinoprostone ovule for cervical ripening before labor induction. However, we categorize the cervix only as soft or stiff in the pre-treatment examination. There is a need for an objective, accessible, and easy-to-use method that can predict dinoprostone treatment efficacy. We measured the thickness of the cervix before treatment and aimed to show at which measurement intervals dinoprostone treatment results in positive vaginal delivery outcomes. In this respect, we presented the first study in the literature as an article.

Materials and methods

In this article, we compiled the analysis of 183 pregnant women from 37–41 weeks from January 2020 to November 2020. We conducted this study in Bursa Yüksek İhtisas Training and Research Hospital, Gynecology and Obstetrics department. The Bursa Yüksek İhtisas Training and Research Hospital ethics committee approved the study (2011-KAEK-25 2019/07-15). The gestational week of all pregnant women included in the study was calculated according to the first-trimester ultrasound, which was correlated with their last menstrual period. Women with fetal macrosomia (>4500 grams), fetal anomaly, previous uterine surgery, short stature (less than 150 cm), occiput posterior fetal position, history of dystocia, and maternal comorbid conditions were excluded from the study.

While performing the essential evaluations (e.g., fetal biometric parameters, estimated fetal weight) before labor induction, we also evaluated the cervix ultrasonographically. We performed cervical length and thickness measurements. We also evaluated cervical maturity by performing a vaginal examination on each pregnant woman.

We observed the sagittal plane using transvaginal ultrasound for cervical length and thickness measurements by placing the probe in the anterior fornix and obtaining the sagittal plane with rotation. We obtained cervical length by measuring the distance between the internal and external cervical os [14-16]. In addition, we measured the outer cervical diameter, in other words, the distance of the cervical canal to the anterior and posterior cervical lips in the same plane, and named this cervical thickness [17-19] (Figure 1).

Figure 1: Cervical thickness measurement figure

Before oxytocin induction, we applied 10 mg of dinoprostone ovule vaginally in sustained release form to pregnant women with a stiff cervix, without dilatation and effacement. When regular uterine contractions started and dilatation of 4 cm occurred or after 12 h, the suppository was removed from the vagina. After a 1-h break, we switched to labor induction with oxytocin. During this period, the ovule was immediately removed in cases of fetal tachysystole or distress or bleeding from maternal spontaneity [5].

Then, we followed up on the latent, active, and second phases of labor. The latent phase of labor was expressed as the time from the onset of labor to 6 cm cervical dilation. The active phase of labor started at 6 cm of cervical dilation. A 4-h threshold for diagnosing labor arrest may be acceptable. The time from full cervical dilation to the delivery of the baby also formed the second stage [20]. We noted the duration of these phases and the fetal head's expulsion by performing digital examinations at recommended intervals [21]. We analyzed the relationship between prolongation in labor processes and arrest situations with ultrasonographic cervical measurements. We defined labor with protraction or arrest in the active or second phase as labor dystocia. We performed Bishop scoring for defining the favorable cervix and considered 6 points and above as successful cervical ripening [22].

Statistical analysis

A Windows-based SPSS 22.0 statistical analysis program was used (SPSS Inc., USA). We examined variables via visual (histograms, probability plots) and analytical methods (Shapiro-Wilk's and Kolmogorov-Smirnov test) to determine whether they were normally distributed. Variables are specified as mean (standard deviation) (X [SD]), the mean difference between groups, 95% confidence interval (95%CI), median (minimum-maximum [min-max]), frequency (n), and percentage (%). Student *t-test* and Mann-Whitney U test compared normally distributed and undistributed variables. Pearson and Spearman's tests were conducted to show relationships between normally and non-normally distributed or ordinal variables. The level of significance was $P \leq 0.05$. For the multivariate analysis, the possible factors identified in previous analyses were further entered into the logistic regression analysis to determine independent predictors of study outcomes. Hosmer-Lemeshow goodness of fit statistics was for evaluating model fit. A 5% type-1 error level was accepted to infer statistical significance. The diagnostic values of cervical thickness and length measures in predicting successful vaginal delivery, labor dystocia, and cesarean delivery were examined by ROC curve analysis. The sensitivity, specificity, and positive and negative predictive values were presented when a significant cut-off value was observed. While evaluating the area under the curve, a 5% type-1 error level was used to accept a statistically significant test variable's predictive value.

Results

In this study, we included 183 pregnant women after exclusion criteria. While the median value of their age was 25 years, the mean week of gestation was 39 weeks and 3 days. In the first evaluation, the mean cervix length values measured ultrasonographically were 31.6 (8.2), and the mean thickness of the cervix was 34.5 (7.5) mm. The mean cervical length/thickness ratio was 0.95 (0.3). In the digital examination, 37.8% of the pregnant women had a hard cervix, 31.1% had a medium, and 31.1% had a soft cervix. While the median latent phase duration of these pregnant women to whom we applied labor induction was 8 h (1.45-24), the active phase duration was 30 min (10-340). While the number of pregnant women ready for induction and achieved adequate patency after dinoprostone was 127 (69.4%), 56 (30.6%) pregnant women could not obtain adequate cervical dilatation. While 124 (67.8%) of the pregnant women were vaginally straight, the rest were subjected to cesarean section (Table 1).

Table 1: Descriptive analysis table according to demographic and clinical characteristics of pregnant women

Characteristics of patients (n=183)	Median (min-max) / Mean (SD)
Age (year)	25 (18-40) #
Parity	1 (0-8) #
Gestational Age (week + day)	39+3 (37-42) #
Labor induction indications (n; %)	Non-reactive NST (50; 27.3)
	Prelabor membrane rupture (29; 15.8)
	Surmaturation (48; 26.2)
	Oligohydramnios (56; 30.6)
Cervical Length (mm)	31.6 (8.2)*
Cervical Thickness (mm)	34.5 (7.5)*
Cervical Length/Thickness Ratio	0.95 (0.3)*
Cervical Consistency (n; %)	Soft (57; 31.1)
	Medium (57; 31.1)
	Firm (69; 37.8)
Dilation (cm)	No (101; 55.2)
	1-2 cm (82; 44.8)
Latent phase duration (hour, minute) (n=169)	8 (1, 45-24) #
Active phase duration (minute) (n=127)	30 (10-340) #
Second stage duration (n=127)	10 (5-90) #
Labor induction indications (n; %)	Non-reactive NST (50; 27.3)
	Prelabor membrane rupture (29; 15.8)
	Surmaturation (48; 26.2)
	Oligohydramnios (56; 30.6)
Adequate cervical ripening after treatment (n; %)	No (56; 30.6)
	Yes (127; 69.4)
Labor (n; %)	Vaginal delivery (124; 67.8)
	Cesarean (59; 32.2)
Cesarean indications (n; %)	Fetal distress (22; 12)
	Labor dystocia (37; 20.2)

Min: minimum, max: maximum, SD: standard deviation, # Descriptive analyses were presented using median (min-max), * for non-normally distributed, and (n; %) for categorical variables. mm: millimeter, n: frequency, % percentage

We performed a correlation analysis between the length and thickness of the cervix and the labor process. Accordingly, the length, thickness, or ratios of the cervix, which we evaluated prenatally, were not correlated with the duration of labor or labor stages. The latent, active phase and second stage duration did not significantly correlate. On the other hand, while the age of the pregnant women was negatively correlated with the thickness of the cervix (P = 0.004), the cervical length/thickness ratio was positively correlated (P < 0.001) (Table 2).

Table 2: Correlation analysis table of cervical length and thickness data with birth parameters in nulliparous women

	Cervical length		Cervical thickness		Length/Thickness ratio	
	r	*P*-value	r	*P*-value	r	*P*-value
Age	0.16	0.104	-0.28	0.004	0.358	<0.001
Gestational Age	-0.12	0.22	0.003	0.97	-0.103	0.29
Latent phase duration	-0.55	0.62	-0.22	0.044	0.13	0.23
Active phase duration	-0.063	0.63	-0.22	0.094	0.015	0.91
Second stage duration	-0.99	0.45	-0.022	0.87	-0.069	0.601

r: correlation coefficient, P < 0.05 was considered significant (Spearmen test)

We divided the pregnant women into two groups: successful and unsuccessful cervical ripening after dinoprostone. There was no difference between the two groups regarding the volunteers' age and gestational week. There was a difference between the two groups regarding the number of births. The thickness of the cervix, which was evaluated ultrasonographically before the treatment, revealed a difference between the two groups (P < 0.001). Accordingly, the mean cervical thickness of the pregnant women with successful cervical ripening was 34.5 (7.5) before treatment, while the mean values of the unsuccessful group were 29.2 (9.1). In addition, cervical length did not differ between the two groups (P = 0.44), while the cervical length/thickness ratio was significantly lower in the group with successful maturation (P < 0.001) (Table 3).

Table 3: Comparison of ultrasonographic and demographic parameters in terms of cervical ripening

	Successful (n=127) X (SD) / Median (min-max)	Non successful (n=56) X (SD) / Median (min-max)	Mean difference (95%CI) / U	*P*-value
Cervical length*	31.6 (8.2)	32.5 (6.8)	0.89 (-1.40 - 3.20)	0.44
Cervical thickness*	34.5 (7.5)	29.2 (9.1)	-5.32 (-6.8 - -2.8)	<0.001
Cervical length/thickness ratio#	0.9 (0.38-2)	1.1 (0.5-2)	2181	<0.001
Age (year)#	25 (18-40)	28 (18-38)	3198	0.27
Parity#	1 (0-8)	0 (0-7)	2370	<0.001
Gestational Age (week + day)#	39 (37-42)	39 (37-42)	3480	0.81

X: mean, SD: standard deviation, %: percent, min: minimum, max: maximum, CI: Confidence interval, U: U value. Descriptive analyzes are presented using (X [SD]) and median (min-max) for normally distributed and non-normally distributed, respectively. Student's t-test *$P < 0.05$ and Mann-Whitney U test # $P < 0.05$ were considered significant.

We performed binary logistic regression analysis to determine the most valuable parameter to affect cervical ripening. Accordingly, the cervical length/thickness ratio was the highest predictor of adequate maturation of the cervix with dinoprostone. Each 1 unit decrease in the length/thickness ratio of the cervix increases the preparation of the cervix for induction by 0.25 times ($P = 0.04$) (Table 4).

Table 4: Binary logistic regression table for cervical thickness and length/thickness ratio in terms of cervical ripening success

Cervical ripening	Parameters	B	Wald	OR	95% CI	*P*-value
Successful	Cervical thickness	0.035	1.4	1.03	0.97-1	0.23
	Cervical length/thickness	-1.38	4.1	0.25	0.7-0.94	0.04

CI (95%); confidence interval, OR: estimated relative risk. Wald: test statistic value. Binary logistic regression was used because the dependent variable consisted of 2 groups. The reference category was taken as the unsuccessful ripening. Parameters found significant in the previous analysis were included in the analysis. Hosmer-Lemeshow model fit was $P < 0.05$.

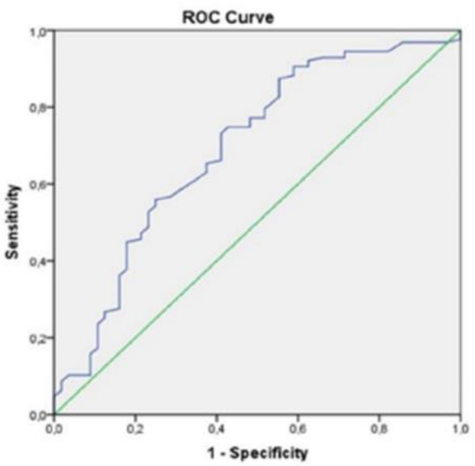
Using the ROC (receiver operating characteristics) curve, we analyzed the chance of predicting the length/thickness ratio of the cervix in successful cervical ripening with dinoprostone treatment. We determined a cut-off value for the cervix length/thickness ratio according to the ROC curve and the area under the curve table (AUC) (Table 5), and the cervical length/thickness parameter had a diagnostic value in predicting successful cervical ripening. As a result, if the cervical length/thickness ratio is <1.06 mm ultrasonographically, a successful and significant response to dinoprostone can be obtained with 73.2% sensitivity and 60.1% specificity ($P < 0.001$) (Table 5) (Figure 2).

Table 5: ROC analysis table in terms of cervical length/thickness ratio threshold value in the prediction of successful dinoprostone therapy

Area Under Curve (AUC)	*P*-value	Cut-off	Sensitivity	Specificity	PPV	NPV
0.693 (0.607 – 0.780)	<0.001	1.06	73.2%	60.1%	80.2%	58.1%

CI: Confidence Interval, PPD: Positive predictive value, NPV: Negative predictive value

Figure 2: Receiver operating characteristic (ROC) analysis chart of predicting the length/thickness ratio of the cervix in successful cervical ripening with dinoprostone treatment



Discussion

In this article, we reviewed the study in which we correlated the effectiveness of vaginal dinoprostone therapy for cervical ripening with cervical length and thickness. Before labor induction, we apply the dinoprostone vaginal ovule as a standard for the cervix to mature sufficiently. We evaluate with cervical examination before this therapy. However, an objective examination or examination method that can show the effectiveness of treatment is not yet available. By evaluating the cervix ultrasonographically before labor induction, we showed that the increase in the thickness of the cervix and the decrease in the cervical length/thickness ratio is predictive of successful dinoprostone treatment in terms of adequate maturation. We showed the cervical length/thickness ratio as the most valuable parameter. Thus, we obtained an objective pre-diagnosis method to prepare the patient for vaginal delivery planned and labor induction. This study will be preliminary in the literature with these findings.

The purpose of cervical ripening is to ease the process of cervical softening, thinning, and dilating with a resultant decrease in failed induction and induction to delivery time. Cervical remodeling is a critical component of the pregnancy process. Collagen degradation, rearrangement, changes in glycosaminoglycans, cytokine release, and increased white blood cell infiltration occur. If induction is indicated and the status of the cervix is unfavorable, agents for cervical ripening may be chosen [5]. The status of the cervix can be determined by the Bishop pelvic scoring system [22].

The currently known and accepted methods for cervical ripening are mechanical cervical dilators and synthetic prostaglandin E1 (PGE1) and prostaglandin E2 (PGE2) treatments [23, 24].

Boulvain et al. [25] showed that in pregnant women with an unfavorable cervix and scheduled for an induction, initial mechanical dilatation is associated with a lower cesarean delivery rate than oxytocin alone. There is insufficient data to evaluate the effectiveness of mechanical methods when compared with prostaglandins [5, 25, 26].

Food and Drug Administration (FDA) approves Misoprostol, a synthetic PGE1 analog, and Dinoprostone, PGE2 preparations, for cervical ripening before labor. Dinoprostone has two forms: a gel containing 0.5 mg of dinoprostone and a vaginal insert containing 10 mg of dinoprostone [5]. Vaginal prostaglandins used for cervical ripening increase the chance of delivery within 24 h but do not reduce the rate of cesarean delivery and increase the risk of uterine tachysystole with associated FHR changes compared with placebo or oxytocin alone [5, 27].

The Bishop score is the cervical assessment method and is still most commonly used in the United States [22]. It seems to be a more available tool than cervical length measurement [28] or fetal fibronectin [29] for assessing the cervical status or predicting successful induction.

Lauterbach et al. [30] performed a 4-year study in nulliparous pregnant women with a Bishop score <5. Accordingly, they compared the results between groups by applying a balloon catheter or vaginal dinoprostone to two groups of patients for cervical ripening. Accordingly, the duration of vaginal delivery was shorter in pregnant women who received a cervical balloon dilator. Bagory et al. [31], in a retrospective study of two years, did not find a significant relationship between misoprostol and dinoprostone treatments in terms of the effect of cervical ripening on vaginal delivery. Garg et al. [32] compared Misoprostol+Foley catheter and Dinoprostone+Foley catheter combinations for cervical ripening in delivery outcomes. In this study, delivery times and outcomes did not differ between the two groups. Chen et al. [7] have a meta-analysis study covering 17,387 pregnant women in 2015. This study compared the efficacy of Foley catheter, misoprostol, and dinoprostone treatments for cervical ripening in labor induction. As a result, no superiority could be shown between the three methods.

Evaluation of the cervix length has been the main subject of many studies in the literature. Numerous studies have reported that an especially short cervix is a sign of premature birth risk [33-37]. In addition, studies are showing the significant effect of cervical length on labor induction and delivery time [38-40]. Park et al. [41] showed that sonographic cervical length was more successful than Bishop's score in predicting the success of labor induction with prostaglandin or oxytocin in their study. Laenciana et al. [42] published that measuring cervical length by transvaginal ultrasonography is a better predictor of successful labor induction than the Bishop score. Cubal et al. [43], in their published study, show that the Bishop score and cervical length are good indicators of successful labor induction, especially in nulliparous women.

While there are many articles about cervical length and its effect on labor, we found no study of cervical thickness. The expression of cervical thickness was previously defined by taking a sagittal section in only one study and was used to calculate the cervical volume. This study showed that cervical volume measurement did not benefit compared to cervical length measurement for predicting preterm birth [44].

As a result of our analyses, measuring the length and thickness of the cervix before using dinoprostone for maturation can result in successful ripening and preparation for induction. The thickness of the cervix is easy to measure and evaluate, as shown in literature examples [1, 17, 44, 45], and can be standardized with more studies. This research is a novel and preliminary study regarding methods and results.

Limitations

Our study had some limitations. The number of pregnant women could have been higher, only nulliparous pregnant women could have been studied, and the data related to delivery duration could have been analyzed. Also, since the score distribution of pregnant women was narrow and there was insufficient data, we could not compare the Bishop score with cervical ultrasonographic parameters. In addition, the number of vaginal deliveries decreased slightly due to pregnant women for whom we decided to have an emergency cesarean section due to the weakening of fetal well-being in the early period after dinoprostone or at the beginning of induction. We also excluded pregnant women who could not obtain an optimal ultrasonographic image due to overall obesity.

In a longer-term study with more pregnant women, the prediction of cervical thickness, especially the duration of labor, the time between induction and delivery, and the cesarean section can be compared.

Conclusion

In this article, we found it meaningful to measure the length and thickness of the cervix ultrasonographically before dinoprostone ovule treatment. The increase in the thickness of the cervix or the decrease in the cervical length/thickness ratio, which we will evaluate before labor induction, may indicate that cervical ripening may be facilitated.

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