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What is The Value of Ultrasonographic Cervical Length Measurement for Predicting Preterm Birth in Asymptomatic Women?

Ultrasonografik Servikal Uzunluk Ölçümünün Asemptomatik Kadınlarda Preterm Doğumu Tahmin Etmedeki Rolü Nedir?

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Özet

Neonatal morbidite ve mortaliteyi azaltmak için prematür doğum riski olan hastaların belirlenmesi oldukça önemlidir. Bu çalışmanın amacı, asemptomatik düşük risk grubundaki hastalarda servikal uzunluk ölçümünün preterm doğumu tahmin etmedeki rolünün belirlenmesi idi. Onaltı-yirmiiki gebelik haftasında olan ve preterm doğum öyküsü olmayan toplam 200 hasta bu prospektif çalışmaya dahil edildi. Servikal uzunluk transvajinal ultrasonografi ile ölçüldü ve servikal uzunluk ölçümünün düşük riskli populasyonda preterm doğumu tahmin etmedeki rolü istatistiksel olarak değerlendirildi. Preterm doğum insidansı %4.5 (9/200) idi. Term ve preterm grupların ortalama yaşları (±S.D.) sırasıyla 27.7±6.98 ve 24.9±4.47 idi (p=0.222). Term grupdaki hastaların ortalama servikal uzunluk ölçümü (35.0±4.57 mm) ile preterm grupdaki hastaların ortalama servikal uzunluk ölçümü (36.5±6.93 mm) arasında istatistiksel fark tespit edilmedi (p=0.887). Sezaryen doğum oranı preterm grupta anlamlı olarak daha yüksekti (p=0.04). Düşük risk grubundaki asemptomatik populasyonda tek başına ultrasonografik servikal uzunluk ölçümünün preterm doğumu tahmin etmedeki rolü sınırlıdır. Bu hastalarda servikal uzunluk taraması yapılmasının önerilebilmesi için kanıtlar yetersizdir. Bu nedenle taramadan fayda görecek hastaların belirlenebilmesi için prospektif geniş çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Preterm doğum, servikal uzunluk, ultrasonografi, asemptomatik, düşük risk

Abstract

Identification of patients who will deliver prematurely is extremely important to decrease neonatal and maternal morbidity and mortality. The aim of this study was to evaluate the value of cervical length (CL) measurement in predicting preterm birth (PTB) in asymptomatic low risk women. A total of 200 consecutive asymptomatic patients between 16-22 gestational age who had no history of PTB previously were included in this prospective study. CL was measured by transvaginal ultrasonography and the predictive value of CL for PTB was evaluated in this low risk population. The incidence of PTB was 4.5% (9/200). The mean age (±S.D.) of the preterm and term groups was 27.7±6.98 and 24.9±4.47 years, respectively (p=0.222). The CLs at 16-22 weeks were not statistically different between the term group (35.0±4.57 mm) and the preterm group (36.5±6.93 mm) (p=0.887). Cesarean delivery rate was significantly higher in preterm group (p=0.04). Ultrasonographic CL measurement alone has limited value in prediction of preterm delivery in a low risk asymptomatic population. Also there is insufficient evidence to recommend routine CL screening in this subpopulation. Further larger prospective studies are needed to identify patients that may benefit most from such screening.

Key words: Preterm birth, cervical length, ultrasonography, asymptomatic, low risk.

INTRODUCTION

Preterm labor is one of the most common reasons for prenatal admission to hospital in worldwide (1,2), however fewer than 10% of patients with symptoms of preterm labor will deliver prematurely (3). Therefore, identification of patients who will deliver prematurely will not only decrease neonatal morbidity and mortality, but also will decrease the number of unnecessary hospitalization and financial cost. Many methods have been attempted to predict preterm birth (PTB) but none of them have fulfilled ideal criteria of screening test. Among these methods, ultrasonographic cervical length (CL) measurement is the most researched one, however, there are conflicting results about the predictive value of CL. Because, some studies have been conducted in symptomatic women (3-10), while others in asymptomatic women at different gestational age and with a different threshold CL values (11-22). As known, women who had PTB previously are at increased risk for PTB in the subsequent pregnancy [23]. However this statement was taken into account in limited studies (13, 19). We, therefore, performed this prospective study to evaluate the predictive value of CL in asymptomatic women at low risk for PTB.

METHODS

Between December 2004 and April 2005, a total of 200 consecutive pregnant patients between 16-22 gestational age admitting to Ankara Etlik Zübeyde Hanım Maternity and Women's Health Research and

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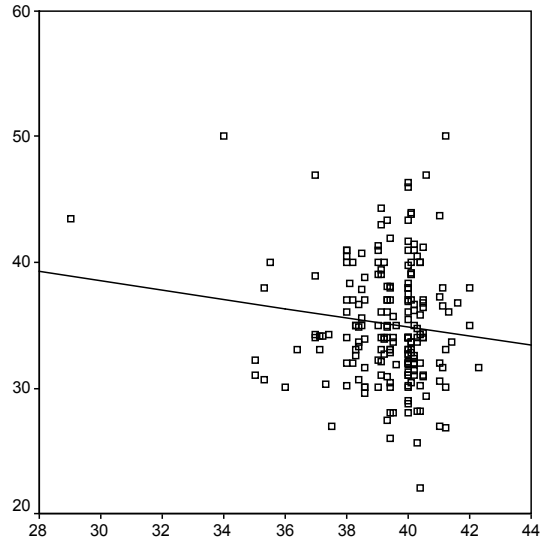

Figure 1. The distribution of CL measurement and gestational age at birth

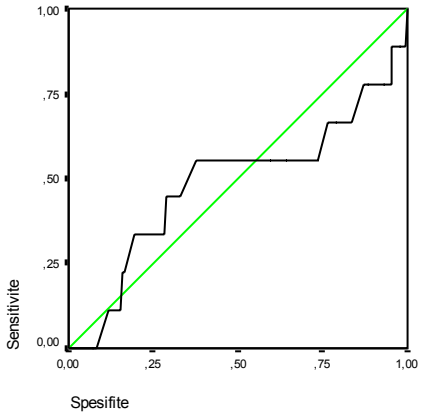

Figure 2. ROC curve

Teaching Hospital for routine antenatal visits without any symptoms of preterm labor were included in this prospective study. This hospital is a tertiary referral center for high-risk pregnancies, with about 18000 deliveries a year. Patients who had multiple pregnancy, cervical insufficiency, fetal anomaly and maternal medical complications such as diabetes mellitus, hypertension, thyroid disorder, history of cervical conization/cerclage and preterm delivery were not enrolled in the study. In all cases, gestational age was calculated from the date of the last menstrual period or by an ultrasound examination in early pregnancy. Ultrasound examination was performed using Aloka Prosound SSD 5500 5.0–6.5-MHz transvaginal probe. The women were asked to empty their bladder before the procedure and a sagittal view of the full length of the cervical canal was obtained. Care was taken not to press onto the cervix with the probe so that the anterior and posterior cervical lips were equal in thickness. CL was measured by placing the calipers at the furthest points at which the cervical walls were juxtaposed. At least three images were obtained and the mean measurement recorded. To eliminate the possibility of interobserver variability in the measurement technique, the first-named author in this paper performed all the ultrasonographic examinations. Demographic and medical data were collected. All patients were followed up to delivery. Outcome variable was the occurrence of spontaneous preterm delivery at < 37 weeks. The ethics committee of our institution approved the study protocol, and the patients gave written consent for inclusion. Spontaneous delivery occurring before 37 weeks was defined as preterm.

A receiver operating characteristic (ROC) curve was constructed for CLs to test the effectiveness of various cutoff points in predicting premature delivery. The areas under the ROC curves were calculated and the sensitivity, specificity, and positive-predictive value (PPV) for the CL of the most appropriate cutoff point were calculated for predicting preterm delivery. CL measurements were expressed as the mean ± standard deviation (S.D.). Student's t-test was used to determine the differences in the CLs of patients who delivered either at term or preterm. A Pearson correlation test was used to test for independence between CL and the gestational week at preterm delivery. The SPSS package (version 11.5) was used for statistical analysis. A value of $P < 0.05$ was considered significant.

RESULTS

The clinical characteristics of 200 women are shown in Table 1. The mean age was 25.0 (range 17-40) and the incidence of PTB was 4.5% (9/200). Clinical and obstetric parameters of patients in preterm and term group are presented in Table 2. The groups were not statistically different with regard to parity, previous miscarriages, education level or cigarette smoking ($p>0.05$). The mean CL of preterm group and term group was 36.5 ± 6.93 mm and 35.0 ± 4.57 mm, respectively ($p =0.887$). Twenty-two percentage (2/9) of patients in preterm group was nulliparous and

Table 1. Clinical characteristics of 200 patients.

	Mean	Standard Deviation	Minimum	Maximum
Age (years)	25,0	4,62	17	40
Body mass index (kg/m^2)	23,5	3,84	16	38
Gestational age (LMP*) (weeks)	18,8	1,47	16,4	22
Gestational age (TVUSG**) (weeks)	18,6	1,55	16	22
Gestational age at birth (weeks)	39,4	1,52	29	42,3
CL*** (mm)	35,1	4,69	22	50

*LMP: Last Menstruel Period
**TVUSG: Transvaginal Ultrasonography
***CL: Cervical Length

Table 2. Comparison of groups according to clinical and obstetric parameters.

	Preterm group	Term group	p
Number of patients (%)	9 (4.5)	191 (95.5)	
Age (years)	27.7	24.9	0.2
CL (mm)	36.5	35.0	0.8
Parity	1	0	0.09
Preterm labor* (n)	5 (55.6%)	6 (3.1%)	<0.001
Cesarean delivery (n)	5 (55.6%)	45 (23.6%)	0.04
Body mass index (kg/m2)	24.3	23.4	0.3

* Previous preterm labor history in the current pregnancy

78% (7/9) was multiparous. One -hundred-and-ninety-one patients who had term delivery 100 (52.4%) were nulliparous and 91(47.6%) were multiparous. There was no statistical difference between groups (p=0.096). We compared delivery mode of these patients and found that cesarean delivery rate was significantly higher in preterm group (Table 2). Furthermore, we evaluated if there was a history of hospitalization due to preterm labor in the present pregnancy, and determined that 5 of 9 patients in preterm group were hospitalized due to preterm labor. The difference was statistically significant (Table2). No correlation between CL and gestational age at delivery was found (rho=-0.074) (p=0.3). The distribution of CL according to gestational age at delivery is shown in Figure 1. Also there was no relation between PTB and CL when cut-off value was regarded as 25mm (P=0.9).

Patients were divided into three groups according to age. There were 17 (8.5%) patients in the <20 years age group, 157 (78.5%) in 20-30 years and 26 (13%) patients in the >30 years age group. The mean CL of patients at <20 years, between 20-30 years and at >30 years were 32.7, 35.2 and 36.2 mm, respectively. There was no significant difference with regard to CL and preterm delivery between groups. ROC curve was constructed for CLs to test the effectiveness of predicting premature delivery. However, the area under the ROC curve was calculated as 0.486 and found insignificant (p=0.888) (Figure 2).

DISCUSSION

This study was conducted on 200 asymptomatic pregnant women who were at low risk for preterm birth due to without any prior spontaneous preterm birth history. The preterm delivery rate in the present study (4.5%) was lower than the reported rate of 8-10% in general population, suggesting that the study population represented predominantly low-risk women. Our results showed that ultrasonographic CL measurement in asymptomatic low risk population is not a good predictor of PTB. PTB is one of the leading causes of perinatal morbidity and mortality (24), thus determining patients who are at high risk group is very important. On the other hand, despite improvement in antenatal follow up programs and intensive research efforts on predicting and preventing PTB, the prevalence still remains at 8-10% (25). Unfortunately the incidence seems to increase in the coming years due to often use of assisted reproductive techniques (26). In clinical practice, evaluation of cervix by digital examination has been used for the determination of high-risk women (27). It was adopted as a simple, cheap and useful method in the assessment of the cervical consistency, shape, station and dilatation, but its subjectivity and insufficiency to evaluate the supravaginal portion and internal cervical os limit the clinical usage (28). Therefore, a number of new methods have been attempted for the prediction of PTB. The most popular one was the evaluation of cervix by TVUSG and it has been suggested as a method for quantitative and qualitative cervical evaluation and considered to decrease inter and intraobserver variations (29). Among the different sonographic parameters used, the majority of investigators have focused on CL measurement as a well accepted and standardized method of cervical assessment. However, there was wide variation in the gestation at which ultrasound cervical length measurement was carried out in women and the definition for thresholds of abnormality. The most common gestation at which ultrasound measurement of cervical length was carried out was in the late second trimester, between 20 and 24 weeks' gestation. The most common threshold used in asymptomatic women was 25 mm at this gestation and this was evaluated in two ideal quality studies (13,22). The outcome frequently used by studies on asymptomatic women was birth before 37 weeks' gestation but among ideal quality studies, the outcome frequently used was spontaneous preterm birth before 34 weeks' gestation. Among symptomatic women, the most common threshold used was 15 mm and the most common outcome used was spontaneous preterm birth within

Table 3. Studies evaluated CL for predicting PTB in asymptomatic women

Study	Number of patients	Gestational age at CL measurement (weeks)
Dilek, 2006	250	22
Hibbard, 2000	760	16-22
Leung, 2005	2880	18-22
Mara, 2002	247	18-20
Taipale, 1998	3694	18-22
To MS, 2001	6819	22-24
Berghella, 1997	96	14-30
Andersen, 1990	113	30
Andrews, 2000	69	20-24
		25-29
Iams, 1996	2915	24-28
Heath, 1998	2567	23

7 days of testing using this threshold (3-10). It is well known that ideal screening test must be easy to utilize, minimally invasive, inexpensive and must have a good predictive value. Unfortunately, with regard to these criterias no ideal screening test for preterm delivery exists at present. Many studies have revealed a relationship between CL and PTB, but most of them reported a low sensitivity, specificity and PPV rates. The prospective study conducted by Tsoi et al. in 2005 is the largest study (510 women) in the literature about the predictive value of CL in symptomatic women. Their results showed a low sensitivity and PPV rate for predicting PTB (3). Also, low sensitivity and PPV rates are reported in asymptomatic population (16-17,19). Studies which have evaluated the predictive value of CL in asymptomatic population are shown in Table 3. As mentioned before, the most common threshold used in asymptomatic women was 25mm. One of the largest trial conducted in 2915 asymptomatic women determined low sensitivity and PPV when the cut off value was set at 26mm (22). Similarly, in another large trial performed by Taipale et al. CL of 3694 asymptomatic patients were analyzed for predicting PTB, the sensitivity was found 19% and PPV 1.8%, when the cut-off value was set at ≤31mm (19). Combined data from the three largest studies involving a total of 7861 women showed that the detection rate of birth before 35 weeks was 34% for a false-positive rate of about 5% and concluded that CL measurement by TVUSG was ineffective to predict PTB in low risk patients (19, 21-22, 30). Conclusively, studies conducted in asymptomatic women showed low sensitivity and PPV as studies conducted in symptomatic women (3-6, 8). Women with a prior spontaneous preterm birth are at three to four times higher risk for a subsequent preterm birth (23). However, in most trials defined above, history of PTB was not taken into account except a few studies. Andrews et al. included 69 women who had PTB history and evaluated the predictive value of short CL <20 gestational weeks. They concluded that women with history of spontaneous PTB who have short CL or funneling are at increased risk of subsequent spontaneous PTB (13). In another study conducted by Owen et al.183 asymptomatic women who previously had experienced a spontaneous birth before 32 weeks' gestation and a CL< 25 mm at the initial sonographic examination was determined to be related to spontaneous preterm birth with a sensitivity, specificity and PPV of 19%, 98% and 75%, respectively (31).

In 2009, a cochrane review concluded that there is insufficient evidence to recommend routine screening of asymptomatic or symptomatic women with CL measurement and also similar suggestions were reported in ACOG Bulletin (32-33). In light of the studies, in asymptomatic population without any risk factor for PTB, suggesting CL measurement as a screening test seems not to be cost effective. The best of our study is the exclusion of patients with a history of PTB, so asymptomatic patients who are at low risk for PTB were included in the study. Therefore, the incidence of PTB was lower than general population. Moreover, limitation of the present and other studies is the small number of PTBs. In conclusion, there is no consensus about the predictive value of short cervix for predicting PTB and also there is insufficient evidence to recommend routine CL screening in asymptomatic women. Our results revealed that CL measurement alone is not a good predictor of PTB especially in asymptomatic low risk population. Further trials are needed to identify the optimum gestation and subgroups that may benefit most from such screening and therapeutic interventions. These trials should ideally be multi-centre, use standardized criteria for defining low and high-risk pregnancy, assess wider-ranging perinatal outcomes in addition to PTD, and evaluate risk–benefit, cost–benefit and quality of life measures.

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