O R I G I N A L   A R T I C L E

Cervical length as a predictor of preterm delivery: gestational age-related percentiles vs fixed cut-offs

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Abstract. *Background:* To determine whether preterm delivery is more effectively predicted by sonographic cervical length measurement using fixed cut-off or gestational age-specific percentiles. *Methods:* One hundred and eight patients hospitalized for suspected preterm labor (PTL) were studied prospectively between the 20th and the 33rd week of gestation. *Results:* Cervical length below 15 mm, 25 mm and the 2.5[th] centile showed substantially equivalent odds ratios for delivery within 7 days (7.5, 7.6, and 7.1, respectively), while for delivery before the 34th week the odds ratios varied between 3.6 with cervical length <2.5[th] centile and 6.2 with cervical length <25 mm. Moreover, the negative predictive value for delivery within 7 days exceeded 90% when cervical length was above 25 mm, the 10th and the 2.5[th] percentile, and 85% when above 15 mm. *Conclusion:* The comparison of fixed and gestational age-specific cut-offs demonstrates a better reliability of fixed cut-offs (15 or 25 mm) in predicting preterm delivery, both before 34 weeks and within 7 days of the ultrasound examination. (www.actabiomedica.it)

Key words: Cervical length, ultrasound, preterm delivery

Introduction

Preterm delivery is the single major cause of neonatal morbidity and mortality, accounting for 65% of neonatal deaths and for 50% of infant neurological disabilities (1). While prevention of preterm delivery (PTD) due to preterm labor (PTL) is a primary goal of obstetricians, its incidence rate does not appear to have decreased over the last 20 years (2). Recently, ultrasound assessment of cervical length, to be used alone or in combination with biochemical tests, has been considered as a possible new method to identify women at high risk for PTD. It has been demonstrated that the combination of short cervical length, previous preterm birth caused by preterm prelabor rupture of membranes (pPROM), and positive fetal fibronectin screening is the most highly associated risk factor for PTD in the current gestation (3).

Transvaginal sonography is considered more reliable than digital assessment of cervical length, which

is generally believed to underestimate the actual measurement by about 14 mm (4, 5). Sonographic cervical length measurement seems to be a simple, effective method in screening patients with suspected preterm labor and in identifying those who do not need any active treatment. For instance, a sonographic cervical length >30 mm has a 97-98% negative predictive value for preterm delivery at ≤37 weeks (6-8).

The purpose of our study was to verify whether PTD is more effectively predicted by sonographic cervical length measurement using fixed cut-off values for the whole pregnancy or gestational age-specific percentiles.

Materials and methods

All patients hospitalized between January 2002 and May 2004 for suspected preterm labor, defined as ≥4 painful uterine contractions every 20 minutes, had

transvaginal scans to determine cervical length. The probe was placed in the anterior fornix of the vagina and a saggital view of the cervix was obtained, with the echogenic endocervical mucosa being used to measure the distance between the internal and the external os. Three consecutive measurements were obtained and, since the shortest measurement is usually associated to uterine contractions, an average of the measurements was preferred. Exclusion criteria were twin pregnancies, singleton pregnancies in which gestational age could not be sonographically determined before the 22nd week, and pregnancies with premature rupture of membranes (PROM) or with cervical dilatation ≥3 cm at digital examination, where the diagnosis of preterm labor was unquestionable. Other exclusion criteria included active vaginal bleeding, placenta previa, and cervical cerclage. The patients gave their informed consent to the prospective observational study. The study protocol was approved by the hospital's ethics board. Data on gestational age, type of and indications for delivery were recorded for all patients. Those cases presenting with maternal or fetal indications for preterm delivery were excluded from the study.

The study was conducted on 108 patients between the 20th and the 33rd week of gestation. The efficacy of sonographic cervical length measurement at admission as a PTD predictor, both within 7 days of the ultrasound examination and before the 34th week, was tested using two constant cut-off values (15 mm and 25 mm) unrelated to gestational age and the 2.5th and 10th percentiles of our reference curve (9). The fixed cut-offs were chosen based on two systematic reviews (10, 11) which reported optimal cut-off values of cervical length as PTD predictors that ranged from 15 to 35 mm, with 25 mm being the most frequently used. In particular, the 15mm cut-off seems to be useful in predicting delivery within 7 days of presentation in women with threatened preterm labor (12).

The results at sonography were blinded to the medical staff. Therefore tocolysis was started based on digital examination soon after the cervical study and regardless of its results. In addition to tocolytics, 24 mg of betamethasone (12 mg/24 hrs) were given to reduce the incidence of respiratory distress syndrome and intraventricular hemorrhages. Those patients who

did not receive tocolytics were put to bed rest. For each cut-off value, we calculated the odds ratio and considered common diagnostic parameters, such as sensitivity, false positive rates, and the positive predictive value. Their respective diagnostic accuracies (the sums of true positives and true negatives expressed as percentages of the total number of cases) were compared using the Mc Nemar tests.

Results

Demographic characteristics and the use of tocolytic treatment are summarized in Table 1. The median maternal age was 32 weeks (range, 17-41) and the median cervical length at admission was 34 mm (range, 3-61). Delivery at <34 weeks of gestation occurred in 25 out of 108 patients (23.1%), who had a median cervical length at admission of 23 mm (range, 3-56). The remaining 83/108 patients (76.8%) who gave birth at ≥34 weeks had a median cervical length at admission of 35 mm (range, 10-61). The patients who delivered within 7 days of ultrasound were 19/108 (17.5%), their median cervical length at admission being 21 mm (range, 3-56) (Fig. 1). Tocolysis was given to all 25 patients who delivered before 34 weeks, including those who delivered within 7 days of ultrasound and to 45 women who delivered after 34 weeks. Univariate analysis of the different cervical length measurements showed that all four considered parameters (Table 2) were associated with a significantly higher odds ratio of preterm delivery within 7 days of ultrasound, ranging from 4.5 (95% CI: 1.41-14.94) for cervical length <10th percentile to 7.66 (95% C.I.: 2.69-21.80) for cervical length <25 mm. The sa-

Table 1. Demographics characteristics of 108 patients and clinical features at study entry *(Data are given as median and range)*

Maternal age (yrs)	32 (17-41)
Gestational age at admission (wks)	29 (20-33)
Gestational age at delivery (wks)	35 (20-41)
Nulliparous No.	41 (37.9%)
Cervical length (mm)	34 (3-61)
Caucasian No.	100 (92.5 %)
African No.	5 (4.6%)
Others No.	3 (2.7%)
Tocolysis No.	70 (64.8%)
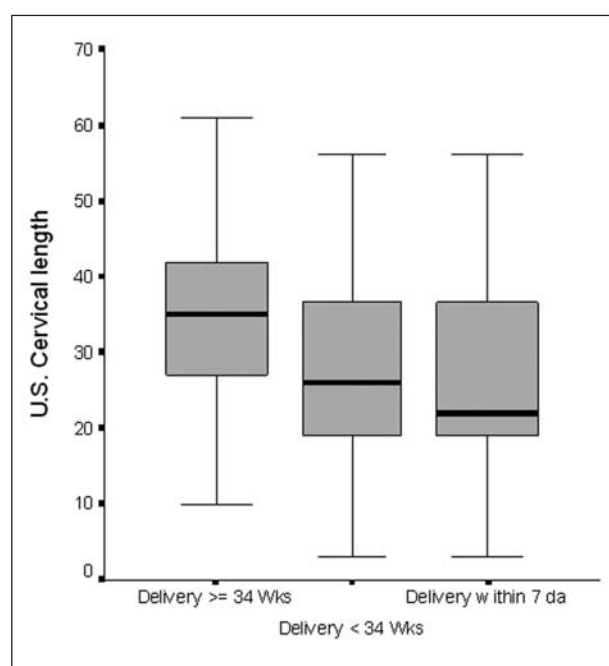
Figure 1. Median Interquantile ranges and Ranges of the ultrasonographic cervical length.

me concordance of parameters was not observed for prediction of PTD before the 34th week (Table 2), because the 10th percentile was not associated with increased risk, unlike the three other cut-offs. For this prediction, the highest odds ratio − 6.27 (95% CI: 2.36-16.65) − was associated also with cervical length <25 mm. The statistical comparison between the diagnostic accuracies of the different cut-offs in predicting preterm delivery within 7 days of ultrasound (Ta-

Table 2. Univariate analysis of delivery within 7 days and before 34 weeks of gestation, based on sonographic cervical length at admission

	Odds ratio	95% CI	P
Delivery within 7 days			
15 mm	7.58	1.81-31.75	0.008
25 mm	7.66	2.69-21.80	0.0001
2.5th centile	7.15	2.30-22.18	0.0001
5th centile	4.59	1.41-14.94	0.015
Delivery before 34 weeks' gestation			
15 mm	4.92	1.35-17.86	0.02
25 mm	6.27	2.36-16.65	0.000
2.5th centile	3.68	1.44-9.41	0.01
5th centile	1.70	0.66-4.39	0.37

ble 3) indicated an 83.3% and a 76.8% rate for the 15mm and 25mm values, respectively, i.e. significantly higher than the 73.1% and 59.2% rates for the 2.5th and 10th percentiles. Furthermore, the fixed cut-off values showed a better diagnostic accuracy (77.7% and 76.8%, respectively) in predicting PTD before the 34th week compared with percentiles (66.6% and 50%, respectively) (Table 4).

Discussion

In our study, only 23% of patients with regular painful contractions gave birth before 34 weeks of gestation and in 17%, delivery occurred within 7 days of ultrasound. Our data analysis confirms that sonographic cervical length measurement is a useful diagnostic tool in predicting PTD, both within 7 days of ultrasound and before the 34th week. For PTD within 7 days, the risk increased 7-fold with cervical length <15 mm and <25 mm, and 4- to 7-fold with cervical length <5th and <2.5th percentiles of our reference curve (Table 2). For PTD before the 34th week, the odds ratio was 6.2 for the 25mm value, 4.9 for the 15mm value, and 3.6 for the 2.5th percentile value (Table 2). Diagnostic accuracies in predicting PTD were definitely better for fixed cut-off values, both for delivery within 7 days (Table 4) and before the 34th week (Table 3). However, they failed to demonstrate significant differences between the 15 and 25 mm thresholds. In prediction of PTD within 7 days, the lower cut-off value of 15 mm − which indicates a remarkable shortening of the cervical canal − had a sensitivity rate as low as 26%, but a very low incidence rate of false positives, corresponding to 4.5%. By contrast, the higher cut-off value of 25 mm had a higher 66% sensitivity rate, but also a higher incidence of false positives, up to 20.7%. The same trend was observed for prediction of PTD before the 34th week.

The 15mm and 25mm cut-offs were constantly below the 10th percentile and very often also below the 2.5th percentile of our reference curve, thus effectively screening those cases with a more marked shortening of the cervical canal and consequently a greater risk of preterm delivery. A critical analysis of our reference curve actually demonstrated higher values for all the

Table 3 - Diagnostic tests and diagnostic accuracy of four sonographic length cut-offs in predicting delivery within 7 days at admission

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Diagnostic accuracy (%)
15 mm	26.3 (5/19)	95.5 (85/89)	55.5 (5/9)	85.8 (85/99)	83.3 (90/108)
25 mm	66.6 (14/21)	79.3 (69/87)	43.7 (14/32)	90.7 (69/76)	76.8 (83/108)
2.5th centile	72.2 (13/18)	73.3 (66/90)	35.1 (13/37)	92.9 (66/71)	73.1 (79/108)
5th centile	78.9 15/19)	55.0 (49/89)	27.2 (15/55)	92.4 (49/53)	59.2 (64/108)

15 mm vs 25 mm p=0.90   15 mm vs 2.5th c p=0.04   15 mm vs 5th c p=0.001
                          25 mm vs 2.5th c p=0.04   25 mm vs 5th c p=0.001
                          2.5th c vs 5th c   p=0.001

Table 4 - Diagnostic tests and diagnostic accuracy of four sonographic cervical length cut-offs in predicting delivery before 34 weeks' gestation at admission

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Diagnostic accuracy (%)
15 mm	24.0 (6/25)	93.9 (78/83)	54.5 (6/11)	80.4 (78/97)	77.7 (84/108)
25 mm	56.0 (14/25)	83.1 (69/83)	50.0 (14/28)	86.2 (69/80)	76.8 (83/108)
2.5th centile	64.0 16/25)	67.4 (56/83)	37.2 (16/43)	86.1 (56/65)	66.6 (72/108)
5th centile	68.0 (17/25)	44.5 (37/83)	26.9 (17/63)	82.2 (37/45)	50.0 (54/108)

15 mm vs 25 mm p=0.91   15 mm vs 2.5th c p=0.009   15 mm vs 5th c p=0.0001
                          25 mm vs 2.5th c p=0.009   25 mm vs 5th c p=0.0001
                          2.5th c vs 5th c p=0.0001

percentiles compared with those reported by other investigators, such as in a previous multicenter study published by Iams et al (8). This could probably be due to differences in the populations studied: Iams's population included a considerable proportion of patients (4.3%) who delivered before 35 weeks and whose cervical length was therefore presumably already reduced. Furthermore, in Iam's study, only the lowest value was recorded after subsequent cervical length measurements.

In one of the most extensive review investigations available at the time of writing, Honest et al. (11) claimed that transvaginal cervical sonography identifies women who are at higher risk of PTD. However, the clinical situation more frequently considered was that of asymptomatic patients at <20 weeks of gestation using a threshold cervical length of 25 mm with PTL before the 34th week as the standard reference. For symptomatic women, the authors stressed that it was not possible to draw the same conclusions due to the paucity of test accuracy. Tsoi et al. (12) reported that among 216 patients with threatened PTL, 37% of those with cervical length <15 mm delivered within 7 days, indicating an odds ratio for delivery of 101 (95%

CI: 12-800; p <0.0001). The same authors found that the 25mm cut-off was the most effective in discriminating between true and false labor in twin pregnancies (13).

Our data indicate that both cut-off thresholds are effective in predicting PTD in singleton pregnancies, but − at least for the 15mm threshold − the odds ratio found in our analysis (OR: 7.5; 95% CI: 1.81-31.75) is definitely lower than that of Tsoi et al. (12) for prediction of PTD within 7 days. In our study, the 25mm threshold was also effective, with a positive predictive value of 43.7% for PTD within 7 days and of 50% before the 34th week. These values are similar to those found by Crane et al. (6), who reported a positive predictive value of 46% for PTD before the 34th week with cervical length <30 mm, but are very different from those of Murakawa et al. (7), who reported a 100% rate with cervical length <20 mm. These remarkable differences suggest the importance of standardization in defining threatened PTL and sonographic cervical assessment.

In conclusion, sonographic cervical length measurement proves to be a simple, effective method for screening patients with increased risk of PTD, both within 7 days of ultrasound and before the 34th week of gestation − even though our data analysis indicates that the probability of having PTD given a positive test is around 50%. Another aspect that should not be underestimated is the negative predictive value exceeding 90%, both for the >25mm value, the 10th and the 2.5[th] percentile. In other words, if a patient with suspected PTL has a sonographic cervical length ≥2.5[th] percentile or ≥25 mm, it can be reasonably estimated that delivery will not occur within 7 days of ultrasound, with a 93% and a 91% probability rate, respectively. Together with clinical considerations to be made on a case-by-case basis, these data could be very helpful in avoiding unnecessary tocolytic and corticosteroid treatment.

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