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Is Midtrimester Cervical Length Associated with Preterm Birth in Women Evaluated for Preterm Labor?

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Abstract

Objective—This article aims to evaluate whether midtrimester cervical length (CL) is associated with improved prediction of preterm delivery in women presenting with preterm labor.

Study Design—This is a retrospective cohort study of women with a singleton gestation who underwent routine CL screening between 18 and 24 weeks of gestation between 2010 and 2014 who were later evaluated for preterm labor. Women were stratified by midtrimester CL quartile. Bivariable and multivariable analyses were performed to identify factors independently associated with preterm birth <37 weeks, <34 weeks, and delivery within 7 days of evaluation. Receiver operating characteristic (ROC) curves were created for multivariable equations with and without CL quartile to determine whether addition of CL improved the predictive capacity of the model for predicting preterm birth.

Result—A total of 460 women were evaluated for preterm labor and had midtrimester CL measurements available. When CL quartile was incorporated into a regression model including demographic and clinical characteristics associated with preterm birth, the area under the ROC curve was not improved (0.775 vs. 0.786, $p = 0.20$).

Conclusion—While a shorter midtrimester CL quartile is associated with an increased incidence of preterm delivery in women evaluated for preterm labor, the addition of this variable to an existing model does not improve prediction of preterm birth.

Keywords

cervical length; preterm labor; preterm birth; preterm birth prevention

Preterm labor and preterm birth are significant sources of both health care spending and perinatal morbidity and mortality in the United States. Approximately 12% of deliveries in the United States occur preterm, with 40 to 45% of those births preceded by spontaneous

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Conflict of Interest
None.

preterm labor.¹ Preterm labor often requires transfer to a tertiary care center, antepartum admission, as well as tocolytic and steroid drug administration, all of which contribute to significant health care spending. Estimates of the annual U.S. cost for treatment of preterm labor exceed \$800 million.²

While these costly interventions are made in an effort to improve neonatal outcomes in the event of preterm delivery, fewer than 30% of women who present with preterm labor will ultimately deliver preterm.³ Furthermore, interventions such as antenatal steroids have a limited window of efficacy, with maximal neonatal benefits afforded if delivery occurs within 7 days of administration.⁴ Yet our current ability to predict delivery in this window is even more limited; a 2009 meta-analysis of 32 studies including more than 5,000 women with symptomatic preterm labor demonstrated that the incidence of preterm birth within 7 days ranged from 1.9 to 29.7%.⁵ If women could be more accurately risk stratified, interventions such as antepartum admission, tocolysis, and steroid administration could be utilized more judiciously.

To risk stratify, obstetricians need tools to be able to predict preterm delivery when a woman presents with preterm labor. There are multiple prediction models available that take into account demographic information as well as clinical factors available at the time of preterm labor evaluation.⁶⁻⁹ However, these models have insufficient sensitivity to be applied clinically.

More objective variables such as transvaginal cervical length and fetal fibronectin testing have also shown utility for predicting preterm delivery, especially when used in combination.¹⁰ Knowledge of transvaginal cervical length at the time of presentation has also been shown to lower the incidence of preterm birth in women with threatened preterm labor.¹¹ However, these two clinical tools are expensive and may not be readily available in many obstetrical triage settings at the time when management decisions must be made. A short midtrimester cervical length has been associated with the risk of preterm birth.¹²⁻¹⁶ With many centers obtaining routine cervical length at the time of the anatomic survey,¹⁷ this clinical data point may be available to incorporate into a model designed to predict preterm birth in women presenting in preterm labor. The primary objective of this study is to evaluate whether the addition of midtrimester cervical length is associated with improved prediction of preterm delivery in women presenting with preterm labor compared with standard clinical assessments alone.

Materials and Methods

This is a retrospective cohort study of women with a singleton gestation who underwent routine cervical length screening between 18^{0/7} and 23^{6/7} gestations from December 2010 to January 2014 and subsequently presented at the Northwestern Memorial Hospital for the evaluation of preterm labor. Women were identified using the umbrella ICD-9 code for preterm labor. Women were included if they were 18 years or older, evaluated between 24^{0/7} and 36^{6/7} for preterm labor, and had a midtrimester cervical length measurement and delivery at the Northwestern Memorial Hospital. Women were excluded if they were diagnosed with rupture of membranes concomitantly with evaluation for preterm labor, were

pregnant with a multiple gestation, underwent an indicated preterm delivery, had a cerclage in place, experienced an IUFD, or if delivery information for the associated pregnancy was not available.

Cervical lengths were obtained transvaginally by ultrasonographers who were trained according to the method of Iams et al.,¹² and all images were reviewed by an attending sonologist. The measured midtrimester cervical length was abstracted from the clinical ultrasound records. If multiple cervical length measurements were obtained, the value taken closest to 20 weeks of gestation was included. For the purposes of the primary analysis, cervical length was divided into quartiles. Demographic and clinical data collected included maternal age, race and ethnicity, insurance status, parity, smoking history, history of a spontaneous preterm birth, body mass index (BMI) at the time of delivery, history of sexually transmitted infection(s), and history of any excisional procedure on the cervix. Details of the preterm labor diagnosis and management were also abstracted, including the cervical dilation and effacement in centimeters on admission as recorded by the clinical team, the administration of betamethasone, and the use of tocolytic medications. For purposes of analysis, the initial cervical dilation was categorized as <1, 1 to 2, or >2 cm and effacement was categorized as a cervical length <1 or ≥1 cm.

The primary outcome was preterm delivery (<37 weeks). Secondary outcomes were delivery before 34 weeks and delivery within 7 days of preterm labor diagnosis. Bivariable analyses were performed using χ^2 or Fisher's exact tests for categorical variables and ANOVA or Kruskal–Wallis tests for continuous variables. A *p*-value of 0.05 defined statistical significance. Multivariable analyses, including covariates associated with cervical length quartile with a *p* < 0.05, were then performed to determine the independent relationship between cervical length quartile and preterm birth outcomes. For the primary outcome of preterm birth <37 weeks, receiver operating characteristic (ROC) curves were created for a model with and without cervical length quartile to assess any change in predictive capacity associated with the incorporation of midtrimester cervical length. Given the relatively limited sample size and risk of overfitting, a sensitivity analysis was performed comparing ROC curves between a model including only cervical dilation on admission and a model that included both cervical dilation on admission and cervical length quartile.

Analyses were performed using Stata version 14.0 (StataCorp, College Station, TX). The study was approved by the Northwestern University Institutional Review Board with a waiver of consent prior to its initiation.

Results

During this study period, 662 women were identified who presented with preterm labor between 24^{0/7} and 36^{6/7} weeks, and then went on to deliver at Northwestern Memorial Hospital. Ultimately, 460 of these women met inclusion criteria (Fig. 1), and 69 (15%) went on to deliver preterm. The median cervical lengths and interquartile ranges for quartiles 1 through 4 were 3.4 cm (3.1–3.6 cm), 4.1 cm (4.0–4.2 cm), 4.6 cm (4.4–4.7 cm), and 5.3 cm (5.0–5.7 cm), respectively.

Patient demographics and clinical characteristics, stratified by cervical length quartile, are shown in Table 1.

Women with a shorter cervical length quartile were more likely to have public insurance and more likely to be nulliparous. Furthermore, women with a shorter cervical length quartile were more likely to initially present with a more advanced cervical dilation and a more effaced cervix. They were also more likely to be given antenatal steroids, suggesting a more concerning clinical presentation. There were no differences across quartiles in maternal age, race/ethnicity, history of spontaneous preterm birth, BMI at delivery, smoking status, history of prior cervical excisional procedure, or prior STI history.

Bivariable analyses of the association between cervical length quartile and preterm birth outcomes are shown in Table 2. Women with the shortest cervical length quartile had a higher risk of preterm birth prior to 37 weeks, relative to the other quartiles. Similarly, women with the shortest cervical length quartile were significantly more likely to deliver within 7 days after presentation. There were no differences in the incidence of preterm birth prior to 34 weeks across the cervical length quartiles.

Due to the observed risk distinction seen in the shortest quartile, cervical length was dichotomized as either ≥ 3 or < 3 cm, as this value represents the 10th percentile for midtrimester cervical length.¹⁶ There were no differences in preterm birth < 37 weeks (14.6 vs. 19.1%, $p = 0.579$), preterm birth < 34 weeks (2.5 vs. 4.8%, $p = 0.430$), or delivery within 7 days of presentation (9.7 vs. 14.3%, $p = 0.452$) between women with a cervical length < 3 cm compared with those with a cervical length ≥ 3 cm.

Table 3 depicts the results of multivariable logistic regressions for each of the preterm birth outcomes. After controlling for insurance status, nulliparity, cervical dilation and effacement on presentation, and receipt of antenatal steroids, midtrimester cervical length quartile was no longer associated with preterm birth < 37 weeks. Similarly, there was no association between cervical length quartile and preterm birth < 34 weeks or delivery within 7 days of presentation. Notably, cervical dilation on admission remained highly associated with each of the preterm birth outcome variables. Incorporating cervical length as a continuous measure did not materially change the results (adjusted odds ratio [aOR] for preterm birth < 37 weeks ≈ 1.03 , 95% confidence interval [CI]: 0.72–1.49; aOR for preterm birth < 34 weeks ≈ 1.42 ; 95% CI: 0.65–3.12; aOR for delivery within 7 days of presentation ≈ 1.03 , 95% CI: 0.65–1.64).

Fig. 2 demonstrates ROC curves for the regression model for the outcome of preterm birth < 37 weeks with and without midtrimester cervical length quartile, controlling for insurance status, nulliparity, cervical dilation and effacement on presentation, and receipt of antenatal steroids. The areas under the curves (AUCs) were not significantly different (0.775 vs. 0.786, $p = 0.20$), suggesting that the addition of midtrimester cervical length did not improve prediction of preterm birth for women presenting in preterm labor. Similarly, the AUCs for the models including only cervical dilation on admission with and without midtrimester cervical length quartile were not significantly different (0.719 vs. 0.715, $p = 0.79$).

Comment

Concordant with prior literature, these data demonstrate a low incidence of preterm delivery for women who present with preterm labor. Our results indicate that, while a shorter cervical length quartile is associated with increased frequency of preterm birth in women who seek evaluation for preterm labor, when incorporated into a prediction model using other variables associated with preterm delivery, the addition of midtrimester cervical length quartile does not improve prediction of preterm birth.

There are several notable limitations to our study including its retrospective design. While we attempted to define women presenting with the diagnosis of preterm labor using appropriate ICD-9 codes, the clinical presentation was often heterogeneous and clear definitions of preterm labor were difficult to define retrospectively. Overall these women were a low-risk cohort, as evidenced by the relative infrequent utilization of antenatal steroids and tocolysis. Inadvertent inclusion of women with preterm contractions but without overt preterm labor would likely have biased our results toward the null hypothesis. However, as this cohort is representative of women who present for evaluation to rule out preterm labor, these results are generalizable to a very relevant clinical scenario. Another limitation is the single institutional design. As our sample was obtained in a tertiary care hospital with a specific management strategy for threatened preterm labor, we cannot assume these results are generalizable to the population as a whole. Despite these limitations, this study is, to our knowledge, the first study to assess the relationship between midtrimester cervical length and preterm birth specifically in patients presenting with preterm labor symptoms.

Preterm labor is a significant health care problem in the United States. Investigating clinically useful models to better predict actual preterm birth has the potential to reduce health care costs without compromising advances made in neonatal outcomes. While a short midtrimester cervical length is associated with an increased risk of preterm delivery, it holds limited clinical applicability in accurately identifying women in preterm labor who will ultimately go on to deliver preterm.

Condensation

Shorter midtrimester cervical length is associated with preterm delivery in women with preterm labor, but does not improve prediction of preterm birth.

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Fig. 1.
Patient flow diagram

Fig. 2. Receiver operating curves for the outcome of preterm birth < 37 weeks. AUC of model without CL quartile $\approx$ 0.775. AUC of model with CL quartile $\approx$ 0.786, $p \approx$ 0.2013. CL, cervical length; AUC, area under the curve

Table 1

Demographic and clinical characteristics stratified by cervical length quartile

	Quartile 1 <i>N</i> ¼ 121	Quartile 2 <i>N</i> ¼ 120	Quartile 3 <i>N</i> ¼ 110	Quartile 4 <i>N</i> ¼ 109	<i>p</i> -Value
CL (cm)	3.4 (3.1–3.6)	4.1 (4.0–4.2)	4.6 (4.4–4.7)	5.3 (5.0–5.7)	<0.001
Maternal age (y)		29.9 ± 6.0	29.4 ± 5.8	29.9 ± 5.8	0.567
Public insurance	85 (70.3%)	75 (62.5%)	58 (52.7%)	50 (45.9%)	0.001
Race/Ethnicity					
Non-Hispanic white	47 (38.8%)	50 (41.7%)	39 (35.5%)	35 (32.1%)	0.602
Non-Hispanic black	23 (19.0%)	14 (11.7%)	19 (17.3%)	23 (21.1%)	
Hispanic	1 (0.83%)	1 (0.83%)	0 (0%)	2 (1.83%)	
Asian	6 (5.0%)	6 (5.0%)	4 (3.6%)	9 (8.3%)	
Other	32 (26.4%)	32 (26.7%)	36 (32.7%)	32 (29.4%)	
Unknown	12 (9.9%)	17 (14.2%)	12 (10.9%)	8 (7.3%)	
Nulliparous	63 (52.1%)	60 (50.0%)	41 (37.3%)	35 (32.1%)	0.004
History of sPTB	13 (10.7%)	5 (4.2%)	8 (7.3%)	7 (6.4%)	0.257
BMI at delivery (kg/m ²)	28.7 ± 5.1	28.5 ± 4.8	30.1 ± 6.9	29.3 ± 5.7	0.120
Current smoker	20 (16.5%)	23 (19.2%)	17 (15.4%)	15 (13.8%)	0.729
Prior cervical excisional procedure	5 (4.1%)	10 (8.3%)	10 (9.1%)	5 (4.6%)	0.303
Prior STI	11 (9.1%)	18 (15.0%)	20 (18.2%)	19 (17.4%)	0.193
Gestational age at evaluation for preterm labor (wk)	32 (29–33)	31 (29–33)	31 (29–33)	31 (29–33)	0.850
Dilation at PTL admission					
< 1 cm	55 (45.8%)	78 (66.1%)	68 (62.4%)	79 (75.2%)	<0.001
1–2 cm	44 (36.7%)	31 (26.3%)	34 (31.2%)	19 (18.1%)	
> 2 cm	21 (17.5%)	9 (7.6%)	7 (6.4%)	7 (6.7%)	
Effacement < 1 cm at PTL admission	23 (19.2%)	10 (8.6%)	10 (9.2%)	6 (5.7%)	0.006
Tocolysis at PTL admission	8 (6.6%)	3 (2.5%)	4 (3.6%)	3 (2.7%)	0.335
Antenatal steroids at PTL admission	28 (23.1%)	12 (10.0%)	10 (9.1%)	10 (9.2%)	0.002

Abbreviations: BMI, body mass index; CL, cervical length; PTL, preterm labor; sPTB, spontaneous preterm birth; STI, sexually transmitted infection. Note: Data are presented as median (interquartile range), mean ± standard deviation, or *n* (%). Values in bold reached statistical significance.

Table 2

Bivariable analysis for preterm birth outcomes

Cervical length quartile	Quartile 1	Quartile 2	Quartile 3	Quartile 4	<i>p</i> -Value
PTB	28 (23.1%)	16 (13.3%)	11 (10.0%)	14 (12.8%)	0.028
PTB < 34 wk	4 (3.3%)	2 (1.7%)	3 (2.7%)	3 (2.8%)	0.881
Delivery within 7 d	21 (17.4%)	7 (5.8%)	11 (10.0%)	7 (6.4%)	0.011

Abbreviation: PTB, preterm birth.

Note: Data presented as *n* (%). Values in bold reached statistical significance.

Table 3

Multivariable analyses for the outcomes of preterm birth < 37 weeks, preterm birth < 34 weeks, and delivery within 7 days of presentation

	PTB		PTB <34 wk		Delivery within 7 d	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
CL quartile						
1 (referent)	1.00	Ref	1.00	Ref	1.00	Ref
2	0.90	0.41–1.98	1.23	0.15–10.07	0.49	0.16–1.46
3	0.55	0.23–1.36	5.48	0.78–38.63	1.16	0.43–3.13
4	1.16	0.49–2.72	2.54	0.36–18.09	0.86	0.28–2.64
Public insurance	1.04	0.54–1.98	2.84	0.42–19.13	2.32	0.97–5.58
Nulliparous	2.38	1.26–4.50	4.11	0.80–21.18	1.81	0.82–4.01
Dilation at PTL admission						
< 1 cm (referent)	1.00	Ref	1.00	Ref	1.00	Ref
1–2 cm	1.70	0.80–3.62	0.30	0.05–1.82	2.41	0.90–6.44
> 2 cm	4.58	1.54–13.66	4.65	0.45–48.22	11.91	3.32–42.76
Effacement < 1 cm at PTL admission	0.19	0.08–0.47	0.78	0.11–5.59	0.17	0.06–0.47
Antenatal steroids at PTL admission	1.97	0.90–4.27	52.99	9.00–312.02	0.84	0.32–2.23

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; CL, cervical length; PTB, preterm birth; PTL, preterm labor.