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Predictive value of midtrimester universal cervical length screening based on parity

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Memorial Medical Center
Abdominal Ultrasound Report

Patient Name: Dombos, Jack Patient ID: 12345
Study Date: 3/3/2014 Gender: M Priority: ROUTINE
Referring MD: Benjamin Shah, MD
Technology: Seth Marks, RDCS
DOB, Age: 10/2/1963, 50y

Indications: Abdominal pain
History/Clinical: Cancer
Procedure: Limited - Liver and Biliary

Liver: A complex mass is identified within the right lobe of the liver.
Length: 11.5 cm Height: 5.84 cm
Width: 6.4 cm Vol: 429324 cm³

Gallbladder: The gallbladder appears unremarkable. No focal abnormality noted.
Length: 5 cm Wall: 2.2 cm
CBD: 0.5 cm

Spleen: The spleen appears unremarkable. No focal abnormality noted.
Length: 9.9 cm Height: 4.5 cm
Width: 5.2 cm Vol: 231.66 cm³

Abdominal Images

Memorial Outpatient Clinic
Lower Extremity Arterial Ultrasound Report

Patient Name: Dombos, Jack Patient ID: 12345
Study Date: 3/3/2014 Gender: M Priority: ROUTINE
Referring MD: Shirley Simmons, MD
Technology: Karen Allen, RDCS
DOB, Age: 10/2/1963, 50y
CPT4: 93925

Indications: Hypertension, Peripheral vascular disease
History/Clinical: Left LE Anomalous ABE
Procedure: Date: 01/03/2014

Doppler	Right	Left
PSV	120	120
EDV	120	120
CFI	120	120
PSV	120	120
EDV	120	120
CFI	120	120
PSV	120	120
EDV	120	120
CFI	120	120
PSV	120	120
EDV	120	120
CFI	120	120

Images

Memorial Medical Center
CIMT Report

Patient Name: Dombos, Jack Patient ID: 12345
Study Date: 3/16/2014 Gender: M Priority: ROUTINE
Referring MD: Shirley Simmons, MD
Technology: Karen Allen, RDCS
DOB, Age: 10/2/1963, 50y

Indications: Bilateral bruits

Images

Carotid IMT

Age	75%	50%	25%
50	0.55	0.50	0.45
60	0.60	0.55	0.50
70	0.65	0.60	0.55
80	0.70	0.65	0.60

Findings: Carotid RI:CCA: Right CIMT - 0.80 mm
Carotid LI:CCA: Left CIMT - 0.65 mm

Summary: Bilateral intimal thickening in the distal common carotid, internal and external carotid artery. The calculated vascular age is not consistent with the patient's age. Right CIMT consistent with a vascular age of 83 years old. Recommend follow up - Carotid Duplex Ultrasound for full evaluation.

Nathan Reed, MD

Memorial Outpatient Clinic
Follow-Up Report

Patient Name: Barnes, Ann Study Date: 09/18/2014 12:47pm
Patient No: 6342195 Referring MD: Brandon Hicks, MD
Height: 61cm Sonographer: Lane Fox, EDDMS
Weight: 172lb DOB, Age: 01/02/1982, 32
LMP: 12/10/2013 Pregnancy: Gravida 2, Para 1
GA by LMP: 40w3d GA Selected: 36w1d (From Known EDD)
GA by Last Study: 35w4d EDD: 10/07/2014
GA by Today's US: 35w4d
History/Indications: Previa Placenta

Fetal Examination, Placenta

Presentations: Floating Breech Fetal Heart Rate: 130 bpm
Gender: Female

Placenta: Placenta Grade III Amniotic Fluid Volume: Subjectively normal

Previa: No previa Appearance: Heterogeneous
Umbilical Cord: 3 Vessels Biophysical Profile: 8/8
Breathing 2, Tone 2, Movement 2, AUV 2

Biometry & Growth

Measurement	GA	Range	Source	% for 36w1d	Ratio	
BPD	8.9 cm	7.9-10.0	Hadlock	48%	11.0/10	0.76 (0.71-0.87)
HC	31.8 cm	28.5-36.6	Hadlock	49%	FL/AC	0.21 (0.20-0.24)
AC	32.2 cm	28.5-36.6	Hadlock	50%	FL/AC	0.99 (0.92-1.11)
FL	4.8 cm	3.9-5.8	Hadlock	32%	Cephal Index	0.79 (0.70-0.88)

GA for sonogram 36w1d (28w5d - 37w4d)
based on (BPD, HC, AC, FL) Hadlock

Fetal Weight Estimate
Weight: 2762 gm (6lb, 10oz (2599 - 3165gm) Hadlock
Normal: 2444 gm (2113 - 3554gm) Hadlock
95% for 36w1d

Fetal Anatomy


Fetal Anatomy	Normal	Abnormal	Suboptimal	Pres. Seen	Fetal Anatomy	Normal	Abnormal	Suboptimal	Pres. Seen
Heart Rate Rhythm	✓				Right Kidney	✓			
Four Chamber	✓				Left Kidney	✓			
Stomach	✓				Bladder	✓			

Clinical Summary: The patient is a 32-year-old, Gravida 2, Para 1 who presents for biophysical profile evaluation and limited evaluation. A single live intrauterine pregnancy at 36w1d is identified. The fetus is in Floating Breech position. The placenta is Previa. Normal amniotic fluid volume. Biophysical profile 8/8. Limited evaluation includes stomach, bladder, kidneys and fetal heart rate. Growth appears normal for gestational age.

Recommendations:
1. Follow-up ultrasound in two weeks.
2. Continue current prenatal care with biweekly office visits.

-Electronic Signature- 09/18/2014 2:22pm
Ann Barnes, MD Finished

Predictive Value of Midtrimester Universal Cervical Length Screening Based on Parity

Joshua I. Rosenbloom, MD, MPH , Nandini Raghuraman, MD, MS, Lorene A. Temming, MD, MSCI, Molly J. Stout, MD, MSCI, Methodius G. Tuuli, MD, MPH, Jeffery M. Dicke, MD, George A. Macones, MD, MSCE, Alison G. Cahill, MD, MSCI

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Abbreviations

AUC, area under the curve; BMI, body mass index; CI, confidence interval; CL, cervical length; PTB, preterm birth; ROC, receiver operating characteristic; sPTB, spontaneous preterm birth; TVCL, transvaginal cervical length; US, ultrasound

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Objectives—To evaluate the effect of parity on performance characteristics of midtrimester cervical length (CL) in predicting spontaneous preterm birth (sPTB) before 37 weeks.

Methods—This was a retrospective cohort study of 13,508 women with no history of sPTB undergoing universal transvaginal CL screening at 17 to 23 weeks' gestation from 2011 to 2016. Patients who declined screening or with unknown delivery outcomes were excluded. Areas under the receiver operator characteristic curves were used to assess and compare the predictive ability of CL screening for sPTB. The sensitivity, specificity, and positive and negative predictive values were estimated for specific CL cutoffs for prediction of sPTB.

Results—There were 20,100 patients, of whom 2087 (10%) declined screening and 4505 (22%) did not meet inclusion criteria. Of the remaining 13,508 patients, 43% were nulliparous. The incidence rates of sPTB were 6.5% in nulliparas and 4.9% in multiparas ($P < .001$). The mean CLs were 39.9 mm in nulliparas and 41.8 mm in multiparas ($P < .001$), and those of the first percentiles were 19.0 mm in nulliparas and 24.0 mm in multiparas. Cervical length was significantly more predictive of sPTB in nulliparas (area under the curve, 0.67; 95% confidence interval, 0.63–0.70; versus 0.61, 95% confidence interval, 0.57–0.63; $P = .008$). At CL cutoffs of 10, 15, 20, and 25 mm or less, the sensitivity was lower in multiparas, and the specificity was comparable between the groups.

Conclusions—Midtrimester CL is less predictive of sPTB in multiparas compared to nulliparas. The poor predictive ability, especially in multiparas, calls into question the value of universal CL screening in this population.

Key Words—cervical length; obstetrics; parity; preterm birth

Spontaneous preterm birth (sPTB) remains a major public health problem, and identification of ways to reduce the rate of sPTB is a priority in obstetric research.¹ Midtrimester universal transvaginal cervical length (TVCL) screening has been proposed as an effective screening tool for preterm birth (PTB), although controversy remains.^{2–8} Indeed routine cervical length (CL) ultrasound (US) is not currently recommended by the International Society of Ultrasound in Obstetrics and Gynecology or the American College of Obstetricians and Gynecologists.^{1,9} Part of the reason for this controversy is that in women with singleton gestations, the sensitivity of a short cervix for PTB is poor, ranging from 16% to 45% with a positive predictive value of

6% to 30% depending on the underlying incidence of PTB and the exact end point studied.^{5,10–12}

Given the limited test characteristics of TVCL screening in the general obstetric population, it would be beneficial to clarify whether the test performs better in a certain subpopulation. In particular, since a history of full-term birth is protective against future PTB, it is unclear how well CL screening performs in multiparous patients with no history of sPTB compared to nulliparous patients.^{13–16} However, current guidelines for midtrimester CL screening do not differentiate between nulliparous and multiparous patients. Therefore, our objective was to evaluate the effect of parity on performance characteristics of midtrimester CL in predicting sPTB before 37 weeks. We hypothesized that single midtrimester TVCL screening would have less predictive utility in multiparous patients with no history of sPTB compared to nulliparous patients.

Materials and Methods

This was a secondary analysis of a retrospective cohort study of all patients undergoing midtrimester TVCL screening from 2011 to 2016 under a universal CL screening program at Washington University School of Medicine in St Louis.¹⁷ Starting in July 2011, our institution initiated universal TVCL screening in women with viable singleton pregnancies without current or planned cerclage, between gestational ages of 17 weeks and 23 weeks 6 days, in an opt-out fashion. Transvaginal CL measurements were obtained by trained sonographers using a standard technique in accordance with the Cervical Length Education and Review Program guidelines (however, the sonographers in our institution are not formally certified by this program).^{17–19} The original study was through 2014, and this study included patients through 2016. The details of the original study have been published previously.¹⁷ The study was conducted after approval from the Washington University School of Medicine in St Louis Human Research Protection Office. A waiver of consent was obtained, and informed consent was not required because of the retrospective nature of the study.

Patients were included in the study if they were carrying a viable singleton gestation and were either nulliparous or had a history of at least 1 prior full-term (≥ 37 weeks) birth and no history of sPTB (defined as

birth from 20 weeks 0 days through 36 weeks and 6 days). Patients with a history of sPTB were excluded, as they are not the intended target of “universal” CL screening but instead undergo alternative prophylactic strategies (eg, 17-hydroxyprogesterone and serial CL measurements with consideration of cerclage).¹⁴ Patients were also excluded if they declined CL measurement (although their baseline characteristics were compared to those of patients who accepted screening) or if their delivery outcome was unknown. Patients with a history of iatrogenic PTB (that is, any PTB unrelated to spontaneous preterm labor or spontaneous preterm premature rupture of membranes) and who had no history of a different pregnancy with a full-term birth were excluded. For patients with more than 1 pregnancy during the study period, only the first pregnancy was included.

Patients with a CL of 20 mm or less were considered to have a short cervix and were offered treatment according to our institutional protocol and national guidelines.¹ Patients with CL of greater than 20 mm but less than 25 mm were considered to have a borderline short cervix and were strongly recommended to return for additional measurement before 24 weeks. If patients had additional CL measurements before 23 weeks 6 days, the shortest one was used for analysis in this study.¹⁷

Clinical and demographic data in our US database includes details regarding medical and obstetric histories, pregnancy complications, and delivery and neonatal outcomes for all women undergoing prenatal US examinations at our institution. Demographic and medical information, including age, race/ethnicity (obtained by self-report), tobacco use, body mass index (BMI), and gestational age, is entered prospectively at the time of the US examination, and neonatal and pregnancy outcomes are obtained after delivery through medical record review or by telephone contact with the patient, provider, or both. We categorized race/ethnicity as African American, white, or other. Gestational age was based on the last menstrual period if in agreement with first-trimester US within 7 days or with a second-trimester scan within 14 days. Otherwise, the estimated due date and gestational age were determined on the basis of the earliest US.

Baseline demographic characteristics were compared between multiparous and nulliparous patients by routine summary measures. We compared CL measurements between nulliparous and multiparous patients, including the mean, standard deviation, and

1st, 5th, and 10th percentiles. We then created receiver operating characteristic (ROC) curves for the relationship between CL and sPTB before 37 weeks and 34 weeks and calculated the area under the curve (AUC) and 95% confidence interval (CI). For comparisons of the AUC between the groups, the method of DeLong et al²⁰ was used. Due to uncertainty regarding the optimal cutoff for a “short cervix,” we investigated cutoffs of 10, 15, 20, and 25 mm and calculated the sensitivity, specificity, positive predictive value, and negative predictive value with 95% CIs for sPTB before 37 and 34 weeks at these cutoffs. We determined the number needed to screen to detect a short cervix at each cutoff, stratified by parity. Next, we compared the incidence of a short cervix in patients who had sPTB by parity. Finally, we conducted a sensitivity analysis excluding all patients with an untreated short cervix or treatment with any modality other than vaginal progesterone alone.

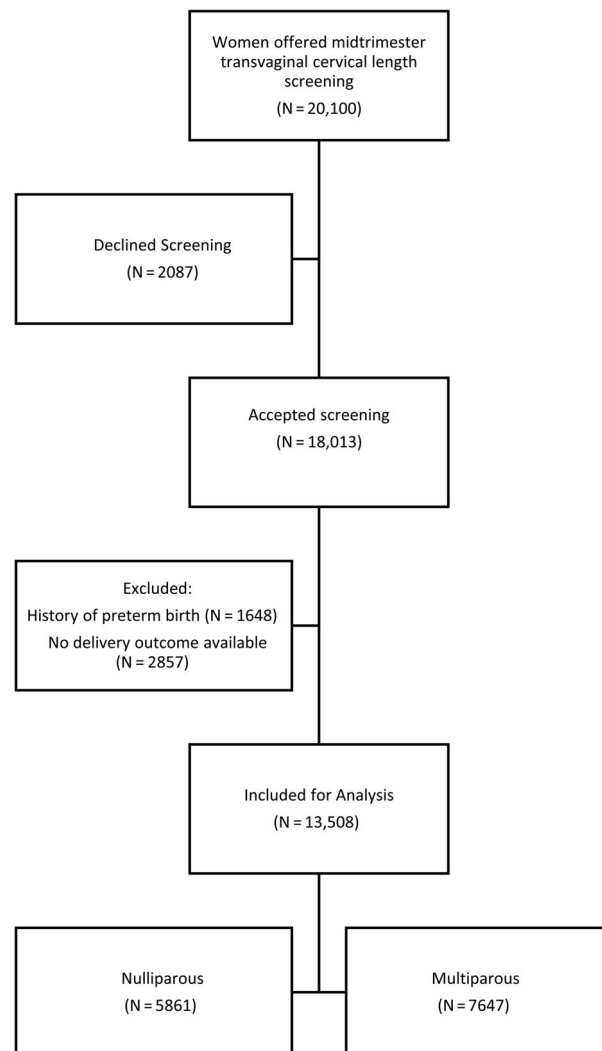
Stata version 13 software (StataCorp, College Station, TX) and SAS version 9.4 software (SAS Institute Inc, Cary, NC) were used for the analysis. We did not perform an a priori sample size calculation because there is no well-established sample size calculation for comparing the area under two ROC curves in independent samples. Two-sided $P < .05$ was considered significant.

Results

During the study period, a total of 20,100 patients were eligible for screening. Of these, 2087 (10%) declined. Patients who declined screening were more likely to be multiparous (63% versus 57%; $P < .001$), to be African American (42% versus 31%; $P < .001$), to smoke tobacco (10% versus 6%; $P < .001$), and to be older (mean age, 28.0 versus 29.4 years; $P < .001$) and had a higher BMI (27.1 versus 26.5 kg/m²; $P = .002$) compared to patients who accepted screening. Of the remaining 18,013 patients, 1648 (9%) had a history of PTB, and 2857 (17% of the otherwise eligible patients) had no outcome data available. Of the remaining 13,508 patients, 5861 (43%) were nulliparous, and 7647 (57%) were multiparous with no history of sPTB (Figure 1). Multiparous patients were older and had a higher BMI than nulliparous patients. Additionally, tobacco smoking was more common in the multiparous group. Multiparous patients were screened

an average of 1 day later than nulliparous patients (Table 1). Birth outcome data were missing from 17% (2857) of otherwise eligible patients (1178 [41%] nulliparous patients and 1679 [59%] multiparous patients). Patients with missing data were compared to the 13,508 patients for whom outcome data was available. The mean CL was the same in nulliparous patients regardless of the availability of outcome data and was 1 mm longer in multiparous patients with outcome data available ($P < .001$). Additionally, patients with missing outcome data were more likely to smoke tobacco, but there were no other significant differences between the group with missing outcome data and the remainder of the patients.

Figure 1. Study flow diagram.



Treatment data were available for 100 of the 122 patients (82%) with a CL of 20 mm or less. Of these patients, 11 (11%) had no treatment; 61 (61%) had vaginal progesterone alone; 2 (2%) had cerclage alone; 1 (1%) had oral progesterone only; 3 (3%) had 17-hydroxyprogesterone only; and 22 (22%) had multiple therapies, including 17 (17%) with cerclage and progesterone, 2 (2%) with multiple forms of progesterone, and 3 (3%) with a pessary, cerclage, and progesterone.

The CL characteristics of each group as well as the outcomes of sPTB before 37, 34, and 28 weeks are shown in Table 2. Multiparous patients had a lower rate of sPTB and a slightly longer mean CL (41.8 versus 39.9 mm; $P < .001$). Additionally, the 1st, 5th, and 10th percentiles of CL were all shorter in nulliparous compared to multiparous patients.

The ROC curves (Figures 2 and 3) showed that TVCL screening performed marginally better in nulliparous patients than in multiparous patients for prediction of sPTB before 37 weeks, with AUCs of 0.67 (95% CI, 0.63–0.70) for nulliparous patients and 0.61 (95% CI, 0.57–0.63) for multiparous patients ($P = .008$). For sPTB before 34 weeks, the AUCs were 0.74 (95% CI, 0.69–0.79) for nulliparous patients and 0.70 (95% CI, 0.64–0.76) for multiparous patients ($P = .30$).

The numbers of patients with and without PTB for each group by CL cutoff are shown in Table 3. The sensitivity was lower in multiparas, and the specificity was comparable between the groups (Table 4).

Table 1. Clinical Characteristics

Characteristic	Nulliparous (n = 5861)	Multiparous (n = 7647)	P ^a
Age, y	27.8 ± 5.8	30.6 ± 5.3	<.01
BMI, kg/m ²	25.9 ± 6.9	27.0 ± 7.6	<.01
Obese (BMI ≥30 kg/m ²)	1137 (19.4)	1835 (24.0)	<.001
Gestational age at screening, wk	19.9 ± 1.2	20.0 ± 1.3	<.01
Tobacco use	260 (4.4)	586 (7.7)	<.01
Race			<.001
African American	1784 (30.4)	2422 (31.7)	
White	3160 (53.9)	3885 (50.8)	
Other or not reported	917 (15.7)	1340 (17.5)	

Data are presented as mean ± SD and number (percent) where applicable.

^aFrom *t* test or χ^2 test.

The same pattern was found for sPTB before 34 weeks (Table 5).

Multiparous patients with sPTB were less likely to have a short cervix compared to nulliparous patients with sPTB. For instance, 58 of 379 (15.3%) of nulliparous patients with sPTB had a CL of 25 mm or less, whereas only 29 of 375 (7.7%) of multiparous patients

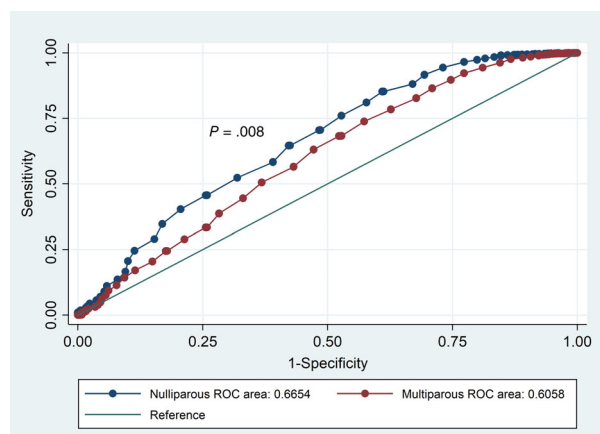
Table 2. Outcomes (n = 13,508)

Outcome	Nulliparous (n = 5861)	Multiparous (n = 7647)	P ^a
Birth outcomes			
sPTB <37 wk	379 (6.5)	375 (4.9)	<.001
sPTB <34 wk	137 (2.3)	108 (1.4)	<.001
sPTB <28 wk	53 (0.9)	47 (0.6)	.052
CL outcomes			
CL, mm	39.9 ± 7.3	41.8 ± 7.4	<.01
10th percentile, mm	32.0	33.0	
5th percentile, mm	30.0	31.0	
1st percentile, mm	19.0	24.0	
CL ≤10 mm (n = 34 [0.3%])	17 (0.29)	17 (0.22)	.44
CL ≤15 mm (n = 68 [0.5%])	40 (0.68)	28 (0.37)	.010
CL ≤20 mm (n = 122 [0.9%])	73 (1.25)	49 (0.64)	<.001
CL ≤25 mm (n = 207 [1.5%])	120 (2.05)	87 (1.14)	<.001
CL in patients with sPTB <37 wk	34.5 ± 10.4	38.5 ± 10.2	<.001

Data are presented as number (percent) and mean ± SD where applicable.

^aFrom *t* test or χ^2 test.

Figure 2. Receiver operating characteristic curves for CL and sPTB before 37 weeks.



with sPTB did ($P = .001$). The same was true at the other CL cutoffs, except that at a cutoff of 10 mm, the difference was no longer statistically significant.

The mean CL in multiparous patients with sPTB before 37 weeks was greater than that in nulliparous patients (34.5 versus 38.5 mm; $P < .001$). The number of patients needed to screen to detect a single case of a short cervix was higher in multiparas compared to nulliparas (Table 6).

In the sensitivity analysis excluding patients with an untreated short cervix or treatment with modalities other than vaginal progesterone alone (remaining 13,470), there was no meaningful change in the results. The AUC for the multiparous patients for sPTB before 37 weeks was 0.60 (95% CI, 0.57–0.63), and for the nulliparous patients, it was 0.65 (95% CI, 0.62–0.68; $P = .026$). Similarly, the sensitivity, specificity, and negative and positive predictive values at the different cutoffs were largely unchanged in this group.

Figure 3. Receiver operating characteristic curves for CL and sPTB before 34 weeks.

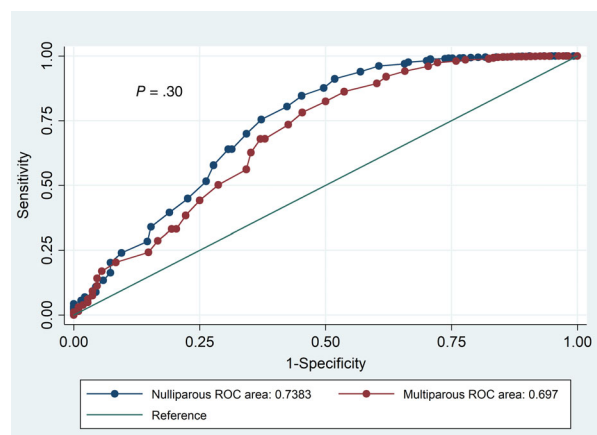


Table 3. Two × Two Tables of CL and Outcome by Parity

CL Cutoff, mm	Nulliparous (n = 5861)				Multiparous (n = 7647)			
	sPTB <37 wk	No sPTB <37 wk	sPTB <34 wk	No sPTB <34 wk	sPTB <37 wk	No sPTB <37 wk	sPTB <34 wk	No sPTB <34 wk
≤10	15	2	13	4	9	8	9	8
>10	364	5480	124	5720	366	7264	99	7531
≤15	25	15	20	20	13	15	11	17
>15	354	5467	117	5704	362	7257	97	7522
≤20	42	31	31	42	20	29	16	33
>20	337	5451	106	5682	355	7243	92	7506
≤25	58	62	40	80	29	58	19	68
>25	321	5420	97	5644	346	7214	89	7471

Discussion

We found that the midtrimester CL is on average longer in multiparous patients without a history of sPTB compared to nulliparous patients and that a short cervix is less predictive of sPTB before 37 weeks in multiparous compared to nulliparous patients. At any cutoff for a short cervix, the number needed to screen to detect a short cervix was lower in nulliparous patients, and there was improved sensitivity for predicting sPTB. However, there was no difference in the predictive ability of midtrimester TVCL screening to predict sPTB before 34 weeks by parity. These findings call into question the value of universal CL screening in multiparous patients without a history of sPTB.

The differences in the predictive value can be explained by the underlying prevalence of the disease (sPTB), which varies in nulliparous versus multiparous patients. However, there were also differences in the sensitivity and specificity, which are inherent properties of the test and are not related to the underlying prevalence of disease. These differences in the sensitivity and specificity of CL screening by parity suggest that the mechanism of sPTB may be different in multiparous compared to nulliparous patients. This finding was supported by the lower incidence of a short cervix in multiparous patients with sPTB. Therefore, TVCL screening in multiparous patients may not assess for the underlying mechanism of PTB in these patients.

To date, there have been only a few studies directly comparing CL in nulliparous patients versus multiparous ones with no history of sPTB. In a prospective study of 1569 patients with no history of preterm delivery undergoing TVCL screening, Orzechowski et al¹⁴ found that a CL of 20 mm or less was more common in nulliparous

Table 4. Test Characteristics for sPTB Before 37 Weeks at Different CL Cutoffs by Parity

CL Cutoff, mm	Nulliparous (n = 5861)				Multiparous (n = 7647)			
	SEN	SPC	PPV	NPV	SEN	SPC	PPV	NPV
≤10	4.0 (2.2–6.4)	100 (99.9–100)	88.2 (63.6–98.5)	93.8 (93.1–94.4)	2.4 (1.1–4.5)	99.9 (99.8–100)	52.9 (27.8–77.0)	95.2 (94.7–95.7)
≤15	6.6 (4.3–9.6)	99.7 (99.5–99.8)	62.5 (45.8–77.3)	93.9 (93.3–94.5)	3.5 (1.9–5.9)	99.8 (99.7–99.9)	46.4 (27.5–66.1)	95.2 (94.7–95.7)
≤20	11.1 (8.1–14.7)	99.4 (99.2–99.6)	57.5 (45.4–69.0)	94.2 (93.5–94.8)	5.3 (3.3–8.1)	99.6 (99.4–99.7)	40.8 (27.0–55.8)	95.3 (94.8–95.8)
≤25	15.3 (11.8–19.3)	98.9 (98.6–99.1)	48.3 (39.1–57.6)	94.4 (93.8–95.0)	7.7 (5.2–10.9)	99.2 (99.0–99.4)	33.3 (23.6–44.3)	95.4 (94.9–95.9)

Data are presented as percent (95% CI). NPV indicates negative predictive value; PPV, positive predictive value; SEN, sensitivity; and SPC, specificity.

Table 5. Test Characteristics for sPTB Before 34 Weeks at Different CL Cutoffs by Parity

CL Cutoff, mm	Nulliparous (n = 5861)				Multiparous (n = 7647)			
	SEN	SPC	PPV	NPV	SEN	SPC	PPV	NPV
≤10	9.5 (5.2–15.7)	99.9 (99.8–100)	76.5 (50.1–93.2)	97.9 (97.5–98.2)	8.33 (3.88–15.2)	99.9 (99.8–100)	52.9 (27.8–77.0)	98.7 (98.4–98.8)
≤15	14.6 (9.2–21.6)	99.7 (99.5–99.8)	50.0 (33.8–66.2)	98 (97.6–98.3)	10.2 (5.2–17.5)	99.8 (99.6–99.9)	39.3 (21.5–59.4)	98.7 (98.4–99.0)
≤20	22.6 (15.9–30.6)	99.3 (99.0–99.5)	42.5 (31.0–54.6)	98.2 (97.8–98.5)	14.8 (8.71–22.9)	99.6 (99.4–99.7)	32.7 (19.9–47.5)	98.8 (98.5–99.0)
≤25	29.2 (21.7–37.6)	98.6 (93.3–98.9)	33.3 (25.0–42.5)	98.3 (97.9–98.6)	17.6 (10.9–26.1)	99.1 (98.9–99.3)	21.8 (13.7–32.0)	98.8 (98.6–99.1)

Data are presented as percent (95% CI). NPV indicates negative predictive value; PPV, positive predictive value; SEN, sensitivity; and SPC, specificity.

compared to multiparous patients, and there was no difference in the odds of sPTB in women with a short cervix (≤ 20 mm) in multiparous versus nulliparous patients. They also reported sensitivity and specificity of a cutoff of 20 mm or less for sPTB before 37 weeks that were somewhat higher than in our study (sensitivity, 20.0% versus 11.1%). Our study differs from their report in a few important ways: our sample size was nearly 9 times larger; we reported on the sensitivity and specificity of TVCL at a number of possible cutoffs; and we used ROC curves to better understand test characteristics. The differences in sensitivity may have been due to different patient characteristics; in their study, 44% of nulliparous patients were African American, whereas in this study, only 30% were.¹⁴ Since CL is more predictive of sPTB in African American compared to non-African American women, this difference in the demographic distribution may underlie the differences in our findings.²¹

Similarly, Facco and Simhan¹⁵ noted that multiparous patients with no history of sPTB had a very low incidence of a short cervix, and therefore, the number needed to screen to prevent a single PTB was considerably higher. On the contrary, in a recent large study by Son et al,²² implementation of a universal CL screening program reduced the rate of sPTB, and this reduction did not differ based on parity. However, their study differed from ours in that only 9.6% of the screened patients were African American. In another example of the way in which the underlying patient population may affect the efficacy of TVCL screening and sPTB, a study comparing outcomes from the Netherlands and Chicago found similar CLs but an increased rate of sPTB before 32 weeks in the Netherlands.²³ Another study from the Netherlands found no difference in the ability of a short cervix to predict sPTB in nulliparous compared to multiparous patients, although the underlying population was quite different from our population.²⁴

Our study had a number of strengths. First, there were more than 13,000 patients in the study, representing

one of the largest studies on this topic to date. Second, all patients underwent TVCL measurement using a standardized protocol in accordance with national guidelines. Third, we had a robust database containing detailed clinical and demographic information.

On the other hand, there were some limitations to consider. Our study was retrospective; however, we had accurate information regarding both the exposure (CL) and the outcome from a validated database.¹⁷ Second, there was heterogeneity in the treatments used for a short cervix, although this has also been seen in similar centers.²² In particular, only 61% of the patients in the study had the recommended treatment (vaginal progesterone) for a short cervix, whereas an additional 17% had progesterone in addition to a cerclage. The fact that patients received different treatments and that not all patients received the current recommended treatment undoubtedly influenced our findings. At the same time, the fact that not all patients accepted or received the recommended treatment may be more representative of the general population, in which there is a diversity of practice patterns.²² Although the fact that patients were treated with any modality will affect the sensitivity and specificity results (compared to an assessment of sensitivity and specificity in untreated patients), this limitation is inherent in any modern assessment of CL performance.¹⁴ Additionally, we had limited clinical information regarding other risk factors for PTB, such as sexually transmitted infections and prior dilation and curettage. Finally, there was no delivery outcome available for 17% of patients. It is possible that inclusion of these patients would have changed the findings of the study, although these patients did not have meaningful differences in clinical characteristics or average CL measurements from those who had delivery information.

In conclusion, the incidence of a short cervix is lower in multiparous patients with no history of sPTB compared to nulliparous patients. As a screening test, TVCL performs worse in multiparous patients with no history of sPTB. Consideration should be given to whether a different cutoff should be used. Importantly, the mean CL in patients with sPTB is well above 25 mm and is even higher in multiparous patients, limiting the sensitivity of TVCL screening, findings that have been seen elsewhere.²⁴ The clinical utility of TVCL screening for prediction of sPTB might be optimized by applying the test in a more nuanced fashion: eg, in patients at higher risk for PTB and with graded cutoffs

Table 6. Numbers Needed to Screen to Detect a Short Cervix by Parity

CL, mm	Nulliparous (n = 5861)	Multiparous (n = 7647)
≤ 10	345 (215–554)	450 (280–723)
≤ 15	146 (108–200)	273 (189–395)
≤ 20	80 (64–101)	156 (118–206)
≤ 25	49 (41–58)	88 (71–108)

Data are presented as number (95% CI).

for the diagnosis of a short cervix based on clinical characteristics. Finally, the results from this study could be used for a cost-effectiveness analysis of universal CL screening in nulliparous versus multiparous patients.

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