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ORIGINAL RESEARCH ARTICLE

Universal cervical length screening for preterm birth is not useful after 24 weeks of gestation

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Abstract

Introduction: Cervical length measurement using transvaginal sonography at 18^{+0}–24^{+0} weeks of gestation is used to identify women at risk of preterm delivery, who may benefit from treatment with progesterone to prevent premature birth. Few and conflicting data exist regarding the predictive value of cervical length measurement performed at later gestational ages. The primary objective of this study was to evaluate the predictive accuracy for spontaneous preterm birth of a single cervical length measurement performed between 24 and 32 weeks of gestation in asymptomatic singleton pregnancies at low risk for spontaneous preterm birth. The secondary objective was to test the predictive accuracy of different cervical length thresholds in the same population.

Material and methods: This was a historical cohort study conducted in a tertiary referral hospital. A total of 2728 asymptomatic women with singleton pregnancy at low risk for spontaneous preterm birth were recruited. Of these women, 1548 had cervical length measured at 24^{+0}–27^{+6} weeks of gestation and 2191 women at 28^{+0}–32^{+0} weeks. In all, 1010 women were present in both gestational age windows. Maternal demographics, medical and obstetrical history, and pregnancy outcome were reviewed. The predictive value of cervical length for spontaneous preterm birth was evaluated through logistic regression analysis. Results were adjusted for confounding factors.

Results: Overall, spontaneous preterm birth occurred in 53/2728 women (1.9%). In both the 24^{+0}–27^{+6} and 28^{+0}–32^{+0} weeks groups, a shorter cervical length was significantly associated with spontaneous preterm birth ($p < 0.01$), but it had a low predictive value, as shown by the receiver operating characteristics curve analysis (areas under the curve 0.62, 95% CI 0.50–0.74 for the 24^{+0}–27^{+6} weeks group, and 0.61, 95% CI 0.52–0.70 in the 28^{+0}–32^{+0} weeks group). When the predictive accuracy for preterm delivery of different cervical length cut-offs was evaluated, the sensitivity

Abbreviations: CL, cervical length; sPTB, spontaneous preterm birth.

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and positive predictive value were low in both gestational age windows, irrespective of the threshold used.

Conclusions: In asymptomatic women with singleton pregnancy at low risk for spontaneous preterm birth, the predictive value of cervical length after 24^{+0} weeks of gestation is low. Therefore, cervical length screening in these women should be discouraged.

KEYWORDS
cervical length, pregnancy, preterm birth, preterm delivery

1 | INTRODUCTION

Preterm birth, defined as birth earlier than 37^{+0} weeks of gestation, is the leading cause of neonatal mortality and morbidity. Worldwide, the incidence of preterm birth is more than 10%.[1,2] Of these, about 70% are spontaneous preterm births (sPTB), the other 30% have a maternal or fetal indication for delivery.[3] Preterm birth prediction tools may be useful to define populations at risk, to understand pathophysiology, and to initiate specific treatment.[4] Besides careful identification of epidemiological risk factors, cervical length (CL) assessment and biological markers have proven useful for screening of women at risk of sPTB during the preclinical stage.[5]

Transvaginal ultrasonography is a reproducible method to measure the CL, a continuous variable that decreases until the time of delivery.[5,6] Universal CL screening at 18^{+0}–24^{+0} weeks of gestation has become usual care in many countries,[7] although some disagreement exists,[8] e.g the Italian Society for Ultrasound in Obstetrics and Gynecology does not endorse this practice.[9] A cut-off of 25 mm at 18^{+0}–24^{+0} weeks has generally been accepted to define a short cervix and a greater risk of sPTB, as it occurs in 1%–3% of the population at 20 weeks and can predict 33.1% of sPTB before 35 weeks of gestation.[10]

In our experience, some practitioners also measure CL at later gestational ages. Nevertheless, few data exist regarding the predictive accuracy for sPTB of CL measured after 24 weeks of gestation. Although it was shown that the sPTB risk increases as the length of the cervix declines,[11–13] most studies do not separate data of pregnancies with or without a previous sPTB.[14] Some authors have suggested that CL after 24 weeks might be useful for prediction of sPTB[5,11–13] and with logistic regression analyses various model-based estimates of sPTB risk have been reported,[5,11–13] but a useful cut-off after 24 weeks of gestation has not been proposed yet.

Our primary objective was to evaluate the predictive accuracy for spontaneous preterm birth of a single CL measurement obtained through transvaginal ultrasound performed between 24^{+0} and 32^{+0} weeks of gestation in asymptomatic singleton pregnancies at low risk for spontaneous preterm birth. Our secondary objective was to test the predictive accuracy of different CL thresholds in the same population.

Key message

Cervical length screening for preterm birth after 24 weeks in asymptomatic, low-risk women has a low predictive value and should not be performed.

2 | MATERIAL AND METHODS

A historical cohort study was conducted on women who had received prenatal care at the Maternity Outpatient Clinic of a tertiary referral hospital between January 2015 and December 2021. Women with a singleton gestation who had CL measured during one or more antenatal visits between 24^{+0} and 32^{+0} weeks of gestation were included. CL measurement was performed by transvaginal ultrasound by trained clinicians, according to the standard technique.[15]

Exclusion criteria included: history of previous sPTB, second-trimester miscarriage or previous conization; use of vaginal or intramuscular progesterone for prevention of preterm birth, placement of a cervical pessary or cervical cerclage, history of at least one episode of uterine activity (painful regular contractions) in the current pregnancy; pregnancy complicated by major fetal anomalies, stillbirth, placenta previa, or placental abruption; or iatrogenic preterm delivery for maternal or fetal indication. We also excluded women who did not deliver in our hospital, because we lack access to data on women who give birth at other centers.

Women were identified using the comprehensive database of antenatal visits in our Maternity Outpatient Clinic. All women who underwent transvaginal ultrasonographic measurement of CL between 24^{+0} and 32^{+0} weeks of gestation were identified, and information regarding maternal demographics, medical and obstetrical history, and progesterone therapy was extracted, using a Microsoft Excel software database. For women who presented more than one pregnancy during the study period, only the first pregnancy was included in the analysis.

Women were divided into two groups, based on the gestational age at which CL measurement was performed: the first group between 24^{+0} and 27^{+6} weeks of gestation, and the second group between 28^{+0} and 32^{+0} weeks. For women who presented more than one CL measurement per group, only the first measurement was included in the analysis. The medical charts of these women were then thoroughly reviewed to record information regarding confirmation of gestational age by first-trimester ultrasonography, complications during current pregnancy, gestational age at delivery, birthweight, and mode of delivery.

2.1 | Statistical analyses

Data analysis was performed using SPSS 20.0 (SPSS Inc.), with separate analysis for the two groups of women previously identified. Data distribution was assessed according to the Shapiro–Wilk's test of normality. Results were reported as absolute and relative frequencies for categorical variables and median and interquartile range for continuous variables. A multiple logistic regression model was used to evaluate the association between CL measurement and sPTB at less than 37 weeks of gestation, adjusting for potential confounders. Odds ratio (OR) and its 95% confidence interval (CI) were reported. To evaluate the predictive capability for PTB of CL performed at 24^{+0}–27^{+6} and 28^{+0}–32^{+0} weeks of gestation, the area under the receiver operating characteristics (ROC) curve (AUC) was calculated. For each threshold of CL the sensitivity, specificity, positive predictive value, negative predictive value, and screen-positive rate were calculated. A *p* value <0.05 was considered significant.

2.2 | Ethics statement

The institutional ethics committee Comitato Area Vasta Centro approved the study (ID 21652) on May 31, 2022.

3 | RESULTS

A total of 6219 ultrasonographic examinations of CL between 24^{+0} and 32^{+0} weeks of gestation were performed in the Clinic during the study period. Of these, 5968 examinations were performed in singleton gestations. After removal of women who met one or more of the previously defined exclusion criteria, 2728 women were included in the study cohort (Figure 1). The demographic and obstetric characteristics and delivery outcomes of the whole cohort are presented in Table 1 and Table 2. Women were then divided into two

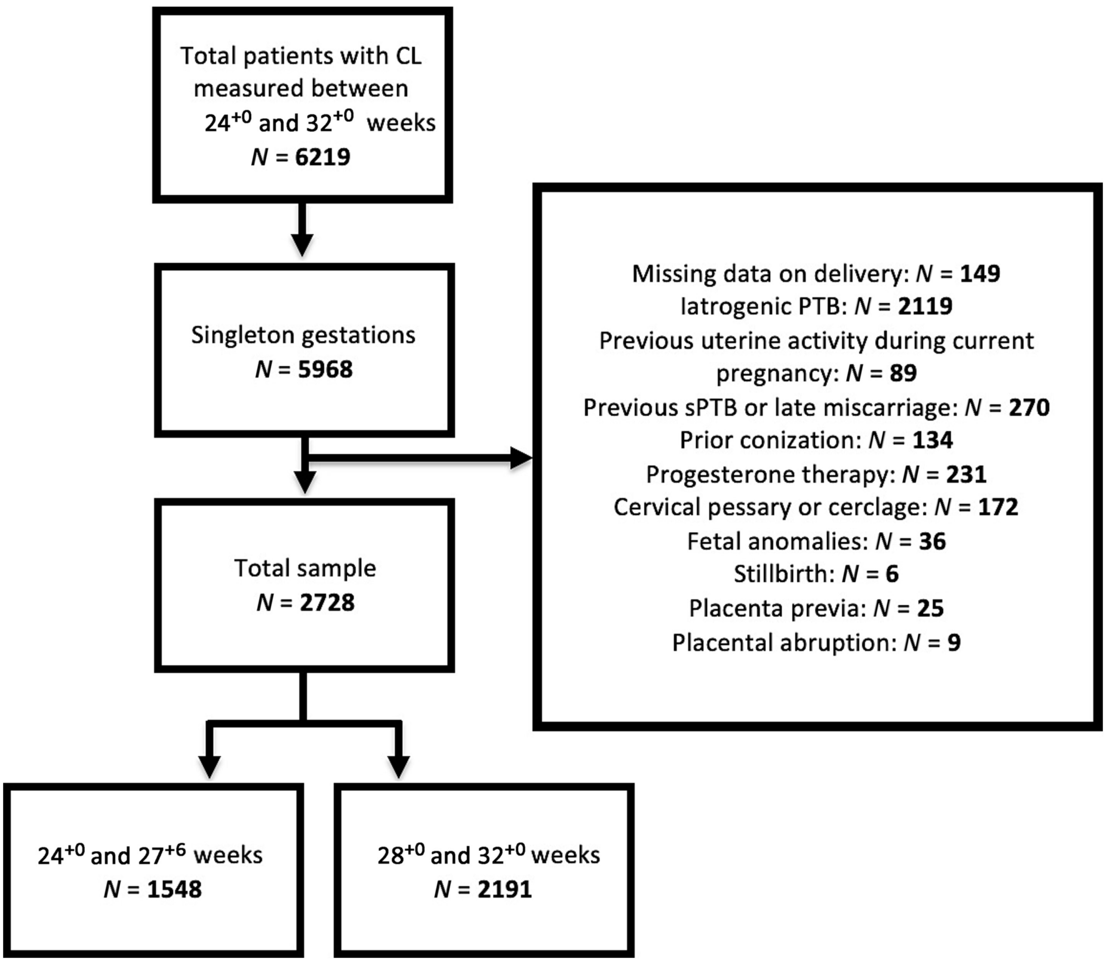

FIGURE 1 Flow chart of the women's selection process.

groups based on the gestational age at which the CL was measured. In all, 1548 women belonged to the first group (24^{+0}–27^{+6} weeks) and 2191 belonged to the second group (28^{+0}–32^{+0} weeks) (Figure 1). In 1010 women, CL measurements were present in both gestational age windows, because CL was repeated on a follow-up visit.

In the first group (CL measured at 24^{+0}–27^{+6} weeks), sPTB occurred in 27 women (1.7%). Table 3 shows term and preterm birth population characteristics compared by logistic regression analysis.

TABLE 1 Maternal characteristics in the whole study cohort (n = 2728).

Age (years)	34 (30–37)
BMI (kg/m^2)	22.3 (20.2–25.4)
Nulliparity	2026 (74.3%)
Ethnicity	
White	2355 (86.3%)
Black	55 (2.0%)
South Asian	127 (4.7%)
East Asian	67 (2.5%)
Mixed	124 (4.5%)

Note: Data are presented as *n* (%) or median (interquartile range).
Abbreviation: BMI, body mass index.

TABLE 2 Delivery outcomes in the whole study cohort (n = 2728).

Gestational age	39^{+2} (38^{+4}–40^{+1})
sPTB <37 weeks	53 (1.9%)
sPTB <34 weeks	8 (0.3%)
Birthweight (g)	3230 (2940–3530)
Mode of delivery	
Vaginal delivery	1740 (63.8%)
Cesarean section	988 (36.2%)

Note: Data are presented as *n* (%) or median (interquartile range).
Abbreviation: sPTB, spontaneous preterm birth.

Cervical length was found to be an independent predictor of sPTB (adjusted OR 0.93, 95% CI 0.91–0.96, p < 0.01): women who delivered prematurely had a significantly shorter CL (median 35 mm), compared with women who delivered at term (median 38 mm). Women who delivered prematurely also had a significantly lower BMI than those who delivered at term, but in both groups the median values were within the normal range. The ROC curve analysis in this group of women (Figure 2) resulted in an AUC of 0.62 (95% CI 0.50–0.74), indicating that CL measurement between 24^{+0} and 27^{+6} weeks of gestation has a low predictive value for sPTB.

In the second group (CL measured at 28^{+0}–32^{+0} weeks), sPTB occurred in 45 women (2%). Again, CL was found to be an independent predictor of sPTB, because it was significantly shorter in women who delivered prematurely compared with women who delivered at term (median 35 mm vs. 37 mm, adjusted OR 0.93, 95% CI 0.91–0.96, p < 0.01) (Table 4). Figure 3 shows the ROC curve in this group. As for the first group, the predictive accuracy of CL for sPTB in this gestational age window was found to be poor, as reflected by an AUC of 0.61 (95% CI 0.52–0.70).

The predictive accuracy of different CL cut-offs was also evaluated. We used fixed thresholds to identify sensitivity, specificity, positive and negative predictive values, and screen-positive rates of different cut-offs, as shown in Table 5 and Table 6. The use of a 25-mm cut-off was associated with low sensitivities (22.2% at 24^{+0}–27^{+6} weeks, and 20% at 28^{+0}–32^{+0} weeks), and low positive predictive values (15.4% and 6.8%, respectively) for sPTB.

4 | DISCUSSION

In this study, we have shown reasons to disagree with CL screening after 24 weeks in singleton asymptomatic pregnancies at low risk because of an unsatisfactory overall predictive accuracy and the low performance of such screening irrespective of the cut-off used. Our results show that the predictive accuracy of CL for sPTB in both gestational age windows is poor, as reflected by AUC,

TABLE 3 Term and preterm birth population characteristics compared by logistic regression analysis—gestational age 24^{+0}–27^{+6} weeks of gestation.

	Preterm birth, n = 27	Term birth, n = 1521	OR (95% CI)
Age (years)	33 (28–36)	33 (30–37)	0.97 (0.91–1.03)
BMI (kg/m^2)	21.3 (18.5–23.9)	22.5 (20.2–25.8)	0.89 (0.79–0.99)
Ethnicity			
White	25 (1.8%)	1338 (98.2%)	Reference
Black	1 (3.6%)	27 (96.4%)	2.86 (0.51–15.95)
South Asian	1 (1.61%)	61 (98.4%)	1.28 (0.24–6.86)
East Asian	0 (0%)	29 (100%)	0.89 (0.05–15.69)
Mixed	0 (0%)	66 (100%)	0.39 (0.02–6.69)
Cervical length (mm)	35 (26–40)	38 (34–41)	0.94 (0.91–0.96)[a]

Note: Results are shown as median (interquartile range) or total number (percentage).
Abbreviation: BMI, body mass index; CI, confidence interval; OR, odds ratio.
[a]Adjusted OR after correction for confounding factors.

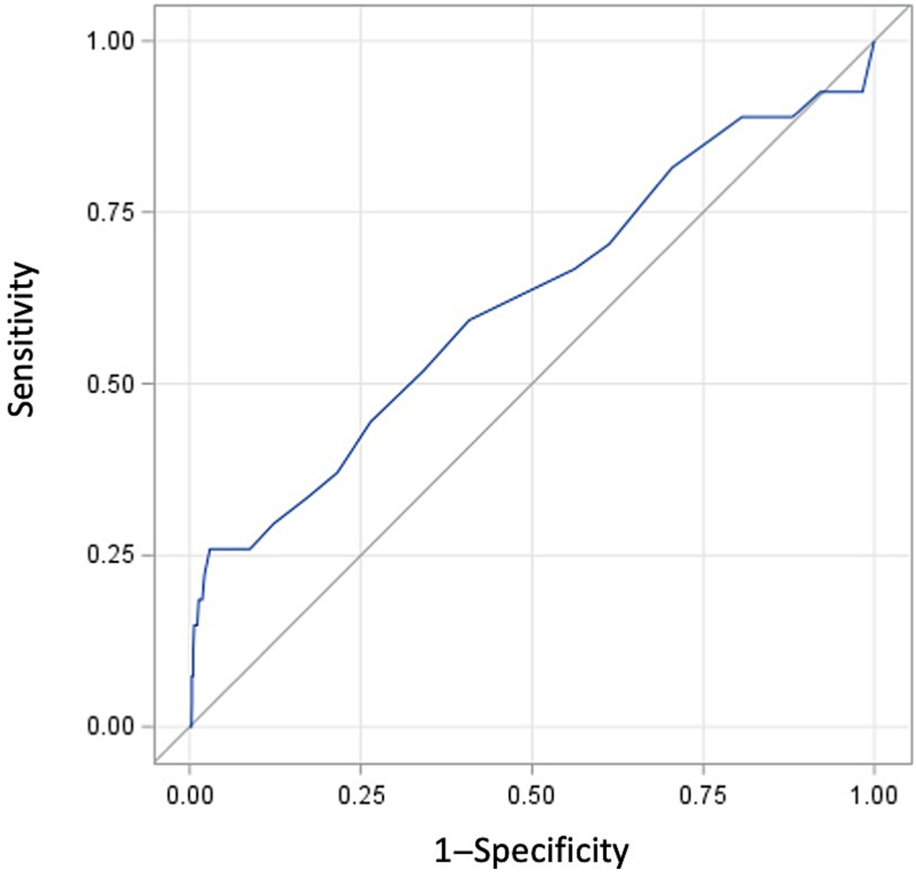

FIGURE 2 Receiver operating characteristics curve analysis for the prediction of preterm birth by cervical length at 24^{+0}–27^{+6} weeks; area under the curve = 0.62; 95% confidence interval 0.50–0.74.

TABLE 4 Term and preterm birth population characteristics compared by logistic regression analysis—gestational age 28^{+0}–32^{+0} weeks of gestation.

	Preterm birth, *n* = 45	Term birth, *n* = 2146	OR (95% CI)
Age (years)	32 (29–38)	34 (30–37)	1.01 (0.99–1.02)
BMI (kg/m^2)	21.3 (19.5–23.9)	22.3 (20.2–25.4)	0.94 (0.87–1.02)
Ethnicity			
White	36 (1.9%)	1839 (98.1%)	reference
Black	2 (4.3%)	44 (95.6%)	2.83 (0.75–10.69)
South-Asian	3 (2.7%)	108 (97.3%)	1.63 (0.53–4.97)
East Asian	2 (3.45%)	56 (96.5%)	2.23 (0.60–8.34)
Mixed	2 (2.0%)	99 (98.0%)	1.27 (0.34–4.66)
Cervical length (mm)	35 (29–37)	37 (32–40)	0.93 (0.91–0.96)[a]

Note: Results are shown as median (interquartile range)/total number (percentage).

Abbreviation: BMI, body mass index; CI, confidence interval; OR, odds ratio.

[a]Adjusted OR after correction for confounding factors.

respectively, of 0.62 and 0.61. Predictive accuracies of different CL cut-offs are also disappointing. There is not a threshold with a sufficient positive predictive value, which reaches a maximum of 28.6% using a 20-mm CL cut-off in the 24^{+0}–27^{+6} weeks of gestation window and 6.8% using a 25-mm CL cut-off in the 28^{+0}–32^{+0} weeks of gestation window. The use of a 25-mm CL threshold, the same used for universal screening in the 18–24 week window, only identifies a small proportion of women who will deliver preterm. The screen-positive rate for CL ≤ 25 mm in our cohort was 2.5% at 24^{+0}–27^{+6} weeks and 6.1 at 28^{+0}–32^{+0} weeks, which is similar to that reported on previous studies in asymptomatic singleton pregnancies that were screened at approximately 24–30 weeks of gestation.[14,16–19]

The prevalence of sPTB in our population was low (1.9%), and is lower than those reported on previous studies (range 4.3%–12.5%).[5,16,17] The difference may be explained by the criteria used

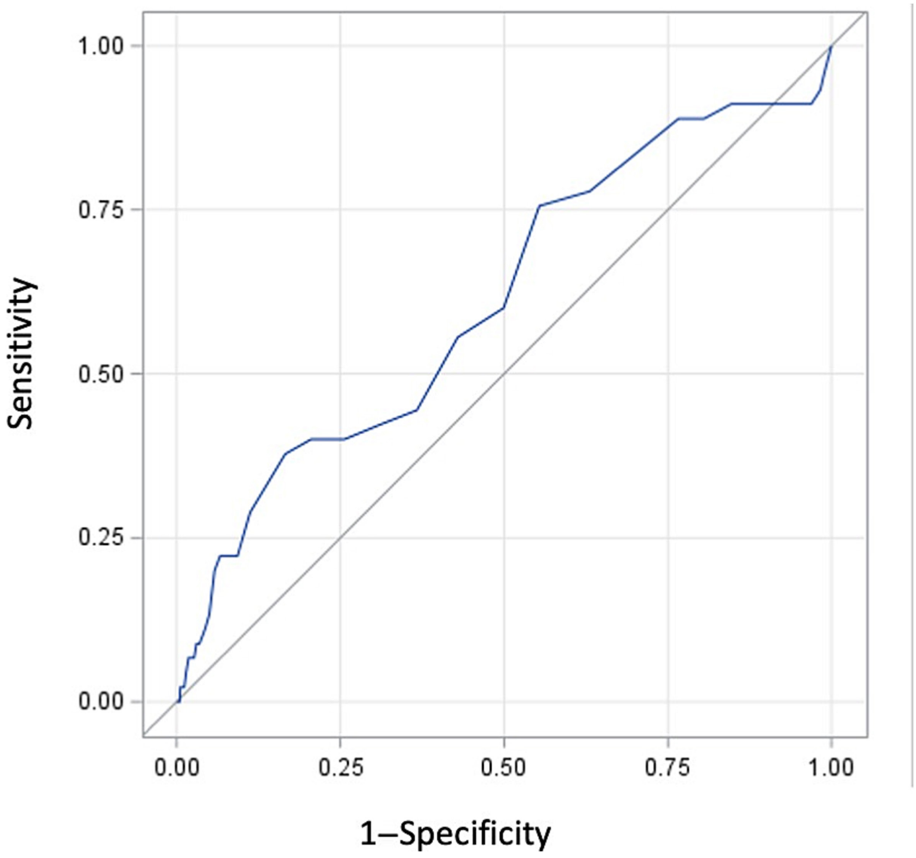

FIGURE 3 Receiver operating characteristics curve analysis for the prediction of preterm birth by cervical length at 28^{+0}–32^{+0} weeks; area under the curve = 0.61, 95% confidence interval 0.52–0.70.

TABLE 5 Predictive accuracy for preterm birth of different CL thresholds—gestational age 24^{+0}–27^{+6} weeks.

Threshold	Sensitivity	Specificity	PPV	NPV	SPR
15 mm	7.4%	99.5%	22.2%	98.4%	0.6%
20 mm	14.8%	99.3%	28.6%	98.5%	0.9%
25 mm	22.2%	97.8%	15.4%	98.6%	2.5%
30 mm	25.9%	91.2%	5.0%	97.8%	9.1%

Abbreviations: CL, cervical length; NPV, negative predictive value; PPV, positive predictive value; SPR, screen-positive rate.

TABLE 6 Predictive accuracy for preterm birth of different CL thresholds—gestational age 28^{+0}–32^{+0} weeks.

Threshold	Sensitivity	Specificity	PPV	NPV	SPR
15 mm	2.2%	98.9%	4.0%	98.0%	1.1%
20 mm	6.7%	97.3%	5.0%	98.0%	2.7%
25 mm	20.0%	94.2%	6.8%	98.3%	6.1%
30 mm	37.8%	83.4%	4.6%	98.5%	17.0%

Abbreviations: CL, cervical length; NPV, negative predictive value; PPV, positive predictive value; SPR, screen-positive rate.

to select our study population, in particular the exclusion of those women with strong risk factors for sPTB. This is both a reassuring finding for the clinician, and an important caveat from a statistical point of view: the lower the prevalence of a disease, the lower the positive predictive value of a screening test; hence the ability of CL measurement to identify high-risk women.

We found no significant difference in the prevalence of sPTB across different ethnicities. However, our analysis might be underpowered to detect differences in the incidence of sPTB between ethnicities, as over 86% of our women were of European descent.

The values of sensitivity, specificity, and screen-positive rates in our study are lower than the ones that led several Institutions to endorse universal CL screening at 18–24 weeks of gestation. Moreover, performing CL measurement after 24 weeks lacks both the advantage of the coincidence with the anatomical scan and, more importantly, an evidence-based intervention to prevent sPTB. In fact, in the absence of a therapy that has proven to be effective, the identification of a short CL in asymptomatic women at low risk might only produce a state of anxiety and concern in women and clinicians. Furthermore, it could bring about detrimental effects, such as rising healthcare costs, and misuse of interventions (hospitalization, tocolysis, induction of lung maturation), with their long-term neonatal effects.[20]

None of the interventions used to prevent sPTB—progesterone therapy, cervical cerclage, and vaginal pessary—have been studied in pregnancies with short CL detected after 24 weeks of gestation. Progesterone has been associated with a significant decrease of sPTB when administered to women with a mid-trimester short CL.[21] Further studies would be needed to assess effective interventions for sPTB prevention in case of CL shortening detected after 24 weeks; for example, it might be appropriate to investigate whether and to what extent progesterone therapy can be useful.

We can identify four main limitations in our study: the retrospective design, the exclusion of women who delivered at other hospitals, which may represent a selection bias, the lack of neonatal follow up, and the inability to estimate the number of women who received prenatal care without CL measurement in our clinic during the study period, which would have allowed us to compare this population with our study cohort. The strengths of this study include the large, homogeneous cohort of women managed in a single tertiary center and the fact that all the ultrasonographic measurements were performed in the same unit by trained physicians, according to a standardized protocol. Moreover, we excluded pregnancies with a history of sPTB, thus allowing us to apply our findings to the general population of pregnancies at low risk for sPTB.

5 | CONCLUSION

The utility of CL measurement has been proven as mid-trimester universal screening[22] and, in high-risk or symptomatic women, as a test to guide management or to drive interventions such as cerclage placement, hospitalization, tocolysis, and induction of fetal lung maturity.[23,24] We acknowledge the importance of this test in the clinical situations mentioned above, but we discourage the use of CL as a universal screening tool for sPTB after 24 weeks. Its use should be limited to the research setting, with the aim of evaluating the utility of interventions, even if belatedly undertaken, to prevent sPTB.

AUTHOR CONTRIBUTIONS

VS: project development, data approval, data analysis, manuscript writing. IA: data management, data approval, manuscript editing. NS: data management, data approval. LT: data approval, data analysis, manuscript editing. CT: data management, data approval. ET: project development, data management, data approval, manuscript editing. MDT: project development, data management, data approval, manuscript editing.

CONFLICT OF INTEREST STATEMENT

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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