Prediction of delivery after 40 weeks by antepartum ultrasound in singleton nulliparous women: a prospective cohort study

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BACKGROUND: Induction of labor at 39 weeks of gestation is associated with better maternal and perinatal outcomes than expectant management. However, a policy of induction of labor implies the identification of women who will deliver after 40 weeks, who are at higher risk of adverse outcome.

OBJECTIVE: This study primarily aimed to elucidate the role of antepartum ultrasound in predicting the onset of spontaneous labor in a cohort of low-risk singleton pregnancies, and secondarily to compare its diagnostic performance with that of other ultrasonographic and clinical parameters.

STUDY DESIGN: This was a prospective study including singleton nulliparous women undergoing a dedicated ultrasound assessment at 36 to 38 weeks of gestation. The primary outcome was delivery ≥40 weeks of gestation. The ultrasound parameters explored were cervical length, posterior cervical angle, angle of progression, and head-perineum distance. Multivariate logistic regression, Kaplan-Meier, and area under the curve analyses were used to test the strength of association and diagnostic performance of variables considered in predicting delivery ≥40 weeks.

RESULTS: A total of 457 women were included, and 49.2% delivered ≥40 weeks. Cervical length was longer (30 vs 19 mm; $P \leq .0001$) and posterior cervical angle wider (105° vs 98°, $P \leq .0001$) in women delivering ≥40 weeks than those delivering <40 weeks. Similarly, head-perineum distance was longer (48 vs 40 mm; $P = .001$) and angle of progression narrower (93° vs 95°; $P = .04$) in pregnancies delivering after 40 weeks. Conversely, there was no difference in the modified Bishop score between the 2 study groups ($P = .689$). In multivariable logistic regression analysis, cervical length (adjusted odds ratio, 1.307) and head-perineum distance (adjusted odds ratio, 1.227) were independently associated with delivery ≥40 weeks. Cervical length showed an area under the curve of 0.896 in predicting a delivery after 40 weeks. Integration of head-perineum distance in the diagnostic algorithm did not increase the performance of the model. A cervical length of 24 mm at 36 to 37 weeks of gestation showed the best combination of sensitivity and specificity in predicting delivery ≥40 weeks, with a shorter latency between ultrasound assessment and birth.

CONCLUSION: Antepartum ultrasound can reliably identify a subset of nulliparous women at higher risk of delivering beyond 40 weeks. A cervical length >24 mm at 36 to 37 weeks of gestation shows the optimal combination of sensitivity and specificity in predicting delivery ≥40 weeks. The findings from this study can help in identifying those women for whom elective induction of labor at 39 weeks of gestation would be beneficial in reducing the risk of adverse pregnancy outcome.

Key words: antepartum ultrasound, cervical length, induction of labor, time of delivery

Introduction

Recent evidence suggests that elective induction of labor (IOL) at 39 weeks of gestation is associated with better maternal and perinatal outcomes than expectant management beyond that gestational age.[1–3] This evidence comes mainly from a large randomized controlled trial carried out in the United States, the a Randomized Trial of Induction Versus Expectant Management (ARRIVE) trial, which shows a reduced risk of hypertensive disorders and a need for cesarean delivery (CD) and neonatal respiratory support in women undergoing elective IOL at 39 weeks.[4–6]

Despite its potential role in improving pregnancy outcomes, a policy of elective IOL would translate to a high economic burden for the national health systems, which have been estimated to be around $2 billion only in the United States.[7]

In 2018, the Centers for Disease Control and Prevention in the United States reported that 57.2% of women deliver between 39 and 40 weeks of gestation, which is consistent with what was reported in Europe.[8–10]

Consequently, a policy of elective IOL at 39 to 40 weeks of gestation would imply the need to identify those women who will deliver after 40 weeks of gestation, who are theoretically at higher risk of adverse pregnancy outcomes.

The integration of clinical parameters, mainly Bishop score and pregnancy characteristics, has been shown to provide moderate accuracy in predicting the likelihood of the onset of delivery in singleton pregnancies. However, this evidence mainly comes from studies including pregnancy beyond term or recruited at the time of IOL. At the same time, there is still a paucity of data on whether clinical assessment may accurately predict the onset of labor before admission to the hospital.[11,12]

Prenatal imaging has been shown recently to predict the likelihood of imminent delivery in nulliparous women. A short cervical length (CL) has moderate value in predicting the onset of spontaneous labor within 7 days from the assessment and can be used reliably as a proxy to identify a subset of women at higher risk of imminent delivery.[13–15] Likewise, it has been previously reported that, in women scheduled for an elective CD, measurement of CL at 35 to 36 weeks of gestation was independently

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AJOG MFM at a Glance

Why was this study conducted?

There is evidence that elective induction of labor at 39 weeks improves maternal and perinatal outcome. Extending induction to all women at 39 weeks of gestation is challenging, with relevant resource implications. The identification of pregnancies that will deliver after 40 weeks is of great clinical interest to focus on pregnancies at risk of complication with advancing gestation and avoid unnecessary induction in women who will deliver spontaneously before 40 weeks.

Key findings

Of singleton nulliparous women studied at 36 to 38 weeks, 49% delivered beyond 40 weeks of gestation, and these pregnancies showed an increased risk of delivering a newborn with a higher birthweight, necessitating emergency cesarean delivery or operative delivery, and spending a longer time in the delivery room. Pregnancies delivering >40 weeks had a longer cervical length and head-perineum distance, wider cervical posterior angle, and narrower angle of progression than those with an early delivery. Cervical length was the most significant parameter, and a value of 24 mm was the best cutoff for predicting those pregnancies that will deliver beyond 40 weeks. Clinical characteristics and Bishop score were not associated with late delivery.

What does this add to what is known?

Antepartum ultrasound may help in identifying women with a higher chance of late delivery. This may be useful in selecting women who can benefit from induction of labor at 39 weeks of gestation.

associated with birth before the scheduled time.[16] More recently, newly reported ultrasound parameters reflecting the uterine and pelvic morphometry, including posterior cervical angle (PCA), angle of progression (AoP), and head-perineum distance (HPD) have been shown to provide an overall high to moderate prediction of imminent delivery in women undergoing IOL or experiencing prelabor rupture of membranes.[17–21]

This study aimed to elucidate the role of third-trimester ultrasound in predicting the onset of spontaneous labor in a prospective cohort of nulliparous low-risk singleton pregnancies. The secondary aim was to compare its diagnostic performance with that provided by the classically reported clinical maternal and pregnancy parameters.

Materials and Methods

Study population

This is a prospective study including singleton nulliparous pregnancies receiving antenatal care from November 2017 to March 2020 at the Division of Maternal Fetal Medicine, Ospedale Cristo Re, Università di Roma Tor Vergata, a hospital with about 2000 deliveries per year. Inclusion criteria were (1) accurate first-trimester pregnancy dating according to crown-rump length at 11 to 14 weeks of gestations, (2) absence of fetal chromosomal or structural anomalies, (3) absence of maternal (diabetes, hypertension, cholestasis, cardiac, and renal diseases) or fetal (small or large for gestational age) complications, (4) spontaneous conception, (5) cephalic presentation, (6) absence of sign of labor (defined as regular painful contractions with cervical change), (7) intact membranes, and (8) delivery in our unit. Exclusion criteria were (1) induction or elective CD before 40 weeks of gestation, (2) incomplete data collection, and (3) lost at follow-up (ie, not delivering in our unit). Maternal characteristics including age, height, weight, body mass index (BMI), ethnicity, and modified Bishop score were prospectively recorded in an electronic database. Additional data collected were gestational age and modality of delivery. The local institutional ethical committee approved the study (Institutional Review Board [IRB] 2017/Ob3), and each woman gave written informed consent to participate.

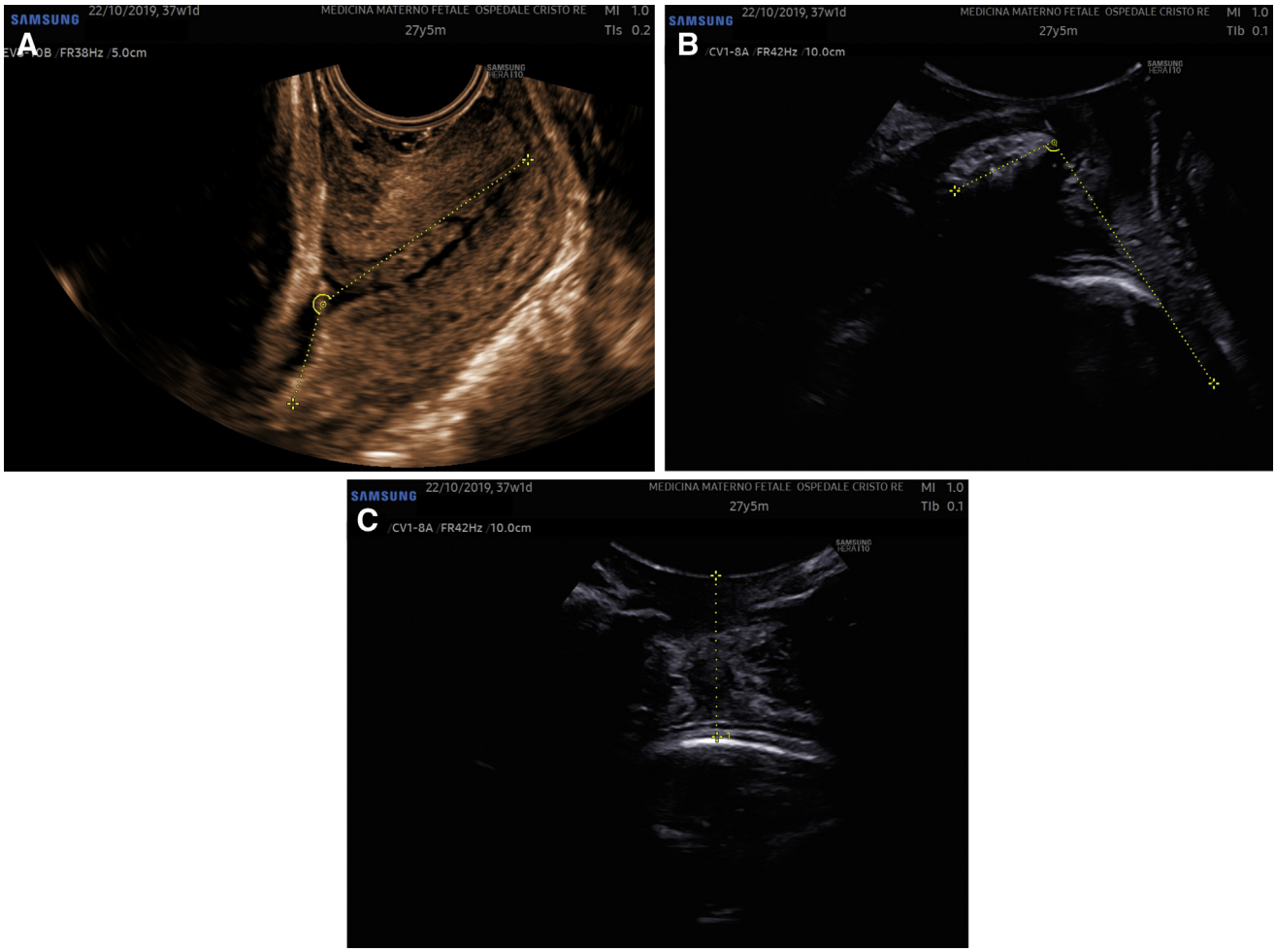
Ultrasound and clinical assessment

Ultrasound assessment was performed at 36 to 38 weeks of gestation in a dedicated clinic for pregnancies planning to deliver in our unit. Two of the authors (G.R. and I.M.) performed all the ultrasonographic recordings at 36 to 38 weeks of gestation. Managing clinicians were blinded to the ultrasound findings.

Ultrasound assessment of the cervix was performed transvaginally following a previously reported technique.[18] Briefly, a sagittal view of the cervix without exerting any compression was obtained. Then, the image was zoomed until the cervix occupied at least two-thirds of the image. The gain was adjusted to obtain a clear view of the cervical canal, and the CL was measured by placing the calipers on the internal and external cervical so. On the same plane, the PCA was evaluated according to a previously reported technique (Figure 1, A).[18] Head circumference, abdominal circumference, and femur length were measured transabdominally according to the International Society of Ultrasound in Obstetrics and Gynecology guidelines, and estimated fetal weight was calculated with the Hadlock-4 formula.[22,23] Transperineal ultrasound was used to measure HPD and AoP.[24] HPD was measured in a frontal transperineal view as the shortest distance from the outer bony limit of the fetal skull to the perineum (Figure 1, B), whereas AoP was measured as the angle between the long axis of the pubic bone and a line from the lowest edge of the pubis drawn tangential to the deepest bony part of the fetal skull (Figure 1, C).

All examinations were performed using the WS80A Elite or Hera 10 ultrasound equipment (Samsung Medison Co, Ltd, Seoul, Republic of Korea) with transabdominal and transvaginal volumetric probes. At the end of the ultrasonographic session, a research midwife (F.A.) blinded to the ultrasound variables performed a clinical evaluation and

FIGURE 1
Ultrasonographic images of a women at 37 + 1 weeks who delivered after 40 weeks



A, transvaginal image of the cervix showing measurements of the cervical length (32 mm) and cervical angle (104°). **B,** Transperineal sagittal view showing measurement of angle of progression (97.3°). **C,** Transperineal transverse view showing measurement of the head-perineum distance (50.1 mm).

FR, frequency.

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assessed the modified Bishop score of each woman.

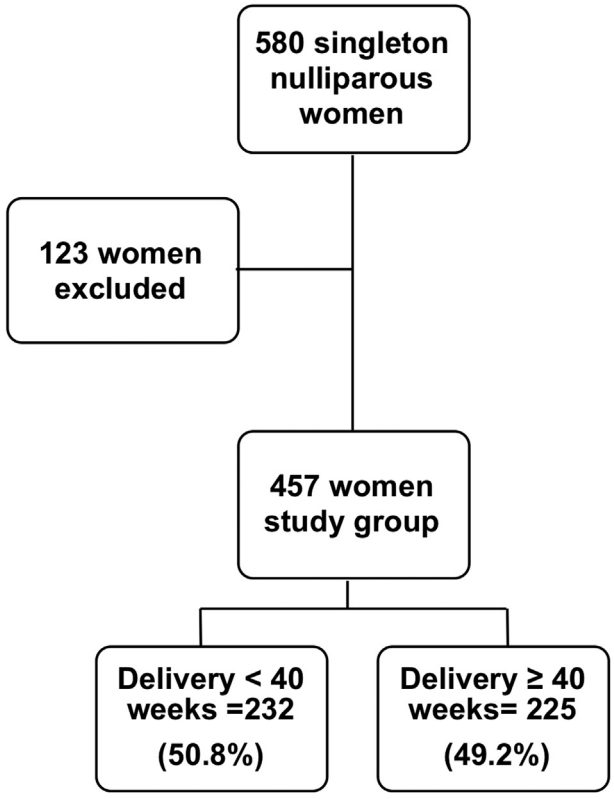
Outcomes measure

The primary outcome was to report the performance of ultrasound in detecting the spontaneous onset of delivery ≥40 weeks of gestation. The secondary outcome was to compare the accuracy of ultrasound with that of the most commonly reported maternal and pregnancy variables, including age, BMI, gestational age at assessment, and Bishop score, in predicting spontaneous onset of labor before 40 weeks of gestation.

Statistical analysis

Data were expressed as median and interquartile range (IQR) or number and percentages. Maternal and fetal characteristics were compared using the chi square test or Fisher exact test for categorical variables, whereas continuous variables were compared using the Mann-Whitney U test. Stepwise forward multivariable logistic regression analysis was carried out to ascertain the strength of association between maternal, fetal, and pregnancy characteristics and time of delivery, and results reported adjusted odds ratios (aORs) with their 95% confidence interval (CI). Only significant variables at univariate analysis were entered in the multivariate model. Collinearity was tested by the Pearson correlation coefficient. Kaplan-Meier survival analysis and Cox regression analysis were used to test the association between the variables analyzed and the time from ultrasonographic examination to delivery. Women induced after 40 weeks of gestation were censored from the analysis. Finally, receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic accuracy of different ultrasound and clinical

FIGURE 2
Flow diagram of study population



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parameters in predicting delivery after 40 weeks. Only variables independently associated with spontaneous onset of labor before 40 weeks of gestation at the regression analysis were computed in the ROC curve analysis. Data were analyzed using Statistical Package for the Social Sciences version 20.0 for Windows (IBM Corp, Armonk, NY), and 2-tailed *P*-values <.05 were considered statistically significant.

Results

During the study period, 580 women were considered eligible for inclusion in the analysis; of these, 123 were excluded for the following reasons: induction or elective CD before 40 weeks of gestation (n=103), lost at follow-up (n=12), and incomplete data collection (n=8), leaving 457 pregnancies available for the analysis (Figure 2).

Spontaneous delivery before 40 weeks occurred in 232 women (50.8%; 95% CI, 0.46−0.55), whereas in the remaining 225 pregnancies (49.2%; 95% CI, 0.45−0.54), it took place after 40 weeks. General characteristics of the study population are reported in Table 1. There was no difference in mean maternal age (*P*=.705), BMI (*P*=.812), ethnicity (*P*=.611), and smoking status (*P*=.689) between women delivering before and after 40 weeks of gestation. Pregnancies delivering ≥40 weeks showed a higher incidence of CD (26.6% vs 18.5%; *P*=.04), a higher birthweight (3610 vs 3410 g; *P*=.0001), and a longer stay in the delivery unit (13 vs 12 hours; *P*=.001) than those delivering <40 weeks. When assessing ultrasound variables, CL was longer (30 vs 19 mm; *P*≤.0001) and PCA wider (105° vs 98°; *P*≤.0001) in women delivering ≥40 weeks. Similarly, HPD was longer (48 vs 40 mm; *P*=.001) and AoP was wider (95° vs 93°; *P*=.04) in pregnancies delivering after 40 weeks. Conversely, there was no difference in the modified Bishop score between the 2 study groups (*P*=.689).

In the multivariable logistic regression analysis, CL (aOR 1.307; 95% CI, 1.246−1.371) and HPD (aOR 1.227; 95% CI, 1.066−1.191) were the only variables independently associated with delivery ≥40 weeks (Table 2).

When assessing the diagnostic performance of the different ultrasound parameters in predicting delivery before 40 weeks of gestation, CL showed an area under the curve (AUC) of 0.896 (95% CI, 0.864−0.928) with a Naegelkerke R^2 of 0.563 in predicting a delivery after 40 weeks. The integration of HPD in the diagnostic algorithm did not increase (De Long *P*=.351) the predictive performance of the model, with an AUC of 0.904 (95% CI, 0.874−0.934; Naegelkerke R^2 of 0.595) (Figure 3).

A CL of 24 mm at 36 to 38 weeks of gestation showed the optimal combination diagnostic accuracy for delivery ≥40 weeks of gestation with a sensitivity and a specificity of 89.3% and 81.9%, respectively, with a derived positive likelihood ratio (LR) of 4.93 and a negative LR of 0.13. At a false positive rate of 10%, the detection rate was 84.6% (95% CI, 80.7−88.6).

When translating these values in a Kaplan-Meier model, women with a CL <24 mm had a shorter interval between ultrasound and delivery than those with a CL ≥24 mm (log-rank test χ^2, 144.9; *P*≤.0001) (Figure 4).

Discussion

Principal findings

The findings from this study showed that antepartum ultrasound could reliably identify a subset of women at higher risk of delivering beyond 40 weeks of gestation, which represents the group of women who would ideally benefit from planned IOL at 39 weeks of gestation to reduce perinatal complications. Pregnancies delivering ≥40 weeks had a longer CL and HPD and a wider CPA and AoP than those delivering <40 weeks of gestation. Conversely, there was no difference in the median Bishop score or maternal and pregnancy characteristics between the 2 study groups. CL and HPD were independently associated with delivery ≥40 weeks. A CL >24 mm showed the optimal combination of

TABLE 1
General characteristics of study population stratified according to time of delivery

Characteristics	Delivery <40 wk N=232	Delivery ≥40 wk N=225	*P* value
Baseline variables			
Maternal age, y	26 (23–30)	26 (24–29)	.705
Maternal height, cm	163 (159–168)	164 (161–168)	.336
Maternal weight, kg	65 (59–71)	65 (59–70)	.866
BMI, kg/m^2	23.3 (20.4–26.2)	23.2 (20.7–26.4)	.812
Ethnicity			.6105
White	221 (95.2)	212 (94.2)	
Other	11 (4.8)	13 (5.8)	
Modified Bishop score	3 (2–4)	3 (2–4)	.333
Smoking	12 (5.2)	14 (6.2)	.689
Ultrasonographic variables			
Gestational age at ultrasound examination, wk	37.0 (36.4–37.4)	36.9 (36.4–37.4)	.463
Estimated fetal weight, g	2730 (2510–2920)	2700 (2440–2910)	.110
Cervical length, mm	19 (14–22)	30 (26–34)	.0001
Posterior cervical angle, °	98 (89–110)	105 (94–115)	.0001
Angle of progression, °	95 (89–100)	93 (90–97)	.046
Head-perineum distance, mm	48 (43–52)	50 (47–53)	.001
Pregnancy variables			
Gestational age at delivery, wk	39.1 (38.4–39.6)	40.7 (40.3–41.0)	.0001
Cesarean delivery	43 (18.5)	60 (26.6)	.0438
Operative vaginal delivery	11 (4.7)	20 (8.9)	.0942
Cesarean delivery or operative vaginal delivery	54 (23.2)	80 (35.5)	.0041
Epidural analgesia	189 (81.5)	192 (85.3)	.3149
Augmentation with oxytocin	89 (38.3)	102 (45.5)	.252
Birthweight, g	3410 (3250–3590)	3610 (3440–3760)	.0001
Umbilical artery pH	7.29 (7.28–7.29)	7.28 (7.27–7.29)	.275
Duration of stay in delivery unit, h	12 (8–16)	13 (10–17)	.001

Data are expressed as median (interquartile range) or number (percentage).

BMI, body mass index.

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sensitivity and specificity in predicting women delivering ≥40 weeks of gestation with an AUC of 0.896. Finally, integration of HPD in this diagnostic algorithm did not increase the predictive performance of the model.

Results

A prior systematic review, including 5 studies (750 nulliparous and parous women), demonstrated that CL measured at ultrasound had a moderate diagnostic accuracy in predicting spontaneous delivery within 1 week.[13] The results from this study confirm these findings and show that using a cutoff value for CL of 24 mm at 36 to 38 weeks can help in identifying a subgroup of women at higher risk of delivering beyond 40 weeks of gestation.

There are still conflicting results on whether CL measured on ultrasound is superior to Bishop score in predicting imminent delivery at term.[25–28] Heterogeneity in inclusion criteria among some of the previously published studies may partially explain the differences in the published literature. In this study, CL measured at 36 to 38 weeks of gestation showed a high diagnostic accuracy in predicting delivery beyond 40 weeks of gestation, supporting its role in stratifying the risk of late delivery in nulliparous women. More recently, new ultrasound parameters, including PCA and transperineal indices of fetal head

TABLE 2
Results of the multivariate logistic regression analysis of independent predictor of delivery ≥40 weeks

Variables	aOR	95% CI	*P*
Cervical length, mm	1.307	1.246–1.371	.0001
Posterior cervical angle, °	1.021	0.999–1.044	.067
Angle of progression, °	0.970	0.958–1.019	.059
Head-perineum distance, mm	1.127	1.066–1.191	.001

aOR, adjusted odds ratio; *CI*, confidence interval.

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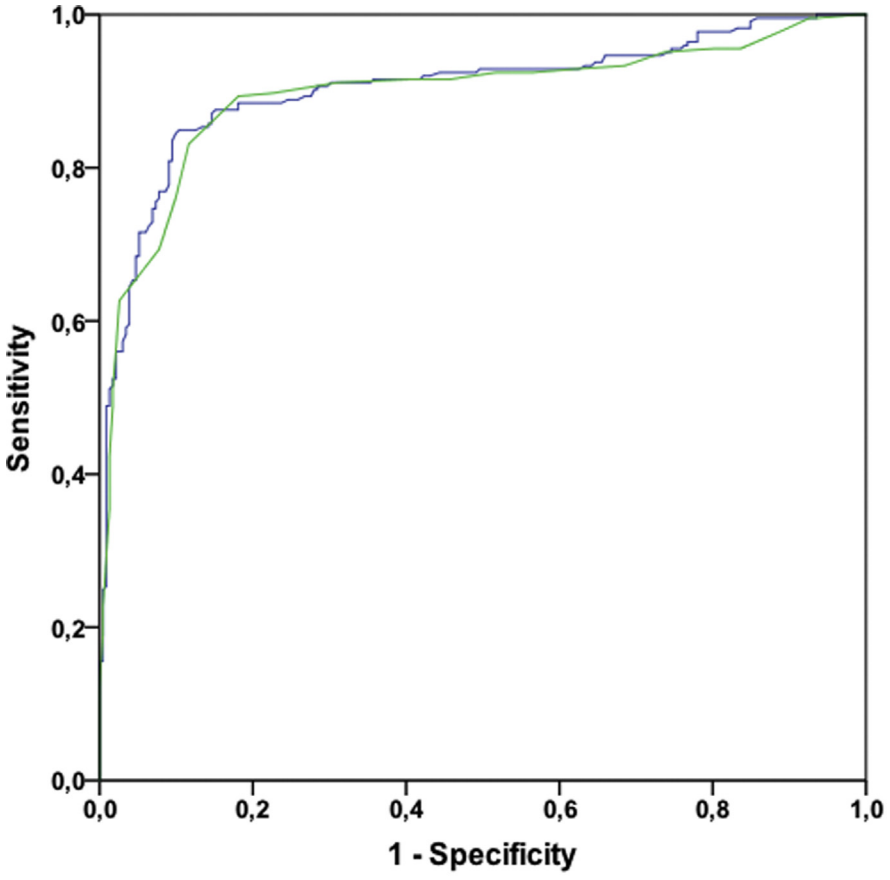
engagement such as AoP and HPD, have been reported to predict the likelihood of vaginal delivery and labor length.[19,20] Rane et al[17] reported that the combination of CL, PCA, and parity provided an optimal prediction of delivery within 24 hours after IOL. To the best of our knowledge, this is the first study analyzing the diagnostic performance of CL, PCA, and other indices of fetal head engagement in predicting delivery beyond 40 weeks of gestation in nulliparous women. Our data show that all these variables were independently associated with the time of delivery. Despite this, when translating these figures into a diagnostic model, the accuracy of CL alone was not improved by integration with other ultrasound parameters.

FIGURE 3
ROC curves of cervical length (*green line*) and a model integrating cervical length and head-perineum distance (*blue line*) in the prediction of delivery ≥ 40 weeks



ROC, receiver operating characteristic.

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Clinical and research implications

The recent ARRIVE trial reported that routine IOL in singleton pregnancies at 39 weeks of gestation is associated with better maternal and neonatal outcomes than expectant management beyond that of gestational age.[5] This trial randomized more than 6000 low-risk nulliparous women at 39 weeks of gestation to either expectant management or induction. Women undergoing induction underwent CD less frequently and had a lower incidence of hypertensive disorders of pregnancy, and newborns were less likely to require respiratory support. These data confirm the findings from previous nonrandomized studies showing that labor induction at 39 weeks may be beneficial in reducing the risk of adverse perinatal outcomes.[2,4,29] Similarly our data also showed, despite the relatively low number of women included, that women delivering <40 weeks underwent CD less frequently. Whether this reduction was related to the relatively small size of the newborn or the more favorable condition of the uterine cervix remains to be established.

Despite this, integrating a policy of routine IOL at 39 weeks for all women may be challenging. Such practice can be perceived as an excessive medicalization of the pregnancy and considered unacceptable by many women and obstetrical care providers. Furthermore, this policy may significantly affect the financial costs of a national healthcare system. More importantly, recent large population studies reported that more than half of women undergo spontaneous onset of labor between 39 and 40 weeks of gestation, making a policy of elective IOL at 39 weeks unnecessary for a large number of these women. It is unlikely that elective IOL would affect the outcome of women who will otherwise

spontaneously deliver before 40 weeks of gestation. On this basis, the risk of adverse perinatal outcome is low before 40 weeks and progressively increases after 41 weeks of gestation. Conversely, the identification of women at high risk of delivering after 40 weeks of gestation would be crucial to undertake intervention (IOL) to reduce the risk of adverse pregnancy outcomes.

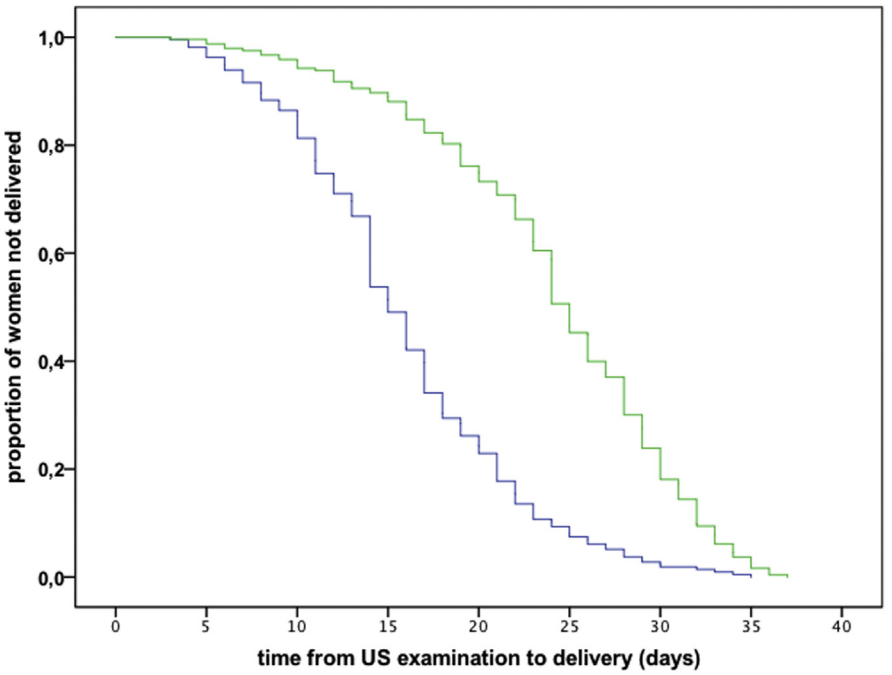
The study's findings provide an insight into the potential role of ultrasound in stratifying the risk of delivery beyond 40 weeks of gestation. Measuring CL at ultrasound between 36 and 38 weeks of gestation would help identify those women at higher risk of late delivery who will benefit from an IOL at 39 weeks of gestation to improve perinatal outcome. Conversely, a short CL on ultrasound may anticipate an imminent delivery and help clinicians decide to defer IOL and wait for spontaneous labor. Despite this, the clinical impact and the cost efficacy of the integration of a policy of routine ultrasound assessment of CL in the third trimester to predict delivery should be tested in large population studies. Further, the medical cost of adding an ultrasound evaluation at 36 to 38 weeks of gestation and the women's perception of excessive medicalization induced by ultrasonographic scan should be considered.

Strength and limitations

The prospective design, inclusion of only nulliparous women, and assessment of maternal and fetal ultrasonographic characteristics in all included cases represent the main strengths of this study. Furthermore, this study explored not only the strength of association between a single ultrasound or maternal variable and the occurrence of late delivery but tried to integrate such parameters into a diagnostic algorithm able to predict this outcome. The major limitation of the study is its cross-sectional nature. It may be speculated that serial measurements of the CL closer to delivery may improve the detection accuracy. However, Meijer-Hoogeveen et al[30] did not report any advantage of repeated CL measurements for the prediction of spontaneous onset of labor at term. Another major limitation of this study is that it was conducted in a single center, limiting the reproducibility of the results. Furthermore, the inclusion of almost exclusively white women may affect the robustness of the results on the basis that the performance of our model may differ in other ethnic groups.

FIGURE 4

Kaplan-Meier estimates of proportions of women not delivered after the ultrasonographic examination, according to cervical length (*blue line*, <24 mm; *green line*, ≥24 mm)



US, ultrasound.

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Conclusions

Antepartum ultrasound can reliably identify a subset of nulliparous women at higher risk of delivering beyond 40 weeks of gestation. A CL >24 mm at 36 to 38 weeks of gestation shows the optimal combination of sensitivity and specificity in predicting delivery ≥40 weeks of gestation. The findings from this study can help in identifying those women for which elective IOL at 39 weeks of gestation would be beneficial in reducing the risk of adverse pregnancy outcomes. ■

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