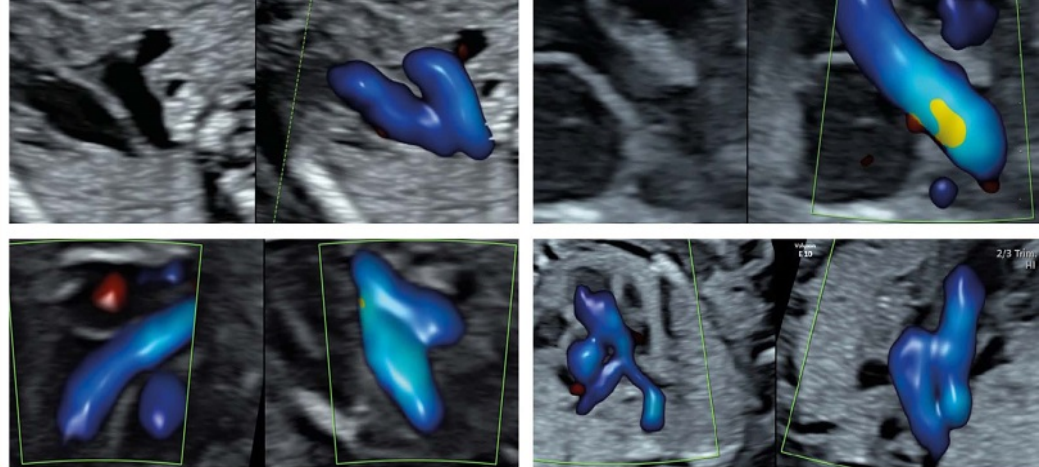# ISUOG Education 2020

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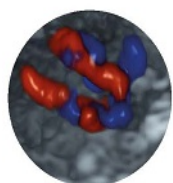
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Serial cervical length measurements after the 1st episode of threatened preterm labor improve prediction of spontaneous delivery prior to 37 weeks' gestation

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Short title: Cervical length and spontaneous preterm delivery

CONTRIBUTION

What are the novel findings of this work?

Women undelivered after their 1st episode of threatened preterm labor are at high risk of delivery < 37 weeks' gestation if their transvaginal cervical length drops below 10 mm at the time of hospital discharge or in the following 4 weeks.

What are the clinical implications of this work?

Transvaginal cervical length assessment could be included in the antenatal care of women discharged from the hospital after their 1st episode of threatened preterm labor to stratify their risk of preterm birth, to rationalize resource-utilization, and to improve pregnancy outcome.

ABSTRACT

Objective: To assess whether repeated cervical length measurements in women discharged from the hospital after their first episode of threatened preterm labor can predict their risk of spontaneous preterm birth

Methods: This is a secondary analysis of a randomized controlled trial on maintenance tocolysis, in which cervical length was measured transvaginally at the time of hospital discharge and respectively after 2, 4, 8 and 12 weeks among women who remained undelivered after their first episode of threatened preterm labor. After univariate analysis, multivariate logistic regression was used to assess if cervical length < 10 mm at the time of hospital discharge or at any follow up evaluation could predict delivery prior to 37 weeks.

Results: 57 out of 226 women (25.2%) discharged with the diagnosis of threatened preterm labor delivered prior to 37 weeks. The risk of spontaneous preterm birth was higher among women with CL < 10 mm compared to those with longer CL at hospital discharge (adjusted OR 3.3; 95%CI 1.2 – 9.2). Moreover, preterm delivery was also more common when CL < 10 was detected up to 2 weeks (adjusted OR 2.9; 95%CI 1.1-7.3) or up to 4 weeks (adjusted OR 7.3; 95%CI 2.3-22.8) post discharge.

Conclusions: women undelivered after their 1st episode of threatened preterm labor remain at high risk of spontaneous preterm birth if their CL drops below 10 mm at the time of hospital discharge or at any follow up visit up to 4 weeks later. CL measurement could be included in the antenatal care of these women, to stratify their risk of preterm birth, and to help clinicians improve pregnancy outcome.

INTRODUCTION

Spontaneous preterm birth (PTB) occurs in 8 to 12% of all pregnancies in developed countries [1], accounting for 80% of perinatal morbidities and 50% of childhood neurodevelopmental disorders [2]. Although approximately 75% of women presenting with threatened preterm labor remain undelivered after a 48-hours course of tocolytics, their risk of preterm delivery remains high, as approximately 30% of them deliver before 37 weeks [3]. Cervical length (CL) measured by transvaginal sonography has been shown to be an accurate predictor of spontaneous PTB among women presenting with painful uterine contractions [4, 5]. However, studies have mainly focused on the role of a single CL measure collected at the time of the initial evaluation for threatened preterm labor. As the potential advantages of repeated CL assessments in identifying women at risk of spontaneous PTB remain speculative, we decided to evaluate whether serial CL measures can predict spontaneous PTB among women who did not deliver after their first episode of threatened preterm labor as they are discharged from hospitals.

METHODS

This is a secondary analysis of a multicenter randomized controlled trial on the efficacy of progestogens for maintenance tocolysis in reducing the rate of preterm birth among women who did not deliver after their first episode of threatened preterm labor. Detailed methodology for the trial is reported elsewhere [6]. Briefly, singleton pregnancies hospitalized at 22^{+0} – 31^{+6} weeks' gestation with painful contractions ($\geq$ 6 in 30 minutes) and cervical changes (i.e. shortening, softening, or dilation on manual examination) who did not experience preterm delivery, were approached for consent if their transvaginal CL measurement at discharge was $\leq$ 25 mm. Women were randomly assigned to receive either a weekly 341 mg intramuscular injection of 17 alpha-hydroxyprogesterone caproate, a daily 200 mg dose of vaginal micronized progesterone, or no treatment until 36 weeks or delivery. Previous spontaneous preterm delivery (20^{+0} – 36^{+6} weeks' gestation), multiple pregnancy, preterm premature rupture of membranes (pPROM), fetal or maternal indications to preterm delivery, Müllerian malformations, prior cervical surgery, cerclage placement in a prior or in the current pregnancy, and persistence of regular contractions at the time of hospital discharge were considered exclusion criteria. Tocolysis and antenatal corticosteroids were administered according to patients' gestational age and national guidelines [7]. Cervical length was measured at the time of discharge with a 7-9 MHz transvaginal probe by trained obstetricians-gynaecologists following the same standardized approach [8]. The original study protocol was approved by the Institutional Review Board of the 5 tertiary care university hospitals where enrolment

occurred. The current secondary analysis was considered exempt to institutional review board approval.

According to the study protocol, follow up appointments were scheduled at 2, 4, 8 and 12 weeks from hospital discharge, to inquire about side effects from the study medications, hospital admissions that might have followed the initial hospitalization, and changes in patients' medical history. On each encounter, obstetrician-gynecologist also performed transvaginal CL measurement. Had patients delivered since the previous clinical encounter, obstetricians-gynaecologists would collect delivery data. Patients who remained undelivered by the last scheduled follow up visit were contacted approximately 2 weeks after their due date, to acquire delivery data.

Our primary objective was to investigate whether the information on CL measured at the time of hospital discharge and at subsequent follow up appointments is useful to predict delivery before 37^{+0} weeks' gestation due to spontaneous onset of labor or premature rupture of membranes (PROM). We chose to categorize CL measurements as < or $\geq$ 10 mm for the following reasons: 1) although midpregnancy CL length $\leq$ 25 mm has a strong association with preterm delivery among asymptomatic patients [9], sensitivity in predicting birth before 37 weeks' gestation among women presenting with uterine contractions is only 70%, with a high false-positive rate of 30% [10]. As less than 10% of women with the clinical diagnosis of preterm labor actually give birth within 7 days of presentation [11], we aimed for a lower CL cut off to increase specificity; 2) despite contrasting opinions, a

midgestation CL inferior to 10 mm has been used by some authors to identify a population at even higher risk of preterm labor, that may benefit from cerclage placement, rather than vaginal progesterone supplementation [12, 13].

As detailed in figure 1, using a transvaginal CL threshold of 10 mm we estimated the risk of preterm delivery at scheduled follow up appointments after hospital discharge: each risk assessment was based on the CL measured from hospital discharge up to that time. At hospital discharge, patients were classified at "low risk" of preterm delivery if their CL measured $\geq$ 10 mm, while "high risk" subjects had shorter CL. Risk of preterm birth was then assessed on all the women who remained undelivered two weeks later (1st follow up visit): pregnancies with CL measurements $\geq$ 10 mm both at that time and at the time of hospital discharge were considered "low risk", while those with CL < 10 mm on at least one of the two assessments were classified "high risk". If delivery hadn't occurred after 4 weeks (2nd follow up visit), pregnancies who maintained CL measurement $\geq$ 10 mm from hospital discharge through the following 2 visits were classified as "low risk", while "high risk" women had shorter CL on at least one of the three assessments. Risk estimates were calculated in a similar fashion on women still pregnant 8 and 12 weeks after hospital discharge (3rd and 4th follow up visits).

Descriptive statistics were used to characterize the socio-demographic features and the obstetric characteristics of women who delivered before and after 37 weeks: categorical variables were presented as absolute and percentage frequencies, and tested with Chi square test or Fisher's exact test as appropriate. Continuous variables were summarized as mean $\pm$ SD and compared with Student's t test. A level of statistical significance of $p \leq 0.05$ was considered.

To control for confounding, multivariate logistic regression models were built to describe the association between the study outcome and CL measured from hospital discharge to each follow-up visit. Socio-demographic variables such as maternal age, BMI at entry to care, ethnicity (Caucasian vs Non-Caucasian), smoking (non-smoking, or smoking stopped prior to conception vs smoking), and education (≤ or > 8 years) were considered as potential confounders, as they are known risk factors for spontaneous preterm birth. Similarly, obstetric features such as parity (nulliparity vs multiparity), tocolysis at the initial hospitalization or at any subsequent hospital admission, urine culture collected on the initial hospitalization, and gestational age at enrolment (≤ or > 28 weeks' gestation) were also taken into account. The area under the ROC curve was used to measure discrimination and calibration of the models. The Kaplan-Meier estimator was used with log rank test to compare how gestational age at delivery varied according to CL risk-category (high vs low risk).

RESULTS

For this analysis, we included 226 of the 235 women with arrested preterm labor and CL $\leq$ 25 mm studied in the original trial: we excluded 2 participants with medically indicated preterm deliveries (due to cholestasis and preeclampsia respectively), and 7 with incomplete information on CL at enrolment (the exact measures were unavailable, despite records indicated if they were < or $\geq$ 15 mm). Spontaneous preterm birth affected 1 out of 4 patients in our study population (57/226).

As detailed in table 1, the baseline socio-demographic characteristics of the women who delivered prior to 37 weeks' gestation due to spontaneous onset of labor or PROM were similar to those who delivered later. The gestational ages at hospital discharge and at all follow up visits were similar between the 2 groups. Women who delivered preterm had significantly shorter CL measurements from hospital discharge through the 3rd follow up visit (p < 0.01), they were more prone to develop pPROM (p < 0.01), they more frequently received tocolysis and had a positive urine culture when initially hospitalized (p = 0.02). Vaginal progesterone was more commonly administered to those who delivered prematurely (p = 0.03). Approximately one in five deliveries after 37 weeks' gestation was medically indicated (p<0.01), while indicated preterm deliveries were excluded from the study population.

Figure 2 shows the cohort of patients followed after hospital discharge, according to their risk of preterm delivery based on serial CL measurements. A CL

cut-off of 10 mm was chosen to distinguish pregnant women at high and low risk of preterm deliveries. In our population, when this cut-off was met at the time of hospital discharge it presented a specificity of 88% and a sensitivity equal to 28% to predict birth before 37 weeks.

Table 2 summarizes the multivariate logistic regression models investigating how changes in CL measurements affected preterm delivery. Each risk assessment was based on the CL measured at that time and on all prior measurements. Pregnancies with at least one CL measurement < 10 mm from hospital discharge to the 3rd follow up visit had a statistically significant 2.9 to 7.3 -fold higher odds of preterm delivery, when compared to women whose cervix persistently remained at or above 10 mm. This association was also confirmed by the Kaplan-Maier estimator (Figure 3). Positive urine culture at the initial hospitalization, smoking, and treatment with vaginal progesterone were also independently associated with the outcome (Table 2). Although the same trends were confirmed, statistical significance was not reached analyzing women still pregnant at the 3rd follow up visit, while insufficient information was available to build a model that could summarize the effects of CL through the 4th visit.

Although CL values measured at the time of discharge were available for all 226 patients, missing values accounted for 27/214 (12.6%), 13/148 (8.8%) and 2/64 (3.1%) of the CL measured respectively at the 1st, 2nd, and 3rd follow up visits. The last observation carried forward was initially used to deal with missing CL measurements (data here displayed); however, similar results were obtained when

missing values were replaced by the following recorded observation, or by the mean value of the previous and the following measurement. Results were no different when the analysis was conducted on the available measurements only, omitting the cases with missing CL data.

The association between CL and preterm delivery was confirmed when the analysis was restricted only to women experiencing spontaneous labor or PROM (i.e excluding those with medically indicated deliveries).

DISCUSSION

Measurement of CL in women presenting with painful uterine contractions prior to 34 weeks' gestation has been shown to predict the majority of those who deliver within 1 [10] or 2 [14] weeks. Amongst symptomatic patients, CL measurement at the time of the initial presentation may be helpful in terms of short-term management, but if the pregnancy continues, further CL evaluations could be useful to determine whether patients remain at risk of spontaneous PTB. Pregnant women who have had an episode of threatened preterm labor comprise a subgroup at high risk for spontaneous preterm birth, as 45% of them are readmitted with a subsequent threatened preterm labor episode, and 25%-30% deliver preterm [3]. Identification of this subgroup of patients becomes pivotal in order to optimize their pregnancy outcomes and rationalize their management. Therefore, we sought to determine if serial CL evaluations in women who overcome their 1st episode of threatened preterm labor, can help identify those who will deliver prior to 37 weeks' gestation.

We concluded that when at least one CL drops below 10 mm after cessation of regular uterine contractions, the odds of spontaneous PTB are 3 to 7-fold higher than among those whose cervix persistently remains at or above 10 mm.

Serial transvaginal CLs have been studied among asymptomatic women [15], while only CL changes from the time of initial presentation have been investigated in symptomatic women. However, to the best of our knowledge, this is the first attempt to investigate the predictive role of serial CL evaluations after the 1st episode of threatened preterm labor. Wagner et al conducted a retrospective study on 310

singleton pregnancies presenting with preterm contractions at 24 to 33 [6/7] weeks of gestation: CL was measured at the time of presentation and on average 3.6 days later [16]. Combination of the first or second CL measurement with the difference between the two was better than a single assessment alone. Sotiriadis et al. examined 122 women with preterm contractions and measured the cervix at presentation and after 24 hours. They also found that the positive predictive value of the first CL assessment was increased by adding the difference between the two measurements [17]. Instead, as Rozenberg et al. examined 109 patients with threatened preterm labor at presentation and 48 hours later, they observed no benefit from adding the difference between the two measurements to the risk calculation based on the first assessment alone [18]. As women were followed with serial cervical evaluations, we identified patients with CL above 10 mm at the time of hospital discharge who experienced cervical shortening in the following weeks and delivered preterm. Therefore, cervical changes monitored over time may better assess the risk of spontaneous PTB than a single CL evaluation, optimizing interventions such as maternal hospitalization, transfer to centers with level III and IV NICUs, antenatal rescue corticosteroids, neuroprotection with magnesium sulfate, and screening for concurrent infections.

There is a well described shortening of cervical length as pregnancy advances, suggesting that the predictive accuracy of sonographic CL in women with threatened preterm labor depends on gestational age at presentation, and that cutoff values predictive of PTL should be gestational age specific [19]. Instead, we showed

that 10 mm is the cutoff value that better identifies women at risk of delivery prior to 37 weeks, independently of the gestational age. Our findings were indirectly supported by previous reports showing that gestational age specific CL values had only modest predictive accuracy for spontaneous PTB among women with threatened preterm labor [19]. Moreover, among asymptomatic women, a midtrimester CL of 10 mm seems to identify a group at particularly high risk of spontaneous PTB. An exploratory subgroup analysis of a systematic review on cerclage placement showed that the intervention prevented spontaneous preterm delivery only when CL was < 10 mm among women without a prior spontaneous PTB [13]. Moreover, vaginal progesterone accounted for a dramatic drop in the rate of preterm birth in women with short cervices and no prior preterm delivery according to a recent systematic review; however, the intervention did not appear to be as beneficial when the cervix was < 10 mm [9].

The main strengths of the study include 1) its prospective design, 2) the use of a standard methodology for CL measurement 3) identification of a population at risk with high numbers of spontaneous PTBs (57/226; 25.2%) 4) patients' recruitment from 5 tertiary care hospitals and 5) a multivariate approach accounting for confounding . However, our study is not without limitations: 1) as we did not record CL upon presentation, some patients may have had a short cervix prior to the beginning of painful uterine contractions; 2) enrollment was based on CL criteria; therefore, our analysis did not account for the role played by cervical dilatation on the risk of spontaneous PTB 3) fetal fibronectin was not systematically evaluated upon

presentation: detection of such glycoprotein could better define the risk of preterm labor among symptomatic patients, and 4) patients were treated according to national guidelines (i.e. for tocolysis, and antibiotic treatment), which could limit the generalizability of our findings.

Our study confirmed the importance of risk factors for PTB such as smoking and UTIs, and corroborated that maintenance tocolysis with progestogens does not lower the rate of preterm delivery. Furthermore, we also showed that vaginal progesterone increases the risk of spontaneous PTB when administered after the 1st episode of threatened preterm labor, as also indicated in the primary analysis of the trial [6]. Given the association between inflammation, infection and preterm delivery [20], we can speculate that suppositories inserted daily into the vagina may favor ascending infections, and promote cervico-vaginal inflammation in women likely to have a pro-inflammatory vaginal milieu related to the recent threatened preterm labor episode.

In conclusion, women undelivered after their 1st episode of threatened preterm labor remain at high risk of preterm delivery if their CL drops below 10 mm at the time of hospital discharge or on any follow up visits up to 4 weeks later, with odds ratios ranging from 2.9 to 7.3. This means that in a population with 10% risk of spontaneous PTL among women with CL above 10 mm after their 1st threatened preterm labor episode, those with a shorter cervix have a 13% to 35% higher risk. Therefore, information on CL measurements could become part of antenatal care in order to stratify the risk of preterm delivery in this population, and help clinicians

utilize resources to improve pregnancy outcomes. Moreover, CL assessment could also reassure mothers about their low risk of preterm delivery when measurements remain above 10 mm, despite a previous hospitalization from threatened preterm labor. Adequately powered prospective studies are necessary to confirm the utility of serial CL assessments in symptomatic patients not receiving additional treatments after their first episode of threatened preterm labor, and to determine the feasibility and the cost effectiveness of such a monitoring program.

The authors report no conflict of interest

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Figure legends

Figure 1: Risk of delivery before 37^{+0} weeks' gestation due to spontaneous onset of PROM according to cervical length measurements

Figure 2: Flow diagram of the patients followed after hospitalization for arrested preterm labor according to their risk of delivery < 37 weeks' gestation based on serial cervical length measurements

Figure 3 Gestational age at delivery according to cervical length risk category

Table 1: Baseline characteristics of the study population according to timing of delivery due to spontaneous onset of labor or PROM

Sociodemographic characteristics	Delivery < 37 weeks	N	Delivery ≥ 37 weeks	N	p
Mean maternal age (years) ± SD	32.6 ± 6.6	56	31.8 ± 5.7	169	0.3*
Mean BMI at booking ± SD	22.9 ± 4.8	56	22.7 ± 4.5	165	0.7*
Number of Non-Caucasian (%)	10 (17.8%)	56	28 (16.6%)	169	0.8**
Number of women with Education ≤ 8 years (%)	17 (30.9%)	55	41 (25.3%)	162	0.4**
Smoking	6 (10.7%)	56	8 (4.8%)	168	0.1
Obstetric Characteristics		N	N	N	N
Number of Nulliparous (%)	34 (62.9%)	54	102 (61.1%)	167	0.8**
Mean GA (weeks) at					
hospital discharge	28.9 ± 2.4	57	28.6 ± 2.3	169	0.5*
1st follow up visit	30.7 ± 2.6	50	30.9 ± 2.6	163	0.5*
2nd follow up visit	32.5 ± 2.8	26	33.4 ± 2.8	118	0.1*
3rd follow up visit	32.1 ± 1.7	7	32.7 ± 2.2	38	0.5*
4th follow up visit	32.8	1	36.3 ± 0.3	3	
delivery	34.1 ± 2.4	57	39.2 ± 1.2	169	< 0.01*
Mean CL (mm) ± DS at					
hospital discharge	16.3 ± 5.8	57	18.2 ± 5	169	< 0.01*
1st follow up visit	15.4 ± 6	51	17.5 ± 5.2	163	< 0.01*
2nd follow up visit	16.7 ± 5.4	27	13.7 ± 6.8	121	< 0.01*
3rd follow up visit	14.5 ± 7.7	7	17.2 ± 5.5	56	< 0.01*
4th follow up visit	23	1	17.2 ± 5.3	12	
Number of women with tocolysis at initial hospitalization (%)	31 (55.4%)	56	64 (37.9%)	169	0.02**
Number of women with positive urine culture at initial hospitalization (%)	13 (25%)	52	19 (12%)	158	0.02**
Number of subsequent hospital admissions due to threatened PTL requiring tocolysis					0.1°
#1 admission	8 (14.4%)	57	11 (6.5%)	169	
#2 admissions	1 (1.8%)	57	1 (0.6%)	169	
Number of with PROM (%)	39 (68.4%)	57	35 (20.8%)	168	< 0.01
Number of courses of antenatal corticosteroids					0.5**
#0	7 (12.3%)	57	32 (19%)	169	
#1	44 (77.2%)	57	119 (70.4%)	169	
#2	6 (10.5%)	57	18 (10.6%)	169	
Type of labor (Number)					0.3°
Spontaneous	48 (84.2%)	57	124 (73.4%)	169	
Induced	6 (10.5%)	57	30 (17.7%)	169	

No labor	3 (5.3%)	57	15 (8.9%)	169	
Mode of delivery (Number)					0.1°
Vaginal delivery	38 (66.7%)	57	123 (72.8%)	169	
Operative vaginal delivery	3 (5.2%)	57	17 (10%)	169	
Cesarean delivery	16 (28.1%)	57	29 (17.2%)	169	
Number of medically indicated deliveries (%)	0 (0%)	57	35 (20.7%)	169	<0.01°
Treatment arm (Number)					0.03**
C+R	15 (26.3%)	57	60 (35.5%)	169	
17P	15 (26.3%)	57	62 (36.7%)	169	
P	27 (47.4%)	57	47 (27.8%)	169	

CL: cervical length *Student's t test ** Chi square test ° Fisher exact test

Table 2: Multivariate logistic regression investigating the risk of preterm delivery from spontaneous preterm labor or pPROM at different time points during pregnancy

Prognostic factors	CL assessment at hospital discharge		CL assessment at hospital discharge and 1st follow up visit		CL assessment from hospital discharge through the 2nd follow up visit		CL assessment from hospital discharge through the 3rd follow up visit	
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
CL								
Low risk	Ref.		Ref.		Ref.		Ref.	
High risk	3.3 (1.2 – 9.2)	0.02	2.9 (1.1-7.3)	0.02	7.3 (2.3-22.8)	<0.01	3.2 (0.3-38)	0.4
Urine Culture								
Negative	Ref.		Ref.		Ref.		Ref.	
Positive	3 (1.3 – 7)	0.01	3.1 (1.2-7.6)	0.01	3.9 (1.2-12.6)	0.02	5.7 (0.6-50)	0.1
Smoking during pregnancy								
No	Ref.		Ref.		Ref.		Ref.	
Yes	3.6 (1.1-12)	0.03	3.9 (1.2 – 13)	0.02	5.5 (1.009-30.6)	0.049	3.7 (0.3-51)	0.3
Treatment								
CTR	Ref		Ref		Ref		Ref	
17P	0.9 (0.3-2.1)	0.7	1.2 (0.5-3.1)	0.6	1.4 (0.3-5.3)	0.6	0.5 (0.3-6)	0.5
P	2.7 (1.2-6.1)	0.01	2.9 (1.2-6.7)	0.02	4.5 (1.3-15.5)	0.002	1 (0.2-7)	0.9

CTR: controls, 17P: 17alpha-hydroxyprogesterone caproate: P: vaginal micronized progesterone

Model on CL assessment at hospital discharge: area under the ROC =0.69

Model on CL assessment at hospital discharge and 1st follow up visit: area under the ROC =0.69
Model on CL assessment from hospital discharge through 2nd follow up visit: area under the ROC =0.76
Model on CL assessment from hospital discharge through 3rd follow up visit: area under the ROC =0.69
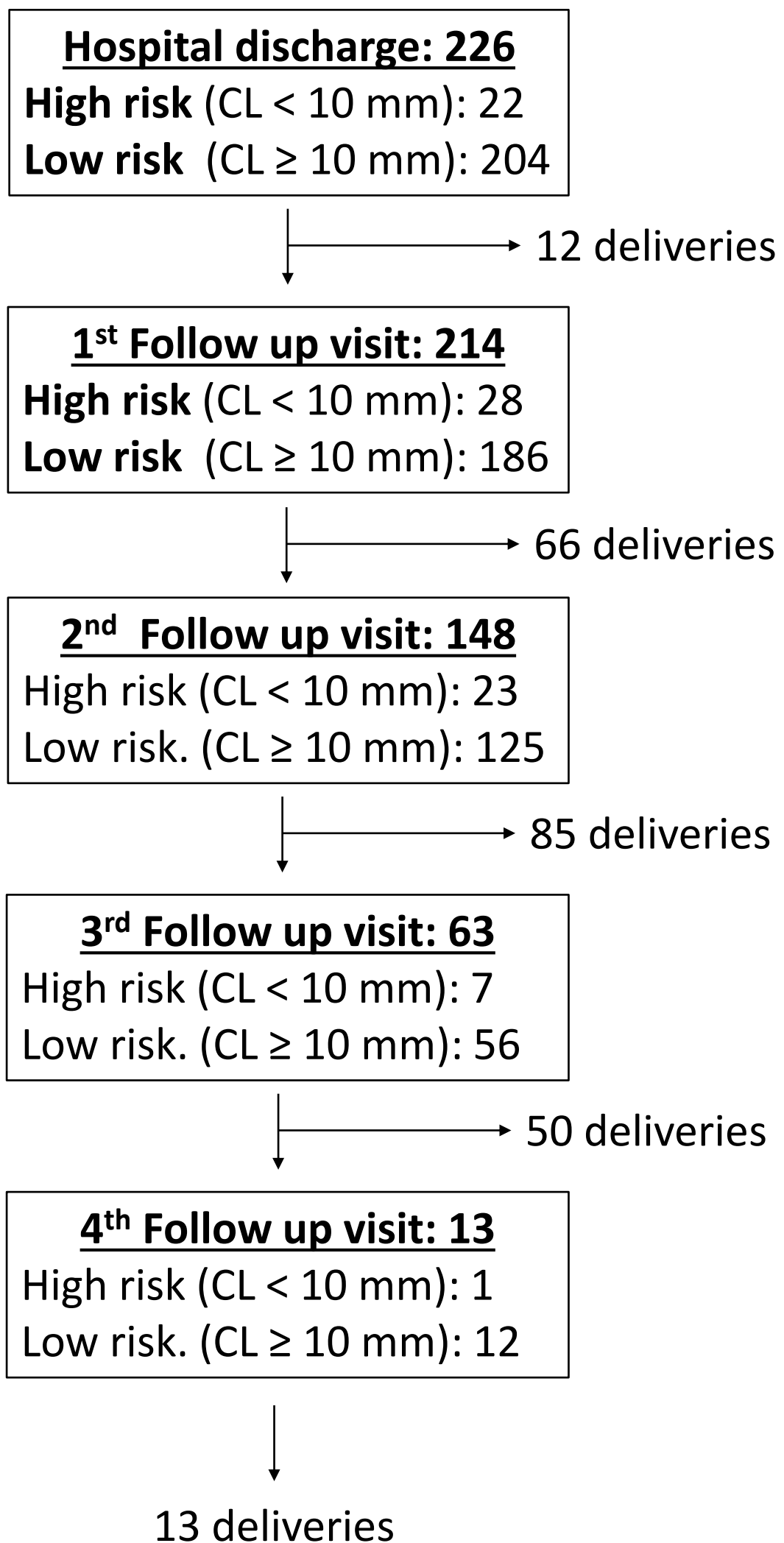
Figure 1: Risk of delivery before 37⁺⁰ weeks' gestation due to to spontaneous onset of PROM according to cervical length measurements

	Hospital discharge	1st follow up visit	2nd follow up visit	3rd follow up visit	4th follow up visit	
	CL < 10 mm					**High Risk**
		CL < 10 mm				**High Risk**
Low Risk	CL ≥ 10 mm		CL < 10 mm			**High Risk**
Low Risk		CL ≥ 10 mm		CL < 10 mm		**High Risk**
Low Risk			CL ≥ 10 mm		CL < 10 mm	**High Risk**
Low Risk				CL ≥ 10 mm		
Low Risk					CL ≥ 10 mm	

Gestational age

CL: cervical length

Hospital discharge: 226
High risk (CL < 10 mm): 22
Low risk (CL ≥ 10 mm): 204

→ 12 deliveries

1st Follow up visit: 214
High risk (CL < 10 mm): 28
Low risk (CL ≥ 10 mm): 186

→ 66 deliveries

2nd Follow up visit: 148
High risk (CL < 10 mm): 23
Low risk. (CL ≥ 10 mm): 125

→ 85 deliveries

3rd Follow up visit: 63
High risk (CL < 10 mm): 7
Low risk. (CL ≥ 10 mm): 56

→ 50 deliveries

4th Follow up visit: 13
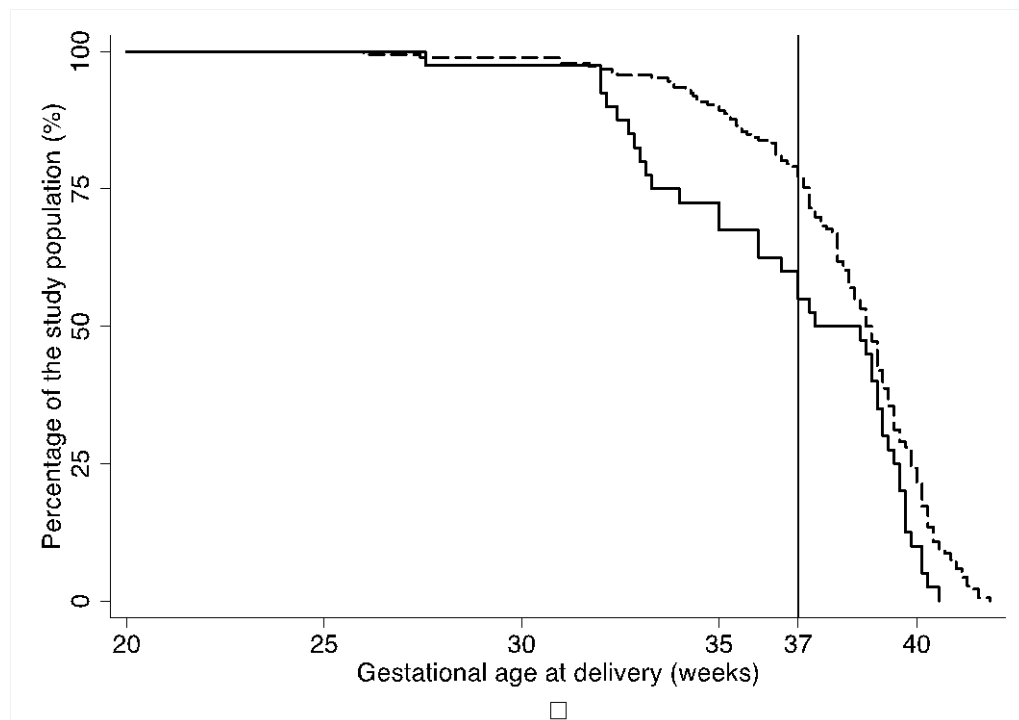High risk (CL < 10 mm): 1
Low risk. (CL ≥ 10 mm): 12

13 deliveries

CL: cervical length
Low risk: patients with cervical length measurements that persistently remained ≥ 10 mm.
High risk: women with at least one cervical length measurement < 10 mm.

Figure 3 Gestational age at delivery according to cervical length risk category

_____ : High risk: women with at least one cervical length measurement < 10 mm.

_ _ _ : Low risk: patients with cervical length measurements that persistently remained ≥ 10 mm.

Log rank test: p = 0.01