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Combined value of placental alpha microglobulin-1 detection and cervical length via transvaginal ultrasound in the diagnosis of preterm labor in symptomatic patients

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Abstract

Aim: We aimed to evaluate the combined value of placental alpha microglobulin-1 (PAMG-1) and cervical length (CL) via transvaginal ultrasound for assessing risk of imminent spontaneous preterm delivery in patients presenting with threatened preterm labor (PTL).

Methods: Clinical exam, PAMG-1 test, cardiotocography, and CL measurement via transvaginal ultrasound were performed on all patients meeting inclusion criteria. Ninety-nine patients at 22^{+0}–36^{+6} gestational weeks with the symptoms of PTL were included. The interval between sample collection and delivery was measured for each method.

Results: Performance metrics were calculated for PAMG-1 test, CL $<$ 25 mm, and contractions $\geq$ 8/h. The sensitivity, specificity, positive predictive value, and negative predictive value for the PAMG-1 test were 100%, 95%, 75%, 100% and 100%, 98%, 88%, 100% for 7 and 14 days, respectively; the respective values for CL $<$ 25 mm were 83%, 59%, 22%, 96% and 79%, 59%, 24%, 94% for 7 and 14 days; and those for contractions $\geq$ 8/h were 42%, 38%, 8%, 83% and 43%, 38%, 10%, 80% for 7 and 14 days. Specificity for the PAMG-1 test was statistically significant ($P < 0.001$) in pairwise comparisons for all other methods. Patients were divided into four groups for analysis of PAMG-1 test performance as follows: CL $<$ 15 mm (100%, 100%, 100%, 100% and 100%, 100%, 100%, 100% for 7 and 14 days, respectively); CL $<$ 25 mm (100%, 94%, 83%, 100% and 100%, 97%, 92%, 100% for 7 and 14 days, respectively); CL of 15–30 mm (100%, 95%, 64%, 100% and 100%, 97%, 82%, 100% for 7 and 14 days, respectively); and CL $\geq$ 30 mm (100%, 100%, 100%, 100% and 100%, 100%, 100%, 100% for 7 and 14 days, respectively).

Conclusion: The use of the PAMG-1 test in patients with a CL of 15–30 mm is highly predictive of imminent spontaneous preterm delivery in women presenting with threatened PTL and could save hospital resources.

Key words: cervical length, placental alpha microglobulin-1, PartoSure, preterm birth, preterm labor.

Introduction

Preterm birth and the complications resulting from its incidence continue to present a challenge to health care globally. According to the most recent systematic analysis, 14.9 million babies were born preterm in 2010, comprising 11.1% of all live births worldwide.[1] Preterm birth rates distribute unevenly across world regions and income levels: the USA has the highest rate of 12% among those countries in the developed world; Germany is at the top in Europe at 9.2%; and the Russian Federation has a rate of 7%.[1] Preterm birth is the leading cause of neonatal and child mortality globally, and in developed countries it accounts for 75% of perinatal mortality and more than

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half of long-term neurocognitive, ophthalmological, and respiratory morbidity.[2]

Women with threatened preterm labor (PTL) between 24 and 34 weeks present at a rate approximately 2–3 times higher than those that go on to deliver.[3] The treatment course for women admitted with a presumed diagnosis of PTL includes interventions with limited efficacy.[4] Tocolytics are used to prolong pregnancy for 2 days to achieve proper action of corticosteroids and for *in utero* transfer to a high risk facility equipped with a NICU; however, no tocolytic drug is associated with a reduction in prenatal or neonatal morbidity, and the use of tocolytics does not lengthen gestation beyond 1 week.[5] Antenatal corticosteroids are the only therapy to show promise in women at risk of preterm delivery between 24 and 34 weeks for the primary purpose of advancing fetal lung development, but there is insufficient evidence to demonstrate any benefit beyond a single course. A survey of 420 European centers revealed that 85% of the obstetric units administered multiple rounds of corticosteroids,[6] counter to the recommended guideline.[7] As the large majority (75–95% of patients with signs and symptoms of PTL) does not deliver within 7 days after presentation,[8] it is a continuous challenge to identify those at risk of imminent delivery from those that can be observed in the outpatient setting. Therefore, it is imperative to improve the identification of women who will go on to deliver within the next 7 days, thereby avoiding unnecessary treatments and reducing health-care costs.

The prevailing methodologies to assess the risk of imminent delivery are imperfect. Cervical length (CL) measurement via transvaginal ultrasound has been widely adopted throughout Europe. While it aids in categorizing women with a long cervix (>30 mm) as low risk and women with a short cervix (<15 mm) as very high risk, it fails to properly establish the risk when CL is equivocal.[4,8,9] Several biomarkers have been investigated for this purpose. Most notably, fetal fibronectin (fFN) was determined to be useful for its high negative predictive value (NPV), but significantly lacks the positive predictive value (PPV) to accurately identify women at risk of imminent delivery. A meta-analysis found the performance of fFN at 100% NPV, but only 15% PPV, rendering the test ineffective when identifying those patients requiring treatment.[10]

The most commonly used and researched fFN-based tests, including Rapid fFN and Quik Check fFN (Hologic), provide qualitative assessment at a threshold of 50 ng/mL. Recently, a version of the test, fFN Q10 (Hologic), was adapted to quantify fFN into five categories (<10 ng/mL, 11–49 ng/mL, 50–199 ng/mL, 200–499 ng/mL, and >500 ng/mL). Quantification of fFN has drawn some interest but lacks true utility, as the likelihood of delivery within 7 days increases only if the patient registers more than 500 ng/mL in her cervicovaginal background, and few patients fall within this category. The vast majority of patients who present to the hospital register <200 ng/mL, yielding a low PPV of only 37% within 14 days.[11] Further research is necessary to understand utility of quantification. Using CL in combination with quantitative fFN shows a slightly improved performance; yet, the best PPV achieved was 28%.[4]

The most recent biomarker introduced into this space is placental alpha macroglobulin-1 (PAMG-1; PartoSure, Parsagen Diagnostics, Inc.). Several trials have already shown the effectiveness of PAMG-1 for assessing the risk of preterm birth, showing PPV as high as 76% and 78%.[9,12] Unlike fFN, PAMG-1 is secreted by the decidua placenta into the amniotic sac and, therefore, may be a more accurate predictor of imminent delivery. Two prevailing theories seek to assert why PAMG-1 may be an effective predictor of PTL: first, it is theorized that transudation of PAMG-1 occurs through chorioamniotic pores in fetal membranes during uterine contractions; and second, the degradation of the extracellular matrix of fetal membranes is due to the inflammatory process of labor and/or infection could allow PAMG-1 to permeate.[13]

We conducted this study to analyze whether the combined use of PAMG-1 and CL measurement would improve identification of women at risk of imminent delivery in the equivocal cervical range between 15 and 30 mm. The parameter was chosen based on previous publications that indicated that patients with CL < 15 mm are at high risk (60–100%) of imminent delivery within 7 days, whereas patients with CL > 30 mm are at low risk (0.7–3%) of imminent delivery within 7 days.[4,8,9] This is the first study to look at this population in combination with the PAMG-1 test. Our aim was to provide better assessment of women who may be monitored in an outpatient setting, significantly reducing unnecessary admissions, alleviating hospital resources, and driving down unnecessary treatment with tocolytics and corticosteroids.

Methods

A prospective study was conducted at the Second Prenatal Unit, D.O. Ott Research Institute of Obstetrics

and Gynecology, North-Western Branch, Russian Academy of Medical Sciences, Saint Petersburg. We assessed the efficacy of the novel kit for the detection of PAMG-1 in the cervicovaginal secretions of pregnant women with clinically intact membranes presenting with signs and symptoms of PTL in predicting time to delivery in combination with CL measurements by transvaginal ultrasound at different cut-off points. The inclusion criteria for the study were as follows: women aged ≥ 18 years with single pregnancy at 22^{+0}–36^{+6} weeks of gestation presenting with self-reported signs, symptoms, or complaints suggestive of PTL. Self-reported signs and complaints suggestive of PTL included: complaints of pain in the abdomen and/or contractions, contractions according to cardiotocography, dull backache, pelvic pressure, bleeding during the second or third trimester, and menstrual-like or intestinal cramping, with or without diarrhea. Additionally, all patients had to have cervical dilatation ≤ 3 cm, and a lack of clinical evidence for preterm rupture of membranes (i.e., intact membranes during vaginal examination). Patients that met the above criteria were invited to participate in the trial and provided informed consent. During the clinical examination at enrollment, subjects who were found to have one or more of the following were deemed ineligible and were not included in the analysis: use of tocolytic medications for treatment of threatened preterm delivery prior to collection of the cervicovaginal specimens or CL measurements; cervical dilatation > 3 cm; suspected placenta previa; gestational age of $<22^{+0}$ or ≥37 weeks; overt rupture of the fetal membranes as indicated by visualized leakage of fluid from the cervical os; heavy vaginal bleeding; symptom (s) not associated with idiopathic threatened preterm delivery, such as trauma; digital examination prior to specimen collection; and enrollment in a tocolytic study. All patients who underwent labor augmentation to enhance the progression of labor or a cesarean section delivery within 14 days of testing were also excluded from the ultimate analysis.

A total of 100 pregnant women with signs and symptoms of PTL were recruited between January 2014 and January 2016. One patient was excluded from the study due to her request not to continue inpatient treatment.

All patients underwent both clinical and laboratory examinations, including: (i) history report; (ii) general clinical and specialized obstetric examinations; (iii) the PartoSure test to determine the presence of PAMG-1 in vaginal secretions; (iv) a vaginal examination to assess the state of the cervix, including, mainly, the degree of softening of the cervical canal and dilatation; (v) transvaginal ultrasound to measure CL; and (vi) assessment of the functional state of the fetus and the nature of uterine activity (cardiotocography). Informed consent was obtained from all patients. The reference method to determine performance metrics was the time interval between testing and imminent spontaneous preterm delivery.

The PartoSure test was performed in accordance with the manufacturer's instructions using the following procedure: (i) a sample of vaginal discharge was collected with a vaginal swab inserted into the vagina for 30 s; (ii) the swab was placed into a vial with solvent and actively rotated for an additional 30 s; (iii) the swab was then extracted from the sample and the test strip was immersed into the vial. The test result was read visually at 5 min by the presence of one or two lines, whereby one line meant that the test was negative, and two lines meant that the test was positive.

After the PartoSure sample was collected, transvaginal ultrasound for the CL measurement was performed using a 5-MHz transvaginal probe, placed in front of the vaginal vault. The patient was in a dorsal lithotomy position with an empty bladder. The CL was measured along its longitudinal axis, defined as the distance between the inner and outer cervix. The CL measurements were done according to the 2015 guidelines by the International Society of Ultrasound in Obstetrics and Gynecolgy.[14]

All patients received therapy aimed at preserving pregnancy (β-adrenoceptor agonists, antagonists, calcium sulfate, magnesium, glucocorticoids). These patients did not receive progesterone treatment, therefore efficacy of preventive use of progesterone could not be considered.

Statistical analysis of the data was performed using Microsoft EXCEL 2007 and IBM SPSS. The Clopper–Pearson procedure was used to calculate 95% confidence intervals.

Results

A total of 100 pregnant patients with signs and symptoms of PTL were recruited between January 2014 and January 2016 at the D.O. Ott Research Institute of Obstetrics and Gynecology. One patient was excluded from the study due to her request not to continue inpatient treatment. Characteristics of the study population are shown in Table 1.

Table 1 Characteristics of study population (n = 99)

Characteristic	Value
Age (years), median (IQR)	25 (23–38)
Weight (kg), median (IQR)	73 (67–103)
Gestational weeks at presentation, median (IQR)	32 (29–36)
Cervical length via transvaginal ultrasound at presentation (mm), median (IQR)	25 (29–36)
Contractions per hour at presentation, median (IQR)	10 (21–40)
Nulliparous	32% (32/99)
Primiparous	30% (30/99)
Multiparous	37% (37/99)
History of premature birth	15% (15/99)
Mild pre-eclampsia	43% (43/99)
Inpatient treatment before this hospitalization	51% (50/99)
History of spontaneous miscarriage (before 22 weeks)	27% (27/99)
Extragenital pathology	65% (64/99)
Infections of the urogenital tract	16% (16/99)
Ovarian failure	21% (21/99)
Threat of termination of pregnancy up to 12 weeks	36% (36/99)
Chronic placental insufficiency, compensated	7% (7/99)

IQR, interquartile range.

At admission, all pregnant women presented with complaints of pain in the abdomen and/or cramping. All patients recorded satisfactory condition of the fetus and irregular contractions during a cardiotocography. Contractions frequency ranged from 2 to 20/h, with a median of 10/h. The PartoSure test was positive in 16 out of 99 patients (16%). Examination via transvaginal ultrasound revealed a shortening of the cervix (<25 mm) in 46% of pregnant women (46 of 99); only three patients (3%) had a cervical cerclage and patients did not receive progesterone treatment as a result of enrollment in this study.

Approximately 15% (15 of 99) of women had a history of PTL and 43% (43 of 99) had mild pre-eclampsia. It should be noted that 51% (50 of 99) of patients had had a prior inpatient hospitalization and this was a repeat visit to the hospital. Due to the small number of patients in each group, it was not possible to conduct subgroup analysis. However, these statistics demonstrate that this was a high-risk group of patients; therefore, despite undergoing a full therapy aimed at maintaining pregnancy, childbirth occurred after administration in 12% (12 of 99) of patients within 7 days and 14% (14 of 99) within 14 days. The PartoSure test was positive in all of these patients.

The performance of both the PartoSure test and CL measurement for the prediction of imminent spontaneous preterm birth within 7 and 14 days of testing is displayed in Table 2. Performance metrics for sensitivity, specificity, PPV, and NPV for the PAMG-1 test were as follows: 100%, 95%, 75%, 100% and 100%, 98%, 88%, 100% for 7 and 14 days, respectively; the same performance metrics for CL < 25 mm were: 83%, 59%, 22%, 96% and 79%, 59%, 24%, 94% for 7 and 14 days, respectively. These results are in line with what was previously found in two publications by Nikolova *et al.*[9,12] As severity of contractions is often taken into account when making a clinical decision, performance metrics for contraction frequency using ≥8/h and ≥12/h as the cut-offs were also calculated. Performance metrics for sensitivity, specificity, PPV, and NPV for contractions ≥8/h were: 42%, 38%, 8%, 83% and 43%, 38%, 10%, 80% for 7 and 14 days, respectively; the same performance metrics for contractions ≥12/h were 17%, 60%, 5%, 84% and 21%, 60%, 8%, 82%% for 7 and 14 days, respectively (Table 2); however, in our study, as in prior publications, they were a poor indicator of preterm delivery.[14]

For a more in-depth analysis, patients were stratified into groups by CL as shown in Table 3 with respective performance metrics listed. The majority of patients (87%) had a short CL of <30 mm, whereas only 13% of patients had a CL ≥ 30 mm. Interestingly, the PartoSure test was positive in only one case in patients with a CL ≥ 30 mm, and this patient went on to deliver within 24 h of presentation. Table 4 shows the proportion of the population falling into each CL stratum as broken down by 5-mm intervals, and the percent of each group that ultimately delivered within 7 and 14 days of testing.

As patients who have a CL < 15 mm are considered very high risk,[4,8,9] we used this cut-off to look at the performance of the PartoSure test. For patients with CL < 15 mm, the PartoSure test result was positive in all but one patient. The patient who had a negative test did not deliver within 14 days of presentation. Despite the administration of therapy, the four women who were in this group and had a positive PartoSure test delivered within 48 h. Performance metrics for sensitivity, specificity, PPV, and NPV for the PAMG-1 test in this group were: 100%, 100%, 100%, 100% and 100%, 100%, 100%, 100% for 7 and 14 days, respectively.

As clinicians often guide the treatment pathway based on CL < 25 mm, we also looked at performance in this group. In our study, 46% of patients had a CL < 25 mm. Performance metrics for sensitivity, specificity, PPV, and NPV for the PAMG-1 test in this group were: 100%,

Table 2 Performance of PartoSure (PAMG-1) test, cervical length < 25 mm and contractions

	SN	SP	PPV	NPV
7 days				
PAMG-1	100% (12/12)	95% (83/87)	75% (12/16)	100% (83/83)
(95%CI†)	[74%–100%]	[89%–99%]	[48%–93%]	[96%–100%]
CL < 25 mm	83% (10/12)	59% (51/87)	22% (10/46)	96% (51/53)
(95%CI†)	[52%–98%]	[48%–69%]	[11%–36%]	[87%–100%]
Contractions				
≥8/h	42% (5/12)	38% (33/87)	8% (5/59)	83% (33/40)
(95%CI†)	[15%–72%]	[28%–49%]	[3%–19%]	[67%–93%]
≥12/h	17% (2/12)	60% (52/87)	5% (2/37)	84% (52/62)
(95%CI†)	[2%–48%]	[49%–70%]	[0%–18%]	[72%–92%]
14 days				
PAMG-1	100% (14/14)	98% (83/85)	88% (14/16)	100% (83/83)
(95%CI†)	[77%–100%]	[92%–100%]	[62%–98%]	[96%–100%]
CL < 25 mm	79% (11/14)	59% (50/85)	24% (11/46)	94% (50/53)
(95%CI†)	[49%–95%]	[48%–69%]	[13%–39%]	[84%–99%]
Contractions				
≥8/h	43% (6/14)	38% (32/85)	10% (6/59)	80% (32/40)
(95%CI†)	[18%–71%]	[27%–49%]	[4%–21%]	[64%–91%]
≥12/h	21% (3/14)	60% (51/85)	8% (3/37)	82% (51/62)
(95%CI†)	[5%–51%]	[49%–70%]	[2%–22%]	[70%–91%]

†95%CI computed by the Clopper–Pearson procedure. CI, confidence interval; NPV, negative predictive value; PAMG-1, placental alpha microglobulin-1; PPV, positive predictive value; SN, sensitivity, SP, specificity.

Table 3 Performance of PartoSure (PAMG-1) test in patients according to CL group

	SN	SP	PPV	NPV
7 days				
CL < 15 mm	100% (4/4)	100% (1/1)	100% (4/4)	100% (1/1)
(95%CI†)	[40%–100%]	[3%–100%]	[40%–100%]	[3%–100%]
CL < 25 mm	100% (10/10)	94% (34/36)	83% (10/12)	100% (34/34)
(95%CI†)	[70%–100%]	[81%–99%]	[52%–98%]	[90%–100%]
CL 15–30 mm	100% (7/7)	95% (71/75)	64% (7/11)	100% (71/71)
(95%CI†)	[59%–100%]	[87%–99%]	[31%–89%]	[95%–100%]
CL ≥ 30 mm	100% (1/1)	100% (11/11)	100% (1/1)	100% (11/11)
(95%CI†)	[3%–100%]	[72%–100%]	[3%–100%]	[72%–100%]
14 days				
CL < 15 mm	100% (4/4)	100% (1/1)	100% (4/4)	100% (1/1)
(95%CI†)	[40%–100%]	[3%–100%]	[40%–100%]	[3%–100%]
CL < 25 mm	100% (11/11)	97% (34/35)	92% (11/12)	100% (34/34)
(95%CI†)	[72%–100%]	[85%–100%]	[62%–100%]	[90%–100%]
CL 15–30 mm	100% (9/9)	97% (71/73)	82% (9/11)	100% (71/71)
(95%CI†)	[66%–100%]	[90%–100%]	[48%–98%]	[95%–100%]
CL ≥ 30 mm	100% (1/1)	100% (11/11)	100% (1/1)	100% (11/11)
(95%CI†)	[3%–100%]	[72%–100%]	[3%–100%]	[72%–100%]

†95%CI computed by the Clopper–Pearson procedure. CI, confidence interval; CL, cervical length; NPV, negative predictive value; PAMG-1, placental alpha microglobulin-1; PPV, positive predictive value; SN, sensitivity, SP, specificity.

94%, 83%, 100% and 100%, 97%, 92%, 100% for 7 and 14 days, respectively.

Patients with a CL of 15–30 mm in this study are of particular interest. Of the 82 women in this group, only 11 patients had a positive PAMG-1 test, with eight patients delivering within 7 days, and nine patients delivering within 14 days. Only two patients with a positive test continued pregnancy after 2 weeks. All other patients were discharged after spending up to 18 days in the hospital and none delivered within 14 days of initial testing. Performance metrics for sensitivity, specificity, PPV, and NPV for the PAMG-1 test in this group were: 100%, 95%, 64%, 100% and 100%, 97%, 82%, 100%, for 7 and 14 days, respectively.

Table 4 Risk of preterm delivery within 7 and 14 days according to CL group with PartoSure (PAMG-1) test

Cervical Length (mm)	PAMG-1 Negative					PAMG-1 Positive					PAMG-1 Positive and Negative				
	n	sPTD within 7 days (%)		sPTD within 14 days (%)		*n*	sPTD within 7 days (%)		sPTD within 14 days (%)		*n*	sPTD within 7 days (%)		sPTD within 14 days (%)	
CL < 15 mm	1	0	0%	0	0%	4	4	100%	4	100%	5	4	80%	4	80%
CL 15–20 mm	3	0	0%	0	0%	6	4	67%	5	83%	9	4	44%	5	56%
CL 20–25 mm	30	0	0%	0	0%	2	2	100%	2	100%	32	2	6%	2	6%
CL 25–30 mm	38	0	0%	0	0%	3	1	33%	2	67%	41	1	2%	2	5%
CL ≥ 30 mm	11	0	0%	0	0%	1	1	100%	1	100%	12	1	8%	1	8%
All cervical lengths	83	0	0%	0	0%	16	12	75%	14	88%	99	12	12%	14	14%

CL, cervical length; PAMG-1, placental alpha microglobulin-1; sPTD, spontaneous preterm delivery.

Discussion

Up to 95% of patients presenting with signs of PTL do not go on to deliver within 7 days.[3] Assessing the risk of preterm birth is of great importance for the objective selection of patients for inpatient treatment, as a false positive diagnosis can result in unnecessary hospitalization and administration of prophylactic treatments, while a false negative diagnosis can place the fetus at risk of mortality and morbidity. Diagnosis includes assessment of symptoms, physical examination of patients, instrumental techniques (including transvaginal ultrasound to measure CL), and biochemical tests for markers of PTL. CL measurement via transvaginal ultrasound is the most widely used method among these, as it is useful to identify low-risk patients presenting with CL ≥ 30 mm; however, it cannot identify patients at risk of imminent delivery in the equivocal range of 15–30 mm. A CL measurement of ≤25 mm is often a standard cut-off for admission, and roughly one-third of women presenting with signs and symptoms of PTL fall within this group measuring ≤25 mm. Of these, relatively few go on to deliver within 7 days,[4] leading to over-hospitalization and unnecessary treatment. Further, this cut-off excludes women with a CL of 25–30 mm, who are still at risk of delivery within 7 days but are frequently sent home. Therefore, imposing a cut-off of 25 mm is an insufficient means of assessing these candidates for admission.[15] As the poor predictive value of CL is well known in these equivocal ranges (15–30 mm), in our study, only seven of 82 patients (8.5%) went on to deliver in this group within 7 days and it has become routine to supplement this diagnostic methodology with a biomarker test.[16]

One limitation to the present study is that in our institution and surrounding facilities, progesterone treatment is not given as a standard of care for women with a short cervix, as is recommended in the medical practice guidelines issued first by the American College of Obstetricians and Gynecologists in 2008[17] and more recently by the Society of Maternal Fetal Medicine in 2011.[18] As a result, we were unable to assess in our study whether those women who had received progesterone treatment prior to enrollment had a lower rate of preterm delivery within 7 or 14 days of presentation compared to those who had not received progesterone treatment prior to enrollment. Such a hypothesis – that is, whether progesterone treatment prior to the onset of PTL symptoms may prolong gestation in women who subsequently experience such symptoms during their pregnancy – is certainly one that should be investigated in future research.

This study evaluated the benefits of combining the PAMG-1 test, commercially known as the PartoSure test, with CL measurement. Alone, the PAMG-1 test had a 100% NPV and a 75% PPV for prediction of imminent spontaneous preterm delivery within 7 days, and a 100% NPV and an 88% PPV for prediction of imminent spontaneous preterm delivery within 14 days. These findings confirm the results of other researchers.[9,12] When used in combination with CL of 15–30 mm, the performance of the PAMG-1 test was 64% PPV and 100% NPV within 7 days and 82% PPV and 100% NPV within 14 days. Although the PAMG-1 test was positive in one additional patient with a CL of 36 mm, who delivered imminently after presentation, the overall risk of the ≥30 mm patient group may be too small to justify routine use of a biomarker test.

Our analysis strongly supports the combinatory use of the PAMG-1 test and CL measurement in women with a CL of 15–30 mm to more accurately identify those at high risk of delivery within 7 and 14 days. The combined use of CL measurement and the PAMG-1 test may result in a reduction of unnecessary

admissions and treatments by approximately 53% compared to CL measurement cut-off of 25 mm alone. Such a reduction could have a significant economic impact on the health-care system and reduce the number of unnecessary treatments administered, which have potential consequences for the mother and the fetus. One shortcoming of our study was that we did not calculate the exact cost of unnecessary admissions in our institution. Future research should focus on calculating the cost–benefit of implementing a strategy that involves the use of the PAMG-1 test in patients with a CL of 15–30 mm: this combinatory strategy for women in the aforementioned equivocal CL range. Admission costs in this group should be compared with a strategy wherein only CL measurement is used, or perhaps, only a biochemical test.

Disclosure

The authors report no conflicts of interest. PartoSure test kits were obtained free of charge. The investigators do not have any financial relationship with the company.

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