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Authors

Wing, Deborah A
Haeri, Sina
Silber, Angela C
et al.

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Original Research

Placental Alpha Microglobulin-1 Compared With Fetal Fibronectin to Predict Preterm Delivery in Symptomatic Women

Deborah A. Wing, MD, MBA, Sina Haeri, MD, MHSA, Angela C. Silber, MD, Cheryl K. Roth, PhD, RN, Carl P. Weiner, MD, MBA, Nelson C. Echebiri, MD, MBA, Albert Franco, MD, Lanissa M. Pappas, MD, John D. Yeast, MD, MSPH, Angelle A. Brebnor, MD, J. Gerald Quirk, MD, PhD, Aisling M. Murphy, MD, Louise C. Laurent, MD, PhD, Nancy T. Field, MD, and Mary E. Norton, MD

OBJECTIVE: To compare the rapid bedside test for placental α microglobulin-1 with the instrumented fetal fibronectin test for prediction of imminent spontaneous preterm delivery among women with symptoms of preterm labor.

METHODS: We conducted a prospective observational study on pregnant women with signs or symptoms suggestive of preterm labor between 24 and 35 weeks of gestation with intact membranes and cervical dilatation less than 3 cm. Participants were prospectively enrolled at 15 U.S. academic and community centers. Placental α microglobulin-1 samples did not require a speculum examination. Health care providers were blinded to placental α microglobulin-1 results. Fetal fibronectin samples were collected through speculum examination per manufacturer requirements and sent to a certified laboratory for testing using a cutoff of 50 ng/mL. The coprimary endpoints were positive predictive value (PPV) superiority and negative predictive value (NPV) noninferiority of placental α microglobulin-1 compared with fetal fibronectin for the prediction of spontaneous preterm birth within 7 days and within 14 days.

RESULTS: Of 796 women included in the study cohort, 711 (89.3%) had both placental α microglobulin-1 and fetal fibronectin results and valid delivery outcomes available for analysis. The overall rate of preterm birth was 2.4% (17/711) within 7 days of testing and 4.2% (30/711) within 14 days of testing with respective rates of spontaneous preterm birth of 1.3% (9/703) and 2.9% (20/701). Fetal fibronectin was detected in 15.5% (110/711), and placental α microglobulin-1 was detected in 2.4% (17/711). The PPVs for spontaneous preterm delivery within 7 days or less among singleton gestations (n=13) for placental α microglobulin-1 and fetal fibronectin were 23.1% (3/13) and 4.3% (4/94), respectively ($P<.025$ for superiority). The NPVs were 99.5% (619/622) and 99.6% (539/541) for placental α microglobulin-1 and fetal fibronectin, respectively ($P<.001$ for noninferiority).

CONCLUSION: Although placental α microglobulin-1 performed the same as fetal fibronectin in ruling out spontaneous preterm delivery among symptomatic women, it demonstrated statistical superiority in predicting it.

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See related editorial on page 1181.

From the University of California Irvine, Orange, California; St. David's Medical Center, Austin, Texas; Summa Health, Akron, Ohio; HonorHealth Scottsdale Shea Medical Center, Scottsdale, Arizona; the University of Kansas, Kansas City, Kansas; Meritus Health, Hagerstown, Maryland; South Shore Hospital, South Weymouth, Massachusetts; Promedica–The Toledo Hospital, Toledo, Ohio; St. Luke's Hospital of Kansas City, Kansas City, Missouri; the University at Buffalo–Women and Children's Hospital of Buffalo, Buffalo, New York; Stony Brook University School of Medicine, Stony Brook, New York; the University of California, Los Angeles, Los Angeles, California; the University of California San Diego, San Diego, California; the University of California, Davis, Sacramento, California; and the University of California, San Francisco, California.

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Each author has indicated that he or she has met the journal's requirements for authorship.

Corresponding author: Deborah A. Wing, MD, MBA, Department of Obstetrics-Gynecology, University of California, Irvine, 333 City Boulevard, Suite 1400, Orange, CA 92868; email: deborahawing@gmail.com.

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Up to 28% of patients presenting with symptoms of preterm labor are admitted to the hospital,[1] but as few as 2.9% will deliver in 7 days or less.[2] An unnecessary admission is estimated in U.S. dollars to be valued at $20,372.[3] Thus, a test that aids in the accurate diagnosis of bona fide preterm labor could reduce admissions and health care costs.

Currently, cervical length measurement using transvaginal ultrasonography and the fetal fibronectin test are used; however, the American College of Obstetricians and Gynecologists Practice Bulletin on the management of preterm labor cautions against the use of either a positive fetal fibronectin result or a short cervix alone to direct patient management as a result of each test's low positive predictive value (PPV).[4] Additionally, fetal fibronectin samples cannot be collected after recent coitus or digital examination; testing requires a speculum and reader, and results take 1–2 hours,[5] possibly up to 24 hours.[6]

Placental α microglobulin-1 is released from decidual cells[7] and found in high concentrations in amniotic fluid. Placental α microglobulin-1 is found in cervicovaginal secretions when spontaneous preterm delivery is imminent, likely attributable to early contractility or inflammation related to preterm labor.[8] Although a recent study suggested improved accuracy with placental α microglobulin-1 compared with transvaginal ultrasonography and fetal fibronectin, it included patients from a high-risk European population who had been screened using transvaginal ultrasonography and therefore is not generalizable to U.S. practice.[9]

Our trial assessed the efficacy of a novel bedside test for placental α microglobulin-1 in predicting spontaneous preterm delivery within 7 and 14 days among symptomatic women presenting to U.S. institutions and compared the performance of this test with fetal fibronectin.

MATERIALS AND METHODS

This prospective observational study enrolled participants consecutively across 15 sites in the United States, some of which were academic medical centers and others of which were community-based affiliates, between April 2015 and July 2016. We invited pregnant women between 24 0/7 weeks and 34 6/7 weeks of gestation who presented with signs and symptoms of preterm labor to participate in the trial and excluded those subsequently determined to have had ruptured membranes or cervical dilatation 3 cm or greater from the analysis. We defined signs or symptoms of preterm labor as uterine contractions, intermittent lower abdominal pain, dull backache, pelvic pressure, bleeding during the second or third trimester, or menstrual-like or intestinal cramping with or without diarrhea. Because one goal of our study was to compare placental α microglobulin-1 with fetal fibronectin in the same population that the fetal fibronectin test is used today, we selected the inclusion and exclusion criteria in consideration of the fetal fibronectin test's limitations to use as approved by the U.S. Food and Drug Administration. Thus, we excluded women if they had received tocolytic medications before the collection of cervical vaginal specimens or if they had placenta previa; moderate-to-gross vaginal bleeding; coitus within the past 24 hours; a cervical cerclage; a history not consistent with idiopathic threatened preterm delivery such as trauma, digital transvaginal ultrasonography, or examination immediately before specimen collection; or if they were enrolled in a tocolytic treatment study.

Each site obtained institutional review board approval and all participants provided written informed consent as a requisite for enrollment. The institutional review boards included the Austin multiinstitutional review board, Chesapeake institutional review board, HonorHealth Research Institute, Meritus Medical Center institutional review board, St Luke's Hospital of Kansas City institutional review board, South Shore Hospital Office of Research, Summa Health System institutional review board, the University at Buffalo institutional review board, the University of California institutional review board Reliance Registry, and the University of Kansas Medical Center Human Research Protection Program. After enrollment, we obtained a medical history for each participant. Study personnel collected placental α microglobulin-1 samples by inserting the sterile swab provided with the placental α microglobulin-1 test kit into the vagina without the use of a speculum for 30 seconds. The specimen was then eluted for 30 seconds through active rotation of the swab in the solvent solution provided with the placental α microglobulin-1 test kit. A second operator not responsible for the care of the patient and out of sight of any health care provider responsible for patient management decisions then inserted the placental α microglobulin-1 immunoassay test strip into the sample and read the results no earlier than 5 minutes and no later than 10 minutes later. Two red lines interpreted visually on the test strip indicated a positive test result and one line indicated a negative test result. Thus, the clinicians managing the care of the participants as well as the participants themselves were

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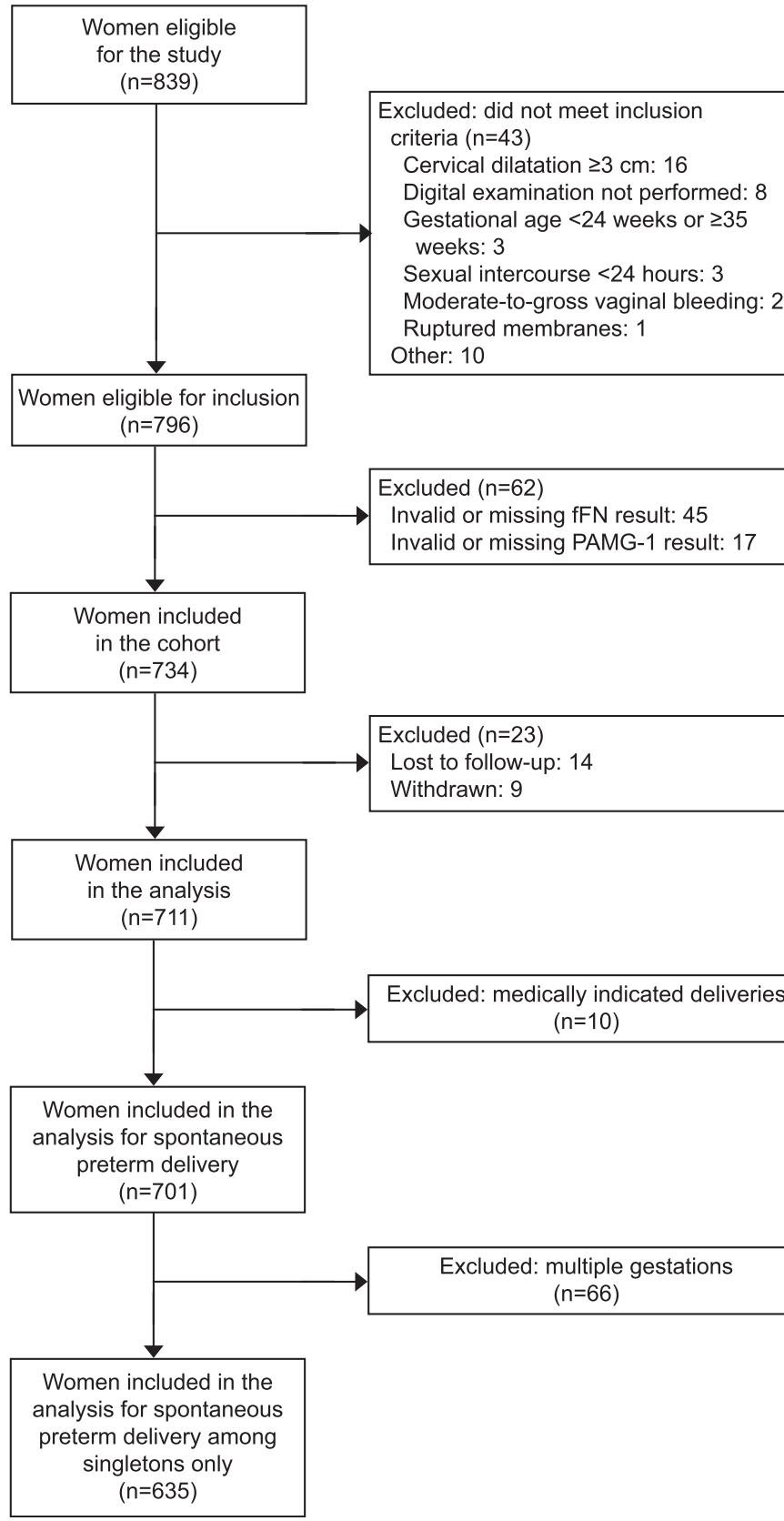

Fig. 1. Study populations used for statistical analyses. fFN, fetal fibronectin; PAMG-1, placental α microglobulin-1.

Wing. Placental α Microglobulin-1 vs Fetal Fibronectin. Obstet Gynecol 2017.

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blinded to placental α microglobulin-1 results. Thereafter, a physical examination including speculum examination was performed to collect a swab of cervicovaginal secretions for fetal fibronectin, as per the manufacturer's requirements and standard practice at the enrolling institutions. The fetal fibronectin test specimen was then sent to a certified laboratory for testing using the U.S. Food and Drug Administration-approved threshold of 50 ng/mL, and results were available to the clinician managing the patient. Cervical length measurements using transvaginal ultrasonography could be obtained thereafter if part of the standard evaluation protocol within a given site.

We collected information regarding labor and delivery and maternal and neonatal outcomes after retrospective chart review. After the single study visit, we held a scripted telephone conversation with each participant at least 21 days after her study visit to facilitate delivery data capture. The scripts used were approved by the institutional review boards.

A clinical consensus panel was chartered and consisted of experts in the field of maternal and fetal medicine who were not otherwise involved with the study. The three members of the clinical consensus panel were responsible for independently evaluating the deidentified medical records of each preterm delivery and categorizing them as either a "spontaneous preterm birth" or a "medically indicated preterm birth" using the following standard definitions: spontaneous preterm birth is defined as delivery occurring subsequent to spontaneous onset of preterm labor or prelabor premature rupture of the membranes or fetal membrane prolapse, regardless of subsequent labor augmentation or cesarean delivery; and a medically indicated preterm birth is defined as delivery occurring as the result of one or more obstetric conditions (eg, placenta previa or multiple gestation) or maternal medical conditions (eg, preeclampsia) that do or do not coincide with spontaneous onset of preterm labor or prelabor premature rupture of the membranes or fetal membrane prolapse.[10] The clinical consensus panel members remained blind to the placental α microglobulin-1 test results during their evaluation and categorization and a consensus assessment (3/3 or 2/3) was utilized to ultimately classify the preterm birth.

Power calculations for testing superiority of placental α microglobulin-1 PPV compared with fetal fibronectin PPV for the prediction of spontaneous preterm delivery at 7 days or less and 14 days were based on a test of inequality for two proportions using a pooled Z-test and $\alpha=0.025$. Power calculations for testing the noninferiority of placental α microglobulin-1 negative predictive value (NPV) compared with fetal fibronectin NPV for the prediction of spontaneous preterm delivery at 7 days or less and 14 days were based on a test of noninferiority of two proportions using proportions with a pooled Z-test and $\alpha=0.025$. Based on these assumptions, it was estimated that 710 participants would provide 80% overall power. Power calculations were conducted using PASS 13, conservatively assuming independent proportions for placental α microglobulin-1 and fetal fibronectin for each coprimary endpoint and time point. Assuming not all participants would be evaluable based on eligibility criteria, and not all test results would be analyzable, planned enrollment for this clinical evaluation was 900 pregnant participants.

We performed the primary endpoint analysis on all evaluable participants with analyzable results from the placental α microglobulin-1 and fetal fibronectin tests as well as known pregnancy outcome. We had

Table 1. Evaluable Participant Demographic and Obstetric Characteristics (N=711)

Characteristic	Evaluable Participants
n	711
Maternal age (y)	
Mean±SD	28.2±5.8
Median	28.0
Range (minimum–maximum)	17.0–44.0
IQR	24.0–32.0
Ethnicity	
Hispanic or Latina	21.4 (148/691)
Not Hispanic or Latina	78.6 (543/691)
Race	
White	67.5 (480/711)
Black or African American	24.5 (174/711)
Native American or Alaska Native	0.6 (4/711)
Native Hawaiian or other Pacific Islander	0.0 (0/711)
Asian	0.8 (6/711)
Other	2.0 (14/711)
Gestational age at sampling (wk)	
Mean±SD	29.7±3.0
Median	29.9
Range (minimum–maximum)	24.0–34.9
IQR	27.4–32.4
Previous term delivery	59.5 (422/709)
Prior preterm delivery	21.4 (152/709)
Previous abortion	39.2 (278/710)
Cervical dilatation 1 cm or less	96.5 (686/711)
Uterine contractions fewer than 4/h	15.4 (28/182)
PAMG-1 detected	2.4 (17/711)
fFN detected	15.5% (110/711)

IQR, interquartile range; PAMG-1, placental α microglobulin-1; fFN, fetal fibronectin.
Data are % (n/N) unless otherwise specified.

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a twofold objective testing two hypotheses simultaneously. The objective of the primary analysis was to demonstrate that the PPV in the placental α microglobulin-1 cohort was greater than the observed PPV rate of the fetal fibronectin cohort. We also tested whether the NPV in the placental α microglobulin-1 cohort was greater than the observed NPV rate of the fetal fibronectin cohort minus the noninferiority margin. We used the generalized estimating equation method of Leisenring et al[11] for the statistical analysis of the superiority of PPV. The statistical noninferiority of NPV was done using the bootstrap resampling method. We produced all tables, listings, and figures using SAS 9.3 or a later version of SAS.

RESULTS

A total of 839 women were enrolled with 711 being evaluable for analysis. One hundred twenty-eight women were not included in the analysis for the following reasons: 45 had invalid or missing fetal fibronectin results (5.4%), 43 did not meet eligibility criteria (5.1%), 17 had invalid or missing placental α microglobulin-1 results (2.0%), 14 were lost to follow-up (1.7%), and nine were withdrawn (1.1%). Overall, 711 of the enrolled participants had evaluable data (84.7%; Fig. 1). Of these, 651 (91.6%) had delivery information obtained from chart abstraction and 60 (8.4%) had delivery information obtained from the follow-up phone calls. In the cases in which delivery information from the follow-up phone call was used in the analysis, delivery information was not available in the patient's medical record.

Most evaluable participants were white, non-Hispanic, and had a mean gestational age of sampling of 29.7 (±SD 3.0) weeks. The overwhelming majority had 1 cm dilation or less at sampling (686/711 [96.5%]). Many had a history of a previous term delivery (422/709 [59.5%]) and 21.4% (152/708) had a prior preterm delivery. Placental α microglobulin-1 was detected in 2.4% (17/711) of participants compared with 15.5% (110/711) in whom fetal fibronectin was detected (Table 1). The prevalence of preterm delivery at 7 days or less and 14 days or less in the study cohort was 2.4% (17/711), of which 13 were singleton gestations, and 4.2% (30/711), of which 21 were singleton gestations. The prevalence of spontaneous preterm delivery at 7 days or less and 14 days or less in the study cohort was 1.3% (9/703), because 8 of the 17 preterm births were medically indicated, as assessed by the clinical consensus panel, and 2.9% (20/701), of which 10 of 30 were medically indicated, as assessed by the clinical consensus panel.

Of the 711 evaluable participants, 10 were medically indicated, as assessed by the clinical consensus panel. After excluding the 10 medically indicated preterm deliveries, 701 evaluable participants remained for analysis for the prediction of spontaneous preterm delivery at 7 days or less and 14 days or less of specimen collection. The PPV for the prediction of spontaneous preterm delivery for both singleton and multiple gestations within 7 days for placental α microglobulin-1 and fetal fibronectin were 18.8% (3/16) and 6.5% (4/94), respectively ($P<.025$ for placental α microglobulin-1 superiority). The NPVs for spontaneous preterm delivery within 7 days were 99.1% (679/685) and 99.7% (591/593) for placental α microglobulin-1 and fetal fibronectin, respectively ($P<.001$ for noninferiority). The PPVs for spontaneous preterm delivery within 14 days for placental α microglobulin-1 and fetal fibronectin were

Table 2. Placental α Microglobulin-1 and Fetal Fibronectin Prediction of Spontaneous Preterm Delivery at 7 Days or Less and 14 Days or Less Among the Whole Cohort of Singleton and Twin Gestations (n=701)

Statistic	PPV	NPV
Spontaneous preterm delivery at 7 d or less		
PAMG-1	19 (3/16) (4–46)	99.1 (679/685) (98.1–99.7)
fFN	6.5 (7/108) (2.7–12.9)	99.7 (591/593) (98.8–100)
P	<.025*	<.001†
Spontaneous preterm delivery at 14 d or less		
PAMG-1	25 (4/16) (7–52)	97.7 (669/685) (96.2–98.7)
fFN	11.1 (12/108) (5.9–18.6)	98.7 (585/593) (97.4–99.4)
P	<.025*	<.001†

PPV, positive predictive value; NPV, negative predictive value; PAMG-1, placental α microglobulin-1; fFN, fetal fibronectin.
Data are % (n/N) (95% CI) unless otherwise specified.
* One-sided *P*-value based on a generalized estimating equation model testing whether or not the slope of the test used variable in the model is equal to 0. *P* value reported for a test of superiority.
† One-sided *P*-value based on a bootstrap resampling method, where a *t* test of the estimates of the difference between the two tests compared with a value of −5% is performed. *P* value reported for a test of noninferiority.

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25.0% (4/16) and 11.1% (12/108), respectively ($P<.025$ for placental α microglobulin-1 superiority). The NPVs for spontaneous preterm delivery within 14 days were 97.7% (669/685) and 98.7% (585/593) for placental α microglobulin-1 and fetal fibronectin, respectively ($P<.001$ for placental α microglobulin-1 noninferiority) (Table 2). Thus, considering both singleton and multiple gestations, we found that the PPV of the placental α microglobulin-1 test was statistically higher than that of the fetal fibronectin while maintaining noninferiority for the NPV. There were no adverse events reported that were associated with either placental α microglobulin-1 or fetal fibronectin use.

Of the 711 evaluable participants, 643 participants had singleton gestations. Of these, 13 had a spontaneous preterm delivery at 14 days or less of specimen collection and eight had a medically indicated preterm delivery at 14 days or less of specimen collection, as assessed by the clinical consensus panel. After excluding the eight medically indicated preterm deliveries, 635 evaluable participants remained for subgroup analysis for the prediction of spontaneous preterm delivery at 7 days or less and 14 days or less of specimen collection among singleton gestations. Placental α microglobulin-1 was detected in 2.0% of participants (13/635) and fetal fibronectin was detected in 14.8% (94/635) of participants (Table 3). The PPVs for spontaneous preterm delivery within 7 days among singleton gestations for placental α microglobulin-1 and fetal fibronectin were 23.1% (3/13) and 4.3% (4/94), respectively ($P<.025$ for placental α microglobulin-1 superiority). The NPVs for spontaneous preterm delivery within 7 days among singleton gestations were 99.5% (619/622) and 99.6% (539/541) for placental α microglobulin-1 and fetal fibronectin, respectively ($P<.001$ for placental α microglobulin-1 noninferiority). The PPVs for spontaneous preterm delivery within 14 days among singleton gestations for placental α microglobulin-1 and fetal fibronectin were 30.8% (4/13) and 9.6% (9/94), respectively ($P<.025$ for placental α microglobulin-1 superiority). The NPVs for spontaneous preterm delivery within 14 days among singleton gestations were 98.6% (613/622) and 99.3% (537/541) for placental α microglobulin-1 and fetal fibronectin, respectively ($P<.001$ for placental α microglobulin-1 noninferiority) (Table 4). The sensitivity and specificity of the placental α microglobulin-1 test were 50.0% and 98.4%, respectively, for delivery at 7 days or less; for fetal fibronectin, these results were 66.7% and 85.7%, respectively (Table 5). Thus, we found that the PPV of the placental α microglobulin-1 test was three to four times higher than that of the fetal fibronectin for each outcome while maintaining noninferiority for the NPV.

Table 3. Demographic and Obstetric Characteristics for Analyzed Singleton Gestations (n=635)

Characteristic	Analyzed Singleton Gestations
n	635
Maternal age (y)	
Mean±SD	28.1±5.8
Median	27.0
Range (minimum–maximum)	17.0–44.0
IQR	23.0–32.0
Ethnicity	
Hispanic or Latina	21.7 (134/618)
Not Hispanic or Latina	78.3 (484/618)
Race	
White	67.2 (427/635)
Black or African American	24.3 (154/635)
Native American or Alaska Native	0.6 (4/635)
Native Hawaiian or other Pacific Islander	0.0 (0/635)
Asian	0.8 (5/635)
Other	2.0 (13/635)
Gestational age at sampling (wk)	
Mean±SD	635
Median	29.8±3.0
Range (minimum–maximum)	30.0
IQR	24.0–34.8
Previous term delivery	60.2 (381/633)
Prior preterm delivery	22.4 (142/633)
Previous abortion	39.0 (247/634)
Cervical dilatation 1 cm or less	97.2 (617/635)
Uterine contractions fewer than 4/h	15.4 (24/156)
PAMG-1 detected	2.0 (13/635)
fFN detected	14.8 (94/635)

IQR, interquartile range; PAMG-1, placental α microglobulin-1; fFN, fetal fibronectin.
Data are % (n/N) unless otherwise specified.

As a result of the low number of patients who underwent transvaginal ultrasonography (125/711 [17.6%]) as well as the inconsistency with which transvaginal ultrasonography was elected to be used, a subgroup analysis investigating the efficacy of this tool in predicting imminent preterm delivery was not possible nor was it possible to evaluate the effectiveness of placental α microglobulin-1 or fetal fibronectin in conjunction with a cervical length measurement.

The ability of other clinical predictors to assess risk of spontaneous preterm delivery was also evaluated (Fig. 2). For the prediction of spontaneous preterm delivery at 7 days or less among singleton gestations, placental α microglobulin-1 had the highest estimates of PPV, NPV, sensitivity, and specificity compared with uterine activity (four or more

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Table 4. Placental α Microglobulin-1 and Fetal Fibronectin Prediction of Spontaneous Preterm Delivery at 7 Days or Less and 14 Days or Less Among Singleton Gestations—Positive Predictive Value and Negative Predictive Value (n=635)

Statistic	PPV	NPV
Spontaneous preterm delivery at 7 d or less		
PAMG-1	23 (3/13) (5–54)	99.5 (619/622) (98.6–99.9)
fFN	4.3 (4/94) (1.2–10.5)	99.6 (539/541) (98.7–100)
P	<.025*	<.001†
Spontaneous preterm delivery at 14 d or less		
PAMG-1	31 (4/13) (9–61)	98.6 (613/622) (97.3–99.3)
fFN	9.6 (9/94) (4.5–17.4)	99.3 (537/541) (98.1–99.8)
P	<.025*	<.001†

PPV, positive predictive value; NPV, negative predictive value; PAMG-1, placental α microglobulin-1; fFN, fetal fibronectin.
Data are % (n/N) (95% CI) unless otherwise specified.
* One-sided *P* value based on a generalized estimating equation model testing whether or not the slope of the test used variable in the model is equal to 0. *P* value reported for a test of superiority.
† One-sided *P* value based on a bootstrap resampling method, where a *t* test of the estimates of the difference between the two tests compared with a value of −5% is performed. *P* value reported for a test of noninferiority.

contractions per hour), cervical dilatation (greater than 1 cm and less than 3 cm), and the presence of vaginal bleeding. The ability of prior preterm birth to assess risk of spontaneous preterm delivery at 7 days or less among singleton gestations was similarly evaluated, although it was the poorest predictor of biomarkers and clinical predictors. The PPV and NPV for spontaneous preterm delivery within 7 days among singleton gestations for prior preterm birth were 1.4% (2/142) and 98.8% (324/328), respectively.

DISCUSSION

We demonstrated that in patients who undergo examination and testing resulting from symptoms of preterm labor, the detection of placental α microglobulin-1 in cervicovaginal secretions is a stronger predictor of spontaneous preterm delivery compared with the detection of fetal fibronectin. Furthermore, we found that fetal fibronectin is significantly more likely to be positive than is placental α microglobulin-1 (15.5% compared with 2.4%, respectively). We found that placental α microglobulin-1 performed similarly to fetal fibronectin in ruling out the risk of spontaneous preterm delivery in 7 days or less and 14 days or less from cervicovaginal sample collection between 24 0/7 weeks and 34 6/7 weeks of gestation with signs and symptoms of early preterm labor, intact amniotic membranes, and minimal cervical dilatation (less than 3 cm). The NPV of placental α microglobulin-1 for prediction of spontaneous preterm delivery at 7 days or less among singleton gestations was comparable with fetal fibronectin's (99.5% compared with 99.6%, respectively [$P<.001$ for noninferiority]), indicating that delivery is highly unlikely within this timeframe when either test is negative. However, the PPV for prediction of spontaneous preterm delivery at 7 days or less after sampling among singleton gestations was greater for placental α microglobulin-1 than for fetal fibronectin (23.1% compared with 4.3%, respectively [$P<.025$]). Thus, the coprimary endpoints of PPV superiority and NPV noninferiority for placental α microglobulin-1 compared with fetal fibronectin were met.

Spontaneous preterm labor is one syndrome with many causes.[10] Consequently, standard medical practice in the United States for the evaluation of women with threatened preterm labor involves historic, clinical, biochemical, and cervical evaluation.[12,13] As such, it is highly improbable that a negative biochemical test result would be considered alone to direct

Table 5. Placental α Microglobulin-1 and Fetal Fibronectin Prediction of Spontaneous Preterm Delivery at 7 Days or Less Among Singleton Gestations—Sensitivity and Specificity (n=635)

Statistic	Sensitivity	Specificity
Spontaneous preterm delivery at 7 d or less		
PAMG-1	50 (3/6) (12–88)	98.4 (619/629) (97.1–99.2)
fFN	67 (4/6) (22–96)	85.7 (539/629) (82.7–88.3)

PAMG-1, placental α microglobulin-1; fFN, fetal fibronectin.
Data are % (n/N) (95% CI) unless otherwise specified.

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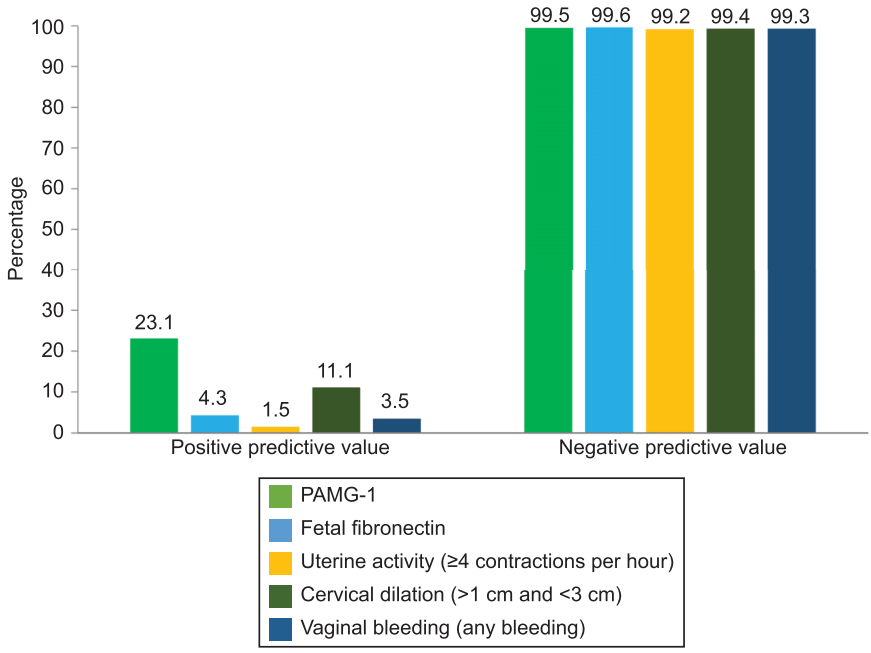

Fig. 2. Performance of risk factors for prediction of spontaneous preterm delivery at 7 days or less of specimen collection for singleton gestations (n=635). PAMG-1, placental α microglobulin-1.

Wing. Placental α Microglobulin-1 vs Fetal Fibronectin. Obstet Gynecol 2017.

management. On the contrary, a clinician is likely to rely on a positive biochemical test result to admit a patient and administer therapeutics and, in this way, use the biochemical test for triaging purposes.[14] In fact, our study showed that greater than 80% of participants treated or admitted for threatened preterm labor did not go on to deliver within 7 days. Thus, the clinical significance of biochemical test performance should not only be placed on its NPV, but also on its PPV and how that PPV in combination with test positivity rate may reduce unnecessary patient interventions.

Previously published reports indicated that placental α microglobulin-1's PPV for prediction of spontaneous preterm delivery among singleton gestations at 7 days or less of presentation ranged from 75.7% to 78.3%.[8,15] Because predictive values are influenced by disease prevalence, we believe the difference between the PPV observed in those studies and ours (23.1%) reflects differences in prevalence rates of spontaneous preterm delivery among the studies' populations. Specifically, those studies' prevalence of spontaneous preterm delivery at 7 days or less of sample collection ranged from 17.2% to 19.8% compared with 2.4% observed in this study. Because those investigations included a European cohort, the higher rates of spontaneous preterm delivery were likely the result of the prominent role played by transvaginal ultrasonography in filtering out lower risk patients, thus enriching the tested patient population for those with a high risk of preterm delivery.

Placental α microglobulin-1 offers a more rapid turnaround time with bedside testing (6 minutes compared with at least 1–2 hours and up to 24 hours for fetal fibronectin).[5,6] Additionally, because the placental α microglobulin-1 test specimen is obtained without speculum examination, it may offer increased comfort for the patient and convenience for the care provider. Lastly, the performance of placental α microglobulin-1 is not known to be affected by recent vaginal examinations or sexual intercourse, because it was previously shown that results obtained before and after digital examination were the same[16] and that placental α microglobulin-1 antibodies do not cross-react with sperm.[17] Together, these advantages may also lead to reduced triage times.

Our study has some important limitations. The rate of spontaneous preterm delivery at 7 days or less and 14 days or less was very low, 1.3% and 2.8%, respectively, and only 13 singleton gestations in the cohort delivered spontaneously within 14 days of sampling. After enrollment, 15% of patients were excluded for various reasons. One third (10) of the 30 deliveries, which occurred within 14 days of study enrollment, were excluded because they were deemed not to have been spontaneous, and we enrolled too few patients with multiple gestations (n=66) or transvaginal ultrasonography (n=125) to conduct subgroup analyses.

In conclusion, we found that placental α microglobulin-1 performed the same as fetal fibronectin in ruling out spontaneous preterm delivery among

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a contemporary cohort of symptomatic women and additionally demonstrated statistical superiority in predicting it. Whether the higher PPV and lower positivity rate of the placental α microglobulin-1 test we observed will ultimately translate into lower rates of unnecessary hospitalizations, interventions, and in utero transfers to higher level-of-care facilities requires further rigorous investigation.

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