Validation of a clinical risk scoring system, based solely on clinical presentation, for the management of pregnancy of unknown location

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Objective: To assess a scoring system to triage women with a pregnancy of unknown location.
Design: Validation of prediction rule.
Setting: Multicenter study.
Patient(s): Women with a pregnancy of unknown location.
Intervention(s): None.
Main Outcome Measure(s): Scores assigned to factors identified at clinical presentation, total score calculated to assess risk of ectopic pregnancy (EP) in women with a pregnancy of unknown location, and a proposed three-tiered clinical action plan.
Result(s): The cohort of 1,400 women (284 ectopic pregnancies, 759 miscarriages, and 357 intrauterine pregnancies) was more diverse than the original cohort used to develop the decision rule. The recommendations of the action plan were low risk, intermediate risk, and high risk; the recommendation based on the model score was compared with clinical diagnosis. A total of 29.4% intrauterine pregnancies were identified for less frequent follow-up observation, and 18.4% nonviable gestations were identified for more frequent follow-up observation (to rule out an ectopic pregnancy) compared with intermediate risk (i.e., monitor in current standard fashion). For a decision of possible less frequent monitoring, the specificity was 90.8% (89.0–92.6) with negative predictive value of 79.0% (76.7–81.3). For a decision of more intense follow-up observation, the specificity was 95.0% (92.7–97.2). Test characteristics using the scoring system were replicated in the diverse validation cohort.
Conclusion(s): A scoring system based on symptoms at presentation has value to stratify risk and influence the intensity of outpatient surveillance for women with pregnancy of unknown location but does not serve as a diagnostic tool. (Fertil Steril® 2013;99:193–8. ©2013 by American Society for Reproductive Medicine.)
Key Words: Ectopic pregnancy, pregnancy of unknown location, risk factors, scoring system

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The presence of abdominal pain and/or vaginal bleeding in a woman known or suspected to be pregnant should be evaluated to investigate the possibility of an ectopic pregnancy (EP) or miscarriage (1). The use of diagnostic algorithms to systematically evaluate all women at risk for an EP has limited the misdiagnosis of an EP and has contributed to the decrease in mortality and morbidity from this life-threatening condition

(2–5). The combination of ultrasound and human chorionic gonadotropin (hCG) determination is the most efficient method of diagnosis for a woman at risk for EP. A solitary hCG value, however, is not sufficient to definitively diagnose an EP and must be interpreted along with ultrasound findings (6–9). Moreover, up to 20% of women who present with first trimester pain and/or bleeding will not have a gestational sac detected by ultrasound (in the uterus or adnexa) and will initially be classified as a pregnancy of unknown location (PUL) (1, 10, 11).

The diagnostic strategy to definitively diagnose a woman with a PUL can be time consuming and cumbersome, and the clinical index of suspicion can affect the frequency and intensity of outpatient follow-up observation (1, 12, 13). Importantly, not all of these women are at equal risk for an EP (14, 15). Individualizing the frequency and aggressiveness of outpatient follow-up observation based on initial risk evaluation would be a much-needed advancement in clinical care. We have demonstrated that for the purpose of clinical prediction it is best to distinguish a potential viable gestation from a nonviable gestation (5) and that the location of an early symptomatic gestation can be predicted, but not diagnosed, solely using information from clinical presentation (5).

Diagnostic models and strategies often result in poorer test characteristics and accuracy in a population distinct from its development (6). Our study validated a clinical prediction rule based on five pieces of information routinely obtained at initial evaluation of a woman with a PUL, distinguishing EPs and miscarriage from ongoing intrauterine pregnancies (IUPs), in a temporally, geographically, and ethnically distinct population from which it was derived. The goal of study was to validate the sensitivity, specificity, and predictive value of the model that can be used to change in the acuity of outpatient surveillance ultimately needed to confirm the diagnosis.

MATERIALS AND METHODS

This study compared the predicted outcome with the actual outcome in a retrospective cohort of woman who had presented with a pregnancy of unknown location. Recommended action based on the total score was proposed by use of a three-tiered clinical plan. Recommendations included low acuity surveillance for low risk (-2 to -1), standard surveillance for intermediate risk (0 to $+4$), and high-acuity surveillance for those with high risk ($\geq +5$). The score-based recommendation was retrospectively compared with definitive clinical diagnosis.

The study was approved by the institutional review boards of the University of Pennsylvania, University of Southern California, and University of Miami. A database of all women in the first trimester of pregnancy (positive pregnancy test or history of a missed period) who present with pain and/or bleeding is maintained at the three centers as part of the Predictors of Ectopic Pregnancy (PEP) study. Data regarding women with a pregnancy of unknown location (PUL) were prospectively entered directly into a computerized database by the clinical staff caring for the patient, including the medical and surgical history, maternal and gestational age, symptoms at presentation (such as pain and bleeding), and diagnostic tests (ultrasound results and hCG level). All women had an initial quantitative hCG value and an ultrasound that was not diagnostic.

Women with a PUL were tracked in this clinical database until they were definitively diagnosed with an EP, a visualized IUP, or a miscarriage according to the consensus definition (10). The diagnosis of miscarriage included women with products of conception identified from the tissue obtained on surgical evacuation of the uterus (histologic IUP), the spontaneous decline of hCG level to ≤ 5 IU/L (spontaneously resolved PUL), or resolution of serum hCG levels after uterine evacuation without evidence of chorionic villi on pathology and without medical therapy (resolved persistent PUL). A visualized IUP was defined as an IUP identified by ultrasound with a yolk sac or a fetal pole. The diagnosis of EP was either a visualized EP (extrauterine gestational sac with yolk sac, or embryonic cardiac activity identified with ultrasound, or an EP visualized at the time of surgery) or a nonvisualized EP (a rising hCG level after uterine evacuation). There were no patients treated medically without confirmation of the location of the gestation (treated persistent PUL).

The scoring system, identical to that used in our previous analysis, assigns values (-1 to $+4$) to each risk factor identified at clinical presentation (Table 1) (5). For each patient, a total score was calculated to assess the risk of a nonviable gestation (miscarriage or EP), which ranged from -2 to $+10$ with a higher score associated with an increased risk of nonviable gestation.

Pearson chi-square tests were conducted to assess demographic, clinical history, and presenting differences between the original (15) and validation cohorts. Logistic regression was used to estimate the association between characteristics at presentation and the primary outcome variable in the new cohort, and to compute odds ratios with 95% confidence intervals. We then compared the strength of the associations in the new cohort with what had been previously demonstrated (15). The original and validation data are presented side by side to facilitate comparisons.

To assess the three-tier plan, the recommendations were collapsed into two binary variables: low-acuity surveillance versus other surveillance (categories of standard surveillance and high-acuity surveillance combined), and high-acuity surveillance versus other surveillance (categories of standard

TABLE 1

Prediction of nonviable gestation by scoring system.

	Variable	Numeric score
1	Age (y)	
	<18	+1
	>38	+3
2	Prior ectopic pregnancy	
	1	+2
	≥2	+3
3	Bleeding	+4
4	Prior miscarriage	
	1 prior miscarriage	−1
5	hCG >2,000 mIU/mL	−1

Note: A total score can range from −2 to +10. A score of −1 or −2 is low risk for nonviable gestation (EP or miscarriage). A total score of 0–4 is intermediate risk for nonviable gestation. A total score of 5 or more is high risk for nonviable gestation. hCG = human chorionic gonadotropin.

Barnhart. Risk scoring system for pregnancy of unknown location. Fertil Steril 2013.