Efficient Use of Early Obstetric Sonography in the Emergency Department Setting

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Objectives—Transvaginal sonography is frequently used in the emergency department (ED) to triage pregnancies of unknown location. The purpose of this study was to examine the utility of sonography in clinically stable patients with β-human chorionic gonadotropin (β-hCG) values below the discriminatory zone.

Methods—We conducted a retrospective cohort study of 408 consecutive ED patients who presented with pregnancies of unknown location and serum β-hCG levels between 5 and 2500 mIU/mL and underwent transvaginal sonography. Women were classified as receiving immediate treatment or expectant management. Predictors associated with immediate treatment were assessed by bivariate analyses and logistic regression.

Results—Of the cohort, 361 women (88.5%) received expectant management, and 6.9%, 3.1%, and 0% of patients with pregnancies of unknown location and β-hCG levels below 1000, 200, and 75 mIU/mL, respectively, received immediate treatment. Compared to the expectant management group, women receiving immediate treatment (n = 47) were further from the last menstrual period (7.86 versus 6.10 weeks; P < .01), were more likely to report pain (59.6% versus 40.2%; P = .01), had higher β-hCG levels (1183 versus 608 mIU/mL; P < .01), and had lower hematocrit levels (35.7% versus 37.0%; P < .01), with pain the most predictive factor for immediate treatment (odds ratio, 5.97; 95% confidence interval, 2.45–14.53). A model combining symptoms, β-hCG, hematocrit, and weeks since the last menstrual period predicted the likelihood of sonography changing management from expectant management to immediate treatment with specificity of 98%.

Conclusions—The diagnostic utility of sonography in clinically stable patients presenting to the ED in very early pregnancy is limited. A model using symptoms, β-hCG, hematocrit, and the last menstrual period may aid clinicians to triage those who would benefit from immediate sonography.

Key Words—early obstetric sonography; ectopic pregnancy; pregnancy of unknown location

The symptoms most often associated with ectopic pregnancy are abdominal pain and vaginal bleeding; however, some may be asymptomatic. Various modalities are used in the evaluation of these women, including hormonal assays for β-human chorionic gonadotropin (β-hCG), clinical examination, and transvaginal sonography.

In gestations longer than 5½ weeks, transvaginal sonography can identify a normal intrauterine pregnancy with almost 100% accuracy.5–7 Although a single serum β-hCG value cannot predict the location or normality of a pregnancy, it can provide a surrogate marker for early gestational age, except in the case of multiple gestations. Above the “discriminatory threshold” level of β-hCG, there should be sonographic evidence of an intrauterine pregnancy using contemporary transvaginal probes in most cases. This threshold value has been reported to be between 1500 and 2500 mIU/mL,8,9 with the upper limit providing higher sensitivity. However, the absence of sonographic findings about this value does not completely exclude the possibility of a normal gestation, especially in the case of a multiple gestation.

Above the discriminatory threshold, sonography can be a valuable tool to aid in the diagnosis of abnormal intrauterine and extrauterine pregnancies or to provide reassurance if a viable intrauterine pregnancy is visualized. Below the discriminatory threshold, a viable intrauterine pregnancy may not yet be visualized. Sonography may reveal signs of a definite ectopic pregnancy (extrauterine gestational sac with a yolk sac or embryo) or a probable ectopic pregnancy (homogeneous adnexal mass or extrauterine saclike structure). However, the sensitivity and specificity of sonography for detecting ectopic pregnancies is 73% to 93% and is greatly dependent on sonographer expertise.4,10,11

Without accounting for β-hCG levels, evidence of a complex adnexal mass is seen in only 60% of ectopic pregnancies and fluid in the cul-de-sac in only 40% of unruptured cases.12 Unless a definitive ectopic pregnancy is visualized, hemodynamically, stable women have a diagnosis of a pregnancy of unknown location and are commonly followed expectantly with another assessment of the β-hCG level in 48 to 72 hours.

The purpose of this study was to examine the utility of immediate sonography in clinically stable patients with pregnancies of unknown location and β-hCG values below the discriminatory zone. Transvaginal sonography was considered to change management if a patient underwent immediate treatment in the ED instead of expectant management. We hypothesized that certain parameters such as the β-hCG level and presence of pain could differentiate which women would benefit from sonography at the initial ED visit.

Materials and Methods

This study was an Institutional Review Board–approved retrospective cohort study of all pregnant women who presented to University of North Carolina, Chapel Hill ED between August 2007 and October 2010 with vaginal bleeding, abdominal pain, or both. Patients were included if they presented to the ED within 12 hours of the first documented serum β-hCG or sonography, were status post therapeutic abortion or documented spontaneous abortion, or did not receive follow-up at our institution. A total of 408 women met all criteria for inclusion.

Sonographic examinations were performed by registered diagnostic medical sonographers (RDMS) using LOGIQ 9 (GE Healthcare, Milwaukee, WI), iU22 (Philips Healthcare, Bothell WA), and Acuson S2000 and Sequoia (Siemens Medical Solutions, Mountain View, CA) ultrasound machines with 5- to 10-MHz transvaginal ultrasound probes and interpreted by physicians board certified in maternal-fetal medicine.

The primary outcome for this study was a change in management due to transvaginal sonography. For this cohort of women with β-hCG levels below the discriminatory zone, it was presumed that patients, had they not undergone sonography, would have had expectant management with another β-hCG value in 48 hours. Sonography was assumed to have resulted in a change in management if the patient received immediate treatment (misoprostol, methotrexate, or surgery) before discharge from the ED. The specific sonographic findings were not considered when segregating patients into groups (ie, the presence of an adnexal mass, free fluid, or complex material inside the uterus); instead, if the patient received immediate treatment, it was presumed that the provider reading the sonogram, the clinician treating the patient, or both felt confident in the diagnosis. Those patients who eventually had a diagnosis and treatment for abnormal intrauterine or extrauter-
ine pregnancies by abnormally rising \( \beta \)-hCG levels or subsequent sonography were not included in the immediate treatment group.

**Exposure and Covariate Assessment**

The primary outcome was immediate treatment, and the primary risk factor was the serum \( \beta \)-hCG value obtained at the ED visit. Additional variables included maternal demographics, risk factors for ectopic pregnancy, presenting symptoms of pain or bleeding, vital signs, and the initial hematocrit value. Patients were classified as clinically stable if they had a heart rate of less than 110 beats per minute and blood pressure of greater than 90/60 mm Hg, no evidence of acute abdomen on examination, and a stable hematocrit value (defined as >30% with no history of anemia or <5% below the previous hematocrit value with a documented history of anemia). Both clinically stable and unstable patients were included in this study because each patient was deemed clinically stable enough to undergo sonography. There were no patients who went to the operating room for suspected ectopic pregnancies during this time frame who did not first undergo sonography.

**Statistical Analysis**

Initially, univariate analyses were conducted to determine the potential relationship between demographic variables, symptoms, vital signs, and laboratory tests and the probability of sonography changing management. The results from the preliminary analyses were used to create a prediction model with a change in management as the dependent variable. All variables that showed a potential relationship with a change in management were initially included in the prediction model along with potential interaction terms. Likelihood ratio tests were conducted, and effect modifiers and predictors that were not statistically significant (\( P < .1 \)) were removed from the model. The independent relationship between each predictor in the final model and the outcome are presented using odds ratios (ORs) with 95% confidence intervals (CIs). The predictive ability of the final model was assessed by goodness of fit (Pearson \( \chi^2 \) test of observed versus predicted responses), classification statistics, and receiver operating characteristic curves. The model was validated by bootstrap stepwise regression validation with the original data set.

**Results**

There were 408 women who met criteria for inclusion in this study. A total of 361 patients (88.5%) underwent expectant management, with most of them (94.7%) receiving instructions for another \( \beta \)-hCG test in 48 hours and the remainder (5.3%) undergoing another sonographic examination in 1 week if evidence of an early intrauterine pregnancy was visualized on sonography (as defined by the presence of a yolk sac or fetal pole). The patients who underwent immediate treatment were further divided into those who underwent emergent management (sent to the operating room for exploration or to control hemorrhage or given methotrexate for presumed ectopic pregnancies) and those who received nonemergent management that could have been safely delayed if desired (treatment for stable patients with a missed abortion). Of the 47 (11.5%) who underwent immediate treatment, 27 were managed emergently and 20 nonemergently (Figure 1). Four of the patients who received emergent management in this group were clinically unstable, all of whom underwent emergent surgical management, 2 for suspected ectopic pregnancies and 2 for incomplete abortions.

Demographics of the two study groups (expectant management and immediate treatment), including age, race, body mass index, and history of ectopic pregnancy risk factors (prior ectopic pregnancy, prior tubal surgery, history of sexually transmitted infections affecting the fallopian tubes, or an intrauterine device in place at the time...
of conception) are shown in Table 1. There was no difference between study groups in age, race, body mass index, or history of ectopic risk factors (Table 1). However, patients who underwent immediate treatment were significantly further from the last menstrual period.

Approximately three-fourths (75.9%) of patients presented with vaginal bleeding (including those with and without pain); 42.4% of patients presented with abdominal or pelvic pain (including those with and without bleeding); and 74 patients (18.1%) presented with both bleeding and pain. Patients in the immediate treatment group were more likely to report pain, have higher β-hCG levels, and have lower hematocrit levels (Table 2). Vaginal bleeding did not differ significantly between groups (Table 2).

The final diagnoses of all patients in the cohort are presented in Figure 2. A total of 67 (16.4%) patients were ultimately treated for an ectopic pregnancy: 44 with methotrexate and 23 with surgical management. Of the 361 patients who received initial expectant management, 81 (22.4%) had a normal rise in β-hCG in 48 hours and went on to have a viable intrauterine pregnancy; 193 (53.5%) had a decrease in β-hCG in 48 hours and had resolution of the pregnancy of unknown location without medical assistance; 44 (12.2%) had a subsequent abnormal rise in β-hCG and received methotrexate for a suspected ectopic pregnancy; 14 (3.9%) had a surgical dilation and curettage for a missed or incomplete abortion; 8 (2.2%) received medical management with misoprostol for missed or spontaneous abortion; and 7 (1.9%) ultimately underwent surgical management of documented ectopic pregnancies. None of the patients who received initial expectant management required a blood transfusion or had other serious morbidity or mortality.

If a stable patient received immediate treatment, it was assumed that the sonographic findings determined the treatment strategy. Although the specific sonographic findings were not used to divide the cohort into groups, 21 of 23 (91%) of patients immediately treated for a presumed ectopic pregnancy had a complex adnexal mass seen on sonography, indicative of a cervical ectopic pregnancy. A total of 80 patients had findings of an adnexal mass on sonography. Of these, 19 underwent immediate treatment for an ectopic pregnancy, and 61 were deemed clinically stable and underwent expectant management. Of the patients with adnexal masses who underwent expectant management, 15 (24.6%) ultimately had a diagnosis of a viable intrauterine pregnancy, and 24 (39.3%) were subsequently treated for an ectopic pregnancy at a later date. The remaining patients had dropping β-hCG values and were followed with resolution of the pregnancy of unknown location. A total of 122 patients (30%) had free fluid present on sonography. Of these, 38 ultimately had a diagnosis of an ectopic pregnancy. Alternatively, of the remaining patients without free fluid

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>EM (n = 361)</th>
<th>IT (n = 47)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>27.9 ± 6.2</td>
<td>27.8 ± 7.3</td>
<td>.950</td>
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<tr>
<td>Race</td>
<td></td>
<td></td>
<td>.437</td>
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<tr>
<td>White</td>
<td>146 (40.5)</td>
<td>16 (34.0)</td>
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</tr>
<tr>
<td>African American</td>
<td>81 (22.4)</td>
<td>7 (14.9)</td>
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<tr>
<td>Hispanic</td>
<td>109 (30.2)</td>
<td>20 (42.6)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>25 (6.9)</td>
<td>4 (8.5)</td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.4 ± 6.9</td>
<td>28.3 ± 6.5</td>
<td>.920</td>
</tr>
<tr>
<td>Weeks by LMP</td>
<td>6.10 ± 1.49</td>
<td>7.86 ± 2.79</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Ectopic risk factor</td>
<td>67 (18.6)</td>
<td>9 (19.1)</td>
<td>.498</td>
</tr>
<tr>
<td>Prior ectopic</td>
<td>30 (8.3)</td>
<td>2 (4.2)</td>
<td></td>
</tr>
<tr>
<td>Tubal surgery</td>
<td>6 (1.7)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>STI</td>
<td>28 (7.7)</td>
<td>4 (8.5)</td>
<td></td>
</tr>
<tr>
<td>IUD in place</td>
<td>4 (1.1)</td>
<td>1 (2.1)</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or number (percent) where appropriate. BMI indicates body mass index; EM, expectant management; IT, immediate treatment; IUD, intrauterine device; LMP, last menstrual period; and STI, sexually transmitted infection.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>EM (n = 361)</th>
<th>IT (n = 47)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Presenting symptom</td>
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<td></td>
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<tr>
<td>Vaginal bleeding</td>
<td>274 (75.9)</td>
<td>35 (74.5)</td>
<td>.566</td>
</tr>
<tr>
<td>Pain</td>
<td>145 (40.2)</td>
<td>28 (59.6)</td>
<td>.012</td>
</tr>
<tr>
<td>Both</td>
<td>58 (16.1)</td>
<td>16 (34.0)</td>
<td>.005</td>
</tr>
<tr>
<td>Clinically stable</td>
<td>361 (100.0)</td>
<td>43 (91.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>β-hCG, mIU/mL</td>
<td>6080 ± 628.0</td>
<td>1183 ± 748.8</td>
<td>.001</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>370 ± 2.6</td>
<td>357 ± 4.0</td>
<td>.033</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or number (percent) where appropriate. β-hCG indicates β-human chorionic gonadotropin; EM, expectant management; and IT, immediate treatment.
on sonography, there were 32 final diagnoses of an ectopic pregnancy. A total of 44 patients (12%) received initial expectant management but were ultimately treated for an ectopic pregnancy. This subset of patients were significantly more likely to have sonographic evidence of a complex adnexal mass (39% versus 12%; \( P = 0.01 \)) and free fluid (43% versus 23%; \( P = .01 \)) than patients who received expectant management and ultimately had normal or abnormal intrauterine pregnancies.

A logistic regression model combining the presence of pain or bleeding, \( \beta \)-hCG and hematocrit levels, and weeks since the last menstrual period was the most parsimonious and predictive for the likelihood of sonography changing management. The goodness of fit test for the model was not significant (\( P = .99 \)), indicating that the model fit well. Reliability of the model was further tested using the area under the receiver operating characteristic curve. This area was fairly high at 0.85. When the model predicted that the probability of sonography changing management was greater than 50%, it was considered a positive test result, and 88% of patients were correctly classified with 98% specificity. A predicted probability of less than 50% had a negative predictive value of 89%.

The model was also used to determine the independent associations between each predictor and the probability of sonography changing management from expectant management to immediate treatment. Women presenting with pain were almost 6 times as likely to undergo a change in management from expectant management to immediate treatment at initial presentation (\( OR, 5.97; 95\% \, CI, 2.45–14.53 \)) independent of other risk factors. Women who presented with vaginal bleeding were twice as likely to have a change in management; however, this finding was not significant (\( OR, 2.23; 95\% \, CI, 0.86–5.77 \)). Gestational age was a significant predictor; for each week from the last menstrual period, the odds of sonography changing management increased by 1.55 (95% CI, 1.29–1.87). The odds of sonography changing management increased by 10% for every 100-mIU/mL increase in the \( \beta \)-hCG value (\( OR, 1.10; 95\% \, CI, 1.05–1.15 \)), and for every 1% increase in hematocrit, the odds of a change in management decreased by 0.87 (95% CI, 0.77–0.97).

Figure 3 displays “efficiency curves” for \( \beta \)-hCG values predicting the likelihood of sonography changing management. Each point represents the probability that sonography will change management below a given \( \beta \)-hCG level. In this study, the lowest \( \beta \)-hCG value at which a patient underwent a change in management was 96 mIU/mL. For those with \( \beta \)-hCG values below 1000 mIU/mL, 6.9% received immediate treatment; the percentages were 3.1% below 200 IU/L and 0% below 75 mIU/mL. At any given \( \beta \)-hCG level, women who presented with pain were more likely than those presenting with bleeding to have sonography change their management from expectant to immediate. In this study, if clinically stable patients without pain and \( \beta \)-hCG values below 2500 mIU/mL were triaged to not undergo sonography, 235 patients (57.6%) would not have undergone it. Of those, 18 (7.6%) required immediate treatment, all for abnormal intrauterine gestations and none for ectopic gestations.

### Discussion

Transvaginal sonography and \( \beta \)-hCG values have become widely used diagnostic tools in the ED evaluation of first-trimester pregnancy complications. This study shows that in the absence of clinical instability, immediate sonography has limited value in some patients with \( \beta \)-hCG values below the discriminatory threshold. To our knowledge, a study investigating which patients might benefit from immediate sonography as opposed to outpatient follow-up has not been reported previously. This study shows that pain is a significant predictor of when sonography will change management, that sonography has limited value at the lower spectrum of \( \beta \)-hCG values, and that a model incorporating presenting symptoms, \( \beta \)-hCG and hematocrit levels, and weeks since the last menstrual period that could be used to triage ED patients to immediate sonography or expectant management with serial \( \beta \)-hCG levels.

In our study of women with \( \beta \)-hCG levels below the discriminatory threshold, pain was the strongest predictor of the need for immediate treatment after sonography. In fact, women with pain were almost 6 times more likely to receive immediate treatment compared to women without pain. Therefore, these women are less likely to receive expectant management, and sonography may be indicated.

![Figure 3. Efficiency curves: probability that sonography will change management under any given \( \beta \)-human chorionic gonadotropin (HCG) value with respect to pain.](image-url)
In addition to aiding in the diagnosis of complicated first-trimester pregnancies, when patients present with moderate to severe pain, sonography can provide valuable diagnostic support for other conditions, including ovarian, uterine, and gastrointestinal disorders. Therefore, we suggest continued liberal use of sonography in the assessment of abdominal and pelvic pain in the setting of early pregnancy.

Gestational age based on the last menstrual period was also a significant predictor of immediate treatment after sonography; for every week from the last menstrual period, patients were 1.5 times more likely to have immediate treatment. This finding is supported by sonographic data that in a normal intrauterine pregnancy, a yolk sac should be visualized at 5½ weeks followed by an embryonic pole at 6 weeks and cardiac activity at 6½ half weeks. With documented β-hCG levels below the discriminatory cutoff in this study, an increase in gestational age was directly correlated with a change in management due to the increased likelihood of the ability to diagnose failed and abnormal intrauterine pregnancies. Concordantly, over one-fourth of the patients who underwent immediate treatment had the diagnosis of a missed abortion and received same-day medical or surgical treatment.

Below a β-hCG level of 75 mIU/mL, no patients in our cohort received immediate treatment after sonography in the ED. Additionally, only 1 patient with an β-hCG level below 100 mIU/mL received immediate treatment in the ED. This patient had an incomplete abortion and underwent dilation and curettage. No patients with β-hCG levels below 100 mIU/mL underwent immediate treatment for an ectopic pregnancy. Although there have been case reports in the literature of ruptured ectopic pregnancies presenting with very low β-hCG values, even with negative urine pregnancy test results,16-18 most of these cases occurred in clinically unstable patients. These patients commonly presented with hypotension, tachycardia, severe pain, an acute abdomen on examination, and low hematocrit levels, indicative of the diagnosis without support from sonography. In these cases, the patients had nondiagnostic findings on sonography but still underwent emergent surgery with an additional delay for the imaging.18 In addition, there are data indicating that most ectopic pregnancies with β-hCG levels of less than 200 mIU/mL do not require surgical intervention, and in fact, many may undergo spontaneous resolution.4,19-21

The positive predictive value of an adnexal mass for the diagnosis of an ectopic pregnancy has been quoted in the literature at between 80% and 90%.5,12 Because we did not perform surgery on all women with adnexal masses, we cannot estimate the positive predictive value of an adnexal mass in our study population. However, it is notable that we had an intrauterine pregnancy rate of 25% in our population of clinically stable patients with β-hCG values below the discriminatory zone and findings of an adnexal mass on sonography. These masses could have been a corpus luteum, a hydrosalpinx, an ovarian tumor, or, less likely, a heterotopic pregnancy that resolved. In addition, free fluid in the pelvis was present in nearly one-third of the patients included in this study; however, less than one-third of those women were treated for an ectopic pregnancy. This finding could be accounted for because many of the sonographic reports did not specify echogenicity of the fluid, most of the reports quoted a “small amount of free fluid,” which could have been physiologic or from a ruptured cyst.

In this study, had this model been applied, in which clinically stable women without pain and with β-hCG values below 100 mIU/mL, 63 patients (15.4%) would not have undergone sonography. None of these patients required immediate treatment. If clinically stable patients without pain and with β-hCG values below 2500 mIU/mL were triaged to not receive sonography, more than half (57%) would not have received it, and whereas 7.6% of those patients required immediate treatment, each was for an abnormal intrauterine gestation, and no ectopic pregnancies would have been missed with the use of these criteria. Therefore, whereas many patients with β-hCG values below the discriminatory zone would still benefit from sonography, the use of this model could reduce the number of unnecessary sonographic examinations by more than half, which could substantially reduce costs and time for smaller institutions where a sonographer or radiologist may not be available in house at all times. Triaging the specific subset of patients who would benefit from sonography by a detailed history, examination, and laboratory values would save time and increase ED turnover without changing outcomes or increasing morbidity.

This study was limited by its retrospective design, which made assessment of pain more difficult. It did not address the risks of women being lost to follow-up during expectant management. However, for most women, the lack of a sonographic examination at the ED visit will likely have little impact on their choice to return for future visits. This study was performed at a single tertiary care center, potentially limiting its external validity. In addition, the model presented in this study was internally validated. To determine external validity, the model should be tested with a new data set.

This study is unique in that it examines the value of sonography for clinical management (instead of diagnostic value) in clinically stable patients with β-hCG values below...
the discriminatory cutoff. Although previous studies have attempted to establish a screening algorithm to predict the location of a symptomatic early gestation,2,23 the goal of this study was to characterize the patients for whom sonography added no benefit in aiding management.

In summary, this study provides evidence that in clinically stable patients presenting to the ED without pain, the clinical utility of sonography is limited when β-hCG values are below the discriminatory zone. By using a combination of presenting symptoms, β-hCG and hematocrit levels, and gestational age based on the last menstrual period, clinicians can effectively utilize ED sonography, appropriately triaging patients to immediate sonography or outpatient follow-up with serial β-hCG levels. Future prospective randomized trials in additional patient populations are needed to validate this model in other populations.

References


Goodman et al—Efficient Sonography in Very Early Pregnancy