Use of a β-hCG Discriminatory Zone With Bedside Pelvic Ultrasonography

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Study objective: We seek to assess the performance of the β human chorionic gonadotropin (β-hCG) "discriminatory zone" when using bedside pelvic ultrasonography in the evaluation of symptomatic pregnant emergency department (ED) patients.

Methods: This was a cross-sectional study of bedside pelvic ultrasonography performed on consecutive pregnant patients in the first trimester who presented to the ED with abdominal pain or vaginal bleeding. Patients received pelvic ultrasonography, serum β-hCG testing, and blinded formal radiologic ultrasonography. All patients were followed for 8 weeks to determine outcomes. The sensitivity and specificity of a discriminatory β-hCG level of 3,000 mIU/mL for the diagnosis of ectopic pregnancy were calculated for patients without an intrauterine pregnancy visualized by bedside ultrasonography.

Results: Thirty-six faculty physicians performed bedside pelvic ultrasonography on 256 patients. There were 161 cases with a confirmed visualizable intrauterine pregnancy and 29 ectopic pregnancies. Bedside ultrasonography identified 115 intrauterine pregnancies. The range of β-hCG for cases of confirmed visualizable intrauterine pregnancy with a nondiagnostic bedside ultrasonography was 15 mIU/mL to 123,368 mIU/mL (median 6,633; interquartile range 1,551 to 32,699). For patients with nondiagnostic bedside ultrasonography, using a discriminatory β-hCG level of 3,000 mIU/mL to further assess for ectopic pregnancy showed sensitivity of 35% (95% confidence interval [CI] 18% to 54%) and specificity of 58% (95% CI 48% to 67%). Finally, the overall sensitivity of bedside pelvic ultrasonography for the detection of intrauterine pregnancy was 71% (95% CI 63% to 78%), and the specificity was 99% (95% CI 94% to 100%).

Conclusion: When bedside pelvic ultrasonography does not demonstrate an intrauterine pregnancy, serum β-hCG level is not helpful in differentiating intrauterine from ectopic pregnancy in symptomatic ED patients. [Ann Emerg Med. 2011;58:12-20.]

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INTRODUCTION

Background

Ectopic pregnancy, a common and potentially fatal condition, must be considered in all first-trimester patients presenting to the emergency department (ED) with abdominal pain, vaginal bleeding, or syncope. Ectopic pregnancy has an overall prevalence of approximately 2% in all pregnancies. Several studies suggest that the prevalence of ectopic pregnancy ranges from 3% to 13% in symptomatic first-trimester ED patients.[1-5] Although early detection during the last 2 decades has greatly improved outcomes, ectopic pregnancy remains a leading cause of maternal morbidity and mortality.[6]

Currently, the diagnostic tests most commonly used to evaluate patients with possible ectopic pregnancy include pelvic ultrasonography and quantitative serum β human chorionic gonadotropin (β-hCG). Pelvic ultrasonography may reveal a normal or abnormal intrauterine pregnancy, ectopic pregnancy, molar pregnancy, or none of the above (also known as an "indeterminate result"). The indeterminate result occurs in approximately 10% to 30% of symptomatic first-trimester patients undergoing radiologic ultrasonography and may represent early intrauterine pregnancy, ectopic pregnancy, or embryonic demise.[7] In such cases, the patient's indeterminate findings are often interpreted in the context of the "discriminatory zone," the level of β-hCG above which the

Editor's Capsule Summary

What is already known on this topic

There is a common belief that intrauterine pregnancies of sufficient size to produce a β human chorionic gonadotropin (β-hCG) level greater than 3,000 mIU/mL can be observed on emergency physician–performed pelvic ultrasonography.

What question this study addressed

Whether emergency physicians can identify intrauterine pregnancy in patients whose β-hCG level exceeds the threshold.

What this study adds to our knowledge

Collectively, the 36 emergency physicians in this study failed to identify an intrauterine pregnancy in 29 of 111 patients who had an intrauterine pregnancy and a β-hCG level greater than 3,000 mIU/mL.

How this is relevant to clinical practice

In this study, when an emergency physician–performed pelvic ultrasonography result was indeterminate for intrauterine pregnancy, serum β-hCG level alone did not differentiate intrauterine and ectopic pregnancy.

sensitivity of ultrasonography for intrauterine pregnancy detection approaches 100%. Using the discriminatory zone combined with the clinical history, providers attempt to differentiate between normal intrauterine pregnancy and abnormal pregnancy, including ectopic pregnancy. Finding a serum β-hCG level greater than the discriminatory zone, in combination with an indeterminate ultrasonography, has been shown to be associated with ectopic pregnancy.[8,9] Typical transvaginal discriminatory zone values in the literature range from 1,500 to 3,000 mIU/mL and have largely been developed according to radiology-performed ultrasonography in outpatients,[10] with intrauterine pregnancy defined as the visualization of a gestational sac.[11-13]

Importance

In recent years, bedside pelvic ultrasonography has shown significant promise in the evaluation of pregnant patients presenting to the ED, allowing for quick and accurate detection of intrauterine pregnancy in 50% to 70% of cases, with a decrease in resource utilization and length of stay.[14-17] However, both the equipment and the examination protocol of bedside ultrasonography usually differ substantially from that used in radiology-performed ultrasonography, and the distinct test performance characteristics of bedside ultrasonography have not been well described. Specifically, it is unclear whether β-hCG has any utility in the setting of bedside ultrasonography performed on symptomatic patients presenting to the ED. Although multiple authors have suggested the use of a cutoff at 2,000 mIU/mL to help determine the disposition of ED patients with an indeterminate bedside pelvic ultrasonography result,[4,18-20] we are unaware of any published data about the clinical performance of this β-hCG discriminatory zone cutoff used after bedside pelvic ultrasonography.

Goals of This Investigation

The purpose of our study was to assess the clinical utility of the traditional β-hCG discriminatory zone in differentiating ectopic from normal pregnancy after indeterminate bedside pelvic ultrasonography in symptomatic pregnant patients presenting to the ED. We hypothesized that the β-hCG discriminatory zone cutoff of 3,000 mIU/mL would not demonstrate test characteristics suitable for differentiating ectopic from normal pregnancy in these patients. Further, we sought to evaluate the β-hCG discriminatory zone for bedside pelvic ultrasonography and to explore whether a revised zone may be more helpful in clinical decisionmaking.

MATERIALS AND METHODS

Study Design

This was a cross-sectional study of emergency physician–performed bedside pelvic ultrasonography in first-trimester pregnant patients presenting to the ED with symptoms of abdominal pain or vaginal bleeding.

Setting

The study was conducted at the University of California, San Francisco, an urban tertiary care university teaching hospital with an annual ED volume of approximately 40,000 patients per year, and was approved by the Committee on Human Research (institutional review board).

Selection of Participants

We attempted to enroll consecutive patients meeting the following inclusion criteria: adult women of reproductive age who presented to the ED with a complaint of vaginal bleeding, abdominal pain, or syncope and had a positive serum or urine pregnancy test result. Exclusion criteria were previous pelvic ultrasonography during the same pregnancy, with available result, or clinical instability as assessed by the attending physician. Research assistants identified potential study candidates by using the ED electronic tracking system or by activation by pager from a clinician during weekdays from 7 AM to 11 PM. Physicians identified patients after hours.

Bedside pelvic ultrasonography was performed and interpreted by attending faculty credentialed in the use of pelvic ultrasonography according to American College of Emergency Physicians' (ACEP's) guidelines. The full details of our credentialing policy have been reported previously.[21] No additional training was conducted for this study.

Data Collection and Processing

Patient consent was obtained by a research assistant or physician. Enrolled patients received a serum CBC count, serum β-hCG measurement, Rh screen (for symptoms of bleeding), and bedside pelvic ultrasonography. A bedside pelvic ultrasonography protocol was instituted such that emergency physician faculty performed an initial transabdominal pelvic scan, using either a SonoSite Micromaxx or M-Turbo (SonoSite Inc., Bothell, WA) with a 5-2 MHz curved probe. Transverse and longitudinal views were obtained and stored. If no obvious intrauterine pregnancy was observed, a transvaginal scan would then be performed using either machine with an 8-5 MHz intracavitary probe.

Operators evaluated the uterus to identify presence or absence of intrauterine pregnancy (as defined by the intrauterine presence of gestational sac containing at least yolk sac or fetal pole), the pelvis for evidence of free fluid, and the adnexa for obvious masses. Physicians documented their interpretation before receiving any subsequent radiology report. For documentation purposes, physicians could interpret their scans in the following 3 ways: intrauterine pregnancy identified, no intrauterine pregnancy identified, or inadequate study. They were also allowed to enter additional free text. Physicians were generally not aware of the results of the β-hCG level at their interpretation because they performed the ultrasonography before it returned, but there was no procedure in place to purposefully blind them from the result. Patients subsequently received pelvic ultrasonography performed by the radiology department (blinded to the results of the bedside ultrasonography) during their ED visit.

Research assistants contacted and performed a standardized interview with all enrolled patients at 8 weeks. The research assistants were blinded to the patients' ultrasonography results (ED and radiology). Patients' clinical records were also reviewed for demographic and clinical history information (age, race, ethnicity, presenting complaint, and risk factors for ectopic pregnancy), as well as formal ultrasonographic interpretation, consultant notes, subsequent clinic notes about the status of the pregnancy, and pathology reports. One research assistant (I.M.) who had been trained by one of the authors (J.C.S.) and had evaluated 10 practice charts with him at the initiation of the project performed the chart review. A standard abstraction form for all patients was used to obtain the chart review data, and the abstractor followed a defined data dictionary for this purpose. Only physician data were reviewed. For any ambiguous entries, the abstractor reviewed the case with one of the authors (J.C.S.); at 2 separate times during data collection, that author reviewed 10 cases with the abstractor to ensure quality of data. The abstractor was not blinded to the study goals and objectives.

Outcome Measures

The bedside ultrasonographic study result was interpreted as positive for intrauterine pregnancy if an intrauterine gestational sac with yolk sac or a fetal pole was visualized.[2] It was interpreted as negative for intrauterine pregnancy if the physician interpreted that no intrauterine pregnancy was visualized or if the interpretation was reported as an inadequate study. The bedside ultrasonographic reporting form did not include a specific category for ectopic pregnancy, and no cases of ectopic pregnancy were positively identified as such on the text portion of the bedside ultrasonographic report. For the purposes of this study, radiology examinations were also interpreted as positive for intrauterine pregnancy if an intrauterine gestational sac with yolk sac or a fetal pole was visualized. The research assistant used a standard abstraction form to record the results from the radiology interpretation. To assess interrater reliability between the research assistant and senior author, a 10% random sample of cases was assessed and showed an actual agreement of 96%, κ 0.92 (95% confidence interval [CI] 0.78 to 1.00).

We created a subset of patients with a confirmed intrauterine pregnancy to assess what proportion of intrauterine pregnancies was actually detected by the emergency physician and then constructed the discriminatory zone for emergency physician ultrasonography. Patients met our definition of a confirmed intrauterine pregnancy for this study only by meeting one of the following criteria: (1) patients who had a gestational sac with yolk sac or a fetal pole visualized by radiologist at initial or subsequent ultrasonography, or (2) confirmed pregnancy at 8-week follow-up clinic visit or telephone call. This definition of confirmed intrauterine pregnancy is not intended to indicate that the intrauterine pregnancy should have been observed at bedside ultrasonography, only that these patients were subsequently proven to have an intrauterine pregnancy that could have been observed if our technology were perfect (as opposed to an intrauterine pregnancy that had already aborted at presentation, which, regardless of technology or serum β-hCG level, would never be visualized). Only patients classified as having a confirmed intrauterine pregnancy by either of these criteria were included in the subset of patients used to evaluate the discriminatory zone for bedside ultrasonography.

Primary Data Analysis

All data were entered into a Microsoft Excel spreadsheet (Version 12.2.8, Microsoft, Redmond, WA). To assess physician compliance with the bedside ultrasonography protocol, we analyzed a 10% random sample of the enrolled patients. One of the authors (R.W.) reviewed the physician note and bedside ultrasonographic images. To evaluate how our test performance compared with that in similar previous reports of bedside pelvic ultrasonography by emergency physicians, we analyzed sensitivity and specificity for the identification of intrauterine pregnancy in our entire data set. To evaluate the test characteristics of the currently defined β-hCG discriminatory zone of 3,000 mIU/mL for the identification of ectopic pregnancy after use of bedside ultrasonography, we analyzed sensitivity and specificity. To assess the discriminatory zone for bedside pelvic ultrasonography, we evaluated only those patients from the data set who had a confirmed

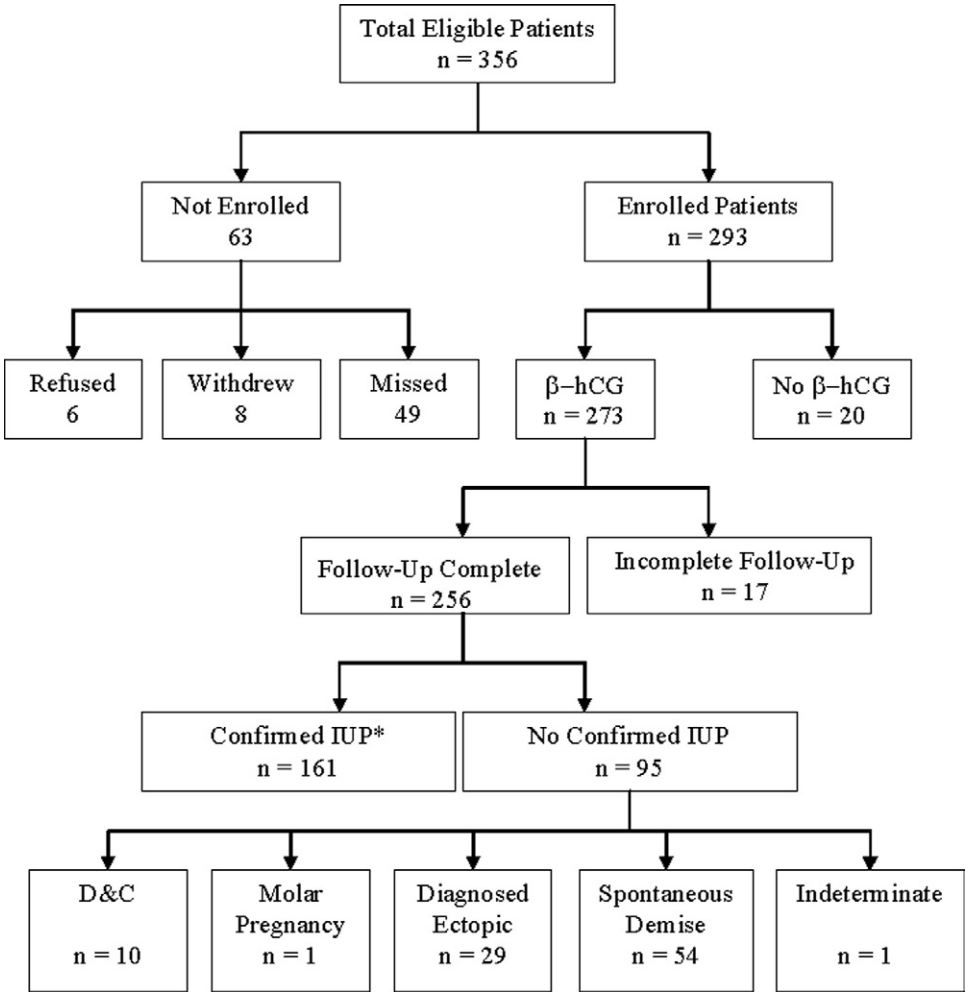

Figure 1. Enrollment process and outcomes of all patient participants. *IUP*, Intrauterine pregnancy; *D&C*, dilation & curettage.

intrauterine pregnancy.[9] We present this data in aggregate and by physician to better represent individual variation in ability to identify an intrauterine pregnancy. To test whether increased experience with ultrasonography may impart a different discriminatory zone among emergency physicians, we planned an a priori analysis of 2 physician subgroups: (1) faculty who enrolled more than 10 patients in the cohort, according to a previous ED study of deep venous thrombosis[22]; and (2) faculty who were trained in the use of ultrasonography during residency. Summary statistics, diagnostic test characteristics, and 95% CIs were performed with Stata (version 10; StataCorp, College Station, TX).

RESULTS

Of 356 adult women of reproductive age who presented to the ED with a complaint of vaginal bleeding, abdominal pain, or syncope and had a positive serum or urine pregnancy test result, 293 were enrolled in the study between January 2007 and June 2009 (Figure 1). We attempted to screen consecutive patients, but 49 of the 356 patients (14%) were never approached (were "missed") by research assistant or physician and were identified only by review of daily discharges from the ED. There were 6 patients who refused to participate and 8 who withdrew before actually receiving ultrasonography. Twenty patients were subsequently excluded because they did not undergo serum β-hCG measurements in the ED. Seventeen patients were excluded because of lack of follow-up (7 of these patients had no intrauterine pregnancy observed by bedside or radiologic ultrasonography and were never treated or contacted again, and 10 of these patients had intrauterine pregnancy observed by the bedside ultrasonography, with no subsequent formal radiologic ultrasonography or clinical follow-up). Thus, 256 patients remained for preliminary analysis. To ensure that physicians followed the bedside ultrasonography protocol (transabdominal first, and if no intrauterine pregnancy was observed, then transvaginal sonography), a review of a 10% random subset showed 92% compliance (95% CI 75% to 98%). Thus, there were 2 of 25 patients for whom the attending physician did not visualize an intrauterine pregnancy on

Table 1. Baseline characteristics of the study populations: (1) 256 patients who were enrolled, received a β-hCG test, and had clinical follow-up available, and (2) the 36 physicians who performed the studies.

Patient Characteristics (n=256)	No. (%)/Median (IQR)
Age, y, mean (SD)	28.4 (7)
Race, No. (%)	
Asian	49 (19)
Black	68 (27)
White	77 (30)
Other	51 (20)
Unknown	11 (4)
Ethnicity, No. (%)	
Hispanic	36 (14)
Non-Hispanic	203 (79)
Unknown	17 (7)
Presenting complaints, No. (%)	
Abdominal pain/cramping	209 (82)
Vaginal bleeding/spotting	167 (65)
Risk factors for ectopic pregnancy, No. (%)	
Previous ectopic pregnancy	9 (3.5)
History of sexually transmitted disease	9 (3.5)
History of intrauterine device	4 (1.6)
β-hCG at enrollment, mIU/mL, median (interquartile range)	10,676 (1,724–51,681)
Physician characteristics (n=36)	
Residency ultrasonographic training, No. (%)	23 (64)
Years of ultrasonographic experience, excluding residency, median (IQR)	3 (3–4)
Number of ultrasonographic studies performed, median (IQR)	5 (2–9)

Table 2. Diagnostic accuracy of emergency physician–performed ultrasonography for the detection of intrauterine pregnancy.*

	Outcome		
EPPU Diagnosis	**IUP**	**No IUP**	**Total**
IUP	114	1	115
No IUP	47	94	141
Total	161	95	256

EPPU, Emergency physician-performed ultrasonography; *IUP,* intrauterine pregnancy.
*Sensitivity=71% (95% CI 63% to 78%); specificity=99% (95% CI 94% to 100%); positive predictive value=99% (95% CI 95% to 100%); negative predictive value=67% (95% CI 58% to 74%).

Table 3. Diagnostic performance of a discriminatory zone of 3,000 mIU/mL for patients with no intrauterine pregnancy by emergency physician–performed pelvic ultrasonography for the detection of ectopic pregnancy.*

β-hCG Level, mIU/mL	Ectopic	No Ectopic	
Positive (≥3,000)	10	47	57
Negative (<3,000)	19	65	84
Total	29	112	141

*Prevalence of ectopic pregnancy with no IUP on EPPU=20.6% (95% CI 14.2% to 28.2%); sensitivity=35% (95% CI 18% to 54%); specificity=58% (95% CI 48% to 67%); positive predictive value=18% (95% CI 9% to 30%); negative predictive value=77% (95% CI 67% to 86%).

transabdominal views and who did not proceed to transvaginal sonography.

Table 1 reports the characteristics of the physician study population, as well as the pregnant women. Thirty-six emergency physicians performed bedside ultrasonographic examinations. Thirteen physicians had not received any ultrasonographic training during their residency. Physicians had a median of 3 years of ultrasonographic experience at the onset of the study, exclusive of residency training (interquartile range [IQR] 3 to 4). One faculty physician was fellowship trained in emergency ultrasonography. Physicians enrolled a median of 5 patients in this study (IQR 2 to 9).

Of the study population of 256 patients, 161 were found to show a confirmed intrauterine pregnancy, leaving 95 who were never proven to have an intrauterine pregnancy that could have been visible at the ED visit. These 95 patients showed eventual clinical outcomes as follows: 54 with spontaneous abortion, 10 with dilation and curettage (with no report of an intrauterine pregnancy), 1 molar pregnancy, and 1 indeterminate (patient still reported irregular bleeding at 8 weeks but also reported never requiring a subsequent ED or clinic visit; she was subsequently lost to follow-up). ED bedside ultrasonography identified 115 intrauterine pregnancies, and all were true intrauterine pregnancies except for 1 case that proved subsequently to be a molar pregnancy. Our overall test characteristics for bedside ultrasonographic identification of intrauterine pregnancy (Table 2) showed a sensitivity of 71% (95% CI 63% to 78%) and specificity of 99% (95% CI 94% to 100%). Positive predictive value was 99% (95% CI 95% to 100%) and negative predictive value was 67% (95% CI 58% to 74%).

Because it is often quoted that in the setting of an indeterminate ultrasonography, finding a serum β-hCG level greater than the discriminatory zone is associated with ectopic pregnancy, we calculated test characteristics for indeterminate bedside pelvic ultrasonography.[8,9] Table 3 shows the diagnostic test performance using a β-hCG cutoff of 3,000 mIU/mL for the diagnosis of ectopic pregnancy in the subset of patients who did not have an intrauterine pregnancy identified by bedside pelvic ultrasonography. Sensitivity was 35% (95% CI 18% to 54%), and specificity was 58% (95% CI 48% to 67%). Positive likelihood ratio was 0.82 (95% CI 0.48 to 1.40), and negative likelihood ratio was 1.13 (95% CI 0.83 to 1.50).

To evaluate whether there may be a different discriminatory zone that applies to bedside ultrasonography, we set up an analysis similar to the one originally described by Kadar et al.[9] From our total 256 patients, 161 (63%) were ultimately classified after follow-up as having an intrauterine pregnancy that was visualizable. Table 4 shows this group of patients and compares those who were diagnosed with intrauterine pregnancy by bedside pelvic ultrasonography with those who were not, stratified by serum β-hCG levels. Although there was no cutoff at which 100% of the intrauterine pregnancies were

Table 4. Discriminatory zone evaluation: Comparison of the number of visualizable intrauterine pregnancies (n=161) that were identified by emergency physician–performed pelvic ultrasonography with those that were not identified at varying serum β-hCG values.

Serum β-hCG Level, mIU/mL	IUP Observed in ED*	No IUP Observed in ED	Total Cases
<3,000	3	18	21
3,000–4,999	5	1	6
5,000–9,999	7	8	15
10,000–24,999	12	8	20
25,000–49,999	30	6	36
50,000–100,000	35	4	39
>100,000	22	2	24
Total	114	47	161

*Defined as yolk sac or fetal parts within gestational sac.

identified, using a β-hCG level of more than 25,000 mIU/mL identified 87 of 99 (88%), and using a level of more than 50,000 mIU/mL identified 57 of 63 (90%). The range of β-hCG for cases of confirmed intrauterine pregnancy with nondiagnostic bedside ultrasonography was 15 mIU/mL to 123,368 mIU/mL (median 6,633; IQR 1,551 to 32,699).

We conducted a similar analysis for our 2 a priori physician subgroups (those enrolling more than 10 patients and those with residency training in ultrasonography) but were unable to identify any important differences when results were compared with the full group analysis. For the subgroup of physicians who performed more than 10 ultrasonography tests in this study (n=4), above a β-hCG value of 100,000 mIU/mL, 100% (5/5) of the intrauterine pregnancies were identified, and above a β-hCG value of 25,000 mIU/mL, 89% (32/36) of the intrauterine pregnancies were identified. For the group of physicians who trained in ultrasonography during residency (n=22), above a β-hCG value of 100,000 mIU/mL, 100% (12/12) of the intrauterine pregnancies were identified, and above a β-hCG value of 25,000, 88% (57/64) of the intrauterine pregnancies were identified. Figure 2 displays the identification of confirmed intrauterine pregnancy by individual physician.

LIMITATIONS

One potential limitation to our study was that 18% of eligible patients were not enrolled. This may have introduced spectrum bias because it is possible that there were differences between this group of patients and the enrolled group.

Another potential limitation is that we did not specifically require physicians to document whether they performed transvaginal ultrasonography in addition to transabdominal ultrasonography. All physicians were trained in both transabdominal and transvaginal ultrasonography, and all had met ACEP guidelines for credentialing. Our ED bedside clinical protocol, as well as study protocol, was to perform transabdominal ultrasonography, and if no identifiable intrauterine pregnancy was found, to then proceed to transvaginal ultrasonography. We have demonstrated that in a random sample of cases, this protocol was followed more than 90% of the time. However, it is possible that if we excluded cases in which only transabdominal sonography was performed, our results would differ.

Additionally, among the key factors that determine the discriminatory zone are operator training and the equipment and scanning protocols used. Certainly, our results reflect our site-specific operator training. However, because we used the ACEP emergency ultrasonography guidelines as the basis for our training and all faculty ultrasonographers met these minimum criteria, our study conditions should be reproducible. Further, our faculty has a wide variation in experience and duration of ultrasonographic use, which is likely similar to that of many EDs nationally. Several of our faculty are particularly interested in ultrasonography, many were trained during residency (23/36), and a smaller proportion trained after residency and may have relatively limited experience. Thus, although the particular training and level of experience probably contribute to the discriminatory zone for our physicians, it seems likely that our current expertise mix is similar to that of many other clinical environments, though distinct from the radiology environment.

In addition, as mentioned above, other key factors in determining the discriminatory zone include the equipment and scanning protocols used, and these may be particular to bedside ultrasonography and the emergency setting. The technology used for formal radiologic ultrasonography (here, an Acuson Sequoia) is widely considered to be more sensitive than the technology used at the bedside in the ED. It is possible that, had the improved technology been available in the ED, the sensitivity of bedside ultrasonography would have been enhanced. However, although this may limit the generalizability of our results, we sought precisely to evaluate the diagnostic performance of bedside ultrasonography in the clinical setting.

Beyond equipment factors, the definition of intrauterine pregnancy used in our protocol required the visualization of a yolk sac or fetal pole, in addition to a gestational sac (a conservative definition of intrauterine pregnancy designed to avoid mistaken identification of a pseudosac as a gestational sac). Although this would not change the performance of bedside ultrasonography relative to radiologic ultrasonography within this study (because radiologic examinations were also interpreted by the same criteria), this definition would shift the discriminatory zone relative to published studies that allowed determination of intrauterine pregnancy by gestational sac alone.[7,23-25]

Finally, our inclusion criteria included the presence of pain or bleeding, and a symptomatic cohort may be expected to have a higher prevalence of abnormal pregnancies (in which the relationship between size/visibility and β-hCG level may be disrupted) than an asymptomatic clinical cohort. Our particular aim was to evaluate the utility of the discriminatory zone in this symptomatic population, and our results are not necessarily directly comparable to a discriminatory zone derived in asymptomatic or mixed populations.

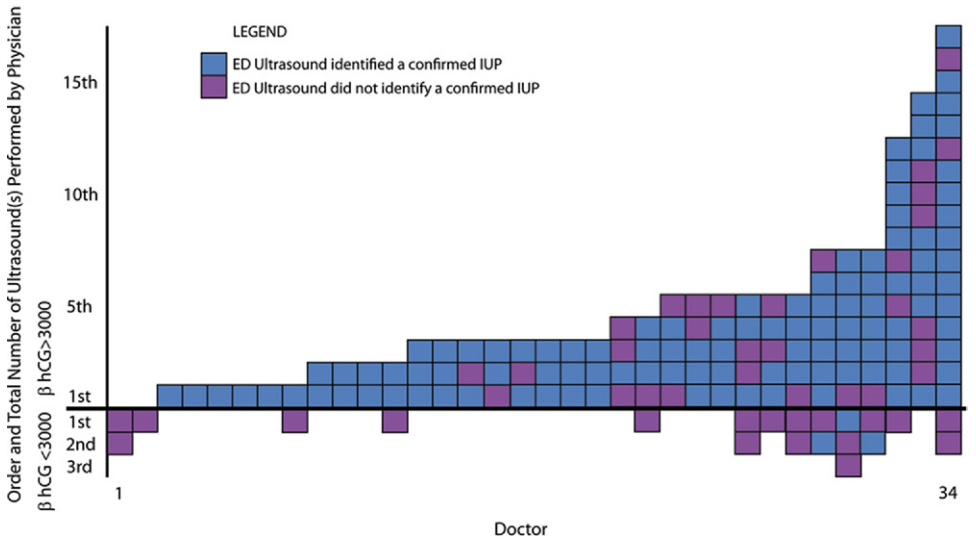

Figure 2. Accuracy of bedside ultrasound examinations for each provider, stratified by discriminatory zone.

DISCUSSION

The correlation of ultrasonographic findings to β-hCG measurements has become a standard part of clinical practice in symptomatic first-trimester patients.[6] Although several authors have suggested extending this approach to symptomatic ED patients with an initial indeterminate bedside ultrasonographic result, this concept has not been rigorously evaluated.[4,18-20] In our study, we found that the test characteristics for a β-hCG cutoff of 3,000 mIU/mL are not acceptable for use in clinical practice when attempting to identify ectopic pregnancy in symptomatic patients with an indeterminate result on bedside pelvic ultrasonography (sensitivity of 35% and specificity of 58%).

In the seminal work by Kadar et al,[9] the initial discriminatory zone was defined with radiology-performed transabdominal ultrasonography in a mixed cohort of outpatients. Intrauterine pregnancy, defined as the visualization of a gestational sac, was not detected in patients with a β-hCG level less than 6,000 mIU/mL. At a level greater than 6,500 mIU/mL, gestational sacs were reliably visualized, resulting in a narrow discriminatory zone of 6,000 to 6,500. This finding subsequently was proven to help further differentiate pregnant patients at risk for ectopic pregnancy who had no intrauterine pregnancy observed on their pelvic ultrasonographic result; those with a low β-hCG level had a reasonable chance of an early intrauterine pregnancy, whereas patients with a β-hCG more than 6,500 mIU/mL had an increased likelihood of ectopic pregnancy.[8] With the advent of transvaginal ultrasonography and high-resolution technology in the following decades, the discriminatory zone values were redefined, resulting in the current accepted lower range of 1,500 to 3,000 mIU/mL.[2,11-13,24] It has been shown that the sensitivity for ectopic pregnancy in this situation ranges from 73% to 93% and is dependent on equipment, gestational age, and operator skill.[6]

In evaluating our data, we first intended to establish its generalizability. We compared the test characteristics of ED bedside pelvic ultrasonography in the identification of intrauterine pregnancy with those of previous studies. We found the data in our study to be similar to reported values from a recent review.[26] Our sensitivity of 71% (95% CI 63% to 78%) compares with 67% (95% CI 59% to 75%) reported by Wong et al,[27] 79% (95% CI 73% to 84%) reported by Mateer et al,[4] and 91% (95% CI 83% to 95%) reported by Durham et al.[28] Our specificity was 99% (95% CI 94% to 100%) and compares with 92% (95% CI 65% to 99%) reported by Wong et al,[27] 100% (95% CI 96% to 100%) reported by Mateer et al,[4] and 100% (95% CI 88% to 100%) reported by Durham et al.[28] The higher sensitivity in the studies by Durham et al[28] and Mateer et al[4] may be accounted for by the fact that both studies used a small, selected group of operators to perform the ultrasonographic examinations in a consecutive sample. Because we have used standardized training and credentialing following the ACEP guidelines and because our test characteristics are similar to those of previous reports, we believe that the subsequent results of our study are likely to be generalizable to those of other groups of ACEP-credentialed physicians.

The primary goal of this investigation was to assess the test performance of a β-hCG cutoff of 3,000 mIU/mL in reference to patients who do not receive a diagnosis of intrauterine pregnancy on bedside pelvic ultrasonography. The low sensitivity (35%) of this β-hCG cutoff derives from the fact that among patients with ectopic pregnancy who have a nondiagnostic bedside pelvic ultrasonographic result, the proportion with a "positive" β-hCG test result (greater than the 3,000 mIU/mL discriminatory zone) is only 35%. The majority of patients with ectopic pregnancy who have an indeterminate bedside pelvic ultrasonographic result have a β-hCG level lower than 3,000 mIU/mL. Overall, this implies that in the setting of

nondiagnostic ED ultrasonography, using a β-hCG cutoff of 3,000 mIU/mL will not aid with the exclusion of ectopic pregnancy; rather, it will miss 65% of the cases.

In our study, of the 256 total patients, 141 had nondiagnostic bedside pelvic ultrasonography. There were a total of 29 cases of ectopic pregnancy. Thus, the prevalence of ectopic pregnancy when no intrauterine pregnancy is observed on initial bedside ultrasonography in our study was 21% (95% CI 14% to 28%). If one uses a β-hCG cutoff of 3,000 mIU/mL, patients with results above this level will have a posttest prevalence of ectopic pregnancy of 18%, and patients with results below this level will have a posttest prevalence of ectopic pregnancy of 23%. Therefore, it does not seem appropriate to use the traditional β-hCG discriminatory zone in clinical algorithms involving bedside ultrasonography in symptomatic ED patients because the test result does not significantly alter the probability of disease.

We turned to the subset of patients who had a confirmed intrauterine pregnancy to evaluate whether a different discriminatory zone might be helpful when bedside ultrasonography is used. Intrauterine pregnancy was visualized by bedside ultrasonography at a β-hCG as low as 1,440 mIU/mL. However, it was not until levels reached 25,000 mIU/mL or higher that we were able to identify more than 80% of cases (Table 4). This results in a wide zone for identifying intrauterine pregnancy with bedside ultrasonography, unlike the narrow discriminatory zone reported by radiologists using different imaging protocols and more sensitive equipment. In evaluation of the data by individual physicians (Figure 2), 47 of 161 (29%) of confirmed intrauterine pregnancies were not diagnosed. The median β-hCG of the 47 missed intrauterine pregnancies was 6,633 mIU/mL (IQR 1,551 to 32,699). Even when we evaluated subgroups that were more likely to have increased experience or training, we found discriminatory zones that were comparable to those of the overall physician group. For patients who do not have an identified intrauterine pregnancy on initial bedside ultrasonographic examination and who are subsequently found to have serum β-hCG levels greater than the traditional discriminatory zone of 3,000 mIU/mL, there is still a high likelihood of intrauterine pregnancy. Thus, emergency physicians should not prematurely counsel patients to expect an adverse outcome if their emergency physician–performed ultrasonographic examination does not reveal an intrauterine pregnancy, regardless of the β-hCG level.

As described above, given the myriad factors that may affect the discriminatory zone, including characteristics of operators, equipment, protocols, and patient populations, it is not surprising that the discriminatory zone for bedside pelvic ultrasonography is notably wider than that for formal radiology-performed studies. ED bedside studies are limited by the use of portable miniaturized ultrasonographic technology, by operator training and experience, and by imaging protocols that are necessarily constrained by the demands of ED setting. However, the finding of a significantly wider discriminatory zone in no way diminishes the valuable contribution of bedside pelvic ultrasonography to the evaluation of women at risk for ectopic pregnancy in the ED. This diagnostic modality remains an efficient means of assessing patients for ectopic pregnancy and was again shown to be highly accurate in our study when an intrauterine pregnancy was identified. There were no patients who received a diagnosis of intrauterine pregnancy by bedside ultrasonography who were subsequently found to have ectopic pregnancy (although one was later found to have a molar pregnancy). Among all patients with complete follow-up, 45% (115/256) received a diagnosis of intrauterine pregnancy by the emergency physician and thus would have required no further emergency evaluation or consultant ultrasonography. However, although no heterotopic pregnancies were identified in our study, in patients who have concerning symptoms the identification of an intrauterine pregnancy does not preclude this diagnosis. Appropriate further evaluation should be obtained if the clinical situation warrants.

This re-evaluation of the discriminatory zone with respect to the specific clinical practice of bedside pelvic ultrasonography in symptomatic ED patients should alert practitioners to avoid the inappropriate interpretation of serum β-hCG level in patients with nondiagnostic results. Although ED bedside pelvic ultrasonographic examinations can reliably exclude ectopic pregnancy when they demonstrate a clear intrauterine pregnancy, the use of the traditional discriminatory zone does not appear to be helpful in the further differentiation of ectopic pregnancy from intrauterine pregnancy when the ultrasonography result does not demonstrate a clear intrauterine pregnancy.

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