

# Subclassification of Indeterminate Pelvic Ultrasonography: Prospective Evaluation of the Risk of Ectopic Pregnancy

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Received for publication August 14, 2001. Revision received November 14, 2001. Accepted for publication December 17, 2001.

Presented at the Society for Academic Emergency Medicine annual meeting, Atlanta, GA, May 2001.

Supported by an institutional seed grant from Boston Medical Center.

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0196-0644/2002/\$35.00 + 0

47/1/122432

doi:10.1067/mem.2002.122432

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**Study objective:** We sought to determine the frequency of ectopic pregnancy among subclasses of indeterminate ultrasonographic examinations.

**Methods:** A prospective observational study was performed from January 1, 1995, to August 31, 2000, on consecutive emergency department patients in the first trimester of pregnancy with a chief complaint of abdominal pain or vaginal bleeding and who had an indeterminate transvaginal ultrasonographic examination at the time of the ED visit. Patients were excluded if lost to follow-up. Ultrasonographic examinations were subclassified into 5 groups (ie, empty uterus, nonspecific fluid, echogenic material, abnormal sac, normal sac) on the basis of a previously published classification system. Patients were followed up until the diagnosis of ectopic pregnancy was either confirmed or excluded. The frequencies of ectopic pregnancy, along with 95% confidence intervals (CIs), were calculated for each of the subclasses. The relative risk of ectopic pregnancy was calculated when appropriate.

**Results:** Seven hundred eighty patients with indeterminate ultrasonographic examinations were identified. One hundred forty-five were lost to follow-up, and therefore, 635 were enrolled. The frequency of ectopic pregnancy for each subclass is as follows: empty uterus, 36 of 259 (13.9%; 95% CI 10.1% to 18.5%); nonspecific fluid, 6 of 127 (4.7%; 95% CI 1.9% to 9.6%); echogenic material, 4 of 93 (4.3%; 95% CI 1.4% to 10.5%); abnormal sac, 0 of 103 (0%; 95% CI 0.0% to 2.9%); and normal sac, 0 of 53 (0%; 95% CI 0.0% to 5.5%). The relative risk of ectopic pregnancy in patients with an empty uterus versus in those without an empty uterus was 5.2 (95% CI 2.6 to 10.2).

**Conclusion:** In our sample, patients with an empty uterus at ultrasonography had the highest frequency of ectopic pregnancy, with a relative risk of ectopic pregnancy 5 times greater than that of the other 4 subclasses.

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[Dart RG, Burke G, Dart L. Subclassification of indeterminate pelvic ultrasonography: prospective evaluation of the risk of ectopic pregnancy. *Ann Emerg Med.* April 2002;39:382-388.]

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## INTRODUCTION

Transvaginal ultrasonography is the test of choice for the evaluation of first-trimester patients with symptoms suggestive of ectopic pregnancy. Identification of an intrauterine pregnancy (IUP) significantly reduces the likelihood of ectopic pregnancy because occurrence of a heterotopic pregnancy, other than in infertility patients, is rare.<sup>1</sup> Specific extrauterine findings increase the likelihood of ectopic pregnancy. These range from an increased volume of cul de sac fluid, cul de sac fluid with internal echoes (suggests the presence of blood), identification of an adnexal mass separate from the ovary, or direct visualization of an extrauterine sac containing a yolk sac or fetus.<sup>2,3</sup> However, when no IUP and no abnormal extrauterine findings are found, the ultrasonographic examination is characterized as indeterminate.<sup>4</sup>

Because approximately 14% of patients with indeterminate ultrasonographic examinations will ultimately be given a diagnosis of ectopic pregnancy,<sup>4</sup> these patients remain at risk. In a prior retrospective study, a classification system was developed to categorize specific endometrial findings identified in patients with indeterminate ultrasonographic examinations.<sup>4</sup> The authors found that the frequency of ectopic pregnancy varied greatly amongst these different subclasses and believed that the use of this system might be helpful in risk stratification. The purpose of this study was to prospectively validate whether this classification system is useful in predicting ectopic pregnancy. A second objective was to determine whether the actual quantitative  $\beta$ -human chorionic gonadotropin ( $\beta$ -hCG) value altered the risk of ectopic pregnancy within each subclass.

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## MATERIALS AND METHODS

A prospective observational study was performed from January 1, 1995, to August 31, 2000, of consecutive first-trimester pregnant women with abdominal pain or vaginal bleeding to determine whether the frequency of ectopic pregnancy varied among subclasses of indeterminate transvaginal ultrasonographic examinations. The site's institutional review board approved this study.

The study was conducted in the emergency department of an academic medical center with an accredited emergency medicine residency program. The ED has an

annual census of approximately 60,000 patients. Patients were eligible if they complained of abdominal pain or vaginal bleeding, had a positive  $\beta$ -hCG test result, and had a transvaginal ultrasonographic examination performed during the ED visit that was classified as indeterminate (ie, it was neither diagnostic of an IUP nor suggestive or diagnostic of an ectopic pregnancy). Ultrasonographic criteria considered diagnostic of an IUP included the presence of an intrauterine gestational sac containing a clearly defined yolk sac or fetal pole. Ultrasonographic criteria considered suggestive or diagnostic of an ectopic pregnancy included visualization of a complex adnexal mass separate from the ovary, identification of an extrauterine sac-like structure with or without a yolk sac or fetal pole, or identification of a moderate to large amount of anechoic fluid or any echogenic fluid in the cul de sac. Patients were excluded for any of the following reasons: if a prior ultrasonographic examination during this pregnancy was diagnostic of an IUP or suggestive of an ectopic pregnancy; if the patient was recently delivered or passed definite products of conception at home or in the ED; if the patient was status after a dilatation and evacuation (D&E) procedure; or if the patient was lost to follow-up.

The treating clinician in the ED identified eligible patients and entered their names and contact information in a patient follow-up book. In addition, the charts of all ED patients were reviewed daily. Any patients who were not listed in the follow-up book and who met eligibility criteria were also enrolled. Approximately 60% of patients were identified from the follow-up book, and the remaining 40% of patients were identified by next day review of ED charts.

The ultrasonographic examinations were initially subclassified by one of the study investigators before any clinical follow-up information was obtained. In addition, the principal investigator reviewed all ultrasonographic reports in batches on an approximately weekly basis as a quality control and to serve as the final ultrasonographic classification. This individual was blinded to any clinical information. Concordance between the initial and final classification was very high, approximately 95%. The limited degree of discordance mainly fell into 2 areas. The first was classification error. The 2 most common examples of this occurred in patients with a gestational sac and a yolk sac but no fetal pole having ultrasonographic examinations classified as indeterminate when they should have been classified as an IUP, or when an isolated but moderate volume of simple fluid was identified in the cul de sac and the ultrasonographic examination was classified as indeterminate when it should have been classified

as suggestive of ectopic pregnancy. The second area of discordance dealt with subjective interpretation of endometrial findings. The 2 most common examples dealt with differentiating a normal sac from nonspecific fluid and differentiating nonspecific fluid from an empty uterus. With the first, if the border was clearly echogenic, we classified it as a normal sac; otherwise, it was classified as nonspecific fluid. The second problem occurred when a tiny amount of endometrial fluid was identified at the time of ultrasonography. If the fluid was just layered in the endometrial cavity, the ultrasonographic examination was classified as empty; if the fluid had a rounded configuration, the ultrasonographic examination was classified as nonspecific fluid.

At our institution, all women of childbearing age with a chief complaint of abdominal pain or vaginal bleeding will have a  $\beta$ -hCG test performed (serum or urine). Patients with positive results have a quantitative serum assay performed. Each patient will then have pelvic ultrasonography performed unless they had a prior ultrasonographic examination during the pregnancy that was diagnostic of an IUP, had fetal heart tones on abdominal examination, or had passed clearly identifiable products of conception. Patients were followed up until a final diagnosis was determined or the patient was lost to follow-up. The diagnostic workup of individual patients was left to the clinicians caring for the patient. Approximately 600 patients per year meet the aforementioned criteria. In practice, essentially all potentially eligible patients had ultrasonography performed. Of the ultra-

sonographic examinations performed, approximately 20% were indeterminate.

All ultrasonographic examination were performed by certified ultrasonography technicians under the direct supervision of a radiology attending physician or resident. In addition, a hard copy of the ultrasonographic scan was reviewed by an attending radiologist with specific expertise in ultrasonography before the dictation of the official report. Ultrasonographic examinations were performed with an Acuson 128 (Acuson, Mountain View, CA) or an ATL Ultramark 9 HDI (Advanced Technologies Laboratories, Bothell, WA) scanner. The Acuson machine used a 5-MHz transvaginal transducer. The Ultramark machine allowed the operator to adjust the frequency of the transvaginal transducer from 5 to 10 MHz.

Indeterminate ultrasonographic examinations were subclassified into 5 groups on the basis of criteria from a previously published classification system (Table 1).<sup>4</sup> The principal investigator, who was otherwise blinded to clinical information, performed the final classification of the examinations on the basis of the text of the official radiology report.

The final diagnosis was categorized by using predefined criteria (Table 2). Information from the ultrasonography report was not used in the determination of the diagnosis of ectopic pregnancy but was occasionally used

**Table 1.**  
Definitions of the subclasses of the indeterminate ultrasonographic examinations.

Subclass	Definition
Empty uterus	Empty endometrial cavity with or without a thickened endometrium.
Nonspecific fluid	Anechoic intrauterine fluid collection of <10 mm in mean sac diameter without an echogenic border.
Echogenic material	Echogenic material within the endometrial cavity without a defined sac or multiple discrete anechoic collections of varying sizes divided by echogenic septations.
Abnormal gestational sac	Anechoic intrauterine fluid collection either of >10 mm in mean sac diameter or with a grossly irregular border.
Normal sac	Anechoic intrauterine fluid collection with an echogenic border and none of the features of an abnormal sac.

**Table 2.**  
Criteria for determining the final diagnosis.

Final Diagnosis	Diagnostic Criteria
Normal IUP	Pregnancy was carried to delivery or, at a later date, had demonstration of a normal IUP with a fetal heartbeat by means of ultrasonography.
Abnormal IUP	(1) Evidence of an abnormal sac, echogenic material, $\beta$ -hCG >3,000 mIU/mL without an intrauterine sac, or decreasing $\beta$ -hCG values before curettage and evidence of chorionic villi at pathology; (2) no villi after curettage but $\beta$ -hCG values that decrease to zero without further intervention; (3) no curettage and $\beta$ -hCG values that decrease to zero without intervention.
Abnormal versus normal IUP	Curettage performed in case of unwanted pregnancy before the exclusion of the diagnosis of a viable IUP with evidence of chorionic villi at pathology.
Ectopic pregnancy	(1) Extrauterine pregnancy visualized at laparoscopy; (2) in patients managed with methotrexate, either identification of an ectopic pregnancy at follow-up ultrasonographic examination or $\beta$ -hCG values that increase or plateau in patients after curettage and without evidence of chorionic villi at pathology.

in differentiating between a diagnosis of normal IUP and abnormal IUP in patients who had a D&E procedure performed.

Pregnancy screening was performed with a urine (Abbott test pack Plus hCG Combo, Abbott Laboratories, Abbott Park, IL) or serum (AxSYM Microparticle Enzyme Immunoassay, Abbott Laboratories) assay. All patients with positive qualitative results then had a quantitative serum test (AxSYM Microparticle Enzyme Immunoassay) performed.

The frequency and 95% confidence intervals (CIs) for the main outcome variable (ectopic pregnancy) was determined for the 5 ultrasonographic subclasses. In addition, the relative risk of ectopic pregnancy was determined where appropriate.

RESULTS

Seven hundred eighty patients with indeterminate ultrasonographic examinations fulfilled eligibility criteria. Of these, 145 were lost to follow-up; therefore, 635 patients were enrolled. The final diagnoses of the study population by subclass are listed in Table 3.

Of the patients with a final diagnosis of abnormal IUP, the diagnosis was confirmed by means of either positive villi at D&E or negative laparoscopy results in 45 of 186 patients with an empty uterus, 34 of 77 patients with nonspecific fluid, 55 of 88 patients with echogenic material, 74 of 100 patients with an abnormal sac, and 7 of 25 patients with a normal sac. Of the 261 patients given a diagnosis of abnormal IUP on the basis of quantitative  $\beta$ -hCG values that fell to zero at follow-up, 4 had a D&E procedure without villi at pathology. Each of these had a greater than 50% decrease in their  $\beta$ -hCG values at the 48-

hour follow-up. An additional 181 patients had no D&E procedure but had a greater than 50% decrease in their  $\beta$ -hCG values at the 48-hour follow-up. Of the remaining 76 patients who had a less than 50% decrease at initial follow-up, the vast majority had a greater than 50% decrease at the second or third follow-up visit. In fact, none of these patients had  $\beta$ -hCG values that plateaued.

Of the entire study population, 46 (7.2%; 95% CI 5.4% to 9.5%) of 635 were given a diagnosis of ectopic pregnancy. The diagnosis was made on the basis of laparoscopy in 21 patients. An additional 21 patients had  $\beta$ -hCG values that increased after D&E, and 2 patients had  $\beta$ -hCG values that remained essentially unchanged 48 hours after D&E. Of the remaining 2 patients, 1 had a  $\beta$ -hCG value that increased from 2,536 to 4,300 mIU/mL with an empty uterus as determined by means of ultrasonographic examination at each of these visits, had a D&E, and then 2 days after the D&E still had a  $\beta$ -hCG value of 3,200 mIU/mL. The last patient had a  $\beta$ -hCG decrease from 4,300 to 3,000 mIU/mL over a 3-day period after D&E.

The frequencies of ectopic pregnancy for each subclass are listed in Table 3. The relative risk of ectopic pregnancy in those with an empty uterus versus those without an empty uterus was 5.2 (95% CI 2.6 to 10.2).

Patients with  $\beta$ -hCG values of less than 1,000 mIU/mL had a higher incidence of ectopic pregnancy overall. In addition, within the subclasses of empty uterus and nonspecific fluid collection, those with  $\beta$ -hCG values of less than 1,000 mIU/mL also had a higher frequency of ectopic pregnancy (Table 4).

We performed a sensitivity analysis to account for potential differential rates in the frequency of ectopic pregnancy among those lost to follow-up in each of the 5

**Table 3.** Final diagnosis of patients according to ultrasonographic subclassification.

Final Diagnosis	Empty Uterus	Nonspecific Fluid	Echogenic Material	Abnormal Sac	Normal Sac	Total
Eligible	310	163	115	123	69	780
Lost to follow-up	51	36	22	20	16	145
Enrolled	259	127	93	103	53	635
Normal IUP	36	41	1	3	25	106
Abnormal IUP	186	77	88	100	25	476
Normal versus abnormal IUP	1	3	0	0	3	7
Ectopic pregnancy	36	6	4	0	0	46
Frequency of ectopic pregnancy, % (95% CI)	13.9 (10.1–18.5)	4.7 (1.9–9.6)	4.5 (1.4–10.5)	0.0 (0.0–2.9)	0.0 (0.0–5.5)	7.2 (5.4–9.5)

subclasses. For 3 of the groups (empty uterus, nonspecific fluid, and echogenic material), we recalculated the rate of ectopic pregnancy, assuming that the actual rate in those lost to follow-up with the same subclass was either 0.5 times or 3 times the measured rate in those in whom a final diagnosis was determined. Because the rate of ectopic pregnancy in the abnormal sac and normal sac groups was 0, we instead used an ectopic pregnancy rate of 10% as the upper limit in calculating the number of ectopic pregnancies in the group lost to follow-up. On the basis of these assumptions, the range of rates of ectopic pregnancy for each of 5 subclasses are listed as follows: empty uterus, 12.7% to 18.3%; nonspecific fluid, 4.2% to 6.8%; echogenic material, 3.9% to 6.1%; abnormal sac, 0.0% to 1.6%; and normal sac, 0.0% to 2.3%.

DISCUSSION

The 5 subclasses of indeterminate ultrasonographic examinations cover a spectrum of endometrial findings that can be seen with an early normal or abnormal IUP. An empty uterus is the earliest finding with a normally developing pregnancy, but it may also be found in the setting of a completed abortion or an ectopic pregnancy. As pregnancy develops further, a small intrauterine fluid collection may be visualized. Fluid collections as small as 2 to 3 mm in mean sac diameter can be identified by means of ultrasonography.<sup>5</sup> However, this ultrasonographic finding is nonspecific because this fluid could also represent a collection of blood within the endometrial cavity. It is not until the sac reaches about 5 to 7 mm that a bright surrounding echogenic border is typically seen.<sup>5</sup> This finding increases the likelihood that the identified fluid collection is actually a gestational sac.<sup>4</sup>

At a gestational sac size of 10 mm, a yolk sac is usually visualized if the pregnancy is viable.<sup>6,7</sup> Identification of a yolk sac provides confirmation that the pregnancy is intrauterine.<sup>8</sup> Although the absence of a yolk sac with a mean sac diameter of 10 mm or greater is highly suggestive of an abnormal pregnancy, other studies have found that a small percentage of pregnancies with this initial ultrasonographic finding will ultimately be found to be viable.<sup>9</sup>

Identification of echogenic material within the endometrial cavity is often found in patients with retained products of conception after a spontaneous abortion. When this finding is identified at ultrasonography, the likelihood of a viable pregnancy is low.<sup>10</sup>

The possibility of an ectopic pregnancy is the major concern in patients with an indeterminate ultrasonographic examination. With ectopic pregnancy, the uterus may be empty; however, fluid collections simulating a gestational sac (pseudogestational sac)<sup>11-14</sup> or echogenic intrauterine material simulating retained products of conception have also been found.<sup>10</sup> In a prior retrospective study, Dart and Howard<sup>4</sup> found that patients with an empty uterus had the highest frequency of ectopic pregnancy (25/94, 27%), followed by those with nonspecific fluid (4/30, 13%), echogenic material (2/39, 5%), an abnormal sac (1/36, 3%), and a normal sac (0/29, 0%). Our results are in concordance with these findings. Patients with an empty uterus were at highest risk, with a relative risk of ectopic pregnancy more than 5 times greater than those without an empty uterus at ultrasonography. Patients with either a nonspecific fluid collection or echogenic material were found to be at intermediate risk. Patients with normal or abnormally appearing sacs appear to be at very low risk for ectopic pregnancy.

Our results demonstrate that the frequency of ectopic pregnancy for each of the subclasses is decreased when the  $\beta$ -hCG value is greater than 1,000 mIU/mL. This was true even in the subclass with an empty endometrial cavity. This finding is in conflict with studies by Kadar et al<sup>15</sup> and Stovall et al.<sup>16</sup> These authors concluded that the absence of a gestational sac in association with a high  $\beta$ -hCG value was strongly suggestive of ectopic pregnancy. However, both studies were performed with older technology. In fact, the study by Kadar et al was performed with transabdominal ultrasonography. A number of studies have demonstrated that ectopic pregnancy occurs up to 4 times more frequently in patients with  $\beta$ -hCG values of less than 1,000 mIU/mL.<sup>17,18</sup> In addition, patients with  $\beta$ -hCG values of less than 1,000 mIU/mL will more often have an indeterminate ultrasonographic examinations

**Table 4.**  
Frequency of ectopic pregnancy stratified by  $\beta$ -hCG value.

Final Diagnosis	$\beta$ -hCG <1,000 mIU/mL, % (95% CI)	$\beta$ -hCG >1,000 mIU/mL, % (95% CI)
Empty uterus	31/173, 17.9 (12.7–24.2)	5/83, 6.0 (2.2–12.8)
Nonspecific fluid	5/41, 12.2 (4.6–25.0)	1/81, 1.2 (0.1–5.9)
Echogenic material	2/19, 10.5 (1.8–30.6)	2/74, 2.7 (0.5–8.4)
Abnormal sac	0/6, 0.0 (0.0–39.3)	0/95, 0.0 (0.0–3.1)
Normal sac	0/7, 0.0 (0.0–34.8)	0/34, 0.0 (0.0–8.4)
Total	38/246, 15.4 (11.3–20.4)	8/367, 2.1 (1.0–4.1)

Quantitative  $\beta$ -hCG values were not available for 22 patients.

compared with those with higher  $\beta$ -hCG values.<sup>18,19</sup> In 1 study,<sup>17</sup> the rate of indeterminate ultrasonographic scans was 5 times higher: 64% when the  $\beta$ -hCG value was less than 1,000 mIU/mL but only 13% when the  $\beta$ -hCG value was greater than 1,000 mIU/mL. Finally, other studies have shown that the likelihood of visualizing an ectopic pregnancy at ultrasonographic examination increases if the  $\beta$ -hCG value is high.<sup>19,20</sup> We believe that these factors in combination contribute to the relatively low rate of ectopic pregnancy in our patients with  $\beta$ -hCG values of greater than 1,000 mIU/mL. Thus, we believe that it is important to emphasize that, when the uterus is empty, clinicians should not be reassured by a low  $\beta$ -hCG value because the risk of ectopic pregnancy in these patients is increased.

A few limitations to our study were identified. First, patients with  $\beta$ -hCG values that decreased to zero without further intervention or who had no chorionic villi at D&E but who had  $\beta$ -hCG values that rapidly decreased to zero were classified as having an abnormal IUP. In fact, some of these patients might instead have had a spontaneously resolving ectopic pregnancy. Therefore, our results probably underestimate the true frequency of ectopic pregnancy in the study population. Although about half of the patients diagnosed with abnormal IUP were classified on the basis of  $\beta$ -hCG values that decreased to zero, 70% of these patients had  $\beta$ -hCG values that decreased by greater than 50% at the 48-hour follow-up. A number of studies have demonstrated that ectopic pregnancy is only rarely diagnosed in patients with  $\beta$ -hCG values that decrease by 50% or greater at initial follow-up.<sup>21,22</sup> Although misclassification might well have occurred, we expect the actual rate of misclassification was low.

If a greater percentage of patients in one subclass was given a diagnosis of abnormal IUP on the basis of these criteria, misclassification bias could be introduced. The subclass of patients with an empty uterus had the highest absolute number of patients and the highest percentage of patients, given a diagnosis on the basis of  $\beta$ -hCG values that decreased to zero. Therefore, relative to other subclasses, the true frequency of ectopic pregnancy in these patients is more likely to have been underestimated.

A second limitation is that ultrasonographic examinations were classified on the basis of the text of the radiology report, rather than on the basis of the hard copy of the ultrasonographic examination. This method was used because a hard copy of the actual ultrasonographic examination was frequently unavailable. It is possible that

some examinations would have been classified differently if the actual hard copy of the examination had been used. We did not find this to be a significant problem in practice because the study criteria used to classify the examinations were routinely reported in the official report. In addition, the net effect of misclassification error tends to make groups more homogeneous, thus making the frequency of ectopic pregnancy among the groups more similar. This effect would decrease the likelihood of detecting a true difference in the frequency of ectopic pregnancy among the subclasses. Because a large difference among the subclasses was seen, we assume the actual effect of any misclassification was small.

Ultrasonographic examinations were performed by experienced operators under the close supervision of individuals with specific expertise in pelvic ultrasonography. Whether our results are generalizable to settings in which the examination is performed by less experienced operators is an area for future study. However, application of this classification system is straightforward because the vast majority of indeterminate ultrasonographic examinations can be subclassified after answering the following 4 questions:

1. Is the endometrial cavity empty?
2. If not, is it filled with echogenic material or a sac-like structure?
3. If a sac is present, is it greater than 10 mm in mean sac diameter?
4. If the sac is less than 10 mm, is an echogenic border present or absent?

Because of the simplicity in applying this system, we believe it could be readily applied at most centers where transvaginal ultrasonography is used.

The number of patients lost to follow-up in our study was greater than the number of patients with ectopic pregnancy. It is possible that the rate of ectopic pregnancy in the individuals lost to follow-up differed from those in whom the diagnosis was confirmed. The sensitivity analysis we performed allowed us to approximate how our results would have been affected by differing rates of ectopic pregnancy among those lost to follow-up in each subclass. Even with the most extreme assumptions, those with an empty uterus would have the highest incidence of ectopic pregnancy, and those with abnormal or normal sacs would have the lowest incidence of ectopic pregnancy.

On the basis of our results, we believe that most clinically stable patients with normal or abnormal sacs can safely be discharged from the ED without further testing, as long as outpatient follow-up can be assured. Patients with either echogenic material or a nonspecific fluid col-

lection are at intermediate risk for ectopic pregnancy. If other clinical findings place the patient at low risk, then close outpatient follow-up without further testing can be reasonably justified. A D&E procedure may be considered in patients with more worrisome clinical findings, as long as the possibility of a viable IUP has been excluded ( $\beta$ -hCG > 3,000 mIU/mL and no intrauterine sac determined by means of ultrasonography, decreasing  $\beta$ -hCG values, and serum progesterone value of < 5.0 ng/mL). Chorionic villi will be identified at pathology in approximately 80% of patients with either nonspecific fluid or echogenic material, effectively excluding the diagnosis of ectopic pregnancy.<sup>23</sup>

Patients with an empty uterus at ultrasonography are at the highest risk for ectopic pregnancy. The optimal diagnostic strategy in these patients is less well defined. D&E can be a useful diagnostic procedure if the possibility of a viable IUP has been excluded, particularly if the endometrial stripe is thickened or the  $\beta$ -hCG value is greater than 1,000 mIU/mL. In these patients, greater than 60% will have chorionic villi identified at pathology.<sup>24</sup> In patients with neither of these findings, the yield of D&E is low because only 15% will have villi identified.<sup>24</sup> Progesterone may also be a useful test in patients with an empty uterus. Patients with progesterone values of less than 5.0 ng/mL are at increased risk for ectopic pregnancy and have a low likelihood of having a viable IUP.<sup>25</sup> Obtaining a repeat  $\beta$ -hCG value in 48 hours is also a useful test. Patients with an empty uterus and rising  $\beta$ -hCG values are at increased risk, especially if the rate of increase is less than 66%.<sup>21</sup> Patients with  $\beta$ -hCG values that decrease by greater than 50% at 48 hours are at low risk.<sup>21</sup> Future research should focus on the development of an optimal diagnostic strategy that incorporates findings on history and physical examination, progesterone levels, and follow-up  $\beta$ -hCG testing, along with the selective use of D&E and laparoscopy.

In summary, the frequency of ectopic pregnancy varies significantly among the 5 subclasses of indeterminate ultrasonographic examinations. Patients with an empty uterus have a fivefold increased risk of ectopic pregnancy. This classification system is a useful tool in identifying patients at increased or decreased risk for ectopic pregnancy.

Author contributions: RGD conceived the study. RGD and LD developed the study methodology. LD and GB collected the study data. RGD drafted the manuscript, and LD and GB contributed substantially to its revision. RGD takes responsibility for the paper as a whole.

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