

Outcome of Patients with an Indeterminate Emergency Department First-trimester Pelvic Ultrasound to Rule Out Ectopic Pregnancy

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Abstract

Objectives: Pelvic ultrasound performed by emergency physicians can identify a definite diagnosis in the majority of symptomatic first-trimester pregnant patients on the initial emergency department (ED) visit. However, a significant minority of such patients are diagnosed as having an indeterminate pregnancy state requiring further testing and consultation. The authors investigated the final outcome of patients with an initial indeterminate ED first-trimester pelvic ultrasound examination in the setting of an interdepartmental protocol to rule out ectopic pregnancy. **Methods:** This was an observational prospective cohort study performed at a regional, urban ED with more than 100,000 patient visits over a 13-month period. Pelvic ultrasound for first-trimester patients was prospectively performed by emergency physicians with gynecologic consultation for lack of intrauterine pregnancy (IUP) ultrasound findings. IUP was defined as a fundal gestational sac with either a yolk sac or a fetal pole. Pelvic ultrasounds were classified into diagnostic categories including definite IUP, embryonic demise, molar pregnancy, definite ectopic pregnancy, and indeterminate. For all patients with indeterminate pelvic ultrasound findings, final diagnostic categories and patient outcome were established by the use of patient records, obstetric ultrasound reports, laboratory studies, operative reports, and pathology reports. All patients with ectopic pregnancy were followed for mode of treatment. Descrip-

tive statistics were calculated. **Results:** A total of 1,490 ED first-trimester pelvic ultrasound examinations were performed over 13 months establishing the following diagnostic rates for initial ED visit: IUP 1,037 (70%), demise 127 (8%), definite ectopic pregnancy 24 (2%), molar pregnancy 2 (<1%), and indeterminate 300 (20%). The 300 indeterminate patients were classified using the above protocol into the following final diagnostic categories: embryonic demise 158 (53%), IUP 88 (29%), ectopic pregnancy 44 (15%), and unknown outcome 10 (3%). Indeterminate patients with ectopic pregnancy were treated with methotrexate in 25 of 44 cases (57%) and surgically in 16 of 44 cases (36%); there were no laparotomies. In contrast, ectopic pregnancy patients diagnosed on initial ED visit were treated surgically in 20 of 24 cases (83%), including four laparotomies. **Conclusions:** The outcome of symptomatic first-trimester patients with indeterminate ED pelvic ultrasounds is poor, with significantly high rates of embryonic demise and ectopic pregnancy. However, those indeterminate patients with the eventual diagnosis of ectopic pregnancy have a higher rate of medical methotrexate treatment and a reduced rate of invasive surgical treatment compared with ectopic pregnancy patients diagnosed at initial ED visit. **Key words:** pregnancy; pelvic ultrasound; ectopic pregnancy. *ACADEMIC EMERGENCY MEDICINE* 2004; 11: 912-917.

Pelvic ultrasound is the primary diagnostic tool in evaluating patients presenting to the emergency department (ED) with symptoms suggestive of ectopic pregnancy.¹⁻³ Most studies by emergency physicians performing pelvic ultrasound show high rates of intrauterine pregnancy (IUP) with lower rates of abnormal pregnancy states on the initial ED visit.^{1,4,5} However, a substantial proportion of first-trimester pregnant patients who present to the ED will initially have an indeterminate pelvic ultrasound.⁵

With findings suggestive of neither ectopic pregnancy, demise, molar pregnancy, nor IUP, the disposition and outcome of those with indeterminate pelvic ultrasound pose a quandary for both the emergency physician and the obstetrical consultant. Many testing algorithms have changed with the increasing use of ED first-trimester pelvic ultrasound to include serial use of quantitative beta-human chorionic gonadotropin (β -hCG) testing, use of bedside endometrial sampling for chorionic villi, and medical methotrexate therapy for ectopic pregnancy.^{3,6} We describe the outcome of patients with an indeterminate ED pelvic ultrasound in the setting of an interdepartmental protocol to rule out ectopic pregnancy.

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METHODS

Study Design. This study was a prospective observational cohort of consecutive first-trimester pregnant

patients who presented to the ED with complaints of abdominal pain, pelvic pain, or vaginal bleeding, and who subsequently underwent an ED pelvic ultrasound. The Institutional Review Board at Carolinas Medical Center approved this study.

Study Setting and Population. The study was conducted over a 13-month period at a regional urban ED with accredited emergency medicine and obstetric residency programs. The ED has an annual census of more than 100,000 visits and serves a mixed socioeconomic population. Emergency physicians perform more than 95% of first-trimester pelvic ultrasounds in this ED.

Inclusion criteria included first-trimester patients who complained of abdominal or pelvic pain and/or vaginal bleeding, had a positive β -hCG result or claimed previous positive testing for pregnancy, and had an ED pelvic ultrasound examination performed by their emergency physician during the ED visit that was classified as indeterminate. Patients were excluded if they had their initial ED evaluation by an obstetrician/gynecologist (Ob/Gyn).

Study Protocol. First-trimester pelvic ultrasound is performed by hospital-credentialed, faculty emergency physicians and faculty-supervised emergency medicine residents using transvaginal ultrasound, transabdominal ultrasound, or both. Ultrasound examinations were performed with a Shimadzu 450XL (Kyoto, Japan) using either a 4–8-MHz 11R endocavitary transducer or a 2–6-MHz 13R curved linear transabdominal transducer. The ultrasound protocol includes examining the uterus in sagittal and transverse planes for identification of the appropriate first-trimester findings of IUP (Table 1). The adnexa and the cul-de-sac are visualized in two planes, and comments are made on abnormalities such as masses, chorionic rings, and a large amount of peritoneal fluid. The pelvic ultrasounds are recorded on thermal images, and attached to an ED ultrasound data sheet. A procedure note is written or dictated for the ED chart. Ob/Gyn consultants may perform ultrasound on the patient again or use the images made by the emergency physician.

The ED first-trimester ultrasound protocol for IUP uses a distinct algorithm (Figure 1) and strict definitions for sonographic findings that may be found during the first-trimester pregnancy (Table 1). Ob/Gyn consultation was obtained for all non-IUP findings. Ob/Gyn consultants usually used a β -hCG discriminatory threshold of 2,000 mIU/mL for the findings of a gestational sac on transvaginal ultrasound, but other factors, such as large fluid collections, adnexal masses, pain level, hemodynamics, desire for the pregnancy, and medical history, were used for deciding on further testing and follow-up.

TABLE 1. Carolinas Medical Center ED Definitions of First-trimester Pelvic Ultrasound Findings

IUP	Fundal gestational sac with yolk sac or fetal pole
Embryonic demise	Gestational sac >10 mm without a yolk sac, gestational sac >18 mm without a fetal pole, or fetal pole >5 mm without cardiac activity
Molar pregnancy	Disorganized cystic areas in large uterus with extremely high β -hCG concentrations
Ectopic pregnancy	Fetal pole, yolk sac in gestational sac, or chorionic ring outside fundus of uterus
Indeterminate	All others

The Ob/Gyn service directed typical management of indeterminate patients. Typically, patients with β -hCG \leq 2,000 mIU/mL were followed-up in 48 to 72 hours at a gynecologist's office or the ED unless they had concerning ultrasound findings, such as large adnexal masses, large peritoneal fluid collections, or comorbidities, that may have prompted further investigation or observation. Patients with β -hCG >2,000 mIU/mL and no identified gestational sac shown by transvaginal ultrasound were interviewed by Ob/Gyn consultants regarding ectopic pregnancy. The patients were queried about their desire for pregnancy, and told of the risk of the procedures or endometrial sampling. They then underwent either very close 48-hour follow-up or endometrial sampling. If endometrial sampling occurred and no endometrial villi were found, these patients were offered medical methotrexate treatment or surgical laparoscopy. Patients with abnormal hemodynamics, peritoneal signs, or evidence of significant hemoperitoneum by ultrasound were taken to the operating room for surgical treatment regardless of β -hCG level.

Measures. The main outcome variable of this study was the final diagnosis of patients with an indeterminate pelvic ultrasound. The clinical course and final classification of patients with indeterminate pelvic ultrasounds were determined by one or more of the following: review of patient records, obstetric ultrasound reports, follow-up clinic records, laboratory testing, operative reports, and pathology reports. A final diagnosis of IUP was assigned if the patient had an appropriate rise in quantitative β -hCG levels (>66% in 48 hours), findings on follow-up ultrasound of IUP, or a subsequent clinic or hospital note indicating IUP. A final diagnosis of ectopic pregnancy was assigned based on operative findings, dilation and evacuation procedures, pathology reports indicating no chorionic villi, or empiric treatment with methotrexate after serial β -hCG levels. A final diagnosis of miscarriage was assigned based on falling β -hCG levels without any treatment, dilation and evacuation findings of fetal structure or chorionic villi, or ultrasound findings of

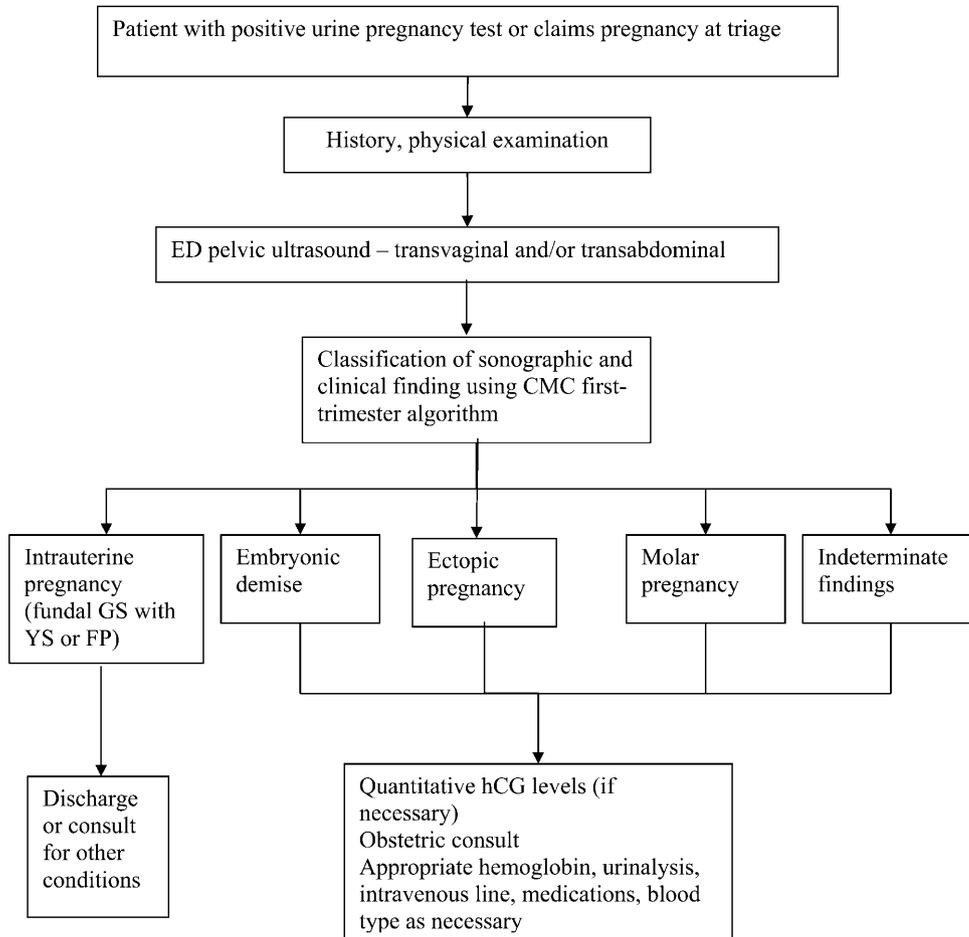


Figure 1. Carolinas Medical Center (CMC) interdepartmental protocol to rule out ectopic pregnancy. GS = gestational sac; YS = yolk sac; FP = fetal pole; hCG = human chorionic gonadotropin.

a clean endometrial stripe on ED or clinic visit after known ultrasound findings of IUP. Patients were assigned a final diagnosis of unknown if there was no follow-up information available on the patient after her initial ED visit.

The therapy for patients with a final diagnosis of ectopic pregnancy was determined in the same manner as above. The patients were classified as receiving methotrexate, surgical treatment, or expectant management. The patients with expectant management, usually with very low quantitative β -hCG levels, had serial β -hCG levels monitored until quantitative β -hCG reached nondetectable levels (<2 mIU/mL).

Data Analysis. Those patients who claimed positive prior pregnancy tests and later had negative pregnancy test results (usually quantitative) were included in the initial population but excluded from data analysis of indeterminate patients, since they were found not to be pregnant.

The proportions and 95% confidence intervals (95% CIs) of the main outcome variable (final diagnosis of patients with an indeterminate pelvic ultrasound) were determined. Analysis of patients with a final

diagnosis of ectopic pregnancy was performed to determine the percentage of specific types of treatment. The Kruskal-Wallis test was used to determine whether there was a relationship between the initial β -hCG value and the final diagnosis. The chi-square test or Fisher’s exact test was used for data measured on the nominal scale. SAS version 8.2 (SAS Institute, Cary, NC) was used for statistical analysis.

RESULTS

A total of 1,512 ED pelvic ultrasound examinations were performed over a 13-month period on suspected first-trimester patients, as shown in Figure 2. A total of 22 patients who claimed prior positive pregnancy testing and underwent pelvic ultrasound were removed from further analysis as a result of subsequent negative laboratory testing for pregnancy. This left a first-trimester population of 1,490 patients, whose initial diagnostic classification after ED pelvic ultrasound is listed in Table 2.

Of those 1,490 patients, 300 (20%) were classified as having indeterminate pelvic ultrasounds on their initial ED visit. These indeterminate patients

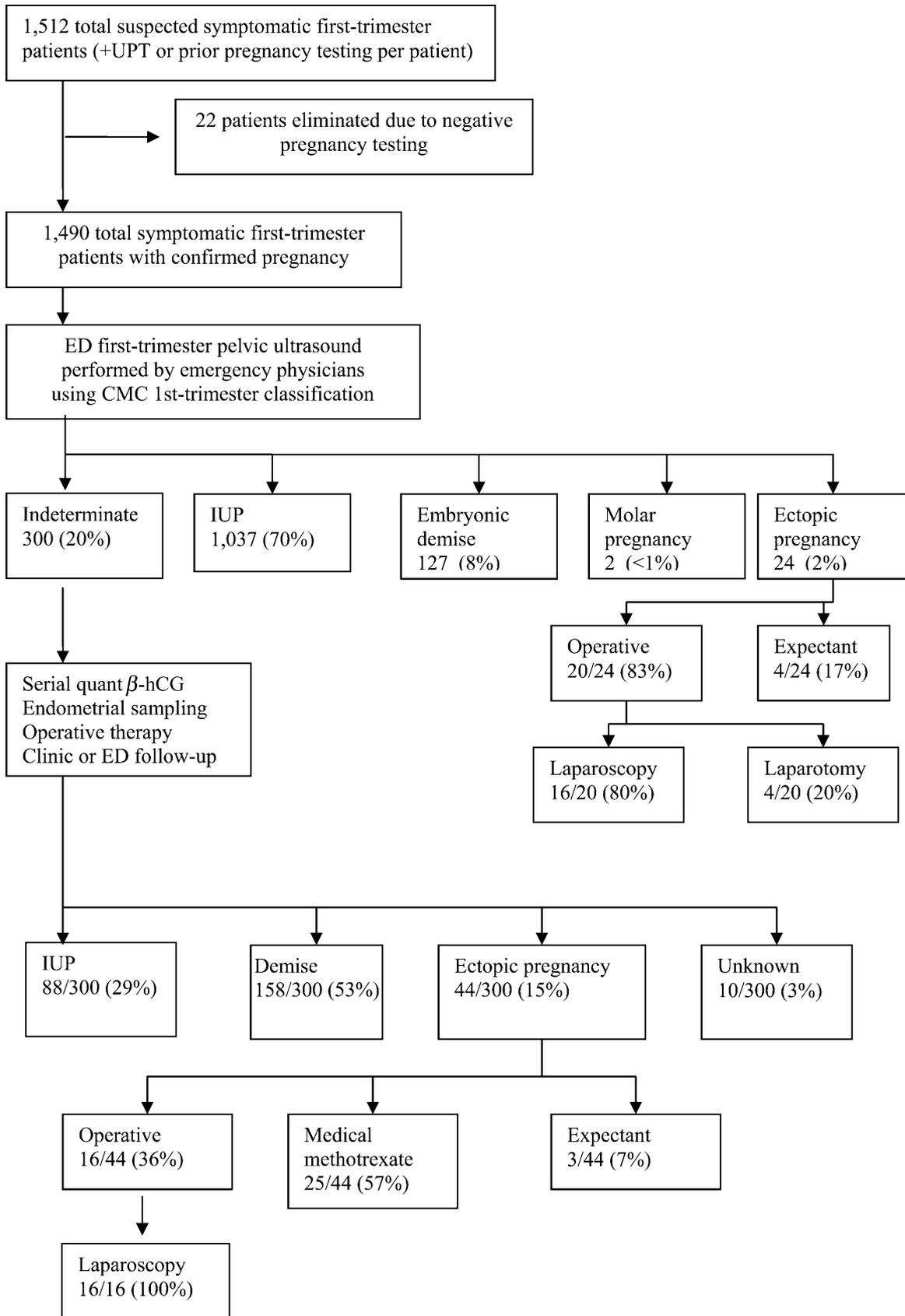


Figure 2. Flow diagram of ED first-trimester pelvic ultrasound patients. UPT = urine pregnancy test; CMC = Carolinas Medical Center; IUP = intrauterine pregnancy; β -hCG = beta-human chorionic gonadotropin.

TABLE 2. Classification of all EM Pelvic Ultrasounds on Initial ED visit

Diagnosis	No. of Patients	Percentages of Diagnoses on Initial ED Pelvic US with 95% CI
IUP	1,037	70% (67%, 72%)
Indeterminate	300	20% (18%, 22%)
Demise	127	8% (7%, 10%)
Ectopic	24	2% (1%, 2%)
Molar pregnancy	2	<1% (0, 0.3%)

US = ultrasound; IUP = intrauterine pregnancy.

underwent testing, procedures, and clinical follow-up as outlined previously to establish final diagnostic categories as listed in Table 3.

The indeterminate patient group had a substantial proportion of embryonic demise and ectopic pregnancy and a low proportion of IUP as a final diagnosis. **In this indeterminate group, initial ED visit median β -hCG values did not significantly differ among the following final diagnoses: IUP (1,304 mIU/mL), embryonic demise (1,572 mIU/mL), and ectopic pregnancy (1,147 mIU/mL); $p = 0.748$, Kruskal-Wallis.**

The treatments for ectopic pregnancy between initial ED visit patients and indeterminate patients are contrasted in Table 4. Patients who were diagnosed as having ectopic pregnancy during the initial ED visit were treated operatively in 20 of 24 patients (83%), with four receiving laparotomy. In comparison, the indeterminate group with ectopic pregnancy received medical methotrexate in 25 of 44 patients (57%) and surgical therapy in 16 of 44 patients (36%). All indeterminate patients with ectopic pregnancy requiring surgery received laparoscopy, with none requiring laparotomy.

DISCUSSION

The typical use of first-trimester pelvic ultrasound by emergency physicians classifies patients into normal IUP, abnormal pregnancy states (including embryonic demise, gestational trophoblastic disease, and ectopic pregnancy), and indeterminate states.^{4,5,7} While the

TABLE 3. Final Diagnosis of First-trimester Pregnant Patients with an Initial Indeterminate ED Ultrasound

Final Diagnosis	No. of Patients	Percentage of Indeterminate Patients with Final Diagnosis (95% CI)
Embryonic demise	158	53% (47%, 58%)
IUP	88	29% (24%, 34%)
Ectopic	44	15% (11%, 19%)
Unknown	10	3% (1.3%, 5.4%)

IUP = intrauterine pregnancy.

TABLE 4. Mode of Ectopic Pregnancy Treatment

Ectopic Treatment	Initial-visit Patients with Diagnosis of Ectopic Pregnancy	Indeterminate Patients with Diagnosis of Ectopic Pregnancy
Operative	83% (20/24)	36% (16/44)
Laparoscopy	16	16
Laparotomy	4	
Medical (methotrexate)	0% (0/24)	57% (25/44)
Expectant	17% (4/24)	7% (3/44)

$p < 0.01$, chi-square test.

diagnosis, management, and outcome are more clear for those patients diagnosed as having IUP and abnormal pregnancy states, the outcome from the ED for patients with indeterminate first-trimester pelvic ultrasounds has not been well described.

This protocol used an operational sonographic definition that reduced ambiguity regarding the definition of IUP by requiring intragestational sac findings of either a yolk sac or a fetal pole. We chose not to include a chorionic ring or a double decidual sign as a sole criterion for IUP, as it has been well described that pseudosacs might have decidual reactions.^{8,9} The definition of embryonic demise was strict so that many of the pregnancies that had abnormal dates, unusual sacs, or small poles were classified as indeterminate until evaluated by the obstetrical consultant or serial follow-up.

Our study confirms previous studies of emergency physician-performed pelvic ultrasound by establishing explicit diagnoses for 80% of first-trimester patients who are symptomatic on the initial ED visit.^{4,5,10} The rate of IUP among these patients is similar to the 60% to 70% as reported previously.⁵ Definite ectopic pregnancy was diagnosed rarely, probably because of the strict definitions of the ultrasound protocol and the “unwritten” pressure to classify examinations as indeterminate without clear findings of an ectopic pregnancy.

Among those with an initial indeterminate pelvic ultrasound, abnormal pregnancy was a frequent outcome. Seventy percent of these indeterminate patients had a failed pregnancy, with most having a miscarriage. Classification by average quantitative β -hCG level did not differentiate final outcome significantly between these indeterminate patients, confirming other studies that suggest a single quantitative β -hCG level is not necessarily helpful in predicting final outcome.^{11,12}

The difference in treatment for those diagnosed as having ectopic pregnancy in the indeterminate group was notable. Patients with ectopic pregnancy diagnosed on the initial ED visit were mostly treated surgically, suggesting that most were ruptured or poor candidates for medical therapy. In contrast, the indeterminate patients with ectopic pregnancy were treated mostly with noninvasive medical

methotrexate. In addition, the lack of laparotomy as the required operation in any of the indeterminate group suggests the stability of these patients to undergo laparoscopy as their operative treatment, even in a delayed fashion. Expectant therapy, although rare, was seen in both initial and indeterminate groups, suggesting a role for careful serial observation in this subset of patients with ectopic pregnancy.¹³

Others have looked at the combination of ultrasound, procedural, and clinical factors that make certain first-trimester diagnoses more common in the indeterminate population. Sonographic endometrial thickness has been examined with varying ability to predict IUP, abnormal, or ectopic pregnancy.¹⁴⁻¹⁶ Endometrial material has been identified as a finding that makes normal IUP unlikely.¹⁷ Peritoneal fluid that is echogenic may be a marker of exudative fluid such as blood found in ruptured ectopic pregnancies.¹⁸ Advanced ultrasound techniques of Doppler interrogation of the pulsatility of the uterine or adnexal structures may also be of some assistance in delineating normal versus abnormal pelvic structures.¹⁸⁻²⁰

This study suggests that those with an initial indeterminate ED ultrasound should be given cautious counseling regarding their rate of normal pregnancy. However, if eventually diagnosed as having an ectopic pregnancy, indeterminate patients are often given less invasive therapy, regardless of the ultimate choice of medical or surgical therapy. ED protocols to rule out ectopic pregnancy that include pelvic ultrasound performed by emergency physicians can stratify first-trimester patients to their therapeutic benefit.

LIMITATIONS

This study was an observational study at a single site with emergency physicians experienced in first-trimester pelvic ultrasound. We did not follow-up patients with diagnoses other than indeterminate and ectopic pregnancy findings, which limits diagnostic comparisons. Sonographically, we did not characterize the endometrium of our indeterminate first-trimester patients in regard to final outcome. Serum progesterone was not used for classification. Further studies on laboratory and sonographic markers for indeterminate patients may be useful.

CONCLUSIONS

The outcome for symptomatic first-trimester patients with an indeterminate ED pelvic ultrasound to rule out ectopic pregnancy is poor, with significantly high rates of embryonic demise and ectopic pregnancy. However, those indeterminate patients with the eventual diagnosis of ectopic pregnancy have a higher rate of medical methotrexate treatment and a reduced rate of invasive surgical therapy compared with ectopic pregnancy patients diagnosed at their initial ED visit.

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