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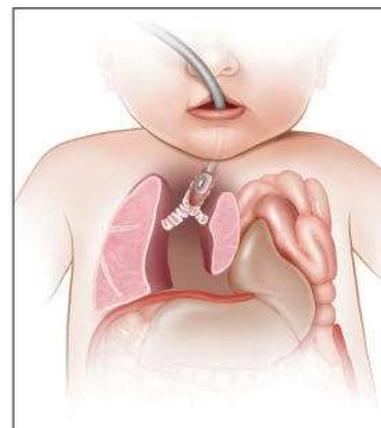
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Adnexal Sonographic Findings in Ectopic Pregnancy and Their Correlation With Tubal Rupture and Human Chorionic Gonadotropin Levels

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Objectives—To determine whether the distribution of transvaginal sonographic findings of ectopic pregnancy has changed since the studies done 20 years ago and to explore the correlation of tubal rupture with transvaginal sonographic findings and human chorionic gonadotropin (hCG) levels.

Methods—Patients with ectopic pregnancy who underwent transvaginal sonography before treatment were included. Sonograms and medical records were retrospectively reviewed. The presence of a tubal ring, the presence of a yolk sac, embryonic cardiac activity, the degree of vascularity on color Doppler imaging, hCG levels, and results of surgery were recorded.

Results—Our study included 231 ectopic pregnancies. A positive sonographic adnexal finding was present in 219 cases (94.8%): adnexal mass in 218 (94.4%) and a moderate-to-large amount of free fluid in 84 (36.4%). The adnexal masses were graded as follows: 1, nonspecific mass (125 cases [54.1% of total]); 2, tubal ring without a yolk sac or embryo (57 [24.7%]); 3, yolk sac but no embryonic heartbeat (19 [8.3%]); and 4, embryo with cardiac activity (17 [7.4%]). The mean hCG level increased as the grade ascended from 1 to 4. Thirty-six patients had tubal rupture at surgery within 24 hours of the sonogram. A moderate-to-large amount of free fluid was significantly associated with tubal rupture ($P < .05$) but had low sensitivity, specificity, and positive predictive value for rupture. Other sonographic findings and hCG levels were not significantly related to tubal rupture.

Conclusions—Transvaginal sonography showed an adnexal abnormality in nearly 95% of our patients with ectopic pregnancy, most commonly a nonspecific adnexal mass. Embryonic cardiac activity was seen in fewer than 10%. Neither sonographic findings nor hCG levels were useful predictors of tubal rupture.

Key Words—ectopic pregnancy; human chorionic gonadotropin; obstetric ultrasound; transvaginal; tubal rupture

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Abbreviations

hCG, human chorionic gonadotropin

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Transvaginal sonography is the imaging method of choice for diagnosing and excluding ectopic pregnancy. It is widely available, well tolerated, and highly sensitive for ectopic pregnancy.^{1,2} The transvaginal sonographic findings in tubal ectopic pregnancy were described in the late 1980s and early 1990s,^{3–5} once transvaginal scanning became widespread. In comparison to transabdominal sonography, transvaginal sonography more often showed an adnexal mass with identifiable features sug-

gestive of an ectopic pregnancy: a tubal ring appearance or the presence of a yolk sac or cardiac activity within the mass. At that time, the frequency of tubal rings was reported to be as high as 71%,⁶ with cardiac activity visible in the ectopic gestation in up to 24%.^{4,7} The ability of transvaginal sonography to diagnose fallopian tube rupture has also been studied, with some suggesting that rupture could be predicted on the basis of transvaginal sonographic findings,^{7,8} whereas others found no sonographic criterion to be a reliable predictor of rupture.⁹

Advances in ultrasound equipment over the past 20 years have led to dramatic improvements in sonographic resolution and performance. In particular, transvaginal sonography is now typically performed at higher frequencies (between 7 and 10 MHz), and harmonic and color Doppler imaging have become generally available. In addition, serum human chorionic gonadotropin (hCG) levels are now readily and rapidly available in the emergency setting. We undertook this study to determine whether the distribution of transvaginal sonographic findings of ectopic pregnancy has changed since the studies done 20 years ago and to explore the correlation of tubal rupture with transvaginal sonographic findings and hCG levels.

Materials and Methods

Institutional Review Board approval was obtained for this study. Using an ultrasound database, we identified all patients who underwent transvaginal sonography between July 1, 2008, and August 31, 2011, with an indication of “rule out ectopic pregnancy” in whom the sonogram showed no sonographic evidence of an intrauterine gestation. Because we use a template reporting system, the terminology “rule out ectopic pregnancy” is used in all of our reports for patients with a positive pregnancy test result who are scanned to determine the pregnancy location when no intrauterine pregnancy is identified. We then reviewed the medical records of these patients. Our study population comprised all patients with pathologic or surgical confirmation of ectopic pregnancy or who had an adnexal mass treated nonsurgically for presumed ectopic pregnancy. If more than 1 sonographic examination was performed before the diagnosis, the sonogram obtained closest to the point of treatment was used for this study.

All sonograms, including images and video clips, were retrospectively reviewed for the presence and characteristics of an adnexal mass and for the presence and amount of free fluid. The reviewer was blinded to the clinical outcome at the time of image review. Adnexal masses were graded using a tiered approach, based on their appearance and

contents, as follows: 1, nonspecific mass (no tubal ring, yolk sac, or heartbeat); 2, tubal ring (echogenic ring with a hypoechoic center but no yolk sac or heartbeat); 3, yolk sac but no embryonic heartbeat; and 4, embryo with heartbeat (Figure 1). Each mass was included in only 1 category: the most advanced grade that applied to it. The size of the mass as reported by the interpreting physician was recorded; if no size was reported, the mass was measured at image review. If more than 1 mass was present, the portion thought most likely to represent the ectopic pregnancy was used for grading and measuring. Masses were measured outer edge to outer edge in 3 planes. When color Doppler imaging of the adnexal mass was performed, the presence and degree of flow were subjectively categorized as trace-to-minimal flow or moderate-to-extensive flow (Figure 2). Color Doppler settings were optimized to detect slow flow.

Free fluid was categorized as none, small, moderate, or large, as follows. Each of 5 locations was evaluated for the presence of fluid: cul-de-sac, right adnexa, left adnexa, above the uterus, and upper abdomen. Fluid seen in 1 location (cul-de-sac or 1 adnexa) was graded as small. Fluid found in 2 locations was graded as moderate. Fluid present in 3 or more locations was graded as large.^{10,11}

The hCG level, if obtained within 24 hours of the index sonogram, was recorded. In the subset of patients who had surgery within 24 hours of the sonogram, the presence or absence of tubal rupture at pathologic examination or surgery was recorded.

Results

Our study set included 231 ectopic pregnancies. These occurred in 227 patients, since there were 4 patients who had 2 ectopic pregnancies during the period of the study. In total, 154 of the 231 cases (66.7%) had surgical and/or pathologic proof of the ectopic pregnancy. The diagnosis was based on sonographic findings in the remaining 77 (33.3%). A positive finding—an adnexal mass and/or a moderate-to-large amount of free fluid—was present in 219 cases (94.8%): an adnexal mass in 218 (94.4%) and a moderate-to-large amount of free fluid in 84 (36.4%). Thirteen patients had no adnexal mass, 1 of whom had a large amount of free fluid, 5 had a small amount of free fluid, and 7 had no free fluid (Table 1).

Among our 231 study cases, sonography showed a grade 1 mass (nonspecific mass) in 125 (54.1%), a grade 2 mass (tubal ring) in 57 (24.7%), a grade 3 mass (yolk sac but no embryonic heartbeat) in 19 (8.3%), and a grade 4 mass (embryonic cardiac activity) in 17 (7.4%). The average size of the mass was 2.2 cm (range, 0.7–8.8 cm; Table 1).

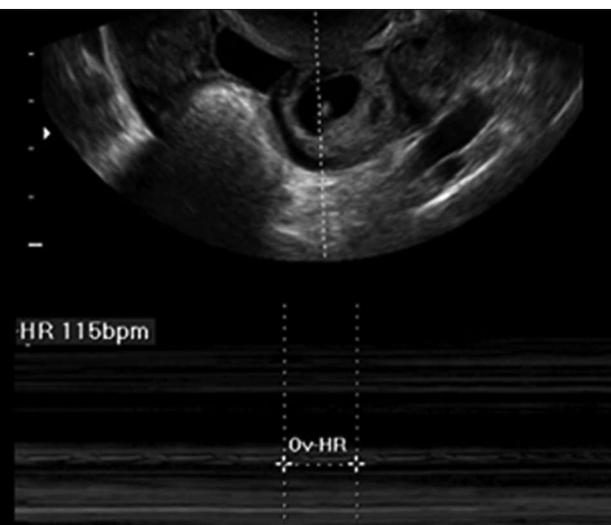
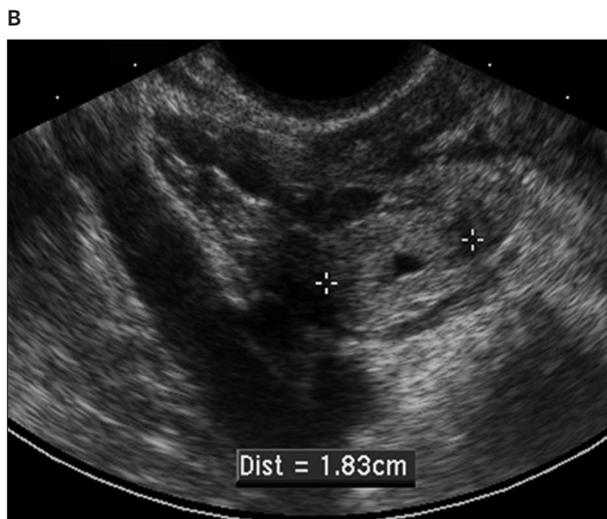
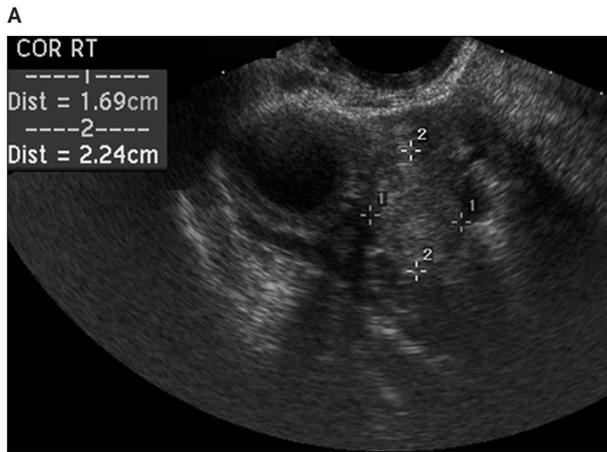


Figure 1. Increasing grades of adnexal masses with ectopic pregnancy. **A**, Grade 1 mass: nonspecific mass. Coronal image of the right adnexa shows a nonspecific echogenic mass (calipers) medial to the right ovary. **B**, Grade 2 mass: tubal ring. Coronal right adnexal image shows a tubal ring (calipers) medial to the right ovary. **C**, Grade 3 mass: yolk sac but no embryonic heartbeat. Coronal image of the right adnexa shows an adnexal lesion containing a yolk sac. **D**, Grade 4 mass: embryonic cardiac activity. Coronal image of the left adnexa shows a tubal ring with a yolk sac (left). An embryonic heartbeat was visible next to the yolk sac and confirmed on M-mode imaging to be 115 beats per minute (right).

Mass size did not show a progressive increase with advancing sonographic grade of the adnexal lesion. Color Doppler imaging of the adnexal mass was performed in 183 cases (Table 1). Flow was trace to minimal in 106 (58%) and moderate to extensive in 77 (42%). There was no

significant relationship between mass type and color Doppler flow ($P = .42, \chi^2$). There was a large amount of free fluid in 48 cases (20.8%), a moderate amount in 36 (15.6%), a small amount in 88 (38.1%), and no free fluid in 59 (25.5%).

Figure 2. Color Doppler interrogation of ectopic pregnancy masses. **A**, Trace to minimal flow. Coronal left adnexal color Doppler image shows only minimal flow medially. **B**, Moderate to extensive flow. Coronal color Doppler image of a right adnexal tubal ring, just medial to the right ovary, shows extensive flow.

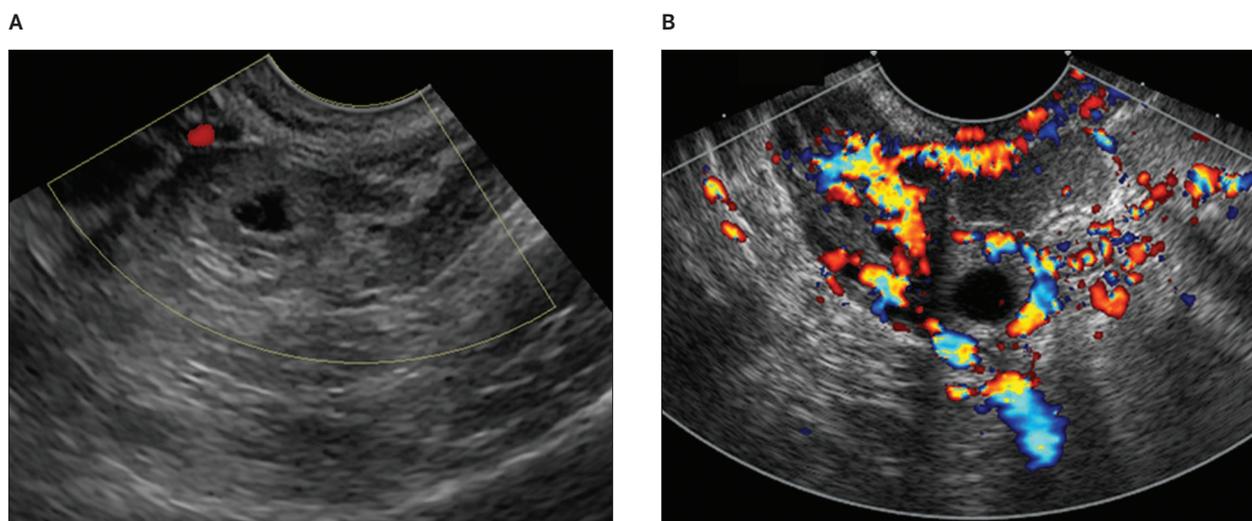


Table 1. Adnexal Characteristics and hCG Levels With Ectopic Pregnancy

Sonographic Finding	n (%)	Mean Size (Range), cm	Color Doppler ^a (When Performed), n (%)		Mean hCG ^{b,c} (Range), mIU/mL
			Moderate/Prominent	Minimal/Trace	
Embryo with cardiac activity (grade 4 mass)	17 (7.4)	2.45 (1.1–6.0)	5 (50)	5 (50)	20,980 (135–107,949) n = 16
Yolk sac (grade 3 mass)	19 (8.3)	2.15 (1.2–6.6)	6 (35)	11 (65)	4,283 (410–14,296) n = 19
Tubal ring (grade 2 mass)	57 (24.7)	1.83 (0.8–6.0)	25 (51)	24 (49)	2,596 (23–16,093) n = 56
Nonspecific adnexal mass (grade 1 mass)	125 (54.1)	2.46 (0.7–8.8)	41 (38)	66 (62)	1,139 (7–12,011) n = 121
No mass and moderate/large free fluid	1 (0.4)				2148 n = 1
No mass and small-to-no free fluid	12 (5.2)				2,553 (164–11,057) n = 12
Total	231		77 (42)	106 (58)	225

^aColor Doppler versus grade of adnexal mass: $P = 0.42, \chi^2$.

^bWithin 24 hours of sonography.

^cHuman chorionic gonadotropin versus presence/absence of cardiac activity: $P < .05, t$ test.

In 225 cases, an hCG measurement was obtained within 1 day of the study sonogram. The hCG levels ranged from 7 to 107,949 mIU/mL, with an average of 3258 mIU/mL. The mean hCG increased with advancing grade (Table 1) and was significantly higher in cases in which cardiac activity was present (20,980 mIU/mL) than in those with no cardiac activity identified (1901 mIU/mL; $P < .01$, t test). Approximately half (112) of the 225 patients in whom an hCG measurement was obtained within a day of the transvaginal sonography had levels of less than 1000 mIU/mL, and 9 (4.0%) patients had levels of less than 100 mIU/mL. Although most patients (174 [77.3%]) had an hCG level of less than 3000 mIU/mL, in 16 patients (7.1%), the hCG level was greater than 10,000 mIU/mL.

Surgery was performed within 1 day of the transvaginal sonography in 143 cases, 36 of whom had ruptured fallopian tubes (25.2%; Table 2). Among these 143 cases, an adnexal mass was present on transvaginal sonography in 135 (94.4%). There was no significant relationship between tubal rupture and the sonographic finding (presence or type) of an adnexal mass ($P = .58$, χ^2); regardless of the findings, approximately 20% of cases were found to be ruptured at surgery. Likewise, the degree of color Doppler flow in the adnexal mass was not significantly related to the presence or absence of tubal rupture ($P = .30$, χ^2).

The rate of rupture was significantly higher when the amount of free fluid was moderate to large compared to small to none (33% versus 17%; $P < .05$, χ^2). However, a moderate-to-large amount of free fluid had poor sensitivity (67%; confidence interval, 49.0%–81.4%), specificity (54%; confidence interval, 44.3%–63.9%), and positive predictive value (33%) for diagnosing tubal rupture. In the single patient with a large amount of free fluid and no adnexal mass identified, no rupture was found at surgery.

An hCG level was available for 139 of the 143 patients for whom the tubal status was known. The relationship between hCG and rupture was not statistically significant, and there was no cutoff level of hCG that predicted tubal rupture. Of note is that 7 of the 72 patients with hCG less than 500 mIU/mL (9.7%) had ruptured fallopian tubes at surgery.

Discussion

There have been major advances in ultrasound equipment in the past 2 decades. The resulting improved resolution raises the question of whether the sonographic findings of ectopic pregnancy described in the early days of transvaginal sonography still apply today. It is possible that improved resolution has resulted in earlier identification of adnexal

Table 2. Adnexal Findings and hCG Levels in Relation to Tubal Rupture Versus Nonrupture

Sonographic Finding	n	Rupture			$P(\chi^2)^a$
		Yes	No	Rupture Rate %	
Adnexal mass					.58 ^b (NS)
Mass with cardiac activity	17	3	14	17.6	
Mass with yolk sac	14	3	11	21.4	
Mass with tubal ring	23	5	18	21.7	
Nonspecific mass	81	23	58	28.4	
No adnexal mass	8	2	6	25.0	
Free fluid					<.05 ^c
None	26	3	23	11.5	
Small	44	9	35	20.5	
Moderate	29	10	19	34.5	
Large	44	14	30	31.8	
Color Doppler					.30 (NS)
Trace/minimal	65	14	51	21.5	
Moderate/prominent	50	15	35	30.0	
hCG, mIU/mL					.62 (NS)
<1000	67	14	53	20.9	
1000–1999	20	6	14	30.0	
>2000	52	14	38	26.9	

^aSonographic finding versus rupture. NS indicates not significant.

^bCombining masses with cardiac activity and masses with a yolk sac into one group and nonspecific masses and no masses into one group because of the small cell size.

^cComparing none/small versus moderate/large.

abnormalities, with a corresponding change in the distribution of imaging findings. Our study addresses this question and provides an updated understanding of the imaging characteristics of ectopic pregnancy and their relationship to fallopian tube rupture.

We found that the percentage of ectopic pregnancies with a yolk sac or cardiac activity was lower than previously reported. Embryonic cardiac activity was found in fewer than 10% of our patients, similar to a recent report² but much lower than in earlier series, in which up to 24% of ectopic pregnancies had cardiac activity.^{4,7} The ectopic pregnancy in more than half of our patients appeared as a nonspecific adnexal mass, which may have represented a blood clot in some cases. Our study confirms the previously published important point that, in a small number of patients, free fluid may be the only sonographic finding of ectopic pregnancy.^{9–12}

In the early 1990s, color Doppler imaging was suggested as a valuable adjunct for the diagnosis of ectopic pregnancy.^{13,14} However, we found color Doppler imaging to be of little clinical value: there was no significant relationship between the color pattern and type of adnexal mass, and the addition of color Doppler imaging to the examination did not improve the ability to predict tubal rupture.

Among our patients who underwent surgery within 1 day of the study sonogram, 25.2% proved to have tubal rupture. However, the overall rate of tubal rupture is likely to be much lower, since the women who underwent surgery were not representative of our entire group. Although our study methods do not allow us to determine the overall rate of tubal rupture with ectopic pregnancy, our results do permit us to conclude, as had been noted previously,^{9,15} that sonographic findings are not reliable predictors of rupture. No single adnexal mass appearance or color Doppler characteristic correlates with the presence or absence of tubal rupture. Only the presence of a moderate-to-large amount of free intraperitoneal fluid was significantly associated with a ruptured fallopian tube, but the finding of this amount of free fluid had poor sensitivity, specificity, and positive predictive value for tubal rupture.

The role of hCG in the diagnosis of ectopic pregnancy is widely debated in the literature. Our study, similar to others,^{8,16–18} shows that hCG levels vary widely in women with ectopic pregnancy, from less than 10 mIU/mL in one of our patients to greater than 100,000 mIU/mL in another, and reinforces the fact that there is no lower-level hCG cutoff value with ectopic pregnancy.¹⁸ The average hCG value increased as the grade of the adnexal mass increased, with the highest average hCG level found in

those with cardiac activity, which also confirms other reports.^{2,8} However, the hCG level did not correlate with the presence or absence of tubal rupture, so this serum measurement has little clinical value if an adnexal mass is seen on sonography.

This study had a few limitations. Measurements of nonspecific adnexal masses were somewhat subjective, since the borders of the masses were not always clear. In particular, some of the poorly defined masses may have represented blood clots, which often do not have discrete margins and may be difficult to measure accurately. Another limitation was that some patients had more than 1 sonographic examination performed before the time of diagnosis. We used the transvaginal sonogram obtained closest to the point of treatment, which may have biased this report toward larger and more advanced adnexal findings. Additionally, some of our patients did not have either surgical or pathologic proof of their ectopic pregnancies but were treated medically.

In conclusion, our findings show that, with ectopic pregnancy, the adnexal findings on transvaginal sonography using current equipment tend to be less advanced than were reported 1 to 2 decades ago. That is, patients are more likely to have a nonspecific adnexal mass than a more advanced finding, such as a yolk sac or embryonic heartbeat in the mass, likely because of diagnosis of ectopic pregnancy earlier in gestation. Imagers should be aware that the sonographic findings of ectopic pregnancy may be quite subtle. Unfortunately, despite the improvement in sonographic equipment and the increased availability of hCG testing, there has been no improvement in the ability of transvaginal sonography to predict fallopian tube rupture.

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