

# The accuracy of transvaginal ultrasonography for the diagnosis of ectopic pregnancy prior to surgery

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**BACKGROUND:** To evaluate the accuracy of transvaginal ultrasonography (TVS) for the detection of ectopic pregnancies (EPs) in women undergoing surgery for presumed ectopic pregnancy. **METHODS:** A prospective, observational study. Women were diagnosed with an EP using TVS if any of the following were noted in the adnexal region: (i) an inhomogeneous mass or blob sign adjacent to the ovary and moving separately from the ovary; or (ii) a mass with a hyper-echoic ring around the gestational sac or bagel sign; or (iii) a gestational sac with a fetal pole with or without cardiac activity. The final diagnosis was based on the findings at surgery and subsequent histology of removed tissues. **RESULTS:** 6621 consecutive women underwent TVS during the study; 200/6621 (3.0%) women were diagnosed as having an EP using TVS. Forty-eight non-surgically managed women were excluded from the analysis. 85.5% of women presented with symptoms and 14.5% were asymptomatic. In 88 (57.9%) cases an inhomogeneous mass or blob sign was visualized and in 20 cases (13.2%) an embryo  $\pm$  cardiac activity. Thirty-one (20.4%) had a hyper-echoic ring in the adnexa. In 11 (7.2%) cases there was no evidence of either an intra-uterine (IUP) or EP on ultrasound. Two (1.3%) IUPs were subsequently diagnosed as heterotopic pregnancies. There was no association between the presenting complaints and TVS findings. 152 surgical procedures were performed. In 5.9% (9/152) of these cases no EPs were confirmed in fallopian tube or pelvis at laparoscopy. In 9.1% (13/143) of cases an EP was visualized at surgery when not seen on the index ultrasound scan. The sensitivity and specificity of TVS to detect EP were 90.9% and 99.9%, respectively, with positive and negative predictive values of 93.5% and 99.8%, respectively. **CONCLUSIONS:** 90.9% of ectopic pregnancies in this study population can be accurately diagnosed using TVS prior to surgery. The diagnosis of an ectopic pregnancy should be based on the positive visualization of an adnexal mass using TVS. This should in turn result in a decrease in the number of false positive laparoscopies.

*Key words:* ectopic pregnancy/adnexal mass/inhomogeneous mass (blob sign)/hyper-echoic ring/transvaginal ultrasonography

## Introduction

Many women of reproductive age present to health professionals in primary and hospital care with lower abdominal pain. Ectopic pregnancy must always be considered in such circumstances. Ectopic pregnancy is the fourth most common cause of maternal death in the United Kingdom, accounting for 80% of early pregnancy deaths in the last triennial report (Lewis and Drife 2004). Women with clinical signs of a ruptured ectopic pregnancy who are haemodynamically compromised should not have surgery delayed to have an ultrasound examination performed. However, the early diagnosis of ectopic pregnancy in clinically stable women with transvaginal ultrasonography (TVS) is not only potentially life saving, but may decrease the number of operative procedures such as diagnostic laparoscopy and dilatation and curettage

(Atri *et al.*, 2003). This early diagnosis of unruptured ectopic pregnancy also allows for consideration of conservative management options such as methotrexate (Hajenius *et al.*, 1997) or even an expectant approach (Korhonen *et al.*, 1994). Should surgery be necessary, a laparoscopic approach should be used in the majority of cases—with advantages in terms of patient recovery time and bed occupancy (Vermesh *et al.*, 1989; Lundorff *et al.*, 1991; Murphy *et al.*, 1992).

Although we acknowledge that the diagnosis of ectopic pregnancy is not usually made based on ultrasound signs alone, we argue that the diagnosis of ectopic pregnancy should be based on the positive visualization of an adnexal mass using TVS rather than on the basis of a scan that fails to demonstrate an intra-uterine gestational sac. If the scan

does not reveal any pregnancy, a knowledge of the behaviour of serial serum hCG and progesterone is essential to evaluate which cases are at risk of developing into ectopic pregnancy. It is still possible to see ultrasound reports that read 'empty uterus, ectopic pregnancy cannot be excluded'. This is not helpful and may result in unnecessary intervention. The aim of this study was to evaluate the role of ultrasonography in the diagnosis of ectopic pregnancy in a scan-based EPU.

## Materials and methods

We undertook a prospective observational study of all women attending the Early Pregnancy Unit (EPU) at St George's Hospital, London, between February 2002 and November 2003, inclusive. All women who presented to the EPU underwent a TVS, using a 5 MHz probe (Aloka SSD 900, 2000 or 4000, Keymed Ltd, Southend, UK and Aloka Co. Ltd, Tokyo, Japan). This was not a screening study for ectopic pregnancy and women either self-referred or were referred by their General Practitioner (GP) to the EPU.

The diagnosis of an ectopic pregnancy by ultrasonography was based on one of the following grey-scale appearances: (i) an inhomogeneous mass or blob sign adjacent to the ovary and moving separately to this; or (ii) a mass with a hyper-echoic ring around the gestational sac or bagel sign; or (iii) a gestational sac with a fetal pole with cardiac activity, i.e. a viable extra-uterine pregnancy; or (iv) a gestational sac with a fetal pole without cardiac activity, i.e. a non-viable extra-uterine pregnancy.

Women were managed expectantly, medically or surgically depending on their clinical state, the size of the ectopic pregnancy, the presence or absence of fetal cardiac activity, the presence or absence of haemoperitoneum in the pouch of Douglas and the level of the serum human chorionic gonadotrophin (hCG).

Ectopic pregnancy visualized at laparoscopy/laparotomy and confirmed on histological examination was used as the gold standard. Women managed non-surgically were however excluded from the final analysis, as histological confirmation of the diagnosis was not possible.

A small minority of women underwent surgery in the absence of a mass at ultrasonography because of pelvic pain and/or the presence of a haemoperitoneum on ultrasound. Although by definition these women had pregnancies of unknown location (PULs), the decision to operate was a clinical one.

Data recorded included the age of the women and length of gestation in days at presentation, presenting complaint, use of contraception, the presence or absence of a corpus luteum, the ultrasonographic appearance of the ectopic pregnancy, the presence or absence of blood in the pouch of Douglas and the levels of serum hCG and progesterone at presentation.

## Statistical analysis

The performance of TVS was evaluated in terms of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

The Chi-squared test was used to assess the relationship between presenting complaint and TVS findings. *P*-values were obtained from the Wilcoxon rank sum tests.

## Results

A total of 6621 consecutive women underwent TVS during the study period. 5840/6621 (88.2%) were given a diagnosis of an early intra-uterine pregnancy or intra-uterine pregnancy using TVS. 581/6621 (8.8%) were classified as pregnancies of unknown location using TVS. 200/6621 (3.0%) of women in this study were diagnosed as having an ectopic pregnancy using TVS. Forty-eight cases managed conservatively (either medically or expectantly) were excluded from the analysis in the absence of confirmatory histology. Eighty-eight (57.9%) cases had an inhomogeneous mass or blob sign, 20 (13.2%) had an embryo  $\pm$  cardiac activity (11 viable and 9 non-viable extra-uterine pregnancies) and 31 (20.4%) had a hyper-echoic ring around the gestational sac (See Table I). The mean age, mean gestation and mean serum hCG levels at presentation are also included in this table for the different TVS subgroups.

There was no significant association between TVS findings and presenting complaint according to the Chi-squared test (See Table II).

The overall mean age was 31.1 years and the overall mean gestational age at presentation was 48.3 days. The mean serum hCG and progesterone levels at diagnosis were 6997.4 IU/l and 29.4 nmol/l, respectively. 85.5% of women presented with symptoms and 14.5% were asymptomatic. Means for the symptomatic group and asymptomatic group were compared (See Table III). There was no statistically significant difference noted between these groups for the mean age, mean gestation, mean serum hCG (*P*-value = 0.44) and mean progesterone levels (*P*-value = 0.22) at presentation.

Presenting complaints included: (1) per vaginal bleeding (PVB) (13.0%), (2) lower abdominal pain (LAP) (30.8%), (3) PVB and LAP (37.0%), (4) query ectopic pregnancy referred from another hospital (2.1%), (5) LAP and previous ectopic pregnancy (2.1%), (6) PVB, LAP and previous ectopic pregnancy (0.7%), (7) unsure dates (4.8%), (8) history of previous

**Table I.** Frequency table for ultrasonographic findings. *n* = 152

USS findings	Frequency	Percentage (%)	Cumulative frequency	Cumulative (%)	Mean age at initial scan (years)	Mean gestation at initial scan (days)	Mean serum hCG at initial scan (U/l)
Inhomogeneous mass	88	57.9	88	57.9	31.5	46.3	2267.6
Embryo with cardiac activity (viable extra-uterine pregnancy)	11	7.3	99	65.2	30.8	48.5	35442.6
Embryo without cardiac activity (non-viable extra-uterine pregnancy)	9	5.9	108	71.1	30.0	58.0	11534.4
Adnexal mass with echogenic/tubal ring	31	20.4	139	91.5	28.9	49.1	5039.1
Pregnancy of unknown location	11	7.2	150	98.7	32.3	45.9	4431.1
Intra-uterine pregnancy	2	1.3	152	100.0	33.0	63.5	117350.0

**Table II.** TVS findings and presenting complaint

TVS findings	Presenting complaints												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Frequency	1	2	3	4	5	6	7	8	9	10	11	12	
Inhomogeneous mass	12	26	32	1	3	0	4	4	1	0	1	1	85
Embryo with or without cardiac activity	1	5	6	0	0	1	3	0	2	0	0	2	20
Adnexal mass with echogenic/tubal ring	3	11	11	2	0	0	0	0	1	1	0	1	30
Pregnancy of unknown location	3	2	5	0	0	0	0	0	0	0	0	0	10
Intra-uterine pregnancy	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	19	44	54	3	3	1	7	4	4	1	1	4	145
Frequency missing = 7													

1. Per vaginal bleeding (PVB); 2. Lower abdominal pain (LAP); 3. PVB and LAP; 4. Query ectopic pregnancy referred from another hospital; 5. LAP and previous ectopic pregnancy; 6. PVB, LAP and previous ectopic pregnancy; 7. Unsure dates; 8. History of previous ectopic pregnancy; 9. Referred from the termination clinic; 10. Maternal anxiety; 11. GP referral not specified; 12. No reason given.

ectopic pregnancy (2.7%), (9) referred from the termination clinic (2.7%), (10) maternal anxiety (0.7%), (11) GP referral not specified (0.7%), and (12) no reason given (2.7%) (see Table III). 85.7% (1–6) of women presented with symptoms and 14.3% (7–12) were asymptomatic. The presenting complaint was not recorded in seven cases.

No corpora lutea were visualized on scan in 52.2% of cases, but were ipsilateral when present in 80.3%. Haemoperitoneum, as defined by the presence of fluid with ground-glass appearance in the pouch of Douglas, was seen in 31% (62/200) of cases. 16.7% (24/143) of women with ectopic pregnancies were using contraception: four intra-uterine contraceptive device, one progesterone only pill, five combined oral contraceptive, nine barrier, one sterilization, three emergency contraception and one depo provera.

Of the 152 surgical procedures performed, there were nine negative laparoscopies, i.e. no ectopic pregnancy was visualized in the fallopian tube or in the pelvis, despite a mass being reported on scan. Six of these cases were subsequently found to have failing intra-uterine pregnancies, one had a failing PUL and two had persisting PUL requiring methotrexate therapy. Thirteen of the 143 (9.1%) of the confirmed ectopic pregnancies visualized at laparoscopy were not seen pre-operatively on TVS. PUL was the initial diagnosis on TVS in 11 of these cases; in three of these cases large uterine fibroids were present and consequently it was not possible to

thoroughly visualize the adnexae. Two women with confirmed intra-uterine pregnancies were subsequently diagnosed as having heterotopic pregnancies at laparotomy. There was a third heterotopic pregnancy in this study that was diagnosed pre-operatively and the woman underwent a laparoscopic salpingectomy followed by an interval termination of pregnancy. Of the ectopic pregnancies visualized at surgery, 93.0% were managed laparoscopically and 7.0% by laparotomy. The sensitivity and specificity of TVS to detect ectopic pregnancy were 90.9% and 99.9%, respectively. The positive and negative predictive values of TVS were 93.5% and 99.8%, respectively (see Table IVa).

When the 48 cases managed conservatively were included, the sensitivity and specificity of TVS to detect ectopic pregnancy were 93.2% and 99.9%, respectively. The positive and negative predictive values of TVS were 95.2% and 99.8%, respectively (see Table IVb).

## Discussion

This study clearly demonstrates the capability of transvaginal ultrasound when used as a single test to positively identify an ectopic pregnancy where present. Although few clinicians would use ultrasound evidence of extra-uterine pregnancy as the primary way to diagnose ectopic pregnancies, our data suggest that ultrasound is a reliable diagnostic tool.

**Table III.** Means for the symptomatic and asymptomatic groups

Reason for presentation	<i>n</i>	%	Mean age at initial scan (years)	Mean gestation at initial scan (days)	Mean serum hCG at initial scan (U/l)	Mean serum progesterone at initial scan (nmol/l)
1. Bleeding	19	13.1	32.2	51.3	4629.9	28.1
2. Pain	44	30.3	31.0	45.7	4742.5	32.2
3. Bleeding and pain	54	37.2	30.7	47.9	6490.1	25.5
4. Query Ectopic pregnancy (EP) referred from another hospital	3	2.1	30.7	46.5	2133.0	19.0
5. Pain and previous EP	3	2.1	34.3	20.0	1319.7	12.7
6. Bleeding, pain and previous EP	1	0.7	33.0	63.0	551.0	178.0
Symptomatic sub-total	124	85.5	31.1	47.2	5324.7	29.4
7. Unsure dates	7	4.8	27.0	49.1	2409.4	30.9
8. Previous EP	4	2.8	32.0	44.0	1491.3	64.3
9. Referred from TOP clinic	4	2.8	26.5	60.0	24828.0	25.0
10. Anxiety	1	0.7	37.0	43.0	3281.0	59.0
11. GP advised USS	1	0.7	39.0	46.0	193.0	4.0
12. No reason	4	2.8	30.8	61.5	10899.3	35.0
Asymptomatic sub-total	21	14.5	29.6	52.1	6304.0	37.0

**Table IVa.** 'True' histological diagnosis versus 'predicted' ultrasound diagnosis on the 152 ectopic pregnancies managed surgically

'True' histological diagnosis	'Predicted' ultrasound diagnosis			
	Ectopic pregnancies	Non-ectopic pregnancies	Total	
Ectopic pregnancies	130	9	139	PPV = 93.5% 130/139
Non-Ectopic pregnancies	13	6469	6482	NPV = 99.8% 6469/6482
Total	143	6478	6621	
	Sensitivity = 90.9% 130/143		Specificity = 99.9% 6469/6478	

**Table IVb.** 'True' diagnosis versus 'predicted' ultrasound diagnosis on all 200 ectopic pregnancies, including those managed conservatively

'True' diagnosis	'Predicted' ultrasound diagnosis			
	Ectopic pregnancies	Non-ectopic pregnancies	Total	
Ectopic pregnancies	178	9	187	PPV = 95.2% 178/187
Non-Ectopic pregnancies	13	6421	6434	NPV = 99.8% 6421/6434
Total	191	6430	6621	
	Sensitivity = 93.2% 178/191		Specificity = 99.9% 6421/6430	

The scans were performed for a multitude of symptoms and not as a 'routine'. The vast majority of women who presented with an ectopic pregnancy were indeed symptomatic and therefore these data can be extrapolated as a diagnostic test to other populations.

The duration of the pregnancy was not influenced by the indication for TVS. There was no statistically significant difference in the timing of the initial scan, regardless of whether the women presented with or without symptomatology (see Table III). Some would argue that the late timing of the scans in this study contributes to the high sensitivity of ultrasonography. This may well be the case, as more advanced ectopic pregnancies tend to be larger at presentation, thus making visualization with TVS more reliable. Women are not screened for ectopic pregnancy in our unit and the apparent late timing of the scan in this study is a reflection of the population studied and not the policy of the unit.

The EPU is a walk-in unit with 7 days a week, 12 h a day open access and no waiting list, therefore women with ectopic pregnancies, in this study population, presented themselves to the EPU at varying gestational ages during the first trimester. Despite the overall mean gestational age, 48.3 days, almost 25% were managed conservatively and only 10 women were unstable at presentation, requiring laparotomy. The authors believe that the late timing of the presentation and first ultrasound scan did not compromise the care of women in this study.

Ideally, scanning and diagnosing women with ectopic pregnancies at much earlier gestations would be preferable. This would enable clinicians to offer more conservative treatment modalities to more stable women with early ectopic pregnancies at lower serum hCG levels. However, this policy would potentially result in more PULs or inconclusive scans, which in turn would result in an increased number of subsequent scans and visits for the women. This would have an implication on resources, not to mention the possible psychological morbidity to the women. We would not advocate

screening for ectopic pregnancy with TVS in asymptomatic women at earlier gestations.

The mean serum hCG at presentation was 6304.0 U/l in the asymptomatic group compared with 5324.7 U/l in the symptomatic group ( $P$ -value = 0.44). These levels seem very high and this is no doubt a reflection of the gestational age at presentation. Such high serum hCG levels would potentially result in a diagnostic suspicion bias, as women with an empty uterus and high serum hCG levels, by definition, are more likely to have an ectopic pregnancy on TVS. However, it is important to remember that these quantitative serum hCG levels were not available at the time of the initial ultrasound scan and therefore they did not influence the ultrasonographer.

Ectopic pregnancy should not be diagnosed on the basis of an absent intra-uterine gestational sac but rather by the positive visualization of an adnexal mass using two-dimensional (2-D) grey-scale TVS. If an EP is present, between 87 and 93% should be identified using TVS prior to surgery (Cacciatori *et al.*, 1990; Shalev *et al.*, 1998). In this study, 90.9% of ectopic pregnancies were positively identified prior to surgery. In a meta-analysis of 10 studies involving a total of 2216 women (565 with ectopic pregnancies and 1651 without ectopic pregnancies) the performance of TVS for the diagnosis of ectopic pregnancy was evaluated (Brown and Doubilet, 1994). Four different ultrasonographic criteria were assessed: criterion A, a gestational sac with a fetal pole with cardiac activity, i.e. a viable extra-uterine pregnancy; criterion B, a gestational sac with a fetal pole without cardiac activity, i.e. a non-viable extra-uterine pregnancy; criterion C, a mass with a hyper-echoic ring around the gestational sac, i.e. an empty 'tubal ring'; and criterion D, an inhomogeneous adnexal mass or blob sign. The positive predictive values (PPV) for criteria A, B and C were 97.8–100%. In our study, the PPV for criteria A, B and C were 100%, in keeping with this data. The PPV for criterion D was 96.3% compared with 88.6% in our study. The high predictive value of TVS as a diagnostic tool in the management of ectopic pregnancies

should reduce the number of unnecessary laparoscopies without significantly compromising the woman's well being. The early detection and classification of an unruptured EP allows conservative management options to be considered (Condous *et al.*, 2003). These include not only medical management in the form of methotrexate, but also expectant management. In this series of 143 consecutive ectopic pregnancies that underwent surgery, 90% were managed laparoscopically as day surgical procedures. Even if surgery is required, diagnosis at an early stage may facilitate minimal access intervention.

This study also confirms previous data regarding the characteristic appearances of ectopic pregnancy on TVS, that the majority of confirmed ectopic pregnancies are seen as an inhomogeneous mass or blob sign (57.9%). 20.4% were visualized as a hyper-echoic ring and only 13.2% were visualized as gestational sac with a fetal pole—55% had positive fetal cardiac activity and 45% had no fetal cardiac activity. All nine negative laparoscopies were pre-operatively classified as inhomogeneous masses using TVS. Misdiagnosis using TVS should be relatively uncommon and in this study the false positive rate was 5.9%.

The negative predictive value (NPV) of TVS in this study is high because of the low incidence of disease within the study population, i.e. a large population of normal women (6478). If the study population had more ectopic pregnancies, the NPV would be far lower.

This cohort of women with diagnosed ectopic pregnancy on ultrasound is separate and distinct to women who have a PUL, where no pregnancy is visualized either inside or outside the uterus. During this same study period, a total of 581 women who came to the department had a PUL and 8% of women in this group of PULs had an underlying ectopic pregnancy. These two groups of women are often thought of as being one and the same. The difference between them relies on the use of ultrasound as a primary diagnostic tool in women with symptoms of pain or bleeding in the first trimester, resulting in improvement of diagnostic standards due to its widespread availability within the unit. In the authors' opinion, ectopic pregnancies could therefore be missed and fall into the PUL group in a unit that is not scan based. This then has implications for the interpretation of hormonal data for departments that rely more on biochemistry than ultrasound. In a scan-based unit, the ectopic pregnancies missed are generally small in size, with relatively low serum hCGs reflecting this. In biochemistry-based centres where ultrasound may not be available, larger ectopic pregnancies may be under-diagnosed. It is here where the use of discriminatory zones is more likely to be useful.

Laparoscopy is the gold standard for the diagnosis of ectopic pregnancy (Ankum *et al.*, 1993). Therefore, the non-surgically managed group of ectopic pregnancies were excluded from the final analysis to avoid selection-bias given the improved sensitivity and specificity when this group were included.

The corpus luteum can be a useful guide when looking for an ectopic pregnancy with TVS. It will be on the ipsilateral side in 70–85% of cases (Walters *et al.*, 1987; Jurkovic *et al.*, 1992). In this study, there was no corpus luteum present in

52.2% of cases. However, when a corpus luteum was present, 80.3% were ipsilateral, in keeping with published data.

Ectopic pregnancy associated with haemoperitoneum on TVS suggests the possibility of tubal rupture, and this situation requires surgical intervention. It is very difficult to quantify the volume of haemoperitoneum on ultrasound scan. The presence of blood in Morrison's pouch, which is compatible with significant haemoperitoneum, was not included in this study. The incidence of haemoperitoneum in this study was 31%, in keeping with published data (18–34%) (DiMarchi *et al.*, 1989; Saxon *et al.*, 1997). Blood in the pouch of Douglas on ultrasound does not imply that tubal rupture has occurred. The majority of ectopic pregnancies in this study group had 'leakage' from the lumen of the fimbrial end of the fallopian tube.

Spontaneous heterotopic pregnancy is rare; between 1:10 000 and 1:50 000 (Condous *et al.*, 2003). In women with assisted conceptions, the incidence is as high as 1% (Condous *et al.*, 2003). During the study period, there were three heterotopic pregnancies out of 200 ectopic pregnancies, which is an extremely high rate (1.5%). This can be attributable to the fact that the EPU is a tertiary referral centre, which receives many high-risk for ectopic pregnancy cases.

The diagnosis of ectopic pregnancy should be based on the positive visualization of an adnexal mass using TVS rather than on the basis of a scan that fails to demonstrate an intra-uterine gestational sac. Our study demonstrates that 90.9% of women who present with an ectopic pregnancy at a mean gestational age of 48.3 days should be diagnosed directly by ultrasound. We believe that such high detection rates are achievable with adequate training in early pregnancy scanning and quality control. Furthermore, should surgery be required, over 90% can be treated laparoscopically in a day surgery setting. We would anticipate that in the future, surgery will become less common for small stable ectopic pregnancies and the use of methotrexate or expectant management will increase.

We believe that the indices referred to in this paper could be used as a standard for quality of care in women with early pregnancy problems presenting to a scan-based unit with minimal access surgical facilities. In a recent survey, only 25% of women undergoing surgery in the UK for ectopic pregnancy have this performed laparoscopically and very few have conservative treatment. Ectopic pregnancies are often not seen on ultrasound prior to surgery. We propose that strict quality assurance guidelines should be set for minimum diagnostic and treatment standards for early pregnancy units. These could be based on the number of pregnancies of unknown location and the prevalence of ectopic pregnancy within this group, the number of ectopic pregnancies visualized prior to surgery, and the number of women managed appropriately either conservatively or with surgery.

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