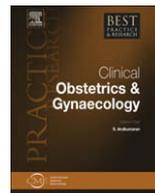




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Diagnosis of ectopic pregnancy with ultrasound

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Transvaginal sonography (TVS) is now the imaging modality of choice for the diagnosis of ectopic pregnancy with overall reported sensitivities of > 90%. Specific sonographic criteria exist for the diagnosis of tubal and non-tubal pregnancies including cervical and caesarean section scar pregnancies. Diagnosis is based on the visualization of an ectopic mass rather than the inability to visualize an intra-uterine pregnancy.

This chapter discusses the specific criteria used for the diagnosis of ectopic pregnancy and examines the literature assessing the accuracy of ultrasound as a diagnostic tool.

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Ectopic pregnancy is a common problem, with over 10,000 diagnosed annually in the United Kingdom.¹ Historically, ectopic pregnancies were diagnosed and managed surgically in symptomatic women, often presenting with the classic triad of symptoms: pain, vaginal bleeding and a history of amenorrhoea. However, now with advances in the use of diagnostic ultrasound and the rapid immunoassay of serum human chorionic gonadotrophin, it is possible to diagnose an ectopic pregnancy at an earlier stage prior to treatment, and even manage them non-surgically using either an expectant or medical approach.²

The introduction of transvaginal sonography (TVS) has revolutionized the diagnosis of many early pregnancy and gynaecological conditions. Studies have shown that it is an acceptable diagnostic procedure for women attending with problems such as pain and bleeding in early pregnancy.^{3,4} TVS has changed the approach to the diagnosis of ectopic pregnancy, from being based on the inability to visualize an intra-uterine pregnancy to one where a positive diagnosis can be made by the visualization of an ectopic mass. It is possible to confirm a diagnosis of an intra-uterine pregnancy earlier and at much lower serum hCG levels with TVS compared with transabdominal sonography (TAS). It is

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reported that using TAS, an intra-uterine sac can be visualized when the serum hCG is > 6500 IU/l.⁵ However, with TVS an intra-uterine sac should be visualized with serum hCG levels as low as 1000 IU/l.⁶ A comparison of TAS and TVS in the diagnosis of ectopic pregnancy has demonstrated sensitivities of up to 77 and 88%, respectively.⁷

Criteria for the TVS diagnosis of ectopic pregnancy

A diagnosis of ectopic pregnancy should be made on the basis of the positive visualization of an extra-uterine pregnancy.⁸ If neither an intra-uterine or extra-uterine pregnancy is visualized on TVS, the woman should be classified as having a “pregnancy of unknown location” and then followed up until the final pregnancy outcome is known. Although the majority of women will be subsequently diagnosed with a failing “pregnancy of unknown location” (PUL) or an intra-uterine pregnancy, data from specialized ultrasound based units show that between 7 and 20% will subsequently be diagnosed with an ectopic pregnancy.^{9–13}

A number of other findings may suggest the presence of an ectopic pregnancy, but are not diagnostic. There may be anechoic or echogenic free fluid within the Pouch of Douglas. Echogenic fluid within the Pouch of Douglas or Morison’s Pouch may suggest haemoperitoneum secondary to a ruptured ectopic pregnancy or a tubal miscarriage, but it may also be seen with the rupture of a haemorrhagic ovarian cyst (Fig. 1). There may also be a collection of fluid within the endometrial cavity often referred to as a “pseudo sac” (Fig. 2). Using TVS it is not difficult to distinguish this from an early intra-uterine gestational sac, which is seen as an eccentrically placed hyper-echoic ring within the endometrial cavity. Table 1 summarizes the specific sonographic criteria used to diagnose the different types of ectopic pregnancy.

Tubal ectopic pregnancy

The majority (~95%) of ectopic pregnancies occur in the Fallopian tube. To make the diagnosis, an ectopic mass should be seen in the adnexa separate to the ovary.⁸ The following may be visualized: (1) an inhomogeneous adnexal mass¹⁴, (2) an empty extra-uterine sac with a hyper-echoic ring¹⁵ or (3) a yolk sac and/or fetal pole with or without cardiac activity in an extra-uterine sac. In a meta-analysis of ten studies, the most appropriate criterion on which to diagnose an ectopic pregnancy was a non-cystic adnexal mass or an inhomogeneous mass with a specificity, positive predictive value, sensitivity and negative predictive value of 98.9, 96.3, 84.4 and 94.8%, respectively.¹⁶ In a recent study looking at the TVS appearance of 388 ectopic pregnancies, 64% had the appearance of an inhomogeneous mass, 22% had an empty gestational sac and 14% had a gestational sac containing a yolk sac or fetal pole.¹⁷



Fig. 1. TVS image of echogenic fluid in the Pouch of Douglas, suggestive of haemoperitoneum following rupture of an ectopic pregnancy.



Fig. 2. TVS image of fluid within the endometrial cavity (“pseudo sac”) as seen in some cases of ectopic pregnancy.

The precise relationship between the appearance of a tubal ectopic pregnancy on TVS, the size of the mass and serum hCG levels is uncertain. In their study on 120 women with ectopic pregnancies, Cacciatore et al. found that serum hCG levels correlated with the size of ectopic gestational sacs but not with the diameter of inhomogeneous adnexal masses.¹⁸ They found that in women with ectopic gestational sacs, the majority of serum hCG levels were high and increasing while in those with an

Table 1
Sonographic criteria used for the diagnosis of ectopic pregnancy.

Type	Image	Criteria	Type	Image	Criteria
	Inhomogeneous mass		Interstitial		An empty endometrial cavity with products of conception located outside of the endometrial echo, surrounded by a continuous rim of myometrium, within the interstitial area.
Tubal	Empty gestational sac	An empty endometrial cavity with: (1) an inhomogeneous adnexal mass or (2) an empty extra-uterine sac or (3) a yolk sac or fetal pole ± cardiac activity in an extra-uterine sac.	Cervical		An empty endometrial cavity, with a gestational sac present below the level of the internal os. An absent “sliding sign” and visible blood flow around the gestation sac using colour Doppler.
	Sac with yolk sac/fetal pole		Caesarean section scar		An empty endometrial cavity and cervical canal with a gestational sac implanted within the lower anterior segment of uterine wall, with evidence of myometrial dehiscence.

inhomogeneous mass the serum hCG levels were significantly lower and most were decreasing. They concluded that visualization of a gestational sac on TVS implies an intact Fallopian tube with a pregnancy that is likely to be growing and visualization of an inhomogeneous mass might well be a collapsed sac, which is less likely to contain active trophoblastic tissue. More recently it has been suggested that visualization of an inhomogeneous mass may represent either an early developing ectopic pregnancy (before a gestational sac is visualized) or a failing ectopic pregnancy.¹⁷ This is because in women initially classified with PULs, with increasing serum hCG levels, who were subsequently diagnosed with ectopic pregnancies, the majority (71%) had the appearance of small inhomogeneous masses.¹⁷

Interstitial ectopic pregnancy

Interstitial or cornual ectopic pregnancies have been reported to account for between 1 and 6% of all ectopic pregnancies.^{19,20} An interstitial pregnancy can be diagnosed if the following criteria are fulfilled: (1) an empty uterine cavity and (2) products of conception located outside of the endometrial cavity and surrounded by a continuous rim of myometrium.²¹

Cervical ectopic pregnancy

Cervical ectopic pregnancies account for less than 1% of all ectopic pregnancies.²² A cervical ectopic pregnancy may be diagnosed using the following criteria: (1) an empty uterus, (2) a barrel-shaped cervix, (3) a gestational sac present below the level of the internal cervical os, (4) the absence of the "sliding sign" (when pressure is applied to the cervix using the probe, in a miscarriage the gestational sac slides against the endocervical canal but does not in an implanted cervical pregnancy) and (5) blood flow around the gestation sac using color Doppler.^{23,24}

Ovarian ectopic pregnancy

Ovarian ectopic pregnancies have an incidence of between 0.5 and 3% of all ectopic pregnancies.²⁵ Surgical criteria for the diagnosis of ovarian ectopic pregnancy have been described: (1) fallopian tubes, including fimbria, must be intact and separate from the ovary, (2) the pregnancy must occupy the normal position of the ovary, (3) the ovary must be attached to the uterus through the utero-ovarian ligament and (4) there must be ovarian tissue attached to the pregnancy specimen.²⁶ However, no specific ultrasound criteria have been described, with ultrasound findings described in individual case reports. A study on six cases of ovarian pregnancies, reported that on ultrasound, these pregnancies appear as on or within the ovary as a cyst with a wide echogenic outside ring.²⁷ The authors reported that a yolk sac or fetal pole was not commonly seen. Care must be taken not to mistake an ovarian ectopic pregnancy with other ovarian pathology.²⁸

Caesarean ectopic pregnancy

Caesarean ectopic pregnancies are thought to comprise 6% of all ectopic pregnancies in women with a previous caesarean section.²⁹ The diagnosis can be made using the following criteria: (1) an empty uterine cavity, (2) a gestational sac located anteriorly at the level of the internal os covering the visible or presumed site of the previous lower uterine segment caesarean section scar, (3) evidence of functional trophoblastic/placental circulation on Doppler examination and (4) an absent "sliding sign".³⁰

Heterotopic pregnancy

A heterotopic pregnancy is diagnosed when you have any of the above types of ectopic pregnancy in conjunction with an intra-uterine pregnancy. Heterotopic pregnancies are more common (1–3%) following in vitro fertilization and fertility treatments involving superovulatory drugs.^{31,32}

Accuracy of TVS in the diagnosis of ectopic pregnancy

The majority of studies on the accuracy of TVS for the diagnosis of ectopic pregnancy relate to the diagnosis of tubal ectopic pregnancies. These studies show TVS to be an accurate diagnostic test for ectopic pregnancy with a high sensitivity (87.0–99.0%) and specificity (94.0–99.9%).^{14,17,33–36} Table 2 summarizes some of the published studies assessing the performance of TVS in the diagnosis of ectopic pregnancy. However, the results should be interpreted with caution as the diagnostic ultrasound examinations were often only performed immediately prior to surgery and were not the only ultrasound examinations performed. Some women will therefore have had initial inconclusive ultrasound examinations and be classified as a PUL before the diagnosis was eventually made on TVS.

To date, only one study has assessed the overall performance of an initial TVS examination in the diagnosis of early pregnancy location within an early pregnancy unit (EPU) setting.³⁶ This was a prospective study on 5318 women attending an EPU over a one-year period. At the initial TVS examination, 91.3% of women had the location of their pregnancy diagnosed – 89.6% intra-uterine pregnancies and 1.7% ectopic pregnancies. The remaining 8.7% were initially classified as PULs. There were three false-positive diagnoses of tubal ectopic pregnancy. The sensitivity of the initial TVS to diagnose ectopic pregnancy was therefore 73.9% with a specificity of 99.9%, a positive predictive value (PPV) of 96.7% and a negative predictive value (NPV) of 99.4%. Twenty-nine out of the 31 ectopic pregnancies in women initially classified with a PUL were subsequently visualized on TVS. This means that the overall sensitivity of TVS to diagnose an ectopic pregnancy was 98.3%, with a specificity of 99.9%, a PPV of 97.5% and a NPV of 100%. This study has shown that a single TVS examination is an effective test for the detection of ectopic pregnancy in women attending an EPU. Not only can nearly 75% of ectopic pregnancies be diagnosed on the basis of a single TVS examination, but also about 90% of women can be reassured that their pregnancy is intra-uterine. This raises the question whether a TVS examination in early pregnancy should be offered as a screening test for ectopic pregnancy. Currently in the UK, it is not routine practice for a woman to have a first trimester ultrasound examination and no study has yet evaluated specifically screening for ectopic pregnancy. However, studies from the Netherlands have shown that the medical and economic benefits of a screening program for asymptomatic women at high risk of ectopic pregnancy is limited.^{37,38} The possible benefits, such as prevention of complications and reassurance, outweigh the possible detriments such as false-positive diagnosis, financial costs and emotional stress.

Why are some ectopic pregnancies not visualized on TVS?

While TVS has a high sensitivity for the detection of ectopic pregnancy, not all of those ectopic pregnancies visualized on TVS are visualized initially and indeed, some are never visualized at all. A quarter of women with ectopic pregnancies are classified as PULs at the time of their first scan.³⁶ There may be a number of reasons why an ectopic pregnancy may not be visualized on TVS. These include poor quality ultrasound equipment or technique, an inexperienced ultrasound operator, increased maternal body mass index or the presence of uterine fibroids or ovarian pathology making visualization of the adnexa difficult. The ectopic pregnancy itself may also have features that made it difficult for visualization at the time of the initial TVS examination. A recent study has compared the TVS findings in women who had their ectopic pregnancies visualized on the initial TVS examination to those initially classified as PULs and visualized on subsequent TVS examinations.¹⁷ Women who were classified as a PUL had a significantly lower mean gestational age and serum hCG level at the time of the initial TVS compared with women who had their ectopic pregnancies visualized on the initial TVS.¹⁷ However, when comparing the serum hCG levels at the time of visualization of the ectopic on TVS there was no significant difference between the two groups. However, women initially classified as PULs had significantly smaller ectopic masses. It would therefore appear that women with ectopic pregnancies who are initially classified as PULs, do not have their ectopic pregnancies visualized on the initial TVS as they are too small and probably too early in the disease process.

Table 2
Summary of studies assessing the performance of TVS in the diagnosis of ectopic pregnancy.

Year	Authors	Total n	Ectopic pregnancy n (%)	Type of study	Population	Type of diagnostic technique	Sensitivity of initial TVS to diagnose EP	Overall sensitivity to detect EP	Overall specificity to detect EP	Comments
1994	Braffman et al.	1427	103 (7%)	Prospective	Women attending the Emergency Department with pain, bleeding or emesis	TAS, TVS and serum hCG levels.	–	99%	84%	<ul style="list-style-type: none"> • 7% (103/1427) had confirmed EP • 45% women had TAS. • 55% women had TAS and TVS. • 93.7% had serum hCG level > 1500 IU/L. • 24%(55/225) had confirmed EP • 84% (46/55) were diagnosed on the initial TVS. • False-positive rate was 1.2%.
1994	Cacciatore et al.	225	55 (24%)	Prospective	Women at increased risk of EP	TVS and serum hCG levels.	84%	84%	98.8%	<ul style="list-style-type: none"> • 45% (380/845) had confirmed EP • PPV 92.5% • NPV 90%.
1998	Shalev et al.	845	380 (45%)	Prospective	Women with presumed EP seen in the Emergency Department	TVS and serum hCG levels.	–	87%	94%	<ul style="list-style-type: none"> • Retrospective review of women with surgically confirmed EP • Prospective observational study • PPV 93.5% • NPV 99.8%
2003*	Atri et al.	143	143 (100%)	Retrospective	Women with surgically confirmed EP	TVS	–	93.8%	–	<ul style="list-style-type: none"> • 2.3% (119/5240) had confirmed EP
2005	Condous et al.	152	143 (94%)	Prospective	Women undergoing surgery for EP suspected on US	TVS	–	90.9%	99.9%	
2007	Kirk et al.	5240	119 (2.3%)	Prospective	Women attending an EPU	TVS	73.9%	98.3%	99.9%	
2008	Kirk et al.	411	411 (100%)	Prospective	Women attending an EPU	TVS	85.9%	94.4%	–	<ul style="list-style-type: none"> • Study of all women with an ectopic pregnancy undergoing a TVS prior to treatment

EP = ectopic pregnancy; TVS = transvaginal ultrasound scan; TAS = transabdominal ultrasound scan; hCG = human chorionic gonadotrophin; EPU = Early Pregnancy Unit; PPV = Positive predictive value; NPV = Negative predictive value.

Summary

Transvaginal sonography (TVS) is now the imaging modality of choice for the diagnosis of ectopic pregnancy. More than 90% of ectopic pregnancies should be visualized on TVS prior to treatment. The majority of these (~75%) will be visualized on the initial TVS examination. Women with a positive pregnancy test in whom neither an intra-uterine or extra-uterine pregnancy is visualized on the initial TVS should be classified as having a PUL. A proportion of these women will subsequently have an ectopic pregnancy visualized on TVS. These ectopic pregnancies were probably too small and early in the disease process to be visualized on the initial TVS.

Practice points

- Transvaginal sonography (TVS) is the imaging modality of choice for the diagnosis of ectopic pregnancy
- Diagnosis should be based on the positive visualization of an ectopic mass rather than the inability to visualize an intra-uterine pregnancy
- More than 90% of ectopic pregnancies should be visualized on TVS prior to treatment

Research agenda

- Identify features that will enable patients to be selected for medical or expectant management

Conflict of interest

None declared.

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