

Ultrasound Evaluation of First Trimester Pregnancy Complications

PRINCIPAL AUTHORS

Lucie Morin, MD, FRCSC, Montreal QC

Michiel C. Van den Hof, MD, FRCSC, Halifax NS

DIAGNOSTIC IMAGING COMMITTEE MEMBERS

Stephen Bly, PhD, Health Canada Radiation Protection Bureau, Ottawa ON

Duncan Farquharson, MD, FRCSC, Vancouver BC

Ms Barbara Lewthwaite, MN, ARDMS, Winnipeg MB

Robert Gagnon, MD, FRCSC, London ON

Shia Salem, MD, FRCPC, Canadian Association of Radiologists Representative, Toronto ON

Amanda Skoll, MD, FRCSC, Vancouver BC

Abstract

Objectives: First, to review normal embryonic development and the sonographic evidence of early pregnancy failure; second, to review sonographic evidence of ectopic pregnancy.

Outcomes: First, prediction of pregnancy failure; second, sonographic identification of ectopic pregnancy.

Evidence: A MEDLINE search and review of bibliographies in identified articles was conducted.

Values: The evidence was reviewed by the Diagnostic Imaging Committee along with the principal authors. A quality of evidence assessment was undertaken as outlined in the report of the Canadian Task Force on the Periodic Health Examination (Table 1).

Benefits, Harms, and Costs: Women presenting with first trimester bleeding may be incorrectly diagnosed with a missed abortion and (or) may be inappropriately reassured about viability. Transvaginal ultrasound provides improved resolution allowing description of early embryonic development characteristics. Improvement in the identification of the sonographic landmarks of normal embryonic development and awareness of the sonographic risk factors of pregnancy failure may lead to more successful management strategies. Diagnosis of suspected ectopic pregnancy often involves an assessment of both hormonal markers and

Key Words: Ectopic, ultrasound, missed abortion, blighted ovum, threatened abortion

sonographic features. Maternal morbidity and mortality can be reduced with an early diagnosis of ectopic pregnancy.

Recommendations: There is good (class A) evidence that current ultrasound technology can distinguish between normal and abnormal pregnancies in the first trimester. There is good (class A) evidence that transvaginal ultrasound in conjunction with quantitative-HCG can diagnose ectopic pregnancy.

J Obstet Gynaecol Can 2005;27(6):581-585

OBJECTIVES

1. To review normal embryonic development.
2. To identify sonographic features of early pregnancy failure.
3. To identify sonographic features of ectopic pregnancy.

THE EMBRYONIC PERIOD

The embryonic period lasts for 8 weeks after conception or 10 weeks after the last menstrual period, although, clinically, gestational age is assigned according to menstrual dating. This is the period of organogenesis and the time when most malformations arise.

The first sonographic evidence of pregnancy is the gestational sac within the thickened deciduas.¹ This sac, which represents the chorionic cavity, is a small anechoic fluid collection surrounded by an echogenic ring that represents trophoblasts and decidual reaction.² With transvaginal ultrasound, it is possible to identify the sac by 4 weeks and 3 days gestation when the mean diameter is 2 to 3 mm.^{1,3}

The yolk sac is the first structure seen within the gestational sac² and, when seen, confirms an intrauterine pregnancy. The yolk sac is seen by transvaginal ultrasound when the mean gestational sac diameter is 5 to 6 mm and should always be visualized when the mean gestational sac diameter is greater than or equal to 8 mm.³

The amnion is a thin, rounded membrane surrounding the embryo and is completely enveloped by the thick echogenic

These guidelines reflect emerging clinical and scientific advances as of the date issued and are subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these opinions. They should be well documented if modified at the local level. None of these contents may be reproduced in any form without prior written permission of the SOGC.

Table 1. Criteria for quality of evidence assessment and classification of recommendations

Level of evidence*	Classification of recommendations†
I: Evidence obtained from at least one properly designed randomized controlled trial.	A. There is good evidence to support the recommendation for use of a diagnostic test, treatment, or intervention.
II-1: Evidence from well-designed controlled trials without randomization.	B. There is fair evidence to support the recommendation for use of a diagnostic test, treatment, or intervention.
II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group.	C. There is insufficient evidence to support the recommendation for use of a diagnostic test, treatment, or intervention.
II-3: Evidence from comparisons between times or places with or without the intervention. Dramatic results from uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category.	D. There is fair evidence not to support the recommendation for a diagnostic test, treatment, or intervention. E. There is good evidence not to support the recommendation for use of a diagnostic test, treatment, or intervention.
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.	

*The quality of evidence reported in these guidelines has been adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on the Periodic Health Exam.³⁷

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on the Periodic Health Exam.³⁷

Table 2. Chronological landmarks in the development of the embryo, as seen on transvaginal ultrasound examination

5 + 0 weeks	Empty gestational sac (mean diameter 10 mm)
5 + 4 weeks	Gestational sac with yolk sac visible
6 + 0 weeks	Gestational sac (mean diameter 16 mm) and yolk sac with adjacent heart beat but small embryo (3mm)
8 + 0 weeks	Embryo with crown/rump length of 16 mm with separate amniotic sac and celomic cavity with yolk sac. Fetal body movements visible, heart rate 175 bpm.

chorion. The yolk sac is situated between the amnion and the chorion. The amnion is thin and difficult to visualize and best seen when perpendicular to the ultrasound beam. The amnion grows rapidly during pregnancy and fuses with the chorion between 12 and 16 weeks of gestation.^{1,3}

The embryo can be identified by transvaginal ultrasound when as small as 1 to 2 mm in length. At 5 to 7 weeks, both the embryo and gestational sac should grow 1 mm daily.¹ Cardiac activity immediately adjacent to the yolk sac indicates a live embryo but may not be seen until the embryo measures 5 mm.^{3,4} From 5.5 to 6.5 weeks, an embryonic heart rate of less than 100 beats per minute is normal. During the following 3 weeks, there is a rapid increase up to 180 beats per minute.^{5,6}

Table 2 summarizes the features of normal early pregnancy.

EARLY PREGNANCY FAILURE

Early pregnancy failure may present with vaginal bleeding and (or) abdominal pain. Differential diagnoses include threatened, inevitable, and missed abortion. The latter can

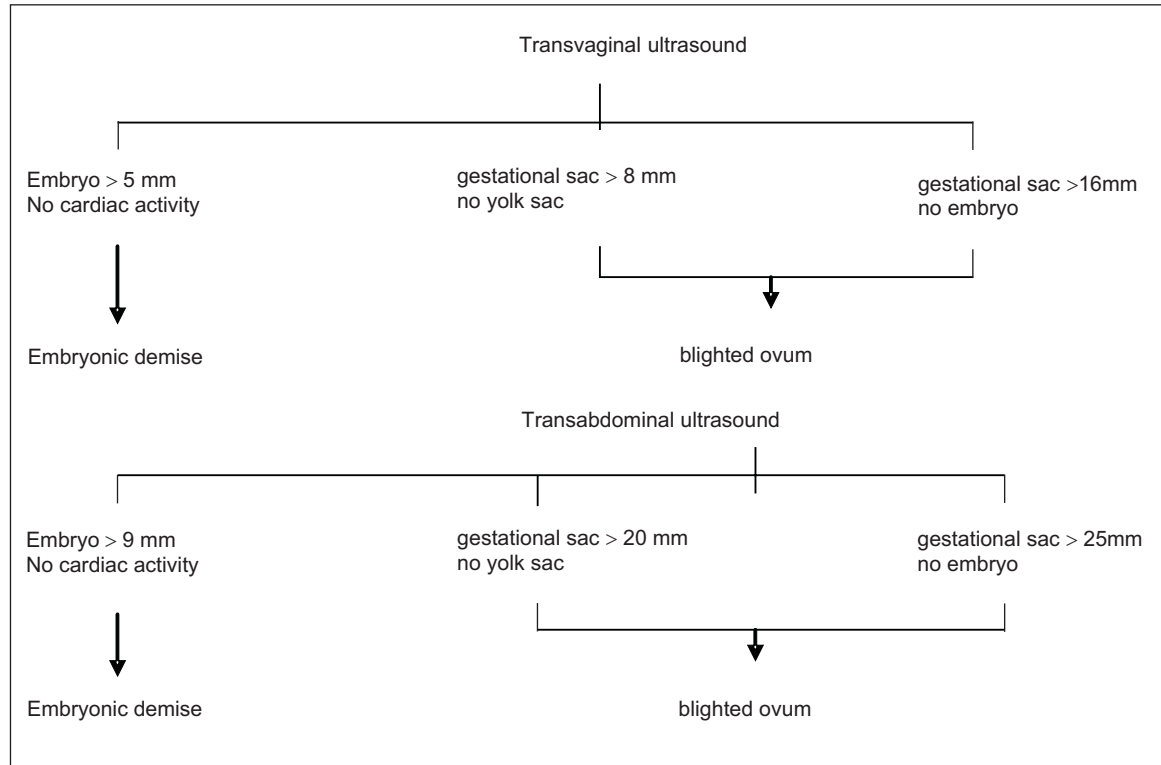
be further subdivided into anembryonic pregnancy (blighted ovum) or embryonic demise. Other differential diagnoses include ectopic and molar pregnancy.

Sonographic diagnosis of embryonic demise can be made when there is no cardiac activity in an embryo greater than 5 mm by transvaginal ultrasound or 9 mm by abdominal ultrasound.⁷

Transvaginal sonographic diagnosis of a blighted ovum is certain when the mean gestational sac diameter exceeds 8 mm without a yolk sac or when the mean gestational sac diameter exceeds 16 mm without an embryo. Transabdominally, a gestational sac greater than 20 mm without a yolk sac or 25 mm without an embryo is diagnostic of a blighted ovum.⁸

Given the possibility of measurement error, it is prudent to allow an additional 1 to 2 mm in gestational sac measurement before considering intervention.⁹ If the gestational sac is smaller than expected, the possibility of incorrect dates should always be considered, especially when there is no pain or bleeding. Under these circumstances, a repeat

Figure 1. Clinical suspicion of early pregnancy failure



transvaginal scan should be arranged after a 1-week interval.¹⁰

Figure 1 depicts the sonographic landmarks of early pregnancy failure.

SONOGRAPHIC FEATURES OF EARLY PREGNANCY FAILURE

Certain sonographic features predict early pregnancy failure including bradycardia (heart rate less than 85 beats per minute) at greater than 7 weeks of gestation,^{6,11-13} a small sac size relative to the embryo (difference of less than 5 mm between gestational sac and crown/rump length),¹⁴ enlarged (≥ 5 to 6 mm) 15 or abnormally shaped (crenelated) yolk sac,¹⁶ and subchorionic hematoma.¹⁷

Spontaneous loss rate in the presence of a subchorionic hematoma is approximately 9%.¹⁸ This risk is increased in women older than 35 and in pregnancy less than 8 weeks.¹⁹

CAUSES OF EARLY PREGNANCY FAILURE

Up to 70% of spontaneous abortions exhibit an abnormal karyotype.^{20,21} Two-thirds will be autosomal trisomies, while the remainder involves monosomy X, structural rearrangements, and other aneuploidies. Only a small percent of early losses related to aneuploidy are due to parental balanced translocations or inversions. Therefore, most women with failed pregnancies and abnormal karyotypes will not have repetitive pregnancy failure.²²

In the absence of a karyotypic abnormality, pregnancy failure can be associated with luteal phase defects, immunological factors, infection, alcohol, smoking, or lethal genetic abnormalities.

ECTOPIC PREGNANCY

The initial diagnostic test in women with suspected ectopic pregnancy is measurement of the serum beta human chorionic gonadotropin (beta-hCG). A negative beta-hCG rules out pregnancy, including ectopic.

Ultrasound that demonstrates an intrauterine pregnancy is reassuring because heterotopic pregnancy occurs in only 1:7000 to 1:30 000 of spontaneously conceived pregnancies.²³ The suspicion of a heterotopic pregnancy should be higher after assisted reproduction techniques because the incidence in this circumstance is up to 1%.^{24,25} The diagnosis of an intrauterine pregnancy involves visualizing a gestational sac within the endometrial cavity showing an embryo or yolk sac or demonstrating a double echogenic ring.²⁶ An intrauterine fluid collection without these characteristics may be a pseudogestational sac. If an intrauterine pregnancy is not demonstrated, the differential diagnosis includes inaccurate dates, complete abortion, and ectopic pregnancy. The sonographic appearance of an ectopic is varied. There may be a simple adnexal cyst, complex adnexal mass, tubal ring, free fluid in the adnexa-cul de sac, a live extrauterine fetus, or an empty uterus with no other sonographic findings.^{27,28}

Table 3. Diagnosis of asymptomatic tubal ectopic pregnancy

Possible ectopic pregnancy	Serum β -hCG level > 1500 mIU/ml Absence of intrauterine pregnancy on transvaginal ultrasound
Probable ectopic pregnancy	Serum β -hCG level > 1500 mIU/ml Absence of intrauterine pregnancy on transvaginal ultrasound Adnexal mass on transvaginal ultrasound
Diagnosis of ectopic pregnancy	Gestational sac inside fallopian tube on transvaginal ultrasound

With the clinical suspicion of ectopic, a normal scan or the presence of a simple cyst carries a low probability of ectopic (5%), while the probability is above 90% with a complex adnexal mass or a tubal ring. A live extrauterine embryo is diagnostic of an ectopic. Isolated free fluid in the pelvis is rarely the only sonographic finding.²⁸

Doppler waveforms from the peritrophoblast have been shown to demonstrate low impedance flow, while colour Doppler may demonstrate an ectopic as a sonographic ring. Doppler does not add clinically useful information when the sonographic features indicate a high or low likelihood of ectopic but may provide important information when other sonographic findings lead to a diagnostic dilemma. For example, with a complex adnexal mass, the finding of low impedance Doppler waveform or a ring on colour Doppler may more strongly suggest an ectopic pregnancy.²⁹

High-resolution ultrasound and the quantitative level of serum beta-hCG are complementary. Most ectopic pregnancies are associated with a disproportionately high level of beta-hCG relative to the size of any intrauterine fluid collection. Failure to detect an intrauterine gestational sac when the beta-hCG values exceed a discriminatory level indicates a high risk of ectopic pregnancy. Most ultrasound laboratories use beta-hCG levels between 1000 to 2000 mIU/ml as the threshold above which an intrauterine gestational sac should be visualized by vaginal ultrasound.^{30–32} With some ectopics, the hCG will show an abnormally low rise, and in this circumstance, a search for ultrasound features associated with ectopic pregnancies should be made.^{33–35}

Table 3, adapted from Yao et al.,³⁶ simplifies the diagnosis of ectopic pregnancy.

Recommendations

1. Sonographic diagnosis of embryonic demise can be made when there is no cardiac activity in an embryo greater than 5 mm by transvaginal ultrasound or 9 mm by abdominal ultrasound.⁷

Transvaginal sonographic diagnosis of a blighted ovum is certain when the mean gestational sac diameter exceeds 8 mm without a yolk sac or when the mean gestational sac diameter exceeds 16 mm without an embryo.

Transabdominally, a gestational sac greater than 20 mm without a yolk sac or 25 mm without an embryo is diagnostic of a blighted ovum⁸ (II-2 A).

2. Given the possibility of measurement error, it is prudent to allow an additional 1 to 2 mm in gestational sac measurement before intervention.⁹ If the gestational sac is smaller than expected, the possibility of incorrect dates should always be considered, especially when there is no pain or bleeding. Under these circumstances, a repeat transvaginal scan should be arranged after an interval of at least one week¹⁰ (II-2 A).

3. Failure to detect an intrauterine gestational sac by transvaginal ultrasound when the beta-hCG value exceeds a discriminatory level (1000 to 2000 mIU/ml) indicates an increased risk for ectopic pregnancy. With a complex adnexal mass or a tubal ring, the probability of ectopic pregnancy is high, while a live extrauterine embryo is diagnostic of an ectopic (II-2 A).

REFERENCES

- Goldstein S. Early detection of pathologic pregnancy by transvaginal sonography. *J Clin Ultrasound* 1990;18:262–73.
- Sauerbrei E, Cooperberg PL, Poland JB. Ultrasound demonstration of the normal fetal yolk sac. *J Clin Ultrasound* 1980;8:217.
- Timor-Tritsch IE, Farine D, Rosen MG. A close look at early embryonic development with the high-frequency transvaginal transducer. *Am J Obstet Gynecol* 1988;159:166–81.
- Levi CS, Lyons EA, Zheng XH, Lindsay DJ, Holt SC. Endovaginal US: demonstration of cardiac activity in embryos of less than 5.0 mm in crown-rump length. *Radiology* 1990;176:71–4.
- Merchiers EH, Dhont M, De Sutter PA, Beghin CJ, Vandekerckhove DA. Predictive value of early embryonic cardiac activity for pregnancy outcome. *Am J Obstet Gynecol* 1991;165:11–4.
- Achiron R, Tadmor O, Mashiach S. Heart rate as a predictor of first trimester spontaneous abortion after ultrasound-proven viability. *Obstet Gynecol* 1991;78:330–4.
- Brown DL, Emerson DS, Felker RE, Cartier MS, Smith WC. Diagnosis of early embryonic demise by endovaginal sonography. *J Ultrasound Med* 1990;9:631–6.
- Levi CS, Lyons EA, Lindsay DJ. Early diagnosis of nonviable pregnancy with endovaginal US. *Radiology* 1988;167:383–5.
- Rowling SE, Coleman BG, Langer JE, Arger PH, Nisenbaum HL, Horii SC. First-trimester US parameters of failed pregnancy. *Radiology* 1997;203:211–7.

10. Hately W, Case J, Campbell S. Establishing the death of an embryo by ultrasound: report of a public inquiry with recommendations. *Ultrasound Obstet Gynecol* 1995;5:353-7.
11. Laboda LA, Estroff JA, Benacerraf BR. First trimester bradycardia a sign of impending fetal loss. *J Ultrasound Med* 1989;8:561-3.
12. Howe RS, Isaacson KJ, Albert JL, Coutifaris CB. Embryonic heart rate in human pregnancy. *J Ultrasound Med* 1991;19:367-71.
13. Falco P, Milano V, Pilu C, Grisolia DG, Rizzo N, Bovicelli L. Sonography of pregnancies with first-trimester bleeding and a viable embryo: a study of prognostic indicators by logistic regression analysis. *Ultrasound Obstet Gynecol* 1996;7:165-9.
14. Bromley B, Harlow BL, Laboda LA, Benacerraf BR. Small sac size in the first trimester: a predictor of poor fetal outcome. *Radiology* 1991;178:375-7.
15. Hurwitz SR. Yolk sac sign: sonographic appearance of the fetal yolk sac in missed abortion. *J Ultrasound Med* 1986;5:435-8.
16. Ferrazzi E, Brambati B, Lanzani A, Oldrini A, Stripparo L, Gueneri S, Makowski EL. The yolk sac in early pregnancy failure. *Am J Obstet Gynecol* 1988;158:137-42.
17. Mantoni M, Pedersen JF. Intrauterine haematoma an ultrasonic study of threatened abortion. *British J Obstet Gynecol* 1981;88:47-51.
18. Pedersen JF, Mantoni M. Prevalence and significance of subchorionic hemorrhage in threatened abortion: a sonographic study. *AJR* 1990;154:535-7.
19. Bennett GL, Bromley B, Lieberman E, Benacerraf BR. Subchorionic hemorrhage in first-trimester pregnancies: prediction of pregnancy outcome with sonography. *Radiology* 1996;200:803-6.
20. Schmidt-Sarosi C, Schartz LB, Lublin J, Kaplan-Graze D, Sarosi P, Perle MA. Chromosomal analysis of early fetal losses in relation to transvaginal ultrasonographic detection of fetal heart motion after infertility. *Fertil Steril* 1998;69:274-7.
21. Ohno M, Maeda T, Matsunobu A. A cytogenetic study of spontaneous abortions with direct analysis of chorionic villi. *Obstet Gynecol* 1991;77:394-8.
22. Goldstein SR, Kerenyi T, Scher J, Papp C. Correlation between karyotype and ultrasound findings in patients with failed early pregnancy. *Ultrasound Obstet Gynecol* 1996;8:314-7.
23. DeVoe RW, Pratt JH. Simultaneous intra- and extrauterine pregnancy. *Am J Obstet Gynecol* 1948;56:1119.
24. Dimitry ES, Subak-Sharpe R, Mills M, Maragara R, Winston R. Nine cases of heterotopic pregnancies in 4 years of in vitro fertilization. *Fertil Steril* 1990;53:107-10.
25. Gamberdella FR, Marrs RP. Heterotopic pregnancy associated with assisted reproductive technology. *Am J Obstet Gynecol* 1989;160:1520-4.
26. Nyberg DA, Laing FC, Filly RA, Uri-Simmons M, Jeffrey RB. Ultrasonographic differentiation of the gestational sac of early intrauterine pregnancy from the pseudogestational sac of ectopic pregnancy. *Radiology* 1983;146:755-9.
27. Fleischer AC, Pennell RG, McKee MS, Worrell JA, Keefe B, Herbert CM, et al. Ectopic pregnancy: features transvaginal sonography. *Radiology* 1990;174:375-8.
28. De Crespigny LC. Demonstration of ectopic pregnancy by transvaginal ultrasound. *British J Obstet Gynaecol* 1988;95:1253-6.
29. Jurkovic D, Bourne TH, Jauniaux E. Transvaginal colour Doppler study of blood flows in ectopic pregnancies. *Fertil Steril* 1992;57:68-72.
30. Stiller RJ, Haynes de Regt R, Blair E. Transvaginal ultrasonography in patients at risk for ectopic pregnancy. *Am J Obstet Gynecol* 1989;161:930-3.
31. Kadar N, Bohrer M, Kemmann E, Shelden R. The discriminatory human chorionic gonadotropin zone for endovaginal sonography: a prospective, randomized study. *Fertil Steril* 1994;61:1016-20.
32. Romero R, Kadar N, Jeanty P, Copel JA, Chervenak FA, DeCherney A, et al. Diagnosis of ectopic pregnancy: value of the discriminatory human chorionic gonadotropin zone. *Obstet Gynecol* 1985;66:357-60.
33. Counselman FL, Shaar GS, Heller RA, King DK. Quantitative b-hCG less than 1000 mIU/mL in patients with ectopic pregnancy: pelvic ultrasound still useful. *J Emerg Med* 1998;16(5):699-703.
34. Kaplan BC, Dart RG, Moskos M, Kuligowska E, Chun B, Hamid M, et al. Ectopic pregnancy: prospective study with improved diagnostic accuracy. *Annals of Emergency Medicine* 1996;28(1):10-7.
35. Falcone T, Mascha EJ, Goldberg JM, Falconi LL, Mohla G, Attaran M. A study of risk factors for ruptured tubal ectopic pregnancy. *J Women's Health* 1998;7(4):459-63.
36. Yao M, Tulandi T. Practical and current management of tubal and nontubal ectopic pregnancies. *Curr Probl Obstet Gynecol Fertil* 2000;23:95-107.
37. Woolf SH, Battista RN, Angerson GM, Logan AG, Eel W. Canadian Task Force on the Periodic Health Exam. Ottawa: Canadian Communication Group; 1994. p. xxxvii.