

Normal and Abnormal US Findings in Early First-Trimester Pregnancy: Review of the Society of Radiologists in Ultrasound 2012 Consensus Panel Recommendations¹

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Abbreviations: β -hCG = beta subunit of human chorionic gonadotropin, CRL = crown-rump length, IUP = intrauterine pregnancy, MSD = mean sac diameter

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SA-CME LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

- Describe issues related to safe interpretation of US findings in first-trimester pregnancy, including definitely normal findings, definitely abnormal findings, and indeterminate findings that require follow-up.
- List criteria that are diagnostic for pregnancy failure and suspicious for pregnancy failure.
- Identify the correct management strategy for a pregnancy of unknown location with normal or near-normal adnexa.

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Since being introduced more than 30 years ago, endovaginal ultrasonography (US) and quantitative testing of serum levels of the beta subunit of human chorionic gonadotropin have become the standard means of establishing the presence of normal intrauterine pregnancy (IUP), failed IUP, and ectopic pregnancy. Appropriate use of these powerful tools requires clear, standardized interpretations based on conservative criteria to protect both the pregnancy and the mother. Since diagnoses are assigned earlier and available medical treatments for ectopic pregnancy and failed IUP are expanding, emphasis must carefully shift toward watchful waiting when the mother is clinically stable and a definitive location for the pregnancy cannot be established with US. To this end and to prevent inadvertent harm to early normal pregnancies, the Society of Radiologists in Ultrasound convened a consensus panel of radiologists, obstetricians, and emergency medicine physicians in 2012 with the goal of reviewing current literature and clinical practices and formulating modern criteria and terminology for the various first-trimester outcomes.

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Introduction

Pelvic ultrasonography (US) and testing of the beta subunit of human chorionic gonadotropin (β -hCG) serum levels are key to diagnosis of early pregnancy and guide management of its associated complications. US imaging in early pregnancy should be primarily endovaginal, with transabdominal imaging used for adnexal masses high in the pelvis and documentation of the amount of free fluid. These tests allow distinction among the diagnostic possibilities of early pregnancy—intrauterine pregnancy (IUP) versus ectopic pregnancy, viable versus nonviable IUP, IUP of uncertain viability, and pregnancy of unknown location—and have contributed to the marked decline in mortality from ectopic pregnancy since the 1980s (1). However, misuse of these tests and misinterpretation of the findings can lead to unintentional harm to potentially viable pregnancies, such as administration of methotrexate for suspected ectopic pregnancy when, in fact, an early IUP is present but not recognized, resulting in embryonic demise or clinically significant birth defects (2). In several case reports, the teratogenic effects of methotrexate in fetuses have been documented (3–5), but inappropriate use of methotrexate due to misdiagnosis is likely underreported in the

TEACHING POINTS

- On the basis of the much higher prevalence of IUP compared with ectopic pregnancy and the fact that a minority of ectopic pregnancies have small intrauterine fluid collections, a nonspecific fluid collection with a smooth, rounded, or oval contour represents an IUP until proven otherwise.
- Because of interobserver variability in endovaginal US measurements of CRL, a 7-mm CRL is necessary to yield a specificity and positive predictive value of 100%, thereby decreasing the likelihood of a false-positive diagnosis associated with a 5-mm CRL cutoff.
- The same reasoning applies to using (a) an MSD cutoff of 25 mm without an embryo as a criterion for pregnancy failure, rather than the previously recommended MSD of 16 mm, and (b) an MSD range of 16–24 mm without an embryo as an indicator of suspicion of pregnancy failure.
- *Pregnancy of unknown location* is the term given to the transient state of early pregnancy during which no definite IUP is visualized at US and the adnexa are normal—in other words, a “normal” pelvic US finding. At this stage, the three main possibilities include early IUP, occult ectopic pregnancy, and completed spontaneous abortion. Unfortunately, a single β -hCG serum level does not allow reliable differentiation among these possibilities.
- In a patient who is hemodynamically stable and has a pregnancy of unknown location, it is less harmful to wait, monitor the β -hCG levels, and repeat the US examination than to presumptively treat an ectopic pregnancy.

medical literature. Given the large number of first-trimester pregnancies that undergo US surveillance, the danger of misdiagnosis potentially causing harm to viable pregnancies should not be underestimated. In 2012, the Society of Radiologists in Ultrasound convened a multi-specialty panel of radiologists, obstetricians, and emergency medicine physicians and established conservative US criteria for definitive diagnosis of pregnancy failure to minimize the possibility of harming a potentially viable IUP (6).

Appreciating the various consensus panel recommendations and implementing them effectively requires a comprehensive understanding of normal and abnormal US appearances during the early first trimester. In this article, we review the normal development of early IUP between 4 and 8 weeks of gestational age and provide a pictorial review of the Society of Radiologists in Ultrasound 2012 consensus panel terminology, as well as diagnostic criteria for nonviable IUP and IUP of uncertain viability. Because of variability in the quality of US images obtained in early pregnancy, standard deviation of measurements, and variance in human development, the criteria are conservative, and the concept of “watchful waiting” in potentially early ectopic pregnancy is emphasized. In addition, this article illustrates the indicators of poor prognosis and addresses management of a pregnancy of unknown location.



Figure 1. Endovaginal US image demonstrates the intra-decidual sign in a pregnant woman with pelvic pain. A 2-mm round gestational sac (arrow) is embedded within the decidual, adjacent to the collapsed endometrial cavity (arrowhead). The MSD is 2 mm, projecting to a gestational age of 4 weeks 4 days.

The role of follow-up pelvic US and monitoring of β -hCG levels is reviewed.

Normal Development of Early IUP between 4 and 8 Weeks of Gestational Age

Gestational age is calculated from the first day of a woman's last menstrual period; however, it is important to appreciate that conception does not take place until after ovulation, approximately 2 weeks after the last menstrual period. This accounts for the 2-week discrepancy between the clinical and histologic gestational age. A gestational sac can first be visualized at endovaginal US at 4.5–5.0 weeks of gestational age as a 2–3-mm rounded intrauterine fluid collection (7). The mean sac diameter (MSD) growth rate is 1.13 mm per day but is often variable (8). Before visualization of a yolk sac or embryo to confirm the fluid collection as a true gestational sac, two signs may be used. The intradecidual sign (Fig 1), defined as an eccentrically located gestational sac within the echogenic decidual, with a relatively undisturbed collapsed uterine cavity visualized as a thin echogenic line, is highly suggestive of an IUP (9–11). The double sac sign (Fig 2), consisting of two concentric echogenic rings surrounding the fluid collection and separated by a thin crescent of endometrial fluid, is a sign of definitive IUP. The outer echogenic ring represents the decidual parietalis, and the inner ring represents the decidual capsularis and chorion (12). The intradecidual sign is visible before the double sac sign because in the intradecidual sign, the gestational sac is not large enough to deform the contour of the uterine cavity, while in the

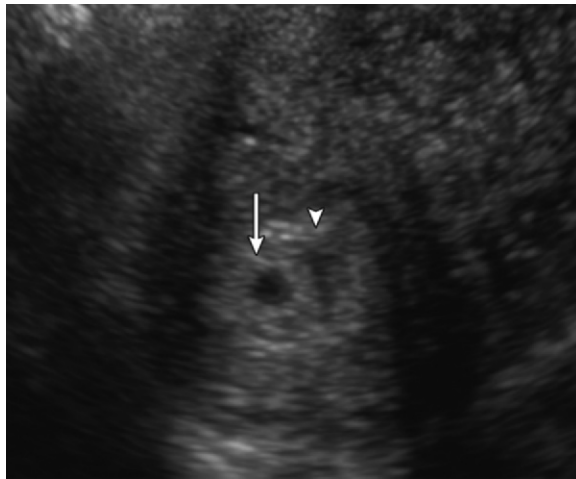
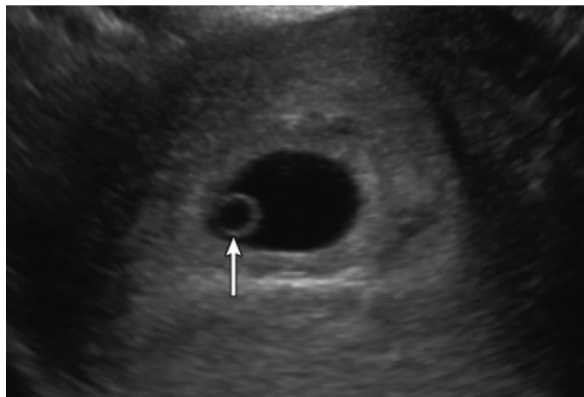
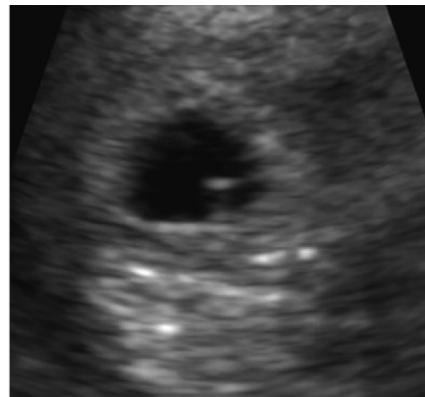


Figure 2. Endovaginal US image shows the double sac sign in a pregnant woman with pelvic cramps. A 4-mm gestational sac is surrounded by two echogenic rings. The inner ring (arrow) represents the decidua capsularis around the chorion, and the outer ring (arrowhead) represents the decidua parietalis. The MSD is 3 mm, projecting to a gestational age of 4 weeks 6 days.



a.



b.

Figure 3. Endovaginal US images show a normal yolk sac at varying stages of early pregnancy. **(a)** The yolk sac (arrow) is an eccentric round echogenic ring within the gestational sac. The MSD is 12 mm, projecting to a gestational age of 5 weeks 6 days. **(b)** The yolk sac is seen as two parallel lines—representing the leading edge and posterior wall—within a small gestational sac. The MSD is 4 mm, projecting to a gestational age of 5 weeks 0 days.

double sac sign, the gestational sac has grown large enough to protrude into the endometrial cavity. The US appearance of early gestational sacs is variable, and while these two signs are highly suggestive of an early IUP, they will be absent in at least 35% of gestational sacs (13). Thus, absence of these signs does not exclude an IUP. A nonspecific, empty, rounded intrauterine fluid collection seen in a pregnant patient has more than a 99.5% probability of representing a gestational sac (14). Therefore, on the basis of the much higher prevalence of IUP compared with ectopic pregnancy and the fact that a minority of ectopic pregnancies have small intrauterine fluid collections, a nonspecific fluid collection with a smooth, rounded, or oval contour represents an IUP until proven otherwise.

The yolk sac is the earliest intragestational sac structure to be visualized at US that can absolutely confirm an IUP. It is the primary maternal-fetal transport system before the establishment of a

fully developed placental circulation (15) and can be visualized at approximately 5.5 weeks of gestational age (1) as a round 3–5-mm structure, usually eccentrically located within the gestational sac (Fig 3a). In gestational sacs at 5.0–5.5 weeks, the yolk sac may sometimes appear as two parallel lines, representing the leading edge and the posterior wall, rather than as a discrete circle (Fig 3b).

The embryo is first visible at approximately 6 weeks of gestational age as a 1–2-mm structure (7,16) at the periphery of the yolk sac. The length of the embryo is measured from the head (crown) to the buttocks (rump), hence the term *crown-rump length* (CRL) (Fig 4), which is the most accurate measurement of gestational age through the first 12 weeks of pregnancy. The embryo should be visualized when the MSD is at least 25 mm (6).

The embryo resides within the amniotic cavity, and the yolk sac resides within the chorionic cavity. The amniotic membrane is thinner than the yolk sac, and although it is seen more easily after

7 weeks (Fig 5), it can be seen as early as 6.5 weeks of gestational age (17). Between 6.5 and 10 weeks of gestation, a linear relationship exists between the diameter of the amniotic cavity and the CRL, with the mean diameter of the amnion 10% larger than that of the CRL (18). In normal gestation, the chorionic cavity, amniotic cavity, and CRL grow proportionally until the onset of fetal urine production at about 10 weeks. The fetal urine disproportionately enlarges the amniotic cavity, which then grows faster than the chorionic cavity, with eventual fusion of the amnion and chorion at 14–16 weeks (19).

Cardiac pulsation in the two paired endocardial heart tubes begins at approximately the 6th week of gestation; thus, it is possible to observe cardiac activity in embryos as small as 1–2 mm. However, absence of cardiac activity in embryos smaller than 4 mm may also be normal (Figs 6, 7) (20). To allow for measurement inaccuracies, differing types of equipment, and other variations in US imaging, the Society of Radiologists in Ultrasound established a measurement of 7 mm and larger as the CRL at which cardiac activity should be present (6). Thus, a definitive diagnosis of failed pregnancy may be assigned only if the embryo is at least 7 mm and lacks cardiac activity. The embryonic heart rate accelerates over the first 6–8 weeks of gestation, with the lower limit of normality near 100 beats per minute at 6.2 weeks of gestation and 120 beats per minute at 6.3–7.0 weeks of gestation (21). Embryonic tachycardia, defined as a heart rate of 135 beats per minute and higher before 6.3 weeks of gestation or 155 beats per minute and higher at 6.3–7.0 weeks of gestation, has been shown to have a good prognosis, with a high probability of a normal outcome (22).

Embryonic morphology is rather featureless until 7–8 weeks, when the spine can be visualized. At approximately 8 weeks of gestation, the head curvature can be separated from the body, and the four limb buds become apparent (23). The rhombencephalon, which is the developing hindbrain, is a prominent landmark at 8–10 weeks of gestation (24), appearing as an anechoic round structure within the head (Fig 5). Intrinsic motion of the embryo may be seen as early as 8.0–8.5 weeks. A timeline of normal early pregnancy development is listed in Table 1.

Abnormal Early IUP

The timing of visualization of early pregnancy landmarks—gestational sac at approximately 5 weeks of gestation, yolk sac at 5.5 weeks, and embryo at 6 weeks, with variation of ± 0.5 weeks (7)—is accurate and consistent. Thus, any deviation from this expected time course may

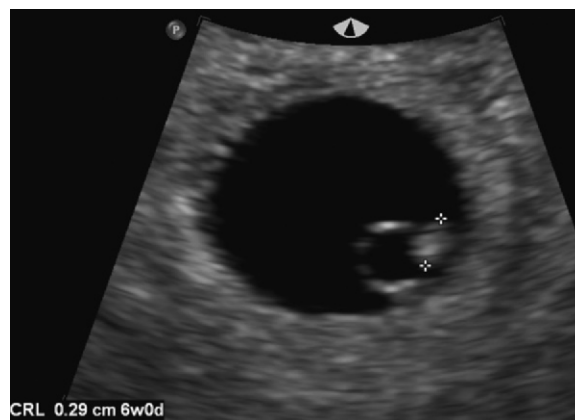


Figure 4. Endovaginal US image in a pregnant woman demonstrates the CRL. The embryo has a CRL of 3 mm (between the caliper marks) and is adjacent to a normal yolk sac. The estimated gestational age is 6 weeks 0 days on the basis of the CRL.

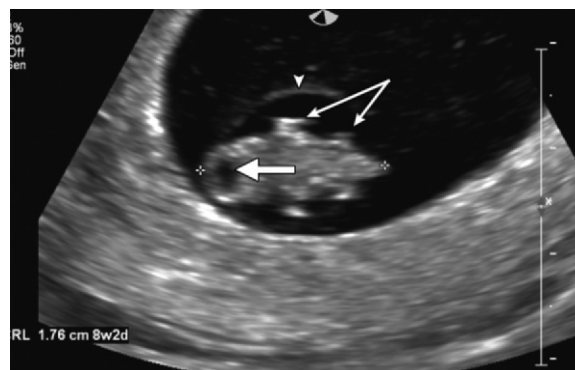


Figure 5. Endovaginal US image in a pregnant patient shows normal amnion and embryo morphology. The embryo (seen between the caliper marks) is within a normal thin-membraned amnion (arrowhead). The embryonic morphology is distinct with the appearance of the rhombencephalon, seen as the anechoic structure within the head (arrow), and the developing limb buds at the periphery of the embryonic trunk (double-headed arrow). The CRL is 17 mm, projecting to a gestational age of 8 weeks 2 days.

be either indicative of or definitive for a failed pregnancy. Discriminatory values for absence of cardiac activity at a certain CRL, absence of an embryo at a certain MSD, and time-based non-visualization of a live embryo were established in the 1980s, when endovaginal US was first deployed. The criteria were based on small cohorts and originated in single-institution academic centers at a time when interobserver variability and standard deviation in measurements were not widely used. More recently, reports of large population-based studies performed by heterogeneous groups of imagers have shown greater variability (25,26). In addition, modern treatment of ectopic pregnancy has shifted to use of nonsurgical therapy. Use of methotrexate instead of surgery does not allow corroboration of the US-based diagnosis and will also potentially harm an IUP. With the goal of absolute certainty

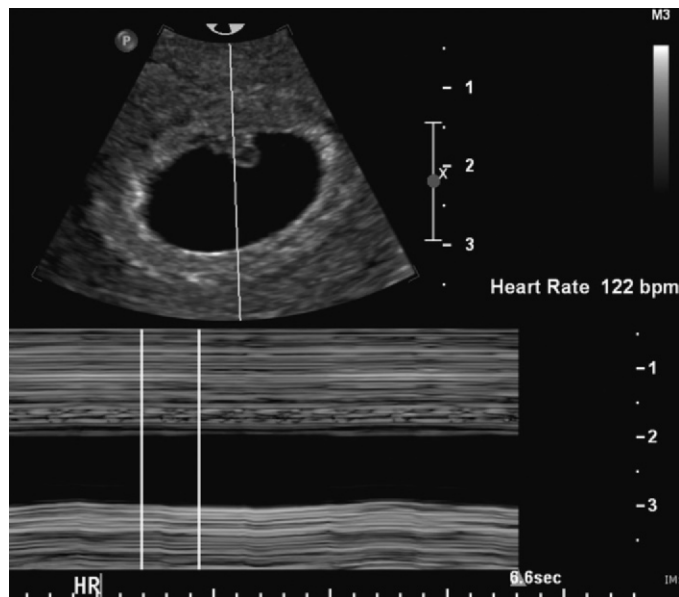
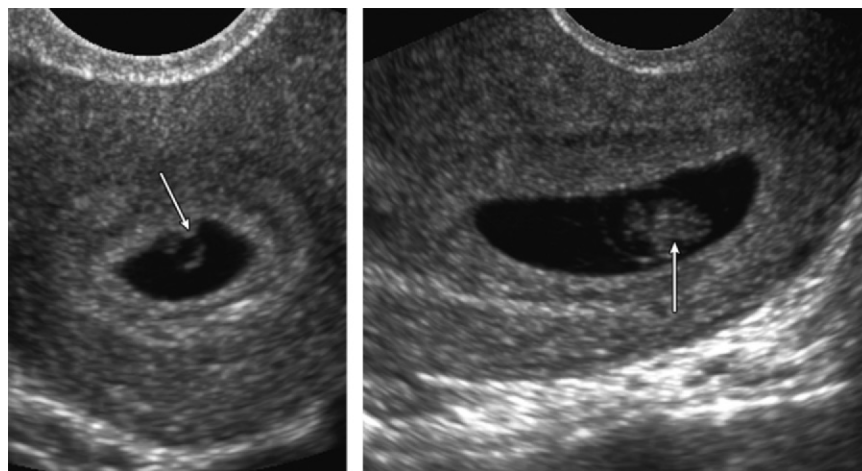


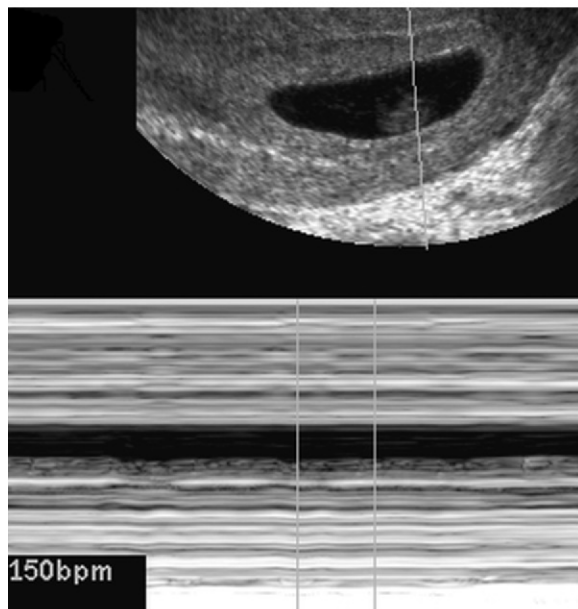
Figure 6. Endovaginal M-mode US image in a pregnant patient demonstrates normal cardiac activity of 122 beats per minute (*bpm*). The CRL is 3 mm, projecting to a gestational age of 6 weeks 3 days.



a.

b.

Figure 7. Endovaginal US images in a pregnant patient with vaginal bleeding and a serum β -hCG level of 5420 mIU/mL (5420 IU/L) show development of cardiac activity. (a) Initial image shows a normal yolk sac and a CRL of 2 mm (arrow), projecting to a gestational age of 5 weeks 6 days. No cardiac activity was detected. (b) Follow-up image obtained 12 days later shows appropriate interval growth of the embryo (arrow). The CRL is 11 mm, projecting to a gestational age of 7 weeks 3 days. (c) M-mode image shows normal cardiac activity of 150 beats per minute (*bpm*).



c.

of pregnancy failure before initiation of irrevocable medical or surgical management, the Society of Radiologists in Ultrasound 2012 consensus panel revisited the traditional discriminatory values to establish more conservative criteria for definitive pregnancy failure (Table 2) and suspicion of pregnancy failure (Table 3) (6).

For many years, an empty gestational sac (without a yolk sac) of 8 mm and larger was considered diagnostic of pregnancy failure, but this criterion is now considered too narrow and has been abandoned (6,25–27).

Previously, a CRL of 5 mm without cardiac activity fulfilled the criterion for pregnancy failure; however, in one series, this resulted in a false-positive rate of 8.3% (25). There have also been reports of embryos with a CRL of 6 mm and no cardiac activity resulting in viable pregnancies (28). Because of interobserver variability in endovaginal US measurements of

Table 1: Timeline of Normal Early Pregnancy Development

Time Period	Developmental Milestone (Threshold)
Week 0	Patient has last menstrual period
Week 2	Conception occurs
Week 4.5–5.0	Gestational sac appears
Week 5.0–5.5	Yolk sac appears
Week 6.0	Embryo appears; cardiac pulsation begins, with a lower limit of 100 beats/min
Week 6.5–7.0	Amniotic membrane appears; cardiac pulsation lower limit is 120 beats/min
Week 7–8	Spine develops
Week 8	Head curvature separates from the body; four limb buds appear
Week 8.0–8.5	Intrinsic motion of the embryo occurs
Weeks 8–10	Rhombencephalon develops

Table 2: US Findings Diagnostic of Pregnancy Failure

Finding	Imaging Appearance
Absent cardiac activity by the time the CRL is a certain size	CRL ≥ 7 mm with no heartbeat
Absent embryo by the time the gestational sac is a certain size	MSD ≥ 25 mm with no embryo
Absent embryo by a certain point in time; requires two US examinations	Absence of embryo with a heartbeat 2 or more weeks after US showed gestational sac without yolk sac Absence of embryo with a heartbeat 11 or more days after US showed gestational sac with yolk sac

Note.—Adapted and reprinted, with permission, from reference 6.

Table 3: US Findings Suspicious for, but Not Diagnostic of, Pregnancy Failure

Finding	Imaging Appearance
Absent cardiac activity by the time the CRL is a certain size	CRL < 7 mm with no heartbeat
Absent embryo by the time the gestational sac is a certain size	MSD of 16–24 mm with no embryo
Absent embryo by a certain point in time	Absence of embryo with a heartbeat 7–13 days after US showed gestational sac without yolk sac Absence of embryo with a heartbeat 7–10 days after US showed gestational sac with yolk sac Absence of embryo 6 or more weeks after last menstrual period
Morphology of gestational sac, amnion, and yolk sac	Empty amnion (amnion seen adjacent to yolk sac, with no visible embryo), enlarged yolk sac (> 7 mm), small gestational sac in relation to size of embryo (< 5 -mm difference between MSD and CRL)

Note.—Adapted and reprinted, with permission, from reference 6.

CRL (29), a 7-mm CRL (Fig 8) is necessary to yield a specificity and positive predictive value of 100%, thereby decreasing the likelihood of a false-positive diagnosis associated with a 5-mm CRL cutoff (6). The same reasoning applies to using (a) an MSD cutoff of 25 mm without an embryo as a criterion for pregnancy failure (Fig

9), rather than the previously recommended MSD of 16 mm (30); and (b) an MSD range of 16–24 mm without an embryo as an indicator of suspicion of pregnancy failure (Fig 10). Using an MSD of 16 mm as a cutoff to diagnose pregnancy failure resulted in a false-positive rate of 4.4% in one series (25). Gestational sacs with

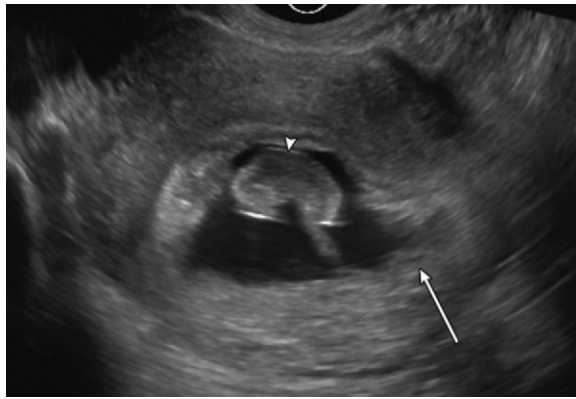


Figure 8. Endovaginal US image shows a nonviable IUP. An amorphous embryo (arrowhead) is seen with a CRL of 20 mm, projecting to a gestational age of 8 weeks 4 days, but there was no cardiac activity. These findings are consistent with a nonviable IUP because the CRL measures at least 7 mm. Note the irregular gestational sac contour (arrow), a sign of poor prognosis.

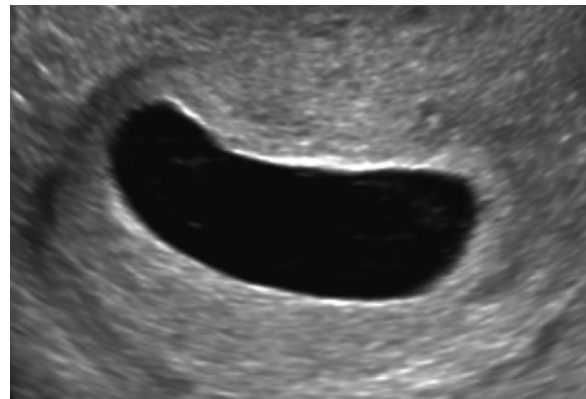
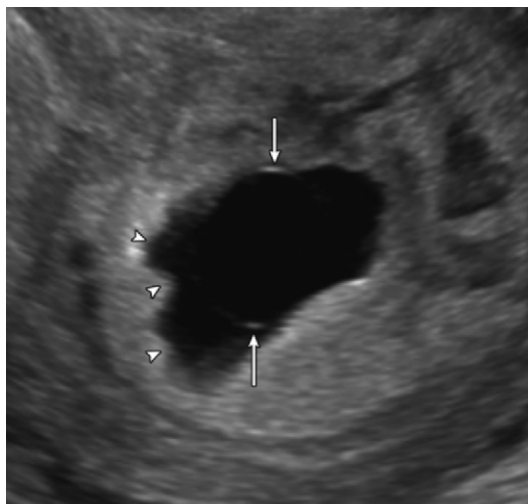
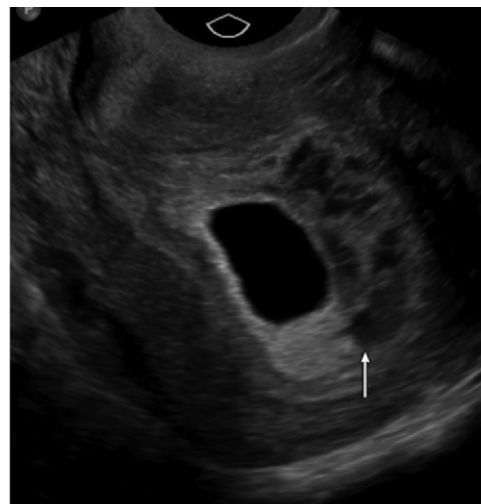


Figure 9. Endovaginal US image demonstrates a nonviable IUP. There is an empty gestational sac with an MSD of 29 mm. Fine linear echogenic debris is noted in the sac, but there is no yolk sac or embryo. The estimated gestational age is 8 weeks 1 day. The findings are in keeping with a nonviable IUP because the MSD measures at least 25 mm.



a.



b.

Figure 10. Endovaginal US images show findings suspicious for but not diagnostic of pregnancy failure at initial US and findings of nonviable IUP at follow-up US. **(a)** Initial findings are suspicious for pregnancy failure but not diagnostic. There is an irregular gestational sac (arrowheads) with an MSD of 17 mm, an enlarged empty amnion (arrows), and no embryo or yolk sac. **(b)** Follow-up image obtained 10 days later shows a nonviable IUP. There is a lack of appropriate interval growth of the gestational sac and no embryo. Note the hydropic changes in the chorionic villi (arrow). The MSD is 19 mm, projecting to a gestational age of 6 weeks 6 days.

mean diameters between 17 and 21 mm and no visible embryo have resulted in viable pregnancies (25,26). Because of interobserver variability in endovaginal US measurements, an MSD cut-off of 25 mm increases the specificity to 100% (29). Not all failed or potentially nonviable intrauterine pregnancies demonstrate a 7-mm CRL without cardiac activity or a 25-mm MSD with no embryo, necessitating additional criteria based on nonvisualization of a live embryo by a certain time interval (Fig 11).

Morphologic assessment of the individual components of a pregnancy—including the gestational sac, the yolk sac, the amnion, the embryo, cardiac activity, and the decidua—is helpful in

evaluating the prognosis of the pregnancy (Table 4). Additional findings that are suspicious for pregnancy failure in the consensus panel criteria include an empty amniotic sac, an enlarged yolk sac, and small gestational sac size relative to embryo size. Given the similar length of the amniotic cavity to the CRL during 6.5–10 weeks of gestation in a normal pregnancy, the presence of an “empty amnion” with no identifiable embryo adjacent to a yolk sac is an indication of poor prognosis (Figs 10a, 12) (31) and should prompt US follow-up. An enlarged yolk sac larger than 7 mm (Fig 13) (15) and small gestational sac size relative to embryo size (defined as less than a 5-mm difference between the MSD and

Table 4: US Indicators of Poor Prognosis in Early Pregnancy

Feature	Imaging Appearance
Gestational sac	Irregular contour, low-lying position
Yolk sac	Calcified, larger than 7 mm
Amnion	Empty, enlarged, or expanded
Embryo	Amorphous shape
Cardiac activity	Bradycardia of 85 beats/min or less
Chorionic villi	Hydropic change
Subchorionic hemorrhage	Large, particularly if it encircles at least two-thirds of the gestational sac circumference

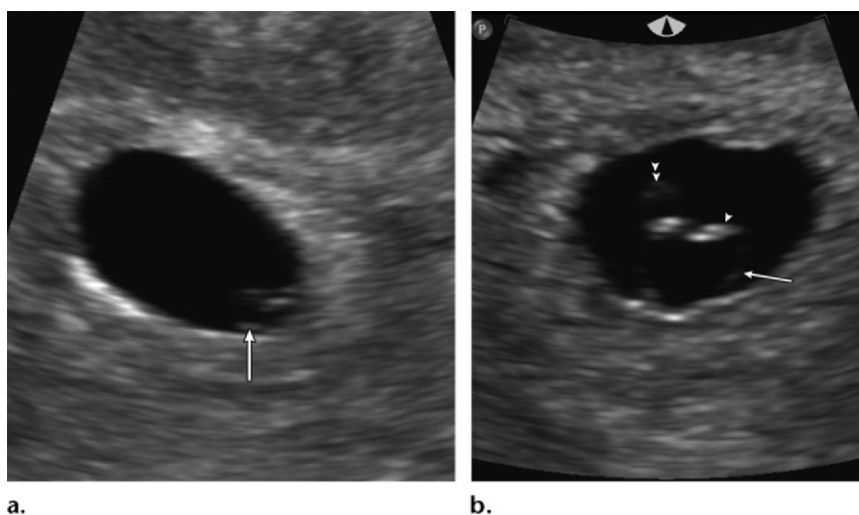
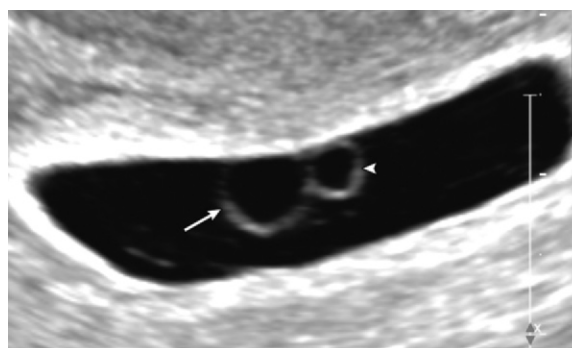


Figure 11. Endovaginal US images show findings of uncertain pregnancy viability at initial US and a nonviable IUP at follow-up US. **(a)** Initial image shows a round gestational sac that contains a yolk sac (arrow) and a possible adjacent embryo. The MSD is 14 mm, projecting to a gestational age of 6 weeks 1 day. **(b)** Follow-up image obtained 13 days later shows lack of appropriate growth of the gestational sac, with an MSD of 16 mm, projecting to a gestational age of 6 weeks 3 days. There is a 4-mm embryo (single arrowhead) within an expanded amnion (arrow). No cardiac activity was detected. A yolk sac is present (double arrowhead). Findings are diagnostic of pregnancy failure.

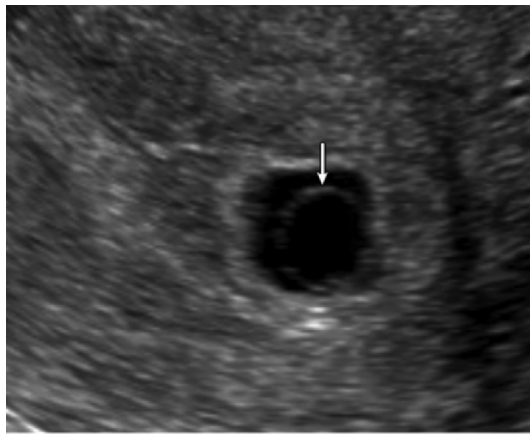
Figure 12. Endovaginal US image demonstrates an “empty amnion,” a sign of poor prognosis. An empty amnion (arrow) is seen adjacent to a normal yolk sac (arrowhead). The MSD is 2.2, projecting to an estimated gestational age of 7 weeks 2 days. An embryo should be present within the amnion in a normal IUP.



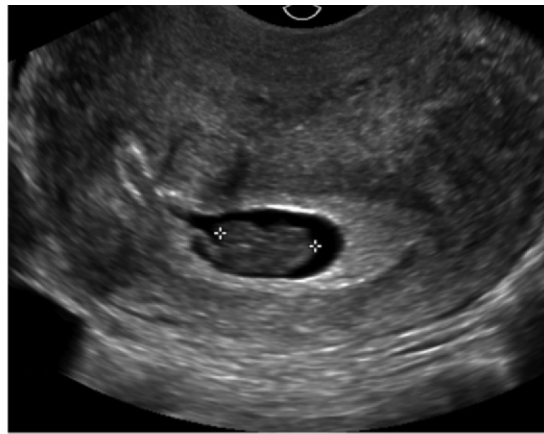
the CRL) (Fig 14) have also been associated with poor pregnancy outcome (32). An irregular gestational sac (lack of a smooth contour and/or presence of a distorted sac shape) is highly suggestive of an abnormal IUP. In one series, this finding had a 100% specificity and a 100% positive predictive value for an abnormal IUP, but it had a low sensitivity of 10% (Fig 10a) (33). The presence of a calcified yolk sac (Fig 15) suggests that the embryonic demise is likely of a relatively

long-standing duration of 2 weeks or longer (34). An enlarged or expanded amnion (amnion too large for the size of the embryo) (17,18) (Figs 15, 16), embryonic bradycardia of 85 beats per minute or less (35), degenerative hydropic changes (Fig 10b) within the chorionic villi, and amorphous shape of the embryo at 7–8 weeks of

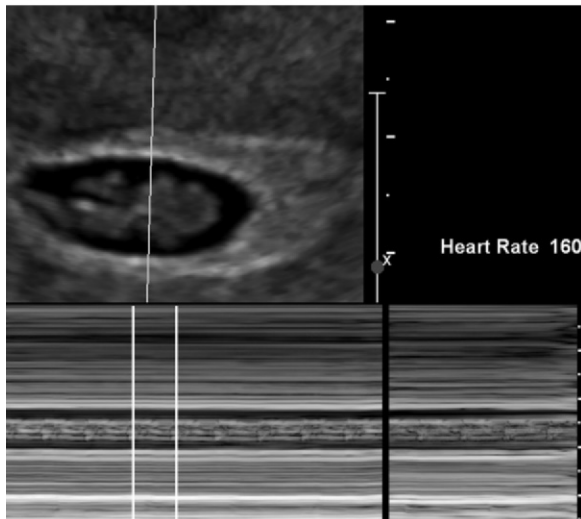
Figures 13, 14. (13) Endovaginal US image shows an enlarged yolk sac, a sign of poor prognosis. An enlarged 7-mm yolk sac (arrow) is seen within an irregular gestational sac with an MSD of 10 mm, projecting to a gestational age of 5 weeks 5 days, and contains no embryo. Findings are suspicious for pregnancy failure but are not diagnostic. (14) Endovaginal US images demonstrate small gestational sac size relative to CRL, a sign of poor prognosis. (14a) Initial image shows a gestational sac with an MSD of 14 mm, projecting to a gestational age of 6 weeks 1 day. The sac contains an embryo with a CRL of 11 mm, projecting to a gestational age of 7 weeks 3 days. The difference between the MSD and CRL is less than 5 mm, a sign of poor prognosis. (14b) M-mode image shows regular cardiac activity of 160 beats per minute. Despite the presence of cardiac activity, the findings are suspicious for pregnancy failure but are not diagnostic. (14c) Follow-up M-mode image obtained 2 days later for vaginal bleeding shows an amorphous embryo (with a CRL of 16 mm) without cardiac activity, in keeping with a nonviable IUP.



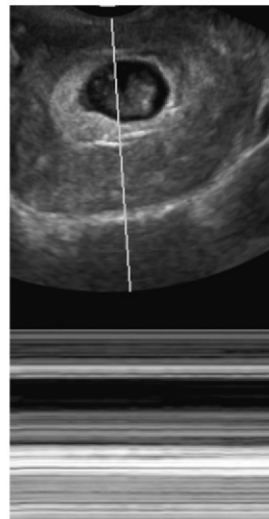
13.



14a.



14b.



14c.

gestation (Fig 8) are also signs of poor prognosis and should prompt US follow-up.

Subchorionic hemorrhage is reported in 18%–22% of first-trimester pregnancies with vaginal bleeding (36,37). The clinical significance depends on the size of the hematoma (Fig 17). The risk of pregnancy loss is doubled in large hematomas, particularly when there is encirclement of more than two-thirds of the chorionic circumference (38). The chorionic bump, thought to represent a small hematoma at the choriodecidual surface that bulges into the gestational sac (Fig 18), is a controversial sign and has been associated with a guarded prognosis (39), but a more recent study demonstrated a more equivocal prognosis (40).

Pregnancy of Unknown Location

Pregnancy of unknown location is the term given to the transient state of early pregnancy during which no definite IUP is visualized at US and the adnexa are normal—in other words, a “normal” pelvic US finding. At this stage, the three main possibilities include early IUP, occult ectopic pregnancy, and completed spontaneous abortion. Unfortunately, a single β -hCG serum level does not allow reliable differentiation among these possibilities (6,41). In the setting of a positive pregnancy test with low β -hCG levels, it may be too early to visualize the site of blastocyst implantation. Despite several studies in which a discriminatory β -hCG level (the value above which

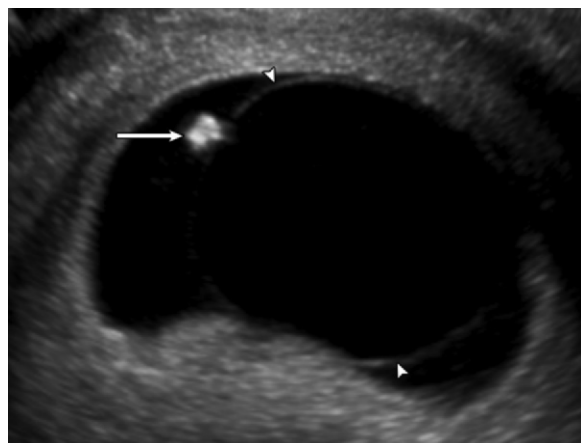


Figure 15. Endovaginal US image shows a calcified yolk sac (arrow), which is a sign of poor prognosis. There is also an enlarged amnion (arrowheads). The CRL (not shown) was 20 mm, projecting to an estimated gestational age of 8 weeks 5 days, and no cardiac activity was seen, findings consistent with a nonviable IUP.

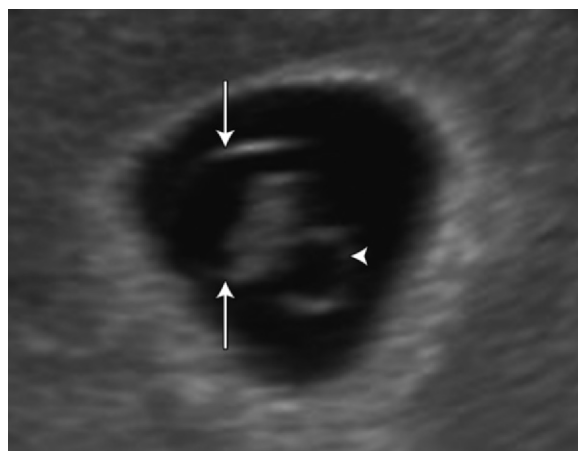


Figure 16. Endovaginal US image shows an expanded amnion (arrows) surrounds a 5-mm embryo that lacked cardiac activity on M-mode images. Note the adjacent yolk sac (arrowhead). The MSD is 14 mm, projecting to a gestational age of 6 weeks 1 day.

an intrauterine gestational sac is consistently seen at US in normal pregnancies) of 1000–2000 mIU/mL (1000–2000 IU/L) was reported, the reliability of the discriminatory level in ruling out a viable pregnancy is less than that reported initially. For example, studies have reported cases of embryos with cardiac activity at follow-up US after initial US showed no gestational sac with a β -hCG level above 2000–3000 mIU/mL (2000–3000 IU/L) (42,43). In addition, a multiple-gestation pregnancy results in higher β -hCG levels at any gestational age compared with those in a singleton pregnancy (7,44). While the probability of an ectopic pregnancy is substantially increased with an empty uterus and higher β -hCG levels, particularly if the level is higher than 3000 mIU/mL (3000 IU/L), there is still a 0.5% likelihood of a viable IUP (6). Thus, in a patient who is hemodynamically stable and has a pregnancy of unknown location, it is less harmful to wait, follow the β -hCG levels, and repeat the US examination than to presumptively treat an ectopic pregnancy. By explaining the limits of our technology, health care providers can help patients appreciate the uncertainty of diagnosis and the need for appropriate follow-up. As so eloquently stated by Doubilet and Benson (14), “First, do no harm.”

Application of Terminology

Accurate interpretation of first-trimester US findings requires application of appropriate and consistent terminology, as set forth by Doubilet et al (6). Figure 19 lists the possible impressions when radiologists dictate the findings of an early-pregnancy US examination. Viable IUP and nonviable IUP findings are straightforward. However, IUP of unknown viability is a broad category and is potentially confusing. To be

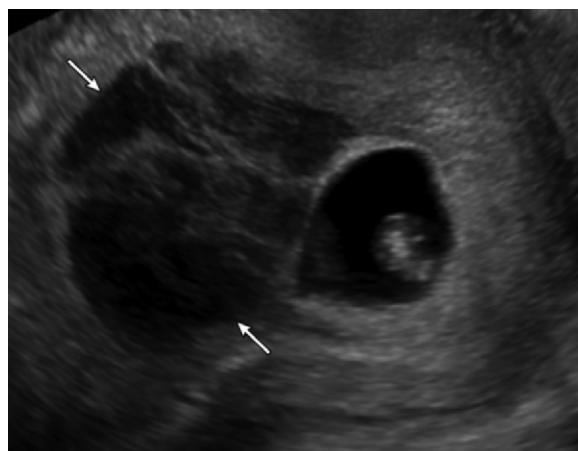


Figure 17. Endovaginal US image shows a large subchorionic hemorrhage. A large hypoechoic collection (arrows) separates the chorion from the echogenic decidua and encircles almost one-half of the circumference of the gestational sac.

precise, IUP of unknown viability can apply to normal situations before development of an embryo that has cardiac activity, including an empty sac, a sac with a yolk sac but no embryo, and a sac with a yolk sac and an embryo smaller than 4 mm but no cardiac activity (20). A second category of unknown viability applies when there are findings suspicious for pregnancy failure (signs of poor prognosis). We have found that using the term *IUP of unknown viability* is more appropriate in this instance because it conveys a sense of caution. Alternatively, for the small gestational sacs, we use the term *early intrauterine gestational sac at ___ gestational age* instead of *IUP of unknown viability* and recommend follow-up US to confirm normal development of the pregnancy.

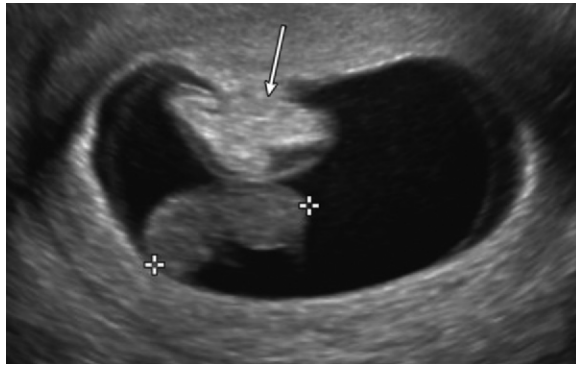


Figure 18. Endovaginal US image shows a chorionic bump. There is a focal echogenic convexity bulging from the echogenic choriodecidual reaction (arrow) into the gestational sac. An amorphous embryo with a CRL of 20 mm, projecting to an estimated gestational age of 8 weeks 4 days, was shown to lack cardiac activity, in keeping with a nonviable IUP.

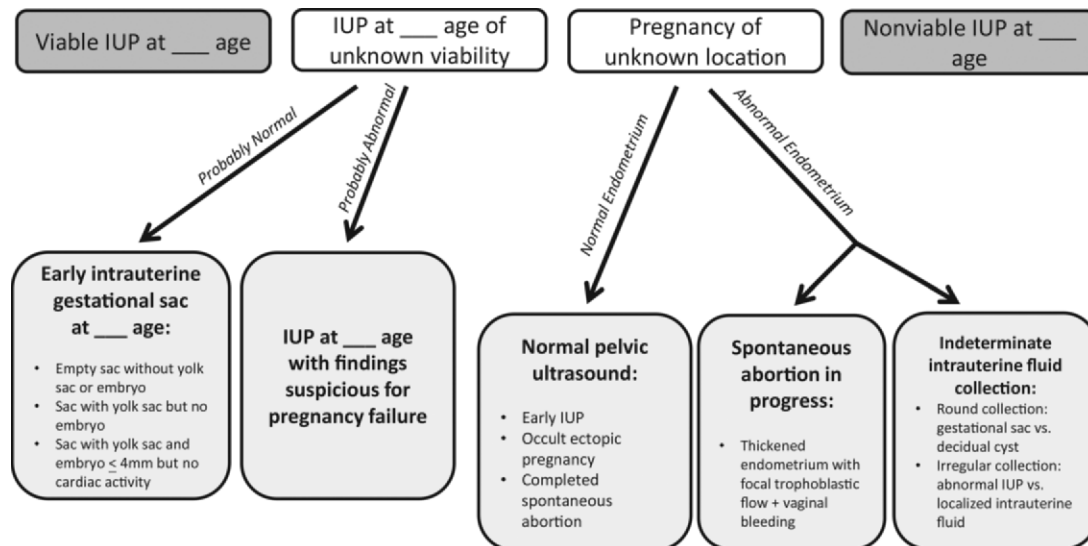


Figure 19. Diagram outlines various early-pregnancy US impressions.

Pregnancy of unknown location has several subsets, and we have encountered these scenarios during application of the terminology to our patient population. With essentially normal pelvic US findings, the differential diagnosis of “very early IUP,” “nonvisualized ectopic pregnancy,” or “completed spontaneous abortion” is provided (Fig 20). When there is vaginal bleeding and a thickened heterogeneous endometrium due to blood products (Fig 21), we have used “pregnancy of unknown location, favoring a spontaneous abortion in progress.” A finding of focal low-resistance arterial trophoblastic flow can be helpful to confirm the intrauterine implantation site in these situations (45). However, spectral Doppler US should not be used in the first trimester if there is a possibility of a normal viable IUP. A third scenario is an indeterminate intrauterine collection. While an intrauterine gestational sac and early IUP may be most likely, the differential diagnosis also includes a decidual cyst (Fig 22) and localized intrauterine fluid (Fig 23) (46). Thus, in these situations, it is recommended that follow-up β -hCG levels be

obtained and that follow-up endovaginal US be performed after 7–10 days.

It is important to note that not all cases fit nicely into the scenarios described previously. For example, in a patient who likely has an intrauterine gestational sac and blood in the pelvis (Fig 24), is the blood due to a leaking hemorrhagic ovarian cyst or a heterotopic pregnancy? If the patient is clinically unstable, she may require surgery to determine the origin of the bleeding. Regardless of the variable imaging features, the principle to remember is that if there is a potential IUP, methotrexate should not be administered to the patient. If the patient is stable, follow-up endovaginal US should be performed, and β -hCG levels should be obtained.

Conclusion

The combination of pelvic US findings and quantitative β -hCG levels provides us with powerful tools in diagnosis of early pregnancy, including normal IUP, nonviable IUP, and ectopic pregnancy. While patients may desire

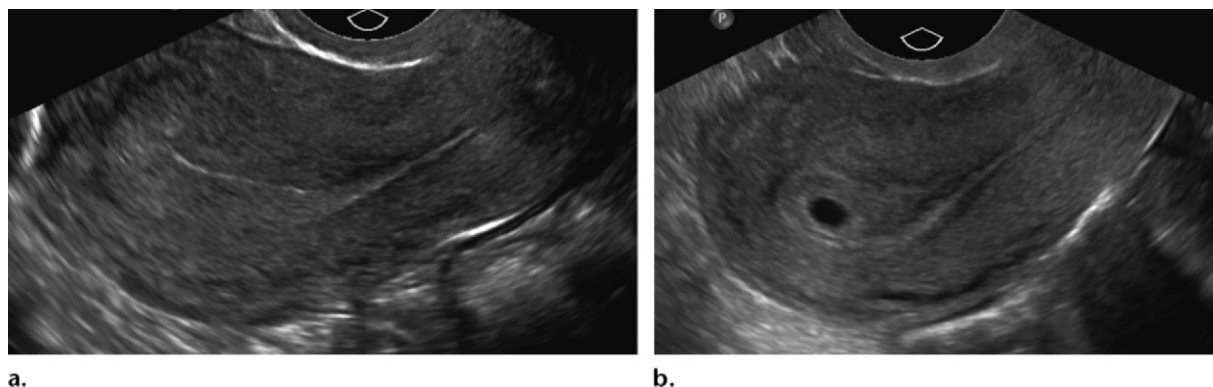


Figure 20. Endovaginal US images in a pregnant woman show a pregnancy of unknown location, with an IUP seen at follow-up US. **(a)** At initial US, the patient had a β -hCG level of 334 mIU/mL (334 IU/L) and demonstrated a normal endometrium, no intrauterine fluid collection, and normal adnexa—essentially “normal” pelvic US findings. The differential diagnosis was early IUP, occult ectopic pregnancy, or completed spontaneous abortion. **(b)** Follow-up image obtained 7 days later shows a rounded intrauterine fluid collection with intradecidual and double sac signs, findings that confirm IUP. The MSD is 6 mm, projecting to a gestational age of 5 weeks 1 day. The β -hCG level increased to 4410 mIU/mL (4410 IU/L).

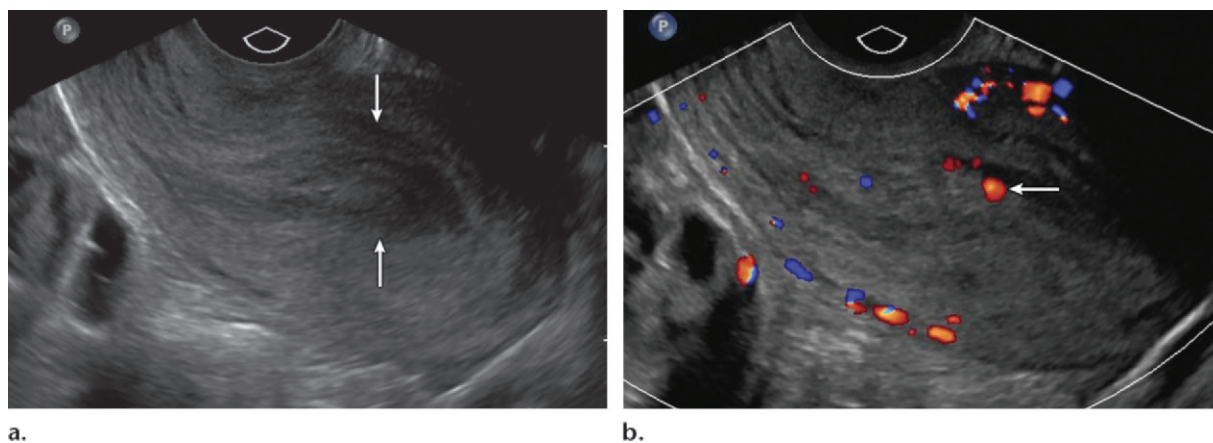
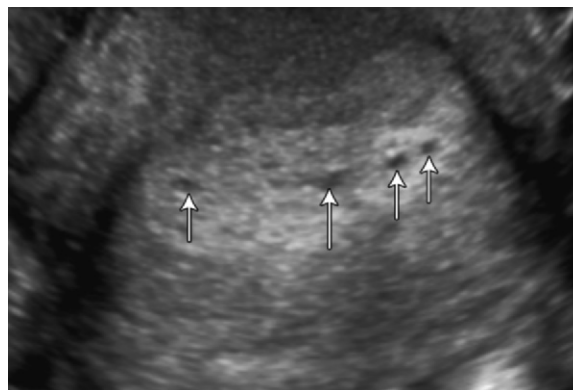


Figure 21. Endovaginal US images in a pregnant woman with vaginal bleeding and a β -hCG level of 24,670 mIU/mL (24,670 IU/L) show a pregnancy of unknown location, with findings favoring abortion in progress. **(a)** Image shows a retroverted uterus with an expanded uterine cavity (arrows) due to heterogeneous echogenic material that represents blood products. No gestational sac is identified. The adnexa are normal, with no blood seen in the pelvis. **(b)** Color Doppler US image shows focal trophoblastic flow at the endometrial-myometrial junction (arrow), a finding that suggests the pregnancy implantation site.

Figure 22. Transverse endovaginal US image in a woman with a β -hCG level of 20 mIU/mL (20 IU/L) shows decidual cysts, which appear as numerous 1–2-mm anechoic cysts (arrows) within the decidual.



definitive results, our goal must be to protect both mother and baby by providing accurate and clear interpretations that lead to intervention only in cases of definitively failed IUP or visualized ectopic pregnancy. It can be much more harmful to intervene in patients with a “pregnancy of unknown location” (because a small percentage of these may be nonvisualized ectopic pregnancies) or in cases of “unknown viability” than to perform follow-up at appropriate intervals by obtaining β -hCG levels and conducting repeat US. The effect of

the increased number of necessary follow-up examinations as a result of these conservative guidelines has been studied, and it is not costly. It has been shown that only 12% of pregnancies

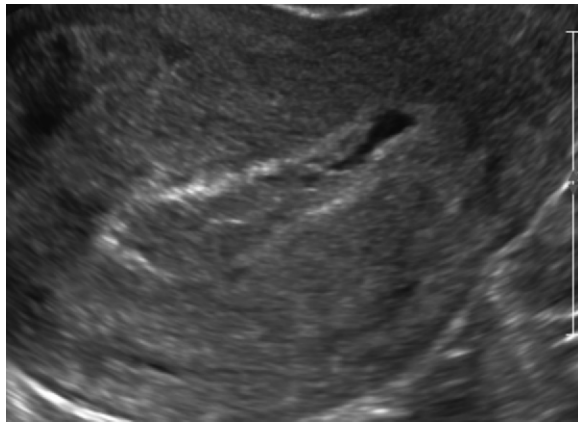
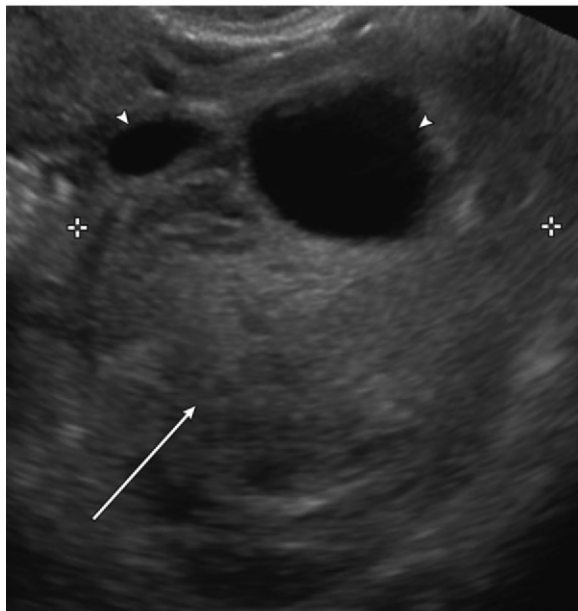


Figure 23. Endovaginal US image in a pregnant patient with right lower quadrant pain demonstrates a pregnancy of unknown location with an indeterminate intrauterine collection. The patient's β -hCG level was 287 mIU/mL (287 IU/L). There is an irregular intrauterine anechoic fluid collection within the lower endometrium, without the intradecidual or double sac signs. The adnexa were normal. The constellation of findings is consistent with pregnancy of unknown location. The patient experienced a spontaneous abortion, and the β -hCG level decreased to 29 mIU/mL (29 IU/L).

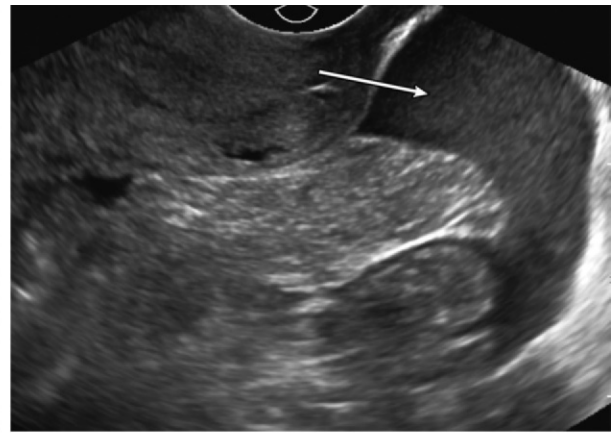


a.



b.

previously categorized as nonviable are placed in the more conservative “suspicious for pregnancy failure” category, necessitating a follow-up examination before treatment (47). Therefore, with safety and cost-effectiveness in mind, discriminatory US landmarks should be set for



c.

Figure 24. Endovaginal US images in a problematic case demonstrate potential IUP and blood in the pelvis in a pregnant woman with acute left pelvic pain and a β -hCG level of 621 mIU/mL (621 IU/L). **(a)** Image shows a round 2-mm sac with an echogenic rim (arrow) within the decidua (intradecidual sign), which is highly likely to be an IUP. The MSD is 2 mm, projecting to a gestational age of 4 weeks 3 days. **(b)** Image shows an enlarged 7 × 5 × 5-cm left ovary (between the caliper marks) that contains an echogenic area (arrow) suspicious for hemorrhage. Note the follicles in the left ovary (arrowheads). **(c)** Image shows a small to moderate amount of complex free fluid (arrow) in the pelvis, a finding that represents blood. The differential diagnosis was early IUP with ruptured left ovarian cyst, heterotopic pregnancy, or ovarian torsion. The patient required surgery because of pain. A normal left fallopian tube was found, as well as a ruptured left hemorrhagic corpus luteal cyst with adjacent blood, which was evacuated in the operating room.

100% specificity at the expense of sensitivity. The Society of Radiologists in Ultrasound 2012 consensus panel of radiologists, obstetricians, and emergency medicine physicians established new terminology and a new set of discriminatory criteria to address these issues. In addition, they recognized a variety of US findings and associated time intervals for which a diagnosis of “suspicion for pregnancy failure” should be used and discussed with the patient. Radiologists should be familiar with the progression of normal and abnormal first-trimester US

findings and develop an understanding of the accepted terminology to use in their interpretations, so that referring physicians will clearly understand our intent and treat their patients safely.

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