Evaluation of Early Pregnancy Failure with Ultrasound

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Abstract: Ultrasound has developed into a powerful tool in the management of early pregnancy failure. However, there is no single finding or measurement that should be used in making a final diagnosis of early pregnancy failure. Instead a combination of clinical, hormonal and ultrasound findings should be used when deciding on the clinical management course.

Key words: Ultrasound, first trimester, pregnancy failure, review.

Learning objectives

- To review the measurements used for dating pregnancies in the first trimester.
- To review the ultrasound criteria used to identify the location of an early pregnancy.
- To review the findings associated with early pregnancy failure.
- To review the importance of a multifactorial approach in the diagnosis of early pregnancy failure and the benefit or serial examinations in the presence of borderline findings.

INTRODUCTION

Who knew that from the technology of World War II would arise obstetric sonography.[1,2] Ultrasound technology has progressed so rapidly in the last 50 years, and now with transvaginal sonography (TVS), it is possible to visualize an embryo when it is in the size of a grain of rice. With the advent of TVS, the first report of an early intrauterine gestation was in Vienna in 1967.[3] This earlier detection has positive implications for earlier detection of pregnancy failure and earlier intervention in ectopic pregnancies. Ultrasound has become the standard by which clinicians diagnose and monitor embryonic age and well-being. This includes ultrasound's utility in evaluation of pregnancy dating, pregnancy failure, ectopic pregnancy, fetal cardiac malformation and chromosomal abnormalities.

DATING

Key to the diagnosis of pregnancy location and early pregnancy failure is the determination of gestational age. Dating by first trimester ultrasound is accurate and also provides useful information in assessing for growth disorders and in planning scheduled delivery times. Multiple measurements have been used including mean gestational sac diameter (MSD), crown-rump length (CRL), and yolk sac diameter. Prior to the identification of a embryo's CRL, it is the MSD that is the most accurate assessment of gestational age.[4] The formula: "menstrual age in days = MSD + 30" can be used to approximate gestational age.[5]

Once an embryo is identified, the most accurate and preferred measurement of pregnancy age is the embryonic size (mm) or CRL at less than 12.5 weeks (Fig. 1).[6-13] The formula, developed by Goldstein in 1994, "Gestational age (days) = early embryonic size (mm) + 42 with a correlation coefficient r = 0.87; 95% confidence limit = +/–3 days," can also be used to approximate gestational age.[10] The CRL can easily be measured transvaginally or transabdominally.

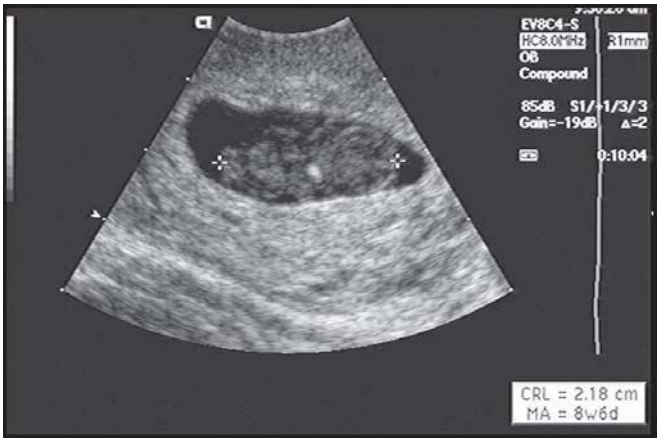

Fig. 1: Crown-rump length (CRL)

LOCATION OF PREGNANCY

Multiple measurements and associated findings have also been used to try and determine whether or not an early pregnancy is intrauterine. These would include: the intradecidual sign, the double decidual reaction, and the yolk sac. Perhaps, the earliest sign to be able to distinguish an intrauterine pregnancy (IUP) is the "intradecidual sign" described by Yeh in 1986.[14] This sign is described as a single rimmed echogenic sac located within a thickened decidua off midline within the uterine cavity. The "intradecidual sign" can be seen by transabdominal sonography (TAS) as early as 3.5 weeks gestation (or 1.5 weeks postconception). Unfortunately, this sign was not reliable when tested with transvaginal sonography and should not be used to differentiate an early IUP from and ectopic pregnancy.[15] When TVS is used to locate a pregnancy, one would expect to be able to see and IUP with a hCG level of 2000 mIU/ml IRP.[16,17] Other authors recommend using a higher hCG discriminatory level such as 3000 to 4500 mIU/ml which will decrease sensitivity but increase specificity so may not be of much clinical utility.[18,19]

The double decidual sign (DDS) was historically one of the first reliable transabdominal and transvaginal sonographic findings used to distinguish an IUP from the pseudosac of an extrauterine or ectopic pregnancy. It was described by Bradley in 1982 as "two concentric echogenic rims" around fluid within the endometrial cavity (Fig. 2). It is send as early as 4.5 weeks gestational age (or 2.5 weeks postconception) by transvaginal sonography.[20] With the advent of transvaginal sonography and thereby earlier detection of the yolk sac, the double decidual sign has become less useful.

The secondary embryonic yolk sac (YS) can be visualized by transvaginal sonography (Fig. 3) at 37 to 40 days and hCG of 2200 mIU/ml, IRP.[16] When a yolk sac is identified, there is 100% positive predictive value of an IUP.[21] However, because a yolk sac may not be present all the time prior to when a normal embryo is identified, YS identification alone is not a reliable single indicator of pregnancy viability.[22,23] The size of a yolk sac has also been associated with pregnancy outcome. There is a 60% positive predictive value of abnormal pregnancy outcome when the YS is greater than 2 standard deviations above the mean sac diameter.[24,25] However, a large YS is, in general, considered a nonspecific finding with early pregnancy failure.[25]

DIAGNOSING PREGNANCY FAILURE

Once a pregnancy is established as intrauterine, the next clinical question to be asked is regarding the pregnancy's viability. Pregnancy failure has been determined with sonography using multiple measurements including the mean gestational sac diameter, embryonic pole, and embryonic heart pulsations. The sonographic diagnostic cut-offs for pregnancy failure vary depending the degree specificity, sensitivity and the different

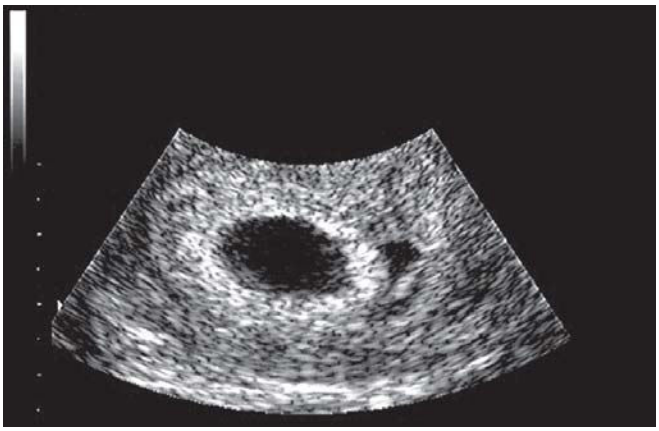

Fig. 2: Double decidual sign (DDS)

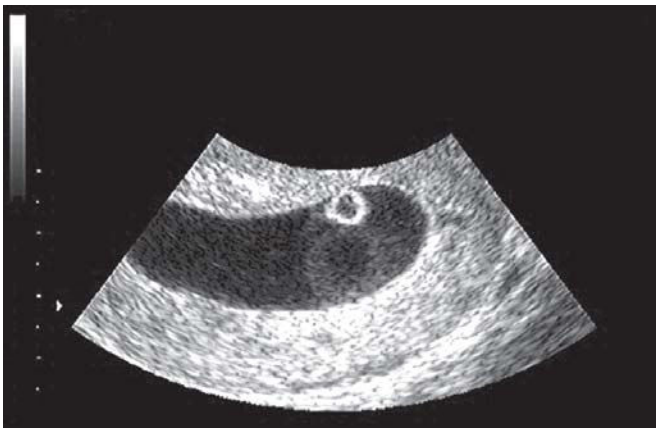

Fig. 3: Yolk sac

author's findings; however, the more common guidelines are summarized in Table 1.[14,16,26-28]

The gestational sac can first be observed by TVS when the sac diameter is 5 mm at approximately 5 weeks gestation (or 3 weeks postconception). Between the fifth and sixth weeks of pregnancy, the MSD increases by approximately l1 mm/day.[29] A small gestational sac as defined in relation to the CRL has been used as a predictor of pregnancy failure.[30-32] In other series, a large gestational sac in the absence of a yolk sac and/or embryo is associated with pregnancy failure. When a yolk sac is not identified by a certain MSD, there is an increase risk of pregnancy failure. Various MSDs have been used to predict pregnancy failure when the yolk sac is absent. It has been suggested that anywhere from 13 to 25 mm for MSD is a good cut-off.[33,34] If you set the cut-off for MSD high enough, however, there is a 100% specificity for abnormal pregnancy outcome. This was demonstrated by Nyberg in 1986. Nyberg proposed using major and minor indicators of pregnancy failure to come up with a 100% positive predictive value. Major criteria were defined as: (i) large size with a MSD > 25 mm without an

Table 1: Guidelines for ultrasound measurements in the first trimester[14,16,26-28]

Documentation of IUP and pregnancy failure	*Detection*		*Discriminatory*	
	Transabdominal	*Transvaginal*	*Transabdominal*	*Transvaginal*
Intradecidual sign	3.5 weeks	Poor indicator		
Double decidual reaction	4-9 weeks	2-9 weeks		MSD 10 mm
Gestational sac		5 mm/4.5 weeks MSD 10 mm		hCG > 2000 mIU/ml, IRP
Yolk sac	MSD 10 mm	37-40 days, MSD 6.7 mm, hCG 2200 mIU/ml, IRP	Poor indicator MSD 20 mm	Poor indicator MSD 13 mm
Embryo			MSD 25 mm	MSD 18-20 mm
Cardiac activity		6 weeks MSD 16 mm fetal pole 3 mm	Fetal pole > 9 mm	Fetal pole > 5 mm

embryo or a MSD > 20 mm without a yolk sac and (ii) distorted gestational sac shape. Minor criteria were defined as: (i) thin decidual reaction (< 2 mm); (ii) week decidual amplitude; (iii) irregular contour; (iv) absent DDS and; (v) low position within the uterus. If one major criteria or three minor criteria were present, there was a 100% predictive value for abnormal pregnancy outcome.[23] With the large degree of variability in MSD cut-offs, MSD is not a good single predictor of pregnancy viability, and instead MSD should usually be used in combination with other findings or in serial ultrasound examinations.[23,35,36]

The documentation of an embryo and its appropriate interval growth with development of a heart pulsation is a positive predictor of pregnancy success. In fact, once an embryonic heart rate is documented by sonography, the miscarriage rate decreases to as low as 10%.[23,37,38] The embryonic heart rate can first be seen by TVS at 36 to 40 days gestation (menstrual age) when the heart tube is just forming (Fig. 4).[39,40] It is expected that an embryonic heart rate may be documented by the time when the CRL is at greater than 4 to 5 mm.[25,41] The embryonic heart rate also has some predictive value in determining pregnancy outcome. The embryonic heart rate at first appearance may be slow but may increase progressively until 9 weeks gestation and then decrease until the end of the first trimester.[42,43] A slow HR between 6 to 8 weeks gestation has been associated with up to a 25% poor pregnancy outcome.[42,44] Although, an embryonic heart rate is not diagnostic of an impending fetal demise, it should warrant a follow-up study.

It is also important to remember that less than expected growth or gestational sac size or low embryonic heart rate may not be associated with pregnancy failure but instead with aneuploidy. Gestational sac morphology, embryonic heart rate and yolk sac morphology all have some value in predicting

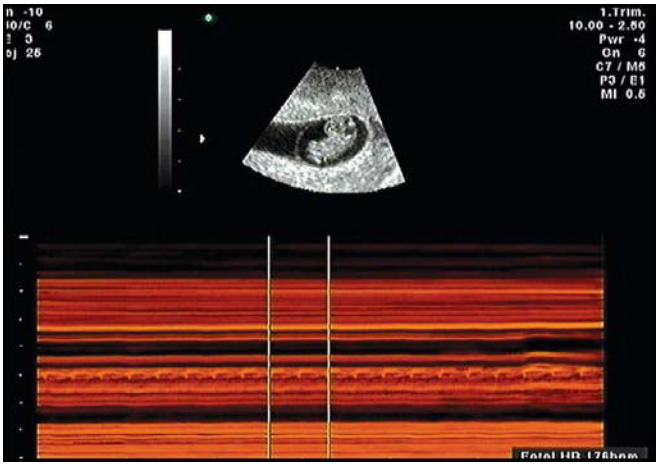

Fig. 4: Embryonic heart rate measured in M-mode

chromosomal abnormalities.[23,45,46] There is, however, contradictory evidence regarding the predictive value of these findings and caution should be used in counseling the patient about genetic testing.[25,47] Given the ability to manage most miscarriages without any medical intervention, it is usually safe for the patient to wait for repeat studies while the certainty of the diagnosis is being made.[48,49]

FIRST TRIMESTER DOPPLER: THE CORPUS LUTEUM AND PREGNANCY FAILURE

More investigational measurements including Doppler and corpus luteum morphology have also been studied as predictors of early pregnancy failure. Doppler has also been used to evaluate the health of the early pregnancy in part by evaluating the early decidual circulation. There is evidence that premature higher resistance maternal circulation within the placenta is

associated with early pregnancy failure. This has been thought to reflect abnormal invasion of the spiral arterioles with decreased cytotrophoblast invasion; and hence, the creation of inadequate low resistance circulation.[50-52] It has been hypothesized that the higher resistance maternal like flow promotes oxidative stress and then further damage to the embryo which may contribute to pregnancy failure.[27] The abnormal placental resistance patterns documented by Doppler and associated with early pregnancy failure are not clinically useful in diagnosing miscarriage. However, the use of Doppler in the late first trimester may become a more useful tool in predicting other developing placental diseases like pre-eclampsia and molar pregnancies.[50,53-60]

Even evaluation of the corpus luteum size and morphology has been investigated to predict early pregnancy failure. Unfortunately, little reliable correlation was found between corpus luteum volume or morphology and hormone (estradiol, progesterone and 17-hydroxyprogesterone) levels.[61]

CONCLUSIONS

Ultrasound is a strong tool on our diagnostic armamentarium, but no single ultrasound measurement can predict pregnancy failure 100% of the time. In conclusion, transvaginal sonography is a powerful tool in diagnosing and treating early pregnancy failure. However, it should not be used in isolation especially if the pregnancy is desired. A combination of clinical judgment, hCG, ultrasound findings and repeat ultrasound and/or hormonal studies should be used in the diagnosis and management of early pregnancy failure.

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