

Re-examining Sonographic Cut-off Values for Diagnosing Early Pregnancy Loss

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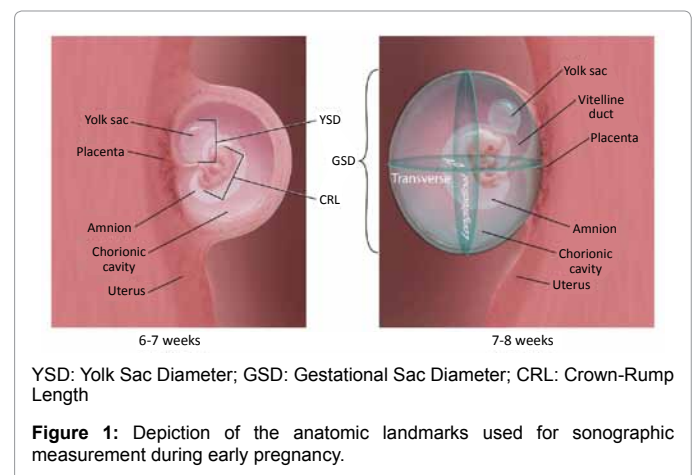
Early pregnancy loss is the most common complication of human pregnancy [1]. Such commonality requires dependable evaluation tools and informed, standardized criteria for accurate diagnosis. A brief perusal of the data on which most of the practitioners who treat women who are newly pregnant have based their recommendations for the sonographic diagnosis of a non-viable pregnancy raises significant concern since most of these data are based on relatively small patient numbers [2-5]. Further, recent studies have shown that the measurements used to determine historically-accepted criteria have fairly wide patient-to-patient, hyphenate intra-observer and inter-observer variability [6]. This makes the inclusion of investigations based upon small patient numbers even more problematic. This unfortunate combination poses an important problem because the diagnosis of failed pregnancy has immense implications to the physical health of the mother and to the emotional well-being of the mother, her partner, her family and her close friends. The criteria for diagnosing a non-viable pregnancy must have a specificity that is as close to 100% as possible. Still, using commonly accepted historical sonographic criteria, authors have shown that between 1 in 100 and 4 in 100 viable pregnancies might be erroneously deemed non-viable [7,8]. If these incorrect diagnoses lead to immediate interventions, some pregnancies will be inadvertently terminated. Such outcomes are unacceptable. There should be near zero tolerance for misdiagnosis. Increased awareness of this too common problem has led to efforts to improve our diagnostic accuracy and has required a stringent re-evaluation of historical diagnostic criteria using investigations that include much larger study populations that have been evaluated using the most sensitive, commonly-available diagnostic modalities. In this case, the most sensitive ultrasonographic technique available for diagnosing an early, non-viable pregnancy is transvaginal sonography.

Since the purpose of this manuscript is to recommend a modern and informed set of ultrasonographic criteria for the diagnosis of a failed pregnancy, it is important to first review the accepted sonographic characteristics of normal pregnancy. While a thickened endometrium may be the only, albeit non-specific, sonographic sign of pregnancy during the first two weeks post-conception, a gestational sac can be first detected by as early as 4 weeks 1 day of gestation using transvaginal sonography [9]; it is typically detectable by 4.5-5 weeks of gestation [10]. The presence of a gestational sac can be easily confused with a non-gestational intrauterine fluid collection (aka pseudogestational sac) and descriptions of an eccentrically-placed intrauterine structure showing a "double decidual sign" have been used to support the presence of a true intrauterine gestation [11]. The visualization of a yolk sac within a gestational sac is the first definitive sonographic sign of an intrauterine pregnancy and is most often detectable using transvaginal sonography when the intrauterine gestational sac has a mean diameter of >8 mm [2]. An embryonic pole might be seen when the gestational sac size is as small as 8 mm [2].

The sonographic measurements most often included among the criteria for diagnosing embryonic viability include the mean gestational sac diameter, the diameter of the yolk sac and the embryonic crown-rump length (Figure 1). While the sensitivity of modern transvaginal sonography is excellent, these measurements are of very small structures. Minute changes in caliper placement when making these measurements

may have substantial effects on dating calculations and viability diagnostics. Herein lays a significant contributor to interobserver and intraobserver variability (Figure 2). It is recommended that the Mean Gestational Sac Diameter (MSD) be measured in the long axis. Averaging of the measurements from three orthogonal planes (Anterior-Posterior (A-P), transverse and longitudinal) gives the MSD, which should be recorded in all studies of pregnancies at less than 10 weeks of gestation and will be used for calculating gestational age in pregnancies less than 7 weeks of gestation. Calipers should be placed at the inner edges of the interface between trophoblast and sac when making these measurements [12]. The yolk sac should be measured in its largest diameter, placing calipers at the center of the typically thickened and highly echogenic yolk sac walls [13]. The crown-rump length measures the longest diameter of an embryo by placing calipers at the most caudad and most cephalad portion of the fetal mass. Prior to about 7 weeks of gestation, measurement is typically of the greatest length that can be visualized, but after 7 weeks, an attempt should be made to measure CRL in a plane that displays the embryo in sagittal section but does not include the yolk sac [14,15].

The recommended revision of the sonographic criteria for diagnosing early pregnancy loss to account for larger available data sets and for patient-to-patient and measurement variations was recently discussed by Bourne and Bottomley [16] in a scholarly review published



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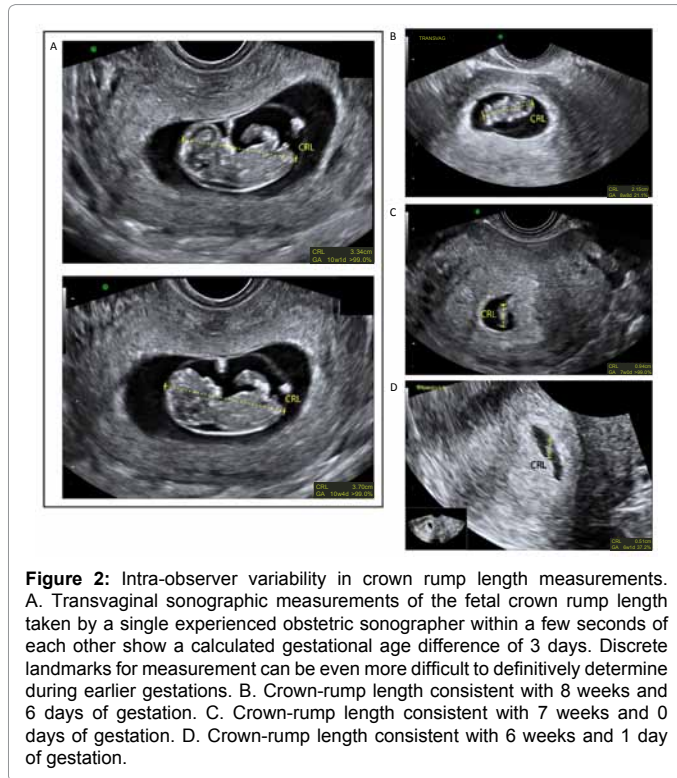


Figure 2: Intra-observer variability in crown rump length measurements. A. Transvaginal sonographic measurements of the fetal crown rump length taken by a single experienced obstetric sonographer within a few seconds of each other show a calculated gestational age difference of 3 days. Discrete landmarks for measurement can be even more difficult to definitively determine during earlier gestations. B. Crown-rump length consistent with 8 weeks and 6 days of gestation. C. Crown-rump length consistent with 7 weeks and 0 days of gestation. D. Crown-rump length consistent with 6 weeks and 1 day of gestation.

in a reproductive subspecialty journal. The authors based their own recommendations on the recently updated criteria for the sonographic diagnosis of early failed pregnancy put forth by the Royal College of Obstetrics and Gynaecology in 2011 [17]. Coming full circle, the RCOG used several recent investigations by the Bourne and Bottomley group to inform their guideline revisions [6,16,18-20]. The recommendations in the Bourne and Bottomley review and those of the Royal College have yet to become standard practice in many countries. However, they are of sufficient significance to advocate wider dissemination to all practitioners who provide recommendations to women with early Pregnancies of Uncertain Viability (PUVs), including obstetricians, gynecologists, family practitioners, nurse practitioners, sonographers and emergency room physicians.

Prior to the publication of these revised recommendations, commonly used criteria included those suggested by governing bodies from the United States, Canada, Australasia and from the Royal College of Obstetrics and Gynecology (Great Britain) prior to recent revision. These are summarized in Table 1. The new recommendations posed by the Bottomly and Bourne group and the RCOG are generally more conservative than prior commonly used criteria in an attempt to avoid misdiagnosis in 100% of cases and to take into account the inter- and intra-observer variability reported by Pexters et al. [6]. Due to the poor reliability of gestational dating that is based on maternal recall of the last menstrual period and the variability of ovulation and conception times within a given cycle, gestational dating based upon last menstrual period is not included in the diagnostic criteria.

It may be useful from an investigational and diagnostic standpoint to categorize early pregnancy losses into anembryonic losses (no detection of a fetal pole prior to pregnancy loss) and early fetal demises (presence of fetal pole without the development of cardiac activity). Consistent with this, the updated RCOG guidelines define early pregnancy loss using one of two criteria:

1. An intrauterine gestation visualized by transvaginal sonography with a mean gestational sac diameter of ≥ 25 mm but without a detectable yolk sac (anembryonic loss)
- or
2. An intrauterine gestation visualized using transvaginal sonography with a fetal crown rump length ≥ 7 mm but no detectable fetal cardiac activity (fetal demise) [17].

Some women will present with pregnancy losses that have occurred prior to reaching the above sonographic sizes. Others will have an intrauterine gestational sac of appropriate size and a yolk sac, but no detectable fetal pole. For these women, a repeat transvaginal ultrasonographic examination should be scheduled at least seven to ten days from the initial study and pregnancy loss diagnosed only if one of the following criteria is met:

1. If an empty gestational sac was initially seen, there has been no growth in the size of the gestational sac and no embryonic structures can be detected.
2. If a gestational sac with a yolk sac was seen on the original study, no embryo can be detected nor fetal CRL measured on the repeat scan. Most consider this an anembryonic loss; although it could be argued that the term should be reserved for pregnancies lacking any embryonic structures, including a yolk sac.
3. If a gestational sac containing an embryo with no fetal cardiac activity was seen on the initial scan, there has been no development of detectable fetal cardiac activity.

The review by Bottomley and Bourne points out that some investigations suggest an even more conservative approach that would remove a lack of gestational sac growth on repeat sonographic studies performed 7-10 days apart from the criteria defining early pregnancy loss [16]. In a prospective study of 1060 consecutive women with intrauterine pregnancies of uncertain viability, Abdallah et al. [19] could not define a lower limit for gestational sac growth that could predict pregnancy loss with 100% specificity. The same investigation also demonstrated that very slow fetal growth could be seen in some viable pregnancies, resulting in a necessity to lower the fetal growth cut-off value for non-viability to < 2 mm/day to attain 100% specificity. This recommendation was not included in the RCOG criteria.

These recommendations are summarized in Figure 3. While these guidelines are based on the best available data to date and are conservative in that they take into account known inter- and intraobserver technical variations, some continue to be based upon under-powered data sets and there remains room for future revision. To this point, the Government of South Australia has put forth even more conservative criteria for the sonographic diagnosis of early pregnancy loss that expand cutoffs to require a > 8 mm fetal pole with lack of fetal cardiac activity to determine non-viability [21]. Once the defining criteria for early pregnancy loss have been met, the patient can be offered therapeutic options. The patient may request and should be offered repeat confirmation of pregnancy failure prior to intervention. Her therapeutic options include expectant management, medical intervention or surgical intervention and all appear to be equally safe in the majority of candidates [22,23]. The relative efficacies of these options, however, appear to differ and to depend on gestational age at presentation and on type of pregnancy loss. A 2005 Cochrane review compared all three approaches and concluded that surgical management was more effective than medical

Governing Body	Recommendations
The Society of Gynecologists of Canada (SGOC) (21)	Embryo >5 mm and absent fetal cardiac activity
	Intrauterine mean gestational sac diameter >8 mm with absent yolk sac
The American College of Radiologists (ACR) (22)	Intrauterine mean gestational sac diameter >16 mm without fetal pole
	Embryonic crown-rump length >5 mm and absent fetal cardiac activity
Royal College of Obstetricians and Gynaecologists (RCOG) and Royal College of Radiologists (RCR) (23)	Intrauterine gestational sac with mean diameter ≥ 20 mm and no yolk sac
	Fetal crown-rump length ≥ 6 mm with absent fetal cardiac activity
Australasian Society for Ultrasound in Medicine (ASUM) (24)	Mean gestational sac diameter ≥ 20 mm with absent embryonic structures
	Embryonic crown-rump length ≥ 6 mm with absent fetal heart rate
Institute of Obstetricians and Gynaecologists, Royal College of Physicians of Ireland (25)	Mean gestational sac diameter >20 mm with absent embryonic structures (embryo or yolk sac)
	Embryonic crown-rump length ≥ 7 mm with absent fetal heart rate

Table 1: Commonly Used Criteria for Sonographic Diagnosis of Early Pregnancy Loss, may Have Specificity below 100% (guidelines prior to recent revisions).

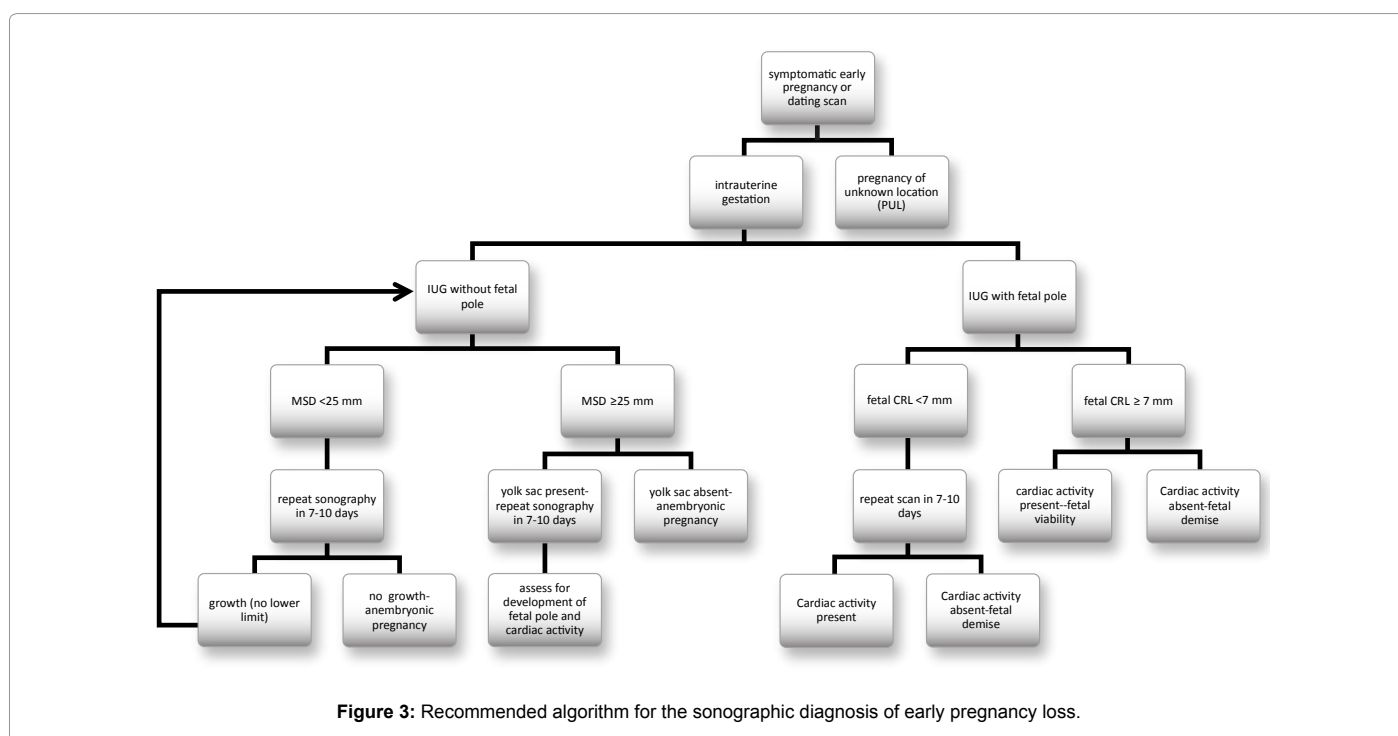


Figure 3: Recommended algorithm for the sonographic diagnosis of early pregnancy loss.

management and medical management more effective than expectant management [24]. Further, total maternal blood loss was decreased with medical and surgical interventions when compared to expectant management. Expectant management of incomplete losses was more effective than expectant management of missed abortions. A 2012 Cochrane comparison of expectant and surgical management of early pregnancy loss confirmed that blood loss and need for transfusion were lower in the surgical management group but that costs were lower with expectant management [25]. Surgical management was more effective than expectant management and risks for infection and for adverse psychological outcomes were similar between the two management approaches. If surgical intervention is chosen, use of vacuum aspiration is safer than the use of sharp curettage [26]. Surgical evacuations can be safely and effectively performed in the clinic setting with excellent patient satisfaction [22].

To summarize, early pregnancy loss is a common complication of pregnancy and patients with isolated and recurrent early pregnancy loss are encountered by many different types of providers. Recent well-informed revisions have been made to the sonographic criteria recommended for the diagnosis of early pregnancy loss and this information should be disseminated to all practitioners who include

newly-pregnant women in their practices. The updated diagnostic criteria that define anembryonic losses and early fetal demises are more conservative than prior guidelines and are based upon new research on larger study populations that consistently utilize transvaginal sonography for the evaluation of early pregnancy. Using the updated criteria, the specificity for diagnosing early pregnancy loss approaches up to 100%. Once a diagnosis of early pregnancy loss has been made, the therapeutic options of expectant management, medical intervention and surgical intervention can be offered. While surgical management is the most effective and medical management is more effective than expectant management, all are acceptable options when the patient has been appropriately counseled.

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