Early (34–56 days from last menstrual period) ultrasonographic measurements in normal pregnancies

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To assess early embryonic growth and development, 361 pregnancies were studied from 34 to 56 days from last menstrual period. All pregnancies had a subsequent successful outcome. Transvaginal ultrasonography was performed using an Acuson 128 X P/10 with a 5–7.5 MHz probe. Gestational sac diameter, embryonic pole length and embryonic heart rates were measured. Embryonic heart rates were determined by M-mode. Gestational sac diameter, embryonic pole length and embryonic heart rate increased linearly relative to gestational age and to each other. Regression equations comparing gestational sac diameter and embryonic pole length as well as comparing embryonic heart rate with gestational sac diameter and embryonic pole length were constructed. To be normal, gestations that have (i) sac diameter of 20 mm and 30 mm should contain at least a 2 mm and 5 mm embryo with embryonic heart rates of at least 75 and 100 beats per min, respectively; and (ii) embryos measuring 2 mm, 5 mm, 10 mm and 15 mm should display embryonic heart rates of at least 75, 100, 120 and 130 beats per minute respectively.

Key words: early gestation/embryonic heart rate/embryonic pole length/gestational sac diameter/transvaginal ultrasonography.

Introduction

Embryonic growth and development during the first trimester of pregnancy have been assessed by ultrasonographic measurements of the gestational sac (Robinson, 1975; Nyberg et al., 1987; Daya et al., 1991; Goldstein et al., 1991), embryonic pole (Dickey et al., 1992; Robinson and Fleming, 1975; Goldstein, 1991; Schats et al., 1991; Tezuka et al., 1991; Hadlock et al., 1992; Rotsztejn et al., 1993; Tadmor et al., 1994; Yapor et al., 1995) and embryonic heart rate (Hertzberg et al., 1988; Levi et al., 1990; Schats et al., 1990; Achiron et al., 1991; Howe et al., 1991; Merchiers et al., 1991; Tezuka et al., 1991; Rotsztejn et al., 1993; Britton et al., 1994; Tadmor et al., 1994; Yapor et al., 1995). We have previously reported that embryonic cardiac activity should be present by day 37 from onset of last menstrual period (LMP) in normal pregnancies (Britton et al., 1994). Other studies have shown that smaller than expected sizes (based upon LMP) of gestational sacs and embryonic poles predict impending pregnancy loss (Bromley et al., 1991; Nazan et al., 1991; Dickey et al., 1992; Goldstein, 1992; Frates et al., 1993). Confusion in interpretation of ultrasonographic findings has occurred when the exact time of conception is not known. Because of the uncertainty of menstrual data, evaluation of embryonic landmarks including gestational sac size, embryonic pole length and embryonic cardiac activity in relation to each other rather than to menstrual age has been advocated (Goldstein, 1992).

Nomograms constructed from regression curves of ultrasonographic measurements to assess gestational growth and development have been largely derived from pregnancies >6 weeks of gestation. Increased resolution provided by newer endovaginal ultrasonic probes allows identification of embryonic structures earlier. To define the relationships between gestational sac size, embryonic pole length and embryonic heart rate, 361 ultrasonographic examinations 34–56 days from LMP during pregnancies that subsequently resulted in normal gestations were studied.

Materials and methods

Diameter of gestational sac, length of embryonic pole and embryonic heart rates were recorded on 361 first trimester ultrasonographic examinations in 235 women from January 1, 1992 to August 1, 1993. All pregnancies resulted from assisted reproductive procedures, hence the day of insemination or embryo transfer was known and used to calculate the menstrual age of pregnancy. All ultrasonographic examinations were performed routinely after the second positive pregnancy test and extended from 34 to 56 days from LMP, normalizing day 14 as the day of ovulation. Pregnancies were included only if it was a singleton gestation and if follow-up beyond the first trimester revealed a normal gestation. All ultrasonographic scans were performed using an Acuson 128 XP/10 (Acuson Computer Imaging, Mountain View, CA, USA) with a 5.0 MHz transvaginal transducer. Both B-mode and simultaneous B- and M-modes were utilized. Gestational sacs were measured in longitudinal and transverse views and their diameters averaged. Embryonic poles were measured in the anterior to posterior dimension. Embryonic heart rates were calculated from frozen M-mode images with electronic calipers.

Gestational sac diameters and embryonic pole lengths were compared with gestational age. Gestational sac diameter was compared with embryonic pole length. Embryonic heart rates were compared with gestational sac diameter and embryonic pole length. Regression analysis with estimation of regression line with 95% prediction intervals was performed using a Systat Inc computer program (Evanston, IL, USA).

Results

Gestational sac diameter, embryonic pole length and embryonic heart rate increased linearly relative to gestational age and to...
Figure 1. Scatterogram of 361 gestational sac diameters (panel A) and embryonic pole lengths (EPL) (panel B) with gestational age from 34 to 56 days from LMP. Panel A: gestational sac diameter in mm = 0.90 (gestational age in days from LMP) - 24.0, \( r = 0.73 \), standard error of estimate = 4.89. Panel B: EPL in mm = 0.67 (gestational age in days from LMP) - 23.66, \( r = 0.87 \), standard error of estimate = 2.65.

Figure 2. Linear regression of mean and 95th percent confidence interval of 361 gestational sac diameters and embryonic pole lengths (EPL) from 34 to 56 days from LMP. EPL in mm = 2.17 + 0.51 (mean gestational sac diameter in mm), \( r = 0.79 \), Fit Std Err = 2.63, FStat = 508.44.

Figure 3. Linear regression of means and 95th percent confidence intervals of 361 gestational sac diameters (panel A) and embryonic pole lengths (EPL) (panel B) with embryonic heart rate (EHR) from 34 to 56 days from LMP. Panel A: EHR in beats per mm = 81.79 + 2.6 (gestational sac diameter in mm), \( r = 0.73 \), Fit Std Err = 15.98, FStat = 357.44. Panel B: EHR in beats per min = 95.72 + 4.65 (EPL in mm), \( r = 0.85 \), Fit Std Err = 12.47, FStat = 787.49.
gestation sacs will contain an embryonic pole measuring at least 2 mm.

Embryonic heart rate has a linear relationship with gestational sac size and embryonic pole length (Figure 3). The regression equations for embryonic heart rate (EHR) in beats per min are:

\[
\text{EHR} = 82 + 2.6 \times \text{gestational sac diameter in mm}
\]
\((r = 0.73, \text{standard error} = 16, FStat = 357)\)

\[
\text{EHR} = 96 + 4.6 \times \text{gestational pole length in mm}
\]
\((r = 0.85, \text{standard error} = 12, FStat = 787)\)

To be within the 95% confidence interval of normal, embryos measuring 2 mm should display an EHR of at least 75 beats/min, 5 mm at least 100 beats/min, 10 mm at least 120 beats/min and 15 mm at least 130 beats/min.

**Discussion**

We have previously reported that in all normal pregnancies EHR can be detected by 37 days from LMP (Britton et al., 1994). Because of uncertainty of exact menstrual age in women spontaneously ovulating, we extended our previous studies on EHR to compare EHR with gestational sac size and embryonic pole length. During the early first trimester (days 34–56 from LMP), gestational sac diameter, embryonic pole length and embryonic heart rate increase linearly relative to each other. To be normal, gestations that have a sac diameter of 15 mm should contain a measurable embryonic pole and a diameter of 20 mm and 30 mm should contain at least a 2 mm and 5 mm embryo with EHR of at least 75 and 100 beats per min, respectively.

The new information provided by this study allows earlier diagnosis of normal growth and development. Using these definitions of normal growth and development, abnormal growth and development can be studied earlier in pregnancy (Coulam et al., unpublished). That these definitions can predict impending pregnancy loss is suggested by a 94% abortion rate (123/144) among women with small for gestational size embryonic pole lengths (data from Figures 1 and 2) Using sonographic measurements, a blighted ovum has been defined as a gestational sac with a mean diameter of 20 mm without an embryo visible (Wilson et al., 1986). Results of the current study would provide a diagnosis of blighted ovum a week earlier with a gestational sac with a mean diameter of 15 mm without an embryo visible. A missed abortion has previously been defined as an embryo of 15 mm length without cardiac activity present (Goldstein, 1995). The diagnosis of missed abortion can now be made 2 weeks earlier with an embryo measuring 3 mm (Figure 3).

The effects of ultrasound on embryonic development during the period of organogenesis are not known with certainty although no reports document adverse effects with current sono- graphic methods used in human gestation. Bioeffects of ultrasound are related to the spatial peak time average intensity and duration of exposure. Ultrasound during pregnancy should be limited to 500 s at a spatial peak time intensity of less than 94 mW/cm² (American Institute of Ultrasound Medicine, 1993). Using these techniques advances in ultrasonographic resolution have allowed identification of embryonic structures very early in gestation (at least by 34 days from LMP). Previously published nomograms were constructed from regression curves with the bulk of the data deriving from small fetuses (embryonic pole length > 18 mm) and then extrapolated back to embryos of 1–2 mm. It is hoped that information obtained from improved ultrasonographic technologies which can differentiate acceptable growth and continued development from a pregnancy which is definitively destined for failure can be used to enhance attempts at improving reproductive outcome.

**References**


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