Determining gestational age in the early fetal period: A comparison of morphometrical parameters

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SUMMARY

Estimation of fetal age is an important component of prenatal evaluation. The measure of the Crown-Rump Length (CRL) by ultrasound is one of the most frequently used methods to determine it. However, in certain pathologies, this measure could lose accuracy, and other measures should be taken to evaluate fetal age and to determine the normal growth of the conceptus. The main objective of this research was to compare different morphometric parameters with CRL in normal human fetuses to determine which of them has a stronger correlation with gestational age to be a useful measure when CRL could not be appropriately evaluated. We measured 10 different morphometric parameters and the weight in 120 human fetuses product of abortion that had externally normal morphology, and a Pearson´s Correlation test was made with each of the parameters with the gestational age determined using the CRL.

Each of the 10 parameters had a significantly strong correlation with CRL. However, some of them have a stronger correlation and should be preferred when CRL is not available. If available, fetal age should be estimated using an ultrasound technique and measuring the CRL. Nevertheless, if an alteration in one of the structures affects its measure, a different parameter should be used. The limitations of each parameter should be noticed before using them.

Key words: Gestational age – Fetal development – Fetal structures – Morphogenesis – Fetal weight

INTRODUCTION

Over the years, different types of measurements have been used to estimate fetal age. Due to its accessibility, ideally, these measurements should be obtained through the use of ultrasound, a low-cost technology, available in most hospitals, which is harmless during pregnancy. The measurement of the crown-rump length is considered the gold standard, as well as the most accurate method for calculating fetal age (Hadlock, 1990). However, in certain situations where the morphology of the fetus is affected due to certain pathologies, some methods of calculation of fetal age may not be accurate (Sherwood et al., 2000). It is known, for example, that the accuracy of measuring biparietal diameter is more likely to be affected by different maternal and fetal factors compared to head circumference (Johnsen et al., 2004).

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Furthermore, different non-pathological variables can also affect the growth of the structures that are used for measurement, and therefore not be as reliable, as the measurement of the abdominal perimeter due to the rapid growth of the abdomen in intrauterine life. As a result, it is necessary to search for alternatives and evaluate their precision.

Research comparing traditional measurement methods to obtain fetal age is quite scarce, since current tendencies include looking for new and modern techniques to estimate fetal age, however not always available (Minier et al., 2014a; 2014b; Pomier et al., 2019). It is necessary to compare the traditional methods in order to find out which is the most accurate in cases where the gold standard cannot be used and no modern technologies to perform these measurements are available.

A pair of studies were made using Multiple Slide Computed Tomography (MSCT) technology, which found that it is possible to calculate the fetal age by evaluating the deciduous tooth gems or the mandible, obtaining a reliable result compared to the measurement of the femoral diaphyseal length (Minier et al., 2014a; 2014b). However, calculating the fetal age with this method may not always be possible, particularly in cases where an MSCT is not available. In another study, authors concluded that orbital measurement using a 3D CT scan could provide a reliable measurement of fetal age, particularly in fetuses with trisomy 21, but this method also becomes unfeasible in cases where the equipment is not available (Pomier, 2009). The measurement of the basilar portion of the occipital bone was also found to be a useful and reliable option for estimating fetal age. Nevertheless, their observations focused on estimating fetal age in fetuses that are the product of abortion, and it is not possible to take this measure in utero by ultrasound (Nagaoka et al., 2012). Likewise, it has been argued that the histological study of the kidney can also be a reliable tool to estimate fetal age (Kumar and Pillay, 1996). Out of the morphological measures, the quantification of surfactant factor produced by type 2 pneumocytes by immunohistochemistry can be used to estimate fetal age, yet both methods are only functional in cases where fetal age is studied in fetuses outside the uterus (Betz et al., 1992).

About the measuring of the ear, several studies have acknowledged the measurement of the external ear as an indicator for either detecting chromosomal abnormalities or determining the fetal age of the product. Sivan et al. (1983) first examined ear length on newborns, determining a parameter to classify small and low set of ears, which was correlated with diagnosing syndromes in pediatric patients.

Chitkara et al. (2000) measured the pinna by sonography, and then developed a nomogram in which the ear was compared to gestational age, and the linear regression found r = 0.96, hence suggesting a high correlation between both variables.

Another study aimed to examine fetal ear length in products with aneuploidy, and not only it was found that these had significantly shorter ears, but also that its length was disproportionate with the biparietal diameter, another measurement used to approximate fetal size (Yeo et al., 2003).

The importance of traditional measurements relies on the fact that they can be calculated in the uterus through an ultrasound, a technology that has a worldwide distribution and is available to the majority of the population. A more accurate gestational age diagnosis using ultrasound could be performed with information about the precision of these measurements.

MATERIALS AND METHODS

This research followed the directions of the Helsinki Declaration and was approved by our institutional ethics committee, with approbation number EB21-00001. A total of 120 human fetuses with normal external morphology and with ages from 12 to 20 weeks of gestation (WOG) were measured using 10 morphometrical parameters; the weight were also determined to compare which of them has a stronger correlation with the gestational age estimated measuring the Crown-Rump Length (CRL) (Paten,1982). The parameters are described, and a graphic description is shown in Fig. 1. The sample size was taken under our laboratory availability of human fetuses.

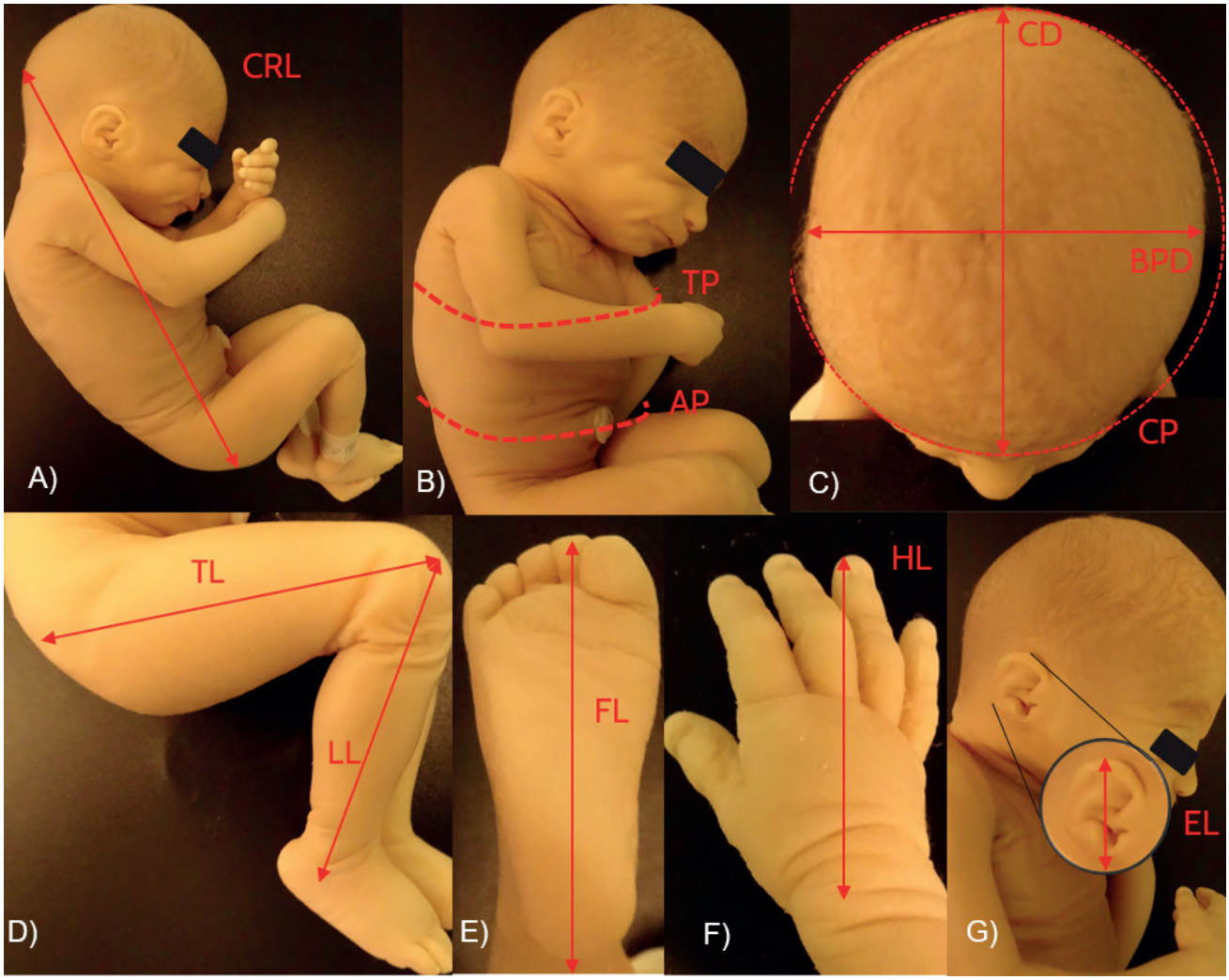

Fig. 1.- Morphometrical parameters to estimate fetal age in a fetus of 20 Weeks of Gestation (WOG). CRL: Crown-Rump Length. TP: Thoracic Perimeter. AP: Abdominal Perimeter. CD: Cephalic Diameter. BPD: Biparietal Diameter. CP: Cephalic Perimeter. TL: Thigh Length. LL: Leg Length. FL: Foot Length. HL: Hand Length. EL: Ear Length.

The Crown-Rump Length (CRL) was measured from the most prominent part of the occiput to the most prominent part of the rump. Thoracic Perimeter (TP) was measured at the level of the nipples. The abdominal Perimeter (AP) was measured around the level of the umbilical cord. Cephalic Diameter (CD) was measured from the sinciput to the occiput. Biparietal Diameter (BPD) was measured as the distance from both parietal bones in the fetus. Cephalic Perimeter (CP) was measured at the level above the eyebrows of the fetus. Thigh Length (TL) was measured from the hip joint to the knee joint. Leg Length (LL) was measured from the knee joint to the ankle joint. Foot Length (FL) was measured from the heel to the most prominent toe. Hand Length (HL) was measured from the wrist joint to the middle finger. Finally, Ear Length (EL) was measured from the helix to the lobule.

A data set was made using the Microsoft Excel 365 Software, and information was processed using the IBM SPSS 24 software. We calculated each measure's mean and standard deviation for each week of gestation from 12 to 20 WOG. This gestational age was previously determined by measuring the Crown-Rump Length (CRL) defined as the preferred measure to estimating fetal age. After corroborating the normal distribution of data with a Kolmorov-Smirnoff test, a Pearson's Correlation test was made from each of the measures and the weight with the CRL to evaluate which had the strongest correlation with this measure.

RESULTS

Results from the mean and standard deviation for each measure at each week of gestation from 12 to 20 WOF are summarized in Table 1.

Table 1. Measures of morphometrical parameters. Each measure is represented as the mean (±SD). HL: Hand Length. LL: Leg Length. FL: Foot Length. TL: Thigh Length. CD: Cephalic Diameter. CRL: Crown-Rump Length. CP: Cephalic Perimeter. TP: Thoracic Perimeter. AP: Abdominal Perimeter. BPD: Biparietal Diameter. EL: Ear Length.

WOG	WEIGHT (gr)	HL (mm)	LL (mm)	FL (mm)	TL (mm)	CD (mm)	CRL (mm)	CP (mm)	TP (mm)	AP (mm)	BPD (mm)	EL (mm)
12	35.75 (5.72)	11.0 (1.41)	17.0 (1.41)	12.5 (0.70)	27.00 (0.00)	57.5 (7.77)	77.5 (0.70)	88.00 (5.65)	73.00 (9.89)	65.00 (16.97)	56.00 (2.82)	6.5 (0.70)
13	54.19 (12.82)	13.62 (1.40)	21.88 (3.21)	15.00 (1.41)	29.88 (2.93)	62.66 (4.89)	92.66 (4.15)	97.33 (8.1)	84.37 (10.56)	75.28 (12.29)	62.50 (4.75)	7.22 (0.91)
14	72.92 (7.94)	15.16 (0.98)	25.00 (2.44)	17.85 (1.57)	35.57 (2.76)	70.00 (3.51)	103.28 (3.98)	108.85 (6.17)	94.42 (6.07)	88.85 (7.22)	66.33 (3.98)	8.50 (0.50)
15	151.24 (41.64)	19.90 (2.42)	36.70 (73.33)	24.22 (2.77)	47.30 (5.85)	92.77 (10.47)	124.11 (8.00)	133.11 (41.80)	128.11 (17.84)	119.88 (18.64)	82.50 (9.20)	11.33 (2.33)
16	208.91 (47.54)	21.28 (2.74)	37.50 (7.80)	27.00 (3.33)	49.81 (6.15)	93.31 (14.41)	133.18 (5.92)	153.36 (14.26)	138.95 (14.44)	136.85 (13.19)	89.91 (4.99)	11.16 (1.02)
17	279.61 (61.04)	25.00 (2.17)	45.21 (4.51)	31.21 (2.52)	55.69 (3.78)	108.68 (12.43)	146.59 (5.47)	159.90 (35.83)	143.04 (32.61)	135.73 (37.41)	100.63 (8.53)	13.45 (1.50)
18	344.19 (65.40)	25.96 (2.76)	47.84 (7.36)	34.88 (2.61)	59.80 (6.74)	111.08 (20.93)	160.12 (8.89)	155.87 (58.59)	163.22 (26.06)	153.59 (24.39)	112.62 (27.15)	15.68 (1.70)
19	421.51 (95.12)	29.86 (3.20)	53.06 (6.87)	38.68 (3.59)	67.06 (6.54)	125.64 (13.16)	171.35 (8.57)	201.78 (22.48)	184.50 (12.43)	177.50 (14.53)	118.90 (6.59)	17.54 (1.29)
20	408.02 (92.95)	31.75 (4.52)	51.50 (5.09)	38.25 (3.05)	63.00 (7.28)	127.71 (7.56)	176.42 (11.54)	201.42 (17.39)	176.66 (11.41)	171.33 (10.51)	121.50 (4.94)	18.32 (2.82)

All of the measured parameters show an increasing pattern as the gestational age increases. However, not all of the measures show a constant increment, as some of them showed periods of greater growth and periods with smaller increments in their size. This is graphically represented in Fig. 2, where the CRL pattern among the studied period is compared with the rest of the parameters measured. In this graphic, CRL is represented with a continuous black line, and it can be observed that, as described by previous authors, it represents the measure with the most constant increment during this period of gestation.

Table 2 shows the results of the Pearson´s Correlation test from each of the measured

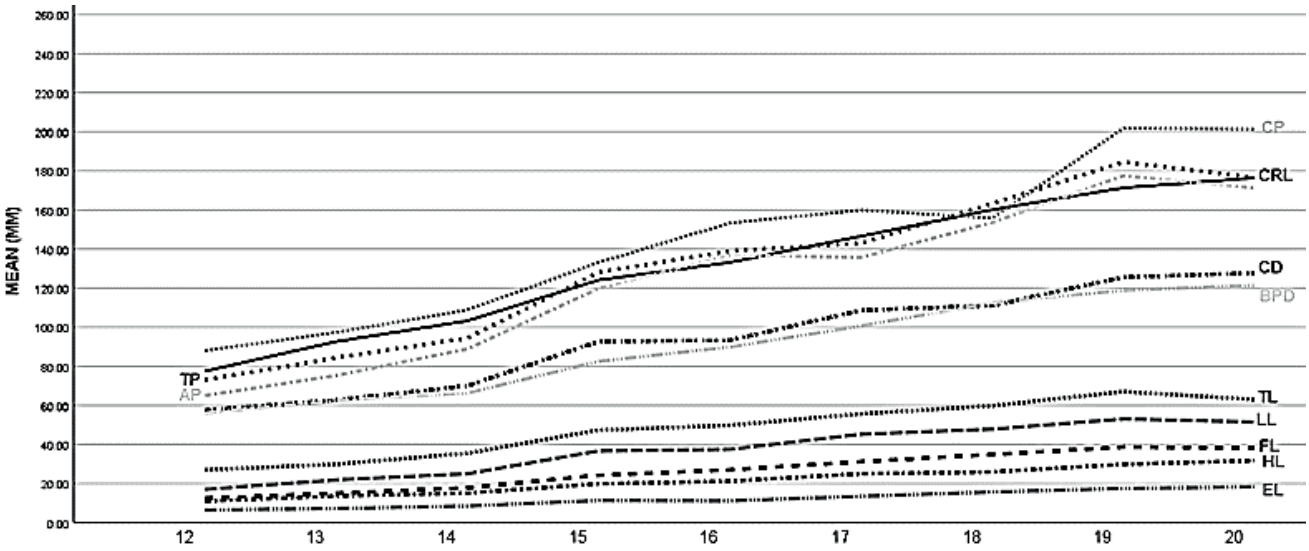

Fig. 2.- Growth pattern of the measured parameters. The CRL shows the most constant increasing pattern.

parameters with the CRL, and, as is shown, all of them have a strong correlation with this measure. Foot Length (FL) and the Biparietal Diameter (BPD) have the next most constantly increasing pattern with the stronger correlation with the CRL. This table could be used as a guide to select a parameter to determine gestational age when CRL could not be used, and this parameter should be selected in the presented order for the accuracy of the age estimation.

Table 2. Pearson´s correlation of each of the measured parameters with the CRL. All of the measures were significant with a p-value <0.01.

MORPHOMETRIC PARAMETER	PEARSON´S CORRELATION TEST
CROWN- RUMP LENGHT (CRL)	1
FOOT LENGHT (FL)	0.997
BIPARIETAL DIAMETER (BPD)	0.996
HAND LENGHT (HL)	0.995
LEG LENGHT (LL)	0.993
CEPHALIC DIAMETER (CD)	0.992
THORACIC PERIMETER (TP)	0.991
TIGHT LENGHT (TL)	0.99
ABDOMINAL PERIMETER (AP)	0.989
EAR LENGHT (EL)	0.989
WEIGHT	0.985
CEPHALIC PERIMETER (CP)	0.973

DISCUSSION

Estimating fetal age is an important part of prenatal evaluation, as it can be a marker of normal development. If possible, fetal age should be determined using non- invasive methods such as the use of different measures through an ultrasound technique. One of the most used measures is the Crown-Rump Length (CRL), which is a constant parameter that strongly correlates with fetal age. We described, as previous authors, that CRL could be the most useful parameter to determine gestational age, since it has significant increases over each week of development, enough to discriminate from one another, making it the most accurate measure (Hadlock, 1990). However, it could be affected by different pathologies that affect its measured components (Sherwood et al., 2000). For example, a patient with anencephaly or cranioschisis would show a smaller length that would not correlate with fetal age properly. On the other hand, a patient with hydrocephaly could show a larger length that also would not be correct (Johnsen et al., 2004). In these cases, a different parameter could be used for estimating fetal age, like the measure of the Foot Length (FL), a simple measure that has shown to strongly correlate with the estimation by CRL. Notice that each of the parameters have their limitations, and they should be considered before using them for the purpose of determining fetal age: for example, the abdominal perimeter is highly influenced by the liver development and the presence or absence of the physiological gut herniation, and thus it should not be used in the period where this herniation takes place. Ear Length (EL), a recently studied structure for determining fetal age, showed a strong correlation with age determined by CRL, however smaller than that from other parameters (Chitkara et al., 2000). However, these structures have an important role when other structures are affected, and their position could be also used as a marker of adequate development (Yeo et al., 2003). Further research should be done to define the normal range for each of the parameters, as this could vary for different characteristics as gender and ethnicity.

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