Ultrasound Obstet Gynecol 2021; **58**: 354–359
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.23690

Crown–rump length measurement error: impact on assessment of growth

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KEYWORDS: crown–rump length; estimated fetal weight; growth scan; large-for-gestational age; measurement error; small-for-gestational age

CONTRIBUTION

What are the novel findings of this work?
Even small errors in the first-trimester measurement of crown–rump length (CRL) significantly affect second- and third-trimester estimated fetal weight (EFW). A measurement error of −2 mm in first-trimester CRL shifts an EFW on the 10th percentile at the 20-week scan to around the 20th percentile. A measurement error of + 2 mm shifts an EFW on the 10th percentile to around the 5th percentile.

What are the clinical implications of this work?
Published data suggest that CRL measurement errors of 2 mm or more are common in clinical practice. Misclassification as small-, appropriate- or large-for-gestational age will commonly occur and affect clinical assessment, patient management and research results. Thus, there is a need to increase awareness of the importance of correct CRL measurement and to reduce measurement error variation through standardization and quality control.

ABSTRACT

Objective *To examine the impact of first-trimester crown–rump length (CRL) measurement error on the interpretation of estimated fetal weight (EFW) and classification of fetuses as small-, large- or appropriate-for-gestational age on subsequent growth scans.*

Methods *We examined the effects of errors of ± 2, ± 3 and ± 4 mm in the measurement of fetal CRL on percentiles of EFW at 20, 32 and 36 weeks' gestation and classification as small-, large- or appropriate-for-gestational age. Published data on CRL measurement error were used to determine variation present in practice.*

Results *A measurement error of −2 mm in first-trimester CRL shifts an EFW on the 10th percentile at the 20-week scan to around the 20th percentile, and the effect of a CRL measurement error of + 2 mm would shift an EFW on the 10th percentile to around the 5th percentile. At 32 weeks, a first-trimester CRL measurement error would shift an EFW on the 10th percentile to the 7th (+ 2 mm) or 14th (−2 mm) percentile; at 36 weeks, the EFW would shift from the 10th percentile to the 8th (+ 2 mm) or 12th (−2 mm) percentile. Published data suggest that measurement errors of 2 mm or more are common in practice.*

Conclusion *Because of the widespread and potentially severe consequences of CRL measurement errors as small as 2 mm on clinical assessment, patient management and research results, there is a need to increase awareness of the impact of CRL measurement error and to reduce measurement error variation through standardization and quality control. © 2021 International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

Knowledge of gestational age is of major importance in many, if not all, aspects of obstetric care. Error and uncertainty in gestational age are associated with a wide range of adverse pregnancy outcomes, including perinatal death[1–3].

For many years, gestational age was determined from the first day of the last menstrual period, but,

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Accepted: 9 May 2021

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nowadays, gestational age is usually derived from the measurement of fetal crown–rump length (CRL) taken during the first-trimester ultrasound scan[4–8], which is carried out for pregnancy dating or as part of screening for aneuploidy[9–12]. Accurate measurement of CRL is essential in many aspects of pregnancy care, such as the interpretation of nuchal translucency thickness and biochemical markers in first-trimester screening for aneuploidy[13–15].

The objective of this study was to examine the impact of CRL measurement error on the diagnosis of small-for-gestational-age (SGA), appropriate-for-gestational-age (AGA) and large-for-gestational-age (LGA) fetuses based on ultrasonographic estimated fetal weight (EFW) during the second and third trimesters of pregnancy.

METHODS

We start by showing how a 2-day difference in gestational age can impact the classification of a fetus in the second trimester as AGA or SGA with EFW $< 10^{th}$ percentile. We then show how this discrepancy can arise from underestimation of CRL in the first trimester by 3 mm leading to a 2-day error in the gestational age of a 20-week scan. Having explained the mechanism, we then show the effects of CRL measurement errors of ± 2 mm, ± 3 mm and ± 4 mm on the percentile ranks for measurements of EFW that would, if measured without error, fall on the 10^{th} and 90^{th} percentiles. We describe a simple measurement error model in which measurements of CRL are composed of the true CRL plus measurement error. The degree of measurement error variation was quantified by its SD. Using this model, we suggest limits on the measurement error SD. These were compared to SDs derived from recent publications[16].

RESULTS

Estimated fetal weight at different gestational ages

To illustrate the process by which a discrepancy in gestational age can impact the classification of a fetus as AGA or SGA, as an example, consider what happens when an EFW of 300 g is interpreted at a gestational age of 20 + 0 weeks (140 days) compared with at 20 + 2 weeks (142 days) (Figure 1). At 140 days, a measurement of 300 g, shown as a solid circle on Figure 1, is well above the 10^{th} percentile and would be interpreted as AGA. At 142 days, the same measurement would be interpreted as SGA. Figure 1b shows the reference distributions of EFW at 140 and 142 days. The percentile rank for the measurement of 300 g at 140 days is 19%. The percentile rank for the same measurement at 142 days is 6%.

Impact of error in first-trimester crown–rump length measurement

Errors in first-trimester CRL measurement lead to the kind of discrepancies illustrated above and in Figure 1. For example, suppose that the true measurement of CRL was 65 mm, giving a gestational age at the first-trimester scan of 90 days. According to this, the 20 + 0-week scan should be scheduled for 50 days later, at a gestational age of 140 days. However, if there was an undermeasurement of 3 mm, giving a CRL measurement of 62 mm instead of 65 mm and a gestational age of 88 days instead of 90 days, the 20 + 0-week scan would be scheduled for 52 days later at a gestational age of 20 + 2 weeks. An EFW of 300 g at this scan would be assessed as a measurement at 20 + 0 weeks and interpreted as AGA. The true interpretation should be at 20 + 2 weeks (142 days) with categorization as SGA.

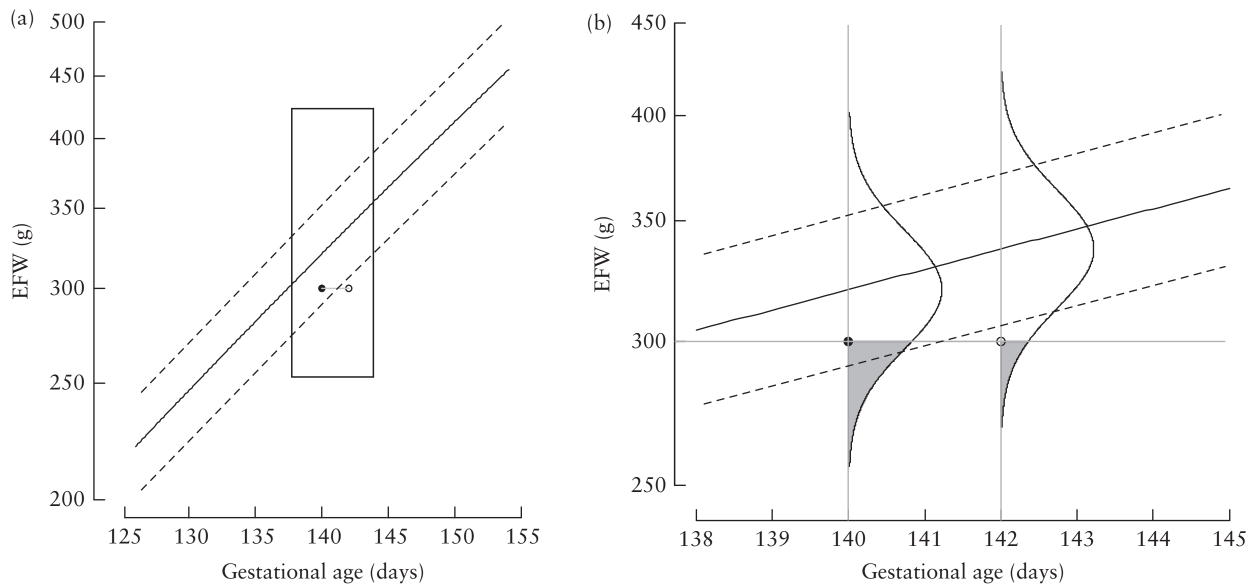

Figure 1 Reference percentile charts for estimated fetal weight (EFW), showing the median (——) and 10^{th} and 90^{th} percentiles (- - -). EFW measurements of 300 g at 140 days' gestation (●) and at 142 days' gestation (○) are shown. The rectangular region is shown enlarged in (b). (b) The reference distributions of EFW at 140 days and 142 days are shown as Gaussian curves. The shaded areas are the percentile ranks for the measurement of 300 g at 140 days and at 142 days. At 140 days, 300 g is on the 19^{th} percentile and, at 142 days, it is on the 6^{th} percentile.

To examine the effect of CRL measurement error at different scheduled visits at gestational ages ranging from 14 to 42 weeks, we applied errors of 0 mm, ± 2 mm, ± 3 mm and ± 4 mm to the first-trimester CRL measurement and computed the percentile ranks of measurements on the 10th and 90th percentiles at the true gestational age. The results are shown in Figure 2, and Table 1 shows these results at 20, 32 and 36 weeks. For negative errors, EFW values are interpreted at earlier gestational ages than they should be and are more likely to be interpreted as AGA. For positive errors, EFW values are interpreted at later gestational ages than they should be and smallness appears more extreme. A notable feature of Figure 2 is that the impact of measurement error decreases with increasing gestational age. This is because the transmission of errors is greater at earlier gestational ages when the percentile charts are steeper. Figure 2 suggests that errors of 2 mm or more may have important impact on clinical management. This raises the question of how often such errors occur and, more generally, the distribution of errors encountered in clinical practice.

In some settings, clinical management is also determined from measurements of fetal head circumference (HC), which is a component of EFW, and standard biometry at the second-trimester scan. A small HC is associated with chromosomal anomalies, genetic syndromes, central nervous system malformations and other adverse outcomes; the smaller the HC, the higher the risk[17,18]. Additional diagnostic procedures and parental counseling are therefore dependent on the HC percentile, and the same effects, information and indications for additional tests apply to fetal abdominal circumference (AC)[19] and femur length (FL)[20] percentiles. The effects of CRL errors on HC, AC and FL percentiles are shown in Figure 3.

Distribution of crown–rump length measurement errors

Numerous studies have quantified measurement error variability in CRL in terms of limits of agreement, SDs of differences between operators, variance components and interclass correlation coefficients[13,14,21]. Results have been presented for intraobserver variation between measurements taken by the same sonographer and for interobserver variation between measurements taken by different sonographers. For the purposes of this paper, we adopted a measurement error model which assumes that CRL measurements comprise the sum of true CRL

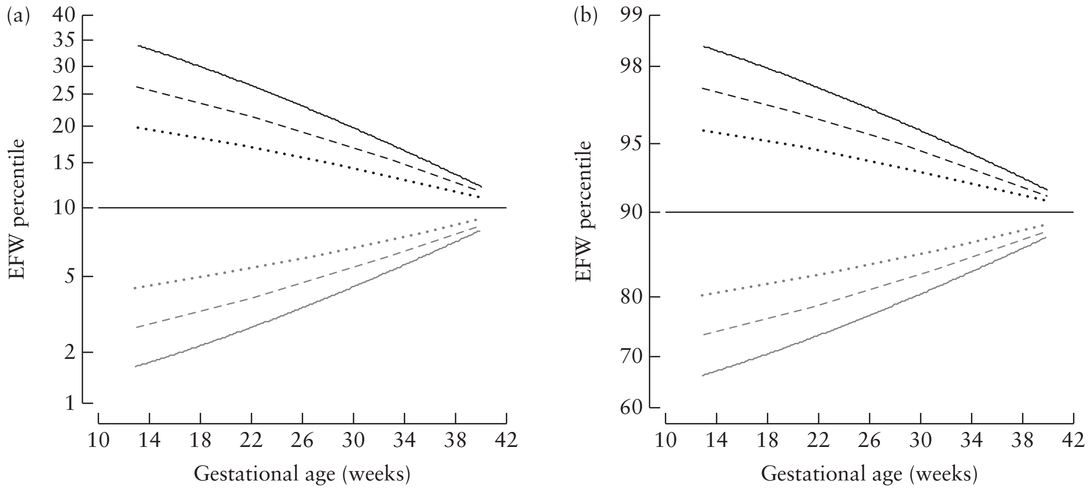

Figure 2 Estimated fetal weight (EFW) percentile according to gestational age estimated with a crown–rump length (CRL) measurement error of −4 mm (——), −3 mm (- - -), −2 mm (·····), + 2 mm (·····), + 3 mm (- - -) or + 4 mm (——) when the true CRL at the dating scan is 65 mm and the true EFW is on the 10th percentile (a) or on the 90th percentile (b).

Table 1 Effect of errors in crown–rump length (CRL) measurement on estimated fetal weight (EFW) percentile when the true CRL at the dating scan is 65 mm and the true EFW is on the 10th or the 90th percentile

	EFW percentile for CRL measurement error of:					
Gestational age	*+ 2 mm*	*−2 mm*	*+ 3 mm*	*−3 mm*	*+ 4 mm*	*−4 mm*
True EFW on 10th percentile*						
20 weeks	5.20	17.64	3.63	22.66	2.48	28.47
32 weeks	7.20	13.64	6.07	15.82	5.09	18.25
36 weeks	8.07	12.34	7.24	13.68	6.49	15.14
True EFW on 90th percentile*						
20 weeks	82.45	94.93	77.67	96.56	72.28	97.74
32 weeks	86.39	92.93	84.33	94.15	82.11	95.21
36 weeks	87.67	92.05	86.41	92.97	85.09	93.82

*No measurement error in CRL.

and a measurement error, according to the relationship: measured CRL = true CRL + error. The measurement error in this model comprises both intra- and interobserver errors. We assumed that the measurement errors follow a Gaussian distribution with a mean of zero, and the corresponding distribution of SDs of 1 mm, 2 mm and 4 mm are shown in Figure 4. Table 2 shows 95% limits for the measurement error, SDs of difference, 95% limits of agreement and interclass correlation coefficients for these error SDs. The interclass correlation expresses the variance (i.e. SD^2) of the true CRLs as a fraction of the variance of the measured CRL. The variance of true CRL will differ depending on the setting. For Table 2, the true CRL is given for uniform distributions across the range 45 to 84 mm, corresponding to gestational ages of 11 to 14 weeks, and for uniform distributions across the range 23 to 84 mm, corresponding to gestational ages of 9 to 14 weeks. The methodology is described in Appendix S1.

DISCUSSION

The preferred method of pregnancy dating is based on the measurement of fetal CRL, and this is recommended by national and international guidelines[22–25]. Our study highlights the impact of CRL measurement error during the first trimester on the assessment of fetal growth during the second and third trimesters. For example, we demonstrated how a CRL measurement error of −2 mm shifts an EFW during the second trimester on the 10th percentile to around the 20th percentile, and an error of + 2 mm shifts an EFW on the 10th percentile to around the 5th percentile (Figure 2). This suggests that the magnitude of measurement error should be restricted to 2 mm or less to limit its effect on the diagnosis of fetal growth abnormality. To restrict errors of this magnitude in 95% of measurements would mean that the error SD should be restricted to 1 mm or less, as seen in Table 2. However, 95% probability intervals for CRL measurement are often reported to be as wide as ± 5 mm, which suggests the impact of CRL measurement bias on pregnancy dating and biometry might exceed what we have shown in this paper.

Some papers have assessed CRL measurement error variability in clinical practice. In a study in which two experienced operators measured CRL in 124 pregnancies, Kagan *et al.* found pooled values for intra- and interoperator variability SDs of 2.5 mm and 2.8 mm, respectively[13]. In a study including 28 experienced operators who measured CRL in 9472 women, Sabria *et al.* found that operator-specific pregnancy-associated plasma protein-A (PAPP-A) multiples of the median values

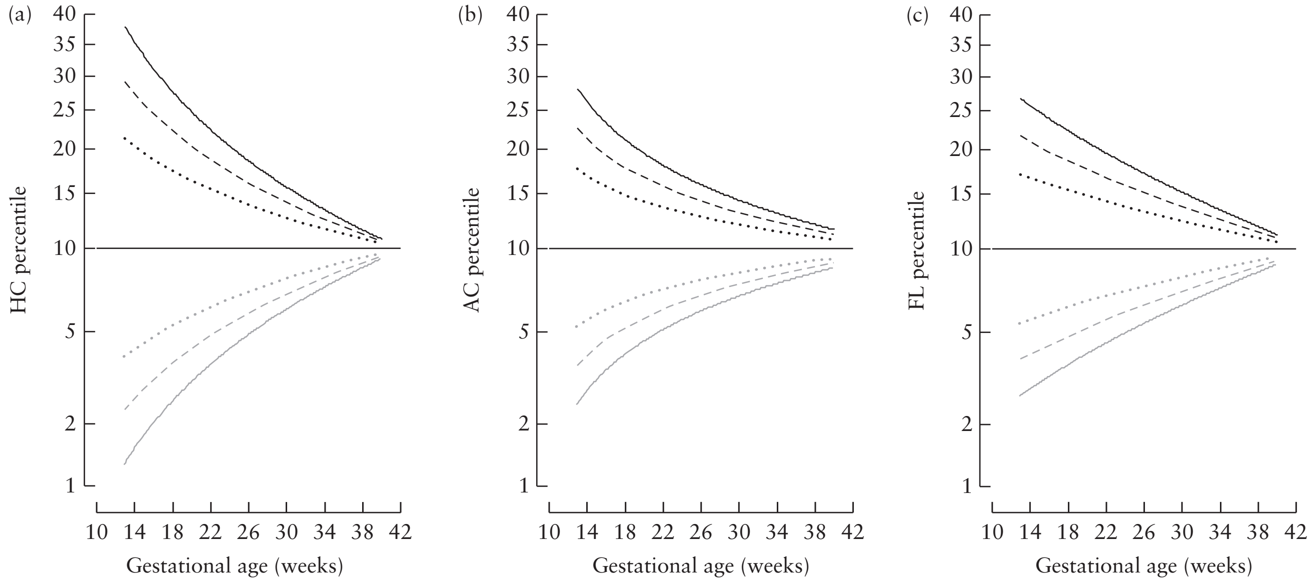

Figure 3 Fetal head circumference (HC) (a), abdominal circumference (AC) (b) and femur length (FL) (c) percentiles, according to gestational age estimated with a crown–rump length (CRL) measurement error of −4 mm (——), −3 mm (– – –), −2 mm (·····), + 2 mm (·····), + 3 mm (– – –) or + 4 mm (——) when the true CRL at the dating scan is 65 mm and the true HC/AC/FL is on the 10th percentile.

Table 2 Different measures of error variation in crown–rump length (CRL) measurement

*Error SD (mm)**	*95% limits (mm)†*	*Difference SD (mm)‡*	*95% LoA (mm)§*	*ICC¶*	*ICC***
1	± 2.0	1.41	± 2.8	0.992	0.997
2	± 3.9	2.83	± 5.5	0.969	0.987
3	± 5.9	4.24	± 8.3	0.934	0.972
4	± 7.8	5.66	± 11.1	0.888	0.951

*SD of measurement error about the true value. †95% limits for the measurement error. ‡SD of the difference between independent measurements. §95% limits of agreement (LoA) for the difference between two independent measurements. ¶**Interclass correlation coefficient (ICC) assuming that the true CRL is distributed uniformly over the range: ¶45 to 84 mm; **23 to 84 mm.

indicated a systematic CRL bias among 36% of the sonographers, and 60% of those had a CRL bias of more than 2 mm[21].

Although there is some degree of heterogeneity amongst the different published studies in terms of methodology, the interobserver measurement error SDs are generally in excess of 1 mm. This has several implications. Misclassification as SGA, AGA or LGA will commonly occur due to errors in CRL measurement. As impaired fetal growth is a risk factor for intrauterine or perinatal death, operative delivery as well as adverse neonatal and long-term outcomes[26–28], misclassification of fetal growth could potentially have severe consequences for short- and long-term pregnancy outcome. Whilst this applies to both singleton and twin pregnancies, possible CRL measurement errors could contribute to misclassification of intertwin CRL discordance, which has been identified as a potential risk factor for adverse outcome and, therefore, of importance for clinical management[29,30].

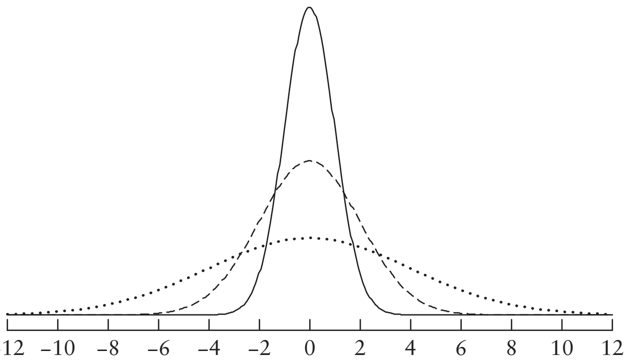

Figure 4 Gaussian distribution of crown–rump length measurement errors with mean of zero and SD of 1 mm (——), 2 mm (- - -) or 4 mm (·····).

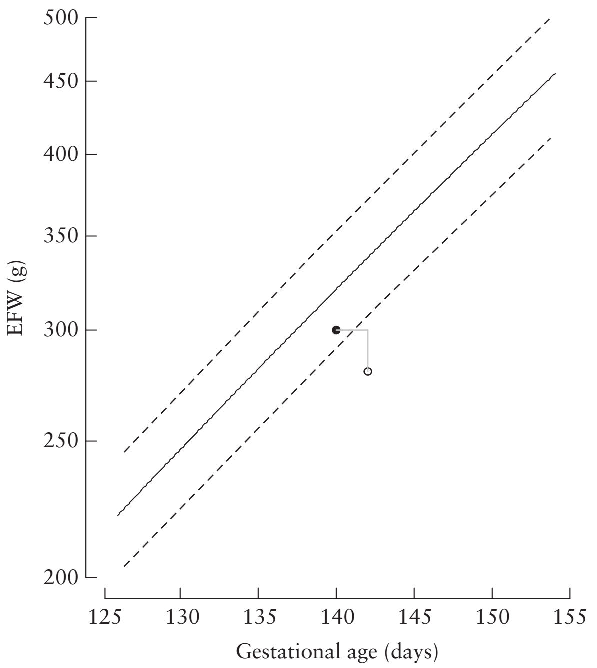

Figure 5 Reference percentile chart for estimated fetal weight (EFW), showing the median (——) and 10th and 90th percentiles (- - -). A true EFW measurement of 300 g at a true gestational age of 140 days (●) is shown, as well as the same measurement with a + 2-day error in gestational age, which shifts the point horizontally, and a −20-g error in EFW, which shifts the point vertically (○).

Classification of growth disorders is also affected by errors in biometric measurements in EFW assessment[31]. The consequence of these measurement errors can also be seen on a percentile chart; the position of a measurement on a percentile chart is shifted horizontally by errors in gestational age that originate from errors in CRL. A measurement error in fetal biometry which shifts the measurement vertically is illustrated in Figure 5.

The reference chart used to evaluate gestational age from CRL measurement has a significant impact on subsequent evaluation of biometry and estimation of fetal weight, as demonstrated recently by Fries *et al.*[32], contributing to the ongoing discussion about which charts and reference populations should be recommended[33,34].

As well as potential misclassification of growth, which is crucial for subsequent clinical management, identification and management of post-term pregnancies can also be affected by CRL measurement error[5]. In addition to the direct and indirect clinical impact of CRL measurement error, there is also an impact on research findings in studies involving CRL-based gestational-age/estimated-due-date data. Bias from ultrasound dating has been estimated to distort the relative risk of preterm or post-term delivery by 10–20%[35], and a recent commentary highlighted the effect of systematic misclassification of gestational age by ultrasound biometry on obstetric epidemiological studies from the Nordic countries[25]. From a resource perspective, growth/gestational-age misclassification due to CRL measurement error entails potential unnecessary follow-up examinations, which could be converted directly to unnecessary healthcare costs and use of resources, as well as a waste of time for the patients and their relatives.

Limiting the impact of crown–rump length measurement error

The method presented in this paper to assess the effect of CRL measurement bias on later biometry/EFW calculations suggests that this bias should be kept below 2 mm, which is in line with the findings of studies on the effect of CRL bias on first-trimester risk calculations for trisomy 21[13]. The need for quality management in fetal biometry has been recognized for decades[36], and different quality-assessment protocols, i.e. using PAPP-A[21] or image scoring systems[37,38], have been suggested. However, despite the increasing use of fetal biometry, most fetal biometric measurements are taken without a system for quality management. In contrast, quality management is an integral part of systems for biochemical measurement. This difference is likely to be a reflection of the way fetal biometric measurements are made by practitioners working autonomously to take measurements from individuals, whereas biochemical measurements are made within a laboratory setting in which quality-management systems have been well-established.

Conclusion

Because of the widespread and potential severe consequences of CRL measurement errors as small as 2 mm on clinical assessment, patient management and research results, there is a need to increase awareness of the impact of CRL measurement error and to reduce measurement error variation through standardization and quality control.

ACKNOWLEDGMENT

This project was supported by a Novo Nordisk Foundation grant (NNFSA170030576).

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Appendix S1 Supplementary methodology

Ultrasound Obstet Gynecol 2021; **58**: 354–359
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.23690

Error de medición de la longitud céfalo-caudal: impacto en la evaluación del crecimiento

RESUMEN

Objetivo Examinar el impacto del error de medición de la longitud céfalo-caudal (LCC) en el primer trimestre sobre la interpretación del peso estimado del feto (PEF) y la clasificación de los fetos como pequeño, grande o adecuado para la edad gestacional en las exploraciones posteriores del crecimiento.

Métodos Se examinaron los efectos de los errores de ±2, ±3 y ±4 mm en la medición de la LCC fetal sobre los percentiles del PEF a las 20, 32 y 36 semanas de gestación y la clasificación como pequeño, grande o adecuado para la edad gestacional. Se utilizaron datos publicados sobre el error de medición de la LCC para determinar la variación presente en la práctica.

Resultados Un error de medición de -2 mm en la LCC del primer trimestre desplaza un PEF en el percentil 10 en la exploración de la semana 20 a alrededor del percentil 20, y el efecto de un error de medición de la LCC de +2 mm desplazaría un PEF en el percentil 10 a alrededor del percentil 5. A las 32 semanas, un error de medición de la LCC en el primer trimestre desplazaría un PEF en el percentil 10 al percentil 7 (+2 mm) o al 14 (-2 mm); a las 36 semanas, un PEF pasaría del percentil 10 al 8 (+2 mm) o al 12 (-2 mm). Los datos publicados sugieren que los errores de medición de 2 mm o más son comunes en la práctica.

Conclusión Debido a las consecuencias generalizadas y potencialmente graves de los errores de medición de la LCC de tan solo 2 mm en la evaluación clínica, el tratamiento de las pacientes y los resultados de la investigación es necesario aumentar la conciencia sobre el impacto del error de medición de la LCC y reducir la variación del error de medición mediante la estandarización y el control de calidad.

顶臀长度测量误差：对生长评估的影响

摘要

目的 检查早期妊娠顶臀长度（CRL）测量误差对估计胎儿重量（EFW）的理解以及后续胎儿生长发育超声检测对小于胎龄儿、大于胎龄儿和适于胎龄儿分类的影响。

方法 我们检查了胎儿顶臀长度测量误差±2mm、±3mm 和±4mm 对在孕 20 周、32 周和 36 周的 EFW 百分位数的影响，以及对小于胎龄儿、大于胎龄儿和适于胎龄儿分类的影响。有关 CRL 测量误差的已发表数据被用于确定在实践中存在的变化。

结果 对早期妊娠 CRL 的-2mm 测量误差将孕 20 周超声检测的 EFW 从第 10 百分位数误算为约第 20 百分位数，而 CRL 的+2mm 测量误差的影响则是将 EFW 从第 10 百分位数误算为约第 5 百分位数。在孕 32 周，早期妊娠 CRL 的测量误差会将 EFW 从第 10 百分位数误算为第 7 百分位数（+2 mm）或第 14 百分位数（-2 mm）；在孕 36 周，EFW 从第 10 百分位数误算为第 8 百分位数（+2 mm）或第 12 百分位数（-2 mm）。已发表的数据表明，2mm 或更大的测量误差在实践中是常见的。

结论 由于在 CRL 测量误差（小至 2mm）在临床评估、患者管理和研究结果上的普遍性及潜在严重后果，有必要提高对 CRL 测量误差影响的意识并通过标准化和质量控制来减少测量误差变化。

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