Current knowledge on the use of ultrasound measurements of fetal soft tissues for the assessment of pregnancy development

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Abstract

Ultrasonography, with its detailed imaging of the fetus, is very widely used in obstetrics. The primary aim of ultrasound scanning in pregnancy is to limit the risk of obstetric complications by early detection of abnormalities, such as intrauterine growth restriction and macrosomia. Currently, morphometric formulae are used for estimating fetal weight. They utilize basic biometric parameters. However, Hadlock formula, used for fetal weight estimation, has an error rate of 20%. For this reason, researchers all over the world have been looking for other sonographic parameters correlating with fetal weight, with a higher predictive value. The current scientific reports indicate that new sonographic parameters, such as soft tissue thickness values, are useful for fetal weight assessment. The measurements can be conducted in various parts of the fetus's body, e.g. thigh, upper arm, abdomen or the subscapular area. Different types of measurements are characterized by different levels of correlation with other sonographic and anthropometric parameters as well as body mass and gestational age. Based on the reports, numerous studies proposing new fetal weight calculation formulae have been produced. Apart from soft tissue, some more advanced and detailed measurements are taken, such as those involving adipose and lean tissue or using three-dimensional ultrasound (3D), for determining fetal weight. Ultrasound measurement of subcutaneous tissue thickness in various parts of the body may prove to be a strong predictor of fetal weight, which is useful for sonographic assessment of pregnancy.

Introduction

Ultrasound is very widely used in obstetrics. It enables detailed imaging of the fetus, among other possibilities. However, it is different at every stage of pregnancy. The use of diagnostic ultrasound begins already at 4–5 weeks of gestation when it is possible to visualize the gestational sac in the uterine cavity. From approximately 5–6 weeks of gestation the embryo's echo is visible[1]. As the pregnancy develops, the number of assessed parameters and the level of difficulty of the ultrasound procedure increase.

The information acquired using this method concerning the developing embryo allow for the prediction, diagnosis and therapy of certain fetal pathologies. The advantages of diagnostic ultrasound primarily include non-invasiveness and ease of the procedure[1]. According to the latest reports, ultrasound scans performed during pregnancy are safe and do not affect fetal weight, premature labor risk, the child's condition at birth or perinatal mortality[2]. Sonography is also associated with certain limitations, especially when the visualization of the fetus is difficult due to unfavorable technical conditions, the mother's obesity, an-

terior placenta or oligohydramnios[3]. The primary aim of ultrasound scanning in pregnancy is to limit the risk of obstetric complications by early detection of abnormalities[1]. These include fetal growth abnormalities such as both intrauterine growth restriction (IUGR) and macrosomia, which are more common in pregnancies complicated by diabetes, obesity, hypertension, nicotine addiction or fetal genetic defects, among other conditions[1].

Fetal growth abnormalities

Over the last few years a larger proportion of neonates with high birth weight for gestational age has been observed. This phenomenon is called macrosomia, which can be defined as fetal weight exceeding 4500 g regardless of the fetal age or exceeding the 90th percentile for a given gestational age and population[1,4]. In pregnancies complicated by diabetes the estimated fetal weight exceeds 4200 g[4]. The prevalence of macrosomia in the general population is 6–14.5% and in women with diabetes 25–42%[5]. The risk factors for macrosomia, alongside maternal diabetes, include maternal obesity, post-term labor, a history of giving birth to macrosomic children, multiparity, advanced maternal age, male fetuses and hyperinsulinemia[4]. Macrosomia is associated with multiple complications, both for the mother and the fetus. For fetuses and neonates these are increased mortality, shoulder dystocia, perinatal trauma (including humerus and clavicle fracture and damage to the brachial plexus), low Apgar score, postpartum hypoglycemia, prolonged jaundice, systemic defects, respiratory problems, calcium deficiency and infections, among other conditions[1,4,5]. For mothers, macrosomia is associated with an increased risk of perinatal trauma such as pelvic diaphragm and anal sphincter damage as well as an increased risk of the delivery by cesarean section and of postpartum hemorrhage[1,4,5]. Early detection of macrosomia allows to avoid the above complications.

Another type of intrauterine growth abnormalities is intrauterine growth restriction. This term is assumed to refer to fetuses whose estimated body weight or abdominal circumference value is below the 10th percentile[6]. The possible cause of intrauterine growth restriction is considered to be impaired circulation of the fetoplacental unit, i.e. placental insufficiency[1,6]. The etiopathogenesis of this condition is still unknown, while the mechanisms responsible for intrauterine growth restriction can be classified as fetal, maternal, placental and environmental factors[1]. The most common factors include maternal age of > 40 years, the mother's short stature, low body mass, arterial hypertension, diabetes with vascular complications, nicotine addiction, obesity, kidney diseases, autoimmune diseases, anemia and cholestasis disease of pregnancy[1,6]. Fetuses with suspected growth deficiency include those with constitutional or genetically-related low body weight as well

as those with pathological conditions such as intrauterine growth restriction. Low birth weight represents an important problem in obstetrics since it is responsible for 69.6% of neonatal deaths and 66.4% of intrauterine deaths[7]. The best diagnostic method for this pathology is regular estimation of fetal weight or measurement of fetal abdominal circumference in high-risk pregnancies[6].

Estimated fetal weight

Currently, morphometric formulae are used for estimating fetal weight. They utilize basic biometric parameters such as biparietal diameter, head circumference, abdominal circumference and femur length[8]. Hadlock and Shepard formulae are most commonly used; however, they have certain limitations. The sensitivity and specificity of Hadlock formula in the detection of fetal macrosomia are 62% and 93%, respectively, and for Shepard formula they are 21% and 99%, respectively[9]. For this reason, researchers all over the world have been looking for other sonographic parameters correlating with fetal weight, with a higher predictive value. The examined fetal parameters include liver dimensions, cerebellar diameter, kidney length, upper arm soft tissue thickness, femur volume and cheek-to-cheek diameter[9–12].

Soft tissue measurements

Fetal abdominal and scapular soft tissue measurements

The current scientific reports indicate that new sonographic parameters such as soft tissue thickness values are useful for fetal weight assessment[4,9,11–14]. The measurements can be conducted in various parts of the fetus's body. For example, subcutaneous tissue thickness can be measured in the thigh, upper arm, abdomen or the subscapular area. Different types of measurements are characterized by different levels of correlation with other sonographic and anthropometric parameters as well as body mass and gestational age. Forouzumer *et al*. demonstrated a strong positive correlation between fetal abdominal soft tissue thickness (FASTT) in the third trimester of pregnancy and fetal weight ($r = 0.86$, $p < 0.001$)[13]. The study included 300 patients between 32 and 42 weeks of pregnancy. The study method involved ultrasound measurement of subcutaneous tissue at the anterior one third of the abdominal circumference between the outer and inner margin of echogenic subcutaneous tissue. The thickness of adipose tissue ranged between 3 mm and 14 mm with a mean of 6.7 mm ± 1.9[13]. Chen *et al*. conducted a more extensive study on 744 patients with physiological pregnancy[14]. They demonstrated that adipose tissue thickness measured in the

second and third trimester of pregnancy at the fetus's abdomen ($r^2 = 0.792$, $p < 0.0001$) and subscapular area ($r^2 = 0.302$, $p < 0.0001$) strongly correlates with fetal age. The method of abdominal adipose tissue measurement was similar to the method described earlier. Fetal subscapular soft tissue thickness (FSSTT) measurement was performed after the whole visualization of the scapula with the caliper positioned between the skin and the subcutaneous tissue margin, perpendicular to the lowest end of the scapula. A study by Rigano *et al.*, who compared three groups of patients: with physiological pregnancy, pregnancy complicated with class 1 gestational diabetes treated with diet and with class 2 gestational diabetes treated with diet and insulin, was even more informative[15]. They observed that birth weight was not significantly different for pregnancies of patients with a normal glucose-tolerance test and patients with gestational diabetes treated with diet and insulin, while for pregnancies complicated with diabetes treated with diet alone birth weight was much higher. Subcutaneous tissue thickness values were significantly different between patients with diabetes and patients with physiological pregnancy between 24 and 35 weeks of gestation, whereas between 36 and 40 weeks of gestation there were no statistically significant differences. In the conclusion to their study, the authors underline that subcutaneous tissue measurement can be another useful parameter for the assessment of diabetes management in pregnant patients[15].

Fetal humeral soft tissue thickness measurement

Fetal humeral soft tissue thickness (FHSTT) can also be measured. Al-Hilli demonstrated in her study that humeral soft tissue thickness is a more sensitive parameter, but less specific than Hadlock formula[3]. It also has a higher negative predictive value than the standard formula. FHSTT measurement involved the visualization of the humerus in the longitudinal section and then the rotation of the transducer by 90 degrees and itis movement towards the head of the humerus in order to measure soft tissues located just below it.

Fetal thigh soft tissue thickness measurement

Another new sonographic parameter is fetal thigh soft tissue thickness (FTSTT)[11]. To date there have been only single reports concerning this parameter; however, the results seem promising. According to Scioscia *et al.*, it strongly correlates with fetal abdominal circumference and birth weight[16]. This conclusion was made based on a study conducted in three stages with 290 patients in total (113, 108 and 69)[16]. The method of measurement involved visualizing the femur in the longitudinal section and freezing the image, and then measuring the distance between the

outer surface of the thigh and the outer surface of the femur, perpendicular to the bone, in its middle part. In the first phase of the study a linear relationship was confirmed between birth weight and head circumference (HC), biparietal diameter (BPD), abdominal circumference (AC), femur length (FL) and FTSTT. The next phase involved determining a new, modified formula for fetal weight estimation using FL and FTSTT measurement. In the last phase fetal weight estimation results obtained using three formulae, two of them well-known: Shepard and Hadlock and the new Scioscia formula were compared. The authors point to the higher accuracy of the new formula ($r = 0.79$), while stressing that both Hadlock and Scioscia formulae give satisfactory results (Bartlett's test: 4.53, $p > 0.05$)[16]. The use of fetal soft tissue measurements for the detection of macrosomia is also being investigated. Han *et al.* demonstrated the utility of FTSTT for the diagnosis of fetal macrosomia, with a sensitivity of 91% and specificity of 94%[17]. They also emphasized that FTSTT, which shows positive correlation with gestational age, can be more useful for fetal weight estimation than other sonographic parameters[17]. This is corroborated by Rotmensch *et al.*, who noticed that such parameters as fetal abdominal circumference, femur length and thigh subcutaneous tissue thickness were significantly higher in pregnancies with macrosomia[9]. The study also investigated a new index, which is the relationship between fetal thigh subcutaneous tissue thickness and femur length; however, no significant differences were demonstrated for macrosomic pregnancies ($p = 0.067$)[9]. In a study by Chauhan *et al.* FTSTT correlation as a predictor of high birth weight was not confirmed; however, as the authors note themselves, there was a large time discrepancy between the different ultrasound scans and delivery, which could have affected the accuracy of the study[10]. The topic of sonographic measurements of FTSTT in uncomplicated pregnancies and high-risk pregnancies was raised in a study by Abdalla *et al.*[18]. They noticed that the higher the FTSTT, the higher birth weight and length are. A statistically significant correlation between FTSTT and body mass of women before pregnancy and before delivery was demonstrated; however, no relationship between FTSTT and body mass increase during pregnancy or BMI of pregnant women was observed. Higher FTSTT values were found in neonates with higher birth weight between 38 and 40 weeks of pregnancy; however, no such relationship was observed for pregnancies at 37 and 41 weeks[18].

Use of fetal soft tissue measurements

Based on the reports above, numerous studies proposing new fetal weight calculation formulae have been produced[16,19,20]. Currently, fetal abdominal circumference is the strongest predictor of fetal weight[19]. However, it has a large risk of error, particularly when it is not possible to ensure optimal conditions for the measurement during the

scan[19]. Obtaining a high-quality ultrasound image is not easy, even for an experienced examiner. Measurements obtained from lower-quality visualizations have a larger error rate. For this reason, Scioscia *et al*. developed a new formula for estimating fetal weight[16]. Based on mathematical analysis they obtained a formula utilizing FL and FTSTT. The advantages of this formula include ease of examination and the possibility to perform measurements when the head of the fetus is located low in the pelvis and is inaccessible to the examiner[16]. Scioscia and Hadlock formulae were considered satisfactory to a similar extent in terms of the ability to estimate the actual fetal weight, with an absolute mean error rate below 15% in over 90% of cases[16,20]. These results are corroborated by a study by Abuelghar *et al*., who first verified the utility of Scioscia formula and then modified it to compare the results obtained using both formulae[20]. According to the authors, both formulae displayed a significant correlation with the neonate's birth weight; however, the strength of the original Scioscia formula was higher: $r^2 = 0.609$ ($p < 0.001$) for the modified formula, $r^2 = 0.957$ ($p < 0.001$) for the original one[20]. However, the results of a study by Barros *et al*. published in 2016 do not confirm this. They observed a weak correlation for weight estimated using the Scioscia formula, which is based only on FL and FTSTT[21]. They also found that using this formula leads to overestimation of larger fetuses and underestimation of smaller ones. The authors believe that the reason for the differences was a low number of macrosomic fetuses included in their study. In this study ultrasound scans were performed by resident physicians with different experience at the admissions department since the aim of the study was to check the use of the formula in such conditions. Kalantari *et al*. also worked on the development of new formulae for fetal weight estimation[19]. The study included various combinations of customarily used sonographic parameters and FTSTT. The formula in which AC, HC and FL were combined with FTSTT displayed the highest predictive strength ($r = 0.77$).

Apart from soft tissue, some more advanced and detailed measurements are taken such as those involving adipose and lean tissue. The results of such measurements are presented in a study by Bernstein *et al*. The measurement involved visualizing the longitudinal section of the long bones – the femur and humerus in this case, and rotating the transducer by 90 degrees in order to obtain the transverse section of the fetal bones[22]. Adipose tissue thickness was the difference between the total subcutaneous tissue and lean tissue thickness, i.e. muscle and bone thickness. The authors noted that both these parameters display a unique growth profile. Due to the accelerated fetal growth in late pregnancy these measurements can be a more sensitive and specific marker of fetal growth abnormalities. They were also used by Larciprete *et al*. and Galan *et al*., among others, as a more precise marker of fetal body structure[23,24].

In comparison with numerous studies on new sonographic measurements in physiological pregnancies and those complicated by macrosomia, only few publications concern FTSTT in pregnancies with IUGR. Balouet *et al*. conducted ultrasound scans on 232 fetuses, only 39 of which were estimated to be too small for gestational age (SGA) [25]. In this group of fetuses the sonographic assessment of thigh soft tissues had a high positive predictive value (74%) in relation to low birth weight with a sensitivity of 74% and specificity of 94%. A study by Larciprete *et al*. estimated adipose tissue and lean muscle tissue of the humerus and femur in addition to fetal abdominal and subscapular soft tissue measurement[23]. The authors of the study noticed significantly lower subscapular, abdominal and humeral subcutaneous tissue values in fetuses with intrauterine growth restriction. It is also one of the few studies which included patients with arterial hypertension (9 out of 14 examined patients had hypertension and 2 out of 14 had pre-eclampsia). An interesting observation in this regard may be a study by Galan *et al*., who studied two populations of pregnant women living at different altitudes 1600 m apart in absolute terms[24]. The authors noticed that abdominal, thigh and upper arm subcutaneous tissue thickness values were lower in the fetuses of mothers living in the region located higher. However, no differences in muscle tissue values were found between the two populations. A different opinion is presented by Hill *et al*., who studied 240 patients for fetal thigh, calf and abdominal subcutaneous tissue parameters. In 13 fetuses intrauterine growth retardation was demonstrated and in 38 high body weight was found. The authors concluded that sonographic parameters could not be treated as reliable predictors in either of the groups[26].

Use of 3D ultrasound

Alongside two-dimensional (2D) sonography researchers are trying to find ways of using three-dimensional ultrasound (3D) for determining fetal weight. The authors of one of the first studies on this subject were Chang *et al*., who created a fetal weight estimation formula based on the analysis of 3D measurements of the thigh. Their formula had a higher accuracy than the methods used to date which utilized 2D measurements. The absolute error rate of the authors' formula was 5.9%[27]. Similarly, Liang *et al*. performed 3D measurements of the upper arm which they used to estimate fetal weight with a higher accuracy than the standard methods[28]. Both studies were preliminary reports and 3D ultrasound measurements constituted the sole variable in the formula used. Schild *et al*., in contrast, developed a formula based on three-dimensional measurements of the abdominal, thigh and upper arm volume of the fetus as well as a standard BPD 2D measurement[29]. The new formula had a much lower mean error rate than

the standard formula based on 2D measurements. Even more precise estimation of body mass in small fetuses (below 1600 g) was achieved by combining 3D measurements with other biometric parameters of the fetus such as FL, HC and BPD[30]. The authors concluded that the use of 3D measurements for fetal weight estimation is more precise, but at the same time more time-consuming: the measurement of each limb lasted 10–15 minutes on average. In order to increase the utility of 3D ultrasound Lee *et al.* in their study aimed to reduce the time needed to perform the measurements to 10 seconds by using a commercial program[12]. A hybrid transducer was used for the examination, which allowed to obtain AC, FL and BPD from volume measurements. The authors concluded that combining AC and BPD measurements with upper arm or thigh volume is associated with more precision. The mean error of fetal weight measurement in relation to the actual fetal weight was 6.6%. In the case of the standard Hadlock formula it was 8.5%.

Conclusion

The correct determination of fetal weight is an important issue in obstetrics since it has a significant impact on the course and end of labor and delivery. Incorrect estimation of fetal weight can result in multiple, often dangerous complications both for the pregnant mother and the fetus. The currently used Hadlock formula for fetal weight estimation has an error rate of 20%, which may depend on the skills of the examiner, equipment base, conditions of the examination as well as the stage of pregnancy or labor. For this reason, new parameters that can be used to predict fetal weight are being reported. The aim of researchers around the world is to find a diagnostic parameter that has as small an error rate as possible, is quick to use and reproducible by different examiners. Fetal soft tissue thickness measurements, both two- and three-dimensional, may prove to be such a parameter. The current reports on the topic are not consistent; studies were often conducted on small groups of patients, which significantly limits the possible application of these measurements in the future. Ultrasound measurement of subcutaneous tissue thickness in various areas of the body may prove to be a strong predictor of fetal weight essential for sonographic assessment of pregnancy.

Conflict of interest

The authors do not report any financial or personal affiliations to persons or organizations that could negatively affect the content of or claim to have rights to this publication.

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Current knowledge on the use of ultrasound measurements of fetal soft tissues for the assessment of pregnancy development

55

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