ISUOG Practice Guidelines: performance of third-trimester obstetric ultrasound scan

Clinical Standards Committee

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INTRODUCTION

Systematic assessment of the impact of routine third-trimester ultrasound examination has provided robust estimates of its diagnostic accuracy for fetal anomalies, small-for-gestational age (SGA) and large-for-gestational age (LGA), as well as some adverse perinatal outcomes. This document outlines recommended guidelines for conducting third-trimester ultrasound examination, encompassing determination of placental location and fetal presentation, measurement of fetal biometry, identification of fetal anomalies, evaluation of amniotic fluid volume and documentation of fetal and uterine artery Doppler findings. The Guideline also addresses third-trimester screening for SGA and macrosomia and evaluates at which gestational age (GA)

the routine third-trimester ultrasound scan should be performed. Finally, it discusses certain situations, such as suspected vasa previa or the combination of low-lying placenta and previous Cesarean section, in which additional steps and detailed assessment should be included in the third-trimester ultrasound scan.

This Guideline does not address whether a third-trimester ultrasound scan should be offered routinely to all low-risk singleton pregnancies, as its availability differs according to resources, and clinicians should follow local guidelines. Furthermore, this Guideline does not address the content, frequency, or GA of third-trimester ultrasound scans in multiple pregnancy, as this is covered in detail in the ISUOG guideline on twin pregnancy[1]. Similarly, it does not address other pathologies or complications that would classify the pregnancy as 'high-risk', such as pre-eclampsia[2], diabetes and fetal growth restriction (FGR)[3], some of which are covered in other ISUOG guidelines. Details of the grades of recommendation and levels of evidence used in ISUOG Guidelines are given in Appendix 1.

THIRD-TRIMESTER ULTRASOUND SCAN

Indications for third-trimester ultrasound scan

The third-trimester ultrasound scan can assess fetal viability, presentation, anatomy and growth, amniotic fluid volume, placental location and fetoplacental Doppler. Less commonly, if the woman has not had a previous ultrasound scan, a third-trimester scan is useful for assessment of GA, or to exclude a suspected multiple pregnancy. There are multiple other indications that can trigger a third-trimester scan, including antepartum bleeding, reduced fetal movements, preterm rupture of the membranes and suspected abnormalities of fetal growth based on physical examination. In addition, ultrasound may be used to guide other procedures in the third trimester, such as external cephalic version. In some settings, routine third-trimester ultrasound may be offered to all women. However, as yet, there is no convincing evidence that routine universal third-trimester ultrasound examination in a

low-risk population improves either perinatal or maternal outcome.

Gestational age for third-trimester ultrasound scan

The optimal GA for performing the third-trimester scan is a trade-off between the optimal visibility of the fetal anatomy and the optimal accuracy of fetal growth assessment, and therefore depends on the objectives of the examination.

Traditionally, the third-trimester scan has been performed at 32–34 weeks. The anatomical examination may be technically easier at this stage, as the rapid growth of the fetus after this window may result in a more flexed position, a relative decrease in the quality of the acoustic window provided by the amniotic fluid and decreased penetration of the maturing fetal tissues, including increasing ossification of bones. On the other hand, the detection of growth deviations, both SGA and LGA, in low-risk cases may be more accurate towards 36 weeks[4–7], which has been an argument for moving the scan to this gestational stage. However, this would not apply to pregnancies at higher risk of complications, in which examination at around 32 weeks, or even earlier, has been proposed[8,9].

Therefore, the timing of the ultrasound scan between 32 and 36 weeks should be decided based on individual maternal and fetal characteristics, the risk level of the pregnancy and local objectives and resources.

Recommendation

- The timing of the third-trimester scan, if indicated, between 32 and 36 weeks, should be decided based on individual maternal and fetal characteristics, the risk level of the pregnancy and local objectives and resources (**GOOD PRACTICE POINT**)

Technique for third-trimester ultrasound assessment

The techniques for ultrasound assessment of fetal biometry and wellbeing, as well as amniotic fluid volume, in the third trimester are similar to those used in the second trimester[10] and should follow the ISUOG fetal biometry guideline[11]. Similarly, the techniques for Doppler ultrasound assessment in the third trimester are similar to those described for use in the second trimester[12]. These descriptions, tailored for use in the third trimester, are included in Appendices 2–4.

GA estimation may sometimes be necessary in late pregnancy, and was the subject of a recent systematic review[13]. In most cases, GA will have been determined at an earlier ultrasound examination, preferably in the first trimester. At 11–14 weeks' gestation, crown–rump length measurements have a half-width 95% prediction interval of around 5 days, meaning that the 'true' GA will be within ± 5 days of the estimated GA 95% of the time[13]. This is the most accurate dating available, and the pregnancy should not be redated using later scans. However, in

women presenting for the first time in the third trimester, the GA should be determined using head circumference (HC) plus femur length (FL), or HC alone, if FL is not available[14]. This method, though ranking highest in a recent systematic review[13], still has a variation of 15 days around the mean at 32 weeks. The head biometry (HC and biparietal diameter (BPD)) may be more difficult to measure accurately in late pregnancy, when the head is deeper in the maternal pelvis. A single-parameter formula using transcerebellar diameter, which is based on the relative sparing of this structure in growth abnormalities, has also been shown to have low 95% prediction[13,15].

Assessment of fetal wellbeing in the third trimester includes umbilical artery Doppler in high-risk pregnancies and, when indicated, should include additional Doppler parameters, such as middle cerebral artery (MCA), ductus venosus and maternal (uterine artery) Doppler velocimetry.

Equipment required for third-trimester ultrasound assessment

The equipment required for third-trimester ultrasound assessment is similar to that for second-trimester ultrasound examination[10] and should include, as a minimum, the following:

- real-time, grayscale ultrasound capability;
- transabdominal transducer with suitable resolution and penetration (usually 2–9-MHz range);
- adjustable acoustic power output controls with output display onscreen;
- freeze-frame capability;
- electronic calipers;
- capacity to print/store images;
- regular maintenance and servicing, important for optimal equipment performance;
- suitable cleaning equipment and cleaning protocols;
- color and pulsed Doppler;
- transvaginal transducer.

Fetal anomalies

Some fetal abnormalities will not be detected at the routine second-trimester anatomy scan, even with the best equipment in the most expert of hands. Broadly, there are two possible reasons for this: first, the anomaly was there but not seen, for example due to technical difficulties, such as increased maternal body mass index or fetal position; second, the natural history of some fetal abnormalities means that they develop or become visible only after the second-trimester scan; these are typically anomalies affecting the genitourinary tract, central nervous system (CNS) and heart.

Drukker *et al.*[16] performed a systematic review of 13 studies, including over 140 000 women, and reported a prevalence of 3.7 per 1000 women with fetal anomalies diagnosed in the third trimester, the most common being

urogenital, CNS and cardiac anomalies (accounting for 55%, 18% and 14%, respectively, of those diagnosed in the third trimester). Similar findings have been reported by several large observational studies and the EUROCAT registry[17–20]. A Cochrane systematic review of two randomized controlled trials (RCTs) comparing universal screening with clinically indicated screening in the third trimester found a greater detection rate of anomalies in the group universally screened[21]. Overall, there was no improvement as a result of universal screening in the neonatal survival rate, albeit the data stemmed from the early 1990s and may not reflect recent advances.

The potential benefits of diagnosing in the third trimester a fetal abnormality not identified at the second-trimester anomaly scan include the opportunity to: arrange for the birth to take place in a center that can provide the appropriate level of neonatal care; allow the parents time and counseling to prepare for the birth of a child with an anomaly; perform prenatal genetic analysis such as third-trimester amniocentesis for chromosomal microarray (CMA) or expand on tests already performed (e.g. expanding on CMA with prenatal exome sequencing); plan neonatal follow-up (which may be missed when the anomaly is not visible on routine neonatal clinical examination); and, where indicated and permitted legally, termination of pregnancy for anomalies with serious implications for the child.

A third-trimester structural examination could include the following.

- *Head*. The size and shape of the fetal head should be assessed. Microcephaly is commonly defined as HC smaller than −3SDs from the mean, and, when pathological, is usually associated with cortical anomalies and a sloping forehead. While fetuses with non-cephalic presentation may have a mild degree of positional elongation of the head (scaphocephaly or dolichocephaly), a marked deformation, especially when combined with a small HC, may be associated with craniosynostoses, as are other deformations (plagiocephaly, brachycephaly, trigonocephaly, cloverleaf skull).

- *Brain*. The symmetry of the hemispheres and the width of the lateral ventricles should be examined, and the texture of the cerebral cortex and parenchyma should be assessed (Figure 1). Intracranial anechoic or hyperechogenic areas are abnormal, as is a smooth cortex (agyria, lissencephaly) or a cortex with too many small (polymicrogyria) or few coarse (pachygyria) sulci. In some cases, anatomy of the brain cannot be seen by the transabdominal route and a transvaginal approach is required.

- *Heart*. The situs, size and symmetry of the heart should be assessed. The screening examination of the heart involves the four-chamber, outflow-tract and three-vessel-and-trachea views (Figure 2)[22]. Normal cardiothoracic circumference ratio in the third trimester is approximately 0.45 and should be no greater than 0.50. Mild asymmetry of the ventricles (right > left) and great arteries (pulmonary > aorta) may be normal in the third trimester, but warrants referral for fetal echocardiography if pronounced (Figure 3)[22].

- *Chest*. The diaphragm should be examined in sagittal and coronal views (Figure 4) (approximately 20% of congenital diaphragmatic hernias are detected only in the third trimester[19]). In addition to cardiac situs, lung texture should be assessed in a transverse view of the chest.

- *Abdomen*. Fluid collections, calcifications and cystic structures should warrant further investigation (Figure 5). Bowel dilatation is a common phenomenon during the third trimester and most pathologies are associated with small bowel dilatation > 14 mm[23].

- *Urinary system*. Approximately 60% of cases of hydronephrosis are detected in the third trimester[19]. Conventionally, the upper normal limit for a renal pelvic anteroposterior (AP) diameter in the third trimester is 7 mm, and an AP diameter > 15 mm is associated with an increased risk for need of postnatal surgery[24,25]. Dilatation of renal calyces and the thickness of the cortex should also be assessed,
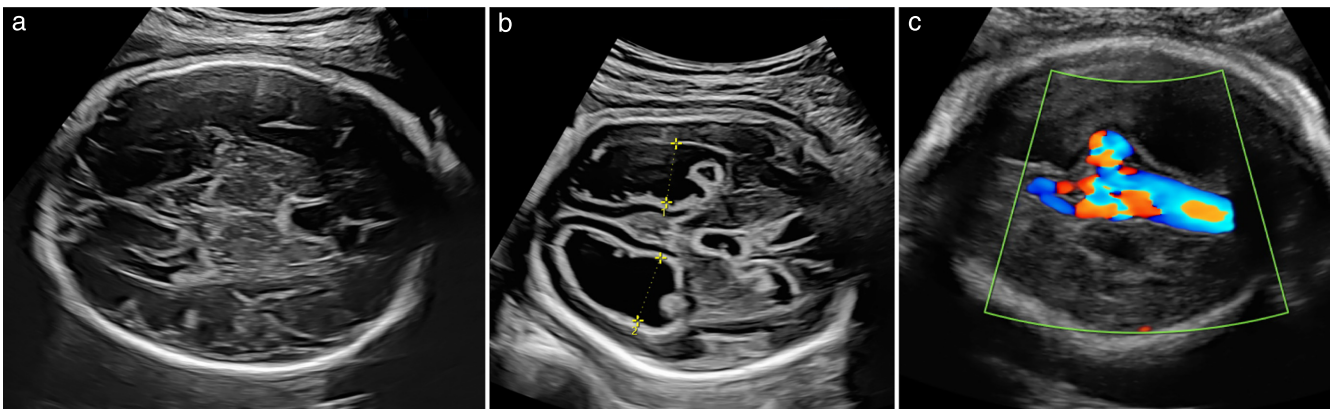

Figure 1 (a) Normal fetal brain configuration on ultrasound imaging in third trimester. (b) Dilatation of third and lateral ventricles, with intraventricular echogenic material (intraventricular hemorrhage Grade 3). (c) Color flow in tubular area that appeared anechoic on B-mode imaging, at midline in posterior part of base of skull (vein of Galen aneurysm).
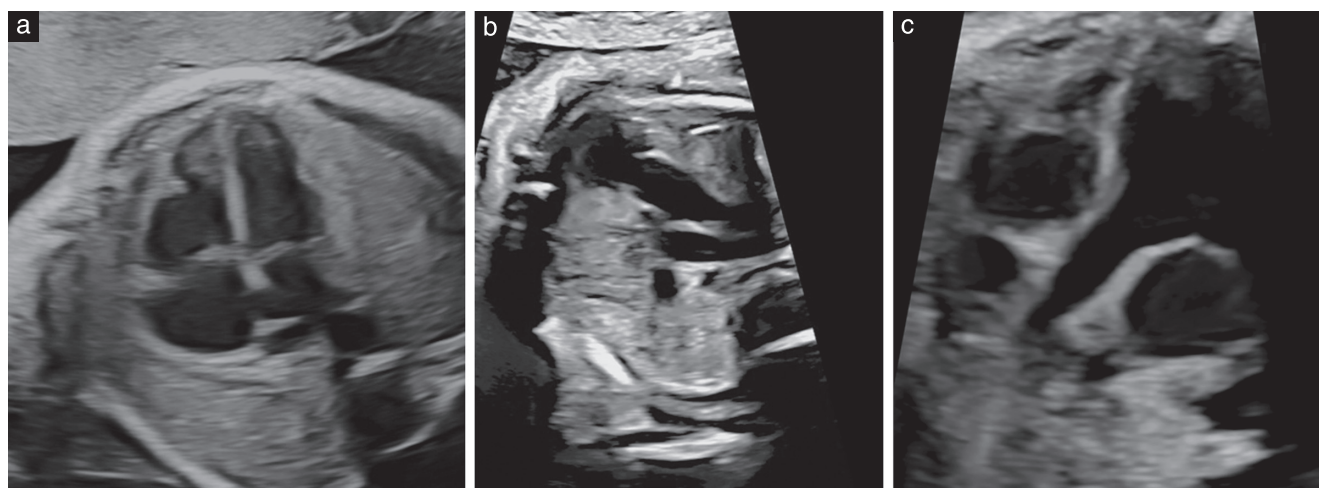
Figure 2 Normal cardiac views in third trimester. (a) Four-chamber view, illustrating symmetry of left and right cardiac chambers. Right-heart elements may appear slightly bigger than left-heart elements, but marked asymmetry should prompt detailed evaluation. (b) Three-vessel-and-trachea view. (c) Left outflow-tract view.

Figure 3 Aorta being significantly smaller than ductus arteriosus on three-vessel view may be indicative of coarctation of the aorta.

as they are associated with postnatal persistence of hydronephrosis (Figure 6)[26]. In the presence of hydronephrosis, the ureters (normally invisible) and the bladder size, wall thickness and emptying should also be assessed.

Recommendations

- Depending on the objectives of the third-trimester scan, anatomical evaluation may be undertaken and, if this is done, should target examination of the head, brain, heart, chest, abdomen and urinary system (**GRADE OF RECOMMENDATION: C**)

Placenta previa

The location of the placenta should be examined in any scan performed in the third trimester. The placental position and its relationship with the internal cervical os should be identified, and the distance of the leading edge of the placenta from the internal cervical os should be documented. Placenta previa represents a risk factor for velamentous cord insertion and vasa previa and these anomalies should be ruled out when assessing women with suspected placenta previa in the third trimester. If the placenta is low, subsequent scans are performed as indicated, to assess whether the placenta has moved clear of the internal cervical os (Figure 7). Women with major placenta previa or a uterine scar may be offered a scan at around 28 weeks, while women with minor placenta previa may be assessed later in the third trimester. Transvaginal ultrasound allows more accurate localization of the placental site, particularly when the transabdominal approach is challenging, such as when the placenta is posterior, or in the presence of maternal obesity or uterine fibroids. A small RCT by Sherman *et al.*[27] ($n = 38$) compared the performance of transabdominal and transvaginal ultrasound in the diagnosis of placenta previa. Randomization was stratified by patient weight and anterior or posterior placental location. Overall, transvaginal ultrasound had a 99% positive predictive value, 98% negative predictive value and 2.3% false-negative rate for diagnosing placenta previa in women in whom this was suspected on transabdominal ultrasound in the second or early third trimester[27,28]. Another study, by Ghi *et al.*[29] ($n = 59$), found that women with placenta previa who had a cervical length ≤ 31 mm on third-trimester ultrasound examination were at increased risk of hemorrhage requiring Cesarean section before 34 weeks' gestation (sensitivity, 83%; specificity, 77%). In particular, the odds ratio for suffering massive hemorrhage requiring emergency Cesarean section was 16.4 (95% CI, 3.4–75.9) in women who had a sonographic diagnosis of placenta previa and a cervical length ≤ 31 mm.

In general, if the leading placental edge is 20 mm or more from the internal cervical os, vaginal birth is considered a safe option. Vaginal birth may also be
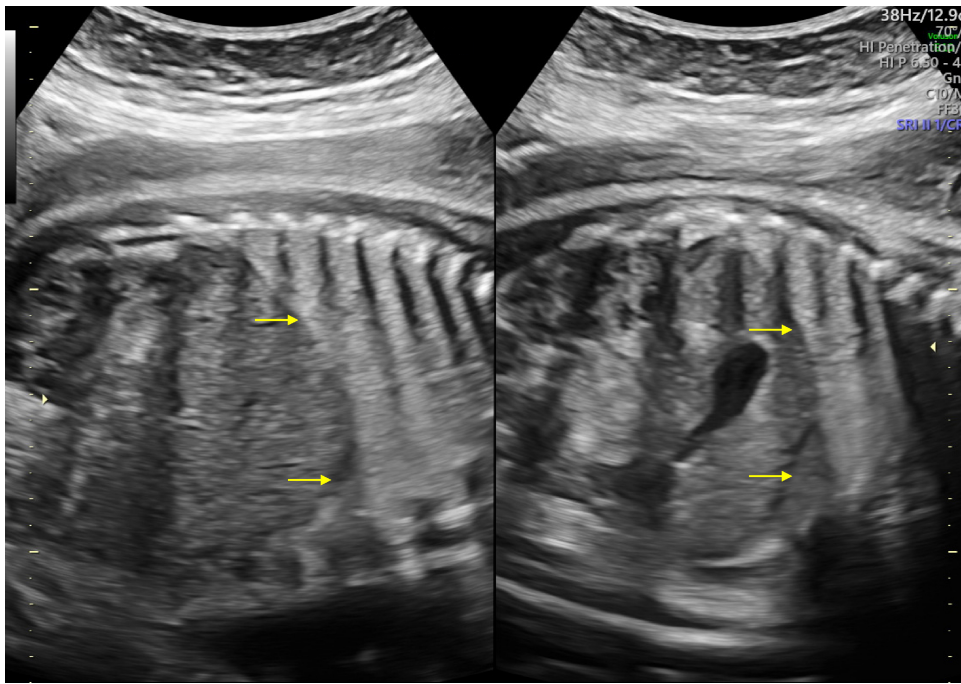
Figure 4 Examination of right and left fetal hemidiaphragm (arrows) in longitudinal view.
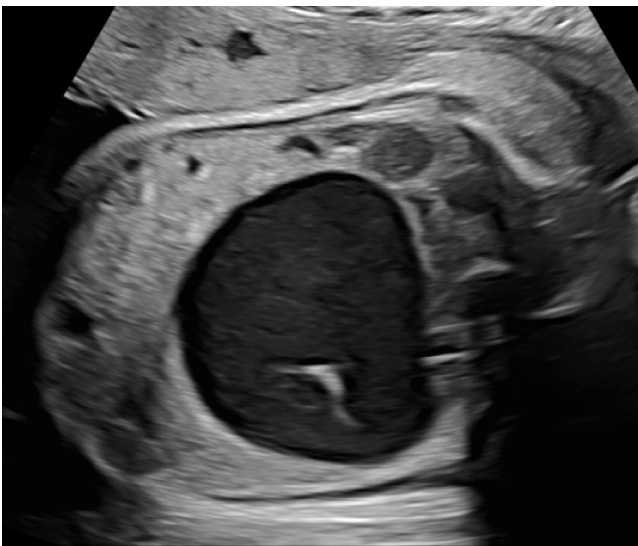

Figure 5 Large fetal ovarian cyst, with incomplete septum and hypoechoic content, indicative of endocystic bleeding (complicated cyst).

considered when this distance is between 10 and 20 mm at 36 weeks' gestation; in these women, the chances of successful vaginal birth ranged from 56% to 93%[28,30]. However, the studies demonstrating this had significant limitations, including small sample sizes, retrospective nature and an observational study design.

Recommendations

- Assessment of placental location should be a component of third-trimester ultrasound (**GRADE OF RECOMMENDATION: C**). Women diagnosed with a low-lying placenta or placenta previa at the routine second-trimester scan should have a follow-up assessment for placental location in the third trimester.
- Women with major placenta previa or a uterine scar may be offered a scan at around 28 weeks, while women with minor placenta previa may be assessed later in the third trimester (**GOOD PRACTICE POINT**)
- The transvaginal approach is preferred in cases of suspected posterior placenta previa (**GRADE OF RECOMMENDATION: B**)

Placenta accreta spectrum

Third-trimester assessment of the placenta is recommended if there is evidence that the lower placental edge reaches or overlaps the internal cervical os at the time of the routine anomaly scan[10]. Conversely, systematic screening for vasa previa or velamentous cord insertion is not recommended in the third trimester, in view of the technical difficulties and lack of robust evidence regarding its usefulness[31,32].

A prior Cesarean birth or uterine surgery, including myomectomy or multiple curettages, in the setting of placenta previa is associated with an increased risk of placenta accreta spectrum (PAS) disorders, which occur when the gestational sac implants and the definitive placenta develops within a uterine scar area[33]. The risk of PAS increases with the number of prior Cesarean sections and ascertainment of the placental position is therefore warranted in these women[34,35]. Prenatal diagnosis of PAS is associated with reduced hemorrhagic morbidity and every woman presenting with clinical risk factors of PAS should be referred for specialized assessment[36]. The diagnostic accuracy of third-trimester prenatal ultrasound in identifying women at high risk
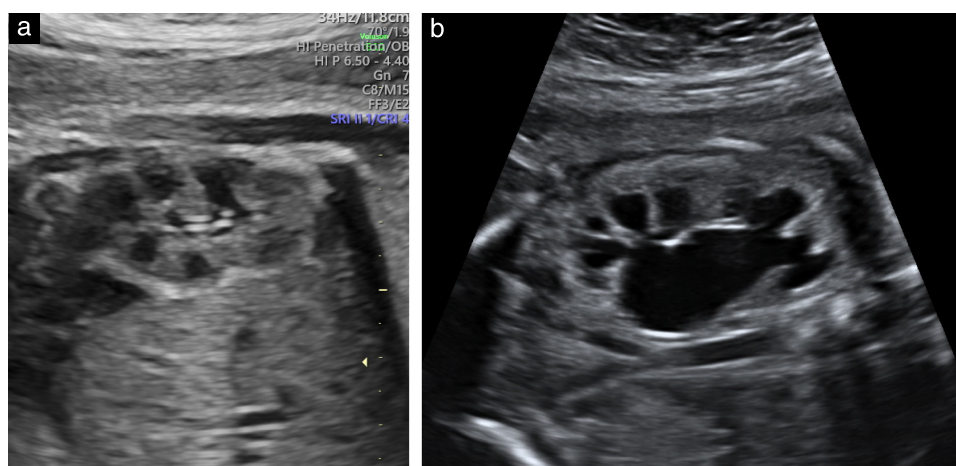
Figure 6 (a) Normal configuration of fetal kidney in third trimester (longitudinal view). Hypoechogenic areas in periphery are renal pyramids. (b) Severe hydronephrosis (coronal view), with dilatation of calyces and thinning of renal cortex.
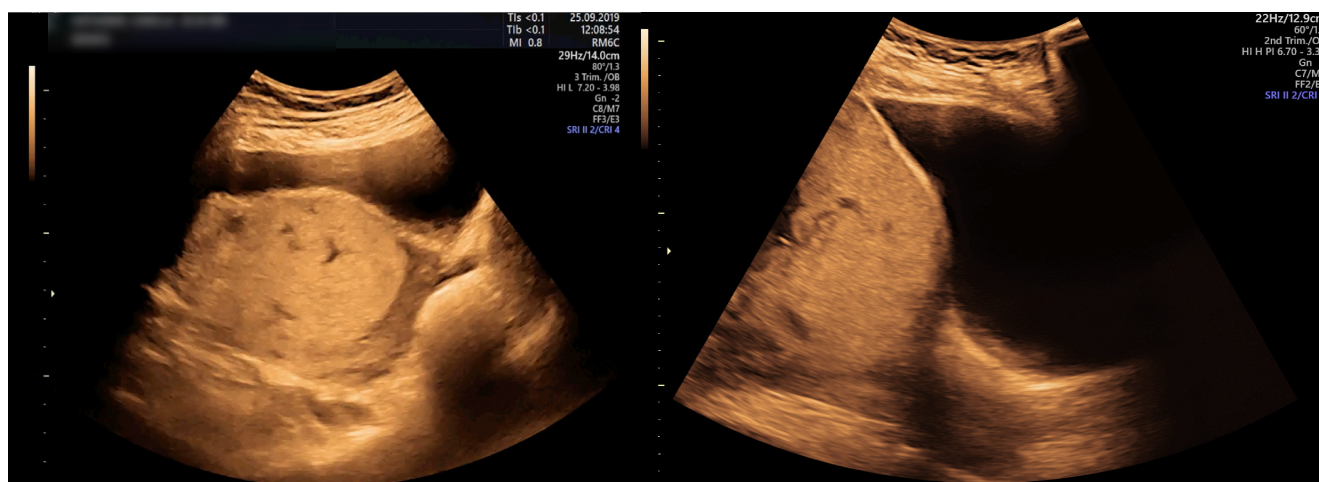

Figure 7 Low-lying placenta. If leading placental edge is 20 mm or more from internal cervical os, vaginal birth is considered a safe option. However, safe vaginal birth may also occur when this distance is between 10 and 20 mm at 36 weeks' gestation.

of PAS has been reported to be around 90% in recent series[37,38]. However, 5–10% of pregnancies complicated by PAS are detected only at the time of Cesarean birth[37,38]. Furthermore, there is still heterogeneity in the reported ultrasound signs associated with PAS. Therefore, irrespective of ultrasound examination, every woman with placenta previa and a prior Cesarean birth or uterine surgery should be considered as a potential case of PAS and managed by a multidisciplinary team in a center with experience in the surgical management of morbidly adherent placenta.

A consensus reached by experts[39] was that the following ultrasound signs of PAS should be assessed in the detailed ultrasound examination to rule out PAS: loss of the retroplacental 'clear zone', myometrial thinning, bladder-wall interruption and the presence of a placental bulge, exophytic mass, uterovesical hypervascularity, placental lacunae and bridging vessels (Figure 8). The optimal combination of ultrasound signs to confirm PAS has not been fully established. A normal hypoechogenic space between the uterus and the placenta is associated

with a reduced risk for clinically significant PAS: from 21% to 5% in women with low-lying placenta or placenta previa in the third trimester of pregnancy, and from 62% to 9% in the subgroup with previous Cesarean section and anterior placenta. An interrupted hyperechogenic interface between the uterine serosa and bladder wall increased the post-test probability of clinically significant PAS from 21% to 85% in women with low-lying placenta or placenta previa and from 62% to 88% in the subgroup with previous Cesarean section and anterior placenta. The presence of multiple ultrasound signs of PAS increases up to 92% the probability of clinically significant disorder in women with previous Cesarean section and anterior placenta[40].

Magnetic resonance imaging (MRI) is a complementary tool with which to assess women at risk of PAS disorders[37,41]. Although the overall diagnostic accuracy of MRI in identifying women at high risk of PAS is no different from that provided by ultrasound, MRI should be considered in the case of inconclusive ultrasound diagnosis or in cases of severe PAS, especially when
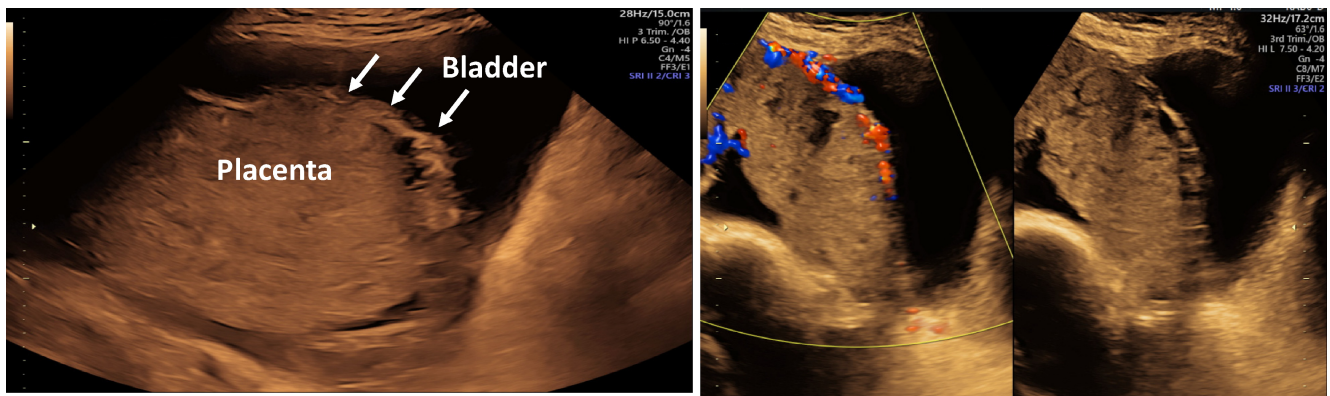
Figure 8 Placenta accreta spectrum. (a) Thickened placenta (arrows) abutting bladder. (b) Placental lacunae with irregular uterovesical interface.

parametrial invasion is suspected, in view of the higher accuracy of MRI in describing the topography of placental extension when compared with ultrasound. MRI is not recommended in cases of placenta previa with no other risk factor for PAS, in view of the low prevalence of morbidly adherent placenta in these pregnancies. Conversely, MRI should be considered in women at risk for PAS in uncommon locations, including those with posterior placenta previa and prior uterine surgery and in those with placental implantation in the area of a myomectomy scar[42]. Longitudinal assessment of fetal growth in the third trimester is not required in women with placenta previa or PAS, unless other risk factors coexist, as the risk of FGR does not seem to be associated independently with morbidly adherent placenta[43].

Recommendations

- Women with placenta previa and prior Cesarean birth or uterine surgery should undergo a detailed ultrasound assessment to rule out PAS disorders (**GRADE OF RECOMENDATION: C**)
- Irrespective of ultrasound findings, a woman with placenta previa and a prior Cesarean birth or uterine surgery should be considered as a potential case of PAS and managed in a center with experience in the surgical management of morbidly adherent placenta (**GOOD PRACTICE POINT**)
- MRI can be considered in pregnancies at risk for PAS in uncommon locations, including pregnancies with posterior placenta previa and prior uterine scarring or if the placenta is implanted in the area of a prior myomectomy (**GOOD PRACTICE POINT**)
- MRI can be considered in the case of inconclusive ultrasound diagnosis or in cases of severe PAS, especially when parametrial invasion is suspected (**GOOD PRACTICE POINT**)
- Longitudinal assessment of fetal growth is not required in women with placenta previa or PAS unless other risk factors coexist (**GRADE OF RECCOMENDA-TION: C**)

Vasa previa

Vasa previa occurs when unprotected fetal vessels (arterial or venous) traverse the membranes overlying the cervix[44], and it is associated with increased perinatal mortality (56%) when not diagnosed prenatally[45]. When it is diagnosed during pregnancy, the perinatal survival is almost 100%, with normal long-term outcomes[45–47]. Ultrasound, in particular transvaginal ultrasound combined with color Doppler, is an accurate tool for the diagnosis of vasa previa (sensitivity, 100%; specificity, 99.0–99.8%)[31]. Vasa previa is characterized by demonstration on transvaginal ultrasound with color Doppler of the umbilical cord inserting into membranes over the cervix, from where unprotected vessels run into the placenta (Figure 9).

The ISUOG guideline on the routine mid-trimester scan states that, in the presence of risk factors for vasa previa, a targeted examination using a transvaginal approach is recommended, depending on experience and resources[10]. The same recommendation can be extended

Figure 9 Vasa previa, defined as unprotected fetal vessels traversing membranes overlying the cervix, or crossing at a distance < 20 mm from internal cervical os.

to the third-trimester scan. These risk factors include placenta previa, second-trimester low-lying placenta, bilobed placenta or placenta with succenturiate lobes, and multiple gestation[28,48]. Ruiter *et al.*[49] in 2016 conducted a systematic review of 13 studies, including 569 410 women. Only two of these were prospective cohort studies; 10 were retrospective cohort studies and one was a case–control study. Of the 325 cases of vasa previa identified, 83% had one or more identifiable risk factors, including placenta previa, bilobed placenta, succenturiate placental lobe, velamentous insertion of the cord or assisted conception, supporting more focused ultrasound assessment of women with one or more of these risk factors, where feasible.

The overall rate of resolution of vasa previa (defined as distance > 20 mm from the internal cervical os) between the second and third trimesters is 23%, depending on factors such as the GA and precise position of the vessels at detection, and the location of the placenta[50,51]. Therefore, when vasa previa has been identified at earlier scans, a reassessment in the third trimester is recommended.

Recommendations

- In the presence of risk factors for vasa previa, a targeted examination using a transvaginal approach is recommended, depending on experience and resources (**GRADE OF RECOMMENDATION: B**)
- When vasa previa has been identified earlier in the pregnancy, reassessment in the third trimester is recommended (**GOOD PRACTICE POINT**)

Breech presentation

Undiagnosed breech presentation at term is associated with an increased risk of perinatal morbidity and mortality. A large study by Wastlund *et al.*[52] published in 2019 assessed 3879 nulliparous women who underwent a research ultrasound examination at 36 weeks' gestation. Breech presentation was diagnosed in 179 (4.6%) of these women at the 36-week scan. In most ($n = 96$) of those women, there was no prior suspicion that the presentation was not cephalic. External cephalic version was offered to all women for whom this was appropriate and was attempted in 84 (46.9%). There was no woman in the entire cohort with undiagnosed breech presentation in labor. Their economic analysis demonstrated that, compared with the current practice of clinically indicated scans, universal near-term ultrasound would virtually eliminate undiagnosed breech presentation in labor and would reduce emergency Cesarean section and vaginal breech birth by 0.7 and 1.0 percentage points, respectively. Such a policy would also reduce the incidence of breech-associated neonatal morbidity and mortality. On average, 40 ultrasound scans are needed to detect one previously undiagnosed breech presentation. Wastlund *et al.*[52] calculated that such a policy would be cost-effective if fetal presentation could be assessed for £19.80 or less per woman.

A more recent study by Knights *et al.*[53] investigated the impact of facility-based third-trimester ultrasound examination and point-of-care ultrasound (POCUS) on undiagnosed breech presentation at term and associated perinatal outcomes in an observational multicenter cohort study. During the study period, all included women received a third-trimester scan. In the institution-based ultrasound cohort, the percentage of all term breech presentations that were undiagnosed was 14.2% before and 2.8% after implementation of a universal screening policy. In the POCUS cohort, the equivalent before and after figures were 16.2% and 3.5%, respectively. Bayesian regression analysis showed that the rate of undiagnosed breech presentation was reduced by 71% following implementation of a universal ultrasound screening policy. This reduction in undiagnosed breech presentation was associated with a moderate-to-high probability of a reduction in: low (< 7) Apgar score at 5 min; hypoxic ischemic encephalopathy (HIE); and perinatal mortality rates.

Given the findings of these two studies[52,53], future studies should focus on exploring the cost-effectiveness of POCUS to determine fetal presentation, given its significantly lower cost compared with facility-based ultrasound examination.

Recommendation

- As ultrasound examination of fetal presentation close to or at the time of delivery can reduce the risk of undiagnosed breech presentation, such an examination should be considered if resources are available (**GRADE OF RECOMMENDATION: B**)

Fetal growth abnormalities

Disorders of fetal growth are associated with increased perinatal mortality and morbidity, as well as long-term developmental abnormalities[3,54].

Large-for-gestational age/macrosomia

As stated in the ISUOG guideline on the assessment of fetal biometry and growth[11], LGA fetuses are typically defined as those with estimated fetal weight (EFW) (or abdominal circumference (AC)) > 90th centile, while macrosomia at term usually refers to a weight above a fixed cut-off (4000 or 4500 g). The main rationale for predicting macrosomia is its association with pregnancy complications, mostly shoulder dystocia.

A systematic review and meta-analysis[55] which included 41 studies and a total of 112 034 women reported that an EFW > 4000 g (or > 90th centile) and AC > 36 cm (or > 90th centile) had a sensitivity of more than 50% in predicting macrosomia at birth (birth weight > 4000 g or > 90th centile), with positive likelihood ratios of 8.74 (95% CI, 6.84–11.17) and 7.56 (95% CI, 5.85–9.77),

respectively. An EFW > 4000 g (or $> 90^{th}$ centile) also had a sensitivity of 22% in predicting shoulder dystocia with a rather modest positive likelihood ratio of 2.12 (95% CI, 1.34–3.35). There were insufficient data to assess other adverse neonatal outcomes associated with fetal macrosomia.

Al-Hafez *et al.*[56], in a systematic review including seven RCTs and 23 643 women, compared detection of LGA (EFW $> 90^{th}$ centile) by routine ultrasound examination with that by serial measurements of the symphysis–fundus height (SFH). They found that the rate of identification of LGA was higher in the routine ultrasound group (30%) compared with that in the serial SFH measurement group (11%), although there was no significant difference in the incidence of LGA at birth (9% in both groups). The same meta-analysis did not find a significant difference in perinatal mortality rate between the two groups (ultrasound group, 0.4% *vs* SFH group, 0.3% (relative risk (RR), 1.14; 95% CI, 0.68–1.89))[56]. Nor were there any significant differences between the two groups in terms of the rates of stillbirth or neonatal death. However, this meta-analysis did not have the power to identify a statistically significant difference in mortality outcomes. Other adverse neonatal outcomes were included as secondary outcomes. No statistically significant differences were identified between the two groups as regards need for resuscitation, admission to a neonatal intensive care unit (NICU), respiratory distress syndrome, Grade 3 or 4 intraventricular hemorrhage or neonatal sepsis.

A secondary analysis of universal ultrasound screening[57], including 3866 nulliparous women, showed that the sensitivity for detection of LGA infants was 27% for selective ultrasonography and 38% for universal ultrasonography. The specificity of both approaches was high (99% and 97%, respectively). Using universal ultrasonography to assess AC growth velocity (ACGV), it was found that, relative to AGA fetuses, LGA fetuses with increased ACGV were at increased risk of any neonatal morbidity (RR, 2.0; 95% CI, 1.1–3.6; $P = 0.04$) and of severe adverse neonatal outcome (RR, 6.5; 95% CI, 2.0–21.1; $P = 0.01$), but LGA fetuses with normal ACGV were not at increased risk.

Screening for LGA is apparently more accurate when performed later in pregnancy. In a large observational study[6], EFW $> 90^{th}$ centile at $35 + 0$ to $36 + 6$ weeks could predict 46% and 65% of LGA $> 90^{th}$ and LGA $> 97^{th}$ centile, respectively, for a screen-positive rate of about 10%[6]. The detection rates were even higher (71% and 84%, respectively) when birth occurred within 10 days following the scan.

Even though routine ultrasound in a low-risk population is predictive of LGA at birth, and performs better than does serial measurement of SFH, it is still debated whether prenatal identification of macrosomia improves perinatal outcome. In a RCT, induction of labor for suspected LGA reduced the risk of shoulder dystocia and associated morbidity, compared with expectant management. Notably, induction of labor in this RCT improved the chance of vaginal delivery and did not increase the risk of Cesarean section[58,59]. Healthcare professionals should balance, as well as discuss with pregnant women, these possible benefits against the potential adverse effects of early-term induction of labor.

Recommendations

- Screening for LGA in the general population may be more accurate when the examination is performed at 36 rather than 32 weeks (**GRADE OF RECOMMENDATION: B**)
- Health professionals should balance the benefits of induction of labor for perceived macrosomia with respect to shoulder dystocia and fractures against the potential adverse effects of early-term delivery (**GOOD PRACTICE POINT**)

Small-for-gestational age/fetal growth restriction

According to the ISUOG guidelines[3,11], SGA is defined as EFW (or AC) $< 10^{th}$ centile, whereas late FGR is defined, according to the 2016 Delphi criteria[60], as a structurally normal fetus with either very small size (EFW or AC $< 3^{rd}$ centile) or with small size ($< 10^{th}$ centile) and Doppler signs suggestive of hypoxia or decelerating growth. The overall prediction rate of SGA/FGR depends on the type of population, definitions and index test, as well as the timing of the third-trimester scan[61]. A meta-analysis of 21 studies in low-risk/unselected populations showed that, for a specificity of about 95%, EFW $< 10^{th}$ centile could predict 38% of cases with birth weight $< 10^{th}$ centile, 54% of cases with birth weight $< 3^{rd}$ centile and 70% of those with FGR[4]. Measurement of AC had similar performance.

While, traditionally, the third-trimester scan has been performed at 32–34 weeks, it appears that a scan later in pregnancy is more effective in predicting SGA/FGR. Two RCTs[7,62] have shown that a scan at around 36 weeks is more effective at detecting FGR than is a scan closer to 32 weeks. The detection rate (39% *vs* 22%)[62], as well as the overall accuracy[7], was higher at the later compared with the earlier scan. A large prospective observational study[5] of 22 000 fetuses showed that the sensitivity of EFW $< 10^{th}$ centile to predict birth weight $< 10^{th}$ centile and birth weight $< 3^{rd}$ centile was 46% and 65%, respectively, when the scan was performed between $35 + 0$ and $36 + 6$ weeks (*vs* 38% and 52%, when the scan was performed between $31 + 0$ and $33 + 6$ weeks). The sensitivity of the late scan was even higher (70% and 84%, respectively) when delivery occurred within 2 weeks following the scan.

Ultrasound assessment of fetuses at increased risk of FGR has the ability to identify those at greatest risk of perinatal complications, and patients with more than double the risk of FGR compared to the general population should undergo evaluation of fetal biometry

and fetal Doppler earlier than the third trimester, between 26 and 28 weeks' gestation[8].

While parameters like uterine artery Doppler and cerebroplacental ratio[63], longitudinal fetal growth assessment[64] and a third-trimester combined screening test[65] may not substantially improve the prediction of SGA/FGR when used in isolation compared to cross-sectional determination of EFW, they constitute key components of the Delphi criteria for diagnosing FGR.

Recommendations

- Screening for SGA/FGR in the general population is more accurate when the examination is performed at 36 rather than 32 weeks (**GRADE OF RECOMMENDATION: B**)
- EFW and AC can be used to screen for SGA/FGR with similar performance (**GRADE OF RECOMMENDATION: C**)

Abnormalities of amniotic fluid volume

The amniotic fluid volume can be assessed semiquantitatively using either amniotic fluid index (AFI) or deepest vertical pocket (DVP). The technique for measuring AF pockets, as described in the ISUOG guideline on the routine mid-trimester scan[10], involves: holding the ultrasound transducer perpendicular to the maternal abdomen; identifying clear boundaries of the upper and lower edges of the pocket of fluid; measuring the largest unobstructed amniotic fluid pocket that is at least 1 cm wide; and using color Doppler to establish absence of the umbilical cord for pools of amniotic fluid where this is not certain (Appendix 3). Typically, oligohydramnios is defined as AFI < 5 cm or DVP ≤ 2 cm[66,67], while polyhydramnios is defined as AFI > 25 cm, or DVP > 8 cm[66,68,69], although GA-specific charts have also been used. Degrees of severity of polyhydramnios have also been proposed for categorization (mild: AFI, 25–30 cm; moderate: AFI, 30.1–35.0 cm; severe: AFI ≥ 35.1 cm), as there seems to be an association between severity and the likelihood of underlying conditions[70,71].

While AFI and DVP have been used interchangeably, AFI may be preferable in assessing polyhydramnios, while DVP may be preferable in assessing oligohydramnios[10,72]. It should be noted that reproducibility of both methods is similarly poor, with wide limits of agreement[73].

Oligohydramnios may be associated with pathology of the fetal urinary system, rupture of the membranes or FGR, or it can be idiopathic. Therefore, recognition of oligohydramnios should lead to a focused anatomical and growth survey, as well as targeted history of fluid loss. The significance of idiopathic oligohydramnios is uncertain; a study defining oligohydramnios as AFI ≤ 5 cm (*n* = 6432 pregnancies, 147 with oligohydramnios) did not report any effects on rate of Cesarean delivery for labor intolerance, NICU admission and neonatal death[74], whereas an older study of 7582 high-risk pregnancies, which defined oligohydramnios as DVP ≤ 2 cm, showed that perinatal mortality increased with decreasing DVP[66,75]. A more recent meta-analysis showed that, compared with pregnancies with normal AFI, those with isolated oligohydramnios had increased risk for meconium aspiration (RR, 2.83), Cesarean delivery for fetal distress (RR, 2.10) and NICU admission (RR, 1.71), while there were too few data to assess the risk for stillbirth[76]. The optimal management of idiopathic oligohydramnios at term is also uncertain. In a small RCT, 87 pregnant women with oligohydramnios beyond 40 weeks were randomized to either induction or expectant management; the perinatal outcomes did not differ between the two arms[77]. A larger multicenter study randomized 1052 pregnant women with a term singleton pregnancy to groups with oligohydramnios defined by either DVP (< 2 cm) or AFI (≤ 5 cm); diagnosis of oligohydramnios was followed by induction of labor. Using AFI resulted in more inductions for oligohydramnios (12.7% *vs* 3.6%) and more frequent abnormal cardiotocography tracings (32.3% *vs* 26.2%), while the rates of NICU admission were similar in the two groups (4.2% *vs* 5.0%)[78].

Polyhydramnios (Figure 10) may be associated with maternal diabetes (20–25% of cases), fetal abnormalities (mostly gastrointestinal obstructions and cardiac and CNS anomalies), placental tumors, fetal infections, conditions that result in anemia and hyperdynamic circulation, and chromosomal and genetic abnormalities, or it can be idiopathic (50–60% of cases)[79,80]. Therefore, identification of polyhydramnios should lead to a detailed sonographic examination of the fetus and placenta, examination for signs of anemia (including MCA peak systolic velocity) and review of the results of any previous screening tests for fetal aneuploidy or congenital infection, as idiopathic polyhydramnios is a diagnosis of exclusion. Although the chance of identifying an underlying cause at initial investigation is not associated with the severity of polyhydramnios, the likelihood of a residual, unrecognized cause increases with increasing severity[70,71]. Even when apparently isolated, polyhydramnios is associated with increased risk of perinatal complications. A recent meta-analysis pooling data from 2392 patients with idiopathic polyhydramnios and 160 135 patients with normal amniotic fluid volume showed that the former were at higher risk of neonatal death (odds ratio (OR), 8.7), intrauterine fetal demise (OR, 7.6), NICU admission (OR, 1.9), macrosomia (OR, 2.9) and Cesarean delivery (OR, 2.3)[81]. On the other hand, idiopathic polyhydramnios can be a transient phenomenon: an observational study of 163 women[82] showed that polyhydramnios can resolve in 38% of cases, especially when diagnosed earlier and characterized by lower AFI. Resolution of polyhydramnios was associated with lower rates of induction for fetal indications, and lower rates of macrosomia and preterm birth, while there were no differences for other perinatal outcomes. There is
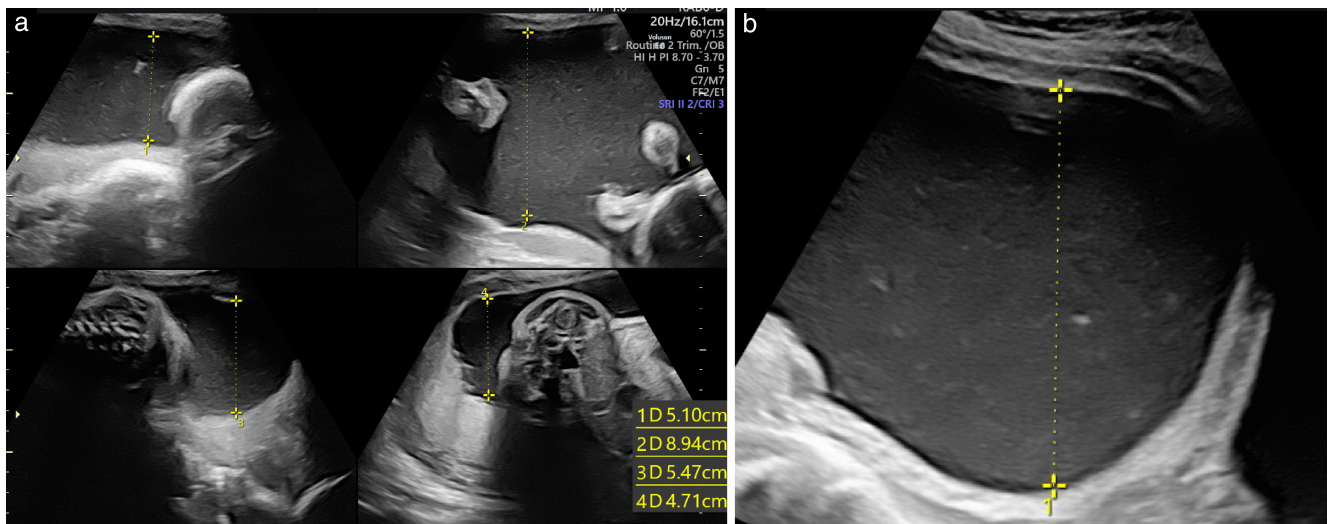
Figure 10 Polyhydramnios, defined as amniotic fluid index > 25 cm (a) or deepest vertical pocket > 8 cm (b).

Figure 11 Relatively uniform mild echogenicity of amniotic fluid is common in third trimester, attributed to presence of vernix.

little evidence regarding the optimal management of cases with mild idiopathic polyhydramnios in the third trimester, as this typically does not require treatment, only follow-up. The management of secondary polyhydramnios depends on the underlying cause, and symptomatic relief for severe polyhydramnios can be achieved with amniodrainage in case of maternal discomfort or dyspnea[83].

A relatively uniform mild echogenicity of the amniotic fluid is common in the third trimester, and is attributed to the presence of vernix (Figure 11).

Recommendations

- DVP is preferred over AFI for diagnosing isolated oligohydramnios, as it is associated with fewer inductions of labor, while having similar perinatal outcomes (**GRADE OF RECOMMENDATION: C**)

- The detection of polyhydramnios should lead to a targeted investigation for underlying causes, as idiopathic polyhydramnios is a diagnosis of exclusion (**GOOD PRACTICE POINT**)

Perinatal mortality

A Cochrane systematic review and meta-analysis by Bricker *et al.*[21] in 2015, including 30 675 women, did not find any significant association between ultrasound performed after 24 weeks' gestation and perinatal mortality (risk ratio, 1.01; 95% CI, 0.67–1.54). However, of the eight studies included in this review, only two were published after 2000, with three published in the 1980s. Moreover, this meta-analysis was not adequately powered to identify a statistically significant difference in perinatal mortality[84].

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CITATION

This Guideline should be cited as: 'Khalil A, Sotiriadis A, D'Antonio F, Da Silva Costa F, Odibo A, Prefumo F, Papageorghiou AT, Salomon LJ. ISUOG Practice Guidelines: performance of third-trimester obstetric ultrasound scan. *Ultrasound Obstet Gynecol* 2024; **63**: 131–147.

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APPENDICES

Appendix 1 Grades of recommendation and levels of evidence used in ISUOG Guidelines

Classification of evidence levels	
1++	High-quality meta-analyses, systematic reviews of randomized controlled trials or randomized controlled trials with very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of randomized controlled trials or randomized controlled trials with low risk of bias
1−	Meta-analyses, systematic reviews of randomized controlled trials or randomized controlled trials with high risk of bias
2++	High-quality systematic reviews of case−control or cohort studies or high-quality case−control or cohort studies with very low risk of confounding, bias or chance and high probability that the relationship is causal
2+	Well-conducted case−control or cohort studies with low risk of confounding, bias or chance and moderate probability that the relationship is causal
2−	Case−control or cohort studies with high risk of confounding, bias or chance and significant risk that the relationship is not causal
3	Non-analytical studies, e.g. case reports, case series
4	Expert opinion
Grades of recommendation	
A	At least one meta-analysis, systematic review or randomized controlled trial rated as 1++ and applicable directly to the target population; or a systematic review of randomized controlled trials or a body of evidence consisting principally of studies rated as 1+ applicable directly to the target population and demonstrating overall consistency of results
B	Body of evidence including studies rated as 2++ applicable directly to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+
C	Body of evidence including studies rated as 2+ applicable directly to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or evidence extrapolated from studies rated as 2+
Good practice point	Recommended best practice based on the clinical experience of the Guidelines development group

Appendix 2

Techniques for assessment of fetal biometry in the third trimester

Appendix 2 summarizes the recommendations of ISUOG guidelines[3,10,11], adapted to the third trimester when necessary. Please refer to the original guidelines for a more detailed description.

Biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL) can be measured routinely for the assessment of fetal size.

Biparietal diameter (BPD) and head circumference (HC) (Figure 12)

Outer-to-outer placement of calipers is preferable when measuring fetal head biometry.

The following criteria ensure optimal acquisition of the imaging plane for measurement of BPD:

- transverse view of the fetal head at the level of the thalami;
- ideal angle of insonation is 90° to the midline echoes, but slight variations are permitted;

Figure 12 Sonographic measurement of fetal head circumference in third trimester.

- symmetrical appearance of both hemispheres;
- midline echo (falx cerebri) interrupted anteriorly only by the cavum septi pellucidi;
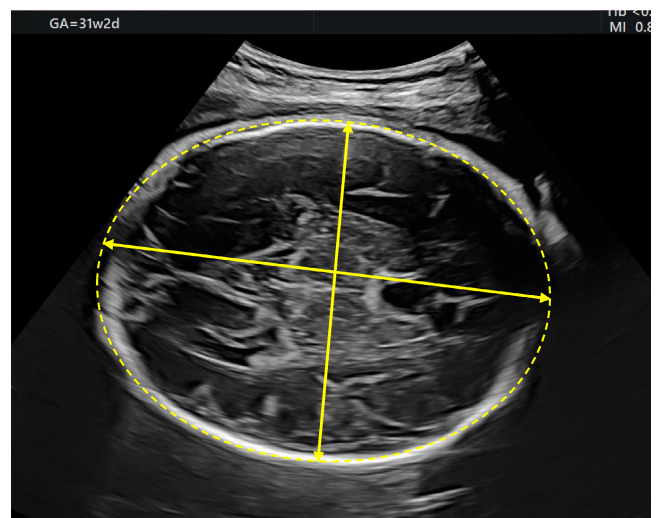- cerebellum not visible.

Abdominal circumference (AC) (Figure 13)

For measurement of AC, the transverse section of the fetal abdomen should be as circular as possible, and the fetal spine preferably in the 3 o'clock or 9 o'clock position. AC is either measured directly at the outer surface of the skin line, with ellipse calipers, or calculated from linear measurements made perpendicular to each other, usually the anteroposterior abdominal diameter (APAD) and the transverse abdominal diameter (TAD).

The following criteria ensure optimal acquisition of the imaging plane for measurement of AC:

- transverse section of the fetal abdomen (as circular as possible);
- umbilical vein at the level of the portal sinus;
- stomach visible;
- kidneys not visible.
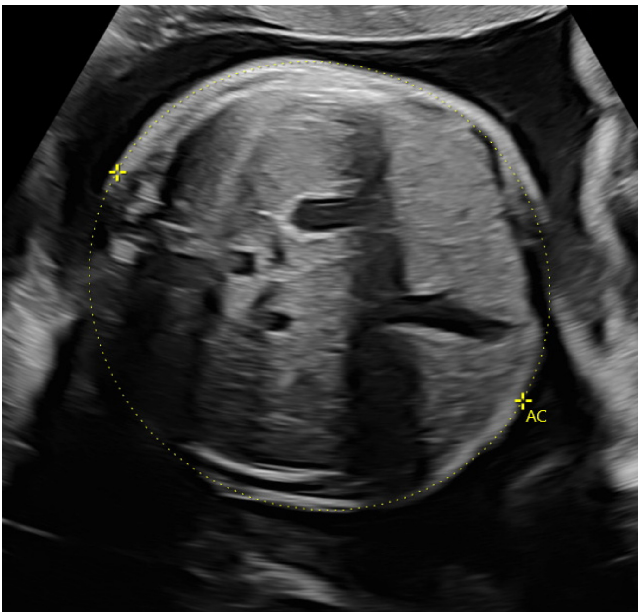
Figure 13 Sonographic measurement of fetal abdominal circumference (AC) in third trimester.

Femur length (FL) (Figure 14)

FL is imaged with both ends of the ossified diaphysis visible. The longest axis of the ossified diaphysis is measured, with the calipers placed at the ends of the ossified diaphysis, without including the distal femoral epiphysis if it is visible. This measurement should exclude triangular spur artifacts that can extend the diaphysis length falsely.

Estimated fetal weight (EFW)

To calculate EFW, the Hadlock-3 formula[85] (HC, AC, FL) is apparently the most stable mathematically, and its use is recommended in most clinical scenarios.
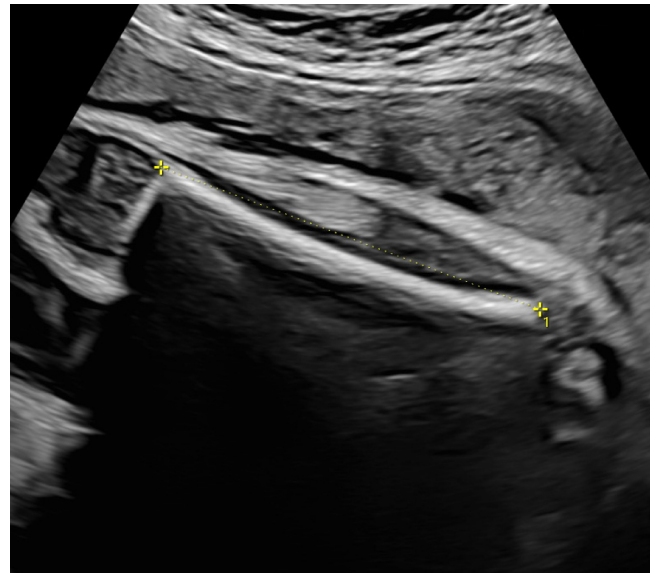

Figure 14 Sonographic measurement of fetal femur length in third trimester.

Appendix 3

Amniotic fluid volume assessment

Appendix 3 summarizes the text and recommendations of the ISUOG guideline on performance of the routine mid-trimester fetal ultrasound scan[10], adapted to the third trimester when necessary. Please refer to the original guideline for a more detailed description.

Amniotic fluid index (AFI) may be preferable in assessing polyhydramnios, while deepest vertical pocket (DVP) may be preferable in assessing oligohydramnios. The amount of amniotic fluid should be evaluated either subjectively, defined as 'normal' or 'abnormal' (reduced or increased), or semiquantitatively, by measurement of the DVP (Figure 15) of amniotic fluid or the AFI
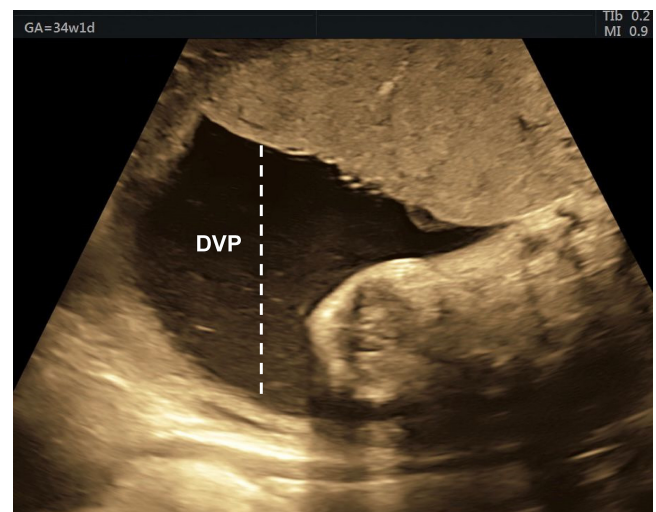

Figure 15 Amniotic fluid assessment using deepest vertical pocket (DVP) in third trimester.

(Figure 10a). For DVP, the largest vertical pocket of amniotic fluid that is free of fetal parts and loops of umbilical cord is measured. DVP ≤ 2 cm or AFI < 5 cm is considered as decreased amniotic fluid volume, DVP > 2 cm and ≤ 8 cm as normal amniotic fluid volume and DVP > 8 cm or AFI > 25 cm, as increased amniotic fluid volume. Reference values for gestational age can also be used.

The technique for performing semiquantitative assessment of the amniotic fluid volume involves:

- holding the ultrasound transducer perpendicular to the maternal position;
- identifying clear boundaries of the upper and lower edges of the pocket of fluid;
- measuring the largest unobstructed amniotic fluid pocket;
- using color Doppler to establish absence of the umbilical cord for pools of amniotic fluid where this is not certain.

Appendix 4

Assessment using Doppler ultrasound

Appendix 4 summarizes the text and recommendations of the ISUOG guideline on the use of Doppler velocimetry in obstetrics[12], adapted to the third trimester when necessary. Please refer to the original guideline for a more detailed description.

Umbilical artery Doppler (Figure 16)

There is a significant difference in Doppler indices measured at the fetal end (intra-abdominal), in a free loop, and at the placental end of the umbilical cord. The impedance i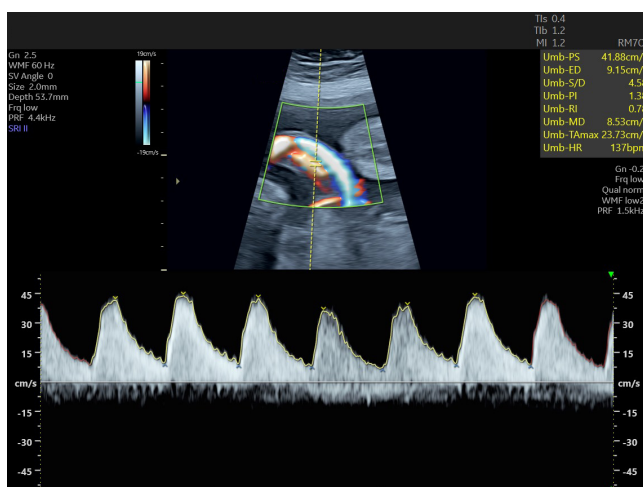s highest at the fetal end, and absent/reversed end-diastolic flow (EDF) is likely to be seen first at this site. For the sake of simplicity and consistency, by convention, measurements should be made in a free cord loop. Umbilical artery Doppler should be assessed in the absence of fetal body or respiratory movements.

Middle cerebral artery Doppler (Figure 17)

For Doppler imaging of the middle cerebral artery (MCA), an axial section of the brain, including the thalami and the sphenoid bone wings, should be obtained and magnified. Color flow mapping should be used to identify the circle of Willis and the proximal MCA, just caudal to the transthalamic plane. The pulsed-wave Doppler gate should then be placed at the proximal third of the MCA, close to its origin in the internal carotid artery (the systolic velocity decreases with increasing distance from the point of origin of this vessel) (**GRADE OF RECOMMENDATION: C**). The angle between the ultrasound beam and the direction of blood flow should be kept as close as possible to 0°. Care should be taken to avoid any unnecessary pressure on the fetal head, as this may lead to increased peak systolic velocity (PSV), decreased EDF and increased pulsatility index (PI). At least three and fewer than 10 consecutive waveforms should be recorded. The highest point of the waveform is considered the PSV (in cm/s). The PSV can be measured using manual calipers or autotrace. PI is commonly reported using autotrace measurement, but manual tracing is also acceptable.

MCA Doppler should be assessed in the absence of fetal body or respiratory movements.
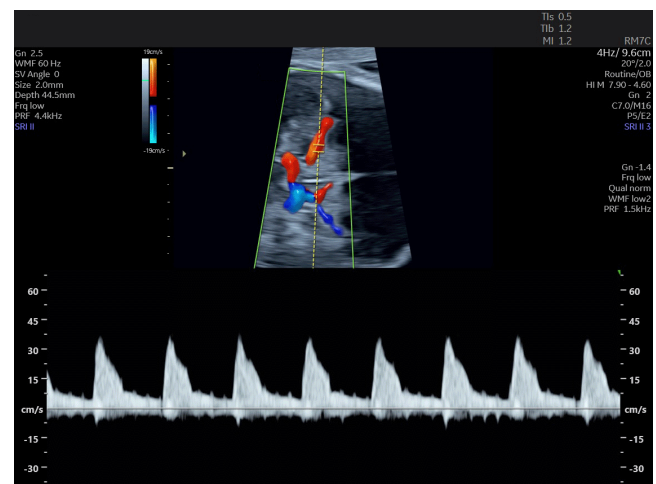

Figure 16 Doppler waveform from umbilical artery obtained transabdominally in third trimester.

Figure 17 Doppler waveform from middle cerebral artery obtained transabdominally in third trimester.

Ductus venosus (Figure 18)

The ductus venosus is visualized on 2D imaging, either in a midsagittal longitudinal plane of the fetal trunk or in an oblique transverse plane through the upper abdomen, as
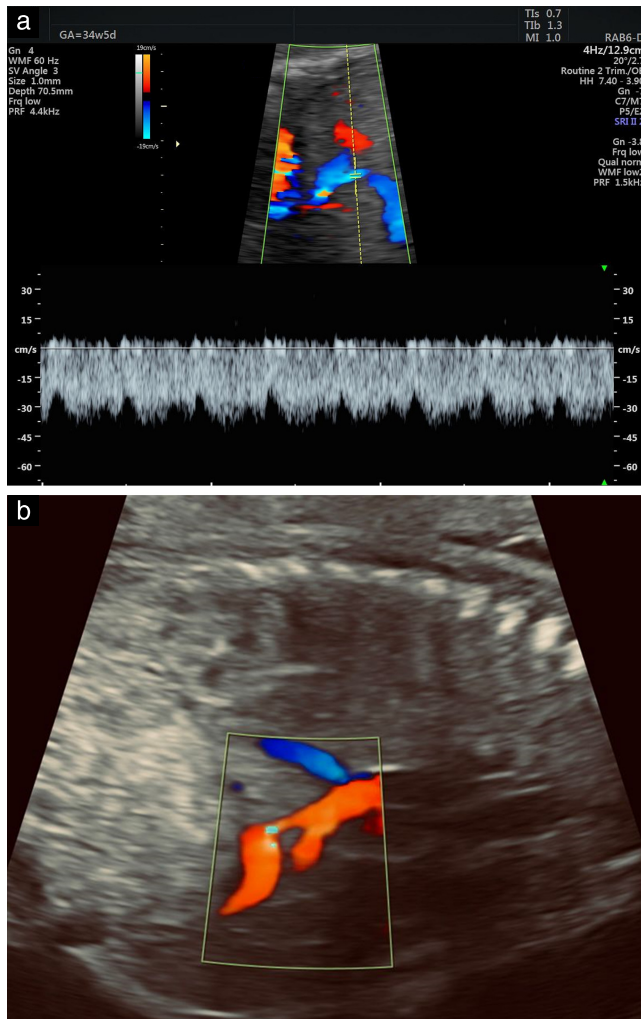
Figure 18 Doppler waveform from ductus venosus obtained transabdominally in third trimester: transverse (a) and longitudinal (b) sections of fetal abdomen.

the continuity of the umbilical vein towards the inferior vena cava. Color flow mapping demonstrating the high velocity at the narrow entrance of the ductus venosus confirms its identification and indicates the standard sampling site for Doppler measurements. Ductus venosus Doppler should be assessed in the absence of fetal body or respiratory movements.

Uterine artery Doppler (Figure 19)

The uterine artery is usually examined transabdominally in the third trimester. The probe is placed longitudinally in the lower lateral quadrant of the abdomen, angled medially in the parasagittal plane. Color flow mapping is useful to identify the uterine artery as it is seen crossing the external iliac artery. The sample volume is placed 1 cm downstream from this crossover point. In a small proportion of cases, the uterine artery branches before the intersection of the external iliac artery. In such cases, the sample volume should be placed on the uterine artery just before its bifurcation. The same process is repeated for the contralateral uterine artery. With advancing gestational age, the uterus usually undergoes dextrorotation. Thus, the left uterine artery does not run as lateral relative to the uterus as does the right.
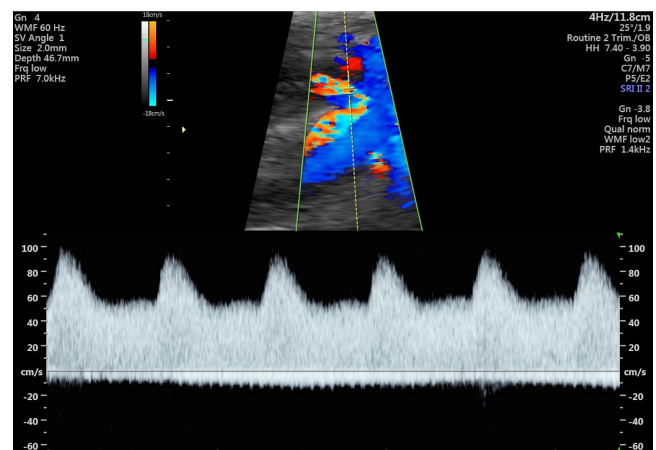

Figure 19 Doppler images with waveform from uterine artery obtained transabdominally in third trimester.