Intrauterine growth restriction

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Members of the guideline group

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Recommendations

- Ultrasonographic measurement of the fetal head, abdomen and femur length should be used to estimate fetal weight and growth where there are identified risk factors for, or suspected growth restriction (strong recommendation). Doppler examination of the umbilical artery flow velocity waveform should be used to diagnose placental cause of intrauterine growth restriction and to guide of clinical management (strong recommendation).
- An overall assessment where the maternal condition, fetal age, weight and growth, amniotic fluid volume, CTG with short variability (STV) and Doppler evaluation included should be done (strong recommendation)
- Delivery should be considered when absent (34 weeks) or reversed (32 weeks) end diastolic blood flow in the umbilical artery (ARED) (strong recommendation).
- Give maternal corticosteroids betamethasone (Celestone Chronodose®) where delivery is planned ≤ week 33 + 6 (strong recommendation)
- Consider giving magnesium sulfate by preterm birth ≤ 31 weeks + 6? (suggestion)
- Low dose aspirin (75mg) should be given as prophylactic treatment from early pregnancy (12 weeks gestation) where there is moderate or high risk of preeclampsia (recommendation)

Litterature:

Pyramidesearch, UpToDate, The Cochrane Library, National Guideline Clearinghouse, Clinical guidelines (US), Royal College of Obstetricians and Gynaecologists (British guidelines), Clinical Guidelines (Canadian), Danish guidelines (dsog.dk), Pubmed.

Definitions

AGA (Appropriate for gestational age) estimated fetal weight (EFW) by ultrasound biometry between 10-90 percentile. SGA (small for gestational age): EFW less than expected in relation to gestational age (EFW <10 percentile or weight deviation> ÷ 14%). IUGR (intrauterine growth restriction, intrauterine growth retardation) involves slow growth by serial measurements. A fetus can be both AGA and have IUGR. Where IUGR is suspected or confirmed Doppler examination of the umbilical artery (UA) can be applied to assess placental insufficiency as the cause of slow growth(1). Approximately ¼- ½ of fetuses who are SGA are constitutionally small and are not

IUGR. It is essential to apply adequate reference values for biometrics and EFW in the assessment of fetal size and growth(2-5), and be aware of the methods strengths and limitations in estimating fetal weight and growth. A precise assessment of the gestational age is a prerequisite for later assessment of weight and growth.

Occurrence
Ca. 10-15% of all pregnancies evaluated for slow fetal growth.

Etiology and risk factors IUGR
Both genetic and environmental factors are decisive for fetal growth. Causes may be divided into fetal, placental, maternal, in one case several factors may be involved.
Fetal causes: Multiple births, chromosome abnormalities, deformities, infections (toxoplasmosis, rubella, CMV herpes simplex, syphilis).
Placental: Abnormal placentation, infarcts, abnormal umbilical cord attachment, bleeding in pregnancy.
Maternal: Preeclampsia, previously given birth to neonate with IUGR or intrauterine death, chronic illness in the mother (hypertension, chronic obstructive pulmonary disease, collagenosis, diabetes mellitus, thrombophilia, kidney disease, anemia), drugs (cytostatics, steroids), high maternal age (> 40 years)(6), mother born with low birthweight (7) nutritional deficiencies, uterine malformations, smoking, substance abuse.

Distinguish between early (<34 weeks) and late IUGR.

Complications
Growth restriction is associated with increased risk of perinatal morbidity and mortality, and may have long term health implications. Also neurological development seems to be influenced by growth restriction(15).

Diagnosis, monitoring, treatment and prophylaxis
Diagnostics
Goals
Clarify whether there are maternal conditions that can be treated, clarify whether the fetus is a healthy SGA fetus or an IUGR fetus,
schedule monitoring of pregnancy, consider intervention measures before (preterm) birth (betamethasone (Celeston®)).

Indication
Identified risk factor (s), low symphysis-fundus (SF) measurements, or that mother feel less fetal movements , or is of the opinion that her uterus is small. Suspected small fetus at ultrasound examination.
Low SF measurement refers to that one SF measurement after week 24 is below the green field at the reference curve (helsekort for gravide). By non- or stunted growth by the SF measurement, the woman should be referred for an ultrasound examination (recommendation). The SF measurement method has a substantial intra- and inter-observer variability and low sensitivity (but better specificity) to identify SGA fetuses. The threshold for referring to ultrasound should be low (8).

With less fetal movements we mean that mother feels less fetal movements than she has done earlier in pregnancy. If substantial and sustained reduction in fetal

movements despite adequate time and concentration, we suggest that the next maternity or out clinic should offer examination of the woman(9 10). There is insufficient evidence to recommend routine counting of fetal movements to avoid intrauterine death in an unselected population(11 12).

Examinations

• Medical history, blood pressure and urine examination and control of gestational age determination

• Fetal biometry and assessment of growth:

Biometry: head size (HC), abdominal circumference (AC) and femur length (FL) and estimation of fetal weight (EFW) using formulas (13-15).

Another approach is to measure biparietal diameter (BPD) and middle abdominal diameter (MAD), and calculate weight deviation percentage (10 percentile = -14% weight deviation, 5 percentile: -20% weight deviation 2.5 percentile = -22% weight deviation).

- Assessment of growth: both a former and current weight estimate are included in the assessment of growth(16).

- If risk factors are identified: we suggest Doppler examination of the uterine arteries (UTA) at approximately gestation 22-24. If UTA Doppler normal is normal we suggest estimation of growth in the 3rd trimester,
  If the UTA Doppler is pathological we suggest monitoring of growth and Doppler examinations every 4 weeks or more frequent.
  • Evaluation of amniotic fluid volume (amniotic fluid index (AFI) or deepest vertical pocket (DVP)), fetal movements and fetal anatomy is recommended. Oligohydramnios when AFI <5 cm or DPV <2cm (17). By anatomical abnormalities, severe early IUGR, or polyhydramnios fetal karyotype and infection serological examination may be appropriate(18).

  Doppler examination of the umbililcal artery (UA) is recommended. This improves precision in the diagnosis of IUGR(19) and clinical management guided by UA Doppler reduces the number of interventions (induction or cesarean) and the risk of perinatal death(1).
  • In early severe IUGR we suggest monitoring with extended feto-maternal Doppler Evaluation (inkl.UA, middle cerebral artery (MCA), ductus venosus (DV), vena umbilicalis(20-21) (UV)) and CTG with short variability (CTG STV) (22). In order to find the optimal time of delivery the MCA Doppler has limited predictive value (severe early IUGR), while changes in the MCA Doppler in to a more pathological pattern may be a sign of worsening the fetal condition and suggests shorter monitoring intervals. In severe early IUGR DV Doppler and CTG with STV should guide the clinician in timing the delivery.
  • Late IUGR less pronounced changes are seen in the UA and DV Doppler, while MCA Doppler and cerebro-placental ratio (MCA PI / UA PI), UTA Doppler, amniotic fluid volume and CTG with STV are useful in timing of delivery (23-27).

  Suggested follow-up and treatment depend on gestational age
  An individual assessment where all information about maternal comorbidities,

risk factors, previous findings, gestational age and development over time is recommended. Current understanding suggests delivery if testing indicates that the risk of fetal death exceeds the risk of neonatal death (death resulting from prematurity). Between gestational week 26-29, each day intrauterine improve neonatal survival by 1-2% (20). By preterm birth before 33 weeks+ 6 days betamethasone (Celeston®) 12 mg intramuscularly in two days is recommended to promote lung maturation and reduce neonatal death and morbidity(28). Magnesium sulphate given before preterm birth is shown to have neuroprotective effect; fewer children getting cerebral palsy. There is still lack of evidence about the optimal treatment regimen (dose and therapeutic window), and the effect on fetuses with IUGR has not been studied (29).
The table below is a suggestion for the handling of IUGR pregnancies by gestational age, but individual adaptation must always be done. In early and severe IUGR, the care should be given by an obstetrician with fetal medicine expertise and in a department with neonatal intensive care unit service.

Gestational week 24+0-33+6	Week 34-36+6	Week >37
AU PI og MCA PI normal: Growth and Doppler assessment after 2 weeks. In severe IUGR with normal Doppler: specialist fetal medicine examination is suggested.	AU PI og MCA PI normal: Growth and Doppler assessment after 2 weeks.	AU PI normal: MCA-Doppler, amniotic fluid amount, CTG with STV. Hvis MCA PI<5 percentile, CPR<1 and/or anomalous CTG consider delivery. Delivery should be considered if EFW <5 percentile (induction before GA 40+2[24;26]), or oligohydramnios or reduced growth (<10-percentile, or increased growth deviation). If observation is chosen; intensive monitoring is indicated[(11)].
AU PI >95 percentile: We suggest to discuss the case with a fetal medicine specialist. Extended feto-maternal Doppler evaluation including amniotic fluid, and CTG with STV. If STV ≤3,0 ms consider delivery.	AU PI >95 percentile: Add MCA-Doppler, amniotic fluid amount and CTG: If normal, reassess in 1 week. *If MCA PI<5 percentile or CPR <1.0 and/or oligohydramnios:* extended feto-maternal Doppler evaluation, CTG with STV 2 times/week. Consider delivery if extended Doppler assessment or CTG abnormal.	AU PI >95 percentile: MCA-Doppler, amniotic fluid amount, and CTG. Delivery should be considered if MCA PI <5 percentile or CPR <1 and/or oligohydramnios or abnormal CTG.

AU ARED: Extended feto-maternal Doppler evaluation every 2.-3. Day. CTG with STV daily Maternal Betametason 12 mg intra-musckulært in 2 days. In DV absent/reversed A-wave, UV pulsations, or STV ≤3.0 ms consider delivery.	AU ARED: CTG and delivery. AED (no positive diastolic flow), CTG and consider delivery.	AU ARED (rare at GA> 37 weeks): CTG and delivery is recommended.

Absolute delivery indications in IUGR

• CTG changes: pre-terminal pattern, complex variable or uniform decelerations, STV ≤ 3.0 ms(22)

• Pathological DV Doppler (reversed or no positive blood flow in the A-wave) Gestational age> 26-28 weeks (30)

• UA Doppler with reversed blood flow in diastole (ARED) by week 32, no positive diastolic blood flow in the UA (AED) by week 34 (31,32)

• When EFW ≤400 and gestational age <26 weeks, the clinician should in consultation with the woman, her partner and neonatologists discuss further conservative management and vaginal delivery

• Estimated fetal weight <5 percentile and (certain) gestational age ≥40+ 2 weeks

Delivery method

• From week 34-36 weeks may fetuses with abnormal UA PI, but positive diastolic blood flow try vaginal delivery with adequate monitoring, if maternal history and fetal condition allows it. Oligohydramnios and changes in MCA, CPR or pathological UTA involve greater risk for asphyxia and acute cesarean delivery (23,27,33)

• When UA ARED before 34 weeks delivery is usually done by cesarean

Recurrence risk and prophylaxis

By IUGR we suggest pathological examination of the placenta.
There is an increased risk of recurrence of IUGR in a subsequent pregnancy (34). Planning of the next pregnancy is recommended, with investigation of the woman, and early dating of a new pregnancy with ultrasound is suggested (35; 36). Monitoring with ultrasound which includes evaluation of growth and Doppler is suggested. Monitoring interval depends on results of the Doppler and growth evaluation at gestational week 22-24. At high or moderate risk of preeclampsia development a low-dose aspirin (75 mg orally daily) from 12 weeks gestation is suggested, as this reduces the risk of developing preeclampsia and IUGR (37).

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