Intrauterine growth restriction (IUGR): Guidelines for definition, recognition and management

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Abstract
Intrauterine growth restriction (IUGR) is an important problem in perinatal medicine. It is the second cause of perinatal mortality after prematurity. The two conditions are often associated in case of iatrogenic prematurity. 52% of stillbirths are associated with IUGR and 10% of perinatal mortality cases in Europe are the consequence of unrecognized severe growth restriction. Moreover IUGR is also associated with increased neonatal mortality and morbidity and it has been suggested that some diseases (metabolic and vascular) evident in adult life are the consequence of fetal growth restriction. In order to improve the perinatal outcome a timely recognition is fundamental. Ultrasonic fetal biometry is the method of choice but it is necessary to respect some criteria remembering that SGA and IUGR are not synonymous and what is important is to detect the “growth” restriction and not to predict the birthweight. After IUGR recognition it is necessary to identify the etiology and in this way to reach a diagnosis. The most common cause of IUGR is the placental obliterative vasculopathy that reduces nutrients and oxygen supply to the fetus. In this condition chronic fetal hypoxaemia occurs that is the reason of the poor perinatal outcome. The clinical management must be therefore based on the assessment of the hypoxaemia.

Key words: intrauterine growth restriction, guidelines, definition, recognition, management

Introduction
Fetal or intrauterine growth restriction (IUGR) is associated with perinatal mortality and morbidity. A satisfactory definition of IUGR has been suggested by the American College of Obstetricians and Gynecologists (ACOG) as describing “a fetus that fails to reach his potential growth”. Small for gestational age (SGA), on the other hand, is a different entity, but is also associated with poor perinatal outcomes. SGA is defined as a birth weight (BW) below a given (usually) the 10th percentile for gestational age. SGA and IUGR are not synonymous. The term IUGR should be used only in regard to the fetus whereas SGA should be used mainly in the newborn (but it can be estimated from somatographic measurements of the fetus). IUGR is ideally detected by a diminished growth velocity of the fetus on serial ultrasonographic scans. In this way, the function of growth becomes the object of interest instead of the result (i.e., birth weight). IUGR is an important clinical problem. The prevalence is about 8% in the general population. It has been shown that 52% of stillbirths are associated with IUGR \( \times 12 \times \) and 10% of perinatal mortality is a consequence of IUGR \( \times 40 \). Up to 72% of unexplained fetal deaths are associated with SGA below the 10th percentile.

The aim of this paper is to review and emphasize important aspects of the identification and management of IUGR as presented in recently published Guidelines [1]. IUGR is a condition with an increased risk of a pathological condition that adversely affects the inherent potential growth of the fetus. Ideally, the diagnosis of IUGR is a two-step procedure: 1) recognition of the growth restriction by ultrasonography, and 2) identification of a specific cause.

Recognition
The recognition of IUGR begins with an accurate gestational age (GA). This is best determined by measuring the crown rump length (CRL) by ultrasound in early pregnancy. Serial ultrasound biometry may then be able to identify the fetus that does not reach its growth potential. Commonly used methods for estimating fetal size are clinical palpation, fundal height (FH) measurement and ultrasonic fetal biometry. Ultrasound must be considered the method of choice as it is highly reliable and reproducible. The commonly used ultrasound biometric parameters in the late 2nd and during the 3rd trimester are the biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL). From these measurements the estimated fetal weight (EFW) can be calculated. The method-error for estimating fetal weight is 7-10%. Fetuses that do not reach their growth potential will still have cerebellar growth until late in the process of IUGR. When gestational age is questionable, the use of the transcerebellar diameter (TCD) may be helpful. AC should be considered as the best single measurement to screen for poor growth because of its good correlation with fetal weight. Selecting a threshold of the 10th percentile for a biometric parameter such as AC or EFW for suspecting or diagnosing IUGR may be a translation of the postnatal SGA newborn concept into fetal life, which is undesirable because it may allow fetuses with restricted growth to be missed if the EFW or AC are above the selected threshold. Uniform criteria for defining a fetus as growth restricted on the basis of biometric parameters are not available, but it is common to use 1.5, 2 or 2.5 SD below the mean for any biometric parameter or combination of parameters. At present, it seems advisable to suspect IUGR when the AC measurement deviate 10% or more from the expected from the individual projected curve of growth. Ideally, early identification of the fetus that does not reach its growth potential should employ population specific growth charts that also take into account other factors influencing fetal growth. Customized growth charts also built

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on homogeneous populations are available and should be used preferentially in order to decrease the rate of false positive diagnoses of IUGR. Successive measurements should be carried out 2 weeks apart. Growth rate tables that take into consideration the time intervals between measurements can also be used. The evaluation of growth velocity with serial measurements offers insight into the characteristics of the growth process and is correlated with perinatal outcomes.

**Etiology**

When IUGR is suspected or diagnosed, it is necessary to distinguish between fetuses that are small but otherwise healthy (i.e. constitutional small, and therefore not growth restricted) and those that are a consequence of an abnormal condition such as a maternal condition (chronic hypertension, pre-gestational diabetes, cardiovascular disease, substance abuse, autoimmune conditions, etc.), a fetal condition (infection, malformation, chromosomal aberration, etc.), or a placental condition (chorioangioma, infarction, circumvallate placenta, confined placental mosaicism, obliterate vasculopathy of the placental bed, etc.). Placental conditions are the most frequent etiology of IUGR.

Obstetrical management depends on the etiology of IUGR. For maternal conditions, such as preeclampsia, management is entirely dependent on the severity of maternal disease. When the etiology is of fetal origin, management may be limited to avoiding prematurity and maternal morbidity. When IUGR is the consequence of a placental etiology (placental insufficiency), management is based on careful fetal assessment in order to detect the optimal time for delivery. The most commonly used methods of monitoring include Doppler flowmetry, cardiotocography, amniotic fluid volume evaluation, fetal biophysical profile and fetal movement counts. Antepartum cardiotocography (CTG), alone or as a part of the fetal biophysical profile, is almost universally used. In order to overcome the great intra- and inter-observer variation in CTG evaluation, computer assisted online evaluation of short fetal heart rate variability is available and offers a more precise prediction of fetal acidemia or demise. Doppler velocity waveform in arteries is mainly influenced by the characteristics of the diastolic phase and reflects the peripheral resistance to blood flow. The pulsatility index (PI) assessment is commonly used. PI values increase as the peripheral resistance increases. In severe IUGR absence of flow in diastole or reverse flow (ARED) can be observed. Perinatal mortality and morbidity are markedly increased in the presence of ARED flow. Study of the umbilical artery Doppler waveforms is fundamental for the identification of restricted blood supply (placental insufficiency) to the IUGR fetus and evidence suggests that Doppler of umbilical arteries may improve the perinatal outcome. Assessment of the Doppler characteristics of the venous system, especially the fetal ductus venous, may also predict adverse outcomes. At present, the best way to detect the optimal timing of delivery based on venous Doppler findings is a matter of debate.

**Conclusions**

In order to improve the perinatal outcome of IUGR fetuses a timely recognition is fundamental.

The methods for identifying IUGR are strongly dependent on the respect of the correct definition without confusing IUGR and SGA that are clinically different conditions. Once detected the growth restriction the identification of the etiology is mandatory in order to perform a rationale management. Chronic fetal hypoxaemia consequence of “placental insufficiency” is observable in 30% of the IUGR. Therefore the management is mainly based on the careful assessment and monitoring of the CFH. Unfortunately it must be accepted that the management of IUGR hypoxaemic fetuses is still empirical (the only effective therapy is the delivery) and in case of prematurity it is a compromise between the risks of intrateneurine demise and of the large prematurity.

**References**