Recommendations and guidelines for perinatal practice

Intrauterine restriction (IUGR)*

Giampaolo Mandruzzato1,2,**, Aris Antsaklis2, Francesc Botet3, Frank A. Chervenak4,Francisc Figueras5, Amos Grunebaum4,1 Bienve Puerto5, Daniel Skupski4,6 and Milan Stanojevic7

1 Department of Obstetrics and Gynecology, Istituto per l’Infanzia, Burlo Garofolo, Trieste, Italy
2 Department Obstetrics and Gynecology, Alexandra Hospital, University of Athens, Greece
3 Neonatology Service, Hospital Clinic, Institut Clinic, Obstetrica, Ginecologia, Neonatologia, Universidad de Barcelona, Spain
4 Weill Medical College of Cornell University, New York, USA and New York Hospital, Queens, New York, USA
5 Fetal medicine Service, Hospital Clinic, Institut Clinic Obstetricia, Ginecologia, Neonatologia, Universidada de Barcelona, Spain
6 New York Hospital, Queens, New York, USA
7 Department Obstetrics and Gynecology, Medical School of University of Zagreb, Sveti Duh General Hospital, Zagreb, Croatia

Abstract

Perinatal mortality and morbidity is markedly increased in intrauterine growth restricted (IUGR) fetuses. Prenatal identification of IUGR is the first step in clinical management. For that purpose a uniform definition and criteria are required. The etiology of IUGR is multifactorial and whenever possible it should be assessed. When the cause is of placental origin, it is possible to identify the affected fetuses. The major complication is chronic fetal hypoxemia. By monitoring the changes of fetal vital functions it is thus possible to improve both management and outcome. The timing of delivery is crucial but the optimal management scheme has not yet been identified. When IUGR is identified at very early gestational ages, serial assessments of the risk of continuing the in utero fetal life under adverse conditions versus the risks of the premature should be performed. Delivery of IUGR fetuses should take place in centers where appropriate neonatal assistance can be provided. Careful monitoring of the IUGR fetus during labor is crucial as the IUGR fetus can quickly decompensate once uterine contractions have started.

Keywords: Fetal assessment; IUGR; neonatal outcome; SGA.

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) [1] 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 [2, 34, 45]. 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 sonographic measurements of the fetus). IUGR is ideally detected by a diminished growth velocity of the fetus on serial ultrasonographic scans [23]. 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 [12] and 10% of perinatal mortality is a consequence of IUGR [40]. Up to 72% of unexplained fetal deaths are associated with SGA below the 10th percentile [14]. The aim of this document is to review and emphasize important aspects of the identification and management of IUGR.

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) restriction 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 biometries 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 [38]. 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% [20, 43]. Fetuses that do not reach their growth potential will still have cerebellar growth until late in the process of IUGR [8].

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 [44]. 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 [7, 46]. 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 on homogeneous populations are available and should be used preferentially in order to decrease the rate of false positive diagnoses of IUGR [9, 13, 22, 24, 36, 37, 42]. Successive measurements should be carried not <2 weeks apart [31, 35]. Growth rate tables that take into consideration the time intervals between measurements can also be used [32]. The evaluation of growth velocity with serial measurements offers insight into the characteristics of the growth process and is correlated with perinatal outcomes [10].

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, obliterator vasculopathy of the placental bed, etc.). Placental conditions are the most frequent etiology of IUGR.

Screening

IUGR is a prevalent and significant public health problem worldwide. In many European countries, four scans are routinely offered during pregnancy and thus screening for IUGR is possible at an early gestational age. The diagnosis of IUGR is non-invasive with few adverse effects, treatment may be available, and early detection and delivery have the potential to improve outcomes [25, 30].

Prevention

Methods of proven efficacy for preventing IUGR are not available. Simple means for preventing this problem are unlikely to be successful because of the multifactorial nature of IUGR. Chronic fetal hypoxemia (CFH) is encountered in about 30% of IUGR, suggesting that prevention of the adverse consequences may be possible after the diagnosis of IUGR [28]. There is some evidence to suggest that perinatal outcome can be improved by optimizing the timing of the delivery.

Obstetrical management

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 [27]. 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 assessment of umbilical artery Doppler may improve perinatal outcome [33]. Assessment of the Doppler characteristics of the venous system, especially the fetal ductus venosus, may also predict adverse outcomes [5, 11, 29, 48]. At present, the best way to detect the optimal timing of delivery based on venous Doppler findings is a matter of debate [18, 39].

There is no evidence that one monitoring method is superior to another.

Based on the best available studies, IUGR can be characterized into several categories on the basis of the ultrasound findings and gestational age, and the following management is suggested.

1. IUGR with normal umbilical artery Doppler waveforms and reassuring tests of fetal well-being
   - Serial biometry, umbilical Doppler and tests of fetal well-being.
2. IUGR with umbilical artery PI >2 SD above the mean for gestational age, presence of diastolic flow and reassuring tests of fetal well-being
   A. Gestational age >34 weeks.
      - Umbilical artery Doppler and tests of fetal well-being twice weekly. Decision for delivery is based on tests results. Trial of labor for vaginal delivery is acceptable.
   B. Gestational age <34 weeks.
      - Umbilical artery Doppler and tests of fetal well-being twice weekly. Consider corticosteroid administration for fetal lung maturation. Decision for delivery is based on test results. Trial of labor for vaginal delivery is acceptable.
3. IUGR with umbilical artery PI >2 SD above the mean for gestational age, presence of diastolic flow and non-reassuring tests of fetal well-being
   A. Gestational age >34 weeks.
      - Daily umbilical artery Doppler and daily tests of fetal well-being. Consider delivery. Trial of labor for vaginal delivery is acceptable.
   B. Gestational age <34 weeks.
      - Corticosteroid administration for fetal lung maturation. Daily umbilical artery Doppler and daily tests of fetal well-being. Consider delivery. Trial of labor for vaginal delivery is acceptable.
4. IUGR with umbilical artery absent diastolic flow. Tests of fetal well-being are usually non-reassuring.
   A. Gestational age >34 weeks.
      - Consider delivery
   B. Gestational age <34 weeks.
      - Corticosteroid administration for fetal lung maturation. Consider delivery.
5. IUGR with reversed diastolic flow in the umbilical artery. Tests of fetal well-being are nearly always non-reassuring.
   A. Gestational age >34 weeks.
      - Extensive counselling on mortality and morbidity. Active or expectant management according to the choice of the family.
   B. Gestational age <34 weeks.
      - Extensive counselling on mortality and morbidity. Active or expectant management according to the choice of the family in concert with the obstetric and neonatal teams. Corticosteroid administration for fetal lung maturation.

Before 33–34 weeks, delivery is a compromise between the risks of fetal demise with continued in utero life under adverse conditions and the risk of severe prematurity. Antenatal corticosteroids administration has a positive effect for both the short- and long-term complications. Clinicians should remember that steroid (betamethazone) administration reduces FHR variability and the number of accelerations. The FHR pattern should be carefully assessed after steroid administration to avoid unwarranted iatrogenic delivery [41]. Counselling must be informative and non-directive, respecting the principle of autonomy of the mother.

Delivery of the IUGR fetus is best performed at a center where intensive neonatal assistance is available. The delivery mode depends on the fetal condition appreciated from fetal evaluations and the tolerance of the fetus to labor. It is not always necessary to perform cesarean delivery for fetuses with IUGR. Also in presence of umbilical artery PI over 2 SD safe vaginal delivery, under close monitoring, can be achieved in 24–40% of the cases [21, 28]. The more pronounced the hypoxemia and acidemia, the more likely the fetus will not tolerate labor and it is less likely that vaginal delivery will be a safe option. IUGR fetuses from a placental or maternal condition are less likely to tolerate labor than those from fetal conditions.

**Neonatal management**

Infants born after IUGR may have significant morbidity, including metabolic (hypoglycemia, dislipidemia), hema-
Recommnedations

1. The terms IUGR and SGA are not synonymous. IUGR is used for the fetus and SGA is used primarily for the newborn. (Level A)
2. IUGR should be defined on the basis of serial measurements showing restricted growth. (Level B)
3. Abdominal circumference measurements are easy to perform and can be used for growth assessment. (Level B)
4. Customized, population-specific growth charts should be used when possible. (Level B)
5. The timely recognition of IUGR improves both management and outcomes. Screening for IUGR should be considered. (Level A)
6. When IUGR is suspected, the etiology should be explored. (Level B)
7. When the etiology is thought to be placental, Doppler study of the umbilical artery allows the identification or exclusion of significant chronic fetal hypoxemia. Close monitoring of Doppler blood flow changes should guide clinical management. (Level A)
8. There is no evidence that one type of monitoring is superior to another. Serial fetal assessment is optimal to identify the best time for delivery. (Level B)
9. Careful monitoring of the IUGR fetus in labor is crucial as a rapid deterioration is possible with uterine contractions. (Level B)
10. Detailed counselling with the family that includes the obstetrician and the neonatologist is recommended. (Level C)
11. Delivery of IUGR should take place where an appropriate neonatal care is available. In utero transport should be preferred. (Level B)
12. After delivery of a neonate with IUGR, early neuroimaging is recommended. (Level B)
13. There is no effective management for the prevention or in utero treatment of IUGR. In case of CFH the only effective therapy is delivery. (Level B)

References
