CPD

Screening – 1 of 2

Fetal growth restriction

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Introduction

Small for gestational age (SGA) fetus is a pregnancy complication occurring in the second half of the pregnancy[1]. It is estimated that a large proportion of SGA pregnancies are having fetal growth restriction (FGR) and the major proportion of FGR pregnancies are also SGA[2]. As FGR has serious short and long term complications, it is important to differentiate SGA fetuses and fetuses with FGR. SGA is routinely defined when the birthweight or estimated fetal weight (EFW) is less than 10th centile for particular gestational age. Significant proportion of SGA is due to constitutional or physiological causes. The diagnosis of FGR ideally requires a serial growth assessment and diagnosis can be confirmed when the fetal abdominal circumference (AC) is below the 10th centile with abnormal Doppler studies. Three to five percent of pregnancies can be complicated with FGR[1]. Most of the available screening methods have been tailored to pick-up SGA fetuses rather than FGR[2].

Two distinct patterns of clinical worsening in FGR have recently been characterized more clearly[3-5]. This difference is determined primarily by the gestational age of disease onset and the placental blood flow resistance. In early onset FGR prior to 34 weeks' gestation neonates have significantly lower expected survival rates than appropriately grown counterparts[6]. The majority of these pregnancies with early-onset FGR show significant umbilical artery (UA) Doppler abnormalities documenting the severity of their placental disease. Late-onset FGR is a significant clinical problem that contributes to over 50% of unanticipated stillbirths at term[7]. This form of FGR often is undetected and offers few Doppler abnormalities and subtle biophysical findings suggesting fetal compromise. Therefore, detection of a FGR fetus is an important objective of antenatal care. In order to pick up SGA fetuses, different screening methods have been evolved.

Gestational age assessment

Precise pregnancy dating in early pregnancy is important in order to determine any deviation of fetal growth in late trimesters. Dating a pregnancy by menstrual history may not be accurate as up to 40% of women are uncertain of their menstrual dates or ovulation may not exactly correspond with the mid menstrual cycle[8]. The National Institute of Clinical Excellence (NICE) has recently recommended that all pregnancies should be dated by fetal crown-rump length (CRL) between 11 and 14 weeks of gestation and by head circumference (HC) thereafter[9].

Abdominal palpation

Leopold's Maneuvers are a systematic way to determine the position of a fetus inside the woman's uterus. These maneuvers are also used to estimate the fetal size[10]. However, its ability to predict fetal weight is limited as few as 30% SGA fetuses can be detected by this method[11].

Symphyseal fundal height (SFH)

SFH measurement is the most commonly used screening tool for SGA. The detection rate of SFH in predicting SGA ranges from 27% to 86%, its specificity from 64% to 88%[12]. This variation is due to different methods of pregnancy dating and different cut-offs used to define SGA[13-15]. Gardosi *et al* created a SFH charts customized for pregnancy characteristics. The authors suggested that using individually adjusted SFH charts (adjusted for physiological variables such as maternal height, weight and parity) might improve precision when screening for FGR[16]. Use of such charts was found to result in improvement in sensitivity up to 48%.

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Ultrasound biometry – gold standard test

A reduced fetal AC on ultrasonographic evaluation is reported to be the most sensitive biometric measurement in predicting SGA (sensitivities of 72.9-94.5% and specificities of 50.6-83.8%). An AC within the normal range reliably excludes FGR, with a false negative rate of less than 10%[17]. The ultrasound EFW has lesser sensitivity than AC in detecting SGA (sensitivities of 33.3-89.2% and specificities of 53.7-90.9%)[17]. Since growth is a dynamic process, serial measurements improve prediction of SGA and FGR. Furthermore, use of customized fetal AC/EFW charts and use of growth velocity in addition to fetal size improves the detection of SGA and FGR[18].

New screening strategies

Scientific advances over the past years have raised the hope that many pregnancy complications are potentially predictable during first and second trimesters[19]. Poor conversion of the spiral arteries reflected in increased uterine artery Doppler resistance, is involved in the genesis of early onset FGR than FGR after 34 weeks. Doppler assessment of uterine artery blood flow resistance may be used to screen for FGR either in the first or second trimesters. It is also becoming increasingly apparent that combining data from maternal characteristics and history with findings of biophysical and biochemical tests can define the patient-specific risk for a FGR[19].

First trimester screening of FGR

Effective screening for FGR in the first trimester may be of value in targeting potential therapeutic agents[20], whereas later identification in the second trimester may be used to undertake intensive monitoring of the pregnancy[21]. Over the last years a number of Doppler ultrasound studies of the uteroplacental circulation have confirmed that increased impedance to flow in these vessels is associated with an increased risk for subsequent development of pre-eclampsia and/or FGR[22].

Transabdominal uterine artery Doppler assessment can be undertaken at 11-14 weeks. A mid-sagittal section of the uterus needs to be obtained, and the cervical canal can be identified. The probe needs to move laterally until the paracervical vascular plexus is observed. Colour Doppler imaging is used to identify the uterine artery as it turned cranially to make its ascent to the uterine body. Measurements are then taken at this point, before the uterine artery branched into the arcuate arteries[23] (Figure 1).

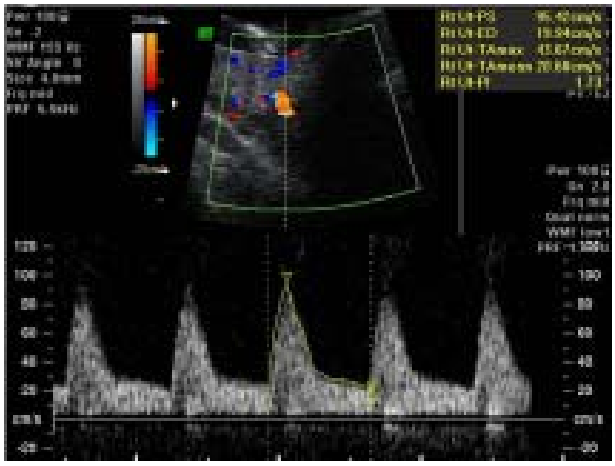

Figure 1. **First trimester uterine artery Doppler wave.**

Dugoff *et al* have assessed the risk of FGR using first uterine artery Doppler at 10-14 weeks and reported that those with a high uterine artery mean resistance index (>75th percentile) were 5.5 times more likely to have FGR[24]. Karagiannis *et al* have demonstrated that an algorithm combining maternal characteristics and biophysical and biochemical tests at 11-13 weeks could potentially identify half of pregnancies that deliver SGA neonates in the absence of PE, at a 10% false positive rate[25] (Table 1).

Second trimester screening of FGR

A study by Gomez *et al* examined uterine artery Doppler at 11-14 weeks and at 19-22 weeks. They have recruited 870 women including 24 cases of preeclampsia (2.75%) and 37 (4.25%) of FGR. Compared to pregnancies with a normal outcome, complicated pregnancies showed a significantly higher prevalence of a bilateral notch and a higher mean pulsatility index in each of the two intervals studied. Women with persistently abnormal mean pulsatility index in the first and second trimester were at greatest risk for adverse perinatal outcome (odds ratio (OR) 10.7; 95% confidence interval (CI) 3.7-30.9), suggesting that the sequence of changes in uterine blood flow between first and second trimesters correlates with the subsequent development of hypertensive disorders and FGR[26]. It is known that detection rate of FGR is lesser than the detection of early onset preeclampsia by second trimester Doppler (60%, 85% respectively). Furthermore, overall detection of FGR is better with second trimester uterine artery Doppler than first trimester Doppler[26] (Table 2).

Table 1. Performance of screening for delivery of SGA neonates by maternal factors only and maternal factors with biophysical markers[+] (uterine artery pulsatility index, mean arterial pressure, fetal nuchal translucency thickness) and biochemical markers[*] (maternal serum pregnancy associated plasma protein-A, free beta-human chorionic gonadotrophin, placental growth factor, placental protein 13, a disintegrin and metalloprotease). Adopted from Karagiannis *et al* 2010[25].

Method of screening	*SGA <37 weeks*		*SGA >37 weeks*	
	DR for FPR 5%	*DR for FPR 10%*	*DR for FPR 5%*	*DR for FPR 10%*
Maternal factors	23.3	35.0	20.8	33.9
Maternal factors plus biophysical markers[+]	33.7	46.8	24.3	36.8
Maternal factors plus biochemical markers[*]	50.1	63.0	29.0	41.7
All markers	60.7	73.2	32.5	45.8

Table 2. Detection rate of SGA/FGR for different screening methods

Test	*Detection rate of early onset SGA (%)*	*Detection rate of late onset SGA (%)*
Abdominal palpation	29	
SFH measurement	30-40	
SFH on customized charts	48	
First trimester uterine artery Doppler	45 (FPR 10%)	35 (FPR 10%)
First trimester uterine artery Doppler, biochemical and maternal characteristics	73 (FPR 10%)	46 (FPR 10%)
Second trimester uterine artery Doppler and maternal characteristics	60	45

Summary

Uterine artery Doppler studies can be used as an effective test in predicting pregnancies at high risk of developing complications related to uteroplacental insufficiency. It can be performed at the same time as routine ultrasound pregnancy assessment. Uterine artery Doppler has a low false positive rate and identifies women who may benefit from increased antenatal surveillance or prophylactic therapy.

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