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A Summary of Chinese Expert Consensus on Fetal Growth Restriction (An Update on the 2019 Version)

Fetal Medicine Subgroup, Chinese Society of Perinatal Medicine, Chinese Medical Association; Maternal-Fetal Medicine Committee, Chinese Society of Obstetrics and Gynecology, Chinese Medical Association; Luming Sun[1,*], Yali Hu[2,*], Hongbo Qi[3,*]

Abstract

Fetal growth restriction (FGR) is a common complication of pregnancy associated with higher rates of perinatal mortality and morbidity, as well as a variety of long-term adverse outcomes. To standardize the clinical practice for the management of FGR in China, Fetal Medicine Subgroup, Chinese Society of Perinatal Medicine, Chinese Medical Association and Maternal-Fetal Medicine Committee, Chinese Society of Obstetrics and Gynecology,Chinese Medical Association organized an expert committee to provide official consensus-based recommendations on FGR. We evaluated the evidence provided by relevant high-quality literature, performed a three-round Delphi study and organized face-to-face meetings with experts from multidisciplinary backgrounds. The consensus includes the definition, prenatal screening, prevention, diagnosis, monitoring and management of FGR.

Keywords: Delphi technique; Fetal growth restriction; Practice guideline

Introduction

Fetal growth restriction (FGR) is associated with elevated rates of perinatal mortality and morbidity and various long-term adverse outcomes. Fetuses experiencing growth restriction are at increased risk of childhood cognitive impairment and a range of adult diseases, including obesity, type-2 diabetes mellitus, cardiovascular diseases, and stroke.[1–4] Therefore, early screening, diagnosis, intrauterine monitoring, and optimized delivery are crucial for FGR. To standardize the clinical management of FGR in China, the Fetal Medicine Subgroup of the Chinese Society of Perinatal Medicine (Chinese Medicine Association) and the Maternal-Fetal Medicine Committee of the Chinese Society of Obstetrics and Gynecology (Chinese Medical Association) organized an expert committee to generate official consensus-based recommendations for FGR.

Methods

A consensus on FGR-related clinical issues was developed by experts reviewing the official FGR guidelines from the American College of Obstetricians and Gynecologists,[5] the Royal College of Obstetricians and Gynecologists,[6] the Society of Obstetricians and Gynecologists of Canada,[7] and the most recent evidence-based clinical research (classification of evidence levels and recommendation grades using the Grading of Recommendations, Assessment, Development, and Evaluations system). Relatively high-level evidence (higher than or equal to level III), along with grade A or B recommendations, that are consistently adopted in other guidelines were cited directly in this consensus. A Delphi technique was used for low-level evidence (lower than level III) and for recommendations that were grade C or below. The Delphi technique aims to refine opinions by consulting with experts and then developing a consensus. The Delphi method is an iterative and anonymous technique based on the scoring of a series of structured statements that are revised, fed back to the participants, and repeated in multiple rounds (in increasing detail) until a consensus has been reached.[8] We performed the Delphi technique over three rounds and successfully reached a consensus based on the situation in China; the consensus served a as grade C recommendation (expert consensus).

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Table 1

Recommendations made by the expert consensus on fetal growth restriction.

Recommendation	Level
Question 1: How should we define fetal growth restriction (FGR)?	
1–1 The definition of a small for gestational age (SGA) fetus: A fetus for which the estimated fetal weight (EFW) or abdominal circumference (AC) $<$ the 10th percentile for gestational age. Not all SGA fetuses have pathological growth restriction. SGA also encompasses a proportion of constitutionally small but healthy fetuses. The establishment of customized growth criteria can improve the sensitivity of prenatal screening for SGA.	C (Expert consensus)
1–2 FGR refers to a fetus that does not reach genetic growth potential due to pathological maternal, fetal, or placental factors. The EFW or AC of FGR is usually $<$ the 10th percentile for gestational age.[6,7]	C (Expert consensus)
1–3 FGR fetuses with an EFW or AC $<$ the 3rd percentile for gestational age, or combined with an abnormal blood flow, are considered to have severe FGR.[9]	C (Expert consensus)
1–4 The definition of an early FGR fetus: $<$32 weeks of gestation, in the absence of congenital anomalies, an AC or EFW below the third percentile or an umbilical artery (UA)—absent end-diastolic flow, or (1) AC or EFW of $<$ the 10th percentile, combined with (2) an uterine artery pulsatility index (PI) of $>$ the 95th percentile and/or (3) a UA-PI of $>$ the 95th percentile.[10]	C (Expert consensus)
1–5 The definition of a late FGR fetus: $\geq$32 weeks of gestation, in the absence of congenital anomalies, an AC or EFW $<$ the 3rd percentile, or at least 2 or 3 of the following: (1) an AC or EFW $<$ the 10th percentile, (2) an AC or EFW crossing percentiles of $>$2 quartiles on growth percentiles, (3) a cerebroplacental ratio (CPR) $<$ the 5th percentile or a UA-PI $>$ the 95th percentile.[10]	C (Expert consensus)
Question 2: How should we screen maternal condition for FGR?	
2–1 Evaluating the maternal factors of FGR is recommended, including pregnancy comorbidities and complications.[5,6]	B
2–2 Screening for autoimmune antibodies should be considered to exclude disorders of the maternal autoimmune system when the pathology of FGR is suspected to be related to placental insufficiency.[11–13]	C (Expert consensus)
Question 3: How should we screen fetal condition for FGR?	
3–1 Detailed ultrasound screening of fetal structure is recommended. If FGR fetuses are accompanied by fetal malformation, then we recommend prenatal diagnostic tests including chromosomal microarrays and karyotyping.[14,15]	B
3–2 Genetic counseling and prenatal diagnosis are recommended for a pregnant woman with FGR diagnosed before 24 weeks of gestation or an EFW below 500 g, regardless of the combination of fetal structural abnormalities.[5,6,16]	B
3–3 Prenatal diagnostic testing with chromosomal microarray analysis can be offered when unexplained isolated FGR is diagnosed at $<$32 weeks of gestation.	C (Expert consensus)
Question 4: Is screening for relevant congenital infections required for FGR?	
4–1 Screening for congenital infections can be offered when FGR is suspected, especially for cytomegalovirus.[17,18] Testing for Zika virus and malaria should also be considered in the context of relevant travel history or location.	C (Expert consensus)
Question 5: How should pregnant women be screened for FGR?	
5–1 All pregnant women should be screened for risk factors for FGR through a review of medical and obstetric history.[19]	A
5–2 The use of maternal fundal height to screen FGR has low sensitivity. Routine measurement of fundal height can help to detect SGA fetuses in areas where other screening tools are not available.[20] Ultrasound evaluation should be performed in cases of clinically suspected FGR.[21]	C (Expert consensus)
5–3 Single serological markers are of limited value when screening aneuploidy for FGR.[22,23]	C (Expert consensus)
5–4 Imaging of the uterine artery with a Doppler system has limited diagnostic accuracy; routine screening is not recommended.[24]	B
Question 6: How do we prevent FGR?	
6–1 Maternal smoking cessation may reduce the risk of FGR.[25]	A
6–2 For pregnant women at a high risk of preeclampsia, prophylactic oral aspirin before 16 weeks of gestation may prevent FGR and preeclampsia.[26]	A
6–3 Low molecular weight heparin is ineffective in preventing FGR for high-risk populations.[27]	A
6–4 There is no evidence to suggest that progesterone and calcium supplementation can prevent FGR.[28,29]	A
Question 7: How do we diagnose FGR?	
7–1 Accurate verification of gestational age is a prerequisite for the diagnosis of FGR.[30]	C (Expert consensus)
7–2 An EFW or AC below the 10th percentile for gestational age can be diagnosed as suspected FGR. Calculation of the EFW or percentile can use either customized standards or unadjusted population standards. The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Asian standard or Hadlock formula is recommended.[31]	C (Expert consensus)
7–3 The etiology and risk factors of FGR should be investigated carefully.	C (Expert consensus)
Question 8: Can monitoring of fetal movements prevent intrauterine death in FGR fetuses?	
8–1 Daily monitoring of fetal movements is recommended for pregnant women with singleton FGR. However, the efficacy of monitoring fetal movements is uncertain with regards to preventing intrauterine death in FGR fetuses.[32,33]	A
8–2 It is recommended that a pregnant woman with FGR who notices reduces fetal movement should be offered further fetal evaluation.	B

(*continued*)

Table 1
(continued).

Recommendation	Level
Question 9: What is the frequency of ultrasound monitoring in FGR to evaluate fetal growth velocity?	
9–1 When dynamic fetal AC or EFW is used to access fetal growth velocity, the interval should be more than 2–3 weeks to minimize the inherent error associated with sonographic measurements and to reduce the false positive rate for diagnosing FGR.[34]	C (Expert consensus)
Question 10: What is the role of Doppler velocimetry in the evaluation of pregnancies complicated by FGR?	
10–1 Umbilical artery Doppler velocimetry plays the most critical role in the management of pregnancies complicated by FGR and could assist obstetric management and reduce perinatal morbidity and mortality.[35]	A
10–2 Ultrasonography at an interval of 1–2 weeks is recommended for FGR fetuses with a normal umbilical artery pulsatility index.[6]	B
10–3 It is important to detect the absence or reversed end-diastolic flow in the umbilical artery of FGR fetuses as this is associated with an increased frequency of perinatal mortality and can affect decisions relating to the termination or continuation of pregnancy.[35]	A
10–4 If the end-diastolic flow is absent or reversed in a fetus with FGR, it is recommended that a pregnant woman should be referred to a medical center with experience in monitoring and treating FGR.	C (Expert consensus)
10–5 Before 32 weeks of gestation, measuring the flow in the middle cerebral artery (MCA) has limited accuracy with regards to the prediction of neonatal acidosis and adverse outcomes for FGR. MCA flow should not be used as the only basis for the time of delivery when end-diastolic flow in the umbilical artery is positive.[36,37]	B
10–6 After 32 weeks of gestation, if the end-diastolic flow of the umbilical artery is positive, a reduction in the MCA pulsatility index ($<$ the 5th percentile) has a predictive value for neonatal acidosis. This can be used as a reference for the timing of delivery.[38]	B
10–7 The assessment of fetal venous flow by Doppler imaging enhances the prediction of acidosis and adverse outcomes.[39]	A
10–8 For preterm FGR with abnormal umbilical artery flow, the assessment of venous flow by Doppler imaging is recommended to help determine the timing of delivery.	C (Expert consensus)
Question 11 What is the role of evaluating amniotic fluid volume in monitoring FGR fetuses?	
11–1 Single deepest vertical pocket measurement to determine oligohydramnios can reduce the false positive rate compared to amniotic fluid index.[40]	A
Question 12 What is the role of computerized cardiotocography (cCTG) in FGR fetuses?	
12–1 cCTG should be offered to FGR fetuses if possible. However, cCTG should not be the only method used for antenatal surveillance.[41]	A
12–2 Of all cCTG indices, the short-term variation of fetal heart rate is valuable for predicting fetal condition.[42]	A
12–3 If a woman is complicated by FGR and in labor, then immediate hospital admission and continuous cCTG are recommended.[6]	C (Expert consensus)
Question 13 How should FGR fetuses be monitored?	
13–1 Once FGR is diagnosed, serial ultrasonography at an interval of 1–2 weeks with monitoring of the amniotic fluid volume and umbilical artery flow by Doppler imaging is recommended. If umbilical artery Doppler velocimetry remains elevated, or even flow by Doppler imaging with absent or reversed end-diastolic velocities, it is recommended that individuals should be referred to medical units with experience of FGR monitoring and management.[6,43]	A
13–2 To date, the optimal strategy for monitoring FGR is a comprehensive evaluation based on the combination of Doppler assessment, amniotic fluid volume, biophysical profile (BPP), cCTG, and fetal growth velocity for fetal surveillance.[44]	C (Expert consensus)
Question 14 How should a woman with an FGR fetus be managed during pregnancy?	
14–1 To date, there is no evidence to suggest any benefit from nutritional supplementation, oxygen therapy, or tocolysis in a hospital, or maternal repositioning to improve fetal growth.[45–48]	A
14–2 Antenatal maternal sildenafil administration for FGR may not improve fetal growth and intrauterine health conditions.[49–51]	B
Question 15 When should a growth-restricted fetus be delivered?	
15–1 The timing of delivery for FGR should be based on a combination of factors, including gestational age, underlying etiology, classification, degree of severity, monitoring indices, and local neonatal intensive care unit capacity.	C (Expert consensus)
15–2 For fetuses less than 24 weeks of gestation or with an EFW $<$500 g, if FGR is evident, then it is recommended that a pregnant woman should receive professional counseling and evaluation at a local prenatal diagnosis center to exclude fetal genetic abnormalities. If Doppler imaging of the umbilical artery is abnormal, then individuals should be counseled carefully regarding fetal prognosis. The attitudes of individuals towards fetuses (whether to continue the pregnancy or not) should be clear; this will help to determine further therapeutic options.	C (Expert consensus)
15–3 For fetuses between 24 and 28 weeks of gestation or with an EFW of 500–1000 g, if Doppler imaging of the umbilical artery is abnormal (absent or reversed end-diastolic flow) and individuals request treatment, it is recommended	C (Expert consensus)

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(continued).

Recommendation	Level
that individuals receive antenatal surveillance and deliver in medical centers capable of managing infants with extremely low birth weight. When an FGR fetus is in a stable condition, the primary hospital should coordinate and communicate with the referral center to strive for the opportunity of intrauterine transport.[5]	
15–4 For FGR fetuses between 28 and 32 weeks of gestation, if Doppler imaging of the umbilical artery is abnormal (absent or reversed end-diastolic flow) combined with an abnormal ductus venosus a-wave (absent or reversed), it is recommended to deliver immediately after corticosteroid therapy for fetal lung maturation. If there is only umbilical artery reversed diastolic flow without any other evidence of fetal distress (such as an abnormal cCTG tracing or an abnormal ductus venosus a-wave, etc.), then delivery is suggested at 32 weeks of gestation.[5,6,43]	C (Expert consensus)
15–5 For FGR fetuses between 32 and 34 weeks of gestation, only with an absence of diastolic flow in the umbilical artery, and without any other evidence of fetal distress (such as abnormal cCTG tracing, a BPP score <4, or abnormal ductus venosus a-wave, etc.), then delivery is suggested at 34 weeks of gestation.	C (Expert consensus)
15–6 Antenatal corticosteroids are recommended if delivery is anticipated before 34 weeks of gestation. In addition, antenatal corticosteroids are recommended for women who are anticipated to deliver between 34 and 37 weeks of gestation, those who are at risk of preterm delivery within seven days, and those who have not received a previous course of antenatal corticosteroids.[5]	A
15–7 For FGR fetuses, if delivery is less than 32 weeks of gestation, then magnesium sulfate should be given for fetal and neonatal neuroprotection.[5]	A
15–8 For FGR fetuses between 34 and 37 weeks of gestation, any single increased umbilical artery pulsatility index should not be taken as an indication for immediate delivery. Recommendations are to assess fetal health comprehensively and follow-up closely. If fetal surveillance indicates a good condition, then delivery is suggested ≥37 weeks of gestation. For FGR fetuses ≥ 34 weeks of gestation, delivery is reasonable if fetal growth arrests for more than two weeks, if oligohydramnios is evident (deepest vertical pocket <2 cm), BPP score < 6, abnormal non-stress test, or confirmed abnormal Doppler modality.	C (Expert consensus)
15–9 Delivery is recommended for FGR fetuses after 37 weeks of gestation. The pros and cons of expectant management and delivery need to be communicated with the pregnant female and her partner/family.	C (Expert consensus)
Question 16 How should the route of delivery be evaluated?	
16–1 FGR is not the absolute indication for cesarean section. However, a planned cesarean is recommended when Doppler imaging of the umbilical artery is abnormal (absent or reversed end-diastolic flow).[5,6]	C (Expert consensus)

Round 1 of the Delphi technique

First, a literature review and face-to-face meetings were carried out. Then some experts participating in telephone or online consultation, to develop a specific questionnaire (questionnaire I) to generate a consensus for FGR. Subsequently, a nationwide panel was asked to propose amendments and determine content; finally, an online version of questionnaire II was created.

Round 2 of the Delphi technique

Next, 20–30 experts who were recognized specialists in this field (each with more than 10-years of experience in the field) were invited to join the Delphi procedure. Participants were asked to answer questionnaire II, submit additional questions and suggest refinements. After meticulously gathering and summarizing the opinions of these experts, we finally reached a consensus and generated Questionnaire III.

Round 3 of the Delphi technique

In round 3, 20–30 experts were invited to answer questionnaire III (half of these were the same as those used in round 2 and half were new); we then collated and summarized the results.

Recommendations (grades A and B) on clinical issues relating to FGR, and the results of the Chinese expert consensus formed through the Delphi procedure, were then integrated to develop the first draft of the "Expert Consensus on Fetal Growth Restriction." The final draft was then modified through face-to-face meetings involving experts from the Fetal Medicine Subgroup of the Chinese Society of Perinatal Medicine (Chinese Medical Association), and online discussion featuring experts with multidisciplinary backgrounds.These guidelines were then revised by experts from the Maternal-Fetal Medicine Committee of the Chinese Society of Obstetrics and Gynecology (Chinese Medical Association).

Results

All recommendations from experts were summarized in Table 1.

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Conflicts of Interest

None.

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