Review Article

Radiological Modalities for the Assessment of Fetal Growth Restriction: A Comprehensive Review

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ABSTRACT

Fetal growth restriction is a significant contributor to fetal morbidity and mortality. In addition, there are heightened maternal risks associated with surgical operations and their accompanying dangers. Monitoring fetal development is a crucial objective of prenatal care and effective methods for early diagnosis of Fetal growth restriction, allowing prompt management and timely intervention to improve the outcomes. Screening for Fetal growth restriction can be achieved via many modalities; it can be medical, biochemical, or radiological. Some recommended combining more than one for better outcomes. Currently, there is inconsistency about the best method of Fetal growth restriction screening.

In this review, a comprehensive evaluation of the current radiological methods used for Fetal growth restriction, including serial growth scan, Doppler velocimetry, and biophysical profile is offered. Limitations, and potential enhancements area were specifically analyzing the effectiveness. Moreover, recently developed experimental radiological techniques were presented and how to integrate them into practice to enhance follow-up performance and results.

Keywords: fetal growth restriction, Doppler, Biophysical profile, radiological screening, Artificial intelligence, machine learning

Introduction

Obstetrical care aims to provide a healthy journey for the mother that ends with the delivery of a safe and healthy baby (1,2). Fetal growth restriction (FGR) or “intrauterine growth restriction” is when a fetus fails to reach its genetically determined weight lacks a common definition, and it can occur due to several factors (3). It could be maternal, placental, or fetal causes or it can be a combination of more than one. On the other hand, a small for gestational age fetus (SGA) is the case when the fetus weight is below the 10th percentile of the norms for that community (4). Table 1. Summarize the main points that distinguish both terms (5).

FGR is a significant contributor to fetal and neonatal morbidity and death. For that, many screening strategies have been adopted to halt its complications on feto-maternal outcomes (6). Screening for fetal growth restriction can be medical, biochemical, and physiological.
Fetal Growth Restriction (FGR) management is a complex dilemma. A critical choice between preventing fetal harm or death by prolonging the pregnancy and the potential risks associated with terminating the pregnancy. This must be grounded on a delicate equilibrium between maternal and family risk factors and the anticipated benefits for the overall feto-maternal outcome (20).

In this review, we will address biophysical screening for FGR, including the ultrasonic parameters, and we will supply a comprehensive appraisal and critique of up-to-date breakthroughs in this rapidly growing field.

**Methods**

The purpose of this review was to bring together data on FGR screening with radiological methods. To ensure a full study of the released work, the methods used a simplified approach that included the steps below:

- A plan was used to find relevant papers using digital libraries, which include databases like Scopus, Web of Science, and Google Scholar.
- A mix of terms and subject titles was used to find articles about fetal growth, fetal growth restriction, intrauterine growth retardation, Doppler, biophysical profile, radiological screening, and babies that

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### Table 1: A comparison between FGR and SGA

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Small for Gestational Age (SGA)</th>
<th>Fetal Growth Restriction (FGR)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definitions</strong></td>
<td>A baby is considered small for its gestational age (SGA) if its birth weight is less than the tenth percentile, which is two standard deviations below the mean for that community</td>
<td>Is diagnosed if physical growth is slow, with an estimated fetal weight is less than the third percentile, with compromised umbilical/cerebral blood flow</td>
</tr>
<tr>
<td><strong>Recently revised</strong></td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>Incidence Interpretation</strong></td>
<td>10-15 percent</td>
<td>May not always be pathological</td>
</tr>
<tr>
<td><strong>An etiology</strong></td>
<td>Constitutional, genetically determined</td>
<td>Placental, maternal, and fetal diseases such as hypertension, infections, etc.</td>
</tr>
<tr>
<td><strong>Impact on fetus</strong></td>
<td>Increased risk, respiratory problems, prematurity, low birth weight</td>
<td>May have a risk or not, depending on the underlying etiology</td>
</tr>
</tbody>
</table>

- **Medical screening** involves Fundal height measurement (FHM)

  It is a simple and cost-effective procedure that is currently included in prenatal screening for pregnant mothers (7). Yet, it is impeded by its lack of precision due to its subjective to the examiner. FHM is influenced by maternal factors such as body weight and size. More importantly, it may fail to detect FGR indicators in its early stages, resulting in delayed diagnosis when options for fetal intervention are limited. The test may yield false-positive results in the case of twins and thus requires confirmation from another test, indicating its limited diagnostic utility (8).

- **Biochemical screening**

  Several biomarkers and inflammatory cytokines (9) were analyzed as Pregnancy-Associated Plasma Protein-A, alpha-1 antitrypsin, and placental growth factor (10)(11). Usually, there is a delay or time lag before the fetal measurements show signs of FGR. Biochemical screening has a higher likelihood of detecting FGR early, however it has poor detection rate and there is no agreement in determining the best time for intervention (12).

- **Biophysical screening**

  Currently, this is the most popular way, including a 2-dimensional ultrasound (US), Doppler study, and biophysical profiling. These tests need serial measurement and repetitions so patient compliance is crucial in the diagnosis (13). These tests are also examiner-dependent, so the inter-observer disparity cannot be excluded. Biophysical is costly, time-consuming, and can lead to higher operative intervention due to their high false positive and negative rates (14).

To date, there are no gold test that could spot FGR, for that utilizing one way of screening alongside other clinical data and maternal risk factors is essential for precise diagnosis and proper management of pregnancies with suspected FGR (15), see Figure 1. To avoid the complications that come with intrauterine growth restriction, it is crucial to take comprehensive steps:

- **Accurate dating establishment** is the first step in diagnosing a fetus with growth restriction, which could be obtained by either LMP or by early US within the 1st trimester (16).
- **Identify the cause**; an extensive medical background.

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**Figure 1. Steps for managing cases with FGR**

**Take appropriate action**

**Close Fetal monitoring**

**Improve uteroplacental flow**

**Control Maternal illnesses**

**Identify the cause**

**Accurate dating**

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are small for their gestational age. To improve the search results, Boolean operators like "AND" and "OR" were used to join keywords. The search looked for papers that were published till 1/2/2024. Fig. 2 shows the study's process and the factors for who was included and who was not included.

Biophysical screening includes Serial growth scan, Doppler, biophysical profiles (BPP), and modified BPP.

Serial growth scan
In basic terms, the weight of the fetus is assessed at a particular moment using conventional measurements such as biparietal profile (BPD), femoral length (FL), head circumference (HC), and abdominal circumference (AC). On the other hand, fetal growth is a dynamic process that involves changes in fetal weight over time. Therefore, at least two ultrasound scans conducted at different intervals are necessary to track this progression (21) (22).

Fetuses with an estimated fetal weight below the 10th percentile, according to the trajectory model, should undergo serial ultrasound scans every 3-4 weeks following diagnosis. This will allow the supervising clinician to periodically evaluate the fetus's viability perinatal risk and determine the appropriate timing for delivery (23). When dealing with pregnancies that have no date or have been poorly dated, accurately diagnosing the incorrect size of the fetus presents a distinct issue. Several specialists recommend scheduling a follow-up ultrasound examination within a period of 3-5 weeks to verify that the development of the pregnancy is progressing in accordance with the predicted pattern, particularly if the fetus seems smaller than anticipated by a difference of more than 21 days based on the last menstrual period (24). Serial ultrasound is an indispensable instrument in identifying growth-restricted fetuses and minimizing the risk of incorrectly diagnosing healthy fetuses as small for their gestational age in high-risk pregnancies. This procedure is both time-consuming and cost-effective. Therefore, Hiersch et al. recommended conducting additional studies to establish the most accurate timing and intervals for performing ultrasound exams (25).

Doppler US:
The Doppler technique is a noninvasive method that utilizes sound waves to quantify the speed and direction of blood flow in different vessels, it provides real-time evaluations, allowing the continuous monitoring of blood flow fluctuations throughout pregnancy (26). It is frequently employed to examine the umbilical artery blood flow in addition to other arteries during pregnancy; see Figure 3, 4 and Table 2, especially for assessing FGR.

Doppler's role in FGR can be summarized into:

Identify FGR:
Doppler results, in conjunction with other clinical and ultrasound characteristics, can assist in diagnosing FGR. Furthermore, it enables the categorization of FGR risk for moms exhibiting abnormal Doppler results, thus empowering obstetricians to identify pregnancies with a heightened risk and adopt suitable management techniques. Timely detection of FGR optimizes treatment and enhances outcomes (35).

Evaluate FGR severity:
Doppler indices abnormality frequently corresponds to the severity of insufficient placental supply and fetal jeopardy. Giving valuable guidance for treatment decisions and optimal timing for interventions (36).
Table 2. The main vessels used in screening for FGR alongside Doppler parameters used and supporting references

<table>
<thead>
<tr>
<th>vessel/Artery; Function/Role</th>
<th>Doppler Indices</th>
<th>Significance in FGR</th>
<th>Supporting references/study findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Umbilical Artery Transports oxygenated blood from the placenta to the fetus</td>
<td>Pulsatility Index (PI), Systolic/Diastolic (S/D) ratio</td>
<td>Increased resistance indicates placental insufficiency, a common cause of FGR.</td>
<td>- Frusca et al. said in low-risk pregnancies, UA Doppler adds no prognostic criteria (27) - Figueras recommended predictive value in high-risk pregnancies, especially if those complicated by preeclampsia or FGR (28) - Anjum et al. said if a normal umbilical artery Doppler is present, a reduced pulsatility index in the middle cerebral artery suggests fetal adaptation (29) - Oyekale et al. There is a debate over the reliance on CPR as an indication for FGR (30) - Seravalli et al. said that although the ductus venosus waveform lacks precise specificity, its association with arterial Doppler gives it significance in evaluating and follow up on FGR fetuses (31) - It plays a crucial role in guiding the therapeutic treatment of fetuses who are at risk of experiencing a decline in cardiovascular health - Pedroso et al. concluded UtA Doppler is not a very accurate predictive test for PE and FGR when used alone. Yet more accurate in detecting preterm PE, its combined use in predictive models is encouraging (32) - Kwok-Yin Leung et al. concluded UtA Doppler is not a very accurate predictive test for PE and FGR when used alone. Yet more accurate in detecting preterm PE, its combined use in predictive models is encouraging (32) - Seravalli et al. said that although the ductus venosus waveform lacks precise specificity, its association with arterial Doppler gives it significance in evaluating and follow up on FGR fetuses (31)</td>
</tr>
<tr>
<td>Middle Cerebral Artery Provides blood to the brain</td>
<td>Absence or reversal of end-diastolic flow</td>
<td>Abnormal Doppler waveforms may suggest fetal hypoxia and the risk of brain damage in cases of FGR.</td>
<td></td>
</tr>
<tr>
<td>Ductus venosus Connects umbilical vein to inferior vena cava, bypassing liver</td>
<td>Aberrant Doppler waveforms</td>
<td>It may indicate fetal cardiac dysfunction and impairment, potentially associated with FGR.</td>
<td></td>
</tr>
<tr>
<td>Uterine Artery Supplies blood to the uterus</td>
<td>Resistance Index (RI), Pulsatility Index (PI)</td>
<td>Increased RI or PI may indicate impaired blood flow, suggesting potential placental issues and an elevated risk of FGR.</td>
<td>- Frusca et al. said in low-risk pregnancies, UA Doppler adds no prognostic criteria (27) - Figueras recommended predictive value in high-risk pregnancies, especially if those complicated by preeclampsia or FGR (28) - Anjum et al. said if a normal umbilical artery Doppler is present, a reduced pulsatility index in the middle cerebral artery suggests fetal adaptation (29)</td>
</tr>
<tr>
<td>Umbilical Vein transport oxygenated and nutrient-rich blood from the placenta to the fetus</td>
<td>Monophasic, non-pulsatile flow (10-15 cm/s)</td>
<td>Assessing risk of perinatal death in FGR</td>
<td></td>
</tr>
</tbody>
</table>

Assess fetal health and well-being:

Serial Doppler tests can monitor alterations in blood flow patterns over a period of time, offering crucial insights into the fetus's reaction to treatments and possible decline (37).

Predict unfavorable consequences:

Aberrant Doppler results, namely the absence or reversal of end-diastolic flow in the umbilical artery (UA) or middle cerebral artery (MCA), are linked to a higher likelihood of perinatal problems such as stillbirth, newborn acidemia, and neurodevelopmental disability (38).

Doppler has its limitations; to begin with, it is reliant on the operator's skill in both acquiring and interpreting images. It cannot conclusively determine the underlying cause of FGR in every instance. Consequently, its predictive value is restricted (39). It is influenced by a broad range of variables since the normal levels vary across different ethnicities. The accuracy of the system is influenced by technical challenges such as movement and location. Furthermore, placental pathology may not be adequately seen by Doppler (40).

There were some concerns that prolonged exposure to the US practically Doppler may have harmful effects on the growing fetuses. Some animal studies reported increased cellular apoptosis however that effect was never reported in humans. Others suggested unwanted thermal effects by Doppler. All these are inconclusive and need further research (41).

To summarize, Doppler ultrasonography is an invaluable technique for evaluating blood circulation in FGR babies. It has a crucial impact on the diagnosis, evaluation of severity, monitoring, and prediction of unfavorable results, eventually leading to enhanced pregnancy outcomes for both women and their infants.

Biophysical profile:

The biophysical profile (BPP) is a 30-minute US examination that evaluates the well-being of the fetus and monitors its cardiac activity. The components consist of a fetal non-stress test, an amniotic fluid index evaluation, fetal breathing movements, full body movements, and limb tone (42), it was explained in details in Table 3.
Table 3. The component of biophysical profile and how is the score giving

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Time</th>
<th>Score giving</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetus breathing movement</td>
<td>Thirty minutes</td>
<td>2 points for active breathing; 1 point for slow or minimal breathing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0 points : NO movement throughout thirty minutes</td>
</tr>
<tr>
<td>Gross fetus body movement</td>
<td>Three 3 body parts</td>
<td>2 points for Vigorous movement involving</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 point for less</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0 points : No movement at all</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 points for active trunk and limb movement</td>
</tr>
<tr>
<td>Muscles tone</td>
<td>Twenty  minutes</td>
<td>1 points for less than that</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0 points for No movement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 points for normal volume</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 point for reduced amount</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0 for absent liquor</td>
</tr>
<tr>
<td>The volume of Amniotic fluid</td>
<td></td>
<td>2 points for normal heart rate tracing in response to fetus movement; i.e. 15 beat acceleration for 15 seconds.</td>
</tr>
<tr>
<td>Non-stress test</td>
<td>Twenty  minutes</td>
<td>1 point for absent acceleration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0 point for fetal heart decertation in response to movement.</td>
</tr>
</tbody>
</table>

The modified Biophysical Profile (MBPP) consists of two components: the Amniotic Fluid Index and the Non-Stress Test (43).

In cases of fetal distress, as in FGR, a decrease in oxygen levels necessitated the implementation of targeted adaptation strategies to provide adequate oxygen supply to various organs. This led to vasodilation in some organs, such as the brain and heart, and constriction in others, such as the kidney and liver (44).

BPP scores should be promptly repeated if the BPP Score is 6 and all of the deducted points are associated with fetal movement. A score ranging from 2-4 is considered disconcerting, and it is recommended to proceed with pregnancy termination.

A score of 0 indicates that fetal asphyxia and death are imminent, and urgent delivery is required (45).

Further testing is required in cases when the AFI examination reveals oligohydramnios, which is an indirect indication of fetal renal perfusion, despite if other parameters appear normal (46).

The BPP possessed the benefit of being very accessible, secure, non-intrusive, and easily obtainable. The evaluation encompasses several characteristics of the fetus’s well-being, resulting in a more comprehensive assessment compared to individual tests (47).

BPP Predicts unfavorable outcomes: An atypical BPP score might suggest an elevated likelihood of problems such as stillbirth, whereas a normal BPP score has a strong positive predictive value for favorable fetal health.

BPP data assist obstetricians in implementing more vigilant surveillance, intervention, or potentially even delivery.

The main drawback of this test is its time-consuming nature, taking around thirty minutes. It exhibits intra-observer variance, meaning that different observers may interpret the results differently. Furthermore, the exam can be influenced by certain medicines such as opiates, magnesium sulfate, corticosteroids, and tocolytics, which can slow down the heart rate and lead to non-reactive cardiac patterns (48).

False positive findings might arise from the infant's deep sleep cycles. Maternal weight might impair visual clarity, necessitating adjustments to the ultrasound's depth and gain (49).

Borade and Sharma discussed that the modified Biophysical Profile is a simple, cost-effective, and time-saving method. It can be utilized as the main antepartum fetal surveillance test to predict perinatal outcomes and offer timely intervention in high-risk pregnancies. However, it does not adequately evaluate fetal breathing, muscular tone, and power (50). Moreover, few studies have been done to validate its use so it currently has low reliability.

Newer radiological markers for FGR evaluation

Shear wave elastography:

Shear wave elastography (SWE) is a developing imaging method that uses US to quantify the tissue stiffness. Recently it gained attention for its possible uses in medicine as FGR (51).

The fact that this technology is noninvasive and radiation-free adds value to its safety for usage in pregnant women and fetuses. The advantage of this procedure that's it could be carried out in the same session and by the same device for fetal and Doppler scan (52).

The test provides a quantitative assessment of tissue stiffness, enabling the evaluation of maturity and development of several fetal organs.

SWE can detect complications at an earlier stage compared to traditional ultrasound and identify FGR babies at a greater risk of experiencing complications, enabling early intervention and enhancing results (53).

It can follow FGR progress and assess the effectiveness of treatment (54).

The end organ damage seen in FGR newborns is also seen, including Liver fibrosis, which is an indicator of long-term liver damage in newborns with growth restriction, and intestinal inflammation, which is a major contributor to perinatal morbidity and death. Finally, it can predict infants who are susceptible to neurodevelopmental issues (55,56).

SWE is a comparatively novel technology that has not yet been extensively implemented in all healthcare settings, and it needs further study to substantiate its therapeutic applicability in FGR. Being operator-dependent makes its precision affected by the proficiency and expertise of the operator. Having a posterior placenta increases the interference with shear wave propagation.

Flow Mediated Dilatation (FMD) and Flow-mediated slowing (FMS)

Studies on flow-mediated dilatation (FMD) and flow-mediated slowing (FMS) in newborns with FGR are scarce. Although these methods are widely accepted for evaluating vascular well-being in adults and older kids, their application in newborns, particularly in FGR, is still nascent (57).

Ultrasonic assessment of FMD of the brachial artery is the standard method to assess endothelial function, and it can proceed with the onset of clinical symptoms (58).
FMS is equivalent to FMD, yet it has not been tested in pregnant moms. Flow Mediated Slowing FMS is calculated by VICORDER® electronically, and it retrieves results for clinical screening and follow-up care and allows interventional strategies to be made (59).

Loibner et al. conducted a pilot study among high-risk pregnancies. The study recommended its use for standard care during pregnancy and predicting accurate clinical outcomes with the advantage of being a straightforward, automated, and operator-independent test technique.

The study compared the findings of FMD and FMS, showing convergence in all 9 cases and suggesting normal endothelium function with a specificity of 100% and a sensitivity of 72.7% (60). However, it is important to note that the study had limitations, and further extensive investigations are required. Despite that research in this technique is in its infancy state; this technique can provide valuable insights into:

- Assessments and evaluation of blood vessel endothelium function, thus providing insights into cardiovascular risks in FGR infants, who are prone to such complications. Anomalous FMD and FMS may suggest initial vascular impairment and maybe forecast forthcoming cardiovascular problems so they can spot a complication (61).
- Implementing FMD and FMS in practice, especially for neonates with FGR, presents; technical challenges while doing the measurements owing to the newborn's tiny stature and their tendency to move (62). Currently, there is a lack of standardized techniques and reference values for neonates, especially for FGR. Further investigation and comprehension are needed to interpret the data within the framework of FGR and its possible influence on vascular health.

**Artificial intelligence and machine learning:**

One area where artificial intelligence (AI) shows great promise is in the field of illness detection and treatment, which is fast becoming an integral part of healthcare. Algorithms powered by artificial intelligence can sift through mountains of medical data, find insights and trends that human physicians would miss, and then propose tailored treatments(63),(64).

Rescinito et al. systemic review and meta-analysis examined using AI/ML models to forecast FGR. The parameters tested in enrolled studies were the fetal heart rate variability, screening of biochemical markers, DNA profiling data, Doppler velocimetry, MRI, and maternal physiological, clinical, or socioeconomic variables (65).

Artificial intelligence and machine learning techniques were effective in accurately predicting and identifying fetuses that are at risk of FGR during pregnancy. The sensitivity of these techniques is 0.84; the specificity is 0.87. The diagnostic odds ratio is 30.97 (95% CI 19.34–49.59), indicating the strength of the association between the AI/ML techniques and risk identification of FGR. The most accurate prediction of FGR was fetal heart rate (FHR) characteristics measured by cardiotocography(66).

AI/ML can enhance the optimization of pregnancy outcomes, but it requires appropriate algorithmic improvement and refinement, which is further emphasized (67). (68).

**Early pregnancy imaging via MRI indices**

Lee et al. conducted a prospective study examining the MRI technique as early as the 14th to 16th week of gestation to forecast the probability of FGR.

They assessed the placenta's ability to maintain a sufficient blood supply to the fetus. When compared to the usual placental ultrasound approach, which may identify decreases in placenta blood flow between 20 to 24 weeks. MRI indices appear to have earlier detection of ischemic placenta. Timely detection of fetal growth restriction and neonates who are undersized for their gestational age at delivery may lead to the formulation of therapeutic strategies for these disorders (69).

**Pulmonary vein Doppler ultrasonography:**

Pham et al. determined that growth-restricted fetuses have a significantly elevated average pulsatility index (PI) in the pulmonary vein. There is a direct relationship between the pulsatility index (PI) of the pulmonary vein and the PI of the umbilical vein in FGR fetuses. Additionally, there is an inverse relationship between the pulmonary vein’s PI and the umbilical artery’s pH(70).

**Early first-trimester pregnancy with contrast-enhanced ultrasound and 3D power Doppler angiography**

Bertholdt et al. designed a study protocol to recruit pregnant women currently at different stages of pregnancy. These women will be divided into three groups based on their gestational ages, Which will be 8, 11, and 13 weeks. A 3-dimensional power Doppler and contrast-enhanced ultrasound techniques will be utilized to collect data on perfusion kinetics and construct 3-D indices to be compared both within and across different gestational ages(71).

**Conclusion and Future Perspective**

The vast emerging technique that arose recently while offering promising results introduces challenges. There is a need for longitudinal studies to validate early promising results—integration of results via multicentric collaborative study. Examine new approaches for understanding the placental function to unravel newer, more efficient interventions, applying AI/ML in screening programs and integrating it into other screening modes.

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**Conflict of Interest**

Authors declare no conflict of interest.

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https://doi.org/10.1097/AOG.0000451759.90082.7b


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