### Doppler assessment of the fetus with intrauterine growth restriction

Society for Maternal-Fetal Medicine Publications Committee, with the assistance of Eliza Berkley, MD; Suneet P. Chauhan, MD; and Alfred Abuhamad, MD



Intrauterine growth restriction (IUGR) is defined as sonographic estimated fetal weight <10th percentile for gestational age. 1 According to the American College of Obstetricians and Gynecologists, IUGR is "one the most common and complex problems in modern obstetrics."<sup>2</sup> This characterization is understandable considering the various published definitions, poor detection rate, limited preventive or treatment options, multiple associated morbidities, and increased likelihood of perinatal mortality associated with IUGR. Suboptimal growth at birth is linked with impaired intellectual performance and diseases such as hypertension and obesity in adulthood.<sup>2</sup>

Current challenges in the clinical management of IUGR include accurate diagnosis of the truly growth-restricted fetus, selection of appropriate fetal surveillance, and optimizing the timing of delivery.<sup>3-5</sup> Despite the potential for a complicated course, antenatal detection of IUGR and its antepartum surveillance can improve outcomes. The purpose of this document is to synthesize and assess the strength of evidence of the current literature regarding the use of Doppler velocimetry of the umbilical artery, middle cerebral artery, and ductus venosus for nonanomalous fetuses with suspected IUGR, and to provide recommendations regarding antepartum management of these pregnancies, in particular for singleton gestations. We acknowledge that defining small for gesta-

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**OBJECTIVE:** We sought to provide evidence-based guidelines for utilization of Doppler studies for fetuses with intrauterine growth restriction (IUGR).

**METHODS:** Relevant documents were identified using PubMed (US National Library of Medicine, 1983 through 2011) publications, written in English, which describe the peripartum outcomes of IUGR according to Doppler assessment of umbilical arterial, middle cerebral artery, and ductus venosus. Additionally, the Cochrane Library, organizational guidelines, and studies identified through review of the above were utilized to identify relevant articles. Consistent with US Preventive Task Force suggestions, references were evaluated for quality based on the highest level of evidence, and recommendations were

**RESULTS AND RECOMMENDATIONS:** Summary of randomized and quasirandomized studies indicates that, among high-risk pregnancies with suspected IUGR, the use of umbilical arterial Doppler assessment significantly decreases the likelihood of labor induction, cesarean delivery, and perinatal deaths (1.2% vs 1.7%; relative risk, 0.71; 95% confidence interval, 0.52–0.98). Antepartum surveillance with Doppler of the umbilical artery should be started when the fetus is viable and IUGR is suspected. Although Doppler studies of the ductus venous, middle cerebral artery, and other vessels have some prognostic value for IUGR fetuses, currently there is a lack of randomized trials showing benefit. Thus, Doppler studies of vessels other than the umbilical artery, as part of assessment of fetal well-being in pregnancies complicated by IUGR, should be reserved for research protocols.

Key words: Doppler, ductus venosus, intrauterine growth restriction, middle cerebral artery, umbilical artery, uterine artery

tional age (birthweight <10th percentile for gestational age) by general population charts vs customized charts is an important issue, but this is not the focus of this clinical opinion.6

#### **Umbilical artery Doppler**

Doppler velocimetry of the umbilical artery assesses the resistance to blood perfusion of the fetoplacental unit (Figure 1, A). As early as 14 weeks, low impedance in the umbilical artery permits continuous forward flow throughout the cardiac cycle. Maternal or placental conditions that obliterate small muscular arteries in the placental tertiary stem villi result in a progressive decrease in end-diastolic flow in the umbilical artery Doppler waveform until absent (Figure 1, B) and then reversed (Figure 1, C) flow during diastole are evident.8 Reversed end-diastolic flow in the umbilical arterial circulation represents an advanced stage of placental compromise and has been associated with obliteration of >70% of arteries in placental tertiary villi. 9,10 Absent or reversed end-diastolic flow in the umbilical artery is commonly associated with severe (birthweight < 3rd percentile for gestational age) IUGR and oligohydramnios. 11,12

Although there are other quantitative assessments of umbilical artery Doppler (eg, resistance index) available, the systolic to diastolic (S/D) ratio and pulsatility index (PI) are commonly used and either may be sufficient to manage most cases of suspected IUGR. When end-diastolic flow is absent, the S/D ratio is immeasurable and PI may be used.

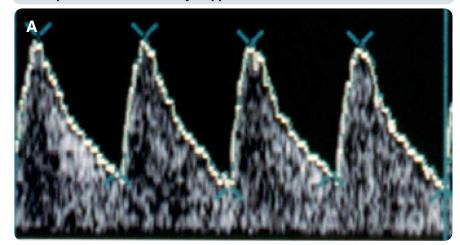
In clinical practice, Doppler waveforms of the umbilical artery can be obtained from any segment along the umbilical cord. Waveforms obtained near the placental end of the cord reflect downstream resistance and show higher end-diastolic flow velocity than waveforms obtained near the abdominal cord insertion. To optimize reproducibility, we suggest interrogating the umbilical artery at the abdominal cord insertion (Table). The S/D ratio and PI should be obtained in the absence of fetal breathing, and when the waveform is uniform. In clinical practice, averaging values of S/D ratios or PIs is unnecessary.

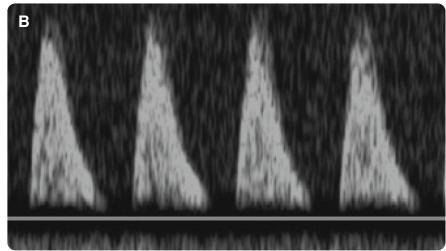
#### **Middle cerebral artery Doppler**

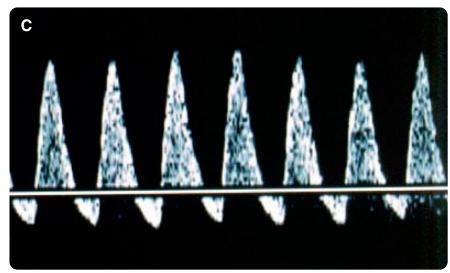
Under normal conditions, the cerebral circulation is a high impedance circulation with continuous forward flow present throughout the cardiac cycle<sup>14</sup> (Figure 2, A). The middle cerebral arteries, which carry >80% of the cerebral circulation, represent major branches of the circle of Willis and are the most accessible cerebral vessels for ultrasound imaging in the fetus. 15 The middle cerebral artery can be imaged with color Doppler ultrasound in a transverse plane of the fetal head obtained at the base of the skull. In this transverse plane, the proximal and distal middle cerebral arteries are seen in their longitudinal view, with their course almost parallel to the ultrasound beam. Middle cerebral artery Doppler waveforms, obtained from the proximal portion of the vessel immediately near the circle of Willis, have shown the best reproducibility<sup>16</sup> (Table). A limited number of studies have noted that middle cerebral artery peak systolic velocity may be a better predictor of perinatal mortality in preterm IUGR than the PI, but additional study is needed to confirm this finding.<sup>17</sup> While angle of correction is not necessary when measuring the middle cerebral artery PI, peak systolic velocity measurement should use angle correction and the angle of incidence should be <30 degrees; optimally as close to 0 degrees as possible.

In the presence of fetal hypoxemia, central redistribution of blood flow results in increased blood flow to the brain, heart, and adrenal glands, and a reduction in flow to the peripheral circulations. This blood flow redistribution, known as the brain-sparing reflex, is

FIGURE 1
Examples of umbilical artery Doppler flow waveforms







**A,** Normal umbilical artery Doppler flow waveform. **B,** Absent and **C,** reversed end-diastolic Doppler flow in umbilical artery.

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Variable	Gestational age, wk	Location	Pitfalls	Abnormal	Abnormality linked with
Umbilical artery	>23	Abdominal cord insertion (preferred), other locations acceptable	Optimally done when no fetal breathing	Decreased end-diastolic flow (includes AEDF, REDF)	Stillbirth Neurological impairment
Middle cerebral artery	>23	Proximal portion of vessel at 0-degree angle of incidence	>30-degree angle of incidence	Increased diastolic flow <sup>a</sup>	Neonatal acidosis Neurological impairment
Ductus venosus	>23	At site of aliasing, where it branches from umbilical vein	Obtaining Doppler of inferior vena cava	Decreased, absent, or reversed flow in a wave	Neonatal acidemia Perinatal mortality
Uterine artery	18-23	As it crosses the hypogastric vessels	Obtaining Doppler of hypogastric artery or vaginal branch of uterine artery	Notching or elevated pulsatility index	Linked in some studies with prediction of IUGR

characterized by increased end-diastolic flow velocity (reflected by a low PI) in the middle cerebral artery (Figure 2, B). 14,18,19 Doppler assessment of brain sparing can also be assessed with the cerebroplacental ratio, defined as middle cerebral artery PI/umbilical artery PI. A fetus is considered to have fetal brain sparing when this ratio is <5th percentile for gestational age. 20,21

#### **Ductus venosus Doppler**

Doppler waveforms obtained from the central venous circulation in the fetus reflect the physiologic status of the right ventricle. Doppler waveforms are obtained from the ductus venosus in a transverse or sagittal view of the fetal abdomen at the level of the diaphragm.<sup>22</sup> By superimposing color Doppler on the gray-scale image, the ductus venosus can be identified as it branches from the umbilical vein (Table). Variable high flow velocities, reflected as a mixture of colors on color Doppler imaging (aliasing), are commonly seen within the ductus venosus, and indicate an appropriate location for Doppler flow interrogation. Ductus venosus Doppler waveforms are biphasic in shape with the first peak corresponding to ventricular systole, the second peak during passive filling in ventricular diastole, followed by a nadir in late diastole with atrial contraction (Figure 3, A). Continuous forward flow throughout

the cardiac cycle is seen in the normal fetus. Decreased, absent, or reversed flow (Figure 3, B and C) in the A wave (atrial contraction) may represent myocardial impairment and increased ventricular end-diastolic pressure resulting from an increase in right ventricular afterload. This abnormal waveform in the ductus venosus has been documented in fetuses with IUGR and linked to an increased neonatal mortality rate. 23,24

#### **Uterine artery Doppler**

Doppler velocimetry of the uterine arteries reveals a progressive decrease in impedance with advancing gestational age. 25,26 This decrease in impedance is thought to reflect a maternal adaptation to pregnancy resulting from trophoblastic invasion of the maternal spiral arterioles in the first half of gestation.<sup>27</sup> The uterine artery can be demonstrated by color Doppler velocimetry as it originates from the anterior division of the hypogastric artery, and just before it enters the uterus at the uterine-cervical junction. Pulsed Doppler velocimetry of the uterine artery should be obtained immediately after the vessel crosses the hypogastric artery and before it divides into the uterine and cervical branches. The ability to obtain the uterine artery Doppler waveforms at all gestational ages is approximately 95-98%.<sup>28</sup>

In early gestation, a notched uterine artery Doppler waveform and low diastolic flow is evident due to high vascular impedance. With advancing gestation, decreasing vascular impedance is reflected by increased flow in diastole and in disappearance of the notch (Figure 4, A). The persistence of a uterine artery notch in the late second and third trimesters has been used to identify abnormal uterine circulation in pregnancy (Figure 4, B). 23,29,30 Caution, however, should be used against relying solely on the presence of a notch in the uterine artery Doppler waveform to define an abnormal uterine circulation given the subjectivity involved in its identification. Thus, clinicians should look also at the PI, with a value >95th percentile for gestational age considered to be abnormal<sup>31</sup> (Table).

#### **Question 1. Should Doppler** ultrasound assessment be performed in low-risk and/or high-risk women as a screening test for IUGR? (Levels II and III)

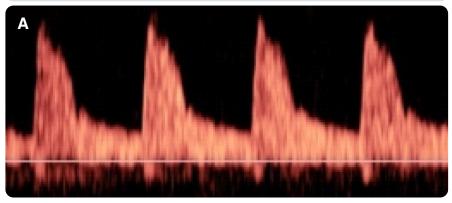
Routine umbilical artery Doppler screening for the subsequent development of IUGR in a low-risk population has not been shown to be effective in predicting IUGR. A metaanalysis of 4 trials (n = 11,375), which included 2 studies of low-risk populations and 2 studies of unselected populations, found no significant difference in antenatal hospital-

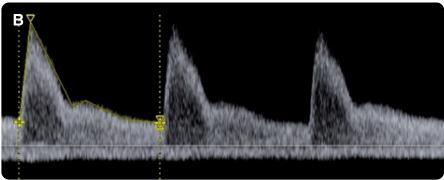
ization, obstetric outcomes, or perinatal morbidities with systematic use of umbilical artery Doppler as compared with control groups.32 The metaanalysis acknowledged that these 4 trials had insufficient power, and that about 30,000 women would need to be randomized to determine if routine umbilical artery Doppler screening in a low-risk population would influence perinatal mortality.32 Thus, until additional randomized trials are completed, Doppler screening of the umbilical artery should not be used routinely in low-risk women to predict IUGR. Among high-risk women, there are no population-based studies regarding umbilical artery Doppler to identify pregnancies complicated by IUGR.

A limited number of studies have evaluated first-trimester uterine artery Doppler velocimetry as a screening test for IUGR. However, the sensitivity is low (12%), precluding its clinical value.33 The 2 largest metaanalyses regarding second-trimester uterine artery Doppler screening reached differing conclusions. Chien et al<sup>34</sup> summarized the result of 28 studies including almost 13,000 women and noted that the likelihood ratio (LR) of an abnormal uterine artery Doppler to identify IUGR was 3.6 (95% confidence interval [CI], 3.2-4.0), and that a negative result carried a LR of 0.8 (95% CI, 0.8-0.9). Cnossen et al<sup>29</sup> identified 61 studies with >41,000 women and noted that an increased PI with notching in low-risk women had a positive LR of 9.1 (95% CI, 5.0-16.7) for IUGR and a LR of 14.6 (95% CI, 7.8-26.3) for newborn birthweight <5th percentile. In high-risk women, the metaanalysis by Cnossen et al<sup>29</sup> noted that an increased RI (>0.58 or >90th percentile) in the second trimester was associated with a positive LR of 10.9 (95% CI, 10.4-11.4), and a negative LR of 0.20 (95% CI, 0.14 - 0.26) for severe IUGR.

In summary, neither umbilical nor uterine artery Doppler velocimetry is recommended as a screening tool for identifying pregnancies that will be subsequently complicated by IUGR because of inconsistent evidence of benefit, and because standards are lacking for the study technique, gestational age at testing, and criteria for abnormal test result.<sup>31</sup>

## FIGURE 2 Examples of middle cerebral artery Doppler flow waveforms





**A**, Normal middle cerebral artery Doppler flow waveform. **B**, Abnormal middle cerebral artery Doppler flow with increased diastolic flow (brain sparing).

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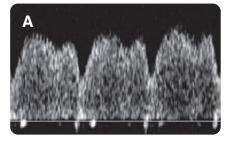
## Question 2. What are the benefits and limitations of Doppler studies of each vessel when IUGR is suspected? (Levels I, II, and III)

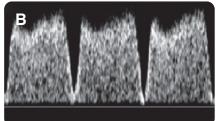
Clinicians have the options of interrogating several vessels, with umbilical artery, middle cerebral artery, and ductus venosus being the ones most studied.

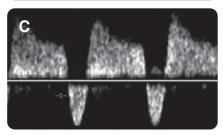
Umbilical artery Doppler evaluation of pregnancies with suspected IUGR has been shown to significantly reduce inductions of labor (relative risk [RR], 0.89; 95% CI, 0.80-0.99), cesarean deliveries (RR, 0.90; 95% CI, 0.84-0.97), and perinatal deaths (RR, 0.71; 95% CI, 0.52-0.98; 1.2% vs 1.7%; number needed to treat = 203; 95% CI, 103-4352) without increasing the rate of unnecessary interventions. 2,35 Compared to not using this type of Doppler, the use of umbilical artery Doppler studies in women with suspected IUGR is associated therefore with maternal and perinatal benefits. Unfortunately, published studies have not typically specified an intervention protocol in response to abnormal umbilical artery Doppler testing results. Nonetheless, umbilical artery Doppler testing should be used in women with suspected IUGR, and may be used to guide the timing of delivery.

Middle cerebral artery Doppler velocimetry has been found to identify a subset of IUGR fetuses at increased risk for cesarean delivery due to abnormal fetal heart rate patterns, and for neonatal acidosis. 21,36 Long-term follow-up of IUGR fetuses with normal umbilical artery Doppler studies but with a middle cerebral artery PI <5th percentile reveals these infants to be at higher risk for poor neurodevelopmental outcome. 37 Despite these associations, middle cerebral artery Doppler testing of suspected IUGR fetuses has not been evaluated in randomized trials, and no specific interventions have been shown to improve outcomes based on abnormal findings.

FIGURE 3
Examples of ductus venosus
Doppler flow wave forms







**A**, Normal ductus venosus Doppler flow. Abnormal ductus venosus Doppler waveform with **B**, absent and **C**, reversed A wave.

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Doppler velocimetry of the fetal central venous circulation helps identify fetuses with suspected IUGR at an advanced stage of compromise.<sup>5,38</sup> Absent or reversed flow in late diastole in the ductus venosus is associated with increased perinatal morbidity, fetal acidemia, and perinatal and neonatal mortality.39-41 In one study of 121 IUGR fetuses, stillbirth was only observed in pregnancies with reversed late diastolic ductus venosus flow.4 Unlike umbilical artery and middle cerebral artery Doppler velocimetry, interrogation of the ductus venosus is difficult because of small vessel size, fetal movement, and waveform similarity to inferior vena cava. There are no randomized trials involving the use of venous Doppler studies in the management of suspected IUGR. A trial is currently underway (Trial of Umbilical and Fetal Flow in Europe: TRUFFLE).<sup>42</sup>

In summary, the umbilical artery is the preferred vessel to interrogate by Doppler flow velocimetry to guide management in pregnancies complicated by suspected IUGR, given lack of randomized trials using Doppler studies of other vessels.

## Question 3. What is the usual progression of Doppler abnormalities in suspected IUGR? Is this progression consistent/reliable? (Levels II and III)

In the presence of hypoxemia, adaptive changes in the fetal circulation can be detected by Doppler ultrasound examination. These changes manifest themselves in a variable fashion in different fetuses, but some general patterns of progression can be recognized. Early adaptation includes preferential shunting and distribution of blood flow to the fetal brain, heart, and adrenal glands at the expense of the splanchnic and peripheral circulation. This adaptive mechanism, termed "brain sparing," is reflected on arterial Doppler ultrasound by increased impedance in the umbilical arteries and decreased impedance in the middle cerebral arteries. As metabolic deterioration occurs and the fetus loses the ability to adapt to hypoxemia, the middle cerebral artery Doppler indices will normalize, with an evident decrease in end-diastolic flow in the cerebral circulation. 5,23,24,43,44

IUGR related to decreased placental function is usually associated with increased umbilical artery impedance, typically followed by brain sparing. With worsening obliteration of placental vessels, venous shunting across the ductus venosus occurs and results in an increase in blood volume to the heart at the expense of the liver. The increase in right ventricle afterload causes further shunting of blood to the left ventricle that improves left ventricular output. Increased end-diastolic pressure in the right ventricle, combined with decreased cardiac compliance, is reflected in a decrease, absence, and ultimate reversal of blood flow in the ductus venosus during the atrial systolic component of the waveform. Increased reversal of flow in the atrial systolic component of the inferior vena cava is also noted. Worsening placental function will lead to increased central venous pressure and umbilical venous pulsations may be seen on Doppler ultrasound. These are changes that may be associated with an abnormal biophysical profile and/or loss of fetal heart rate variability.

When the ductus venosus and umbilical venous Doppler studies become abnormal, the risk for stillbirth increases dramatically, compared to when only the umbilical and middle cerebral artery Doppler studies are abnormal. <sup>45</sup> Although this is not a sufficient reason to recommend routine usage of such testing, it might be utilized by centers with experience in venous Doppler. Using the combination of arterial and venous Doppler testing can result in identification of the majority of fetuses with acidemia (sensitivity 70-90% and specificity 70-80%). <sup>46,47</sup>

The sequence of arterial and venous Doppler findings is mostly limited to the preterm idiopathic IUGR fetus and has not been well documented in gestations at >34 weeks.<sup>20,36,48</sup>

In summary, in preterm IUGR fetuses there does appear to be a natural progression of changes in the Doppler of umbilical artery, middle cerebral artery, and ductus venosus, but it has a large variability in manifestation.

# Question 4. What Doppler study regimen should be initiated for suspected IUGR? What other antepartum testing may be helpful in this setting? (Levels I, II, and III)

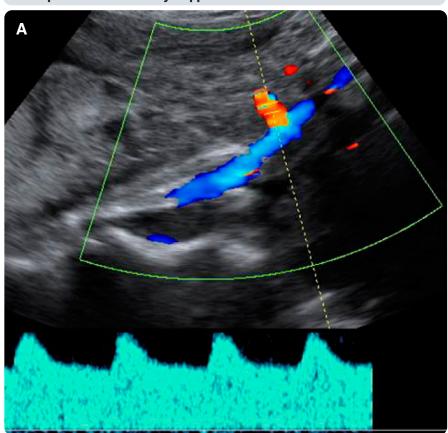
Umbilical artery Doppler evaluation of the fetus with suspected IUGR can help differentiate the hypoxic growth-restricted fetus from the nonhypoxic small fetus, and thereby reduce perinatal mortality, and unnecessary interventions. <sup>2,8,35,49-52</sup> Umbilical artery Doppler studies to assess for the presence of increased placental impedance and fetal cardiovascular adaptation to hypoxemia should be initiated when IUGR is suspected and the fetus is considered potentially viable. Umbilical artery Doppler studies may help guide decisions regarding obstetrical interventions for the IUGR pregnancy, as shown in Figure 5.

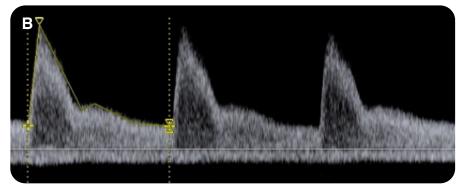
Since there are no randomized trials with adequate sample size to assess the optimal frequency of umbilical artery Doppler assessment with IUGR, suggested protocols vary.<sup>53</sup> While some advocate weekly Doppler assessment, others recommend testing at 2- to 4-week intervals. 38,54 When Doppler abnormalities are detected in the fetal arterial circulation, weekly follow-up Doppler studies are considered usually sufficient if forward umbilical artery end-diastolic flow persists.<sup>3</sup> In the absence of specific data regarding the optimal frequency of testing, experts have recommended Doppler surveillance up to 2-3 times per week when IUGR is complicated by oligohydramnios, or absent or reversed umbilical artery end-diastolic flow.<sup>48</sup>

When the estimated fetal weight is <10th percentile, fetal surveillance is recommended because of the recognized association between IUGR and neonatal morbidity and mortality, and this may be initiated as early as 26-28 weeks. 2,55 Traditional surveillance of the IUGR fetus has relied on fetal heart rate testing by cardiotocography or ultrasound-derived biophysical profile testing. Twice weekly nonstress testing with weekly amniotic fluid evaluation, or weekly biophysical profile testing, is commonly recommended when IUGR is suspected<sup>56,57</sup> (Figure 5). The combination of ultrasound and cardiotocographic surveillance techniques has been shown to improve outcome for IUGR fetuses. 58,59

#### **Question 5. What interventions are** available and should be considered based on abnormal fetal Doppler velocimetry studies? (Levels II and III) Umbilical artery Doppler blood flow studies can be used clinically to guide interventions such as the frequency and type of other fetal testing, hospitalization, antenatal corticosteroid administration, and delivery (Figure 5). Sometimes these Doppler studies can also help defer intervention. For example, in cases with suspected IUGR and absent or reversed end-diastolic flow <25 weeks, aggressive obstetrical interventions may be deferred until a later gestational age given the poor prognosis

FIGURE 4
Examples of uterine artery Doppler flow waveforms

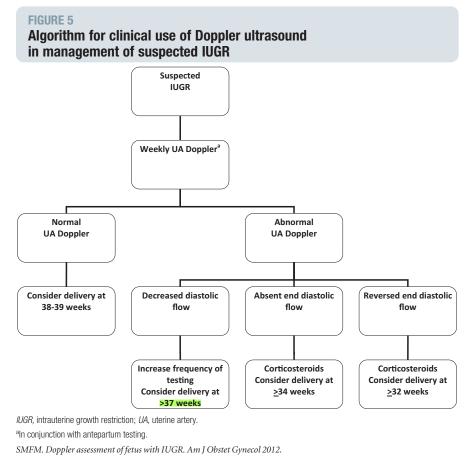




**A,** Normal and **B,** abnormal uterine artery Doppler flow. SMFM. Doppler assessment of fetus with IUGR. Am J Obstet Gynecol 2012.

for survival and intact survival in this situation. However, when the decision is made to perform antenatal surveillance and there is willingness to perform cesarean delivery for fetal indication, then antenatal corticosteroids should be considered under this circumstance.

There are no randomized studies that evaluate the effect of any intervention based on fetal Doppler blood flow testing specific to the IUGR fetus. Once the umbilical artery Doppler flow becomes abnormal in suspected IUGR, especially in cases of absent or reversed flow, nonstress tests, and/or biophysical profiles can be performed twice weekly, or more often. Although there are no randomized studies to guide the decision to hospitalize, admission may be offered once fetal testing more often than 3 times per week is deemed necessary.



Although there is ample evidence regarding the benefits of administration of antenatal corticosteroids before spontaneous preterm births, some have raised concern for its administration for the growth-restricted fetus with abnormal umbilical artery Doppler studies. In the original trial by Liggins and Howie<sup>60</sup> there was an excess of fetal deaths among women with pregnancy-related hypertension and IUGR. The potential reason for the increased mortality is the transiently increased physiologic and metabolic demands associated with administration of glucocorticoids. Overall, though, published evidence supports use of corticosteroids for IUGR, and close observation for 48-72 hours is reasonable. 61 When absent or reversed umbilical artery end-diastolic flow is noted <34 weeks, antenatal corticosteroids should be administered (Figure 5). Subsequent to steroid administration, there may be transient return of enddiastolic flow in about two thirds of the

cases, attributed to altered tone of the placental vasculature.62

Umbilical artery Doppler can guide timing of delivery (Figure 5). If the umbilical artery Doppler and the antepartum course are reassuring, delivery of IUGR pregnancies may be postponed until 38-39 weeks.<sup>2,63</sup> For pregnancies complicated by IUGR with absent enddiastolic umbilical artery flow, provided other fetal surveillance has remained reassuring, delivery at 34 weeks should be considered.<sup>2,17,38</sup> For IUGR with reversed end-diastolic umbilical artery flow, antenatal corticosteroid administration followed by delivery at 32 weeks should be considered.<sup>64</sup>

#### RECOMMENDATIONS

#### Levels II and III evidence. level C recommendation

1. Doppler of any vessel is not recommended as a screening tool for identifying pregnancies that will subsequently be complicated by IUGR.

#### Levels I evidence. level A recommendation

2. Antepartum surveillance of a viable fetus with suspected IUGR should include Doppler of the umbilical artery, as its use is associated with a significant decrease in perinatal mortality.

#### Levels II and III evidence, level C recommendation

3. Once IUGR is suspected, umbilical artery Doppler studies should be performed usually every 1-2 weeks to assess for deterioration; if normal, they can be extended to less frequent intervals.

#### Levels II and III evidence, level C recommendation

4. Doppler assessment of additional fetal vessels, such as middle cerebral artery and ductus venosus, has not been sufficiently evaluated in randomized trials to recommend its routine use in clinical practice in fetuses with suspected IUGR.

#### Level I evidence, level A recommendation

5. Antenatal corticosteroids should be administered if absent or reversed end-diastolic flow is noted <34 weeks in a pregnancy with suspected IUGR.

#### Levels II and III evidence, level C recommendation

6. As long as fetal surveillance remains reassuring, women with suspected IUGR and absent umbilical artery end-diastolic flow may be managed expectantly until delivery at 34 weeks.

#### Levels II and III evidence. level C recommendation

7. As long as fetal surveillance remains reassuring, women with suspected IUGR and reversed umbilical artery end-diastolic flow may be managed expectantly until delivery at 32 weeks.

#### **Quality of evidence**

The quality of evidence for each included article was evaluated according to the categories outlined by the US Preventative Services taskforce:

- Properly powered and conducted randomized controlled trial; wellconducted systematic review or metaanalysis of homogeneous randomized controlled trials.
- **II-1** Well-designed controlled trial without randomization.
- **II-2** Well-designed cohort or case-control analytic study.
- II-3 Multiple time series with or without the intervention; dramatic results from uncontrolled experiments.
- III Opinions of respected authorities, based on clinical experience; descriptive studies or case reports; reports of expert committees.

### Recommendations are graded in the following categories:

#### Level A

The recommendation is based on good and consistent scientific evidence.

#### Level B

The recommendation is based on limited or inconsistent scientific evidence.

#### Level C

The recommendation is based on expert opinion or consensus.

This opinion was developed by the publications committee of the Society for Maternal-Fetal Medicine with the assistance of Eliza Berkley, MD, Suneet P. Chauhan, MD, and Alfred Abuhamad, MD, and was approved by the executive committee of the society on Dec. 21, 2011. Drs Berkley, Chauhan, and Abuhamad, and each member of the publications committee (Vincenzo Berghella, MD [Chair], Sean Blackwell, MD [Vice-Chair], Brenna Anderson, MD, Suneet P. Chauhan, MD, Joshua Copel, MD, Cynthia Gyamfi, MD, Donna Johnson, MD, Brian Mercer, MD, George Saade, MD, Hyagriv Simhan, MD, Lynn Simpson, MD, Joanne Stone, MD, Alan Tita, MD, MPH, PhD, Michael Varner, MD, Deborah Gardner) have submitted a conflict of interest disclosure delineating personal, professional, and/

or business interests that might be perceived as a real or potential conflict of interest in relation to this publication.

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The practice of medicine continues to evolve, and individual circumstances will vary. This opinion reflects information available at the time of its submission for publication and is neither designed nor intended to establish an exclusive standard of perinatal care. This publication is not expected to reflect the opinions of all members of the Society for Maternal-Fetal Medicine.