Uterine artery Doppler flow studies in obstetric practice

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Summary

In women who develop preeclampsia there is a pathological increase in placental vascular resistance should be detectable by abnormal Doppler flow studies of the maternal uterine vessels.
In women considered at low risk with abnormal early pregnancy uterine artery Doppler studies are needed. Until such time as these are available, routine uterine artery Doppler screening of women considered at low risk is not recommended. Uterine artery Doppler screening of high-risk women appears to identify those at substantially increased risk for adverse pregnancy outcomes. and interventions that might improve clinical outcomes.
Abnormal testing in these women could potentially lead to increased surveillance and interventions that might improve clinical outcomes.

Key words: uterine artery , Doppler flow, preeclampsia, SGA.

Introduction

In normal pregnancy, placental trophoblast cells invade the inner third of the myometrium and migrate the entire length of the maternal spiral arteries what optimizes delivery of oxygen and nutrients to the fetus. In women who develop preeclampsia there is failure of trophoblast invasion of the uterine muscalar wall with the result that the spiral arteries retain the muscle elastic coating and impedance to blood flow persists [1]. Theoretically, a pathological increase in placental vascular resistance should be detectable by abnormal Doppler flow studies of the maternal uterine vessels, and this could offers the potential to detect women at risk for diseases like preeclampsia.

Also, abnormal uterine artery Doppler studies in both the first and second trimester have been shown to be associated with subsequent perinatal complications.

Uterine artery Doppler studies in normal pregnancy

Schulman and colleagues determined that in the non pregnant state there is a rapid rise and fall in uterine artery flow velocity during systole and a "notch" in the descending waveform in early diastole. During pregnancy, they noted a significant increase in uterine artery compliance between 8 and 16 weeks, which continued to a lesser extent until 26 weeks' gestation [2].

The majority of research has centered on an elevation in the RI or PI, or the persistence of a uterine artery diastolic notch to detect the presence of increased uteroplacental vascular resistance. Criteria for an abnormal RI have varied from a single cut off (eg, RI > 0.58) to a percentile cut off value (eg, 75th, 90th, 95th). The Gomez et al evaluated the uterine artery PI in the first trimester, and was able to identify 30.8% of pregnancies that subsequently developed severe pregnancy complications by using the 95th percentile as a cut off [3].

In order to increase the sensitivity and specificity of this technique Papageorghiou et al9 combined maternal history with uterine artery Doppler to determine a patient's specific risk. Accepting a false positive rate of 25%, they were able to identify 67.5% of women who would subsequently develop preeclampsia [4]. A recent metanalysis concluded that a PI with notching had the best predictive value for pregnancy outcomes [5]. It appears that as the impedance to flow increases in the placenta there is in late systole or early diastole, or an increase in downstream resistance as the relatively inflexible distal artery recoils from distention caused by the systolic pulse. This is manifested as an early diastolic notch in the Doppler wave form. Most studies use subjective criteria for the definition of a diastolic notch, but a drop of at least a 50 cm/s from the maximum diastolic velocity is a reasonable criterion after 20 weeks [6]. In a screening program of 2058 unselected women, Bower et al identified women with a uterine artery diastolic notch present or a high RI (95th percentiles) at 18-22 weeks, and repeated testing for these women at 24 weeks [7]. Uterine artery notching was defined subjectively but the authors demonstrated concordance in subjective criteria among sonographers before the study was performed. Three hundred twenty-nine (16%) women had abnormal RI values and/or uterine artery notching on the first evaluation, with 104 women having persistently abnormal testing. The presence of a diastolic notch was a better predictor of preeclampsia than an elevated RI.

In an evaluation of women at increased risk for preeclampsia or growth restriction, compared the diagnostic accuracy of gestational-aged adjusted 90th and 95th percentile cut offs for RI at 20, 28, 36 weeks' gestation with a cut off of 0.58, and the presence or absence of a diastolic notch. They concluded that 20 weeks' gestation was the optimal time for testing, with an abnormal value being defined as above the 90th percentile. The presence of a diastolic notch carried a 57% positive predictive value for subsequent severe complications and 93% predictive value for any complication [8]. Although this combination had the strongest positive predictive value, the sensitivity remained low for any complications (21%) and for severe complications (27%). In summary, there are no current standards for gestational age at testing or criteria for an abnormal uterine artery Doppler study. Once adequately trained in the technique, a reasonable approach would be to use an ultrasound machine with the capability to perform continuous wave and/or pulsed wave Doppler studies of the uterine, arcuate, and subplacental arteries. In 1 report, a proper waveform could be obtained within 20 minutes in all cases [9]. The RI, with gestational age appropriate cut offs, is the most commonly used index. However, [8] Chan et al. showed little difference between using a RI >0.58 or a RI above the 95th percentile, and both were more effective at predicting an adverse outcome when combined with the presence of a diastolic notch [8,9]. A reasonable definition for a diastolic notch is a drop of at least 50 cm/s from the maximum diastolic velocity. PI has been less commonly reported, but using levels above the 95th percentile or a PI>1.6 appears to be appropriate. Recent reports show some utility in assessment of uterine artery flow in the first trimester. However, the second trimester has yielded more consistent results. Performance at 18-20 weeks'gestation is a reasonable approach. There is some evidence that repeating the tests at 24-26 weeks may add further benefit [10].

Screening in low risk populations

Abnormal uterine artery Doppler studies in both the first and second trimesters have been shown to be associated with subsequent perinatal complications. For women with abnormal testing in the first trimester, the likelihood ratio (LR) for the development of preeclampsia is approximately 5, while those with normal Doppler flow studies have an LR of 0.5. Similarly, an abnormal test carries an LR of 2 for fetal growth restriction, with an LR of 0.9 after a normal test result. Though this relationship persists with testing in the second trimester, the sensitivity may be lower [11]. However, Antsaklis et al found the sensitivity and specificity of screening for preeclampsia to be 81% and 87% at 20 weeks, and 76% and 95% at 24 weeks' gestation [12].
The utility of uterine artery Doppler assessment was published by Chien and colleagues in 2000 [13]. Strict criteria regarding diagnostic interventions and outcome measures were used for inclusion. Twenty-eight studies met their criteria, encompassing a total of 12,994 patients. Analysis of studies involving low risk populations revealed that an abnormal velocity waveform with or without a diastolic notch carried an LR of 6.4 for subsequent development of preeclampsia (95% confidence

interval (CI), 5.7-7.1), and a negative result carried an LR of 0.7 (95% CI, 0.6-0.8). Women with a positive test had an LR of 3.6 (95% CI, 3.2-4.0) for the development of fetal growth restriction and a negative result carried a 0.8 LR (95% CI, 0.8-0.9). Results for the prediction of perinatal death were less robust with an LR of 1.8 (95% CI, 1.2-2.9) for a positive test result, and 0.9 (95% CI, 0.8-1.1) for a negative result. A recent metanalysis found a positive LR for preeclampsia of 7.5 (95% CI, 5.4-10.2) and a negative LR of 0.59 (95% CI, 0.47-0.71), and for severe preeclampsia a positive LR of 15.6 (95% CI, 13.3-17.3) and a negative LR of 0.4 (95% CI, 0.2-0.6). Furthermore, in women with abnormal uterine artery Doppler studies a positive LR of 9.1 (95% CI, 5.0-16.7) and a negative LR of 0.89 (95% CI, 0.85-0.93) were found for the occurrence of growth restriction [13].

Abnormal uterine artery Doppler studies: treatment of women considered at low risk

Several studies have evaluated the potential benefits of therapeutic interventions for those with abnormal uterine artery Doppler studies. One of the largest, by Goffinet et al, was a multicenter trial of 3317 pregnant women [14]. Low risk gravidas with an abnormal uterine artery Doppler between 20 and 24 weeks' gestation were treated with of 150 mg aspirin daily until 36 weeks' gestation. They found no significant reduction of intrauterine growth restriction and preeclampsia when these women were compared with women who did not receive aspirin therapy, and concluded that there was no justification for screening and treatment with uterine artery Doppler in low risk populations. In a analysis of a recently published prospective study of antioxidant therapy for the prevention of preeclampsia that found no significant benefit from 1000 mg of vitamin C and 400 IU of vitamin E given daily to at-risk woman, those with abnormal uterine Doppler studies at 18-22 weeks' gestation also failed to benefit from therapy (preeclampsia; 24% vs 25%; relative risk (RR), 0.95; 95% CI, 0.40-2.29;) [15].

Screening in high risk populations

Restriction of screening to populations at increased risk for adverse outcomes can improve the predictive value of the test. Based on this principle it is plausible that uterine artery Doppler studies could prove more useful when performed on at-risk women. The metanalysis by Chien et al included 12 studies of high risk patients which met stringent inclusion criteria [13]. The LR for preeclampsia after an abnormal test was 2.8 (95% CI, 2.3-3.4), resulting in an increase in the pretest probability from 9.8-23%. Similar results were obtained for the prediction of fetal growth restriction, with an LR of 2.7 (95% CI, 2.1-3.4), with the probability increasing from 17.8-36.7% with a positive test. The LR of perinatal death after an abnormal test was 4.0 (95% CI, 2.4-6.6), increasing the pretest probability from 8.9-27.8%. A recent metanalysis on uterine artery Doppler and adverse pregnancy outcomes in high risk gravidas included 83 studies with approximately 18,000 women, and found that the presence of notching had a positive LR of 20.2 (95% CI, 7.5-29.5) and a

negative LR of 0.17 (95% CI, 0.03-0.56) for preeclampsia. In the same analysis women with an RI > 0.58 had a positive LR of 10.9 (95% CI, 10.4-11.4) and negative LR of 0.20 (95% CI, 10.4-11.4) for growth restriction. Though an effective intervention to avoid complications has not been identified for high risk women with an abnormal uterine artery Doppler study, it is plausible that testing could be used to select those who are at lower risk based on a reassuring test.

The patient with a negative study could then undergo fewer evaluations during the pregnancy, with a reduction in health care costs and time lost. Axt-Fliedner et al. [16] considered this possibility in a prospective study of at risk singleton pregnancies (history of essential hypertension or preeclampsia, prior infant with fetal growth restriction or intrauterine death, or prior placental abruption). Bilateral uterine artery notching was associated with a positive predictive value of 33% (RR, 12.7) for a composite morbidity defined as the occurrence of preeclampsia or fetal growth restriction requiring delivery before 34 weeks, or fetal demise or placental abruption at any gestational age. Alternatively, the negative predictive value was also high at 93-97%. The highest negative predictive value (97%) was seen for women with both a normal RI and the lack of bilateral uterine artery notching. The authors concluded that high-risk women who had normal uterine artery Doppler studies at 19-26 weeks' gestation could be considered to be a low risk group suitable to less intensive antenatal care. Subsequent studies have also found high negative predictive values among high-risk populations. Harrington et al found reassuring testing to carry a negative predictive value of 99.2% for preeclampsia, 95.9% for SGA, 100% for abruption, and 97.7% for stillbirth and/or neonatal death [17]. Similarly, Frusca et al. found superimposed preeclampsia to develop in 12% of women with abnormal flow studies and in none of those with reassuring studies among 78 gravidas with chronic hypertension. The rate of fetal growth restriction was also low among women with reassuring Doppler studies (2% vs 52%) [18].

Conclusion

The predictive value of Doppler testing in a low risk population of women appears to below, and currently there are no available interventions to prevent adverse outcomes based on an abnormal result. Effective interventions to prevent late pregnancy complications (preeclampsia, growth restrictions) in women considered at low risk with abnormal early pregnancy uterine artery Doppler studies are needed. Until such time as these are available, routine uterine artery Doppler screening of women considered at low risk is not recommended. Uterine artery Doppler screening of high-risk women (eg, history of chronic hypertension or preeclampsia, prior fetal growth restriction, or stillbirth) with singleton gestations appears to identify those at substantially increased risk for adverse pregnancy outcomes. Abnormal testing in these women could potentially lead to increased surveillance (earlier and more frequent assessment of fetal growth and maternal clinical condition) and interventions that might improve clinical outcomes. However, further study is needed to determine which high-risk conditions are amenable to such screening, what testing regimen is optimal for a normal or abnormal test in these women, and what interventions based on these findings will improve pregnancy outcomes. At this time, the evidence does not support routine screening with uterine artery Doppler in any particular group of patients.

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