Role of Doppler Velocimetry of Uterine Artery in Obstetrics: Review Article

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Abstract

Uterine artery Doppler studies detect the pathological increase in the placental vascular resistance. In high-risk patients, abnormal studies of Uterine artery Doppler can identify the adverse outcomes during pregnancy. Well-timed interventions in these patients may improve the maternal and the neonatal outcome. Uterine artery Doppler in combination with maternal characteristics for the screening of low-risk patients is useful to predict the hypertensive disorders.

Keywords: Doppler studies; Pregnancy; Uterine artery

Introduction

In the present era, one of the commonest pregnancy complication with the highest incidence of maternal and perinatal mortality and morbidity worldwide is arterial hypertension [1].

Abnormal uterine artery Doppler studies commonly indicate the rise in the resistance of the placental vascular bed and which is usually associated with the increasing incidence of pregnancy complications like fetal growth restriction and pre-eclampsia. Timely and early interventions in these patients with abnormal Doppler studies can prevent or reduce maternal and fetal/neonatal morbidity and mortality. Many studies have reported that the abnormal doppler studies are associated with the perinatal complications. Nowadays research activities are mainly focused on the early identification of the risks so that the early interventions can be taken, thus improving the outcome. In this review, the role of Doppler studies of uterine arteries has been discussed in both the low and high-risk group. Prophylactic treatment in low-risk patients with abnormal Doppler studies of uterine arteries has also been discussed.

Placental Changes in Pregnancy

Transport of nutrients and oxygen to the fetus is mainly by the placenta. The development of the placenta is dependent on its implantation and the invasion of the trophoblastic tissues. Trophoblastic cells of placenta invade the adjacent portion of myometrium and the total length of the maternal spiral arteries which ensures the function of the placenta. There are two stages of the placental development, the first stage development is from 8 till 12 weeks of gestation and the trophoblastic cells invade from the proximal till the intra-decidual part of the spiral arteries. The second stage of placental development started from 14 weeks of a period of gestation and the trophoblastic cells invade unto the myometrial portion of the spiral arteries. Loss of elastic and smooth muscle layers of the placental spiral arteries converts the circulation between uterus and placenta into a low resistance and high capacitance system [2,3].

Placental changes are completed by 16-18 weeks of gestation. In some patients, there is a failure of the placental development and trophoblastic cell invasion. In these patients, there is the increased resistance in the uteroplacental circulation and which is mainly because of the persistence of the elastic portion of the muscle layer in the placental spiral arteries. These defective changes in the placental vasculature lead to hypoperfusion, oxidative stress, and hypoxic injury. Derangement in placental trophoblastic differentiation can lead to obstetric complications like fetal growth restriction and pre-eclampsia which is associated with the fetal morbidity and mortality.

Defective implantation may also be associated with placental abruption, preterm labor and second-trimester miscarriages [4].

There is an association found between the defective placental development and the levels of vasoactive factors in the circulation which leads to endothelial dysfunction as a result of the abnormal adaptation of maternal vascular system [5]. Placental products are released into the circulation during its development. These products act as biochemical markers in the circulation and reflect the defective placentation and its pathophysiology. These markers are useful for the prediction of late pregnancy complications if measured in the early trimesters. They include PAPP-A, inhibin A, sFlt-1, PGF, activin-A and sEng.

Doppler Studies of Uterine Arteries in Normal Pregnancy

In a normal pregnancy, there is a significant increase in the compliance of the uterine arteries usually between 8 to 16 weeks of gestation. This increase is continued till 26 weeks but to a lesser range [6]. The Systolic/Diastolic ratio of uterine arteries in Doppler studies is usually ≤ 2.6 in a normal pregnancy [7]. When the ratio exceeds this level or there is a notch in the waveform, the pregnancy is complicated by intrauterine growth retardation, premature birth, stillbirth, placental abruption and maternal pre-eclampsia. Uterine arteries Doppler velocimetry is an essential ingredient of optimum pregnancy surveillance.

Review of literature has demonstrated a strong correlation between abnormal waveforms and fetal-maternal disease. There is a possible role of Doppler studies of uterine arteries as a screening test in routine antenatal care [8].

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Elevation in the Resistive index (RI) or pulsatility index (PI) or presence of a diastolic notch in the uterine artery denotes the high resistance uteroplacental vasculature. Criteria for the abnormal values of RI varies from a percentile to a single cut-off value. Almost 30.8% of antenatal patients, later on, developed pregnancy complications if 95th percentile is taken as a cutoff for the PI value measured in the first trimester [9].

Patients clinical history if combined with the Doppler study of the uterine artery, the sensitivity and specificity of this technique can be increased [10]. It was shown in the multiple studies that the PI value along with the diastolic notching in the Doppler waveform of uterine artery considered best to anticipate the consequences of pregnancy [11]. Appearance of the diastolic notch is the result of increased impedance to flow in the placental vasculature. A sensible criterion used for the diagnosis of the diastolic notch is fall of minimum 50 cm/s from the maximum value of the diastolic velocity beyond 20 weeks of a period of gestation [12]. Diastolic notch presence is a more useful parameter for the prediction of pregnancy complications like pre-eclampsia than an increased RI, showed by multiple research studies.

It has been showed by many studies that the most favorable time for performing the uterine artery Doppler Studies is 20 weeks gestation with the cut-off value of 90th percentile. Abnormal Doppler defined as the value more than the 90th percentile. Diastolic notch is a very useful parameter and its presence is associated with 57% PPV for later development of severe complications and 93% for any kind of complication but the sensitivity for the test remained low which is 27% for severe and 21% for any kind of complication [13]. RI is the most frequently used index and cut-offs appropriate for gestational age are available. Many studies have proved that the diastolic notch and the RI value, when used as a combined parameter, is more efficacious in anticipating the adverse pregnancy outcomes [14]. Some of the recent research studies have shown the usefulness of the Doppler studies of the uterine artery in the early trimester but the second trimester had more appropriate results. Appropriate timing to perform Doppler velocimetry of uterine artery is at 20 weeks’ gestation but a repeat testing at 24 weeks may have an additional benefit [15].

**Doppler Studies in Low-Risk Patients**

Increased incidence of perinatal complications has been shown to be associated with the abnormal values of the Doppler studies in the second and first trimester. Second trimester Doppler studies have been analyzed in multiple studies as an anticipating marker for the development of late-onset complications like intra-uterine growth restriction and pre-eclampsia. Uterine arteries Doppler velocimetry in the early trimester is the center of attraction nowadays. Many studies have been done to study the association between Doppler studies and untoward pregnancy outcomes by the measurement of various techniques and indices. Overall, first trimester Doppler velocimetry predicts early onset pre-eclampsia better than late onset. Sensitivity in anticipating untoward pregnancy complication like prior onset pre-eclampsia and intra-uterine growth restriction is almost 40-70% when Doppler velocimetry is used as a single marker in low-risk pregnant population. Maternal characteristics and biochemical markers when combined with the pulsatility index of the uterine artery in the 1st trimester, early onset pre-eclampsia detection rate is above 90% [16]. The various combination of these tests and their validity in different patients will be the focus of research in the future. The ideal combination of all these tests and their validation in the various patient will be the focus of future research.

The likelihood ratio for the prediction of pre-eclampsia in cases of abnormal Doppler velocimetry is around 5, while with normal studies of uterine artery Doppler it is only 0.5. Similarly for the intra-uterine growth restriction likelihood ratio is around 0.9 with normal studies and 2 with abnormal studies [17]. Many studies have shown the utility of Doppler velocimetry of uterine arteries for the anticipation of hypertensive disorders in pregnancy and intra-uterine fetal growth restriction [18].

Scadiuzzi et al. have done a prospective study in 2016 involving 162 low-risk singleton pregnancies to study the maternal parameters (maternal ethnicity, age and parity) and Doppler velocimetry of uterine artery in 1st and 2nd trimester as anticipating factors for the prediction of early onset pre-eclampsia. This study showed that combined analysis of these factors for the early trimester screening is very useful for the prediction of early onset pre-eclampsia and other hypertensive disorders [19].

Review of various studies comprised of low-risk pregnant females has shown that the likelihood ratio for the development of hypertensive disorders especially pre-eclampsia in a case of abnormal Doppler studies with or without the presence of a diastolic notch is around 6.4. Similarly, for the intra-uterine growth restriction, it is 3.6 for positive screening and 0.8 for negative screening. Analysis results for the perinatal deaths were not that robust and likelihood ratio showed to be around 1.8 for positive screening and 0.9 for negative screening.

A recent analysis showed that for the pre-eclampsia the likelihood ratio for positive screening was around 7.5 and around 0.59 for negative screening while it increases in case of severe pre-eclampsia which was approximately 15.6 for positive screening and 0.4 for negative screening. Furthermore, for the fetal growth restriction likelihood ratio was 9 with positive screening and 0.89 for negative screening [18].

**Treatment of Low-Risk Population with Abnormal Doppler Velocimetry of Uterine Artery**

There are multiple studies involving patients with abnormal Doppler velocimetry of uterine artery in which the utility of therapeutic interventions has been analyzed.

Goffin et al have done one of such kind of the largest study, which comprised of 3317 pregnant patients [20]. Low-risk pregnant females with abnormal Doppler studies detected between 20 to 24 weeks of the period of gestation were given 150 mg OD dose of aspirin till 36 weeks of the period of gestation. According to this study, when a comparison was done between treated and the non-treated group it was found that there is no remarkable reduction of incidence of intra-uterine growth restriction and pre-eclampsia. Thus concluded from this study that there is no requirement of screening and any therapeutic interventions in these patients.

In another study it was found that in low-risk patients with abnormal Doppler velocimetry treatment with vitamin C and E have no benefit. Doses used for therapeutic interventions were 1000 mg of vitamin C and 400 IU of vitamin E.

Cochrane review involving 32,891 women in 46 trials, published in 2007, found that the aspirin treatment is associated with the 17% reduction in the likelihood of development of hypertensive disorders and especially pre-eclampsia, relative risk 0.83 and 0.77-0.89 (95% confidence interval) [21]. Use of antiplatelet drugs significantly decreases the probability of pre-eclampsia. These antiplatelet drug use, in addition, associated with a 10% decrease in small for gestational age.
and 8% decrease in the likelihood of preterm birth. Lastly, 14% decrease in the probability of fetal and neonatal deaths.

Bujold et al. have done an analysis, reviewed 27 RCT’s comprised of 11,348 women and it was found that if aspirin was started at 16 weeks of the period of gestation or much earlier there is a remarkable decrease in the incidence of pre-eclampsia and intra-uterine growth restriction than the later initiation of therapy [22].

Another meta-analysis was done recently by Vela et al. in 2014 comprised of 55,974 pregnant women, they have found that Doppler velocimetry of uterine artery in the first trimester is a helpful screening test for anticipating pre-eclampsia and unfavorable pregnancy outcomes. On the basis of the number of patients who need treatment, the study showed that in the screen positive low-risk patients with abnormal Doppler study, aspirin treatment is justified and a reasonable therapeutic intervention [23].

### High Risk Pregnant Females Screening

Doppler velocimetry of uterine artery, when done exclusively in high-risk patients, can increase the prediction value of the screening test. They are more useful in high-risk patients as compared to the low-risk population. Chien et al. have done a meta-analysis which includes included 12 studies of high-risk patients [18]. This analysis showed that abnormal uterine artery Doppler studies increase the pre-test probability for prediction of pre-eclampsia from 9.8 to 23%, for intra-uterine growth restriction from 17.8 to 36.7% and for perinatal death from 8.9 to 27.8%. In an another meta-analysis, 83 studies were reviewed and involving 18,000 pregnant women. This study concluded that the presence of a diastolic notch carried a positive likelihood ratio of 20.2 and negative likelihood ratio of 0.17 for early onset pre-eclampsia. For intra-uterine growth restriction if the RI value is more than 0.58 then the positive likelihood ratio was 10.9 and negative likelihood ratio was 0.20.

Moijan et al have done one analysis in 2014 for the diagnostic assessment of Doppler velocimetry of uterine artery for prognostication of untoward pregnancy outcomes and they have concluded that almost 88.2% patients developed pre-eclampsia and 23.5% had fetal growth restriction. For the detection of pre-eclampsia, the PI of uterine artery had to be >1.45, the sensitivity of 79%, specificity of 95.5%. For fetal growth restriction, it had to have a sensitivity of 57%, specificity of 96.5%, positive predictive value of 23.5% and NPV of 99.2% [24].

In high-risk patients with abnormal Doppler velocimetry, any effective interventions have not been diagnosed which can avoid complications but the Doppler velocimetry can identify the population at low risk. In these low-risk patients, antenatal visits are reduced and thus reducing the time spent and health care system cost.

A prospective study was conducted in 2005 by Axt-Fliedner et al. [25], comprised of high-risk singleton pregnancies. They have shown that the negative predictive value is highest (97%) when the RI value is normal and there was an absence of a diastolic notch in uterine arteries.

The final conclusion was that the high-risk patients could be categorized as a low-risk group if the Doppler parameters were normal around 19-26 weeks and these patients are suitable for less intensive antenatal monitoring.

Harrington et al concluded that a negative predictive value for pre-eclampsia developed in 12% of patients with abnormal Doppler velocimetry. Patients with chronic hypertension and normal test none had developed complications out of 78 patients. Similarly, the incidence of small for gestational age was also less in patients with a normal study of Doppler velocimetry of uterine arteries [27].

### Conclusion

The Doppler studies in combination with the maternal characteristics as a first-trimester screening are useful to anticipate hypertensive disorders in a low-risk group. In low-risk patients with an early derangement of Doppler studies, effective interventions are required to prevent late pregnancy complications like intra-uterine growth restriction and pre-eclampsia. The first trimester Doppler studies have a better detection rate for early onset pregnancy complications like early onset pre-eclampsia and small for gestational age than the late onset complications. Because of the low sensitivity, this test cannot be used as an isolated disease marker. Further research studies are required to assess the role of Doppler velocimetry of Uterine arteries as a screening test in a low-risk population.

Screening in high-risk patients like the previous history of pre-eclampsia or chronic hypertension, stillbirth and prior fetal growth restriction, will identify the patients at increased risk of late complications or adverse pregnancy outcomes. These high-risk patients will have increased monitoring and effective interventions can improve outcome or prevent the untoward pregnancy outcome.

### References


