Utility of uterine artery Doppler ultrasound imaging in predicting preeclampsia during pregnancy: a meta-analysis

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Abstract

Aims: Accurate prediction of preeclampsia could improve maternal outcomes. However, the role of uterine artery Doppler ultrasound in predicting preeclampsia remains unclear. Materials and methods: We comprehensively searched several electronic databases, including PubMed, EMBASE, the Cochrane Library, and Web of Science, covering studies published from the time of database creation to September 23, 2023. Studies on the predictive value of uterine artery Doppler ultrasound for preeclampsia were included. The primary pregnancy outcome was preeclampsia. The risk of bias was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 scoring scale. Results: The use of resistance index (RI) for predicting preeclampsia demonstrated the highest sensitivity of 0.73 (95% confidence interval [CI], 0.30–0.94) and specificity of 0.90 (95% CI, 0.72–0.97), with a pooled area under the curve value of 0.91 (95% CI, 0.88–0.93). The use of pulsatility index (PI) for predicting preeclampsia showed a sensitivity of 0.65 (95% CI, 0.45–0.81) and specificity of 0.88 (95% CI, 0.77–0.94). Furthermore, preeclampsia prediction via notching showed a sensitivity of 0.54 (95% CI, 0.38–0.68) and specificity of 0.89 (95% CI, 0.79–0.95). Conclusions: These findings highlight the varying predictive performance of different preeclampsia indices. PI and RI demonstrated moderate-to-high sensitivity and specificity, whereas notching exhibited relatively lower sensitivity but comparable specificity. Further research and validation are warranted to consolidate these results and enhance the accuracy of preeclampsia prediction.

Keywords: preeclampsia; Doppler ultrasound; uterine artery; meta-analysis

Introduction

Preeclampsia, a multisystem disorder, manifests as the emergence of hypertension and proteinuria beyond the 20th week of gestation [1]. This disorder causes profound complications during pregnancy, including pulmonary edema, acute renal failure, and coagulopathy [2]. Globally, preeclampsia is one of the leading causes of maternal morbidity and mortality and is known to exert its harmful effects on the fetus [3]. Furthermore, preeclampsia predisposes the mother to enduring health consequences such as cardiovascular disease [4]. The incidence of preeclampsia varies between 3% and 5% across different racial and environmental contexts as well as diagnostic criteria employed [5-7].

The etiology of preeclampsia encompasses multiple mechanisms, among which inadequate placental implantation is believed to play a key role. Inadequate invasion of trophoblasts into the maternal deeper myometrial arteries results in aberrant remodeling of spiral arteries [8,9]. Consequently, these defective spiral arteries exhibit higher resistance and diminished oxygenation compared with their normal counterparts, culminating in placental ischemia, hypoxia, and necrosis. Necrotic trophoblasts release antiangiogenic factors and proinflammatory cytokines into the maternal circulation, eliciting a systemic response in endothelial cells. These cascading events contribute to the clinical manifestations of preeclampsia, which typically manifest several weeks after the initial insult [10,11].
Currently, the American College of Obstetricians and Gynecologists recommends relying on the patient’s medical history as the screening approach for preeclampsia [12]. However, the preeclampsia detection rate using this method is only ~30% [13]. Therefore, researchers have conducted numerous studies to develop predictive tests for preeclampsia that can improve the accuracy and efficacy of screening methods. One such noninvasive method for assessing placental perfusion is the evaluation of uterine arteries (UtA) using Doppler ultrasound velocimetry [14]. Abnormal UtA velocimetry serves as an indicator of incomplete remodeling of spiral arteries [15]. Thus, uterine artery Doppler ultrasound is a promising method for detecting preeclampsia during pregnancy. This study aimed to assess the accuracy of uterine artery Doppler ultrasound in predicting preeclampsia during pregnancy.

Materials and methods

This meta-analysis did not involve any participants and therefore did not require ethics approval or informed consent. This study was registered in PROSPERO under the following ID: CRD42023480091.

Search strategy
We searched PubMed, EMBASE, the Cochrane Library, and Web of Science for randomized clinical trials and observational studies conducted from database creation to September 23, 2023, in which uterine artery Doppler imaging was used to predict preeclampsia. The terms “preeclampsia,” “pregnancy,” “uterine artery Doppler,” “sensitivity,” “specificity,” and “prediction” were searched individually or in combination. Only studies involving humans and published in English were included in the analysis, and the detailed search strategy is presented in Supplemental File 1.

Inclusion and exclusion criteria
The inclusion criteria were as follows: Studies (1) focusing on pregnant women, (2) involving the use of uterine artery Doppler ultrasound, and (3) published in English. The exclusion criteria were as follows: (1) abstracts, letters, talks, and reviews; (2) studies in which uterine artery Doppler ultrasound was not used; and (3) duplicate studies involving data already included in the meta-analysis.

Data extraction
Two reviewers independently analyzed all included studies and extracted the following data: names of authors, year of publication, type of study, Doppler ultrasound parameters, geographical region, type of data set, sample size of experimental and control groups, and sensitivity and specificity data.

Quality assessment
Two reviewers independently scored the quality of the included studies using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) criteria [16]. In the QUADAS-2 scoring scale with a maximum score of 7, each study was scored according to whether it met seven criteria: “yes” (score of 1) and “unclear” or “no” (score of 0).

Statistical methods
All data were analyzed using STATA software version 15.0. The diagnostic efficacy of different parameters of uterine artery Doppler ultrasound in predicting preeclampsia was measured based on sensitivity, specificity, and subject operating characteristic curve (SROC). Posterior density plots were used to indicate the relative importance of two included parameters. SROC was constructed based on the sensitivity and specificity values. The Deek’s funnel plot asymmetry test was used to detect publication bias.

Results

Basic characteristics of the included studies
In total, 2471 studies were found to be potentially eligible after a thorough literature search. After removing 1766 duplicates, 705 studies remained. After excluding 9 reviews or letters and 531 off-topic articles, 165 studies remained. After reading the full-text we found that 19 studies satisfied the inclusion criteria and were finally used in our analysis (fig 1).

The main characteristics and QUADAS-2 scores of the included studies are shown in Table 1. These 19 stud-
ies included 573 patients with preeclampsia and 7419 healthy controls. Preeclampsia was diagnosed during pregnancy via uterine artery Doppler ultrasound. All studies were mostly conducted in Asian populations and were published between 2008 and 2022. All studies used in-hospital data as the primary dataset. Most of the studies were prospective, and only two were retrospective. Most studies were of good quality, with 12 studies of high quality (QUADAS-2 score of ≥6). Detailed quality assessment is shown in Table II.

### Table I. The main characteristics of the 19 studies included in this meta-analysis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Region</th>
<th>Dataset type</th>
<th>Parameters</th>
<th>N, Test</th>
<th>N, Control</th>
<th>QUADAS</th>
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<tbody>
<tr>
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<td>RI</td>
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<td>297</td>
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<td>Hospital</td>
<td>PI, Notching</td>
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<td>421</td>
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<td>Hospital</td>
<td>PI</td>
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<td>412</td>
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<td>PI</td>
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<td>167</td>
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<td>RI</td>
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<tr>
<td>Shahid 2021 [28]</td>
<td>Retrospective</td>
<td>Pakistan</td>
<td>Hospital</td>
<td>Notching</td>
<td>40</td>
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<tr>
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<td>124</td>
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<td>RI, Notching, S/D</td>
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<td>480</td>
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<td>PI</td>
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<td>Hospital</td>
<td>PI</td>
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<td>Austria</td>
<td>Hospital</td>
<td>Notching</td>
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<td>356</td>
<td>7</td>
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PI, pulsatility index; RI, resistance index; S/D, systolic/diastolic ratio

### Efficacy in predicting preeclampsia

A total of 19 studies were analyzed, of which 11 used pulsatility index (PI) for predicting preeclampsia. The pooled sensitivity of PI in predicting preeclampsia was estimated to be 0.65 (95% confidence interval [CI], 0.45–0.81), with a corresponding specificity of 0.88 (95% CI, 0.77–0.94) (fig 2), and the pooled area under the curve (AUC) value was 0.86 (95% CI, 0.82–0.88) (fig 3).
Table II. Assessment of the validity of individual studies with Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool for the 19 included studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk of bias</th>
<th>Applicability Concerns</th>
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<tbody>
<tr>
<td></td>
<td>Patient Selection</td>
<td>Index Test</td>
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<tr>
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<td>Bhattacharyya 2012 [27]</td>
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<td>Stoensescu 2021 [30]</td>
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<td>Choorakutti 2022 [34]</td>
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<td>Springer 2020 [35]</td>
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وصلات خارجية:
[17] Okwudire 2019
[18] Puttapitakpong 2016
[19] Maged 2017
[20] Trongpisutsak 2021
[22] Melchiore 2008
[23] Fouad 2016
[25] Prajapati 2013
[26] Fratelli 2008
[27] Bhattacharyya 2012
[28] Shahid 2021
[29] Khanam 2021
[30] Stoensescu 2021
[31] Das 2022
[32] Nagar 2015
[33] Verma 2016
[34] Choorakutti 2022
[35] Springer 2020
[36] 36
[37] 37
[38] 38
[39] 39
[40] 40

Regarding the resistance index (RI), data from seven studies were available for analysis. The pooled sensitivity of RI in predicting preeclampsia was estimated to be 0.73 (95% CI, 0.30–0.94), with a specificity of 0.90 (95% CI, 0.72–0.97) (fig 4), and the pooled AUC value was 0.91 (95% CI, 0.88–0.93) (fig 5).

Regarding notching as a predictor of preeclampsia, data from eight studies were available. The pooled sensitivity of notching was estimated to be 0.54 (95% CI, 0.38–0.68), whereas the corresponding specificity was 0.89 (95% CI, 0.79–0.95) (fig 6), and the pooled AUC value was 0.79 (95% CI, 0.75–0.82) (fig 7).

Publication bias

The Deek’s funnel plot revealed no publication bias (p=0.10, p=0.16, p=0.45) (Figs S1–S3 in Supplemental File 1).

Discussions

During pregnancy, uterine artery Doppler ultrasound is used to predict preeclampsia. However, previous research has shown the limited accuracy of this technique owing to varying false-positive and false-negative results, varying predictive effects in primigravid and transient women, different regional effects, and differences in the optimal threshold [36,37]. Many studies have explored the value of Doppler indicators in predicting preeclampsia, but the results are inconsistent. A previous meta-analysis indicated that uterine artery RI and PI are better predictors than the uterine arterial blood flow rate [38]. However, other studies have revealed that an RI of ≥0.58 and blood flow rate of >105 ml/min were more accurate predictors at ~20 weeks of gestation [39,40]. However, it
remains controversial whether the Doppler index of the right uterine artery is better than that of the left uterine artery in predicting preeclampsia. A study revealed that the right side RI of ≥0.61 and right side blood flow rate of >123 ml/min were independent predictors of preeclampsia [41]. In contrast, another study reported that the predictive ability of the left and right uterine artery indices is equivalent [42]. This may be due to differences in individual arterial structure and blood flow variability. In addition, the position of the placenta affects Doppler prediction ability. A previous study reported that hemodynamic changes were more pronounced in the posterior placenta than in other regions, with a higher predictive power of PI and RI [40]. Although a study demonstrated that placental position does not affect the predictive value of Doppler index [43], the use of RI in the current study showed a high accuracy of 0.91 (95% CI, 0.88–0.93), with corresponding sensitivity and specificity of 0.73 and 0.90, respectively. Based on the results of the 19 studies included in this meta-analysis, the diagnostic accuracy of PI and RI was found to be superior to that of other indices. The results also showed that the accuracy, sensitivity, and specificity of PI were 0.86, 0.65, and 0.88, respectively, consistent with the findings of most previous studies.

Although uterine artery Doppler ultrasound is important in predicting preeclampsia during pregnancy, its predictive ability is limited by many influencing factors, resulting in different research results. To improve prediction accuracy, both sensitivity and specificity need...
to be considered, but predictive indicators are often selected based on specificity. This is because excessively high false-positive results may increase maternal anxiety and lead to a large number of unnecessary interventions. According to previous studies, false-positive rates of up to 25% can induce stress and cause pregnant women to undergo unnecessary medical interventions [44,45]. Reducing the cutoff value of the Doppler index can improve sensitivity; however, the corresponding specificity will also decrease, leading to more false positives. Thus, it is important to consider the risks of false negatives for both the mother and child during birth. For instance, vitamin C or E supplements have proven ineffective in preventing preeclampsia or its complications [46,47]. Therefore, sensitivity and specificity should be carefully considered when selecting parameters and adjusting thresholds for predicting precursor rows.

Although Doppler ultrasound is a noninvasive and painless imaging technique [48], its clinical application requires an expensive color Doppler ultrasound machine, routine instrument maintenance to ensure imaging precision, and specialized training in blood flow parameter measurements [49]. Operator experience and equipment parameters strongly influence Doppler ultrasound results, and standardized training and optimized equipment settings are needed to obtain consistent results [50].

Doppler ultrasound appears to have a less favorable predictive ability for preeclampsia in some developing countries, including Mexico [51], Nigeria [52], and India [53], compared with that in developed countries.

Limitations

In this study, 9 of the 19 studies included participants from Asia, and the results may not be globally representative. The gestational age of most pregnant women was >20 weeks, which may lead to a bias. Therefore, more convincing findings are warranted to analyze the potential influences of certain studies.

Conclusions

A meta-analysis of 19 studies showed that different uterine artery Doppler ultrasound parameters showed varying predictive performance for preeclampsia. In particular, PI and RI showed high sensitivity and specificity; therefore, they can be used as selective indicators for predicting preeclampsia. However, owing to regional differences in research and the tendency to prioritize specificity for predicting preeclampsia, the overall prediction accuracy may be biased because of different prediction objectives.

Conflict of interest: none

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References


