Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis

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CRD summary
This review found that Doppler ultrasonography was a better predictor of pre-eclampsia than of intrauterine growth restriction; pulsatility index, alone or combined with notching, in the second trimester was the most predictive Doppler index. In addition to other limitations, most of the authors’ conclusions were based on results from single studies so cannot be considered reliable.

Authors’ objectives
To investigate the value of Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction.

Searching
MEDLINE, EMBASE, The Cochrane library and Medion were searched to April 2006 without language restriction. Search strategies were presented. Reference lists of included articles were checked, and relevant experts contacted for additional studies.

Study selection
Studies which used Doppler assessment of the main uterine arteries in the first and second trimesters (after 16 weeks) of pregnancy were eligible. Pregnant women in any health care setting and at any risk of pre-eclampsia and intrauterine growth restriction were considered. As a reference standard pre-eclampsia was defined as high systolic (≥140 mmHg) or diastolic (≥90 mmHg) blood pressure with proteinuria (as defined in the review) after 20 weeks’ gestation; intrauterine growth restriction was defined as birth weight below the 10th centile for the population. Other definitions were provided for different severities. Studies had to provide data sufficient to create 2x2 tables of diagnostic accuracy.

Doppler ultrasonography was generally performed between 18 and 24 weeks’ gestation during a routine scan. The median rate of pre-eclampsia across all women was 4.9% and the mean of intrauterine growth restriction in low-risk women was 8.2%.

Four reviewers independently performed the study selection, with disagreements resolved by consensus or another reviewer.

Assessment of study quality
One reviewer assessed study quality using the QUADAS tool for diagnostic studies.

Data extraction
Data were extracted separately to generate 2x2 tables, and sensitivity and specificity, for the predictive accuracy of a range of Doppler indices for predicting pre-eclampsia and intrauterine growth restriction. It seemed that at least two reviewers performed the data extraction.

Methods of synthesis
The bivariate model was used to meta-analyse sensitivity and specificity estimates and generate pooled estimates with 95% confidence intervals (CI). Where several thresholds for a Doppler index were reported, the authors analysed the most common one. The pooled estimates were used to generate summary positive and negative likelihood ratios (LR+, LR-). Subgroup analyses for outcome severity, patient risk, gestational age at testing, use of preventive interventions and study quality were performed.

Results of the review
A total of 83 studies were included. Over 70% met QUADAS criteria for avoidance of verification bias, independence of reference tests and blinding of assessment of index test. Studies scored poorly on descriptions of selection criteria and reference tests, blinding assessment of reference test and data availability.
Pre-eclampsia: There were 74 studies, of which 69 were cohort studies, with 79,547 women (range 28 to 16,808).

In low and unspecified risk patients, pre-eclampsia was best predicted in the second trimester by increased pulsatility index with notching (LR+ 7.5, 95% CI 5.4 to 10.2; LR- 0.59, 95% CI 0.47 to 0.71; one study), followed by bilateral notching (LR+ 6.5, 95% CI 4.3 to 8.7; LR- 0.61 95% CI 0.44 to 0.79; 17 studies).

In high-risk patients, pre-eclampsia was best predicted in the second trimester by unilateral notching (LR+ 20.2, 95% CI 7.5 to 29.5; LR- 0.17 95% CI 0.03 to 0.56; one study), or increased pulsatility index with notching (LR+ 21.0, 95% CI 5.5 to 80.5; LR- 0.82 95% CI 0.72 to 0.93; one study).

Using preventive treatment was not found to improve predictive performance. When using only high quality studies pre-eclampsia in low-risk women was best predicted in the second trimester by unilateral notching (LR+ 12.5, 95% CI 5.1 to 20.0; LR- 0.45 95% CI 0.09 to 0.80).

Intrauterine growth restriction: There were 61 studies, of which 57 were cohort studies, with 41,131 women (range 28 to 7,851).

In low-risk patients, intrauterine growth restriction was best predicted in the second trimester by increased pulsatility index with notching (LR+ 9.1, 95% CI 5.0 to 16.7; LR- 0.89 95% CI 0.85 to 0.93; one study).

In high-risk patients predictive performance was deemed to be low for all indices. Using preventive treatment was not found to improve predictive performance.

Results for other Doppler indices, severe outcomes and first-trimester assessment were also presented.

Authors' conclusions
Doppler ultrasonography was a better predictor of pre-eclampsia than of intrauterine growth restriction. A pulsatility index, alone or combined with notching, in the second trimester, was the most predictive Doppler index.

CRD commentary
This review addressed a valid research question with appropriate review criteria. A suitable search was conducted and it appeared that some effort was made to identify unpublished material. Some action was taken to reduce reviewer error and bias at most stages of the review process. Study quality was assessed and appeared variable; most studies had poor quality in some assessed areas.

Studies were combined in meta-analyses suited to diagnostic tests, which accounted for correlation between the sensitivity and specificity. Analyses were conducted for a very large number of Doppler indices without consideration of the potential for finding favourable results purely by chance when performing multiple analyses. Most indices were investigated in only a few, or only one, study which increased this risk of chance findings. Confidence intervals were wide for most results. The use of the positive likelihood ratio alone to determine the best index to use was also of doubtful validity.

As most of the authors' conclusions are based on results from a single study, their conclusions cannot be considered to be reliable.

Implications of the review for practice and research
Practice: The authors suggested that the pulsatility index, alone or combined with notching, should be the Doppler index used in practice.

Research: The authors suggested that research should focus on combining Doppler ultrasonography with other tests.

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