Ophthalmic artery Doppler in the prediction of preeclampsia

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The ophthalmic artery is an easily accessible vessel for Doppler assessment that provides information on the less accessible intracranial circulation. In women with preeclampsia, compared with normotensive pregnant women, there is a decrease in impedance to flow and an increase in velocities in the flow velocity waveforms from the ophthalmic arteries. This study aimed to report the methodology for ophthalmic artery Doppler and summarize findings from the clinical implementation of such assessment in the prediction of pre-eclampsia. The Embase and MEDLINE were searched from inception to November 2020 to identify studies reporting on the use of ophthalmic artery Doppler in the prediction of preeclampsia. Of note, 2 small studies in high-risk pregnancies, one at 11 to 14 weeks' gestation and another at 20 to 28 weeks' gestation, reported differences between women who developed preeclampsia, compared with unaffected pregnancies, in ophthalmic artery Doppler and suggested that this is a useful biomarker for screening for preeclampsia. Another small study in high-risk pregnancies at 18 to 23 weeks' gestation reported that there was no marked difference in ophthalmic artery Doppler indices between the preeclampsia and unaffected groups. In addition, 2 recent, large observational studies in unselected pregnancies at 19 to 23 and 35 to 37 weeks' gestation, respectively, reported that, first, it is necessary to record waveforms from both eyes to get reproducible results; second, the waveform from the ophthalmic arteries is characterized by 2 systolic peaks and the ratio of the second to the first peak systolic velocity was increased in women who developed preeclampsia; third, in the study at 19 to 23 weeks' gestation, the peak systolic velocity ratio was superior to the uterine artery pulsatility index, mean arterial pressure, serum placental growth factor, and soluble fms-like tyrosine kinase-1 as individual biomarkers in the prediction of both preterm and term preeclampsia and the peak systolic velocity ratio improved the prediction of preeclampsia provided by all the other biomarkers; and fourth, in the study at 35 to 37 weeks' gestation, the peak systolic velocity ratio improved the prediction of subsequent development of preeclampsia provided by maternal factors alone and combinations of maternal factors with mean arterial pressure, uterine artery pulsatility index, placental growth factor, and serum placental growth factor. The ophthalmic artery Doppler provides a useful biomarker for the prediction of preeclampsia.

Key words: biomarker, competing risks model, mean arterial pressure, peak systolic velocity, placental growth factor, sensitivity, soluble fms-like tyrosine kinase-1, uterine artery

Introduction

The ophthalmic artery is the first branch of the internal carotid artery and is an easily accessible vessel for Doppler assessment that provides information on the less accessible intracranial circulation. In the 1990s, cross-sectional studies reported that in women with preeclampsia (PE), compared with normotensive pregnant women, there is a decrease in impedance to flow and an increase in velocities in the flow velocity waveforms from the ophthalmic arteries.[1−3]

The objectives of this article were to report the methodology for ophthalmic artery Doppler and summarize findings from the clinical implementation of such assessment in the prediction of PE.

Description of the Method

The mother is placed in the supine position and placed to rest for 5 minutes. A 7.5-MHz linear transducer is then placed transversely and gently over her closed upper eyelid after application of conduction gel. Color flow Doppler is used to identify the ophthalmic artery, which is found superior and medially to the hypoechoic band representing the optic nerve (Figure).[4] Pulsed-wave Doppler is then used to record 3 to 5 similar waveforms. The angle of insonation should be kept at <20°, the sample gate is set at 2 mm to cover the whole vessel, the depth is 3.0 to 4.5 cm, the high-pass filter is 50 Hz, and the pulse repetition frequency is set at 125 kHz. To minimize any potential adverse effects on the eyes, the duration of the examination of each eye is a few seconds, and a special preset should be used with a marked reduction in output power and maximum mechanical index of 0.4.

The waveform from the ophthalmic artery is characterized by 2 peaks in systole (Figure). The following 4 indices are used for analysis: first peak systolic velocity (PSV), second PSV, pulsatility index (PI), and ratio of second to first PSV. The first PSV and PI are automatically obtained by the machine, the second PSV is measured manually, and the

ratio of the second to first PSV is calculated.

A study in which waveforms were obtained in sequence from the right eye, left eye, and again right eye and then left eye found that there was good correlation between the first and second measurements from the same eye but poorer correlation in the first and second measurements between the 2 eyes.[5] It was estimated that the best performance of screening for PE was achieved by taking the average of 4 measurements (2 from each eye); satisfactory results were also achieved by taking the average of 1 measurement from each eye.

Prediction of Preeclampsia

Traditional methods

Effective prediction of preeclampsia can be achieved in screening by a combination of maternal demographic characteristics and medical history with biomarkers[6]; useful biomarkers at 11 to 13 weeks' gestation are uterine artery PI (UtA-PI), mean arterial pressure (MAP), and serum placental growth factor (PlGF)[7]; useful biomarkers at 19 to 24 weeks' gestation are UtA-PI, MAP, PlGF, and serum soluble fms-like tyrosine kinase-1 (sFlt-1)[8]; and useful biomarkers at 35 to 37 weeks' gestation are MAP, PlGF, and sFlt-1.[9]

Ophthalmic artery Doppler

The 3 small studies in high-risk pregnancies examined the potential value of the ophthalmic artery Doppler in screening for subsequent development of PE.[10–12] In these studies, only the right ophthalmic artery was examined. In the first study, 440 pregnancies were examined at 11 to 14 weeks' gestation, and the authors reported that in the group that developed PE, compared with unaffected pregnancies, the second PSV was increased; all other indices were not markedly different.[10] Screening by maternal demographic characteristics and medical history identified 45% of cases of PE, at 10% false positive rate (FPR); addition of ophthalmic artery second PSV was associated with a small improvement in the detection rate (DR) to 48%. In the second study, 347 pregnancies were examined at 20 to 28 weeks'

gestation, and the authors reported that in the group that developed PE, compared with unaffected pregnancies, the second PSV was increased and, in screening by this marker, the DR for PE was 70% at an FPR of 25%.[11] In the third study, 372 pregnancies were examined at 18 to 23 weeks' gestation, and the

authors reported that in the group that developed PE, compared with unaffected pregnancies, there was no marked difference in second PSV, second to first PSV ratio, or PI.[12]

In 2 recent prospective observational studies, we examined 2853 unselected pregnancies at 19 to 23 weeks' gestation

FIGURE
Color flow demonstration of the left ophthalmic artery
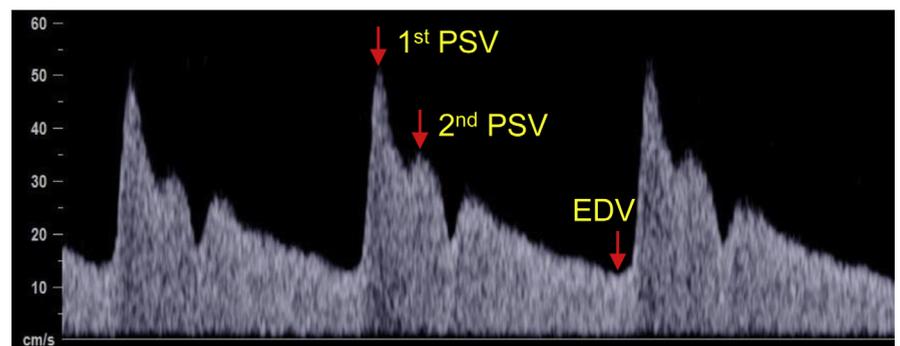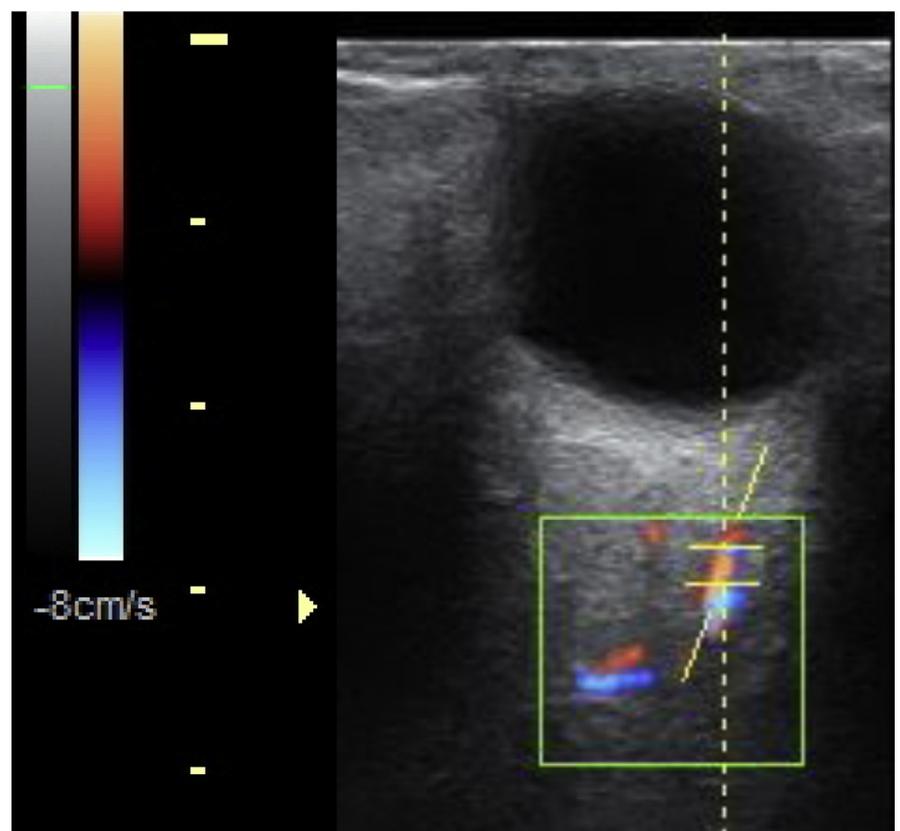
At the bottom is the flow velocity waveform from the ophthalmic artery obtained by pulsed-wave Doppler illustrating the first PSV, second PSV, and EDV.

EDV, end-diastolic velocity; *PSV*, peak systolic velocity.

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TABLE 1

DR, at 10% false positive rate, of delivery with PE at <37 and ≥37 weeks' gestation in screening at 19 to 23 weeks' gestation by maternal factors, ophthalmic artery second to first PSV ratio, and combinations with MAP, UtA-PI, serum PlGF, and sFlt

Method of screening	DR of PE at <37 wk PSV ratio		DR of PE at ≥37 wk PSV ratio	
	No	Yes	No	Yes
Maternal factors	56	80	34	46
+MAP	69	83	42	51
+UtA-PI	75	86	41	51
+PlGF	76	86	31	44
+sFLT	60	81	31	45
+MAP+UtA-PI	81	88	47	54
+MAP+UtA-PI+PlGF	86	90	45	53
+MAP+UtA-PI+PlGF+sFLT	85	90	43	51

DR, detection rate; *MAP*, mean arterial pressure; *PE*, preeclampsia; *PlGF*, placental growth factor; *PSV*, peak systolic velocity; *sFlt*, soluble fms-like tyrosine kinase-1; *UtA-PI*, uterine artery pulsatility index.

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and 2287 unselected pregnancies at 35 to 37 weeks' gestation.[13,14] We conducted Doppler studies twice in each eye and used the average of the 4 measurements for analysis. In both study groups, we found that the second to first PSV ratio was the only ophthalmic artery index that provided useful prediction of PE; the PSV ratio was increased in PE pregnancies, and the deviation from normal was greater for earlier PE than later PE. In the study at 19 to 23 weeks' gestation,

the PSV ratio was superior to MAP, UtA-PI, PlGF, or sFlt-1 as individual biomarkers in the prediction of both preterm and term PE (Table 1).[13] The PSV ratio improved the prediction of both preterm and term PE provided by MAP, UtA-PI, PlGF, and sFlt-1, both individually and in various combinations between each other. In the study at 35 to 37 weeks' gestation, the PSV ratio improved the prediction of PE with delivery at any stage after assessment provided by maternal factors alone and combinations of maternal factors with MAP, UtA-PI, PlGF, and sFlt-1 (Table 2).[14] The PSV ratio also improved the prediction of PE with delivery at <3 weeks from assessment.

Conclusion

Ophthalmic artery Doppler provides a useful biomarker for the prediction of PE. ∎

TABLE 2

DR, at 10% false positive rate, of delivery with PE within 3 weeks and at any time after assessment at 35 to 37 weeks' gestation by maternal factors, ophthalmic artery second to first PSV ratio, and combinations with MAP, UtA-PI, serum PlGF, and sFlt

Method of screening	DR of PE at <3 wk PSV ratio		DR of PE at any time PSV ratio	
	No	Yes	No	Yes
Maternal factors	31	69	25	51
+MAP	74	83	54	63
+UtA-PI	43	71	31	53
+PlGF	73	81	60	66
+sFLT	84	88	67	71
+MAP+PlGF	85	89	68	71
+MAP+sFLT	91	93	73	74
+MAP+PlGF+sFLT	93	93	76	77

DR, detection rate; *MAP*, mean arterial pressure; *PE*, preeclampsia; *PlGF*, placental growth factor; *PSV*, peak systolic velocity; *sFLT*, soluble fms-like tyrosine kinase-1; *UtA-PI*, uterine artery pulsatility index.

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