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Effects of age on the peak ratio of ophthalmic artery Doppler

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Abstract

This study aimed to investigate the effects of age on the peak ratio (PR) of ophthalmic artery (OA) Doppler.

The initial peak velocity (P1), second peak velocity (P2) and PR of OA were detected by color Doppler ultrasonography in 147 healthy subjects. All of the subjects were divided into 6 groups (G1-G6) according to the age. (G1, 20-29 years; G2, 30-39 years; G3, 40-49 years; G4, 50-59 years; G5, 60-69 years; and G6, 70 years or older). The blood pressure and heart rate were also examined before ultrasonography. The influences of age, blood pressure and heart rate on the P1, P2, and PR were further evaluated.

There were significant differences in the P2 and PR among different age groups except for P1. There were no significant differences in the P2 and PR between the first 2 groups, neither among the latter 4 groups. Nevertheless, P2 and PR in the first 2 groups were significantly different from those in the latter 4 groups. In addition, both P2 and PR (not P1) increased significantly with age, systolic and diastolic blood pressure. P1, P2 and PR were not related to heart rate. Both P2 and PR were closely related to the age. PR also had a weak relationship with systolic blood pressure.

Both P2 and PR of OA Doppler increase with age. Concern should be raised when P2 and PR are used to evaluate the hemodynamic change of OA.

Abbreviations: OA = ophthalmic artery, PR = peak ratio, P1 = initial peak velocity, P2 = second peak velocity.

Keywords: age effect, color Doppler ultrasound, ophthalmic artery, peak ratio

1. Introduction

Ophthalmic artery (OA) Doppler is a useful tool for the evaluation of orbital circulation in the pregnant women with preeclampsia.[1–6] Given that there are embryological, anatomical and functional similarities between OA and intracranial arteries, Doppler ultrasonography of OA has been used to examine the intracranial circulation. The most frequently used Doppler parameters are peak systolic velocity, end diastolic velocity, pulsatility index and peak ratio (PR). Among them, PR is the best value to evaluate the orbital circulation.[4–6] The increase in the PR indicates the orbital or cerebral hyperperfusion.[1,5,7,8] The higher the PR, the more serious the preeclampsia is.

Age is an important variable related to the pathogenesis of some ocular diseases such as age-related macular degeneration, glaucoma and vascular occlusive diseases. Consistent with the vascular system in other organs, ocular perfusion also decreases with the increase in age as a function of both increased vascular resistance and decreased vessel density. Doppler parameters of OA also have close relationships with age.[9–12] In 1995, 2 studies investigated the effects of age on the OA Doppler, and their results consistently showed the peak systolic velocity and end diastolic velocity correlated negatively with age.[9,10] Another 2 studies revealed that the vascular resistance increased with age.[11,12] All these studies indicate the reduced ocular perfusion with age.

PR was first introduced by Nakatsuka et al in 2002 as a sensitive index to evaluate the orbital circulation in preeclampsia women.[7] Studies have investigated the correlation between gestational age and PR,[6,13–16] but the effect of age on the PR is still poorly understood. The rate of pregnancy at advanced maternal age (≥35 years) or very advanced maternal age (≥45 years) is raising worldwide in the last decades, especially in high income countries.[17–19] Therefore, the effect of age on the PR should be clarified before it was used to evaluate the orbital circulation. The present study was to investigate the influence of age and other various factors (height, body weight and blood pressure) on the PR.

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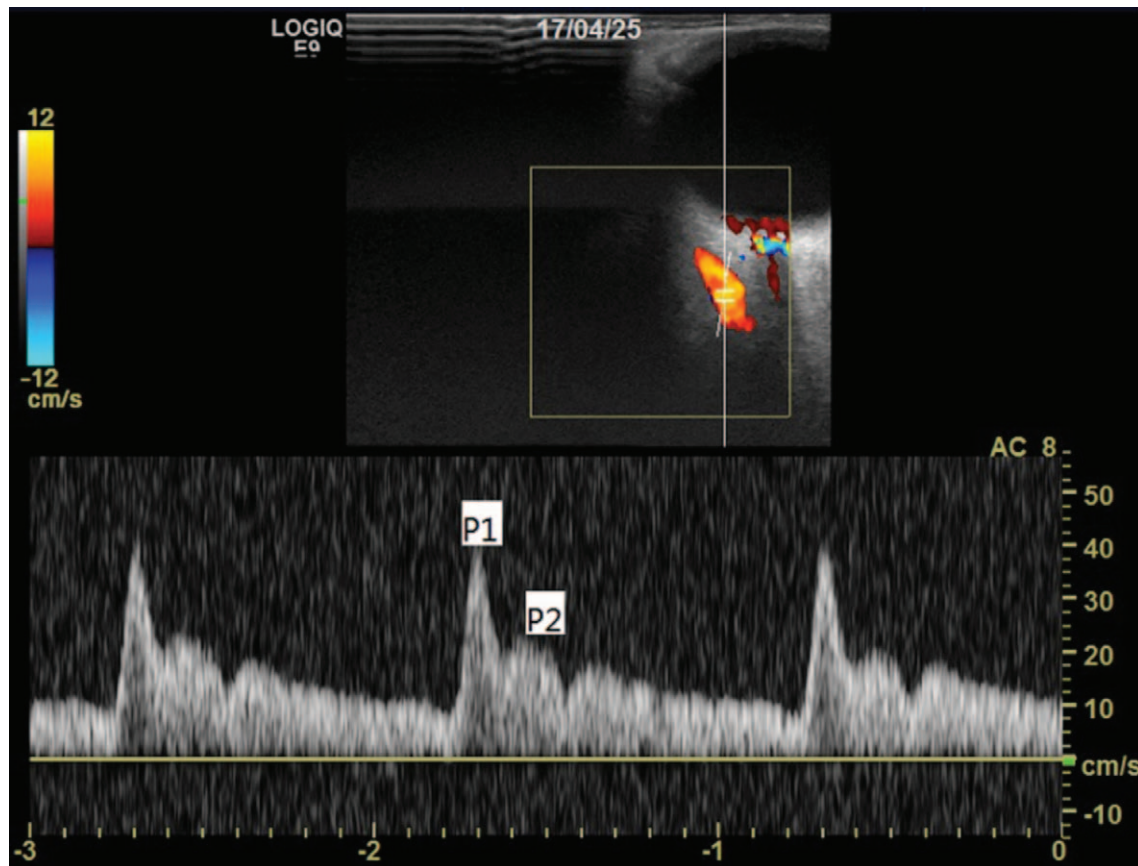
Figure 1. Measurement of P1 (initial peak velocity) and P2 (second peak velocity).

2. Materials and methods

2.1. Study Population

A total of 147 healthy female subjects aged 20 to 86 years were recruited. The subjects were divided into 6 groups according to the age (G1, 20-29 years; G2, 30-39 years; G3, 40-49 years; G4, 50-59 years; G5, 60-69 years; and G6, 70 years or older). All the subjects had no history of ocular diseases, diabetes mellitus, cardiovascular diseases, ocular or systemic hypertension, and smoking. None were taking systemic drugs or topical ocular medications. Written informed consent was obtained from all participants before the study. The study was approved by the Research Ethics Committee of our Institute.

2.2. Data Collection

After rest for at least 10 min, blood pressure (BP) and heart rate (HR) were measured using an electronic sphygmomanomety (Omron HEM-7111, Omron, Tokyo, Japan) with the subjects in a sitting position. Doppler waveforms of OA were acquired by an investigator using LOGIQ E9 (General Electric Company, Fairfield, CT) with a 6-15 MHz linear transducer. The examined eye of each subject was chosen randomly because previous study has shown no significant differences in the Doppler parameters between 2 eyes.[15] Subjects were all examined in a supine position. Ophthalmic arterial examinations were performed as described previously.[20] After 5 flow velocity waveforms in similar size and shape were acquired by spectral Doppler imaging, the initial peak velocity (P1) and second peak velocity (P2) were manually measured from a single waveform. PR was defined as the ratio of P2 to P1 (Fig. 1).[7]

2.3. Statistical analysis

All the statistical analyses were performed with SPSS version 17.0 software (IBM Corporation, Armonk, NY). Measurement data are presented as means ± standard deviations, and compared with the analysis of variance in each group. LSD method was used to determine which means were different. The effects of age, systolic blood pressure (SBP), diastolic blood pressure (DBP) and HR on the PR, P1 and P2 were evaluated by simple linear regression analysis and multiple regression analysis. A value of $P < .05$ was considered statistically significant.

3. Results

A total of 147 healthy female subjects were included in the present study. The mean age was 45.2 ± 16.8 years (range: 20 to 80 years). The average HR was 73 ± 6 beats/min (range, 60 to 90 beats/min). Their mean SBP and DBP were 124.3 ± 8.1 mmHg and 80.1 ± 4.1 mmHg, respectively. The mean P1, P2, and PR were 33.41 ± 7.71 cm/s, 22.52 ± 6.82 cm/s, and 0.68 ± 0.14, respectively. The HR, SBP, DBP, P1, P2, and PR in each group are shown in Table 1.

Table 1

The age, HR, SBP, DBP, P1, P2, and PR in each group.

Group	Age (yr)	HR (beats/min)	SBP (mm Hg)	DBP (mm Hg)	P1 (cm/s)	P2 (cm/s)	PR
G1 (n=33)	23.6±2.4	74.5±7.3	113.9±5.3	76.3±2.7	34.2±7.1	18.0±5.6	0.52±0.08
G2 (n=30)	34.6±2.8	71.4±5.3	123.0±4.9	79.1±2.8	33.8±7.2	19.8±4.5	0.59±0.08
G3 (n=23)	45.4±2.6	71.8±4.5	128.1±4.6	81.1±2.8	33.4±7.3	25.1±5.4	0.76±0.08
G4 (n=26)	53.8±2.2	72.0±4.8	129.4±3.8	82.9±2.7	34.5±9.2	26.1±7.0	0.76±0.10
G5 (n=20)	63.9±3.2	76.0±6.0	130.7±4.8	83.1±3.9	31.5±7.1	25.0±6.8	0.79±0.09
G6 (n=15)	74.3±4.8	75.8±5.3	125.5±9.9	80.1±5.7	31.5±8.9	24.4±8.1	0.77±0.13
Total (n=147)	45.2±16.9	73.3±5.9	124.3±8.1	80.1±4.1	33.4±7.7	22.5±6.8	0.68±0.14

HR, heart rate; SBP, systolic blood pressure; DPB, diastolic blood pressure; P1, initial peak velocity; P2, second peak velocity; PR, peak ratio.
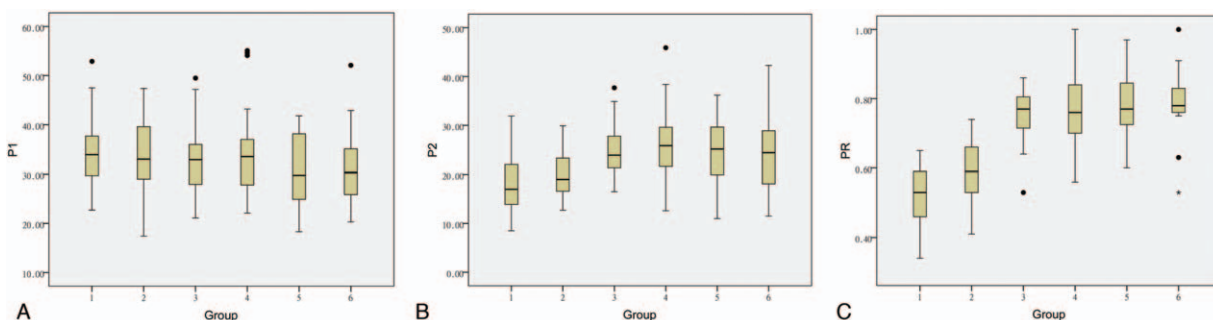

Figure 2. A. Box plots of P1 in each group. B. Box plots of P2 in each group. C. Box plots of PR in each group.

Analysis of variance rejected the hypothesis of equality of P2 and PR in all groups (both $P<.001$). Comparisons with LSD method showed there was no significant differences in the P2 and PR between G1 and G2 groups. Also, no significant differences were observed in the P2 and PR among G3, G4, G5, and G6groups. However, the P2 and PR in the G1 and G2 groups were significantly different from those in the other 4 groups. These results indicate P2 and PR increase since the subject is older than 40 years. Analysis of variance accepted the hypothesis of equality of P1 in all groups ($F=0.808$, $P=.546$). Distributions of P1, P2 and PR are shown separately in box plots (Fig. 2A-C).

As shown in Table 2, Pearson regression analysis indicated both P2 and PR (not P1) increased significantly with age (Fig. 3A-C), SBP and DBP. P1, P2 and PR had no relationships with HR. Multiple regression analysis showed both P2 and PR were closely related to age. PR had a weak, but significant relationship with SBP.

4. Discussion

With the development of social industrialization, increasing women choose to bear child at an advanced age.[21] In China, after the releasing of 2-child policy, there is a significant increase in the percentage of elderly parturient women.[22] Studies have reported that advanced maternal age (≥35 years) or very advanced maternal age (≥45 years) is closely related to the adverse pregnancy outcomes, including low birth weight, premature birth, preeclampsia, severe preeclampsia and other diseases.[23,24] Among these diseases, preeclampsia is 1 of the most common disorders that cause high maternal and fetal morbidity and mortality worldwide. It's a systemic vascular disease involving the endothelial dysfunction with vasospasm, arterial constriction, and decreased intravascular volume.[25] PR is a best OA Doppler parameter used to assess the severity and progression of preeclampsia.[4–6] Although it's well-accepted that the resistance of arterial walls tends to increase with age,[26] the influence of age on the PR has never been evaluated.

Table 2

The correlation coefficient and *p* values of the simple linear regression and multiple linear regression.

	Simple linear regression analysis			Multiple linear regression analysis		
	P1	P2	PR	P1	P2	PR
Age	−0.096	0.420[a]	0.715[a]	−0.114	0.247[a]	0.553[a]
SBP	−0.007	0.379[a]	0.576[a]	0.049	0.12	0.195[b]
DBP	−0.008	0.307[a]	0.450[a]	0.009	0.053	0.055
HR	−0.016	0.059	0.081	0.001	0.026	0.017

HR, heart rate; SBP, systolic blood pressure; DPB, diastolic blood pressure; P1, initial peak velocity; P2, second peak velocity; PR, peak ratio.
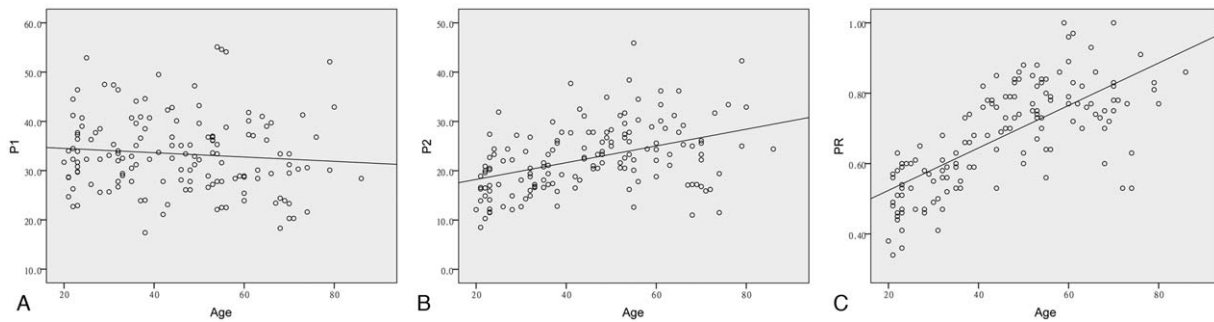[a] $P<.001$.
[b] $P<.05$.

Figure 3. A-C: Scatterplots show no significant correlation between age and P1, but close relationships of age with P2 and PR.

In this cross-sectional study, results showed both PR and P2 of OA Doppler were closely related to the age. The correlation between PR and age was moderate (partial correlation r = 0.553), while the correlation between P2 and age was week (partial correlation r = 0.247). The P2 and PR increased significantly in women older than 40 years. No relationship was found between P1 and age. To the best of our knowledge, the present study for the first time evaluated the effect of age on the PR and P2 of OA Doppler.

PR is the only Doppler parameter used to assess OA. The elevation of PR, the ratio of P2 and P1, is associated with decreased P1 or increased P2 after the protodiastolic notch. In the present study, P1 had no relationship with age, but P2 correlated positively with age. Thus, the elevation of PR in our study might be mainly ascribed to the rise of P2.

The average PR in our study was 0.68 ± 0.14, much higher than that in young population. In a study of Lockhart et al.,[27] the mean PR was 0.58 (range, 0.55-0.61) in ten young men (age 18 to 28), similar to that reported by Alves et al (average PR, 0.58 ± 0.11).[16] Similarly, the PR of left eyes of low risk pregnancy women was 0.58 ± 0.16.[15] We speculate that 1 of the main reasons for this variation is the age difference among these studies. In our study, a wide range of population (mean age, 45.2 ± 16.8 years) was included, and the subjects had a relatively advanced age as compared to other studies. Multiple regression analysis also showed moderate correlation between PR and age. Estimation based on determination coefficient (R^2) suggests that about 30.58% of variation was caused by age. Thus, age should be considered when PR is used in clinical pratice.

P2 is also a sensitive marker of the maternal vascular changes. Matias et a,[28] reported that P2 > 22.11 cm/s was the best cut-off for predicting preeclampsia, with a diagnostic sensitivity of 70% and specificity of 75%. In their study, the mean P2 was 19.29 ± 6.72 cm/s, lower than that in the present study (22.52 ± 6.82 cm/s). This discrepancy might be related to the difference in the age. However, in another study[16] conducted in a young population (average age, 26.1 ± 6.7 years), the P2 (21.07 ± 7.62 cm/s) was similar to our finding. This may be explained by the weak positive relationship between P2 and age as shown in the multiple regression analysis (partial correlation r = 0.247).

In availabe studies, P1 in normal controls varies noticeably. This might be ascribed to the differences in the devices, the sites of examination, and the observers' experience. In addition, the correlation between age and P1 is also conflicting. Kaiser et al. and Harris et al,[11,29] found that there was no significant relationship between P1 and age. However, Williamson et al and Chan et al,[10,30] found that P1 had a weak negative relationship with age. Our findings were consistent with those reported by Kaiser et al and Harris et al,[11,29].

In the present study, despite the significant correlation between SBP and PR, the R^2 was very low (0.038). DBP and HR showed no significant influence on the measured variables. Therefore, in clinical practice, BP and HR may not interfere with the interpretation of P1, P2 and PR of the OA. This is consistent with that reported by Kaiser et al,[29]. Of note, both BP and HR were in normal range in our study. Therefore, this conclusion should not be applied to subjects with abnormal BP or HR. More studies are needed to investigate the relationships of Doppler parameters with hypertension or hypotension.

In summary, our study indicates that P2 and PR of OA Doppler increase with age. Age is a crucial variable that should be considered when the P2 and PR are used to evaluate the hemodynamic change of OA, especially in women older than 40 years. The reference range of P2 and PR should be established in different age groups before the clinical application.

Author contributions

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Supervision: Zhi-Xian Li.
Writing – original draft: Xi-Yue Yang.
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