Usefulness of color Doppler imaging of orbital arteries in young hypertensive patients

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ABSTRACT

Color Doppler imaging (CDI) is an established method for investigating ocular blood flow characteristics, and several blood flow parameters can be obtained from the velocity wave. This study evaluated CDI parameters in hypertensive subjects by measuring flow velocities, resistive index, and the pulsatility index of ocular arteries. One hundred young hypertensive patients and 50 age- and gender-matched healthy controls were recruited for the study. CDI parameters of the ophthalmic artery, central retinal artery, and posterior ciliary artery were measured in all subjects. Doppler index cutoff points were calculated using area under the curve with 95% confidence intervals. Results showed that Doppler parameters were significantly higher in subjects diagnosed with hypertension in the young compared to controls.

KEYWORDS Color Doppler imaging; Doppler parameters; hypertension in young; ophthalmic artery; peak ratio

Hypertension in the young (HY) is defined as a systolic blood pressure >140 mm Hg and/or a diastolic blood pressure >85 mm Hg or a history of antihypertensive therapy in the age group 19 to 39 years.¹ Hypertension is the leading cause of death worldwide. Globally and locally, there has been an increase in hypertension in children, adolescents, and young adults <40 years.² A large part of the increased prevalence can be attributed to lifestyle factors such as diet and physical inactivity, which lead to overweight and obesity. Most young patients ($>90\%$) will have essential or primary hypertension, whereas only a minority ($<10\%$) will have secondary hypertension.³ Hypertension alters vascular resistance in the eyes and is a major risk factor for arteriosclerosis; advanced arteriosclerosis occurs with increasing age, which indicates a long duration of hypertension. Color Doppler imaging (CDI) is an established method for investigation of ocular and orbital blood flow characteristics.

METHODS

This cross-sectional study was undertaken in the Department of Radiology at a tertiary care hospital in India over the 2-year period from January 2016 to December 2018. Before subjects were recruited, the study protocol was

approved by the institutional ethics committee, in accordance with the ethical principles for human investigation outlined by the Second Declaration of Helsinki, and written informed consent was obtained from all patients.

A total of 100 cases of HY diagnosed at our hospital and 50 age- and gender-matched healthy controls were recruited for the study. Cases of HY were grouped into two categories: Group 1a consisted of patients with comorbidities, which included diabetes, hypercholesterolemia, and smoking history ($n = 50$), and group 1b consisted of patients without comorbidities ($n = 50$). Controls were subjects without stroke matched to cases by age, gender, and risk factors like diabetes, hypertension, smoking, and hypercholesterolemia. Patients were excluded from the study if they had grade 1 retinopathy that could interfere with atherosclerotic changes or had diabetes mellitus, glaucoma, age-related macular degeneration, high myopia, or a history of laser photocoagulation or prior ophthalmic surgery. A fundus screening examination was performed in all patients by a trained ophthalmologist using direct and indirect ophthalmoscopy. CDI parameters of the ophthalmic artery (OA), central retinal artery (CRA), and posterior ciliary artery (PCA) were measured in all subjects, and results were tabulated for comparison. The peak ratio, which is the ratio of the values for the peak diastolic velocity (after the protodiastolic notch)

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and the initial peak (peak systolic velocity), was calculated for OA, and Doppler index cutoff points were calculated using area under the curve with 95% confidence intervals.

For this study, HY was defined as blood pressure $\geq 140/90$ mm Hg on two occasions and/or treatment for hypertension in the age group 19 of 39 years. Diabetes mellitus was defined as presenting with a history of diabetes mellitus; being on diet control, hypoglycemic drugs, or insulin treatment; or having a random blood sugar >200 mg/dL during the hospital stay. A current smoker was defined as someone who self-reported smoking within the calendar year prior to the year of diagnosis, and an ex-smoker was defined as an ever smoker who had quit smoking for more than one calendar year prior to the diagnosis year. A nonsmoker was defined as one who did not meet the criteria for ever smoker, current smoker, or ex-smoker. Hypercholesterolemia was defined as having a diagnosis of hypercholesterolemia, being on a prescribed diet or lipid-lowering agents, or having a fasting cholesterol level >200 mg/dL.

Blood pressure was measured using a mechanical sphygmomanometer in the hospital setting after 15 minutes of comfortable sitting. The average of three blood pressure measurements was calculated. The diagnosis of hypertension was based on the eighth report of the Joint National Committee.³ Height and weight were measured according to standardized protocols and body mass index was calculated.

The left and right eyes were studied in all patients to assess resistive index (RI), pulsatility index (PI), peak systolic velocity (PSV), and end diastolic velocity (EDV) of the OA, CRA, and PCA. All CDI examinations were performed with the patient after 10 minutes of rest by the same experienced sonologist using a GE LOGIQ P5 analyzer with a 7.5-MHz linear transducer. Before the examination, CDI was performed with the gain adjusted to avoid artefactual color noise, thus allowing detection of low velocities. Scans of the eye were performed with the patient in the supine position with head tilted at an angle about 30° , with eyes closed. The transducer was applied to the closed upper eyelid using a gel coupling agent, with the examiner's hand resting on the orbital margin to minimize the applied pressure to the eye globe and the orbit. The angle of the transducer was 30° to 60° during the examination. After the exclusion of orbital pathologies by B-mode, CDI was performed. The patients were asked to remain in the same position for assessing the RI, PI, PSV, and EDV of OA, CRA, and PCA.

Subjects were asked to look to the other side during evaluations of the right or left eye for orbital parameters of OA. The optic nerve was taken as reference for all of the measurements. Blood flow velocity of the OA was measured nasally directly after crossing the optic nerve approximately 2 to 3 cm behind the globe, and an angle correction was applied between the transducer and the vessel according to the vessel course. Blood flow velocities in the CRA were measured within the optic nerve head shadow 3 to 5 mm behind the posterior margin of the globe. Blood flow velocity of the

nasal and temporal PCA were examined approximately 5 to 10 mm behind the globe and the results were averaged. Once the location of arterial blood flow within the OA, CRA, and PCA was determined, fine movements of the probe provided sufficient length of the vessels to give the strongest and most uniform readings of arterial flow. PSV (the highest velocity achieved during systole), EDV (the lowest velocity achieved during diastole), and RI $([PSV - EDV]/PSV)$ of assessed vessels were measured for every patient. All ultrasonographic assessments were performed by the same experienced radiologist to prevent interobserver variabilities, and intraobserver variability for CDI measurements was $<5\%$. Doppler parameters of both right and left OA, CRA, and PCA were determined by an average of two point measurements. Intraclass correlation coefficients were calculated for the same patient characteristics measured on left and right sides by calculating color Doppler indices of OA, CRA, and PCA from 100 cases of HY and 50 matched controls. Intraclass correlation coefficients varied around a median value of 0.0112. The investigator was masked for the hypertension data, and all readings were taken and interpreted by the same investigator.

Descriptive statistics were reported using numbers and percentages for categorical variables. Analysis was done using Microsoft Excel 2013, SPSS Statistical Package Version 20.0, and IBM SPSS Statistics for Windows Version 20.0. Mean RI values (mean of the right and left eye RI values), mean PI values, mean PSV values, and peak EDV values of OA, CRA, and PCA were calculated. Kolmogorov-Smirnov tests were used to test the normality of data distribution. The data were expressed as arithmetic means and standard deviations. The chi-square test was used to compare the categorical variables between groups. One-way analysis of variance with post hoc Bonferroni and Kruskal-Wallis tests was used in normally and nonnormally distributed continuous data, respectively. Independent sample *t* test was used to compare continuous variables between two hypertensive groups. Pearson's correlation analysis and *P* values were calculated to compare demographic data, biochemical variables, clinical characteristics, and orbital CDI parameters in HY subjects and control groups, and $P < 0.05$ was considered statistically significant. Receiver operating characteristic curves were used to determine the predictive power of the OA Doppler indices for identification of HY by comparing subject groups 1a and 1b.

RESULTS

Demographic data, biochemical variables, clinical characteristics, and orbital Doppler parameters of the 100 HY subjects and 50 controls are presented in [Table 1](#). There were no statistically significant differences in gender, age (32.5 vs 31.7 years), or body mass index (29.0 vs 29.7) between the control and hypertensive subjects. There were significant differences between the two groups in clinical characteristics such as systolic blood pressure, diastolic blood pressure, and

Table 1. Demographic data, biochemistry variables, clinical characteristics, and orbital Doppler parameters of young hypertensive patients and controls^a

Patient characteristic	HY group (n = 100)	Control group (n = 50)	t Test	P value ^b
Age (years)	32.5 ± 3.5	31.7 ± 3.8	0.64	0.24
Gender (male/female)	53/47	26/24	0.34	0.58
BMI (kg/m ²)	29.0 ± 5.3	29.7 ± 3.9	0.26	0.77
Smoking	42/100	—	—	—
Urea (mg/dL)	32.8 ± 5.4	32.1 ± 3.3	0.18	0.93
Creatinine (mg/dL)	0.8 ± 0.1	0.8 ± 0.1	0.19	0.91
AST (U/mL)	30.5 ± 11.8	29.6 ± 10.8	0.39	0.52
ALT (U/mL)	28.6 ± 11.8	27.3 ± 10.4	0.42	0.50
Total cholesterol (mg/dL)	178.3 ± 41.7	174.2 ± 39.1	−2.01	0.04
Triglycerides (mg/dL)	178.6 ± 98.4	174.2 ± 89.2	0.22	0.82
HDL (mg/dL)	34.5 ± 8.1	37.3 ± 10.2	0.63	0.08
LDL (mg/dL)	107.4 ± 32.5	102.7 ± 28.9	0.86	0.06
Systolic BP (mm Hg)	132.5 ± 34.0	120.5 ± 20.5	4.67	0.001
Diastolic BP (mm Hg)	90.5 ± 11.0	72.5 ± 7.5	6.42	0.002
Mean arterial pressure (mm Hg)	134.7 ± 22.3	112.7 ± 14.4	6.19	0.004
Mean RI of OA	0.7 ± 0.1	0.7 ± 0.04	−3.53	0.01
Mean PI of OA	1.64 ± 0.52	1.22 ± 0.44	−3.39	0.03
Mean PSV of OA (cm/s)	27.2 ± 13.7	24.8 ± 9.1	−3.11	0.04
Mean EDV of OA (cm/s)	10.1 ± 5.4	8.8 ± 4.4	2.28	0.03
Mean RI of CRA	0.66 ± 0.08	0.64 ± 0.05	−4.20	0.02
Mean PI of CRA	1.5 ± 0.5	1.2 ± 0.4	−3.98	0.03
Mean PSV of CRA (cm/s)	26.4 ± 11.6	22.2 ± 8.7	−3.42	0.04
Mean EDV of CRA (cm/s)	10.3 ± 4.4	8.1 ± 3.9	2.67	0.04
Mean RI of PCA	0.7 ± 0.1	0.7 ± 0.03	−3.83	0.02
Mean PI of PCA	1.7 ± 0.6	1.2 ± 0.4	−3.71	0.04
Mean PSV of PCA (cm/s)	29.6 ± 14.3	25.1 ± 10.7	−3.56	0.05
Mean EDV of PCA (cm/s)	9.9 ± 5.1	8.7 ± 4.4	2.84	0.04

^aAll measurable values were tabulated with mean ± standard deviation.

^bIndependent sample *t* test was used except in the case of age (chi-square test) and triglycerides and diastolic BP (Mann-Whitney *U* test).

ALT indicates alanine transaminase; AST, aspartate transaminase; BMI, body mass index; BP, blood pressure; CRA, central retinal artery; EDV, end diastolic velocity; HDL, high-density lipoprotein; HY, hypertension in the young; LDL, low-density lipoprotein; OA, ophthalmic artery; PCA, posterior ciliary artery; PI, pulsatility index; PSV, peak systolic velocity; RI, resistive index.

mean arterial pressure but no statistically significant differences in biochemical variables such as urea, creatinine, aspartate transaminase, alanine transaminase, triglycerides, high-density lipoprotein, and low-density lipoprotein.

Compared with the control group, the HY group had a significantly higher mean RI of OA, CRA, and PCA; a significantly higher mean PI of OA, CRA, and PCA; a significantly higher mean PSV of OA, CRA, and PCA; and a significantly higher mean EDV of OA, CRA, and PCA (Table 1). When group 1a and group 1b were compared,

there were significant statistical differences in mean RI, mean PI, mean PSV, and mean EDV of OA; mean RI, mean PI, mean PSV, and mean EDV of CRA; and mean RI, mean PI, mean PSV, and mean EDV of PCA (Table 2). In bivariate analysis, mean RIs of OA, CRA, and PCA were significantly correlated with the duration of hypertension ($P = 0.04$) and smoking history ($P = 0.04$) (Figure 1).

Analysis of the risk factors for HY showed that orbital color Doppler parameters correlated positively with smoking and hypercholesterolemia but not with age and gender. The

Table 2. Demographic data, biochemistry variables, clinical characteristics, and orbital Doppler parameters of young hypertensive groups and controls^a

Patient characteristics	HY group 1a (n = 50)	HY group 1b (n = 50)	Control group (n = 50)	One-way ANOVA (F value) ^b	P value
Age (years)	32.2 ± 3.4	32.7 ± 3.6	31.7 ± 3.8	2.16	0.29
Gender (male/female)	26/24	27/23	26/24	1.84	0.62
BMI (kg/m ²)	29.8 ± 5.4	28.1 ± 5.1	29.7 ± 3.9	1.72	0.79
Smoking	28/50	14/50	—	4.37	0.04
Hypertension duration (years)	3.7 ± 1.3	3.3 ± 1.4	—	4.46	0.04
Urea (mg/dL)	33.4 ± 5.8	32.3 ± 4.9	32.1 ± 3.3	1.29	0.99
Creatinine (mg/dL)	0.85 ± 0.12	0.83 ± 0.12	0.82 ± 0.12	1.39	0.97
AST (U/mL)	31.6 ± 12.2	29.5 ± 11.5	29.6 ± 10.8	2.02	0.59
ALT (U/mL)	29.8 ± 12.4	27.4 ± 11.1	27.3 ± 10.4	2.37	0.51
Total cholesterol (mg/dL)	182.4 ± 42.6	174.2 ± 40.7	174.2 ± 39.1	4.26	0.05
Triglycerides (mg/dL)	182.9 ± 102.6	174.1 ± 94.2	174.2 ± 89.2	1.55	0.89
HDL (mg/dL)	32.6 ± 7.2	36.4 ± 8.9	37.3 ± 10.2	3.42	0.08
LDL (mg/dL)	111.7 ± 34.7	103.1 ± 30.3	102.7 ± 28.9	3.83	0.06
Systolic BP (mm Hg)	134.0 ± 36.0	131.0 ± 32.0	120.50 ± 20.5	27.8	0.001
Diastolic BP (mm Hg)	93.0 ± 12.0	88.0 ± 10.0	72.5 ± 7.5	14.35	0.003
Mean arterial pressure (mm Hg)	137.7 ± 24.0	131.7 ± 20.7	112.7 ± 14.4	11.17	0.004
Mean RI of OA	0.7 ± 0.1	0.7 ± 0.1	0.7 ± 0.04	6.82	0.01
Mean PI of OA	1.8 ± 0.6	1.4 ± 0.5	1.2 ± 0.4	4.29	0.04
Mean PSV of OA (cm/s)	28.2 ± 14.6	26.2 ± 12.8	24.8 ± 9.1	4.01	0.05
Mean EDV of OA (cm/s)	10.8 ± 5.8	9.4 ± 5.0	8.8 ± 4.4	5.32	0.03
Mean RI of CRA	0.7 ± 0.1	0.6 ± 0.1	0.6 ± 0.05	4.94	0.01
Mean PI of CRA	1.6 ± 0.5	1.4 ± 0.5	1.2 ± 0.4	4.29	0.04
Mean PSV of CRA (cm/s)	28.4 ± 12.4	24.5 ± 10.7	22.2 ± 8.7	4.22	0.05
Mean EDV of CRA (cm/s)	10.8 ± 4.5	9.8 ± 4.2	8.1 ± 3.9	4.51	0.03
Mean RI of PCA	0.8 ± 0.1	0.7 ± 0.1	0.7 ± 0.03	6.42	0.02
Mean PI of PCA	1.8 ± 0.6	1.6 ± 0.5	1.2 ± 0.43	4.11	0.04
Mean PSV of PCA (cm/s)	30.4 ± 15.8	28.7 ± 12.7	25.1 ± 10.7	4.37	0.04
Mean EDV of PCA (cm/s)	10.4 ± 5.3	9.4 ± 4.8	8.7 ± 4.4	4.93	0.03

^aAll measurable values were tabulated with mean ± standard deviation.

^bOne-way analysis of variance with a post hoc Bonferroni was used except in the case of age (chi-square test), hypertension duration (independent sample *t* test), and triglycerides and diastolic BP (Kruskal-Wallis test).

ALT indicates alanine transaminase; AST, aspartate transaminase; BMI, body mass index; BP, blood pressure; CRA, central retinal artery; EDV, end diastolic velocity; HDL, high-density lipoprotein; HY, hypertension in the young; LDL, low-density lipoprotein; OA, ophthalmic artery; PCA, posterior ciliary artery; PI, pulsatility index; PSV, peak systolic velocity; RI, resistive index.

receiver operating characteristic curves showed a higher probability of HY for peak ratio values >0.71 (*Figure 2*).

DISCUSSION

The current study demonstrates for the first time that CDI is sensitive enough to assess hemodynamic changes in HY. The peak ratio, which is a ratio of the values for the

peak diastolic velocity (after the protodiastolic notch) and the initial peak (PSV), was first described in 2002 in studies by Nakatsuka et al.⁴

Abnormal results in retrobulbar CDI examination include elevated resistance in OA, CRA, and PCA, which are associated with pathognomonic acute painless visual field loss, optic disc edema, and ischemic optic neuropathy.⁵ Reduced blood flow velocities of the OA, CRA, and PCA

Figure 1. Scatter diagrams demonstrating the association between hypertension duration and the resistive index of (a) the ophthalmic artery, (b) the central retinal artery, and (c) the posterior ciliary artery.

are consequences in patients with systemic hypertension and have a poor prognosis due to increased resistance and reduced posterior circulation.⁶ Early diagnosis and intervention can result in improvement of the retrobulbar circulation with optic nerve decompression and might be beneficial for the treatment of the above-mentioned conditions and help

revert changes back to normal. CDI may detect chronic perfusion deficits of retrobulbar vessels in acute circulatory abnormalities.⁷ The only disadvantage of CDI of orbital arteries is the close contact between the eyelids and the transducer that must be established. Some pressure may be applied to the globe, particularly when the examiner is not familiar with the method. Williamson et al,⁸ however, have shown that this influence can be minimized with experience. Repeated measurements of the same subject by the same or different trained examiners have shown that the results of velocity measurements may be well reproduced.

The advantage of using the RI value is that it is not dependent on Doppler angle, unlike PSV and EDV, which change based on Doppler angle. OA is representative of peripheral arteries and confers anatomical advantages for detecting Doppler flow because of the absence of ultrasonic-positive obstacles such as bones and fat tissue, the good sonolucency of the eyeball, and the near-vertical angle of the OA to the transducer. Hemodynamic Doppler flow patterns may reflect peripheral vascular resistance. The technical reproducibility of OA Doppler imaging is well established in the ophthalmological field with sufficient observer experience. The relationship between OA Doppler findings and systemic atherosclerosis, however, remains unclear.

A limited number of studies have been performed to investigate the CDI orbital artery parameters in hypertensive patients. Taylor and Holland⁹ reported that the RI values of the CRA, PCA, and OA in hypertensive patients were significantly increased compared with those of normal controls. Ahmetoglu et al¹⁰ also indicated that the RI of the OA, CRA, and PCA in hypertensive patients were significantly increased, and the treatment of hypertensive patients with candesartan significantly decreased RI values of the CRA, PCA, and OA. As an affirming finding, Karadeniz-Bilgili et al⁵ found increased RI values in hypertensive patients compared to healthy subjects. Akal et al¹¹ found a higher RI of PCA levels and similar OA and CRA levels in geriatric hypertensive patients compared to healthy subjects. The RI of the orbital arteries in hypertensive patients with or without retinopathy has not yet been investigated and compared. Dimitrova et al¹² reported that RIs of OA, CRA, and PCA are significantly increased in patients with diabetic retinopathy compared to control subjects. Tamaki et al¹³ also suggested that RI of OA is significantly higher in patients either with or without diabetic retinopathy than in normal subjects. Basturk et al¹⁴ showed higher RI values of the orbital arteries in patients with diabetic retinopathy than in patients without retinopathy.

Orbital hyperperfusion in patients with preeclampsia was also described by Ohno et al,¹⁵ Ayaz et al,¹⁶ and Diniz et al.¹⁷ In the current study, the increased values of this index in patients with HY suggest that there is a reduction in the impedance to flow in the OA. Further, there was a significant difference ($P < 0.05$) between RI, PI, PSV, and EDV values of OA, CRA, and PCA in HY subjects and

Figure 2. Receiver operating characteristic curves for the (a) resistive index, with area under the curve of 0.78 (95% confidence interval, 0.68–0.89; cutoff point, 0.669), and (b) pulsatility index, with area under the curve of 0.79 (95% confidence interval, 0.68–0.90; cutoff point, 1.262).

healthy controls (*Tables 1 and 2*). Akal et al¹¹ evaluated RI values of OA, CRA, and PCA in patients with hypertensive retinopathy and found no significant difference compared to patients without hypertensive retinopathy.

In conclusion, in investigating CDI orbital arteries, the current study found that Doppler parameters were significantly higher in subjects diagnosed with HY compared to controls.

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