Original Article

Evaluation of resistive index using color Doppler imaging of orbital arteries in geriatric patients with hypertension

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Background and Aim: Resistive index (RI) is an indirect measurement of blood flow resistance that can be used to evaluate vascular damage in ophthalmologic disease. The purpose of this study was to evaluate the association between RI values of orbital arteries using the color Doppler imaging (CDI) in geriatric hypertensive patients with or without retinopathy. **Setting and Design:** Designed as a cross-sectional study. **Materials and Methods:** We evaluated 60 geriatric patients with hypertension (Group 1) and 30 healthy subjects (Group 2). Further, the patients with hypertension were grouped into two: Group 1a consisted of patients with retinopathy (n = 30), and group 1b consisted of patients without retinopathy (n = 30). The mean RI values of ophthalmic artery (OA), central retinal artery (CRA), and posterior ciliary artery (PCA) were measured using CDI. **Results:** Compared to group 2, group 1 had significantly higher mean resistive index of PCA levels (P = 0.017), whereas there were no statistical difference in mean resistive indexes of OA and CRA (both P > 0.05). Besides, there were no statistical difference in mean resistive indexes of OA, CRA, and PCA between the group 1a and group 1b (P > 0.05 for all). Mean resistive indexes of OA, CRA, and PCA were significantly correlated with the duration of hypertension (r = 0.268, P = 0.038; r = 0.315, P = 0.014; r = 0.324, P = 0.012, respectively). **Conclusions:** Our study indicates that RI might be a useful marker for the ocular hemodynamic of retinal vessels, provides morphologic and vascular information in hypertension and hypertensive retinopathy.

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The Resistive Index (RI) is a widely used measure of resistance to arterial flow and is calculated from the color Doppler imaging (CDI).[1,2] CDI is a noninvasive, safe, and useful method, which provides morphologic and vascular information in various diseases. Circulatory parameters in the retrobulbar blood vessels are one of them.[3-7] Hypertension alters vascular resistance in eyes, and is a major risk factor for arteriosclerosis, and advanced arteriosclerosis occurs with increasing age which indicates long duration of hypertension. Previously, a little number of studies in literature has been performed to evaluate the RIs of orbital arteries in patients with hypertension.[8-11] Beyond these studies, we aimed in the present study to evaluate the association between RI values of orbital arteries in geriatric patients with hypertension. Moreover, we compared these levels in hypertensive patients with or without retinopathy.

Materials and Methods

This cross-sectional cohort study was conducted at Harran University, School of Medicine, Sanliurfa/Turkey. Prior to subject recruitment, the study protocol was reviewed and approved by the local ethics committee, in accordance with the ethical principles for human investigations, as outlined by the Second Declaration of Helsinki, and written informed consents were obtained from all the patients.

From March-2012 to November-2012, consecutively 60 geriatric patients with hypertension (Group 1) and 30 age-gender-matched healthy controls (Group 2) were recruited for the study. Further, the patients with hypertension were grouped into two: Group 1a consisted of patients with retinopathy (n = 30), and group 1b consisted of patients without retinopathy (n = 30). The exclusion criteria were as follows: Patients with grade 1 retinopathy that could interfere with the atherosclerotic changes, diabetes mellitus, eyes that had an ophthalmic condition that could interfere with the ophthalmic arteries, such as glaucoma, age-related macular degeneration, high myopia etc., as well as those with laser photocoagulation or previous ophthalmic surgery. Fundus examination was performed in all patients by a trained ophthalmologist using direct and indirect ophthalmoscopy. The RI of the ophthalmic artery (OA), central retinal artery (CRA), and posterior ciliary artery (PCA) were measured in all patients.

Blood pressure was measured using a mechanical sphygmomanometer in the medical office setting. In each subject, after 15 minutes of comfortably sitting, the average of three blood pressure measurements was calculated. The diagnosis of hypertension was based on the seventh report of the 'Joint National Committee.'[12] Height and weight were measured according to standardized protocols. Body mass index was calculated as the weight in kilograms divided by the height in meters squared (kg/m^2).

The left and right eyes were studied in all patients to assess resistive indexes of the OA, CRA, and PCA. All CDI examinations were performed with the patient after 10 minutes of rest by the same experienced sonographer using a Hitachi EUB 515 (Hitachi Medical Corp, Tokyo, Japan) analyzer with

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a 7.5-MHz linear transducer. Before the examination, CDI was performed with the gain adjusted to avoid artifactual color noise, thus allowing detection of low velocities, and the room temperature was brought to optimal level. Scans of the eye were performed in the supine position with head tilted at an angle about 30^o, with eyes closed. The transducer was applied to the closed upper eyelid using an ophthalmic sterile gel, with the examiner's hand resting on the orbital margin to minimize the applied pressure to the eye globe and the orbit. Angle of the transducer was taken 30-60 degrees during the examination. After the exclusion of orbital pathologies by B-mod, CDI was performed. The patients were asked to be at the same position for assessing the RI of CRA and PCA and were asked to look the other side during evaluating right or left eye for assessing the RI of OA. Optic nerve was taken as reference for all of the measurements. Blood flow velocity of OA was measured nasally directly after crossing the optic nerve approximately 2-3 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 3-5 mm behind the posterior margin of the globe. Blood flow velocity of the nasal and temporal PCA were examined approximately 5-10 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. Peak systolic velocity (PSV; the highest velocity achieved during a systole), end diastolic velocity (EDV; the lowest velocity achieved during a diastole), and resistive index (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 were <5%. Because of the measurements depend on inter- and intraobserver variability and the age, a standardized international value does not exist for RI levels; therefore, measured levels are used only for comparisons.

All blood samples were collected from an antecubital vein with the patient in the supine position after a 12-hour overnight fast. Serum urea, creatinine, fasting blood glucose, aspartate aminotransferase, alanine aminotransferase, triglycerides, total cholesterol, high-density and low-density lipoprotein cholesterol levels were determined using the commercially-available assay kits (AbbottÒ, Abbott Park, North Chicago, Illinois, USA) with an auto-analyzer (AbbottÒ, Abbott Park, North Chicago, Illinois, USA).

Statistical analyses were performed using SPSS for Windows version 17.0 (SPSS, Chicago, IL, USA). Mean RI values (mean of the right and left eyes RI values) of the 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 ANOVA* with a *post-hoc Bonferroni and Kruskall Wallis* tests were respectively used in normally and non-normally distributed continuous data. *Independent sample T*-test was used for comparison of continuous variables between two hypertensive groups. *Pearson's correlation* analysis was used to examine the association of demographic and biochemical variables with orbital Doppler indexes in hypertensive patients. A two-sided $P < 0.05$ was considered statistically significant.

Results

Clinical, laboratory, and demographic characteristics of controls and hypertensive subjects were presented on Table 1. There were no statistical differences in gender, age, and body mass index between the controls and hypertensive subjects ($P > 0.05$ for all). Compared to group 2, group 1 had significantly higher mean resistive index of PCA levels ($P = 0.017$), whereas there were no statistical difference in mean resistive indexes of OA and CRA (both $P > 0.05$).

In hypertensive retinopathy group (Group 1a), we examined 24 patients with grade 2 and 6 patients with grade 3 retinopathy and did not encounter grade 4 retinopathy patients. Compared to group 1a and group 1b, there were no statistical difference in mean resistive indexes of OA, CRA, and PCA ($P > 0.05$ for all) [Table 2].

In bivariate analysis, mean resistive indexes of OA, CRA, and PCA were significantly correlated with the duration of hypertension (r = 0.268, $P = 0.038$; r = 0.315, $P = 0.014$; $r = 0.324$, $P = 0.012$, respectively) [Fig. 1]. Whereas, both in group 1 and group 2, there were no correlations between the resistive indexes of OA, CRA, PCA, and the age (In Group 1: *r* = -, 084, *P* = 0.524; r = 0, 032, *P* = 0.810; r = -, 012, *P* = 0.926, respectively) (In Group 2: r = -, 201, *P* = 0.286; r = -, 310, *P* = 0.095; *r* = 0, 099, *P* = 0.603, respectively).

Discussion

To the best of our knowledge, this is the first report to evaluate the RI of orbital arteries in geriatric patients with hypertension, and is the first study that compared

Table 1: Comparison of the demographic, laboratory, and clinical characteristics of hypertensive and control patients

Patient characteristics	Group 1 (*n*=60)	Group 2 (*n*=30)	*P*
Gender, male/female	31/29	13/17	0.507*
Age, years	72.55±4.59	71.46±4.15	0.264†
BMI, kg/m^2	29.82±6.03	30.16±3.77	0.741†
Urea, mg/dL	34.32±6.73	34.30±3.60	0.988†
Creatinine, mg/dL	0.86±0.18	0.87±0.18	0.842†
AST, U/mL	31.10±10.22	29.13±11.17	0.422†
ALT, U/mL	30.10±10.47	27.33±11.83	0.283†
Total cholesterol, mg/dL	176.33±39.31	195.23±41.46	0.043†
Triglyceride, mg/dL	181.23±115.31	181.33±98.55	0.758‡
HDL, mg/dL	33.56±8.83	37.30±9.18	0.071†
LDL, mg/dL	106.86±34.82	121.30±31.18	0.051†
Systolic BP, mmHg	134.58±15.76	122.00±8.86	<0.001†
Diastolic BP, mmHg	81.50±10.01	74.66±7.76	0.002‡
Mean RI of OA	0.72±0.07	0.70±0.05	0.141†
Mean RI of CRA	0.66±0.08	0.64±0.07	0.230†
Mean RI of PCA	0.71±0.06	0.68±0.05	0.017†

All measurable values were given with mean±standard deviation. BMI: Body mass index, AST: Aspartate transaminase, ALT: Alanin transaminase, HDL: High density lipoprotein, LDL: Low density lipoprotein, BP: Blood pressure, RI: Resistive index, OA: Ophthalmic artery, CRA: Central retinal artery, PCA: Posterior ciliary artery, *Chi-square, †independent sample *T* test, ‡Mann-Whitney U tests were used hypertensive patients with or without retinopathy. The main findings of this study were that, (i) RI of PCA in hypertensive patients was higher than patients without hypertension, (ii) RIs of patients with or without retinopathy were not different, (iii) and RIs were correlated with the duration of hypertension.

Table 2: Comparison of the demographic, laboratory, and clinical characteristics of hypertensive (with or without retinopathy) and control patients

Patient characteristics	Group 1a (*n*=30)	Group 1b (*n*=30)	Controls (*n*=30)	*P*
Gender, male/female	14/16	17/13	13/17	0.561*
Age, years	73.43±4.69	71.90±4.40	71.46±4.15	0.200†
HT Duration,	7.26±2.66	7.96±3.14	-	0.356‡
BMI, kg/m^2	29.17±7.53	30.46±4.05	30.16±3.77	0.626†
Urea, mg/dL	35.43±8.68	33.20±3.79	34.30±3.60	0.340†
Creatinine, mg/dL	0.85±0.18	0.86±0.19	0.87±0.18	0.959†
AST, U/mL	32.86±8.61	29.33±11.48	29.13±11.17	0.306†
ALT, U/mL	32.00±9.96	28.20±10.78	27.33±11.83	0.216†
Total cholesterol, mg/dL	181.66±37.72	171.00±40.77	195.23±41.46	0.069†
Triglyceride, mg/dL	195.93±129.52	166.53±99.14	181.33±98.55	0.722§
HDL, mg/dL	35.56±9.17	31.56±8.13	37.30±9.18	0.041†
LDL, mg/dL	107.80±37.34	105.93±32.72	121.30±31.18	0.165†
Systolic BP, mmHg	136.16±15.18	133.00±16.43	122.00±8.86	<0.001†
Diastolic BP, mmHg	82.66±9.71	80.33±10.33	74.66±7.76	0.005§
Mean RI of OA	0.720±0.068	0.714±0.080	0.70±0.05	0.287†
Mean RI of CRA	0.648±0.091	0.684±0.058	0.64±0.07	0.095†
Mean RI of PCA	0.713±0.064	0.706±0.053	0.68±0.05	0.067†

All measurable values were given with mean±standard deviation.
BMI: Body mass index, AST: Aspartate transaminase, ALT: Alanin transaminase, HDL: High density lipoprotein, LDL: Low density lipoprotein,
BP: Blood pressure, RI: Resistive index, OA: Ophthalmic artery, CRA: Central retinal artery, PCA: Posterior ciliary artery, *Chi-square, †one way ANOVA with a post hoc Bonferroni, ‡independent sample *T* test, §Kruskall Wallis tests were used

CDI may be a method for evaluation of vascular hemodynamics of retinal vessels, provides morphologic and vascular information in various diseases such as in hypertension. The pathogenesis of essential hypertension is multi-factorial, and many patients with ocular problems such as glaucoma, central retinal vein occlusion, and diabetes mellitus also have essential hypertension.[13] The RI has been proposed as a measure of distal vascular resistance and is reported to be linearly related to vascular resistance in both *in vitro* and *in vivo* studies. Hypertension causes elevation of the RI, indicating increased peripheral resistance or a vasospasm.[10,14,15]

In literature, limited number of studies has been performed to investigate the RI values of the orbital arteries in hypertensive patients. Taylor *et al*. reported that the RI values of the CRA, PCA, and OA in the hypertensive patients were significantly increased when compared with those in normal controls.[9] Ahmetoglu *et al*. also indicated that the RI of the OA, CRA, and PCA in the hypertensive patients were significantly increased, and the treatment of hypertensive patients with candesartan significantly decreased RI values of the CRA, PCA, and OA.[10] As an affirming finding, Karadeniz *et al*. have found increased RI values in hypertensive patients compared to the healthy subjects.[11] In our study, we found only a higher RI of PCA levels, and similar OA and CRA levels in geriatric hypertensive patients compared to the healthy subjects.

The OA originates from the internal carotid artery and enters the orbital cavity through the optic canal. It is a medium-sized muscular artery (1.33 ± 0.33 mm). The CRA and PCA are the ocular branches of the OA.[11,16] The major source of blood flow to the optic nerve head is in most cases derived from the PCA, whereas the CRA supplies the blood flow to the retina. The flow of the CRA is similar to that of the OA, with a lower systolic peak.[11,13] The spectrum of the PCA is also like that of the CRA; however, the diastolic flow of the PCA is higher than that of CRA, thus reflecting low-resistance vascular channels of the choroid.[17] Because of these different features of the PCA, although not definitely, PCA might be firstly affected by hypertension than those of the other orbital arteries as is found in our study.

The RI of the orbital arteries in hypertensive patients with or without retinopathy has never been investigated and compared yet. However, comparison of the diabetic patients with or without retinopathy has been investigated. Dimitrova *et al*. reported that, RI of OA, CRA, and PCA are significantly increased in patients with diabetic retinopathy

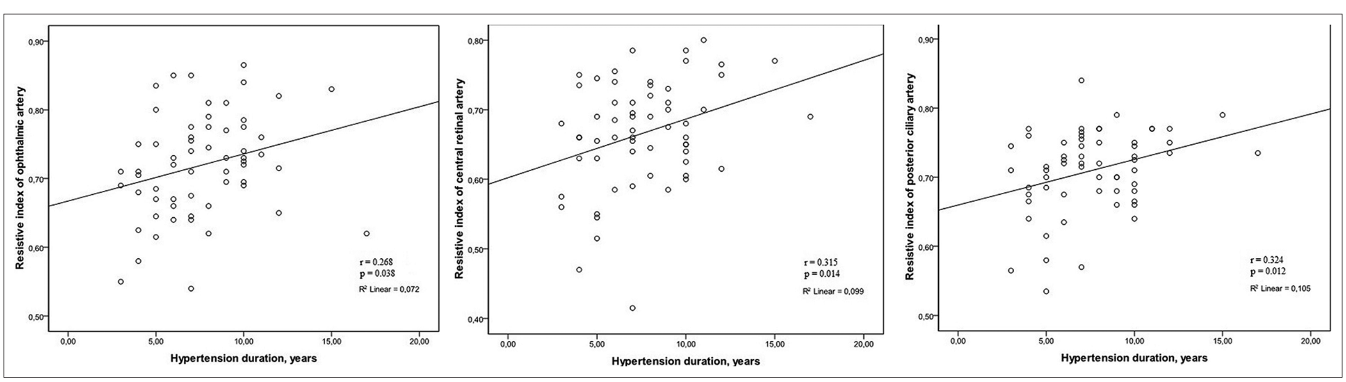

Figure 1: Graph demonstrating the association between the hypertension duration and the RIs of the orbital arteries

than in control subjects.[18] Tamaki *et al*. also suggested that, RI of OA is significantly increased in patients either with or without diabetic retinopathy than in normal subjects.[19] Basturk *et al*. have also showed increased RI values of the orbital arteries in diabetic retinopathy patients than patients without retinopathy.[6] In our study, all orbital RI values of patients with hypertensive retinopathy were found to be similar compared to patients without retinopathy.

Certain limitations of the present study should be considered. First of all, sample size was relatively small and design of the study was cross-sectional. Second, comparison of our results with younger individuals, although we selected geriatric cohort individuals, the investigation would perhaps provide deeper insight into the ophthalmic arteries in patients with hypertension and might add to the value of our manuscript. Finally, another potential limitation was operator-dependent nature of ultrasonography although it is non-invasive, easily performed, and confidential method for evaluating CDI.

In conclusion, our study differed from the previously published studies that have investigated the RI values in geriatric patients with hypertension, and also compared patients with or without retinopathy. CDI allows rapid, non-invasive evaluation of the orbital hemodynamic abnormalities. Therefore, when hypertension is diagnosed, orbital RI values should be measured by CDI to early predict orbital complications, and future prospective studies on ocular circulation are needed to address this issue.

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