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Comparative Study of Orbital Doppler Parameters in Hypertensive Patients With and Without Retinopathy

AYA M.S. ALY, M.Sc.*; ALIA M. NOURELDINE, M.D.**; AMR A.H. GADALLA, M.D.* and ABO ELMAGD ELBOHY, M.D.*

The Department of Diagnostic & Interventional Radiology and Ophthalmology Department**, Faculty of Medicine, Cairo University*

Abstract

Background: Hypertensionis a major risk factor for the development of cardiovascular disorders. Years before end organ damage is clinically evident, hypertension is considered a silent killer. Since retinal arterioles share anatomical and physiological properties with cerebral and coronary microcirculation, and can be monitored easily and non-invasively, it can thus be considered an in vivo window into the human circulation. Color Doppler Imaging (CDI) is a well-established technology for determining the parameters of orbital blood flow.

Aim of Study: To compare changes of color Doppler imaging (CDI) in the ophthalmic artery and its branches in hypertensive patients with retinopathy and without retinopathy in relation to their fundoscopic changes.

Patients and Methods: This observational study included 80 hypertensive patients, divided into 3 groups according to Wong and Mitchell Classification: No retinopathy (Group 1), with mild-moderate Retinopathy (Group 2), and with severe Retinopathy (Group 3). All did Orbital CDI in which Ophthalmic Artery (OA), Central Retinal Artery (CRA) and Ciliary Arteries (CA) were identified. Peak systolic velocity (PSV), End Diastolic velocity (EDV) and Resistivity Index (RI) were measured.

Results: CRA RIwas highest in G3 (p=0.05). OA EDV was significantly higher in G1 vs G3 (p=0.013). On the contrary, OA RI was lower in G1 vs G2 (p=0.010), and vs G3 (p=0.000). HTN duration showed a significant negative correlation with CRA EDV (r=-0.237, p=0.034); a significant positive correlationwith CRA RI (r=0.280, p=0.012) as well as with CA RI (r=0.288, p=0.010). Regarding HTN control, CRA PSV and EDV were significantly higher in stage 1 HTN (p=0.033 and 0.036 respectively), while CRA RI was significantly higher in isolated systolic HTN (p-value 0.029). OA PSV was signficnatly lower among patients with isolated systolic HTN vs controlled and stage 1 HTN patients (p=0.004 and 0.009).

Conclusion: RI of orbital arteries mainly OA and CRA, may serve as good predictors for microvascular changes of the retina especially in patients with poorly controlled HTN of long duration.

Correspondence to: Dr. Aya M.S. Aly, The Department of Diagnostic & Interventional Radiology, Faculty of Medicine, Cairo University

Key Words: *Orbital Doppler – Vascular alterations – Hypertensive retinopathy.*

Introduction

A major risk factor for the development of cardiovascular disorders is Hypertension. It is a chronic illness affecting 26% of the world's population **[1]**. Unfortunately, there is still a lack of awareness, treatment and control of hypertension. Years before end organ damage is clinically evident, hypertension is considered a silent killer. Since retinal arterioles share anatomical and physiological properties with cerebral and coronary microcirculation, and can be monitored easily and non-invasively, it can thus be considered an in vivo window into the human circulation **[2]**.

Retina is supplied by two branches of the Ophthalmic Artery (OA): The central retinal artery (CRA) and the posterior ciliary arteries (PCA) **[3]**. The CRA, running lengthwise to the optic nerve, pierces the lamina cribrosa and arrives at the optic disc nasal to the posterior pole. It then splits into superior and inferior branches, which continue to divide to nourish the inner retinal layers **[3]**.

Color Doppler Imaging (CDI) is a well-established technology for determining the parameters of orbital blood flow. It's an ultrasonographic technique that scans the state of circulation in many eye disorders and retinal vascular diseases **[4]**. Low blood flow velocities and increased resistance of the OA, CRA, and PCA are outcomes in patients with systemic hypertension which cause impaired ocular circulation. Early diagnosis and management can improve the orbital circulation which may prevent severe complications and enhance previous changes **[5]**.

In this study, we aimed to compare the different CDI parameters of orbital vessels in hypertensive patients with retinopathy and others without retinopathy, to detect correlations with different disease variables such as duration and control.

Patients and Methods

This is a cross-sectional studythat took place in Cairo University Hospitals between November 2020 till August 2021. The CDI was performed in the Radiology Department, Faculty of Medicine, Cairo University. It included a total of 80 hypertensive patients, randomly selected from outpatient clinics of the same hospital. All patients received a detailed explanation of the study design and aims, and signed an informed consent. The study protocol was revised and approved by the Research Ethics Committee, Faculty of Medicine, Cairo University (Code: MS-455-2020) and followed the tenets of the Helsinki declaration.

Study population:

Inclusion criteria: Hypertensive patients 30 years old or above randomly selected from ophthalmology outpatient clinics.

Exclusion criteria: Patients with vascular retinopathies other than HTN (e.g., diabetic retinopathy, retinal artery or vein occlusion, hereditary systemic angiopathy); patients with glaucoma, history of laser photocoagulation, previous intravitreal injections, congenital anomalies or any inflammatory process involving the eye and globe. Patients with corneal thinning such as severe Keratoconus, corneal ectasia or scleral thinning were also excluded for risk of perforation. Cardiovascular patients, chronically ill (e.g., nephropathy) patients and who took any medications that have a direct or an indirect effect on the circulation hemodynamics such as altering platelet aggregation or decreasing blood lipids, were excluded.

Data collection:

Patients had their demographics (age and gender) recorded, and a review of their medical history including personal and family history, history and duration of systemic diseases, history of ocular diseases. HTN duration and control were recorded. All patients had a thorough ophthalmological examination, including Best Corrected Visual Acuity (BCVA) using Snellen's chart, slit lamp examination, assessment of intraocular pressure by Goldmann's applanation tonometry, and dilated fundus examination by binocular indirect slit-lamp biomicroscopy. Patients were divided according to Wong and Mitchell Classification into 3 groups. Group 1: Without hypertensive retinopathy, Group 2: With mild-moderate Retinopathy, and Group 3: With severe Retinopathy.

Color doppler imaging:

CDI scan was performed to all patients by a single experienced ultrasonographer using the same machine and the same setting. The operator was blind to the patients' clinical data and fundus examination findings. The study was performed using the ultrasound and Color Doppler machine (TOSHIBA TUS A-500, Toshiba medical systems corporation, JAPAN) using linear array probe (L11-13 MHZ). Patients were placed in supine position, instructed to keep their globes straight ahead while closing their lids. A copious acoustic coupling gel amount was administered to the closed upper eyelid and the probe was gently positioned, avoiding excessive pressure on the globe. The ultrasonographer hand rested either on the patient's cheek or forehead for fine manipulation of the probe. We used the preset for small parts to allow vascular low flow detection with low pulse repetition frequency, low filter and high gain. At first, the eye globe is identified using the B-modescan, then the optic nerve was identified as the hypo-echoic structure behind the globe. The optic nerve would then be used as a hallmark. Depth, gain, time gain compensation and focus were accustomed to clearly detect the whole orbital cavity and its contents. Color mode was then turned on, adjusting velocity and gain to just below the noise floor, till we obtained the optimum quality. The CRA was identified running within the optic nerve, PCAs were located on both sides of the optic nerve and the OA was identified at the apex of the orbit, running from temporal to nasal aspect crossing over or below the optic nerve. Regarding PCAs, they arise as nasal and temporal trunks from the OA, then they divide into short and long branches. We scanned PCAs at the main trunk before their division. For each artery, we measured PSV, EDV, RI while adjusting sample volume to 1mm. Since the angle can't be fixed at zero in advance, the cursor was kept parallel or near parallel the direction of blood flow (according to the vessel direction), usually at an angle minor than 60°. Doppler filter was kept at 70 hertz (low filter setting) and again we increased the gain until the noise appeared in the Doppler spectrum then we decreased the gain just below the noise floor.

Outcome measures:

1- Comparing CDI parameters (PSV, EDV and RI) of each of the OA, CRA and PCA between Groups 1,2 and 3.
2- Comparing CDI parameters (PSV, EDV and RI) of each of the OA, CRA and PCA based onHTN control categories.
3- Correlation between the HTN duration and CDI parameters (PSV, EDV and RI) of each of the OA, CRA and PCA.

Statistical analysis:

Statistical analysis was conducted using SPSS 22nd edition, numeric variables were presented in mean ± standard deviation and were compared using one way ANOVA between <2 groups and post HOC pairwise comparison after normality testing. Categorical variables were presented in frequency and percentage and were compared using Chi^2 test. Pearson correlation test was used to assess the correlation between 2 numeric variables. Any *p*-value <0.05 was considered significant.

Results

80 hypertensive patients were included in our study with a mean age of 55 ± 12 years and 48(60%) were females. Fundus examination revealed that 47.5% had no hypertensive changes (Group 1), while 36.3% had mild-moderate changes (Group 2) and 16.3% had severe changes (Group 3). Regarding HTN control, 52 patients were found to be controlled on medications and 28 non controlled: 18 with stage 1 HTN (130-139mmHg systolic BP or 80-89mmHg diastolic BP) and 10 patients of isolated systolic HTN. CRA PSV and CRA EDV showed higher values in females vs males (both *p*=0.008). Similarly, CA PSV and CA EDV were found to be higher in females vs males (*p*=0.002 and 0.003 respectively).

1- *Comparing CDI parameters (PSV, EDV and RI) of each of the OA, CRA and PCA between Groups 1,2 and 3:*

Comparing CDI parameters of CRA, PCA and OA between Group 1,2 and 3 showed differences, some were significant and others were not. Detailed results are shown in Table (1).

Table (1): Comparing CDI parameters of OA, CRA and PCA between Group 1,2 and 3.

	Group 1		Group 2		Group 3		ONE WAY ANOVA	
	Mean	SD	Mean	SD	Mean	SD	F	*p*-value
CRA PSV	10.58	2.25	10.77	6.96	10.04	2.83	0.111	0.895
CRA EDV	3.55	1.47	4.22	3.57	3.09	0.87	1.192	0.309
CRA RI	0.67	0.07	0.63	0.07	0.69	0.08	3.014	0.05
PCA PSV	14.08	5.92	1320	4.91	15.42	3.77	0.804	0.451
PCA EDV	5.54	2.54	4.99	2.27	5.13	1.69	0.489	0.615
PCA RI	0.61	0.07	0.63	0.08	0.66	0.11	1.673	0.195
OA PSV	24.45	10.09	23.58	9.41	24.56	11.28	0.075	0.927
OA EDV	7.72	3.23	6.36	3.30	4.81	2.25	4.569	0.013
OA RI	0.68	0.53	0.73	0.08	0.79	0.04	18.415	0.000

Significant *p*-values are in Bold.

2- *Comparing CDI parameters of each of the OA, CRA and PCA between the HTN categories:*

As mentioned above, patients were found to fall in 1 of 3 categories regarding HTN control: Controlled, Stage 1 HTN or Isolated Systolic HTN. Comparison of each artery's CDI parameters between the 3 categories was done using post HOC pairwise test after normality testing. Regarding CRA,PSV and EDV were significantly higher among patients with stage 1 HTN compared to controlled patients (*p*=0.033, 0.036 respectively); while CRA RI was significantly higher among patients with isolated systolic HTNvs patients with stage 1 HTN (*p*=0.029). As for OA, only the PSV was signficnatly lowest among patients with isolated systolic HTN in comparison to controlled and Stage 1 HTN patients (*p*=0.004 and 0.009 respectively).

3- *Correlation between the HTN duration and CDI parameters of each of the OA, CRA and PCA:*

Upon doing correlation between HTN duration and CDI parameters of different arteries, OA did not show significant results, while some of the CRA and CA parameters showed significant correlations and are well presented in Tables (2,3).

Table (2): Correlation between duration of hypertension and CRA measurements.

	CRA PSV	CRA EDV	CRA RI
Duration of HTN:			
Correlation coefficient	–0.166	–0.237	0.280
p-value	0.142	0.034	0.012
Total number	80	80	80

Significant *p*-values are in Bold.

Table (3): Correlation between duration of hypertension and CA measurements.

	CA PSV	CA EDV	CA RI
Duration of HTN:			
Correlation coefficient	0.009	–0.116	0.288
p-value	0.935	0.305	0.010
Total number	80	80	80

Significant *p*-values are in Bold.

Discussion

Our study included 80 hypertensive patients with a mean age of 55.5±12.5 years, 60% were females, and 40% were males. The mean age reported in our patients was lower than that reported by Akal et al., *[6]* who were the first to compare parameters of orbital arteries using CDI in geriatric hypertensive patients with or without retinopathy, where they reported a mean age of 71.55±4.6 years for their patients.

The results of our current study showed that CRA RI was significantly higher in patients with hypertensive retinal changes, being higher the more severe is the retinopathy. In addition, CRA RI showed a positive correlation with duration of hypertension. All parameters of CRA were significantly correlated with the degree of control of hypertension: PSV and EDV were significantly higher in stage 1 HTN, while RI showed was significantly higher in isolated systolic HTN. This somehow shows agreement with results of Ahmetoglu et al. *[7]* despite the different study grouping. Ahmetoglu et al., *[7]* highlighted that RI of all orbital arteries were higher among patients with hypertension compared to normal controls, but he added that RI was significantly decreased after medical control of hypertension, which agrees with our CRA parameters, being significantly better in the controlled group who are compliant and responsive to treatment. This agrees with our hypothesis that hypertensive retinopathy changes can be reversed if early detected and managed properly, since arterial parameters are better in the controlled patients.

On the other hand, OA RI and EDV were significantly higher and lower respectively in patients with hypertensive fundus changes, while its PSV was correlated with the degree of control of HTN. As for PCAs, only the RI was correlated with HTN duration. This also agrees with Ahmetoglu's study *[7]*, and with Karadeniz et al., *[8]*. Who reported significant decrease only in the OA RI and PCAs RI after antihypertensive treatment. Similarly, the study by Reddy et al. *[5]*, in 2019 who studied 100 hypertensive patients by CDI in comparison to 50 healthy matched controls, stated that RIs of OA, CRA and CA were significantly higher in hypertensive patients.

Despite the agreement of many studies with our results, Akal et al., who, as previously mentioned,in 2014 conducted the first study comparing CDI orbital parameters in HTN patients with and without retinopathy, concluded that there were no statistical differences in mean RI of OA, CRA, and PCA *[6]*. Our explanation to this is the older age group of their study geriatric population, which may have led to dual pathology: HTN and atherosclerotic changes without HTN. Their patients mean age was 71.55±4.6 years while ours was 55.5±12.5 years.

In this study, duration of HTN showed a significant negative correlation with CRA EDV, a weak positive correlation with CRA RI, and a significant positive correlation with CA RI. These results were similar to those reported by Akal et al., *[6]* with positive correlation between HTN duration and CRA RI (r=0.31 and p=0.014) and with PCA RI (r=0.32, and p=0.012).

In contrast, PCA RI was significantly correlated with duration of hypertension but all parameters of PCA did not differ significantly according to the presence or the degree of retinopathy. This is in contrary to previously mentioned studies *[5-8]*.

In addition, we found that there was a statistically significant difference in CRA PSV and EDV based on the HTN control category. CRA PSV and EDV were significantly higher among patients with stage 1 HTN, while CRA RI was significantly higher among patients with isolated systolic hypertension, which is the most common form of HTN.

Limitations: Our study had limitations, first the relatively small sample which was a reflection of the Covid-19 era during which this study was conducted. In addition, we did not assess the different anti-HTN treatment modalities and their correlation with the HTN control category, or with the hemodynamic changes.

Conclusion:

CDI can be used for assessment of hypertensive retinopathy, using RI of orbital vessels mainly OA and CRA, as good predictors for microvascular changes of the retina especially in patients with poorly controlled HTN or with long duration. CDI, being an available, noninvasive, safe and rapid tool, has the potential to be used as a prognostic tool to detect "functional" retinoapthy before its clinical appearance. And this conclusion of ours agrees with Prathibha et al., *[9]* who studied the orbital vessels flow changes in hypertensive and diabetic patients; where they noted significant changes in blood flow velocities and resistance in cases with retinopathy compared to patients with normal fundi. They also recommended that CDI can actually offer prognostic values regarding altered orbital hemodynamics even before retinopathy changes appear. It is also of great usefulness in case of media opacity, where other imaging investigations and even clinical examination may be challenging.

Authors contribution statement:

AMN contributed to writing the report, extracting and analyzing data, interpreting results, creating 'Summary of findings' tables and provided feedback on the report. AMS was responsible for writing the protocol and report, conducting the search, extracting and analyzing data, updating reference lists and creating 'Summary of findings' tables. AEE

was responsible for designing the review protocol, screening potentially eligible studies, conducted the meta-regression analyses, writing the report, and interpreting results. AAH provided feedback on the report.

Conflict of interest:

The authors declare that they have no conflicts of interest concerning this article.

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دراسة مقارنة لمؤشرات الدوبلر الملون لدى مرضى ارتفاع ضغط الدم المصابين وغير المصابين باعتلال الشبكية

الغرض: مقارنة التغيرات فى تصوير دوبلر الملون فى الشريان العينى وفروعه لدى مرضى ارتفاع ضغط الدم المصابين باعتلال الشبكية وبدون اعتلال الشبكية فيما يتعلق بالتغيرات لقاع العين.

المنهجية: شملت هذه الدراسة الرصدية ٨٠ مريضًا يعانون من ارتفاع ضغط الدم، مقسمين إلى ٣ مجموعات وفقًا لتصنيف وونغ وميتشل: لا يوجد اعتلال شبكية (المجموعة ١)، مع اعتلال شبكية خفيف إلى متوسط (المجموعة ٢)، ومع اعتلال شبكية شديد (المجموعة ٣).

خضع جميعهم لتصوير دوبلر ملون مدارى تم فيه تحديد الشريان البصرى والشريان الشبكى المركزى والشرايين الهدبية. تم قياس السرعة الانقباضية الذروة وسرعة النهاية الانبساطية ومؤشر المقاومة.

النتائج: كانت مقاومة الشريان المركزى للشبكية فى المجموعة الثالثة هى الأعلى. وكانت السرعة الانبساطية فى نهاية الشريان العينى أعلى بكثير فى المجموعة الأولى مقارنة بالمجموعة الثالثة. على العكس من ذلك، كانت مقاومة الشريان العينى أقل في المجموعة الأولى مقارنة بالمجموعة الثانية والمجموعة الثالثة. أظهرت مدة ارتفاع ضغط الدم وجود علاقة سلبية معنوية مع السرعة الانبساطية لنهاية الشريان الشبكى المركزى. هناك علاقة إيجابية معنوية مع مقاومة الشريان الشبكى المركزى وكذلك مع مقاومة الشريان الهدبى. فيما يتعلق بالتحكم فى ارتفاع ضغط الدم، كانت السرعة الانقباضية القصوى للشريان الشبكى المركزى والسرعة الانبساطية النهائية أعلى بكثير فى ارتفاع ضغط الدم فى المرحلة الأولى، فى حين كانت مقاومة الشريان الشبكى المركزى أعلى بشكل ملحوظ فى المرضى الانقباضيين المعزولين. ارتفاع ضغط الدم. من ناحية أخرى، كانت السرعة الانقباضية القصوى للشريان العيني أقل بشكل ملحوظ بين المرضى الذين يعانون من ارتفاع ضغط الدم الانقباضى المعزول مقارنة بمرضى ارتفاع ضغط الدم الخاضع للسيطرة والمرحلة الأولى.

الاستنتاج: مقاومة الشرايين بشكل رئيسى الشريان العينى والشريان الشبكي المركزى، قد تكون بمثابة تنبؤات جيدة لتغيرات الأوعية الدموية الدقيقة فى شبكية العين خاصة فى المرضى الذين يعانون من ارتفاع ضغط الدم الذى لا يمكن التحكم فيه بشكل جيد لمدة طويلة.