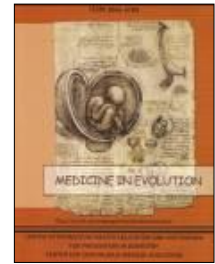


THE RELATIONSHIP OF VARIOUS RETINAL LESIONS AND HYPERTENSION IN A TIMIS COUNTY POPULATION



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ABSTRACT

Purpose. Our purpose was to describe the relationship of various retinal lesions to hypertension in a population of individuals without diabetes mellitus or other known retinal vascular diseases from Timis County, Romania.

Methods. Our study included 2142 patients (1378 men and 764 women), aged 40-65 years who were examined for retinal microvascular changes by retinal photographs in Ophthalmology Clinic Timisoara between March 2008 and May 2011.

All participants underwent anamnesis, a brief physical examination, lab tests (including fasting glucose level, HbA1c, total cholesterol level, LDLc, HDLc, hemoglobin, creatinine clearance), ECG, blood pressure evaluation and ophthalmic examinations.

Results. We included in our study 2142 patients (1378 men-64, 33%, 764 women), mean age 54 ± 10 years. The mean follow-up period was 26±12 months.

We found hypertension in 600 patients (382 men-63.66%, 218 women). Out of all the study participants, we found changes at eye examination (retinal lesion) in 534 patients (25%): focal and general arteriolar narrowing in 262 patients (12. 23%); arteriovenous nicking in 168 patients (7.84%); microaneurysms, hemorrhages and exudates (retinopathy) in 104 patients (4.85%). We found hypertensive retinopathy in 210 patients (35%) from the hypertension group with statistic significance as compared to nonhypertensive group (35% vs. 21%, p<0.001); focal and general arteriolar narrowing in 108 patients (18% vs 10%, p< 0.001); arteriovenous nicking in 60 patients (10% vs. 7%, p<0.001); microaneurysms, hemorrhages and exudates (retinopathy) in 42 pts (7% vs. 4%, p<0.001). No patient had disc swelling or optic nerve oedema.

Conclusion. Our results showed that retinal lesion represented by focal and global arteriolar narrowing, by arteriovenous nicking and retinopathy are common in people with hypertension, especially in those with poor control of raised blood pressure despite antihypertensive treatment. We believe that further studies are necessary to evaluate the importance of detecting retinal lesion for assessing the risk of future cardiovascular disease, stroke and kidney damage in this population.

Key words: hypertension, retinal lesion.

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INTRODUCTION

The signs of hypertensive retinopathy can be broadly classified into arteriolar changes (generalized arteriolar narrowing, focal arteriolar narrowing, arteriovenous nicking and arteriolar wall opacification) and more advanced retinopathy lesions (microaneurysms, blot and flame-shaped hemorrhages, cotton-wool spots, hard exudates and optic disk swelling). With the exception of disk swelling, these signs can be detected fairly frequently in adult populations, even in person's

without a known history of hypertension¹⁻⁵. The prevalence of retinopathy in nondiabetic populations has been far greater than the 0.8% originally reported by the Framingham Eye Study⁶, ranging instead from 7.8% to 9.8% in more recent reports^{1,3,7-8}.

Our purpose was to describe the relationship of various retinal lesions and hypertension in a population of individuals without diabetes mellitus or other known retinal vascular diseases, from Timis County, Romania.

MATERIAL AND METHOD

Our study included 2142 patients (1378 men and 764 women), aged 40-65 years who were examined for retinal microvascular changes by retinal photographs in Ophthalmology Clinic Timisoara between March 2008 and May 2011.

All participants underwent anamnesis, a brief physical examination, lab tests (including fasting glucose level, HbA1c, total cholesterol level, LDLc, HDLc, hemoglobin, creatinine clearance), ECG, blood pressure evaluation and ophthalmic examinations.

We excluded from our study patients with history of stroke or transient ischemic attack; significant peripheral vascular disease (previous surgery or symptoms of intermittent claudication); aortic aneurysm; diabetes mellitus (fasting glucose > 126 mg/dl or receiving insulin or oral hypoglycemic treatment); thyroid disease; nephrotic syndrome or patient with prior coronary arteries diseases (history of angina, previous myocardial infarction). Out of the patients included in our study, 600 (382 men and 218 women) were hypertensive (on the basis of systolic and diastolic blood pressure measured at three

consecutive visits-more than 140 systolic or/and 90 diastolic mmHg, measure in a rest condition with a mercury sphygmomanometer, hypertension diagnostic was confirmed by a cardiologist). The characteristics of study population are shown in Table I.

Procedures. At the baseline examinations, blood pressure (BP) was measured three different times, after patients had been seated for at least 5 minutes, using a mercury sphygmomanometer with an appropriate cuff size. Systolic and diastolic blood pressures (SBP and DBP) were recorded from the first and fifth Korotkoff sounds. Hypertensive subjects were divided into 3 groups: controlled (using medication, normal BP at examination), uncontrolled (using medication, elevated BP at examination), and untreated (elevated BP at examination, but not using medication). The complete history of cardiovascular disease was taken and an ECG was performed and interpreted by a cardiologist; complete blood analysis was done before inclusion in our study.

The photographs were read in a masked manner by 2 trained graders,

and the presence of any retinal changes was recorded. All participants underwent a detailed ocular examination, after pupillary dilation, 30° stereoscopic retinal photographs of the macula, optic disc, and other retinal fields of both eyes were taken, using a fundus camera (model FF3; Carl Zeiss Meditec, Oberkochen, Germany). We used Keith, Wagener, and Barker classification to describe all retinal changes (Table II).

We have documented the following individual lesions as present versus absent: generalized and focal arteriolar narrowing, arteriovenous nick-

ing, retinal hemorrhage and exudates, microaneurysms and disc swelling. When both eyes of a participant were discrepant in the presence of a lesion, the grade assigned to him/her was that of the more severely involved eye.

Statistical analysis. We used the MedCalc Software for calculating the relative risk, confidence interval, prevalence proportion. The results for continuous variables were given as mean \pm SD and for categorical variables as percentage. The limit of P value of statistical significance was considered $p < 0.05$.

Table 1 Baseline characteristics

	Mean \pm SD
Age	55 \pm 8 years
Systolic blood pressure	128 \pm 9 mm Hg
Diastolic blood pressure	82 \pm 9 mmHg
Men, %	1378, 64%
Total cholesterol	185 \pm 68 mg%
LDLc	144 \pm 64 mg%
Smokers, %	1071, 50%
Fasting glucose	82 \pm 12 mg%
Serum creatinine level	0.84 \pm 0.12 mg%

Table 2 Keith, Wagener, and Baker classification of hypertensive retinopathy

Grade I	slight or modest narrowing of the retinal arterioles, with arteriovenous ratio \geq 1:2
Grade II	modest to severe narrowing of retinal arterioles (focal or generalized), with arteriovenous ratio $<$ 1:2 or arteriovenous nicking
Grade III	bilateral soft exudates or flame-shaped hemorrhages
Grade IV	bilateral optic nerve oedema

RESULTS

We included in our study 2142 patients (1378 men-64.33%, 764 women), mean age 54 \pm 10 years. The mean follow-up period was 26 \pm 12 months.

We found hypertension in 600 patients (382 men-63.66%, 218 women).

After initial evaluation of blood pressure 360 patients (60%) had first stage hypertension, 180 patients (30%) second stage hypertension and 60 patients (10%) third stage hypertension. No patient had malignant hypertension in initial evaluation.

From total population included in our study we found modification on eye examination (retinal lesion) in 534 patients (25%): focal and general arteriolar narrowing in 262 patients (12.23%); arteriovenous nicking in 168 patients (7.84%); microaneurysms, hemorrhages and exudates (retinopathy) in 104 patients (4.85%).

We found hypertensive retinopathy in 210 patients (35%) of the hypertension group with statistic significance as compared to nonhypertensive group (35% vs. 21%, $p < 0.001$): focal and general arteriolar narrowing in 108 patients (18% vs. 10%, $p < 0.001$); arteriovenous nicking in 60 patients (10% vs. 7%, $p < 0.001$); microaneurysms, he-

morrhages and exudates (retinopathy) in 42 patients (7% vs. 4%, $p < 0.001$). No patient had disc swelling or optic nerve oedema. The characteristic lesion according to the type of hypertension is shown in Table III.

Those patients whose blood pressure remained elevated despite treatment had higher incidence of any retinal lesion compared with patients' controlled elevated blood pressure.

The positive predictive value for hypertension of the retinal lesions was as follows: 41.2% (108/262 subjects) for focal and general arteriolar narrowing; 35.7% (60/168 subjects) for arteriovenous nicking; 40.4% (42/104 subjects) for retinopathy.

Table 3- Proportion of the cases according the etiopathogeny

Lesion	Arteriolar narrowing	AV nicking	Retinopathy
Hypertension			
Treated and controlled	72 (12%)	10 (1.6%)	3 (0.5%)
Treated and uncontrolled	26 (4.3%)	33 (5.5%)	12 (2%)
Untreated	10 (1.6%)	17 (2.83%)	27 (4.5%)

DISCUSSIONS

In cardiovascular risk stratification of hypertensive patients an important role may have recognition of hypertensive retinopathy because poorly controlled systemic hypertension causes damage to the retinal microcirculation⁹.

The retinal microvascular changes can be reliably documented by retinal photographs. In general, reproducibility from photographs has been found to be excellent for well defined retinopathy signs¹⁰⁻¹⁴.

Our data show a relation of systemic hypertension with the increased incidence of retinopathy in subjects without diabetes.

In the Beaver Dam Eye Study¹ among those examined, 2,151 (69.1%)

were normotensive and 963 (30.9%) were hypertensive at baseline. Over the five-year period, retinopathy developed in 175 (6.0%), arteriolar narrowing in 282 (9.9%) and arteriovenous nicking in 201 (6.5%) nondiabetic subjects.

In the Framingham Eye Study, ophthalmoscopes screening examinations revealed that 19 (0.8%) of subjects without history of diabetes (n=2375) had signs of retinopathy, 14 of whom had history of hypertension, three had branch vein occlusion, one had diabetes mellitus discovered at the follow-up examination, and one had no other cause of the retinopathy determined⁶.

In Evans County, Georgia, retinopathy was present in 2.3% of white males and 4.9% of white females whose

diastolic blood pressure was greater than 100 mm Hg. (15) In a population-based study of 855 men 50 years of age in Gothenburg, Sweden, mean systolic and diastolic blood pressures were significantly ($P<.05$) higher in those subjects with arteriolar narrowing and retinopathy than in those without these signs ¹⁶. In our study the presence of hypertensive retinopathy was detected using stereoscopic retinal photographs of the macula, optic disc, and other retinal fields of both eyes and interpreted by two experienced non-ophthalmologists. The incidence of retinopathy was higher in women, data similar with other study ¹⁷.

Low sensitivity of retinal abnormalities associated with hypertension indicates that hypertensive retinopathy is not common in hypertensive people. Less than half the retinal changes associated with hypertension cannot be explained by high blood pressure (low positive predictive value). In both the Beaver Dam eye study and the Blue

Mountains eye study little difference was found in the presence of hemorrhages and exudates between normotensive and hypertensive people aged over 65. Various other conditions have been associated with hypertensive retinopathy, such as ethnicity, smoking, intima-media thickness, carotid plaque score, carotid artery stiffness, serum cholesterol concentration, diabetes, and body mass index. The high specificity indicates that hypertensive retinopathy is rare in patients with normal blood pressure. Half the people without hypertensive retinopathy, however, still have hypertension (low negative predictive value).

A number of important limitations of this study should be mentioned. The people in our study were white Caucasians aged between 40-65 years. Thus, caution should be taken when extending these findings to other segments of the population – older and younger age groups, other ethnic groups, etc.

CONCLUSIONS

Our results showed that retinal lesion represented by focal and global arteriolar narrowing, by arteriovenous nicking and retinopathy are common in people with hypertension, especially in those with poor controlled raised blood pressure despite antihypertensive treat-

ment. We believe that further studies are necessary to evaluate the importance of detecting retinal lesion for assessing the risk of future cardiovascular disease, stroke and kidney damage in this population.

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