Relationship of Age-Related Macular Degeneration and Risk Factors of Cardiovascular Diseases

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Introduction. Age - related macular degeneration (ARMD) is one of the most common causes of blindness in the elderly people. Atherosclerotic damage and its' related cardiovascular diseases (CVD) are well-known significant factors, predisposing the development of the age-related macular degeneration (ARMD) through the disturbances on blood flow in the choroidal circulation [1]. Alternatively, it has been hypothesized that atherosclerotic processes, including inflammation and lipid deposition, directly affects Bruch's membrane and retinal pigment epithelium promoting development of ARMD [2]. The data about the relation of risk factors and conditions such as hypertension, angina or atherosclerosis for developing the age-related macular degeneration are controversial [13]. It is still unknown whether the prevalence of abnormal carotid artery thickening, severe carotid artery atherosclerosis and stenosis, is greater in patients with ARMD as compared to patients without ARMD.

The aim of this work is to evaluate how the presence of CVD, CVD risk factors, severity of carotid atherosclerosis and CVD treatment are related to ARMD development.

The objectives:

1. To assess the influence of separate CVD risk factors and manifestation of CVD (stable angina pectoris, myocardial infarction or stroke) on ARMD development.
2. To evaluate how atherosclerotic changes in carotid arteries (CA) and CA stenosis are related to ARMD.
3. To find out the influence of medications (beta-blockers, ACE inhibitors / angiotensin II receptor blockers (ARB), calcium channel blockers, statins, antiplatelet drugs) for CVD treatment on ARMD development.

Methods. This was a cross-sectional study. 210 patients (130 women and 80 men) older than 50 years with suspected ARMD admitted to the Department

of Eye disease and the Department of Cardiology during the period from 2014.09.22 till 2016.09.21 were enrolled in the study.

The study population was divided into two groups – control non-pathologic group (patients without ARMD) and pathologic group (patients with ARMD). The patients with any of the following criteria were excluded from the study: glaucoma, uveitis, high refractive error, diabetes mellitus, stroke, acute myocardial infarction, severe heart failure, renal insufficiency (GFR < 30 ml/min), respiratory insufficiency or other severe life-threatening conditions, oncological and mental disorders.

An informed consent was obtained from all of them as approved by the Ethics Committee Bioethics edition number P1-NO-2-13.

All the patients were asked to fill in questionnaires about risk factors (such as ARMD anamnesis in relatives, arterial hypertension (AH), smoking, alcohol consumption, nutrition habits), constitution parameters (the height and weight), medications, which they were using. The presence of angina pectoris, MI or stroke was defined according to physician's diagnosis or patient's reported anamnesis.

High resolution vascular ultrasonography was performed to all the patients. Intima – media thickness (IMT) and presence of plaques in carotid arteries were assessed using 2D-mode vascular ultrasound (7 MHz ultrasound transducer). Common carotid artery (CCA) 1 cm before and under the bifurcation, the carotid artery bifurcation (CAB) and internal carotid artery (ICA) on both sides were evaluated, according to Mannheim's criteria [14], atherosclerotic plaque was defined as the structure which goes into the lumen of the artery at least 0.5 mm or ≥50% of the total value of the IMT. CA IMT was defined as increased when it exceeded the 0.9 mm. Probability of CA stenosis was estimated using peak-systolic and end-diastolic velocities obtained by pulse-wave Doppler.

All the patients underwent ophthalmologic assessment. The presence of ARMD was determined by systematic grading of stereoscopic color fundus photographs.

Statistical analysis was performed using SPSS 21.0 and Microsoft Excel 2016 software. Different statistical methods such as student T tests, ANOVA, $\chi 2$ test, multifactorial logistical regression analysis were used. The value of $p<0.05$ was considered as significant.

Results. The study population was divided into two groups according to the presence of ARMD: non-pathologic (116 patients) and pathologic (94 patients) groups. In our study women were more likely to have ARMD (there were 58.5% (55) women in pathologic group), however women were significantly older (mean age - 69.44 y. of women vs. 65.65 y. of male; $p = 0.015$), so we need more studies for determining differences between genders in developing AMD.

ARMD was established in 44.76% (94 patients) of our study population. ARMD was diagnosed significantly more frequent in patients with angina

pectoris, previous MI or stroke than in patients without CVD (40.9%; n=38 vs. 21.2%; n=24, respectively, p= 0.02).

72 (76.6%) patients with ARMD suffered from AH, while 56 patients (49.1%) had AH in the control group (p< 0.001).

There were no statistically significant relation between ARMD presence and overweight, alcohol consumption, family history of CVD or smoking.

The intima-media thickness of CCA was significantly higher in patients with ARMD (Table 1). The multiple logistical regression analysis revealed that IMT of CCA more than 0.9 mm increases likelihood of ARMD 8.22 times (95% CI 1.63-41.4) in analysed population and it is significantly higher in women than in men (16.7 (95% CI 1.86-15.6) vs. 2.01 (95% CI 0.17-24.4), respectively).

There were no statistically significant differences of intima-media thickness in CB and IC, end-diastolic and peak-systolic velocities and atherosclerotic plaque presence between the patients who had ARMD and those who did not. The consumption of cardiovascular medications (beta-blockers, ACE inhibitors / angiotensin II receptor blockers (ARB), calcium channel blockers, statins, antiplatelet drugs) was not significantly different between pathologic and control groups.

Table 1. Intima – media thickness of common carotid artery, the carotid artery bifurcation and internal carotid artery

	Control group	**AMD group**	**P value**
R CCA anterior wall, mm	0.718 ± 0.180	0.770 ± 0.194	0.258
R CCA posterior wall, mm	0.657 ± 0.134	0.734 ± 0.198	< 0.001*
R CB anterior wall, mm	0.751 ± 0.200	0.711 ± 0.148	0.552
R CB posterior wall, mm	0.683 ± 0.169	0.692 ± 0.151	0.010*
R ICA anterior wall, mm	0.655 ± 0.176	0.638 ± 0.167	0.421
R ICA posterior wall, mm	0.577 ± 0.137	0.583 ± 0.138	0.016*
L CCA anterior wall, mm	0.773 ± 0.175	0.718 ± 0.167	0.592
L CCA posterior wall, mm	0.749 ± 0,195	0.686 ± 0.157	0.007*
L CB anterior wall, mm	0.710 ± 0.156	0.710 ± 0.190	0.321
L CB posterior wall, mm	0.667 ± 1.640	0.695 ± 0.183	0.017*
L ICA anterior wall, mm	0.650 ± 0.146	0.647 ± 0.148	0.681
L ICA posterior wall, mm	0.587 ± 0.129	0.568 ± 0.121	0.348
CCA >0.9 mm	46.6 %	54.3 %	0.267

*Significant at P <0.05. R - right, L- left, CCA- common carotid artery; CB- carotid bifurcation; ICA- internal carotid artery, ARMD - age – related macula degeneration.

Conclusions

1. We did not find any significant relation between ARMD and investigated separate CVD risk factors. Arterial hypertension was significantly more common in patients with ARMD than in control group.

2. CCA intima-media layer thickness (IMT) was significantly higher in patients with ARMD. If CCA intima-media thickness was > 0.9 mm, the risk of AMD was increasing 8.22 times.

3. Different classes of cardiovascular system affecting medications have not significant influence on ARMD development in our study population.

We show a relation of cardiovascular diseases as stable angina, previous infarction or stroke but not cardiovascular risk factors with the incidence of ARMD. There is a need for further research of underlying biological processes explaining the relationship of carotid IMT and carotid plaques and the incidence of ARMD.

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Aim: to evaluate how the presence of CVD, CVD risk factors, severity of carotid atherosclerosis and CVD treatment are related to ARMD development.

Methods: all patients filled in questionaires about CVD risk factors, presence of angina pectoris, MI. Vascular ultrasonography was performed to all patients to assess IMT, presence of plaques, peak systolic and end-diastolic velocities in carotid arteries. All patients underwent ophthalmologic assessment to evaluate the presence of ARMD.

Design: this was a cross-sectional prospective study.

Conclusion: CCA IMT was significantly higher in patients with ARMD. We did not find significant relation between ARMD and investigated separate CVD risk factors.