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Relationship between Carotid Artery Intima-Media Thickness and Choroidal, and Ganglion Cell- Inner Plexiform Layer Thickness

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Abstract

Background and objective: To assess the relationship between common carotid artery intima-media thickness (CIMT) and the choroidal, and ganglion cell - inner plexiform layer (GCIPL) thickness.

Materials and methods: This cross-sectional study comprised 50 patients with cardiovascular disorder. CIMT, choroidal thickness thickness at subfoveal, perifoveal and peripapillary locations and GCIPL thickness were measured.

Results: Patients with CIMT value ≥0.8mm was accepted as group 1 (n=23) and <0.8mm was accepted as group 2 (n=27). CIMT was inversely associated with GCIPL thickness and choroidal thickness at all points. However, this relation was not statistically significant for both GCIPL thickness and choroidal thickness except some, random points ($p<0.05$).

Conclusion: Although the relationship seems to be weak, these results may support that systemic vascular disorders such as atherosclerosis and cardiovascular disease can lead to structural changes in choroid and retinal ganglion cell layer. Therefore, such diseases should be considered for choroidal structure evaluation.

Keywords: Choroidal thickness; Ganglion cell - inner plexiform layer thickness; Carotid artery intima-media thickness; Atherosclerosis

Introduction

The blood supply to the retina and choroid circulation is mostly provided by the ophthalmic artery which is a branch of the internal carotid artery (ICA). Atherosclerosis is the major factor in producing carotid artery stenosis or occlusion, and carotid artery intima-media thickness (CIMT) is a surrogate marker for the presence and progression of atherosclerosis [1,2]. Systemic arterial hypertension is one of the major risk factor for atherosclerosis [3,4]. Also several other factors including age, cholesterol, smoking and diabetes mellitus have been proved to affect the risk of atherosclerosis, and high CIMT values are associated with these risk factors [3,5-7]. In addition to this, hypertension, smoking and diabetes mellitus have been found to be associated with decreasing of choroidal thickness [8-10]. Based on these relationship, we hypothesized that CIMT which is an accepted marker of atherosclerosis may have a relation with choroid and retina. The purpose of this study was, therefore, to assess the relationship between common CIMT and the choroidal, and ganglion cell-inner plexiform layer (GCIPL) thickness.

Materials and Methods

Fifty subjects referred to radiology department were included in the study. Out of 50 patients, 12 would undergo coronary angiography, 8 would undergo bypass surgery, 6 would undergo cardiac valve surgery and others had myocardial infarction or angina pectoris in their anamnesis. All study participants had best corrected visual acuities of 20/25 or more, a refractive error in the range +3.0 to –3.0 diopters and intraocular pressure (IOP) lower than 21mmHg. Those with systemic or ocular disease (glaucoma, uveitis, high myopia, age-related macular degeneration, diabetes mellitus, etc.) and/or a history of ophthalmic surgery that may have affected the choroidal vascular network were excluded. Measurement of CIMT were made by

one sonographer, blinded to patient's clinical characteristics and retinal measurements, according to standard recommendations [11,12]. The IMT was measured on the far wall of the middle segment of the common carotid artery as the distance between the lumen-intima interface and the media-adventitia interface at 10mm proximal to the bifurcation. All participants were examined with Cirrus HD-OCT (Carl Zeiss Meditec, Inc, Dublin, CA). A horizontal and a vertical scan were taken utilizing the high-definition scan protocol which was composed of a single, 6mm raster scan consisting of 4096 A-scans. Both scans were taken through the optic nerve and macula. Choroidal thickness was measured perpendicularly from the outer edge of the hyper reflective RPE to the inner sclera at subfoveal area and 500µm intervals temporal, nasal, superior and inferior from the fovea, up to 1500µm. Also, peripapillary choroidal thicknesses was measured at the superior, inferior, nasal and temporal quadrants at 500µm intervals, from beginning of the RPE up to 1500µm, along the line of the RPE. One of two eyes which had better signal strength was included in the study, and eyes with signal strength lower than 6 were excluded from the study. Scan interpretations and measurements were performed by a blinded investigator. Average GCIPL thicknesses were obtained from retinal OCT scans. All statistical data were analyzed using SPSS version 18.0 (SPSS Inc, Chicago, IL, USA). Values were expressed as mean±standard deviation. The normality of the values was analyzed by using Shapiro-Wilk test. Independent samples t test or Mann-Whitney U test was used according to the Shapiro-Wilk test result. Differences were considered significant at $p<0.05$. Correlations between the variables were investigated by using Spearman correlation coefficients. The reproducibility of choroidal thickness measurements was calculated via intra class correlation coefficient.

Results

Patients with CIMT value of at least 0.8mm were accepted as group 1(n=23) and less than 0.8mm were accepted as group 2 (n=27). The mean CIMT value was 0.98±0.3mm in group 1 and 0.57±0.12mm in group 2 ($p<0.001$). The mean GCIPL was 80.17±9.02 in group 1 and 83.81±6.88 in group 2 ($p=0.113$). The rate of hypertensive patients was 18/23 in group 1 and 17/27 in group 2 ($p=0.239$). Differences in age, sex, AL, spherical equivalents between the groups were not significant ($p>0.05$). Table 1 shows demographic and clinical features of the groups. Table 2 shows choroidal thickness measurement differences between group 1 and 2, and also shows the intra class correlation coefficient analysis of the results of the evaluator author at two different time point. Intra class correlation coefficient ranged from 824 to 996, and these results supported the reliability of the measurements. Subjects in group 1 had thinner choroidal thickness at all parafoveal and peripapillary points. However, the differences between the groups were not statistically significant ($p>0.05$). Table 3 shows correlation analysis results between choroidal thickness and CIMT in all individuals (group 1 plus group 2). There was negative correlation at all points however the differences were not statistically significant at locations ($p>0.05$). Also there was an insignificant negative correlation between the CIMT and mean GCIPL thickness ($r= -0.233$, $p=0.103$).

Table 1: Demographic and clinical features of the groups. CIMT: Carotid artery Intima-Media Thickness, GCIPL: Ganglion Cell-Inner Plexiform Layer.

Parameters	Group 1 (N=23)	Group 2 (N=27)	P Value
Age (years)	61±8	58±4	0.07
Female/male n	10/13	14/13	0.555
Axial length (mm)	23.2± 0.7	23.06±0.6	0.335
Spherical equivalent (diopter)	0.3±1.2	-0.4±1.6	0.119
Hypertension n(%)	18(78%)	17(62%)	0.239
CIMT (mm)	0.98±0.3	0.57±0.12	<.001*
GCIPL	80.17±9.02	83.81±6.88	0.113

*Statistically significant differences; Values are expressed as mean SD.

Table 2: Choroidal thickness measurement differences between the groups, and intraclass correlation coefficient at the same points.

Parameters	Group 1	Group 2	P Value Mann-Whitney U Test	Intraclass Correlation Coefficient	P Value
Subfoveal choroidal thickness	241±69	248±77	0.768	996	<.001
Parafoveal choroidal thickness locations					
Temporal 500µm	222±66	243±73	0.294	981	<.001
Temporal 1000µm	214±69	238±66	0.209	971	<.001
Temporal 1500µm	210±64	231±59	0.23	956	<.001
Nasal 500µm	228±61	238±81	0.622	950	<.001
Nasal 1000µm	216±63	238±77	0.276	953	<.001
Nasal 1500µm	206±68	223±70	0.393	951	<.001
Superior 500µm	226±68	252±65	0.178	960	<.001
Superior 1000µm	223±60	246±58	0.184	917	<.001

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Superior 1500µm	215±63	244±58	0.106	871	<.001
Inferior 500µm	223±64	246±77	0.272	950	<.001
Inferir 1000µm	218±57	242±83	0.051	943	<.001
Inferior 1500µm	221±56	254±87	0.126	925	<.001
Peripapillary Choroidal thickness locations					
Temporal 500µm	105±30	125±38	0.057	835	<.001
Temporal 1000µm	150±52	173±56	0.154	918	<.001
Temporal 1500µm	172±59	202±71	0.108	926	<.001
Nasal 500µm	123±58	141±49	0.477	939	<.001
Nasal 1000µm	159±71	168±65	0.142	918	<.001
Nasal 1500µm	171±68	185±74	0.485	915	<.001
Superior 500µm	116±33	134±39	0.152	824	<.001
Superior 1000µm	150±48	172±58	0.156	901	<.001
Superior 1500µm	180±62	185±69	0.798	936	<.001
Inferior 500µm	96±24	116±42	0.052	929	<.001
Inferior 1000µm	113±33	133±48	0.116	935	<.001

Table 3: Correlation analysis results between choroidal thickness and carotid intima-media thickness.

Parameters	R	P Value
Subfoveal choroidal thickness	-0.08	0.579
Parafoveal Choroidal thickness locations		
Temporal 500µm	-0.241	0.091
Temporal 1000µm	-0.252	0.078
Temporal 1500µm	-0.303	.032*
Nasal 500µm	-0.167	0.247
Nasal 1000µm	-0.322	0.022
Nasal 1500µm	-0.223	0.12
Superior 500µm	-0.248	0.116
Superior 1000µm	-0.342	0.015
Superior 1500µm	-0.29	0.086
Inferior 500µm	-0.349	.013*
Inferior 1000µm	-0.211	0.063
Inferior 1500µm	-0.216	0.076
Peripapillary choroidal thickness locations		
Temporal 500µm	-0.313	0.054
Temporal 1000µm	-0.214	0.135
Temporal 1500µm	-0.324	0.122
Nasal 500µm	-0.334	.018*
Nasal 1000µm	-0.228	0.111
Nasal 1500µm	-0.2	0.163
Superior 500µm	-0.318	0.052
Superior 1000µm	-0.342	.015*
Superior 1500µm	-0.227	0.113
Inferior 500µm	-0.263	0.066
Inferior 1000µm	-0.326	.021*
Inferior 1500µm	-0.251	0.077

*Statistically significant differences; Values are expressed as mean±SD.

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Discussion

Carotid artery stenosis and/or obstruction are most often due to arteriosclerotic vascular disease. CIMT measurement has been used to assess atherosclerosis [1,2]. We demonstrated that patients with high CIMT values had slightly thinner choroidal thickness. Although the relationship seems to be weak CIMT was inversely associated with choroidal thickness in all peripapillary and parafoveal areas. There have been several reports investigating the relationship between ocular structures and carotid vessels [13-17]. Agladioglu et al. [13], found that choroidal thickness was negatively correlated with ICA diameter and ICA resistance index in healthy volunteers. Torres et al. [14], demonstrated that CIMT was inversely associated with retinal arteriolar diameters and directly associated with retinal venular diameters in patients with hypertension. Kang et al. [15], showed a sub foveal thinning of the choroid in three patients with high-grade internal carotid artery stenosis by enhanced depth imaging (EDI) OCT. The relation between ICA and retinal or choroidal circulation may implicate that vascular damage in large arteries might associate with disturbance of microcirculation. High CIMT values may possibly reflect reduced blood flow in choroidal blood vessels that may have an effect on retinal/choroidal function resulting in choroidal thinning and decreasing of ganglion cell thickness. In another study including patients with different degrees of internal carotid artery stenosis, OCT showed thinning of retinal ganglion cell and nerve fiber layers [16]. In the present study, OCT scans revealed slight thinning of the GCIPL thickness. However, GCIPL in different quadrants and retinal nerve fiber layer (RNFL) were not evaluated in this study. We have a few limitations, one of them is small sample size. Also, as RNLF thickness was not measured we could not completely evaluate the relationship between CIMT and retina. Another major drawback was the hypertension, although there was no significant difference in hypertension rates between the groups, choroidal thickness might have been affected by the hypertension [8]. Thus, the relationship between CIMT and choroidal thickness may not has been demonstrated clearly. In conclusion, these results may support that systemic vascular disorders such as atherosclerosis and cardiovascular disease can lead to structural changes in choroid and retinal ganglion cell layer. Therefore, such diseases should be considered for choroidal structure evaluation. Also, despite all limitations the present study can guide for the further studies with a larger cohort size to evaluate the relationship between CIMT and choroidal/retinal changes, and to use adapted OCT parameters for the evaluation of atherosclerosis and atherosclerotic diseases.

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