Exp Biomed Res 2023; 6(4): 298-307 **DOI: 10.30714/j-ebr.2023.195**

Experimental Biomedical Research *Original article*

Choroidal structural changes after phacoemulsification in eyes with age-related macular degeneration

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ABSTRACT

Aim: To evaluate the changes in choroidal vascular structures in patients with dry age-related macular degeneration (AMD) and healthy controls (No-AMD) after phacoemulsification.

Methods: This prospective study was conducted in 34 eyes of 19 patients in the AMD group and 32 eyes of 20 patients in the no-AMD group who had uneventful phacoemulsification. Best-corrected visual acuity, slit-lamp biomicroscopy, and intraocular pressure were recorded. Choroidal thickness (CT) measurements of the subjects were obtained using enhanced depth imaging optical coherence tomography (Edi-OCT) (RS-3000 Advance, Nidek, Japan), and choroidal vascular index (CVI) was calculated by using the binarization method at baseline and postoperatively at months 1 (M1) and 3 (M3) and the results were compared.

Results: There was no significant difference between the patients in terms of age and gender (p=0.069, p=0.855 respectively). The mean CVI at baseline was 0.644 ± 0.019% in the AMD group and 0.657 ± 0.021% in the no-AMD group (*p=0.025)*. In the AMD group, the CVI increased significantly in M3 compared to preoperative values (p=0.001). There was no significant difference between the two groups in terms of CT in baseline, M1, and M3 (p>0.05). There was a significant increase in CT in M1 compared to preoperative values in both groups (p=0.026 and p=0.050, respectively).

Conclusion: Although the preoperative CVI was lower in the AMD group than in the no-AMD group, there was a greater increase in CVI after phacoemulsification in the AMD group. While CT values return to normal after phacoemulsification sooner, CVI remains elevated for a longer period.

Key words: Age-related macular degeneration, choroidal thickness, choroidal vascular index, phacoemulsification.

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Received: 2023-08-08 / Revisions: 2023-08-22

Accepted: 2023-08-24 / Published online: 2023-09-20

Introduction

Two of the most widespread eye diseases of aging and the most important causes of vision loss are cataract and age-related macular degeneration (AMD) [1-3].

AMD is an irreversible degeneration that results in a gradual decline in central vision and total loss of vision [3]. The vast majority of AMD is the dry type, which is identified by the occurrence of drusen and damage to the cells of the retinal pigment epithelium (RPE) [4] and high-dose vitamin supplements are commonly used to decrease the occurrence of exudative type [5]. While it may be asymptomatic in the early stages when only drusen is present, irreversible loss of central vision occurs in advanced stages characterized by geographic atrophy [6].

Phacoemulsification which is often used for cataract surgery is currently the most commonly performed intraocular surgery. It has greatly improved visual outcomes, especially for elderly patients [7].

The choroid is essential for delivering nutrients and maintaining proper volume and ocular metabolism [8]. Photoreceptor dysfunction can be caused by abnormal choroidal blood volume [7].

Numerous studies and analyses have shown that even simple phacoemulsification can cause choroid disorders, particularly an elevation in choroid thickness (CT) [3,6-14].

Patients with AMD who undergo phacoemulsification for visually significant cataracts can experience a significant improvement in their quality of life [2,15-17]. Although phacoemulsification can effectively treat visual loss caused by cataract, some medical professionals believe that it may also raise the risk of exacerbating underlying AMD, potentially leading to further harm to vision acuity [1,18-20].

Enhanced depth imaging optical coherence tomography (Edi-OCT) provides an easy, noninvasive way to image the choroidal stromal and vascular structures in greater depth and detail [7,21]. Choroidal vascular index (CVI) is a biomarker used to study blood vessels in the choroid, the ratio of the vascular lumen (luminal area- LA) to total choroidal area (TCA). CVI is used to overcome the limitation of CT measurement alone, as it is more stable than CT and less affected by physiological factors [14,22]. Our aim in this study was to investigate the impact of phacoemulsification on the structures of choroidal blood vessels in patients with AMD after cataract surgery using EDI-OCT. To our knowledge, there is no study in the literature showing how the CVI value changes after phacoemulsification in AMD patients. We hypothesized that examining CVI could offer further insights into the underlying mechanisms of AMD, whether cataract surgery should be performed, or the timing of surgery.

Materials and methods

This cross-sectional prospective study was carried out in the Department of Ophthalmology at Fatih Sultan Mehmet Training and Research Hospital. The study was approved by the Fatih Sultan Mehmet Training and Research Hospital Ethics Committee (FSMEAH-KAEK 2022/11) and conducted based on the guidelines of the Declaration of Helsinki. Informed consent was obtained from the participants and archived with the authors.

We carried out a prospective clinical study on 34 eyes with dry type AMD (AMD group) and 32 eyes without AMD (No-AMD group) that underwent phacoemulsification for senile cataract without any complications during the operation.

To be considered for inclusion in the study, participants had to have cataract with or without dry type age-related macular degeneration. The diagnosis of AMD was determined according to the established criteria by the Age-Related Eye Disease Study [5]. The hardness of cataracts was assessed and graded using the Lens Opacities Classification System (LOCS 3) [23].

Those patients who had severe cataract that could lead to low Edi-OCT quality, glaucoma (intraocular pressure (IOP) >21 mmHg), retinal disease, uveitis, refractive error of $\geq \pm 3.00$ D, diabetes mellitus, or other systemic diseases that could affect the choroid were excluded. Also, the study did not include cases of advanced AMD with geographic atrophy affecting the fovea, or any signs of exudative AMD.

All participants underwent ocular examination, which included measurement of

best corrected visual acuity (BCVA, the logarithm of the minimum angle of resolution) and IOP with noncontact pneumatic tonometry (RK-1a Auto Ref/Keratometer, Nidek, Japan) examination of the anterior segment with slit-lamp biomicroscopy, and the posterior segment with pupil dilation. CT and CVI values were evaluated using Edi-OCT (RS-3000 Advance, Nidek, Japan).

OCT scans were performed without pupil dilation at the same time of day (between 9:00 and 11:00 am) to avoid daily variations in CVI and CT by a single operator blinded to the groups preoperatively, 1 month (M1), and 3 months (M3) postoperatively. CT was measured with the manual caliper provided by the computer program and represented as the 1500 μm wide area within the subfoveal space extending vertically from the outer edge of the RPE to the border between the choroid and sclera.

To determine CVI, the choroid's grayscale images were converted to binary using the ImageJ 1.51s software program (National Institutes of Health, Bethesda, MD, USA) with a semiautomated strategy. The Edi-OCT scan images were initially transformed into 8-bit images using the default setting. Niblack's automatic thresholding tool was used to determine the boundary between the luminal area (LA) and the stromal area (SA) by manual drawing. The total of LA and SA is represented by TCA, and the CVI was determined by dividing LA by TCA.

An experienced ophthalmologist (AA) performed all measurements 3 times and the average of the 3 measurements was reported.

The phacoemulsification was performed through a 2.4mm clear cornea incision using a standard technique while the patient was under topical anesthesia by the same experienced surgeon using the Constellation® vision system (Alcon, Fort Worth, TX, USA). An acrylic intraocular lens was successfully implanted in the capsular bag without any intraoperative complications. All of the patients received identical postoperative treatment, which included the use of dexamethasone and moxifloxacin eye drops. Each patient was discharged with the same prescriptions, consisting of dexamethasone eye drops (decreased gradually from 4 times a day to 1 time per day) and moxifloxacin eye drops (4 times a day for 2 weeks) postoperatively.

Statistical analysis

The data's descriptive statistics included the use of mean, standard deviation, median, minimum, maximum, frequency, and ratio values. The Kolmogorov-Smirnov test was used to measure the distribution of variables. For the analysis of quantitative independent data, both the independent sample t-test and Mann-Whitney u-test were utilized. Paired-sample t-test and Wilcoxon test were used in the analysis of quantitative dependent data. The chi-square test was used in the analysis of qualitative independent data. The analysis was conducted using the SPSS 28.0 program. If the *p*-value was less than 0.05, it was deemed significant.

Results

A total of 66 eyes of 39 patients were included in the study. Nineteen patients (34 eyes) were with cataract and dry AMD (AMD group) and 20 patients (32 eyes) were with cataract and without AMD (No-AMD group). AMD group comprised 8 (42.1%) women and 11 (57.9%) men with a mean age of 74.3 ± 6.5 years and the no-AMD group comprised 9 (45.0%) women and 11 (55.0%) men with a mean age of 69.3 ± 7.9 years. There was no significant difference between the patients in terms of age and gender (p=0.069, p=0.855 perspectively). There was no significant difference between the groups in terms of the operated eye sides of the patients (p=0.611). The

characteristic features of the groups are shown in Table 1.

There was no significant difference between the groups in terms of preoperative BCVA (p=0.292). There was a statistically significant increase in BCVA at M1 and M3 compared to the baseline in both groups (p<0.001 for all changes). But BCVA at M1 and M3 was significantly higher in the control group (p=0.006 and p=0.014, respectively) (Table 2).

There was no significant difference between the two groups in terms of preoperative IOP (p=0.097). There was a statistically significant decrease in IOP at M1 and M3 compared to the baseline in both groups (p<0.001 for all changes). IOP at M1 and M3 was significantly lower in the control group (p=0.005 and p=0.008, respectively). BCVA and IOP changes in baseline, M1, and M3 in AMD and No-AMD groups are shown in Table 2.

Table 1. The descriptive datas of the groups.

Parameters		**No-AMD group**	**AMD group**	***p***	
Age (years) (Mean ± SD)		69.3±7.9	74.3±6.5	0.069	m
Gender (n, %)	**Male**	11 (55)	11 (57.9)	0.855	X^2
	Female	9 (45)	8 (42.1)		
Side (n, %)	**Right**	14 (43.8)	17 (50)	0.611	X^2
	Left	18 (56.3)	17 (50)		

[m] Mann-whitney u test / [X^2] Ci-square test. AMD group, age related macular degeneration with cataract; No-AMD group, with cataract; sd, standard deviation.

Table 2. Changes in BCVA and IOP of the groups.

Parameters	**No-AMD group**					**AMD group**				***p***	
	Mean ± SD			**Median**		**Mean ± SD**			**Median**		
BCVA											
Baseline	0.53	±	0.19	0.50		0.49	±	0.19	0.50	0.292	m
M1	0.06	±	0.08	0.00		0.14	±	0.11	0.15	***0.006***	m
M3	0.04	±	0.06	0.00		0.09	±	0.09	0.10	***0.014***	m
Change to baseline											
Baseline-M1	-0.47	±	0.18	-0.40		-0.35	±	0.23	-0.30	***0.015***	m
*p**	***0.000***			W		***0.000***			W		
Baseline-M3	-0.49	±	0.17	-0.45		-0.40	±	0.21	-0.35	***0.025***	m
*p***	***0.000***			W		***0.000***			W		
IOP											
Baseline	13.4	±	3.4	12.5		14.4	±	2.3	14.5	0.097	m
M1	10.9	±	3.0	11.0		12.9	±	2.6	13.0	***0.005***	m
M3	10.6	±	3.1	11.0		12.4	±	2.3	12.0	***0.008***	m
Change to baseline											
Baseline -M1	-2.5	±	2.8	-2.0		-1.5	±	3.0	-1.0	0.192	m
*p**	***0.000***			W		***0.001***			W		
Baseline-M3	-2.8	±	3.6	-2.0		-2.1	±	3.0	-2.0	0.405	m
*p***	***0.000***			W		***0.001***			W		

*AMD group, age related macular degeneration with cataract; No-AMD group, with cataract; BCVA, best corrected visual acuity (LogMAR); IOP, intraocular pressure (mmHg); sd, standard deviation; baseline, before cataract surgery; M1, one month after cataract surgery; M3, three months after cataract surgery; p *, comparison between baseline and M1 results; p **, comparison between baseline and M3 results.*

Table 3. Changes in CVI and CT of the groups.

Parameters	**No-AMD group**				**AMD group**				***p***	
	Mean ± SD			**Median**	**Mean ±SD**			**Median**		
CVI										
Baseline	0.657	±	0.021	0.660	0.644	±	0.019	0.643	***0.025***	m
M1	0.659	±	0.020	0.655	0.648	±	0.019	0.650	0.057	m
M3	0.662	±	0.018	0.659	0.658	±	0.016	0.662	0.847	m
Change to baseline										
Baseline-M1	0.00	±	0.02	0.00	0.00	±	0.02	0.01	0.603	m
*p**	0.525			w	0.081			w		
Baseline-M3	0.01	±	0.02	0.01	0.02	±	0.02	0.02	0.158	m
*p***	0.078			w	***0.001***			w		
CT										
Baseline	182.5	±	43.7	171.5	196.1	±	41.7	186.0	0.139	m
M1	198.3	±	43.8	207.0	207.7	±	43.4	224.0	0.276	m
M3	198.0	±	48.6	212.5	193.2	±	45.2	188.0	0.833	m
Change to baseline										
Baseline-M1	15.8	±	30.8	5.5	11.6	±	28.3	2.0	0.627	m
*p**	***0.026***			w	***0.050***			w		
Baseline-M3	12.4	±	34.2	-1.0	3.0	±	33.0	-1.0	0.447	m
*p***	0.518			w	0.861			w		

*[m] Mann-whitney u test / [w] Wilcoxon test. AMD group, age related macular degeneration with cataract; No-AMD group, with cataract; CVI, choroidal vascular index; CT, choroidal thickness; sd, standard deviation; baseline, before cataract surgery; M1, one month after cataract surgery; M3, three months after cataract surgery; p *, comparison between baseline and M1 results; p**, comparison between baseline and M3 results.*

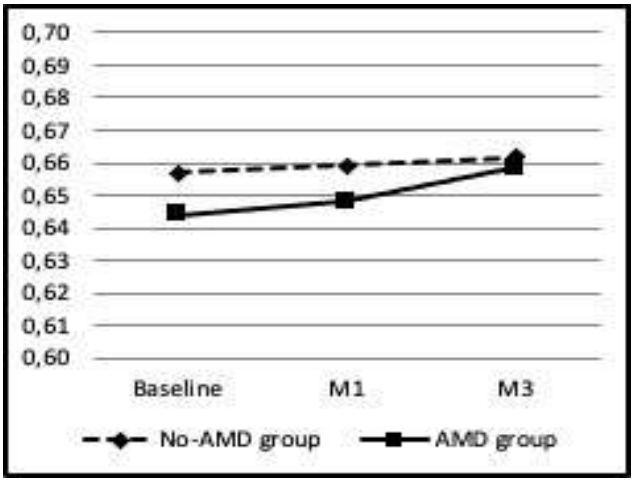

Figure 1. Time course of choroidal vascular index of the groups. (AMD group, age-related macular degeneration with cataract; No-AMD group, with cataract; baseline, before cataract surgery; M1, one month after cataract surgery; M3, three months after cataract surgery).

The AMD group's baseline CVI value was significantly lower (p=0.025).

Although there was an increase in CVI value at M1 and M3 compared to the baseline in both groups, the increase in M1 was statistically significant in the AMD group (p<0.001) (Figure 1.).

There was no significant difference between the two groups in terms of CVI values in M1 and M3 (p>0.05). There was no significant difference between the two groups in terms of CT values at the baseline, M1 and M3 (p>0.05). There was a significant increase in CT values at M1 compared to preoperative values in both groups (p=0.026 and 0.050 respectively). While the CT value at M3 could not regress to the preoperative value in the no-AMD group, it becomes thinner than the

baseline in the AMD group. Table 3 lists changes in CVI and CT of the groups.

Discussion

This study compared CT and CVI values of patients with and without AMD before and after cataract surgery. To the best of our knowledge, this is the first study evaluating CVI values after phacoemulsification in AMD patients.

In our study, the preoperative CVI value was lower in the AMD group. The CVI value continued to increase for 3 months postoperatively in both groups but the increase was greater in the AMD group. CT value increased in both groups in the 1 month postoperatively and began to regress in the 3 months postoperatively. The decrease in CT value was faster and greater in the AMD group.

The most widely performed surgery in ophthalmology is phacoemulsification, which can cause inflammation in multiple eye tissues, including the choroid [3,10]. This could be due to the induction of pro-inflammatory molecules as a result of surgery due to ultrasound power, IOP fluctuation, and activation of reactions caused by excessive light entering the eye [1,2,7,8,19,20]. Moreover, the utilization of an artificial lens may result in increased exposure to light and damage ultraviolet rays [1].

Inflammatory factors have also been linked to the development of AMD [1]. Likewise, it is believed that the progression of AMD is linked to oxidative damage and inflammation occurring in RPE, resulting in the formation of the drusen [24].

There are studies that an increase in CT after phacoemulsification [3,7-14]. A significant increase at M1 and a decrease at M3 in CT values was observed in our study.

The increased inflammation in the choroid with cataract surgery may increase the permeability of the perifoveal capillaries due to damage to the blood-aqueous barrier [12]. Subsequently leading to the change of choroidal vascular structures resulting in alterations in CT and CVI values. Another potential reason is a decrease in IOP following cataract surgery. After phacoemulsification, a decrease in IOP can lead to an increase in ocular perfusion pressure, and as a result, CT and CVI increase [14,25,26]. In our study, IOP values were significantly decreased in both groups after surgery.

Yiu et al. demonstrated that the blood flow in the choroid of the eye was affected in individuals with worsening AMD. However, after adjusting for age and refractive error, the researchers did not observe any significant difference in CT among patients with AMD [24].

Gudauskienė et al. reported that AMD patients had thinner CT before cataract surgery. This could be attributed to the lack of small choroidal vessels, narrowing of the choriocapillaris lumen, and reduction in blood flow in AMD. Similar to our study, they found increased CT in 1 month after cataract surgery in AMD patients and controls. Unlike us, the increase in CT was still observed in the AMD group 3 months after cataract surgery [3]. Jonas et al. found no difference in CT values postoperatively when they compared eyes with and without AMD [27].

The use of CVI could be a promising noninvasive method for examining structural changes in the choroid and monitoring the development of exudative AMD.

Studies are showing lower CVI values in AMD patients [21,28]. The reason for the low preoperative CVI value and rapid decrease after 1 month in CT value in AMD patients in our study may be the decrease in choroidal blood flow. In our study, the increase in CVI was present for longer and was greater after phacoemulsification in the AMD group.

After cataract surgery, the choroid may undergo changes that could potentially exacerbate pre-existing macular degeneration [1,19,20].

There are concerns among researchers that phacoemulsification may increase the risk of developing exudative AMD [18-20]. There are also publications reporting that phacoemulsification does not accelerate AMD progression [29-33].

During cataract surgery, the macula in individuals with AMD may be more susceptible to phototoxic damage due to its pre-existing unhealthy state. During cataract surgery, prolonged surgery and bright light settings can pose a potential risk for phototoxic damage to the macula [8,34]. Also, the small changes in CT after phacoemulsification may affect the onset of AMD [10]. We utilized low-energy ultrasound and completed the phacoemulsification process in a brief amount of time.

Eyesight is increased by cataract surgery in AMD patients [1,2,30,35]. The increase in vision has been reported to depend on initial visual acuity, duration and severity of AMD disease (2). In some studies, it was reported that AMD patients who had cataract surgery had better visual acuity and quality of life in the short term than those who did not, the long-term results are unknown [1,35]. In our study, postoperative visual improvement was achieved in both groups, but recovery was faster in the non-AMD group.

Although baseline CVI is lower in diseases such as AMD and diabetic retinopathy, the increase in CVI after cataract surgery was found more in these patients. They are worse affected than the normal population [26,36].

There are some limitations to the current study. Firstly, the analysis of CVI may be affected by the omission of recording the average ultrasonic emulsification time and the cumulative dissipated energy. Secondly, the group of patients studied was not sufficiently large, and we only evaluated the short-term effects of surgical intervention on CVI. More research with larger samples and longer follow-up times is needed.

In conclusion, based on our analysis, it appears that phacoemulsification can result in the enlargement of choroidal vascular structures within a month post-surgery. CT values began to return to baseline 1 month postoperatively, while CVI values, a more stable marker, remained elevated for longer. CVI increase was higher in AMD patients after cataract. However, in our study, cataract surgery increased visual acuity without a risk of developing exudative AMD.

A comprehensive assessment of the long-term impact of phacoemulsification on CVI change can offer critical insights into the possible correlation between phacoemulsification and choroidal disorders like AMD.

Funding: *The authors received no financial support for the research, authorship, and/or publication of this article.*

Conflict of interest: *The authors declare that they have no conflict of interest.*

Ethical statement: *The study was approved by the Fatih Sultan Mehmet Training and Research Hospital Ethics Committee (FSMEAH-KAEK 2022/11).*

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