



Original research

# Choroidal thickness changes following cataract surgery in patients with type 2 diabetes mellitus

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## Abstract

**Purpose:** To evaluate the choroidal thickness changes after cataract surgery in type 2 diabetic patients.

**Methods:** Three groups of patients were enrolled into this prospective study. Group A included diabetic patients without diabetic retinopathy (DR) or with mild non-proliferative diabetic retinopathy (NPDR) who underwent phacoemulsification, Group B included non-diabetic patients with significant cataract who underwent phacoemulsification, and Group C included diabetic patients without DR or with mild NPDR who followed up without surgical procedure. Choroidal thickness in 5 points (subfoveal and 500  $\mu$  temporal, nasal, superior and inferior to the fovea) and central macular thickness were measured before surgery using enhanced depth spectral domain optical coherence tomography. Patients were re-evaluated 1 week, 1 month, and 3 months after operation and compared with the baseline values.

**Results:** In total, 63 eyes from 63 patients were enrolled to this study, including 21 eyes in Group A, 22 eyes in Group B, and 20 eyes in Group C. After three months of follow-up of the patients, choroidal thickness in all measured points was decreased significantly, and central macular thickness was increased significantly following cataract surgery in diabetic eyes (Group A); meanwhile, both choroidal thickness and central macular thickness were increased significantly in non-diabetic eyes (Group B). In Group C, choroidal thickness and central macular thickness had no significant changes, after three months.

**Conclusion:** Unlike in non-diabetic eyes, choroidal thickness in diabetic patients decreased following cataract surgery.

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**Keywords:** Choroidal thickness; Diabetic retinopathy; Cataract surgery; Phacoemulsification; Optical coherence tomography

## Introduction

Diabetes mellitus (DM) is one of the most frequent metabolic disorders worldwide and its prevalence has been increasing in adults in the last decades secondary to changes in lifestyle.<sup>1–3</sup> Diabetic retinopathy (DR) is a micro vascular complication of DM that may account for 4.8% of all cases of blindness in the world.<sup>4</sup>

The principle pathogenesis of DR is the breakdown of the blood-retinal barrier (BRB), retinal vascular integrity impairment and hemodynamic abnormalities.<sup>5</sup> Clinical and

experimental data suggests that choroidal vascular abnormalities may play an important role in the pathogenesis of DR.<sup>6</sup> In the previous studies, different choroidal changes including choriocapillaris obstruction, vascular degeneration, choroidal neovascularization, and choroidal aneurysms have been reported in patients with DR.<sup>7–9</sup>

Today, neurodegeneration has become suggested as a new pathophysiological model in the early stages of DR.<sup>10</sup> Retinal neurodegeneration is characterized by reactive gliosis, neuronal apoptosis, glutamate excitotoxicity, reduction of neuroprotective factors, and neurovascular coupling impairment.<sup>11–14</sup> However, it is controversial that retinal neurodegeneration is an independent element in the pathogenesis of DR, or it is secondary to retinal vessels damage.<sup>15</sup>

Until recently, indocyanine green angiography (ICG), laser Doppler flowmetry, and ultrasound were used for the evaluation

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of choroid, but these techniques provide no anatomical information.<sup>16</sup> Enhanced depth imaging optical coherence tomography (EDI-OCT) can provide reliable and reproducible measurement of choroidal thickness.

One of the most important causes of visual impairment in patients with DM is the accelerated development of cataract.<sup>17</sup> There are some reports of DR progression after cataract surgery.<sup>18–20</sup> This progression may be due to increased release of pro-inflammatory mediators such as vascular endothelial growth factors (VEGFs), interleukin 1 (IL-1), and hepatocyte growth factor (HGF) into the aqueous humor.<sup>21</sup> These post-operative inflammations may have resulted in vascular abnormalities in the retina and choroidal layers and exacerbated the DR after cataract surgery in patients with DM. Vascular changes in the choroid may lead to choroidal thickness changes.

According to our knowledge, there is only one study on the evaluation of the choroidal thickness changes following cataract surgery in diabetic patients, and it showed that in diabetic eyes with DR (with or without macular edema), central macular thickness increased 1 month following phacoemulsification, but subfoveal choroidal thickness remained stable and was not mirrored by central macular thickness; however, this finding was not compared with the control group.<sup>22</sup> In the present study, we used EDI-OCT to evaluate choroidal thickness changes following phacoemulsification in patients with DM and compared it with non-diabetic healthy subjects.

In this study, we used EDI-OCT to evaluate choroidal thickness changes following phacoemulsification in patients with DM and compared it with non-diabetic healthy subjects.

## Methods

This prospective study included 63 eyes of 63 patients who referred to the Ophthalmology Clinic of Baqiyatallah Hospital in Tehran, Iran. Approval for this project was obtained from the institutional review board of Baqiyatallah University of Medical Sciences. The study followed the tenets of the Declaration of Helsinki. Written informed consent was obtained in all cases.

Patients were divided into 3 groups: Group A included patients with type 2 DM without DR or with mild non-proliferative DR (NPDR) that underwent phacoemulsification surgery due to visually significant cataract, Group B included non-diabetic patients who underwent phacoemulsification surgery, and finally, Group C included patients with type 2 DM and without significant cataract who did not required cataract surgery. Only the right eye of patients in Group C were included.

The disease severity was defined based on the clinical findings and using the International Clinical Disease Severity Scale for DR.<sup>23</sup> Eyes with “mild NPDR” were determined by the presence of a few microaneurysms. All fundus examinations were done by a single vitreoretinal specialist (A.A.).

Patients with history of previous ocular surgery or trauma, history of glaucoma, uveitis or other ocular disorders, and history of any systemic disease other than DM were excluded.

Also, diabetic patients (in Groups A and C) with DR more than mild NPDR, with proliferative diabetic retinopathy (PDR), with diabetic macular edema, or history of intravitreal anti-VEGF injection or laser therapy were excluded. Only patients with spherical equivalent between  $-3$  and  $+3$  diopters were included. Patients with dense cataract especially with advanced posterior subcapsular cataract that may restrict OCT imaging with adequate quality were excluded. Also, patients with any intraoperative complications or postoperative cystoid macular edema (CME) were excluded.

Complete ophthalmic examination included best corrected visual acuity (BCVA) measurement, slit-lamp examination, intraocular pressure measurement, and fundoscopy was performed. EDI-OCT using Heidelberg SD-OCT (Heidelberg Spectralis software version 5.3.2; Heidelberg Engineering; Germany) was done 1 day before surgery and then 1 week, 1 month, and 3 months after operation. All OCT scans were performed by the same experienced operator who was masked to identify the treatment groups of all of the patients. All scans were done between 11 and 12 o'clock.

Choroidal thickness measurements were done by a single vitreoretinal specialist (T.H.) who was masked to identify of the study group of all of the patients. Choroidal thickness was measured using the caliper found on the Spectralis software from the hyper-reflective band corresponding to Bruch's membrane beneath the retinal pigment epithelium (RPE) to the chorio-scleral junction. For each case, choroidal thickness was measured at subfoveal area and at 500  $\mu$  temporal, nasal, superior, and inferior from subfoveal point. Cases with poor image quality were eliminated.

Cataract surgery in all cases was performed by a single surgeon (J.K.) using the same machine (Infiniti Vision System, Alcon). Acrylic intraocular lens was implanted in the capsular bag in all cases. No intraoperative complications happened in any cases. Topical chloramphenicol eye drops were administered for 1 week and topical betamethasone eye drops were administered for 1 month in all cases who underwent phacoemulsification surgery (Groups A and B).

The main outcome in this study was choroidal thickness changes after cataract surgery.

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp, Armonk, NY, USA). Normality of distribution was examined by the Kolmogorov–Smirnov test. The difference in the frequency of qualitative variables in two or more groups was assessed using Chi square test. Student's *t*-test and one-way ANOVA test were used to see the difference in mean in two and more than two groups, respectively. *P*-value less than 0.05 was considered statistically significant.

## Results

A total of 63 eyes from 63 consecutive patients (33 male and 30 female) with a mean age of  $63.15 \pm 7.39$  years were included in this prospective study. Group A included 21 eyes of 21 diabetic patients without DR or with mild NPDR who underwent phacoemulsification surgery and completed 3

Table 1  
Baseline demographic data of patients in the 3 groups.

	Group A	Group B	Group C	P-value
Case number	21	22	20	
Age (mean ± SD)	62.09 ± 6.31	64.45 ± 5.63	61.32 ± 6.92	0.681
Sex				0.866
Male	10 (47.62%)	12 (54.55%)	11 (55%)	
Female	11 (52.38%)	10 (45.45%)	9 (45%)	
Baseline BCVA (logMAR)	0.51 ± 0.27	0.43 ± 0.18	0.23 ± 0.15	0.000
Subfoveal choroidal thickness	253.23 ± 33.14	278.33 ± 36.73	250.54 ± 29.18	0.003
Central macular thickness	249.34 ± 24.37	256.45 ± 17.48	257.72 ± 26.82	0.510

BCVA: Best corrected visual acuity.

months follow-up. Group B included 22 eyes of 22 patients without DM in which phacoemulsification was performed and completed 3 months follow-up. Group C included 20 eyes of 20 diabetic patients (the right eye in all cases) without DR or with mild NPDR and without visually significant cataract and completed 3 months follow-up. Patient demographic data for each group is recorded in Table 1.

There was no statistically significant difference in baseline and also final BCVA between Group A and Group B. BCVA improved significantly at 3 months postoperative examination in Group A and Group B ( $P = 0.001$  and  $P = 0.001$ , respectively) and remained stable in Group C ( $P = 0.17$ ).

At baseline, there was no significant difference regarding choroidal thickness in all measured points between diabetic patients in Group A and Group C; however, choroidal

thickness in both Group A and Group C was significantly thinner than non-diabetic subjects in Group B.

Baseline mean subfoveal choroidal thickness in 41 diabetic eyes in Groups A and C ( $253.14 \pm 35.42 \mu$ ) was significantly less than subfoveal choroidal thickness in 22 non-diabetic eyes in Group B ( $278.33 \pm 36.73 \mu$ ) ( $P = 0.001$ ). Also, choroidal thickness in the temporal, nasal, superior, and inferior regions in diabetic eyes (41 eyes) were significantly less than choroidal thickness in the corresponding regions in 22 non-diabetic eyes (Table 2).

Mean subfoveal choroidal thickness and choroidal thickness at temporal, nasal, superior, and inferior regions progressively decreased at 1 week, 1 month, and 3 months after operation in patients in Group A, but these values progressively increased in patients in Group B. Progressive thinning of choroid in all measured points in Group A and progressive thickening of choroid in all measured points in Group B at 1 week, 1 month, and 3 months follow-up period were statistically significant compared to baseline values (Table 3). Choroidal thickness in all 5 measured points had no significant changes during follow-up period in patients in Group C (Table 3).

The mean changes in subfoveal choroidal thickness from baseline were  $-6.65 \pm 6.88$ ,  $2.86 \pm 12.87$ , and  $1.9 \pm 4.60$  at one week,  $-13.00 \pm 11.10$ ,  $9.63 \pm 17.31$ , and  $1.10 \pm 5.05$  at

Table 2  
Comparison of choroidal thickness in different measured regions in diabetic (includes both Group A and Group C eyes) and non-diabetic eyes at baseline.

Choroidal thickness	Diabetic eyes	Non-diabetic eyes	P-value
Subfoveal	251.14 ± 35.42	278.33 ± 36.73	0.001
Temporal	244.46 ± 36.29	276.12 ± 34.22	0.001
Nasal	242.63 ± 35.17	264.61 ± 36.33	0.021
Superior	238.39 ± 36.06	260.64 ± 33.74	0.018
Inferior	238.85 ± 37.54	259.78 ± 33.67	0.017

Table 3  
Choroidal thickness in all 5 measured points and central macular thickness in the 3 study groups. All comparisons were performed compared to the baseline values.

		Baseline	1 week (P-value)	1 month (P-value)	3 months (P-value)
Group A	Subfoveal	253.23 ± 33.14	246.24 ± 33.12 ( $P = 0.001$ )	246.11 ± 27.54 ( $P = 0.017$ )	240.66 ± 36.94 ( $P = 0.003$ )
	Temporal	244.44 ± 36.43	239.47 ± 35.43 ( $P = 0.004$ )	240.23 ± 41.35 ( $P = 0.014$ )	232.64 ± 37.25 ( $P = 0.004$ )
	Nasal	241.62 ± 35.38	237.82 ± 35.37 ( $P = 0.008$ )	237.38 ± 40.44 ( $P = 0.040$ )	232.71 ± 37.45 ( $P = 0.005$ )
	Superior	238.65 ± 36.91	235.49 ± 35.24 ( $P = 0.011$ )	233.54 ± 39.33 ( $P = 0.022$ )	229.72 ± 36.42 ( $P = 0.001$ )
	Inferior	239.44 ± 37.43	234.42 ± 35.36 ( $P = 0.002$ )	234.22 ± 42.63 ( $P = 0.023$ )	230.95 ± 36.04 ( $P = 0.001$ )
	Central macular thickness	249.34 ± 24.37	250.82 ± 0.2041 ( $P = 0.271$ )	261.04 ± 36.82 ( $P = 0.003$ )	265.86 ± 19.69 ( $P = 0.007$ )
Group B	Subfoveal	278.33 ± 36.73	281.24 ± 39.01 ( $P = 0.074$ )	287.54 ± 43.90 ( $P = 0.017$ )	297.06 ± 44.25 ( $P = 0.005$ )
	Temporal	267.12 ± 34.22	271.52 ± 35.65 ( $P = 0.027$ )	275.52 ± 39.29 ( $P = 0.008$ )	282.64 ± 40.87 ( $P = 0.007$ )
	Nasal	264.61 ± 36.33	268.63 ± 39.95 ( $P = 0.000$ )	273.45 ± 40.18 ( $P = 0.031$ )	281.54 ± 42.27 ( $P = 0.011$ )
	Superior	260.64 ± 33.67	265.13 ± 36.64 ( $P = 0.013$ )	267.61 ± 37.25 ( $P = 0.022$ )	272.41 ± 37.73 ( $P = 0.017$ )
	Inferior	259.78 ± 33.67	263.45 ± 38.76 ( $P = 0.065$ )	265.54 ± 38.64 ( $P = 0.016$ )	272.28 ± 38.42 ( $P = 0.011$ )
	Central macular thickness	256.45 ± 17.48	255.73 ± 27.51 ( $P = 0.062$ )	263.49 ± 29.83 ( $P = 0.017$ )	269.83 ± 16.85 ( $P = 0.003$ )
Group C	Subfoveal	250.54 ± 29.18	249.34 ± 38.55 ( $P = 0.092$ )	249.04 ± 67.96 ( $P = 0.096$ )	249.62 ± 86.30 ( $P = 0.076$ )
	Temporal	245.29 ± 44.42	243.57 ± 92.24 ( $P = 0.087$ )	245.24 ± 12.46 ( $P = 0.089$ )	244.04 ± 39.96 ( $P = 0.083$ )
	Nasal	243.35 ± 13.14	242.24 ± 47.67 ( $P = 0.077$ )	244.56 ± 26.25 ( $P = 0.092$ )	243.53 ± 62.54 ( $P = 0.121$ )
	Superior	240.36 ± 36.61	242.44 ± 53.24 ( $P = 0.072$ )	240.35 ± 37.83 ( $P = 0.152$ )	240.22 ± 21.60 ( $P = 0.141$ )
	Inferior	237.60 ± 69.49	238.75 ± 66.37 ( $P = 0.183$ )	237.14 ± 73.84 ( $P = 0.092$ )	239.24 ± 25.95 ( $P = 0.076$ )
	Central macular thickness	257.72 ± 26.82	255.73 ± 32.15 ( $P = 0.241$ )	259.33 ± 26.61 ( $P = 0.152$ )	257.93 ± 31.93 ( $P = 0.208$ )

one month, and  $-11.95 \pm 13.00$ ,  $14.05 \pm 20.04$ , and  $0.95 \pm 4.85$  at 3 months in Group A, Group B and Group C, respectively. At one week, the changes were significantly different between Group A and Group B ( $P = 0.001$ ), between Group A and Group C ( $P = 0.014$ ), and also between Group B and Group C ( $P = 0.011$ ). At one month postoperative follow-up, the changes were significantly different between Group A and Group B ( $P = 0.000$ ), between Group A and Group C ( $P = 0.000$ ), and between Group B and Group C ( $P = 0.011$ ). At 3 months, the changes were significantly different between Group A and Group B ( $P = 0.000$ ), between Group A and Group C ( $P = 0.000$ ), and between Group B and Group C ( $P = 0.043$ ).

Central macular thickness increased significantly 3 months after cataract surgery in both Group A and Group B and remained stable in Group C (Table 3); however, no cases of diabetic macular edema were developed postoperatively.

## Discussion

The choroidal vasculature is affected by metabolic changes in diabetic patients and may be effective in the pathogenesis of DR.<sup>6</sup> Today, EDI-OCT has allowed evaluating the choroidal thickness changes, which may be useful for the evaluation of diabetic eye disease.<sup>24</sup>

In this study, we assessed the choroidal thickness changes following cataract surgery in diabetic patients and compared it with non-diabetic individuals. At baseline, subfoveal choroidal thickness was thinner in diabetic eyes than non-diabetic eyes. The choroid is the main source of oxygenation and nutrition of the outer retinal layers and RPE,<sup>16</sup> and choroidal thinning in diabetic eyes may be related to the decrease of the choroidal blood flow and tissue hypoxia in diabetic eyes.<sup>25–27</sup> Altinkaynak et al. compared the subfoveal choroidal thickness in 56 patients with congestive heart failure (CHF) with 56 healthy individuals.<sup>28</sup> They reported that subfoveal choroidal thickness was significantly thinner in patients with CHF ( $181.2 \pm 80.23$  mm) than normal eyes ( $283.6 \pm 52.4$  mm). Also, they found that subfoveal choroidal thickness was significantly correlated with the ejection fraction of the left ventricle. They concluded that choroidal thinning may be due to insufficient choroidal blood flow and may result in photoreceptor dysfunction. Many previous studies showed that choroidal thickness decreased in diabetic eyes compared with non-diabetic eyes.<sup>6,29–31</sup>

Cataract is one of the main causes of visual impairment in the old ages, especially in diabetic patients, and cataract surgery is the most frequent ocular surgery in the world.<sup>32</sup> Aslan Bayhan et al. evaluated the choroidal thickness changes following phacoemulsification surgery in 38 eyes from 38 healthy individuals.<sup>33</sup> They reported that choroidal thickness in all measured points significantly increased one month after operation. Noda and coworkers found that subfoveal choroidal thickness increased one month following cataract surgery and did not return to baseline preoperative values at 6 months follow-up period.<sup>34</sup> In another study, Pierru et al. found that subfoveal choroidal thickness increased after cataract surgery and reached its highest values one month following surgery;

however, subfoveal choroidal thickness decreased at 3 months follow-up after operation.<sup>35</sup> In the present study, we found that subfoveal choroidal thickness and also choroidal thickness in other measured regions increased significantly in healthy non-diabetic eyes and reached its highest values at 3 months postoperative examination. This finding is compatible with previous studies.<sup>33–35</sup>

The exact mechanism of choroidal thickening following cataract surgery is not fully understood. It may be due to up-regulation of prostaglandins, free radicals or growth factors, or other pro-inflammatory cytokines after phacoemulsification surgery.<sup>36–38</sup> This inflammatory cascade may activate secondary to surgical trauma or prolonged light exposure during or after operation.<sup>38,39</sup> Surgical trauma may lead to the release of prostaglandins and pro-inflammatory cytokines in the aqueous humor. Also, these inflammatory mediators may pass to the posterior segment, including the retina and choroid, and result in inner and outer BRB dysfunction.<sup>40</sup>

In the present study, we found that unlike non-diabetic eyes, subfoveal choroidal thickness and choroidal thickness in other regions decreased significantly after cataract surgery in diabetic eyes. Brito et al. evaluated retinal and subfoveal choroidal changes after phacoemulsification surgery in diabetic patients.<sup>22</sup> They divided 35 eyes from 35 diabetic patients into 3 groups: patients with DR and without macular edema, patients with DR and with macular thickening in OCT, and patients with clinically significant macular edema (CSME). Intravitreal bevacizumab was injected in eyes with CSME at the time of cataract surgery. The authors reported that at one month postoperative examination, no significant changes in subfoveal choroidal thickness was detected in any of studied groups; however, central macular thickness increased significantly with the exception of patients with CSME who received simultaneous intravitreal bevacizumab. They concluded that postoperative inflammation can cause significant macular thickening without detectable choroidal thickness changes. Unlike Brito et al.'s study, we included only diabetic eyes without DR or with mild NPDR. In our study, subfoveal choroidal thickness decreased significantly after cataract surgery in diabetic eyes. It may be secondary to exacerbation of hypoxia in the compromised choroidal vascular network in diabetic eyes secondary to intraocular inflammatory process or elevation of free radical levels in the eyes following cataract surgery.

Previous studies showed that DR progressed after cataract surgery in diabetic patients<sup>41,42</sup>. Our results suggest that one of the possible mechanisms for progression of DR may be choroidal hypoxia manifested as choroidal thinning.

In the present study, choroidal thickness in diabetic patients who were followed without cataract surgery (Group C) remained stable during 3 months follow-up, meaning that cataract surgery was a major cause of choroidal thickness reduction in diabetic patients in which phacoemulsification was done (Group A).

Many studies reported that both central macular thickness and subfoveal choroidal thickness increased following cataract surgery in healthy non-diabetic individuals.<sup>34,43</sup> Our study showed that central macular thickness increased following



cataract surgery both in diabetic and non-diabetic eyes. Therefore, in non-diabetic eyes, both central macular thickness and choroidal thickness increased after cataract surgery while in diabetic eyes, central macular thickness increased but choroidal thickness decreased. In the Brito et al. study, central macular thickness increased significantly one month after cataract surgery in diabetic eyes, but subfoveal choroidal thickness had no significant changes.<sup>22</sup> The author hypothesized that choroidal changes in diabetic eyes may be independent of the BRB status. The choroidal thickness changes after cataract surgery in diabetic eyes in our study were not mirrored by central macular thickness, and this was compatible with Brito et al.'s results. Therefore, in diabetic eyes, some different mechanisms than non-diabetic eyes may lead to the reduction of choroidal blood flow and hypoxia and finally result in DR exacerbation or progression.

This study has several limitations including a small sample size and short follow-up period. Likewise, we have no axial length data; however, patients with high refractive errors were excluded. The possibility of choroidal thickness measurement errors due to manual measurement and choroidal thickness measurement by a single grader are other limitations. Also, we did not separate patients without DR and patients with mild NPDR in diabetic groups.

In conclusion, our study shows that in diabetic eyes, central macular thickness increased but choroidal thickness decreased following phacoemulsification; however, in non-diabetic eyes both central macular thickness and choroidal thickness increased. Reduction in choroidal thickness may be secondary to choroidal blood flow suppression and subsequent choroidal hypoxia and finally may lead to DR progression. Further study is required to document this relationship and guide the prevention of choroidal thinning following cataract surgery in diabetic patients.

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