Changes in Chorioretinal Flow Index after Cataract Surgery: An Optical Coherence Tomography Angiography Study

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Abstract

PURPOSE: Pseudophakic cystoid macular edema (CME) occurs in up to 2% of uneventful cataract surgeries. This study evaluates changes in macular blood flow succeeding uneventful phacoemulsification cataract extraction among otherwise visually healthy subjects.

METHODS: This prospective study included 18 eyes of 18 patients undergoing routine phacoemulsification. Optical coherence tomography angiography (OCT-A) was performed using the Angio-Retina 6x6mm protocol with the XR Avanti Angio-Vue system (Optovue Inc., Fremont, California) prior to the surgery and 4-8 weeks thereafter. Exclusion criteria included motion artifacts, segmentation errors and signal strength index (SSI) ≤ 40 . The main outcome measure was change in flow index (FI) measured in all 4 retinal segmentation layers within an area of 1mm diameter around the foveal center.

RESULTS: Following surgery, a significant increase in SSI (46.65 ± 8.62 versus 53.12 ± 8.07 , $p=0.01$), superficial plexus FI (0.98 ± 0.23 versus 1.16 ± 0.16 , $p=0.02$) and deep plexus FI (0.54 ± 0.46 versus 0.93 ± 0.39 , $p=0.01$) was found. No significant changes were noted in the outer retina or the choriocapillaris.

CONCLUSION: The study demonstrates a significant increase in FI in the superficial and deep retinal plexus following uneventful cataract surgery, with the greatest changes occurring in the latter. These findings corroborate evidence from structural imaging and support the vascular etiology of pseudophakic CME.

Introduction

Cataract surgery is the most common surgical intervention in ophthalmology.[1] In spite of the overall high rate of success and excellent outcome profile of this procedure worldwide,[2] post-operative complications may appear in up to 5% of the cases, and may occur even after uneventful surgery. Clinical pseudophakic cystoid macular edema (CME), also termed Irvine-Gass syndrome, has been reported in 0.1 to 2.35% of patients undergoing cataract surgery.[3] This condition typically appears 6-10 weeks after cataract extraction and involves cystoid thickening of the macular center which may lead to decrease in visual acuity. Although the etiology of this condition is yet to be fully elucidated, it is postulated that increased vessel permeability may underlie the pathogenesis of this phenomenon. Risk factors for pseudophakic CME include vitreoretinal traction, and posterior capsular rupture resulting in vitreous prolapse.[3] The clinical hallmark of this condition is the appearance of macular cystoid thickening, associated with a decrease in visual acuity. The gold-standard for the diagnosis is fluorescein angiography (FA) which demonstrates a petaloid pattern of macular leakage associated with hyperfluorescence of the optic nerve head.[4] Sub-clinical pseudophakic CME, in which similar angiographic alterations are unaccompanied by decrease in visual acuity (better than 20/40), occur in up to 20 - 54.7% of phacoemulsification cataract surgeries.[5]

Whereas the mechanism of pseudophakic CME is not fully understood, increased vessel permeability due to post-surgical cytokine release is considered a key causative factor of a blood-retinal-barrier compromise.[3, 6, 7] Further evidence on the pathophysiology of pseudophakic CME is derived from recent studies which demonstrated choroidal thickening after uneventful cataract surgery using enhanced-depth-imaging OCT.[8–12] These studies demonstrated an increase in choroidal subfoveal thickness up to 6 months following surgery,[10] with a greater increase among patients who developed pseudophakic CME, thus further supporting the inflammatory mechanism of pseudophakic CME.[12] Additional pathomechanistic factors suggested include macular phototoxicity due to exposure to ultra-violet radiation from the operating microscope[13] and retinal metabolic changes.[5]

Optical coherence tomography angiography (OCT-A) is a novel non-invasive technology enabling to image the choroid and the retina, with the capacity to quantitatively and qualitatively evaluate the blood flow within them. The technology is based on spectral-domain OCT (SD-OCT) with an added split spectrum amplitude decorrelation angiography (SSADA) algorithm. The latter enables *in vivo* imaging of red blood cells based on consecutive B-scans.[14] The collected information is depicted as *en-face* images of 4 different layers: (1) Superficial capillary plexus in the ganglion cell layer of the retina, (2) Deep capillary plexus: between the inner and outer plexiform layers, (3) Outer retina normally devoid of vasculature and (4) Choriocapillaris, the innermost vascular plexus of the choroid supplying the retinal pigment epithelium and photoreceptors. The software derives 2 major measurements: vessel density (VD), defined as the percentage area occupied by the blood vessels, and flow index (FI) which is the average flow signal in the area of interest, calculated as the average decorrelation value in the region of interest. The software is also able to calculate the area of the foveal avascular zone (FAZ).[15]

In the present study we aimed to investigate the alterations in macular blood flow following uneventful cataract extraction among otherwise visually healthy subjects. Such information would shed light on the processes taking place in the macula following cataract surgery, and may deepen our understanding of the pathophysiology of pseudophakic CME and other macular changes noted after this procedure.

Methods

Patient Population

This prospective study performed in the department of Ophthalmology, Rambam Health Care Campus, Technion Israel Institute of Technology Haifa, Israel, was approved by the institutional ethical committee and adhered to the tenets of the declaration of Helsinki. Patients scheduled to undergo routine cataract surgery were offered to participate in the study. Informed consent was obtained from all patients. Inclusion criteria were age over 18 years, a clinically and visually significant cataract warranting surgical intervention, and good view of the ocular fundus which allowed acquisition of high-quality images of the retina with a minimal OCT signal strength index (SSI) of 40. Preoperative exclusion criteria included past or present ophthalmic inflammatory diseases, planned cataract extraction in combination with an additional ophthalmic procedure, and dense cataract hindering view of the posterior pole and thwarting

acquisition of reliable imaging. Patients who developed inflammatory or infectious post-operative complications were also excluded from the study.

Visits and Data Collection

At baseline, all patients underwent a thorough ophthalmic examination including best corrected visual acuity, objective refraction, slit-lamp biomicroscopy, and measurement of the intraocular pressure. Pharmacologic pupil dilation facilitated ophthalmoscopic examination and OCT-A imaging of both eyes. Data collected for each patient consisted of demographic details including age, gender, laterality of the operated eye (right/left), past medical history of systemic diseases, past ophthalmic history with attention to previous operations, inflammatory conditions or regular use of eye drops, and history of ocular trauma. Additional ophthalmic measures obtained at baseline included axial length, best corrected visual acuity, cataract severity and morphology (nuclear, anterior cortical, posterior subcapsular) according to the Age-related eye disease (AREDS) clinical lens grading scale.[16]

All baseline tests were performed approximately 2 weeks prior to the operation. At the follow-up examination, performed within 4-8 weeks post-operatively, a similar set of measures was obtained from each patient. Records of intra-operative complications were reviewed and collected. Routine post-operative treatment, employed in all patients, consisted of ofloxacin 0.3% (Oflox, Allergan Pharmaceuticals Ireland Castlebar Road Westport, Co, Mayo) and dexamethasone disodium phosphate 0.1% (Sterodex, Doctor Fisher Pharmaceutical Labs, Tel-Aviv).

OCT Angiography Imaging

In all patients OCT-A imaging was performed using the Angio-Retina 6 x 6 mm protocol with the XR Avanti Angio-View system (Optovue Inc., Fremont, California). This platform is based on Spectral-Domain OCT and performs 70,000 axial scans per second. Each B-scan is obtained from 304 A-scans. Comparing consecutive B-scans allows flow identification.[17] Care was taken to obtain images with reliable quality and an SSI > 40.[18–20] Patients in whom acquisition of a reliable image (without motion artifacts or segmentation errors) was impossible were excluded from the study. Measures of Flow index (FI) were obtained for all 4 retinal segmentation layers within an area of 1 mm diameter around the foveal center.

Statistical analysis

Statistical analysis was performed using Minitab 19 software (Minitab Inc., State College, Pennsylvania, USA). The comparison of continuous variables was performed using the Wilcoxon Signed Rank test. Values are presented as average $\pm$ standard deviation. P-value of less than 0.05 was considered statistically significant.

Results

Demographic and Preoperative Parameters

Included in this study were 18 eyes of 18 patients with a mean age of 70.9 ± 7.8 years of which 38.9% (n=7) were female. Best corrected visual acuity pre-operatively was LogMar 0.34 ± 0.16 and was improved to LogMar 0.154 ± 0.065 after surgery (p-value < 0.01). Nuclear cataract was the morphology found in the majority of eyes (n=15/18, 83%) with an average grade of 2.38 ± 0.53 , while that of the posterior subcapsular cataract was 2.17 ± 0.76 . The mean axial length was 24.1 ± 1.8 mm.

Flow Index Values

Figure 1 shows the *en-face* images of all 4 layers obtained from one patient, before and after surgery. The flow in the deep retinal plexus appeared more enhanced post-operatively. To quantitatively assess changes in macular blood flow after cataract surgery, the FI values of the different retinal segmentation layers obtained before and after surgery were compared (Table 1). Notably, following surgery there was a significant increase in the FI measures from the superficial plexus (0.98 ± 0.23 versus 1.16 ± 0.16 , p=0.02) and deep retinal plexus (0.54 ± 0.46 versus 0.93 ± 0.39 , p=0.01) among the entire study group (figure 2). Consistently, the ratio between flow indices postoperatively compared to baseline was 1.18:1 and 1.72:1 in the superficial and deep plexuses, respectively. In addition, an improved SSI was also noted postoperatively (46.65 ± 8.62 versus 53.12 ± 8.07 , p=0.01). No significant changes were noted in the outer retina or in the choriocapillaris layers.

Table 1
A comparison of flow indices before and after phacoemulsification cataract surgery.

Parameter	Preoperative	Postoperative	Ratio	*P-Value
SSI	46.65 ± 8.62	53.12 ± 8.07	1.14	0.01
Superficial plexus	0.98 ± 0.23	1.16 ± 0.16	1.18	0.02
Deep retinal plexus	0.54 ± 0.46	0.93 ± 0.39	1.72	0.01
Outer retina	1.32 ± 0.07	1.26 ± 0.20	0.95	0.08
Choriocapillaris	1.83 ± 0.11	1.76 ± 0.28	0.96	0.69
*Wilcoxon Signed Rank test was used for analysis				
SSI: signal strength index				

Discussion

This prospective study evaluated the OCT-A derived retinal FI values of subjects undergoing routine phacoemulsification cataract surgery at baseline as well as after the procedure. Following cataract extraction, there was a significant increase in the FI measures obtained from the superficial plexus as well as deep retinal plexus, with the greatest changes occurring in the latter. In contrast, no significant changes in FI measures were noted in the outer retinal layer and choriocapillaris. As can be expected in

conjunction with improved media clarity, a significant improvement in SSI values was also noted following surgery.

The most significant change in FI was measured in the deep retinal plexus. Indeed, previous studies have reported an increased perfusion of the inner plexuses following cataract surgery.[21] Yu et al. reported a significant increase in OCT-A derived flow indices in both superficial and deep capillary plexuses following cataract surgery among a cohort of 12 patients.[21] Interestingly, Pilotto et al. reported a temporary increase in vascular area density and vessel density index in both the intermediate and deep capillary plexuses, but not the superficial plexus.[22] The increased measures, noted in 9 patients, appeared one day following surgery, but normalized one week postoperatively.[22] In our study, OCT-A derived measures of macular blood flow were not obtained during the first postoperative week, whereas emphasis was placed on the 4-8 week postoperative period, when the occurrence of pseudophakic CME is most frequently encountered.[3] Perhaps, differences in the OCT-A machines and postoperative care regimens employed in the aforementioned study may explain the seemingly contradicting results. The results of our study are supported by those of Zhao et al. who employed the same OCT-A system and reported an increase in the total vessel density, representing measures from all retinal layers combined, as well as a decrease in FAZ area following cataract surgery.[18] The rise in the macular FI measures found in the current study could be attributed to the secretion of pro-inflammatory factors from the anterior segment, which migrate through the Cloquet canal to the posterior ocular segment. Such inflammatory cytokines may induce vasodilation which leads to an increase in vascular flow within the retinal capillary plexus and explains the elevation in FI found in our study.[3]

Recent studies employing enhanced depth imaging (EDI)-OCT demonstrated macular choroidal thickening following cataract surgery.[10–12] This technique involves acquisition of cross sectional macular images enabling enhanced visualization of the choroidal layers. However, EDI-OCT does not provide direct assessment of the choroidal vascular blood flow. In our current study no postoperative changes in the FI from the choriocapillaris were depicted on OCT-A. This discrepancy in results may be due to the development of choroidal leakage manifesting as choroidal thickening on EDI-OCT, yet not visualized on OCT-A technology as the flow is typically too slow. Alternatively, the changes may result from alterations occurring in deeper layers of the choroid which are not imaged on OCT-A. Previous studies evaluating changes in flow using OCT-A after cataract surgery did not consistently report data regarding the outer layers.[18, 21] Pilotto et al. reported an insignificant increase in choroidal thickness following surgery, but did not report on blood flow or perfusion measures in this vascular layer.[22] The authors postulated that a local choroidal inflammatory response may contribute to choroidal thickening detected at 1 month in their study.

Several studies, including the PREMED study[23] have reported on the successful prevention of pseudophakic CME using bromofenac 0.09% and dexamethasone 0.1% eye drops. It is of interest whether these treatments may impact the changes in FI measures identified in the current study following phacoemulsification cataract surgery. In the current study no patients developed pseudophakic CME and thus a comparison between patients with or without this condition was not performed. Future studies

examining a correlation between changes in flow measures and the development of pseudophakic CME will perhaps identify risk factors for this condition. Future studies examining a correlation between changes in FI and the development of pseudophakic CME may identify risk factors for this condition and assess the etiologic role of such a rise in causing pseudophakic CME.

Despite its prospective nature, our study has several limitations, first of which is its relatively small sample size. However, repeated OCT-A images obtained longitudinally from the same patients before and after surgery allowed for a paired analysis with an adequate power, compared to a non-paired analysis. Larger studies may be warranted to validate our findings. An additional potential limitation is that due to the inherent nature of this study, baseline SSI values among eyes with cataract were considerably lower compared to the corresponding values obtained after surgery from the same eyes, thus potentially compromising the quantitative measures obtained at baseline and affecting our results. To address this limitation, only patients with an SSI value of 40 or higher at baseline were included in our study. This cut-off is in consistency with previous studies of eyes with potential media opacities. [18–20]

Altogether, our prospective OCT-A imaging study demonstrates a significant increase in the macular blood flow among eyes undergoing routine cataract extraction, with FI measures from the superficial and deep retinal plexuses demonstrating the largest changes. These findings corroborate evidence from structural imaging and histopathological studies, and support the vascular etiology of pseudophakic CME.

Declarations

Compliance with Ethical Standards

No funding was received for this study

Ethical approval

This article does not contain any studies with animals performed by any of the authors

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Figures

Figure 1

en face images of the four retinal segmentation layers obtained from a single patients at baseline (a, c, e, g), and after surgery (b, d, f, g). An increased flow can be appreciated in the deep retinal plexus (c, d).

Figure 2

A comparison of the flow indices in the different retinal vascular layers segmented by OCT-A (superficial plexus, deep plexus, outer retina and choriocapillaris), before (pre) and after (post) cataract surgery. The dots represent the mean and the errors bars represent the standard error.