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The influence of high myopia and hyperopia on the retinal and the optic disc vascularization after uncomplicated phacoemulsification – preliminary report

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ABSTRACT

Aim of the study: To evaluate the influence of phacoemulsification on macular and the optic disc vascularization and its association with different axial lengths, in particular high myopia and hyperopia.

Material and methods: Forty eyes of 40 patients with cataract were assessed pre-operatively and 1 month after surgery. Patients were divided into three groups: Group 1 included patients with hyperopia, Group 2 included patients with high myopia and Group 3 included healthy persons without hyperopia or myopia. Examinations included measurement of best corrected visual acuity, intraocular pressure, axial length, a slit lamp biomicroscopy and OCT angiography.

Results: The mean BCDVA significantly improved in all groups. Pre-operatively, no significant differences between the groups were present, however, post-operatively, the mean macular volume was much larger in the hyperopic and myopic groups, when compared to the normo-axial group. There was a significant increase in the vessel density and length of the superficial plexus of the macula in groups 1 and 3. Deep plexus macular vessel length increased significantly in group 3. Changes in the optic disc area size, as well as Cup-to-disc ratio (C/D ratio) were insignificant. The retinal nerve fiber layer thickened postoperatively in all groups, although it was only significant in the hyperopic group. Preoperatively, the myopic group had a much thinner mean RNFL than the other groups. Radial peripapillary capillary density increased significantly in group 2 and group 3 postoperatively.

Conclusions: This study reveals retinal microvascular changes in highly myopic and hyperopic eyes, which correlates with axial length. Both axial length extremes presented a worse retinal vascular architecture, but improved after the phacoemulsification surgery in terms of vascularity.

KEY WORDS: OCT angiography, OCTA, high myopia, hyperopia, axial length.

INTRODUCTION

Although cataract is operated and treated extensively in the developed world, it continues to be the leading cause of reversible blindness globally, accounting for 51% of cases of blindness [1].

Many factors may affect the post-operative prognosis, they are either patient dependent, such as advanced age or presence of other ocular and non-ocular comorbidities [2], or surgeon dependent, mainly occurrence of perioperative or postoperative complications [3]. Other known factors which can influence postoperative outcome, include: the age, high technical complexity of the procedure (partially connected to the advancement of cataract), ocular or general coexisting diseases (diabetes, various diseases affecting the retina), and the presence of perioperative complications, such as posterior capsular rupture or vitreous hemorrhage [3].

As the prevalence of high myopia has been rising globally [4], the axial length of the cataract population has yet to be extensively investigated in terms of post-operative prognosis, in particular regarding the vascularity of the macula.

Myopia is defined as a refractive pathology with a spherical equivalent of < –0.5 Diopters in a non-accommodating eye, with a further division to high myopia with a spherical equivalent of < –6.0 D. Myopia can be divided into: refractive, axial and corneal curvature-related. Myopia can be defined by the axial length of the eye, with myopic eyes having an axial length of > 24 mm, and high myopic eyes an axial length of > 26 mm [5].

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The prevalence of myopia is rather variable in the younger age groups and stable in adulthood, this is largely owing to the early age of onset of myopia. With regards to possible causes of myopia, the importance of genetic and/or environmental factors in myopia development is still debatable [6]. School myopia (juvenile-onset myopia) is considered to be more dependent on environmental factors rather than genetic ones, an idea supported by the substantial rise in myopia prevalence in regions with social norms of abundant near work and scarce outdoor activities [5]. A couple studies reported Alaskan Eskimos were found to have a sharp increase in myopia prevalence when they were introduced to modernized mandatory education during early life [7]. A large scale meta-analysis associated prolonged near work with increased risk of myopia, estimating an average increase of 2% per 1 diopter-hour of near work performed per week [8], and with the recent rise in computer and mobile phone usage, a rather large proportion of the young population is at risk of myopia development [9]. Nonetheless, one must not exclude the importance of genetics in the development of juvenile onset myopia, as comparative studies done on parents and twins do support a contributory role [10]. A few protective factors were evaluated, hyperopia during childhood with a refractive error of +0.75 D was linked with a lower risk of myopia development later on [11], as well as outdoor exposure consisting of as little as 40 minute intermittent daily activities decreasing myopia onset by 9% in 3 years [5]. It was hypothesized that outdoor light exposure plays a protective role in myopia by stimulating release of retinal dopamine, a speculation supported by animal studies where the protective effect is replicated or blocked by a dopamine antagonist [12].

Myopia (with a stronger association in the case of high myopia) is linked with a few other ocular pathologies, with studies showing an increased risk of cataract [13] and glaucoma [14], and a decreased risk of age related macular degeneration [15]. Pathological myopia, defined as high myopia with degenerative alterations of the posterior pole including the sclera, choroid and retinal pigment epithelium layer, is a rising public health concern. The effect of high myopia on the eye structure has been well documented in the past. Histopathological findings described a thinned sclera and retina in eyes with markedly higher axial length, however the first generations of OCT devices did not find any correlation between the axial length and mean macular thickness [16]. More recently, newer generation devices, so called ultra-high-resolution OCT, were able to depict the separate layers of the retina using automated separation algorithms, an advancement which allowed the study of individual intraretinal layers and their thickness. Different regions of the retina had unique alterations, with the central macular region presenting only thickening of the outer segment of the receptors (myoid and ellipsoid areas) with increasing axial length, while the more peripheral areas were found to have all retinal layers affected by thinning, with the exception of the inner plexiform and ganglion cell layers [17].

With the increasing global prevalence of refractive errors and hyperopia being the most common refractive error during childhood [18], it is rather surprising that the vast majority of research on the topic remains focused on myopia rather than hyperopia. This selection bias is mainly due to the lower prevalence among younger individuals and the different mechanism of progression, with hyperopia often developing at a young age and remaining rather stable throughout life [19, 20], unlike myopia which often develops in older children and tends to progress gradually [21]. Lower prevalence and a stable course, in addition to accurate measurement struggles in the hyperopic population, many of whom have hyperopia coinciding with amblyopia, have left the hyperopes mainly classified into other subcategories such as amblyopia and pediatric vision.

Hyperopia, also known as far-sightendness or hypermetropia, is a refractive condition in which light rays entering the globe in the state of relaxed accommodation focus on a point situated further than the retina. Hyperopia can be classified according to its etiology and effect on the eye, whereas simple hyperopia is a phenomenon which is mainly axial in its nature [21], it could also be due to decreased converging power of the cornea or the lens [18]. Pathologic hyperopia originates in developmental, traumatic, or primary disorders of the eye such as cataract, aniridia, microphthalmia and nanophthalmia [18]. Another subclass is functional hyperopia where the source of the condition lies in accommodative dysfunction, with some cycloplegics causing a relatively transient hyperopia [18].

As with other refractive errors, hyperopia can be classified according to the degree of refractive error, with low hyperopia being below +2 D, moderate hyperopia between +2.25 D and +5 D, and high hyperopia above +5 D, with the latter cases possibly presenting blurred optic disc margins or pseudo-papilloedema distinguishable from authentic papilloedema by the presence of normal sized vessels and surrounding retina [18]. A meta-analysis investigating the prevalence of hyperopia has concluded a decrease of prevalence with age, as an average prevalence of 5% at age 7, progresses to 2-3% between the ages of 9 and 14, and dropping even further to 1% at the age of 15 [18].

Hyperopia during early life tends to be a precursor of other eye related defects, oculo-motoric or sensory issues, in particular accommodative esotropia, anisometropia, and amblyopia. Despite its association with the above conditions, no specific consensus has been accepted by the global eye care community as to the cut-off values or age at which refractive correction should be established. Asthenopia including fatigue and eye pain while reading, along with squinting when looking at near objects are frequent early clinical manifestations in hyperopic children [22]. Hyperopic eyes also tend to possess a more shallow anterior chamber, increasing the risk of narrow-angle glaucoma developing [22].

The need for a mean of refractive correction (whether glass lenses, contact lenses, or refractive surgery) depends on the severity of hyperopia, with mild cases (often up to + 3 D

if asymptomatic) usually not requiring treatment. Lenses used are convex in their shape, converging the light into the eye in the correct focal point on the retina [18].

It has been found that there is a connection between refractive errors and different types of cataract. In a population-based study, it was found that patients with nuclear and posterior subcapsular cataract had a higher prevalence of myopia while the prevalence of hyperopia was lower in those with cataract. High myopia was seen in higher grades of nuclear cataract. The high percentage of hyperopia was also significant in patients with cortical cataract [19].

AIM OF THE STUDY

The purpose of this study is to evaluate the association of different axial lengths, in particular myopia and hyperopia, with the macular vasculature, as well as phacoemulsification surgery and its possible influence on the macular and the optic disc vascularization.

MATERIAL AND METHODS

The study was a prospective, observational study. The analyzed data were gathered prospectively from a non-randomized consecutive series of patients. Patients were enrolled to the department of ophthalmology, Medical University of Lodz, for cataract surgery from tertiary eye clinics in the district of Lodz, Poland. Cataract patients with varying axial lengths who were scheduled for phacoemulsification surgery with intraocular lens (IOL) implantation were selected for the study. In the instance where both eyes were qualified to participate in the study, both eyes were studied after each eye's separate phacoemulsification.

All patients gave an informed consent to participate in the study. All tenets of the Declaration of Helsinki were followed for all study protocols. The study was approved by the Bioethics Committee of the Medical University of Lodz (approval number RNN/69/20/KE).

All the study participants signed informed consent forms and had the contents of the above-mentioned forms explained to them.

All patients had undergone complete ophthalmologic examination and included the measurement of best corrected distance visual acuity (BCDVA) using standard Snellen charts, the measurement of intraocular pressure (IOP), the measurement of axial length (AL) with partial coherence interferometry (IOLMaster), a slit lamp biomicroscopy, as well as a dilated fundus evaluation. Every patient's medical and family histories were collected to assess compatibility.

The inclusion criteria for the study were the presence of a nuclear or cortical cataract with no concomitant intraocular disease, IOP of 21 mm Hg or lower, and separate ranges of ALs for each study group; the myopic group consisted of individuals with an AL of 26.0 mm or longer, the hyperopic group an AL of 21.0 mm or shorter, and the control group had patients with ALs between 22.0 mm and 25.0 mm.

Exclusion criteria were: any previous ocular surgery or laser procedures, as well as any present or previous ocular or systemic diseases that might affect the results. Eyes not fitting the AL ranges, IOP higher than 21 mm Hg, a history of ocular trauma or severe intraocular disease, or any abnormal intraocular finding in the region of the macula with the possibility of it affecting visual acuity were excluded. Other causes for exclusion included poor OCT images quality due to severe cataracts or unstable fixation, as well as intraoperative or postoperative complications.

Lastly, the COVID-19 pandemic forced the study to end preemptively as quarantine regulations were enforced.

All patients underwent an OCT examination using a high-speed spectral-domain optical coherence tomography device (OPTOPOL Technology, software version: "9.5.0"). Macular scans were of 6.0 mm × 6.0 mm dimensions. En face retinal angiograms were formed by the projection of a signal originating from the inner limiting membrane (ILM) to the retinal pigment epithelium (RPE). Images with a signal strength index of more than 40 and relatively no residual motion artifacts were saved for future analysis. Outlining of the foveal avascular zone (FAZ) was performed for area and circumference measurement using the software provided by the OCTA manufacturer (The parafoveal region was defined as an annulus contained between an inner diameter of 1.0 mm and an outer diameter of 3.0 mm, and the perifoveal region was defined as an annulus with an inner diameter of 3.0 mm and an outer diameter of 5.0 mm. Vessel densities of the above-mentioned areas were automatically calculated by the OCT system.

Macular retinal thickness was calculated along the retinal vascularization in the retinal map mode, measured starting from the ILM and until the middle of the RPE and Bruch membrane complex. The inner retina was defined as the layer of the retina between the ILM and outer IPL, and the outer retina was situated between the outer IPL and the middle of RPE and Bruch membrane complex. The mean thickness of the retina at a specific point was defined as retinal thickness. The 1.0 mm ring zone at the center of the macula was defined as the fovea, and the OCT system supplied automatic calculations of the mean full, inner, and outer retinal thicknesses of the above-mentioned 3 areas.

All ophthalmologic measurements, including best corrected distance visual acuity (BCDVA), intraocular pressure (IOP), axial length (AL), and OCT, were performed before the cataract surgery, and were repeated during the follow up visit 1 month after the procedure. All measurements were done between 9:00 AM and 1:00 PM to avoid diurnal variation.

All surgical procedures were performed using the Centurion phaco machine (Alcon, Fort Worth, USA). After topical anesthesia was administered (1% lidocaine gel), a 2.2 mm corneal incision with a self-sealing nature was performed, followed by continuous capsulorhexis, hydrodissection, phacoemulsification, and finally removal of the residual lens cortex by irrigation-aspiration. Implantation of a foldable IOL (Aspira AO, Human Optics, Germany) was then carefully performed into the capsular bag. Lastly, injection of cefuro-

Table I. BCDVA at baseline and 1 month post-operatively

Statistic	G1 pre	G1 post	G2 pre	G2 post	G3 pre	G3 post
Minimum	0.03	0.30	0.02	0.20	0.20	0.60
Maximum	0.50	0.80	0.50	1.00	0.60	1.00
Mean	0.31	0.57	0.23	0.57	0.46	0.91
Standard deviation (n)	0.14	0.19	0.17	0.25	0.12	0.15
p-value	0.009		0.006		0.001	

Table II. Macular volume at baseline and 1 month post-operatively

Macular volume	G1 pre	G1 post	G2 pre	G2 post	G3 pre	G3 post
Minimum	2.53	2.68	2.14	2.48	2.32	2.39
Maximum	8.28	9.49	8.92	9.40	8.66	3.01
Mean	6.74	6.21	5.10	6.02	6.20	2.79
Standard deviation (*n*)	2.02	2.82	2.45	2.61	2.28	0.16
p-value	0.432		0.641		0.013	

Table III. Retinal thickness (µm)

Retinal thickness (µm) at the foveal region						
	G1 pre	G1 post	G2 pre	G2 post	G3 pre	G3 post
Minimum	103.00	153.00	168.00	187.00	202.00	196.00
Maximum	334.00	441.00	388.00	325.00	268.00	241.00
Mean	219.10	241.00	249.33	246.75	227.29	213.00
Standard deviation (*n*)	60.66	75.42	58.42	38.18	18.67	12.77
p-value	0.572		0.141		0.024	
Retinal thickness (µm) at the parafoveal region						
Statistic	**G1 pre**	**G1 post**	**G2 pre**	**G2 post**	**G3 pre**	**G3 post**
Minimum	160.50	188.00	220.75	178.50	245.75	252.50
Maximum	321.75	377.00	357.25	320.25	329.50	319.00
Mean	264.38	295.08	290.15	282.28	294.25	294.64
Standard deviation (*n*)	52.90	48.92	42.22	44.44	16.60	16.53
p-value	0.275		0.742		1.000	

xim (Aprocam, Thea) into the anterior chamber was done. After the surgery, a combination of antibiotic and steroid was administered topically 4 times a day to avoid complications for a duration of 3 weeks.

All calculations were performed for the significance level $\alpha = 0.05$ using Microsoft Excel and AddinsoftXLStat 2008 software. As the examined groups were small, statistical analysis was performed using nonparametric tests. Pre- and postoperative values in the same group were compared using Wilcoxon signed-rank test. Statistical significance between unpaired data (independent samples) was determined using Mann-Whitney U test. Differences were considered statistically significant at $p < 0.05$.

RESULTS

Forty eyes of 40 patients with senile cataract participated in the study and were assessed at baseline pre-operatively and 1 month after the surgery. The study patients were divided into three study groups based on their axial length.

Group 1 consisted of 10 eyes of 10 patients with hyperopia. This group included 6 women (60%) and 4 men (40%), aged from 62 to 87 years old (mean age was 72 ±8 years old).

Group 2 consisted of 13 eyes of 13 patients with high myopia. This group included 10 women (77%) and 3 men (23%), aged from 50 to 84 years old (mean age was 65 ±11 years old).

Group 3 consisted of 17 eyes of 17 healthy persons without hyperopia or myopia. This group included 10 women (58,8%)

Table IV. FAZ parameters – area, perimeter and circularity

FAZ area (mm^2)						
	G1 pre	G1 post	G2 pre	G2 post	G3 pre	G3 post
Minimum	0.220	0.180	0.060	0.060	0.110	0.090
Maximum	0.749	0.839	0.580	0.650	0.590	0.500
Mean	0.496	0.457	0.306	0.274	0.302	0.285
Standard deviation (*n*)	0.134	0.160	0.146	0.195	0.126	0.105
p-value	0.275		0.945		0.210	
FAZ perimeter (mm)						
Statistic	**G1 pre**	**G1 post**	**G2 pre**	**G2 post**	**G3 pre**	**G3 post**
Minimum	2.460	2.290	1.210	1.160	1.580	1.740
Maximum	4.132	4.392	4.870	3.590	3.540	4.120
Mean	3.312	3.111	2.567	2.317	2.550	2.571
Standard deviation (*n*)	0.446	0.505	0.891	0.743	0.518	0.576
p-value	0.160		0.945		0.909	
FAZ circularity						
Statistic	**G1 pre**	**G1 post**	**G2 pre**	**G2 post**	**G3 pre**	**G3 post**
Minimum	0.400	0.440	0.270	0.400	0.260	0.210
Maximum	0.740	0.700	0.770	0.670	0.780	0.740
Mean	0.562	0.579	0.585	0.558	0.580	0.553
Standard deviation (*n*)	0.104	0.075	0.134	0.095	0.152	0.155
p-value	0.798		0.944		0.147	

and 7 men (41,8%), aged from 27 to 85 years old (mean age was 72 ±13 years old).

The mean axial length was 20.49 ±0.47 mm in group 1, 27.79 ±3.08 mm in group 2, and 23.06 ±0.8 mm in group 3.

The mean BCDVA was 0.31 ±0.14 for group 1, 0.23 ±0.17 for group 2, and 0.46 ±0.12. The mean IOP was 15.34 ±2.78 mmHg for group 1, 14.45 ±2.78 mmHg for group 2, and 13.36 ±3.22 mmHg for group 3.

At the follow up visit, 1 month after the surgery, the mean BCDVA significantly improved in each of the groups (all $p < 0.01$; Table I), and a noticeable difference was found to exist between group 1 and 3, and 2 and 3, both at baseline and 1 month after the surgery (all $p < 0.05$).The visual acuities are summarized in Table I.

There was no significant difference in the decrease of IOPs in the groups ($p = 0.065$, $p = 0.199$, and $p = 0.581$ respectively) and between different groups.

A decrease in the mean macular volume was noticed in the normo-axial patient group ($p = 0.013$; Table II), although no statistically significant changes were present in the hyperopic and myopic groups ($p = 0.432$ and $p = 0.641$ respectively). Pre-operatively, no statistically significant differences between the groups were present, however, post-operatively, the mean macular volume was much larger in the hyperopic and myopic groups compared to the normo-axial group ($p = 0.010$ and $p = 0.013$ respectively). The macular volumes are summarized in Table II.

A decrease in the mean retinal thickness at the foveal region was found to occur in the control group (group 3), however no significant difference was present in groups 1 and group 2 ($p = 0.572$ and $p = 0.141$ respectively). Additionally, no statistically significant difference was noticed between the different groups 0. At the parafoveal region, no significant difference was present comparing pre and 1 month post-operatively in the groups, as well as comparing between the different groups at each visit. The mean retinal thickness at the foveal and parafoveal region is summarized in Table III.

A small decrease in the mean **foveal avascular zone (FAZ) area** was present in each group, however no statistical significance could be attributed to it (Table IV). Comparing between the groups, the FAZ area was much larger in the hyperopic group pre-operatively compared to the myopic or control groups ($p = 0.014$ and $p = 0.003$ respectively). Post-operatively, a much larger relative decrease in the FAZ area was noticed in the hyperopic group compared to the control group ($p = 0.007$), with no statistical significance found comparing the other groups.

Similar results were described in the mean **FAZ perimeter**, where no statistically significant difference was present in the individual groups comparing pre and at the 1 month follow-up, however the FAZ perimeter was much larger in the hyperopic group pre-operatively compared to the myopic or control groups ($p = 0.004$ and $p = 0.002$ respectively).

Table V. Parameters of macular vessels

	G1 pre	G1 post	G2 pre	G2 post	G3 pre	G3 post
Macular vessel density of the superficial plexus						
Minimum	22.900	30.200	18.300	35.100	23.800	31.400
Maximum	37.100	37.000	37.500	39.900	39.600	40.600
Mean	31.340	34.740	32.283	37.275	34.124	37.187
Standard deviation (*n*)	3.762	2.115	5.858	1.533	3.945	2.074
p-value	0.049		0.078		0.002	
Macular vessel length of the superficial plexus						
Minimum	14.100	14.400	11.700	17.300	13.200	16.400
Maximum	17.600	24.600	20.200	19.300	18.400	19.500
Mean	15.780	17.340	17.200	18.363	16.376	17.920
Standard deviation (*n*)	1.040	2.690	2.494	0.638	1.379	0.896
p-value	0.020		0.461		0.001	
Macular vessel density of the deep plexus						
Minimum	34.800	33.700	30.900	36.000	37.800	39.800
Maximum	40.900	41.500	42.200	43.500	43.000	43.500
Mean	38.660	38.530	38.367	40.925	41.229	42.133
Standard deviation (*n*)	1.917	2.491	3.136	2.514	1.476	0.950
p-value	0.846		0.148		0.011	
Macular vessel length of the deep plexus						
Minimum	18.300	17.100	19.100	18.800	18.300	18.900
Maximum	21.100	24.500	23.000	21.300	21.200	20.900
Mean	19.370	19.270	20.533	20.213	19.465	19.967
Standard deviation (*n*)	0.982	2.120	1.226	0.785	0.648	0.603
p-value	0.557		0.641		0.025	

Post-operatively, a much larger relative decrease in the FAZ perimeter was noticed in the hyperopic group compared to the control group ($p = 0.008$), with no statistical significance found comparing the other groups .

No significant difference was noticed in relation to FAZ circularity comparing in the groups pre and post-operatively or between the separate groups. The FAZ parameters are summarized in Table IV.

There was a significant increase in the **vessel density** of the superficial plexus of the macular region in groups 1 and 3 ($p = 0.049$ and $p = 0.002$ respectively; Table V).Comparing between the groups, no significant difference was noticed pre-operatively, yet at the 1 month follow up, group 1 showed a significantly smaller increase in the macular vessel density of the superficial plexus compared to group 2, and a larger increase in vessel density compared to group 3 ($p = 0.011$ and $p = 0.003$ respectively).

There was a significant increase in the mean vessel length of the macular region in groups 1 and 3 ($p = 0.02$ and $p = 0.001$ respectively; Table V). Pre-operatively, comparing between the groups, group 1 had a significantly smaller mean macular vessel length in comparison to group 2 ($p = 0.03$), with no significant difference present between the other groups. At the 1 month follow up, group 1 showed a larger relative increase in the macular vessel length of the superficial plexus compared to groups 2 and 3 ($p = 0.028$ and $p = 0.046$ respectively), with no difference found in the comparison between the other groups.

In the deep plexus, macular vessel density increased significantly in group 3 ($p = 0.011$), but no statistically relevant changes were present in the other groups. A comparison between the groups revealed a substantially smaller deep plexus vessel density pre-operatively in group 1 and 2 compared to group 3 ($p = 0.001$ and $p = 0.007$ respectively). Post-operatively, the only significant difference between the groups was between group 1 and 3 ($p = 0.0001$; Table V).

Similarly to deep plexus vessels density, deep plexus mean macular vessel length increased significantly in group 3 ($p = 0.025$), however no significant differences were noticed in the other groups pre and post-operatively or between the separate groups (Table V).

Changes in the optic disc area size in the groups and between the groups were found to be statistically insignificant (all $p > 0.05$; Table VI).

Table VI. Parameters of the optic disc

	Optic disc area					
	G1 pre	G1 post	G2 pre	G2 post	G3 pre	G3 post
Minimum	1.680	1.600	1.050	0.950	1.670	1.410
Maximum	2.530	2.700	3.370	5.840	2.560	2.510
Mean	2.191	2.224	2.298	2.299	2.124	2.047
Standard deviation (*n*)	0.272	0.328	0.626	1.355	0.294	0.306
p-value	0.069		0.652		0.461	
Optic disc rim size						
Minimum	1.160	1.440	0.450	0.360	0.540	0.850
Maximum	2.530	2.700	3.150	2.790	2.160	1.970
Mean	1.864	1.912	1.496	1.151	1.391	1.383
Standard deviation (*n*)	0.456	0.398	0.813	0.657	0.406	0.321
p-value	0.313		0.164		0.820	
Cup/Disc ratio						
Minimum	0.000	0.000	0.000	0.000	0.000	0.000
Maximum	0.310	0.240	0.790	0.940	0.750	0.740
Mean	0.158	0.151	0.398	0.386	0.326	0.308
Standard deviation (*n*)	0.136	0.101	0.270	0.295	0.217	0.226
p-value	0.054		0.910		0.053	

No significant difference was found in the optic disc rim size when comparing pre and post-operatively in the 3 groups ($p = 0.313$, $p = 0.164$, $p = 0.820$ respectively; Table VI). Group 1 was found to have a substantially larger mean optic disc rim area pre-operatively compared to group 2 and group 3 ($p = 0.033$ and $p = 0.022$ respectively). At the 1 month follow up visit, group 1 showed a mild increase in the disc rim area compared to the substantial decrease in disc rim area in group 2, and the mild decrease in disc rim area reported in group 3 ($p = 0.004$ and $p = 0.003$ respectively).

Cup-to-disc ratio (C/D ratio) changes in the groups were found to be statistically insignificant (all $p > 0.05$; Table VI), however, group 1 had a noticeably lower C/D ratio pre-operatively compared to group 3 ($p = 0.035$). Comparison between the other groups pre and post-operatively yielded no statistically relevant results.

The retinal nerve fiber layer was shown to thicken post-operatively in all three groups, although the increase in thickness was only statistically significant in the hyperopic patient group ($p = 0.001$; Table VII). Preoperatively, the **myopic** group had a much thinner mean RNFL thickness compared to the hyperopic group ($p = 0.004$) and the normo-axial group ($p = 0.010$). Post-operatively, the RNFL of the **myopic** group was still the thinnest out of the three groups, although that difference was only statistically significant when comparing the myopic group to the hyperopic group ($p = 0.006$).

Radial peripapillary capillary (RPC) density was found to increase significantly in group 2 and group 3 after the surgery ($p = 0.004$ and $p = 0.001$ respectively; Table VII). Group 3 had a significantly larger increase in RPC density post operatively compared to group 1 ($p = 0.012$), with other comparisons between the groups showing no statistical significance.

Radial peripapillary capillary length has noticeably increased in group 3 ($p < 0.002$), with no other significant changes in the other groups (Table VII). Comparing between the separate groups, there was a significantly smaller increase in RPC length in group 2 compared to group 3 ($p = 0.003$), with the rest of the comparisons between the group showing no statistically significant changes.

DISCUSSION

In this study, the changes in retinal vascularization at the macular region post cataract surgery were studied among patients with varying ocular axial lengths. OCT Angiography has been used in a number of studies to assess retinal microvasculature in the variable axial lengths [23, 24] and in the cataractous population [25], however, retinal vascularization was never assessed in a common study group, as cataractous eyes are often excluded in studies of axial length, and usually only normo-axial patients are included in studies of cataractous lenses.

Visual acuity has improved in all three study groups, with a significantly lower starting BCDVA present in the hyperopic and myopic patient groups compared to the control group. This significant BCDVA difference between the axial extremes and the control groups persisted post-operatively, as was expected. There was no significant difference in the decrease of IOPs between all the examined groups.

Table VII. RNFL thickness and RPC parameters

	G1 pre	G1 post	G2 pre	G2 post	G3 pre	G3 post
Retinal nerve fiber layer (RNFL) thickness						
Minimum	88.000	91.000	31.000	36.000	75.000	76.000
Maximum	107.000	108.000	95.000	99.000	117.000	119.000
Mean	99.286	101.667	74.714	75.400	95.000	96.714
Standard deviation (*n*)	6.474	4.967	20.575	23.329	10.710	10.912
p-value	0.001		0.188		0.066	
Radial peripapillary capillary (RPC) density						
Minimum	26.733	26.967	27.967	32.167	28.000	33.500
Maximum	37.400	37.767	36.800	36.833	38.900	40.767
Mean	32.880	33.393	33.172	35.093	33.024	36.602
Standard deviation (*n*)	3.081	2.858	2.122	1.690	3.176	2.421
p-value	0.508		0.004		0.001	
Radial peripapillary capillary (RPC) length						
Minimum	15.367	16.167	14.967	16.467	15.000	17.767
Maximum	18.867	20.233	24.033	26.967	20.567	21.133
Mean	17.715	17.943	18.717	19.474	17.476	19.333
Standard deviation (*n*)	1.015	1.152	2.261	2.856	1.458	0.974
p-value	0.820		0.074		0.002	

A decrease in the mean macular volume was noticed in the normo-axial patient group. Post-operatively, the mean macular volume was much larger in the hyperopic and myopic groups compared to the normo-axial group. This phenomenon requires further studies, as its cause is not clear.

Mean retinal thickness at the foveal region was shown to decrease in the control group, with no other statistically significant difference noticed in and between the groups. Similarly, no statistically significant differences were noticeable at the parafoveal region.

Hyperopic patients were recorded to have a significantly larger FAZ area and perimeter pre-operatively, compared to myopic or normo-axial patients, and demonstrated a substantially greater relative decrease in the FAZ area and perimeter after the surgery compared to the other groups. Although the relative difference in FAZ area and perimeter between the hyperopic and myopic groups was not maintained significant post-operatively ($p = 0.051$ and $p = 0.064$ respectively), a trend can be seen, and the statistical insignificance could be attributed to the small patient sample size. No statistically significant difference could be attributed to the changes in FAZ circularity of the three patient groups.

All three study groups demonstrated a significant increase in macular vessel density at the level of the superficial plexus, with the myopic group exhibiting the largest relative increase, followed by the hyperopic and lastly normo-axial patient group. Despite the fact that the increase in the myopic group was not statistically significant ($p = 0.078$), a trend could be seen as the increase was in accordance with the other patient groups, and the statistical insignificance could be attributed to the small number of patients in the myopic group. Pre-operatively, the differences in vascular density at the superficial plexus between the groups were statistically insignificant, however, at the 1 month follow up, the hyperopic group had a noticeably lower vascular density at the level of the superficial plexus compared to the myopic and hyperopic group. The reason for this effect is not clear.

Hyperopic patients had significantly shorter vessels at the superficial macular plexus pre-operatively compared to their axial counterpart, the myopic patient group. This could simply be a matter of axial length, as, if the axial length of the eyeball is shorter, so is the collective vessel length. Vessel length increased in all three groups, but that increase was relatively larger in hyperopic patients compared to myopic and normo-axial patients. Although the increase in the myopic group is not of statistical significance, a trend could be noticed as all three groups presented an increase in vessel length and density at the level of the superficial plexus, and therefore the statistical insignificance could be due to the small patient sample size. A possible explanation is that the device evaluates the mean length of all vessels it can detect in the examined area, post-operatively the vessel density increased which suggests that the vessel width increased and therefore that the device could detect more vessels, which showed as an increase of the mean vessel length. This strongly suggests that there was an increase in the retinal perfusion post-operatively.

At the level of the deep plexus, hyperopic and myopic patients possessed a significantly lower macular vessel density

compared to normo-axial individuals at baseline. This suggests that both extremes have changes in the level of the deep plexus. The gap in deep plexus vascular density between the hyperopic and normo-axial patients was maintained at the 1 month follow up as the hyperopic group didn't show a statistically significant change whereas the normo-axial eyes had increased vessel density. This suggests that both very short and very long eyes have a worse retinal micro-vascularity than average-axial length eyes. It's possible that the retinal vessel density in hyperopic eyes were more crowded on the level of the optic disc and this influenced the lack of their density change postoperatively. The association between high myopia, hyperopia, and decreased vascular density in the superficial and deep macular layers is described in literature [30, 38], and supports our findings. Macular vessel length at the level of the deep plexus was found to increase in the control group, although no other statistically significant changes were present when comparing in and between the groups.

Changes in the optic disc area showed no statistically significant differences in and between the groups, however, the disc rim area was noticeably larger in the hyperopic group preoperatively compared to the myopic and normo-axial patient groups. This statistically significant difference was also present at the 1 month follow up, with the hyperopic group continuing to have the largest rim area out of the three groups.The cup-to-disc ratio has decreased in the hyperopic and normo-axial groups in a statistically insignificant manner ($p = 0.054$ and $p = 0.053$), yet this could be merely due to the small patient sample size. Hyperopic eyes also possessed a lower C/D ratio preoperatively compared to normo-axial and myopic eyes. Although the comparison of the hyperopic to myopic group was statistically insignificant ($p = 0.055$), it suits the statistically significant comparison in disc rim area size, and thus fits a trend. The lower ratio could be due to the hyperopic group having a smaller cup, which influenced the C/D ratio.

All three study groups showed a noticeable increase in retinal nerve fiber layer (RNFL) thickness, which although was the only statistically significant in the hyperopic group, fits the current literature [26] supporting the increase in RNFL thickness, and could simply be attributed to the small sample size. The myopic group had a thinner RNFL compared to the other groups both pre and post-operatively, with that difference being only statistically insignificant when compared to the normo-axial group post-operatively, an insignificance which could be attributed to the small patient sample size. High axial length eyes are strongly associated with a thinner RNFL [27]. The increase in RNFL thickness could be simply due to falsely low measurements, as improved signal transmission and reflection from the retina after removal of the cataract reveal a more accurate assessment [28].

Myopic and normo-axial eyes had a significant improvement in radial peripapillary capillary density, with that increase being smaller in myopic eyes. No statistically significant difference was present between the groups pre-operatively, but the normo-axial group had a markedly increased RPC density compared to the hyperopic group post-operatively. Radial peripapillary capillary length showed a similar rise to the RPC density, with normo-axial eyes improving significantly. Myopic eyes also showed a mild increase in RPC length ($p = 0.074$), which although was statistically insignificant, is nonetheless supported by the increased RPC density detected in the group, and therefore could be attributed to the small patient sample size. The increase was milder in eyes of higher axial length compared to normo-axial eyes ($p = 0.003$).The smaller improvement of peripapillary capillary density in the myopic group compared to the normo-axial group could be due to the degenerative changes myopic eyes often undergo, more specifically retinal thinning and peripapillary atrophy [29].

Early studies using fluorescein angiography were very limited in the number of visible capillaries, with visibility decreasing tremendously along the edge of the foveal avascular area (FAZ), resulting in detection of only 40% of capillaries located further than 900 μm from the FAZ. In addition, only 43% of the smaller size capillaries (ranging from 4 to 5 μm) were detected, suggesting that fluorescein angiography capillary visibility is dependent on the retinal depth and capillary size [30]. Iafe *et al*. [31] demonstrated that mean capillary density, in both the inner and outer capillary plexuses, decreases with the patients age, while the FAZ increases with the patients age.

The foveal pit and FAZ have been studied thoroughly in relation to their role and function in vision, with early reports using fluorescein angiography to define their size and shape. Nowadays however, the incorporation of OCT and OCT devices into the studying of the eye has provided an extraordinary new approach to observe these retinal landmarks. A study done using an adaptive optics scanning laser ophthalmoscope (AOSLO) recorded FAZ areas ranging from 0.05 to 1.05 mm^2 as well as foveal pit volumes ranging from 0.022 to 0.190 mm^3, with significant correlation between the FAZ and foveal pit area, depth, and volume [32]. Multiple OCTA studies reported similar results, with additional data comparing between the average superficial and deep FAZ layers having a mean area of 0.24 mm^2 and 0.38 mm^2 respectively, a 0.14 mm^2 difference [33]. With regards to high myopia, an inverse correlation was found between the thickness of the retina and the size of the FAZ, and thus patients with higher axial length which tend to have a thinner retina, presented a larger FAZ [33].

Ocular vascular alterations have been reported in myopic patients in numerous studies. Histological evaluation of enucleated globes with high axial length revealed major thinning of the choroid, choriocapillary and retinal pigment epithelium loss. Scleral thinning would begin in proximity to the equator, with the thinnest scleral area being the posterior pole [34]. Although these findings may seem promising, observations acquired from non-living myopic patients may be tainted with post-mortem changes, and thus an in vivo approach was necessary. One of the first methods used to observe the retinal microcirculation in live myopic patients was fluorescein angiography, performed by Avetisov *et al.* [35] in

a group of myopic patients. They observed decreased retinal blood flow in the group of patients with myopia compared to the control group. Alongside the delay of retinal blood flow, myopic eyes also had smaller vessel diameter, apparent in both retinal arterioles and venules, possibly due to the degenerative changes that myopic eyes undergo, such as retinal thinning and peripapillary and chorioretinal atrophy [36–38]. An imaging technique developed more recently, optical coherence tomography angiography (OCTA), was used in a study done by Hua *et al.* [39] comparing moderate and high myopia patients to a group of normal axial length patients. They noticed an association between decreased vascular density in the superficial and deep macular layers and myopic eyes, more specifically longer axial length and degree of myopia. Additionally, the thickness of the ganglion cell complex (composed of the 3 inner retinal layers, inner plexiform, ganglion cell, and nerve fiber layers) was associated with the macular vascular density, possibly shedding light on the reason behind the decreased vascularity; a lower ganglion cell count in the ganglion cell complex would require less oxygen for its normal function, perfusion would diminish, and ultimately result in decreased macular vascularity.

With the limited research on the topic of hyperopia, even less research is done on the long term effects of the condition on the retinal vascularity. Studies performed using an OCT device have reported that axial length has an effect on peripapillary retinal nerve fiber layer thickness (RNFL), with a considerable difference between myopic, emmetropic, and hyperopic eyes [40], however, the above-mentioned difference is nullified once correction for magnification error is applied through the modified Bennet formula [41]. A study done on a group of children with hyperopic anisometropic amblyopia has found that the study eyes had a significantly lower foveal, superficial capillary plexus and deep capillary plexus vascular density, in addition to an increased central macular thickness [42]. Whether this effect is caused by the amblyopia or the increased axial length is not conclusive, however Li *et al.* [23] described a negative association between retinal vascularization and axial length in a group of myopic patients, thus supporting the latter variable.

Overall, a number of reasons could be the cause of the changes in retinal vasculature. A decrease in IOP pressure was reported to increase fundus pulsation amplitude by Weigert *et al.* [43], however no significant change in IOP was detected in our study. Another possibility is post-operative inflammation, where proinflammatory cytokines rise post-operatively, causing vasodilation and damage to the blood-retinal barrier [44]. An increase in light exposure after the opaque lens removal might also have an effect on the retinal vascularity and metabolic demand, however no clear consensus is present on the matter [45]. Whether these factors are present in varying degrees in the radical axial extremes is questionable.

The limitations of the study include: a small number of participating patients (resulting from the meticulous exclusion criteria, low prevalence of high myopia and hyperopia, and the abrupt interruption of data collection caused by the preemptive suspension of all scheduled cataract surgeries during the COVID-19 pandemic), a relatively low reliability factor of angio-OCT considered sufficient for reliable assessment of vascular structures (caused by a limited number of patients), high BCVA difference between groups suggesting differences in the transparency of optical centers (which could potentially influence the difference in visualization), as well as short time between the surgery and postoperative measurements (which could have a possible effect of postoperative inflammatory reaction on the evaluation of morphological and vascular parameters).

Nevertheless, this study examined numerous patients from the neglected and under-researched axial extremes, reporting differences in improvement post cataract removal. Because of the above-mentioned limitations, we assume that this study is preliminary requires further investigation. It is also our recommendation that future studies should include a larger number of patients, so that diagnostic and prognostic parameters could be calculated with a higher reliability.

CONCLUSIONS

This study reveals retinal microvascular changes in highly myopic and hyperopic eyes, which correlates with axial length elongation and shortening respectively. Both axial length extremes presented a worse retinal vascular architecture, but mostly improved after the phacoemulsification surgery in terms of vascularity, which was similar to the normo-axial patients.

DISCLOSURE

Authors declare no conflict of interest.

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