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A novel index for predicting macular thickening after cataract surgery

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Abstract. – PURPOSE: In this study, we tried to investigate weather or not the preoperative anterior chamber depth, the lens thickness (LT) and the relation between these variables by the ratio (K) of the distance from the corneal peak to the posterior side of the lens (A) (K = A/LT) could be predictive for a surgically induced foveal thickening following uneventful cataract surgery in normal, emmetropic eyes.

PATIENTS AND METHODS: A total amount of 45 eyes, 25 females and 20 males, were enrolled in this study and underwent uncomplicated phacoemulsification under topical anesthesia. A complete ophthalmological examination was performed preoperatively, including refraction, best corrected visual acuity, slit-lamp examination, biometry and optical coherence tomography of both eyes. These examinations, with the exception of the biometric examination, were repeated one day, one week and four weeks after surgery.

RESULTS: The K ratio was positively correlated with the macular thickness changes after cataract surgery. The Pearson correlation analysis of K ratio and foveal tickness changes was 0.792 (y = 36.457x – 52.558, R2 = 0.6266).

CONCLUSIONS: A novel ratio that incorporates preoperative ocular parameters has been described. It could be easily measured in a clinical setting, and appears to be strongly predictive for macular thickening following cataract surgery. Of course, further studies enrolling a larger amount of patients are necessary in order to confirm these preliminary data.

Key Words:
Macular thickening, Cataract surgery, Phacoemulsification, Optical Coherence Tomography (OCT), Visual acuity.

Introduction

Foveal thickness changes after cataract surgery have already been reported[1]. However, at this time, it's not completely understood what may influence the postoperative macular thickening: thus the macular edema (ME) remains a major cause of visual decrease after cataract surgery[2]. The reported percentages regarding incidence of angiographic ME (3-70%) or clinically relevant ME (0-22%) vary in different papers, depending on the technique employed for cataract surgery, the diagnostic method utilized and the underlying comorbidities[3,4].

In the last five years, Optical Coherence Tomography (OCT) imaging of the retina has been established as a non-invasive alternative to fluorescein angiography (FAG) for the diagnosis of macular pathologies[5]. In the past, the comparability of OCT-measured macular changes after cataract surgery was limited, and therefore, the results were often contradictory. The variability in these results was mainly due to different generations of OCT sets, to different analysis parameters and probably to high incidence of measurement artefacts[6-8].

Thanks to the high resolution of the new Stratus OCT™ and its adapted software for accurate analysis of the results, subtle changes in macular thickness can now be detected by a standardized protocol[9,10].

Notwithstanding these influences on the measured values, the OCT-based macular thickness evaluation after cataract surgery is increasingly quoted to quantify postoperative outcomes of ocular treatments[1,3,11].

However, the relation between anterior chamber depth (ACD), lens thickness (LT) and macular thickness (MT) after cataract extraction has not been well described at this time.

In this study, we tried to investigate weather or not the preoperative anterior chamber depth, the lens thickness (LT) and the relation between these variables by the ratio (K) of the distance from the corneal peak to the posterior side of the

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lens (A) (K=A/LT) could be predictive for a surgically induced foveal thickening following uneventful cataract surgery in normal, emmetropic eyes.

Materials and Methods

A total amount of 45 patients (mean age 72.9±8.1 years; 25 females and 20 males), were enrolled in the study and underwent uncomplicated phacoemulsification under topical anesthesia in one of their eyes. All subjects were caucasian Italians. 28 contralateral eyes were phakic and 17 contralateral eyes were pseudophakic with caratact surgery performed more than 12 months prior to recruitment. Patients were eligible when media opacity due to cataract was moderate and OCT examination could be performed in both eyes.

Exclusion criteria were the following: media opacification for other reasons than cataract, retinal pathologies, glaucoma, uveitis, amblyopia, age-related macular degeneration, diabetes mellitus or other systemic diseases that could affect the eye. More than 45% of the scheduled patients were not recruited because of these strict criteria.

The study was approved by the Institutional Ethics Committee and patients were enrolled in the study if listed for elective cataract surgery and intraocular lens (IOL) implantation. After its full explanation, all patients had to sign a written informed consent to be enrolled in the study. The study complied with the Declaration of Helsinki.

Preoperative Examination

All patients underwent preoperatively to a complete ophthalmologic examination, including refraction, best-corrected visual acuity (BCVA) test, slit-lamp examination, biometry and OCT of both eyes. These examinations, with the exception of the biometric examination, were repeated one day, one week and four weeks after surgery.

Bilateral biometric data such as axial length and ACD were obtained preoperatively by means of IOLMaster 500® (Zeiss-Meditec, Jena, Germany) and documented for statistical analysis.

The IOLMaster 500® uses the principle of partial coherence interferometry (PCI) to measure the axial length of the globe whereas the ACD is measured along the visual axis from the corneal epithelium to the anterior surface of the crystalline lens by optical principles using a non-PCI method.

The IOLMaster 500® takes five simultaneous ACD measurements and the mean of these five readings is used only. Subjects were asked to blink just before measurements were taken in order to spread an optically smooth tear film over the cornea.

The A-scan ultrasound (US) was used to measure the LT after ocular topical anesthesia was obtained by means of 0.4% oxybuprocaine eye drops (Benoxinato Cloridrato Intes, Alfa Intes, Casoria, Naples, Italy) instilled in supine subjects.

Two ophthalmic technicians performed the measurements independently. The A-scan US measurement was made with a handheld 10 MHz probe with sound velocity setting of 1641 m/s for the lens. The patients were asked to look at a blinking light located into the ultrasound probe that was gently placed on the central cornea, using the pupil as a reference for a correct position. The device performed automatically 10 consecutive measurements of axial length, ACD, LT, and vitreous chamber depth. A special care was taken in order to ensure that all measurements were on-axis and without indentation. The readings were obtained when a satisfactory scan image was achieved. A good image was defined as one with well-defined echoes corresponding to the cornea, the anterior and posterior poles of the crystalline lens, and the posterior wall of the eye. The LT measurements were based on the average of 10 consecutive measurements. The measurement series were repeated if the standard error (SE) of the 10 programmed consecutive measurements was > 0.12 mm. If three consecutive measurements were not able to achieve SE ≤ 0.12 mm, the LT was considered unmeasurable.

Optical coherence tomograms were acquired through dilated pupils by using the OCT3 (Stratus OCT™, Carl Zeiss Ophthalmic Systems, Inc. Hymphrey Division, Dublin, CA, USA). The standard fast macular thickness scan protocol was selected to obtain six consecutive macular scans focused on the fovea and equally spaced 30° apart. To centre the scan, the patient's fixation and the operator's recognition of retinal landmarks were used. In all scans, images with a signal strength (OCT-SS) below 5 have not been used for analysis. To determine foveal thickness, the OCT-images were analysed with the Stratus OCT-software (Version 4.0). Mean minimal foveal thickness was defined as the average thickness at the intersection of six radial scans (six data points).

Surgical Technique

During three days before surgery, all patients received an identical preoperative topical treatment with antibiotic (Exocin®, Allergan, Irvine, CA, USA) eye drops, three times daily in both eyes.

Mydriasis was then obtained one hour before surgery by means of diclofenac 0.1% and tropicamide 1% eye drops, every 20 minutes for three times. Topical anesthesia was performed shortly before surgery by using a solution of lidocaine 4% administered in the inferior fornix of the lying patients for three times, two minutes apart. Additionally 25 units of 2% lidocaine was injected in the anterior chamber through the side-port before filling it with Viscoat®. No systemic sedatives were used.

All patients underwent clear corneal phacoemulsification performed by the same experienced surgeon (MC) through the following steps: 1.2 mm side port incision, anterior chamber filling with Viscoat® (Alcon Laboratories, Fort Worth, TX, USA), 2.75 mm superior or temporal clear corneal incision, continuous circular capsulorexis, hydrodissection with balanced saline solution (BSS), cataract extraction by "stop and chop" endocapsular phacoemulsification technique with the Alcon Series 20000 Legacy® Phaco-Emulsifier Aspirator (Alcon Laboratories, Fort Worth, TX, USA) equipped with a flared regular 30° tip, enlargement of the corneal incision to 4.1 mm, anterior chamber filling with IAL-F® (1.8% sodium hyaluronate, Fidia Farmaceutici SpA, Abano Terme (PD), Italy), Acrisof® SA60AT (Alcon Laboratories, Fort Worth, TX, USA) foldable IOL implantation in the capsular bag with forceps, removal of the viscoelastic solution and filling of the anterior chamber with BSS.

After surgery, all patients received the same standard steroid/antibiotic eye drops (Doricum, Laboratoires Théa, Clermont-Ferrand, France) four times daily for the first week, thereafter tapered to end in three weeks.

Statistical Analysis

Sample size calculation and statistical analysis were performed by means of two standard software programs (BIAS 4.0, Ackermann, Frankfurt, Germany; SPSS 11 for MacOS-X, SPSS Inc., Chicago, IL, USA). The sample size was calculated for a significance level of 0.05 and a power of 0.8[12]. The intraindividual difference of OCT foveal thickness of operated eye vs contralateral eye was calculated in order to reduce the variability of retinal thickness measurements. The parametrical Student's *t*-test was performed on this data to detect postoperative changes in macular thickness ($p < 0.05$). Wilcoxon test, Mann-Whitney U-test and Kruskal-Wallis test were used to evaluate non-parametric distributed values such as the OCT-SS and the LogMAR-BCVA. Mann-Whitney U-test, linear regression analysis and Spearman correlation analysis were carried out to compare BCVA, OCT-SS and biometric data with OCT-measured macular thickness. Significance was assessed at the 5% level.

Results

Baseline and demographic characteristics are summarized in Table I. The mean age of the enrolled patients was 66 years ± 2.2 standard deviation (SD).

Mean LT was 4.3 mm (SD ± 0.51), mean distance from the corneal peak to the posterior side of the lens was 7.52 mm (SD ± 0.54) and mean ACD was 3.23 mm (SD ± 0.35). A novel ratio called K and based on the distance from the corneal peak (A) to the posterior side of the lens and the LT (K=A/LT) was evaluated in all patients and its mean value was 1.76 ± 0.13 SD.

The mean preoperative BCVA was 0.5 logMar whereas it increased to 0.0 logMar four weeks after surgery (Table II).

The mean OCT-measured foveal thickness was 169.3 ± 25.55 micron (preoperatively), 170.2 ± 28.27 micron (one week after surgery), 181 ± 27.47 micron (four weeks after surgery) ($p = 0.019$). The mean difference between four weeks after surgery and baseline was 11.68 ± 7.75 micron. However, in our study this postoperative foveal thickening did not influence the postoperative visual acuity recovery.

We noted that the retinal thickening was inversely correlated with LT and proportionally associated with deeper ACD although not at a significant level. On the other hand, the K ratio was positively correlated with the increasing macular thickness changes after cataract surgery. The Pearson's correlation between K ratio and foveal tickness changes was 0.792 ($y = 36.457\times - 52.558$, $R^2 = 0.6266$) (Figure 1).

Discussion

The occurrence of subclinical macular edema after uneventful cataract surgery has become an

Table I. Baseline demographic features, pre- and postoperative OCT values.

						Pre op			1 Week			1 Month				
Patients	Lens	Pachy	Acd	A-value	K-Ratio	m_180	m_90	m_t	m_180	m_90	m_t	m_180	m_90	m_t	DIFF	Age
P.A.	3.57	538	3.57	7.14	2.000	169.0	162.0	165.5	185.0	158.0	171.5	175.0	189.0	194.0	28.5	76
D.A.	4.27	558	3.41	7.68	1.799	183.0	171.0	177.0	190.3	179.7	185.0	171.3	186.3	191.0	14.0	73
M.P.	4.53	522	3.37	7.9	1.744	140.0	158.0	149.0	181.0	177.7	179.3	155.3	163.0	159.2	10.2	70
V.E.	5.09	565	3.02	8.11	1.593	199.0	205.0	202.0	183.0	188.0	185.5	196.0	216.0	207.0	5.0	86
G.D.	4.61	539	3.21	7.82	1.696	162.0	131.0	146.5	145.5	134.0	139.8	140.0	156.0	155.0	8.5	53
S.F.	4.47	567	3.16	7.63	1.707	165.0	157.0	161.0	165.0	186.0	175.5	162.0	187.0	174.5	13.5	71
P.E.	4.69	543	2.98	7.67	1.635	158.0	167.5	162.8	164.3	200.5	182.4	173.0	171.3	170.0	7.3	70
B.F.	3.86	537	3.15	7.01	1.816	155.0	142.0	148.5	168.0	144.0	156.0	143.3	146.7	160.0	11.5	79
C.G.	4.26	620	3.55	7.81	1.833	190.0	195.0	192.5	180.0	193.0	186.5	173.7	188.3	210.0	17.5	64
M.A.	4.64	529	2.96	7.6	1.638	138.7	139.0	138.8	159.3	151.3	155.3	152.0	152.0	152.0	13.2	84
M.R.	4.64	527	3.04	7.68	1.655	162.0	205.0	183.5	164.3	189.7	177.0	162.3	156.7	195.0	11.5	70
L.D.B.	3.76	538	3.03	6.79	1.806	162.7	172.0	167.3	226.7	259.0	242.8	182.7	187.7	180.0	12.7	73
D.R.	2.99	555	2.67	5.66	1.893	199.0	202.0	200.5	203.7	202.0	202.8	213.0	209.3	222.0	21.5	81
C.G.	3.76	535	3.17	6.93	1.843	142.0	162.7	152.3	143.3	170.7	157.0	147.3	164.0	169.0	16.7	77
G.U.	3.76	473	2.98	6.74	1.793	163.7	184.0	173.8	134.7	155.3	145.0	183.3	136.7	185.0	11.2	78
A.L.	4.78	471	3.16	7.94	1.661	179.7	186.3	183.0	183.3	175.7	179.5	175.7	192.0	190.0	7.0	72
F.A.	3.86	526	3.38	7.24	1.876	165.5	197.0	181.3	159.3	160.0	159.7	189.3	185.7	197.0	15.8	80
G.I.	3.93	535	3.39	7.32	1.863	130.0	180.0	155.0	132.0	179.7	155.8	161.0	157.3	166.0	11.0	71
B.K.	4.01	553	3.5	7.51	1.873	216.0	207.7	211.8	210.7	220.7	215.7	231.3	236.3	233.8	22.0	59
T.M.	4.67	581	3.83	8.5	1.820	158.7	162.0	160.3	158.3	169.3	163.8	166.0	160.0	177.0	16.7	72
S.M.	4.68	546	2.67	7.35	1.571	256.0	207.0	231.5	279.7	217.5	248.6	281.0	277.0	235.0	3.5	78
D.R.	4.56	515	2.94	7.5	1.645	193.0	209.0	201.0	189.0	206.5	197.8	201.0	198.3	208.0	7.0	68
V.A.	4.62	530	3.12	7.74	1.675	166.0	173.7	169.8	162.7	180.0	171.3	166.7	174.3	175.0	5.2	74
C.E.	4.09	547	4.17	8.26	2.020	185.0	188.5	186.8	147.3	170.7	159.0	193.0	195.0	209.0	22.3	75
E.R.	4.26	487	3.34	7.6	1.784	185.0	187.0	186.0	161.7	158.7	160.2	156.7	160.0	192.0	6.0	77
P.M.	5.45	502	2.44	7.89	1.448	163.0	167.7	165.3	170.0	185.0	177.5	177.0	172.7	174.8	9.5	76

LENS: lens thickness; PACHY: corneal pachymetry; ACD: anterior chamber depth; A-VALUE: distance from the corneal peak to the posterior side of the lens; K-RATIO: ratio of the distance from the corneal peak to the posterior side of lens and lens thickness; PRE OP: pre-operative OCT scan values; DIFF: difference from baseline.

Table II. Pre- and postoperative visual acuity (VA. logMar) for each patient.

Patients	VA PRE	VA POST	Patients	VA Pre	VA Post
A.L.	0.4	0.0	L.D.B.	0.4	0.0
B.C.	0.4	0.0	L.F.	0.4	0.0
B.F.	0.4	0.0	L.M.	0.4	0.1
B.K.	0.4	0.0	L.M.	0.4	0.1
B.M.	0.4	0.0	M.A.	0.4	0.1
C.A.	0.4	0.0	M.D.	0.4	0.1
C.E.	0.6	0.2	M.L.	0.4	0.1
C.G.	0.6	0.0	M.P.	0.3	0.0
C.G.	0.6	0.0	M.R.	0.3	0.0
C.I.	0.6	0.1	N.C.	0.3	0.0
C.T.	0.6	0.1	P.A.	0.3	0.0
D.A.	0.6	0.1	P.A.	0.4	0.1
D.A.	0.6	0.1	P.A.	0.4	0.2
D.P.	0.6	0.1	P.E.	0.4	0.1
D.R.	0.6	0.1	P.E.	0.4	0.0
D.R.	0.6	0.1	P.M.	0.4	0.1
E.R.	0.6	0.1	S.F.	0.4	0.2
F.A.	0.4	0.0	S.M.	0.3	0.0
G.A.	0.4	0.0	S.O.	0.3	0.0
G.D.	0.4	0.0	T.M.	0.3	0.0
G.I.	0.4	0.0	V.A.	0.3	0.0
G.U.	0.4	0.0	V.E.	0.3	0.0
I.C.	0.4	0.0	Mean	0.5	0.0

issue of safety for this frequent operation since studies have found postoperative angiographic leakage in a high percentage (from 19% up to 88%) of the cases, also reporting that the occurrence of leakage was more evident six weeks after surgery[13-15]. The significant increase of OCT-measured foveal thickness that we found in our operated eyes seems to confirm the high appearance of subclinical alterations involving the macular blood retinal barrier (BRB) during the postoperative period. Other published OCT studies found similar results[1,16,17]. At the same time, our study could not detect a negative impact of these changes on BCVA.

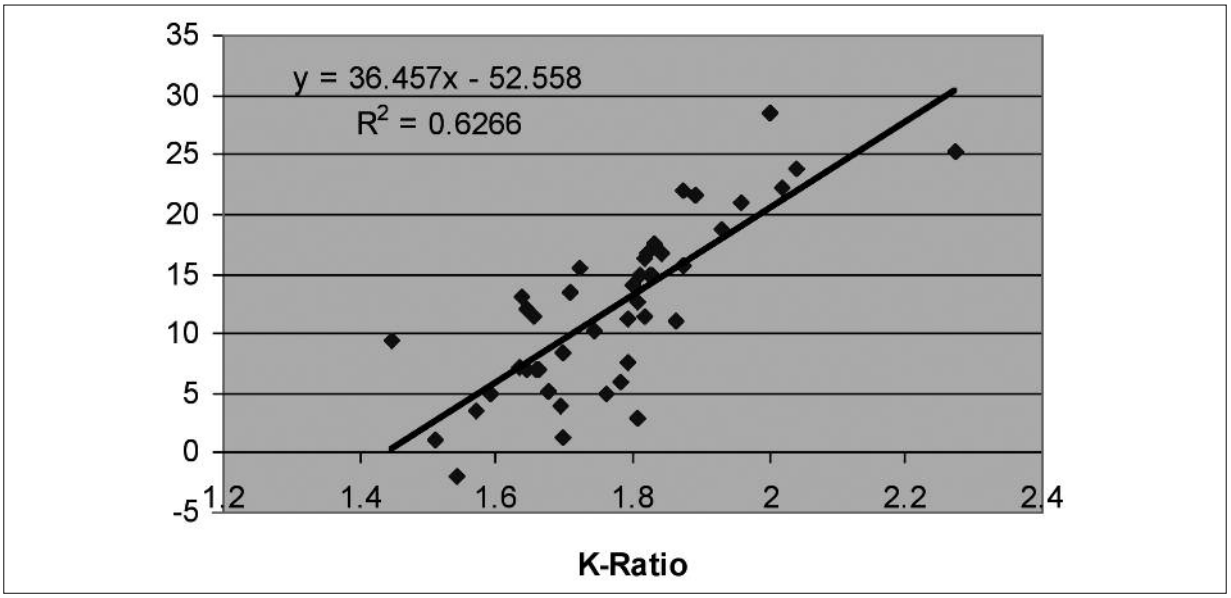

Figure 1. The K ratio was positively correlated with the increasing macular thickness changes after cataract surgery.

Macular thickness can vary relatively in the normal population[18]. Therefore, it's often difficult to define the differences between a subclinical thickening and a foveal edema[19,20]. Given the concept that retinal thickening is a continuous process followed by macular edema, a small increase of macular thickness should be regarded as predictor of pathological changes. However, despite the use of same generation of OCT sets, recent studies displayed heterogeneous results in the measurement of retinal thickness changes after cataract surgery[1,16,17]. Differences in the recruitment criteria could be a reason for these contradictory results.

Moreover, there are conflicting reports regarding the influence of cataract surgery on OCT-measured macular thickness. For example, Van Velthoven et al[21] reported that image quality and retinal thickness measurements were influenced by cataract type (cortical more than nuclear) and concluded that OCT imaging is influenced by cataract that may cause underestimation of retinal thickness. On the other hand, Ching et al observed in a large prospective trial of 131 eyes a decrease in retinal thickness at two, four, eight weeks after surgery in comparison to preoperative measurements[22]. However, this trend has not been observed by other authors.

Furthermore, many parameters should be taken into account by evaluating OCT-measured retinal thickness: circadian fluctuations, pupil size, cataract, mechanical factors, different OCT instruments[23-27]. The influence of these parameters can be significantly reduced by using an intraindividual adjustment with the contralateral eye, as we did in our study, and a Stratus OCT™, an instrument that already demonstrated reproducible measurements of macular thickness[28].

The pathogenetic reasons for a subclinical increase in central foveal thickness should be similar to those leading to the development of a pathological ME: e.g. vitreous mechanical traction and inflammation, intraocular pressure, increased levels of vascular endothelial growth factor and others[25,26]. However, it should be emphasized that all these factors are still not completely understood.

In our study, we found that the retinal thickening was inversely correlated with LT and proportionally associated with deeper ACD although not at a significant level. On the other hand, the K ratio was positively correlated with the increasing macular thickness changes after cataract surgery, suggesting that higher values of the K ratio could theoretically represent an index risk for the possible development of a clinically significant ME.

Conclusions

We describe a novel ratio that incorporates preoperative ocular parameters, which can be easily measured in a clinical setting, and appears to be strongly predictive for retinal thickening following cataract surgery. However, although this index might be useful for the daily clinical practice, further studies enrolling a larger amount of patients and a longer follow up are needed before any firm conclusion can be made. Moreover, some potentially important surgical dynamic parameters such as effective phacoemulsification time, irrigation time and pressure, vacuum, entire surgical duration as well as phaco energy[12] have not been recorded and statistically analysed in this study.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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