Coll. Antropol. **37** (2013) 3: 841–845
Original scientific paper

Macular Thickness after Glaucoma Filtration Surgery

Antonio Sesar[1], Ivan Ćavar[1], Anita Pušić Sesar[1], Mia Zorić Geber[2], Irena Sesar[1], Katia Novak Lauš[2], Zoran Vatavuk[2] and Zdravko Mandić[2]

[1] Clinical Hospital Mostar, Department of Ophthalmology, Mostar, Bosnia and Herzegovina
[2] University of Zagreb, University Hospital Center »Sestre milosrdnice«, Department of Ophthalmology, Zagreb, Croatia

A B S T R A C T

The aim of present study was to analyze early postoperative changes in the macular area using optical coherence tomography (OCT) after uncomplicated glaucoma filtration surgery. This prospective study included 32 patients (34 eyes) with open-angle glaucoma, which underwent trabeculectomy with or without use of mitomycin C. Exclusion criteria were macular edema, uveitis, age-related macular degeneration, blurred optical media, secondary glaucoma and angle-closure glaucoma. All standard clinical examinations were made before surgery, at the 2nd day, 1 week and 1 month after surgery. Tomography of the macula was performed during every examination using Cirrus HD OCT for the analysis of central subfield thickness. Results show that thickening of the macula was slightly higher 1 week and 1 month after operation in comparison with baseline end 2nd day postoperativelly. There was no significant difference in the change of macular thickness in patients who have used topical prostaglandins compared with those who have used other topical medications. Also, there was no difference in macular changes between patients treated with or without mitomycin C. In conclusion, we found a slight subclinical increase in macular thickness after uncomplicated trabeculectomy, for which we considered that was the result in reduction of intraocular pressure after glaucoma surgery. Macular thickening after glaucoma filtering surgery could be a physiological reaction to the stress of the retina caused by a sudden reduction of intraocular pressure and it is the consequence of altered relationship between capillary pressure and interstitial fluid pressure.

***Key words**: macular thickness, glaucoma, trabeculectomy, optical coherence tomography, intaocular pressure, starling forces*

Introduction

Macular edema has been represented as significant cause of visual impairment after cataract surgery and other types of ocular surgical procedures. Cystoid macular edema (CME) often appears after complicated operation, although it is known that it can occur after uncomplicated cataract surgery[1–5]. Improvement of surgical techniques has led to a reduction in the incidence of CME[2,6], and it also reduced a chance for development of macular thickening[7,8]. Optical coherence tomography (OCT) allows us three-dimensional image of the retina at high resolution, provide the insight of the subtle changes that can occur in the macula after cataract surgery and give us possibility of quantitative and qualitative analysis of the macular area. It has been shown that subclinical thickening of the macula can occur after modern cataract surgery[9–11], however the changes are described after femtosecond laser-assisted phacoemulsification[8]. Although many etiological factors are associated with the development of edema, the most accepted point of view is that inflammatory mediators from the anterior chamber diffuse posteriorly into the vitreus causing the leakage from retinal blood vessels[12,13].

Contrary to the development of macular edema after cataract surgery, changes in the macula after glaucoma filtering procedure are not so well described. Ocular hypotony is well known complication after glaucoma surgery, which can lead to a decline in visual acuity in the early postoperative period[14]. Post-trabeculectomy hipotony may be associated with various complications such as

Received for publication July 10, 2013

maculopathy, endophthalmitis, corneal changes, accelerated cataract progression, ciliochoroidal detachment and suprachoroidal hemorrhage[15–18]. Hypotony maculopathy is characterized by optic disc swelling, venous tortuosity and radial chorioretinal folds that can lead to significant visual loss after glaucoma filtering surgery[19,20]. Although ultrasound measurements showed increased thickness and volume of the ocular wall[21], only the usage of OCT provides the insight into the structural changes in macular area after glaucoma filtering surgery[20]. It has been shown that hypotony maculopathy can be characterised with serous macular detachment and CME[22]. Proposed hypothesis is that hypotony causes breakdown of the blood-aqueous barrier, which results in the release of inflammatory mediators[23]. Furthermore, lowering of intraocular pressure after glaucoma surgery may be responsible for the moderate, temporary increase in foveal retinal thickness[24]. Retinal thickening could be followed by decrease in visual acuity in patients with hipotony after filtering procedure[25].

The aim of present study was to analyze early postoperative changes in the macular area after uncomplicated glaucoma filtration surgery in eyes that have not developed hypotony maculopathy.

Materials and Methods

This prospective study was conducted between February 2011 and February 2012 in Clinical Hospital »Sestre milosrdnice«, Zagreb, Croatia. The following inclusion criteria were: 1. fornix-based trabeculectomy with or without use of antimetabolites for open-angle glaucoma, 2. ophthalmoscopically normal retina with adequate fundus visibility. Exclusion criteria were any ocular diseases that can affect the study results such as macular edema, uveitis, age-related macular degeneration, history of previous ocular surgery, intraoperative complications, conditions with blurred optical media, secondary glaucoma and angle-closure glaucoma. The presence of mild diabetic retinopathy without macular edema and early age-related macular degeneration showing drusen did not constitute exclusion criteria. Overall, 43 patients (45 eyes) gave their informed consent prior to inclusion into the study. Development of hipotony maculopathy was the reason for exclusion of 2 eyes from the study. In 6 eyes there were complications (hyphema, corneal edema) that did not allow a high quality imaging by retinal OCT, while 3 patients after surgery have not completed all examinations.

The remaining 32 patients (34 eyes) were operated by the filtering procedure, trabeculectomy with mitomycin C (0.4 mg/ml, applied for 2 minutes) in 18 patients and trabeculectomy without antimetabolites in 16 patients. Preoperatively, 25 patients used topicaly prostaglandins, while only 9 patients used other topical medications in the treatment of glaucoma.

All patients underwent a standard eye examination, including best-corrected visual acuity, intraocular pressure measurement by Goldmann aplanation tonometry, slit lamp biomicroscopy, ophthalmoscopy with 90 diopter lens and measurement of macular thickness by OCT. Examination was performed before surgery, 2nd day, 1 week and 1 month after surgery.

Tomography of the macula was performed during every examination on the Cirrus Spectral-domain, high definition OCT (software version 3.0; Carl Zeiss Meditec, Dublin, CA, USA) through dilated pupils. The calculations were made on the basis of data from analytical program Macular Thickness: Macular Cube 512x128, derived from retinal clip, size 6 x 6 mm, with a focal point in the foveola. Thickness values were obtained from the central field, 1 mm diameter circle (central subfield thickness). We have determined a significant macular thickening as the value of one standard deviation of the mean preoperative thickness, which was 17 μm.

Postoperative treatment included a combination of antibiotics and steroids (Maxitrol, Alcon, Puurs, Belgium), given topically 4 times daily, with dose reduction within one month of surgery.

The results were analysed with statistical programme SPSS 17.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Kolmogorov-Smirnov test was used for the analysis of equality of continuous distributions. For normal distribution, mean and standard deviation were used to present mean value and dispersion measure. Furthermore, in order to compare these variables Repeated measure tests with posthoc LSD test, and Pearson Correlation test for testing correlation between the variables, were used. Chi-square test was used for testing nominal variables. P value less than 0.05 was considered as significant.

Results

Average age of all examinees was 68.5±7.7 years. The youngest patient was 51, and the oldest 84 years of age. In the study participated 20 (58.8%) men and 14 (41.2%) women. Distribution of glaucoma types is presented in Table 1.

Macular thickness changed from the values 248.76± 17.49 before and 248.64±17.97 two days after surgery to the values 253.11±16.64 one week after and 253.38± 16.16 one month after surgery. Results show that thickening of the macula was slightly higher 1 week and 1 month after operation in comparison with baseline end 2 days postoperativelly ($p<0.001$). There were 7 diabetic patients without macular edema, who did not have sig-

TABLE 1.
TYPES OF GLAUCOMA THAT ARE PRESENT IN THE PATIENTS INCLUDED IN THE STUDY

Type of glaucoma	Number of patients (%)
Primary open-angle glaucoma	21 (61.8)
Pseudoexfoliation glaucoma	12 (35.3)
Pigmentary glaucoma	1 (2.9)

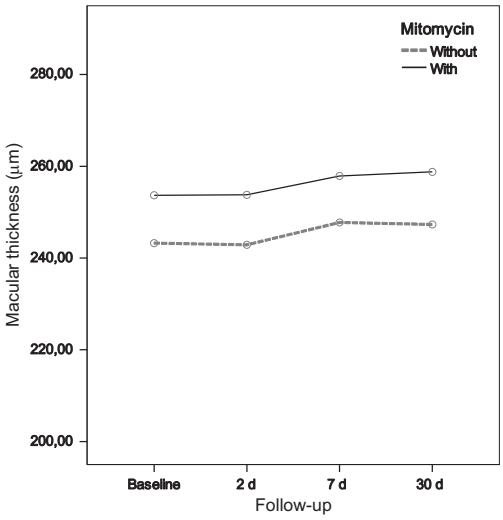

Fig. 1. Follow-up of retinal thickness for patients operated with or without mitomycin C.

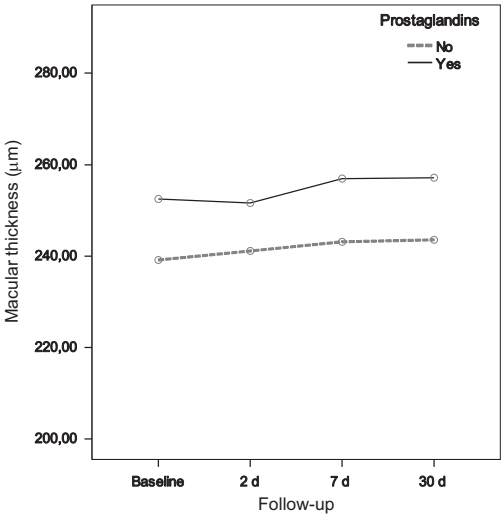

Fig. 2. Follow-up of retinal thickness for patients who preoperatively used topical prostaglandins or other antiglaucomatous medicaments.

nificant variations in macular thickness compared to patients without diabetes (data not shown).

Overall, 18 patients were operated with mitomycin C and 16 patients without use of antimetabolites. There was no significant difference in the change of macular thickness at all time points between these two groups of patients (Figure 1, p=0.852).

Although the group of patients who used prostaglandins to treat glaucoma showed a slight thickening of the macula 1 week postoperatively, there was no statistically significant difference in the change of macular thickness values over the time between the above mentioned two groups of patients (Figure 2, p=0.516).

The correlation between macular thickness, visual acuity and intraocular pressure was analysed. No significant correlation was found between changes of macular

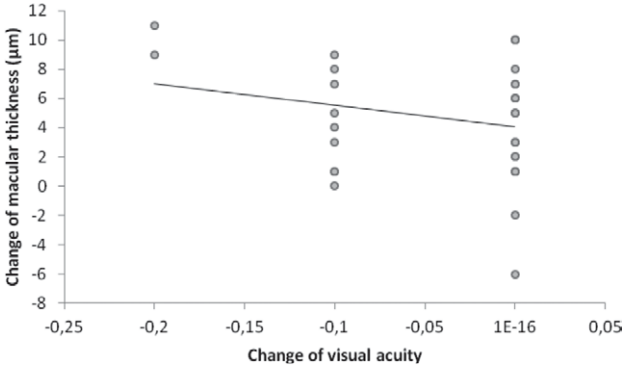

Fig. 3. Correlation between changes of macular thickness and visual acuity.

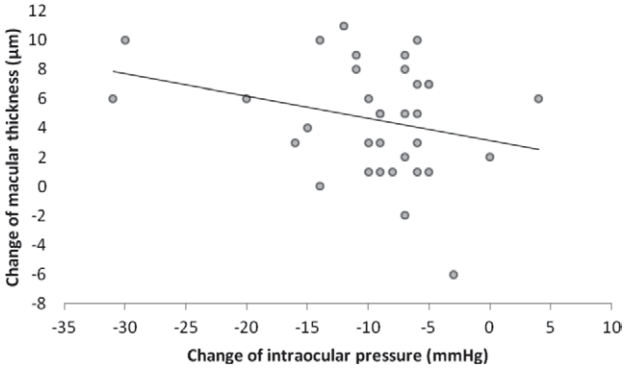

Fig. 4. Correlation between changes of macular thickness and intraocular pressure.

TABLE 2.
PROPORTION OF PATIENTS SHOWING A POSTOPERATIVE INCREASE IN MACULAR THICKNESS

Increase of macular thickness	Number (%) of eyes	
	>17µm compared to baseline	>5% compared to baseline
Yes	2 (5.88)	3 (8.82)
No	32 (94.12)	31 (91.18)
Total	34 (100.0)	34 (100.0)

thickness and visual acuity (Figure 3, P=0.179), as well as between changes of macular thickness and intraocular pressure (Figure 4, P=0.116).

The proportion of patients showing an increase in macular thickness 17 µm or increase 5% in comparison to baseline is shown in Table 2. Significant thickening 17 µm was present in only 2 patients (5.88%), while thickening 5% was recorded in 3 (8.82%) patients.

Discussion

The purpose of this study was to investigate the effect of uncomplicated trabeculectomy on central retina in the

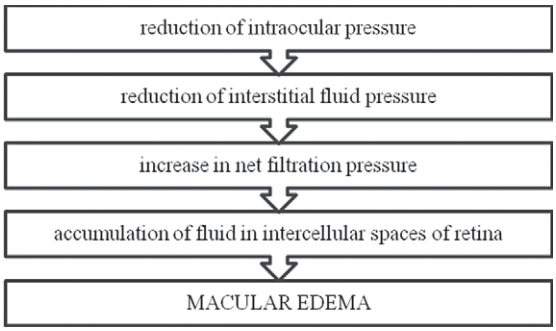

Fig. 5. Macular edema as a result of reduction of intraocular pressure.

early postoperative period during 4 weeks. Our results show a slight thickening in the macula 1 week and 1 month after surgery, althought the proportion of patients who developed significant macular thickening is relatively small. Németh and Horóczi, by using ultrasound, revealed increased thickness and volume of the ocular wall after trabeculectomy, explaining that these changes might be caused by ocular hypotonia and postoperative inflammation[21]. Measurements by OCT showed reduction in macular thickness after normalization of intraocular pressure in the eyes with hypotonia after filtering procedure[25]. Lima et al have reported an increase in macular thickness in 8 of the 14 studied patients with prolonged postoperative hypotonia and without clinically visible maculopathy[26]. Karasheva et al have reported significant reduction of intraocular pressure and increase in macular thickness after filtering surgical procedures in all visit within a month of surgery. Although they did not confirm correlation between the changes in the thickness of the retina and IOP, it was considered that the reduction of intraocular pressure after filtration surgery results in a moderate increase in foveal thickness[24].

Arcieri et al revealed that the usage of prostaglandin analogues may lead to disruption of the blood-aqueous barrier and development of cystoid macular edema in some patients with pseudophakia and aphakia[27]. Our findings show that there was no significant difference in the change of macular thickness in patients who have used topical prostaglandins compared with those who have used other topical medications. Also, there was no difference in macular changes between patients treated with or without mitomycin C.

Additionally, Aydin et al have found increased thickness of the retinal nerve fiber layer, which significantly correlates with the reduction of intraocular pressure after glaucoma filtering surgery[28]. Studies by other authors have shown a significant correlation between changes in macular thickness and changes in the thickness of retinal nerve fiber layer in glaucoma patients[29,30]. Also, the relationship between IOP value and changes in macular thickness are described after cataract surgery. Lee et al described a significant negative correlation between intraocular pressure and macular thickness, where the increase of IOP was accompanied by a decrease in macular thickness in the early postoperative period within 12 hours after phacoemulsification[31]. Albeit the attention of researchers was mostly focused on the anterior segement of the eye and related complications, as well as on the changes in the peripapillary retinal nerve fiber layer, the exact mechanism and incidence of macular edema after filtering procedures are not yet fully understood.

It is known that the interstitial fluid pressure in tightly encased tissues, such as eye, is for a several milimeters of mercury lower than the pressure which makes tunica on the tissue. Reduction of intraocular pressure leads to a reduction in interstitial fluid pressure and increase gradient of capillary pressure / pressure of the intercellular space, resulting to increase in net filtration pressure (Figure 5). Therefore, fluid and dissolved substances increasingly leak in the intercellular space leading to the consequent elevation in macular thickness and development of macular edema[32].

The above mentioned pattern of »Starling forces« (capillary pressure / interstitial fluid pressure) could play a role in reducing macular volume in glaucomatous eyes compared to normal eyes. Lederer et al have shown that the progression of glaucoma and higher values of intraocular pressure lead to a reduction in macular volume[33]. Furthermore, Barišić et al have found decreased values of macular volume and average macular thickness in glaucoma patients in comparison to healthy subjects[34]. It is considered that the loss of retinal ganglion cells in advanced glaucomatous disease could be responsible for reduction in retinal thickness[35]. In reverse, higher intraocular pressure leads to an increase in interstitial fluid pressure, lowering the net filtration pressure and increasing absorption of fluid from the intercellular space into the capillaries, respectively thinning the retina.

In conclusion, we found a slight subclinical increase in macular thickness after uncomplicated trabeculectomy, for which we considered that was the result in reduction of intraocular pressure after glaucoma surgery. Macular thickening after glaucoma filtering surgery could be a physiological reaction to the stress of the retina caused by a sudden reduction of intraocular pressure and it is the consequence of the altered relationship between capillary pressure and interstitial fluid pressure.

REFERENCES

1. ROSSETTI L, AUTELITANO A, Curr Opin Ophthalmol, 11 (2000) 65. — 2. JAFFE NS, CLAYMAN HM, JAFFE MS, Ophthalmology, 89 (1982) 25. — 3. MANDIĆ Z, PETRIĆ I, BENČIĆ G, VATAVUK Z, BOJIĆ L, Coll Antropol, 29 (2005) S9. — 4. CAGINI C, FIORE T, IACCHERI B, PICCINELLI F, RICCI MA, FRUTTINI D, Curr Eye Res, 34 (2009) 1036. DOI: 10.3109/02713680903288937. — 5. VUKICEVIC M, GIN T, AL-QURESHI S, Clin Experiment Ophthalmol, 40 (2012) 282. DOI: 10.1111/j.1442-9071.2011.02638.x. — 6. AH-FAT FG, SHARMA MK, MAJID MA, YANG YC, J Cataract Refract Surg, 24 (1998) 801. — 7. GHOSH S, ROY I, BISWAS PN, MAJI D, MONDAL LK, MUKHOPADHYAY S, BHADURI

G, Acta Ophthalmol, 88 (2010) 102. DOI: 10.1111/j.1755-3768.2010.01896.x. — 8. NAGY ZZ, ECSEDY M, KOVÁCS I, TAKÁCS Á, TÁTRAI E, SOMFAI GM, CABRERA DEBUC D, J Cataract Refract Surg, 38 (2012) 941. DOI: 10.1016/j.jcrs.2012.02.031. — 9. SOURDILLE P, SANTIAGO PY, J Cataract Refract Surg, 25 (1999) 256. — 10. DEGENRING RF, VEY S, KAMPPETER B, BUDDE WM, JONAS JB, SAUDER G, Graefes Arch Clin Exp Ophthalmol, 245 (2007) 18. DOI: 10.1007/s00417-006-0377-4. — 11. GHARBIYA M, CRUCIANI F, CUOZZO G, PARISI F, RUSSO P, ABDOLRAHIMZADEH S, Eye, 27 (2013) 605. DOI: 10.1038/eye.2013.28. — 12. URSELL PG, SPALTON DJ, WHITCUP SM, NUSSENBLATT RB, J Cataract Refract Surg, 25 (1999) 1492. — 13. MIYAKE K, OTA I, MAEKUBO K, ICHIHASHI S, MIYAKE S, Arch Ophthalmol, 117 (1999) 34. DOI: 10.1001/archopht.117.1.34. — 14. SCHWENN O, KERSTEN I, DICK HB, MÜLLER H, PFEIFFER N, J Glaucoma, 10 (2001) 85. — 15. COSTA VP, ARCIERI ES, Acta Ophthalmol Scand, 85 (2007) 586. — 16. BORISUTH NS, PHILIPS B, KRUPIN T, Curr Opin Ophthalmol, 10 (1999) 112. — 17. BRUBAKER RF, PEDERSON JE, Surv Ophthalmol, 27 (1983) 281. — 18. TULI SS, WUDUNN D, CIULLA TA, CANTOR LB, Ophthalmology, 108 (2001) 1808. — 19. DELLAPORTA A, Am J Ophthalmol, 40 (1955) 781. — 20. GOODKIN ML, GREWAL DS, GREENFIELD DS, J Glaucoma, 19 (2010) 349. DOI: 10.1097/IJG.0b013e3181bd59c. — 21. NÉMETH J, HORÓCZI Z, Int Ophthalmol, 16 (1992) 355. — 22. KOKAME GT, DE LEON MD, TANJI T, Am J Ophthalmol, 131 (2001) 384. — 23. BENSON SE, MANDAL K, BUNCE CV, FRASER SG, BMC Ophthalmol, 5 (2005) 7. DOI: 10.1186/1471-2415-5-7. — 24. KARASHEVA G, GOEBEL W, KLINK T, HAIGIS W, GREHN F, Graefes Arch Clin Exp Ophthalmol, 241 (2003) 170. DOI: 10.1007/s00417-003-0628-6. — 25. KLINK T, LIEB WE, GÖBEL W, Ophthalmologe, 97 (2000) 353. — 26. LIMA VC, PRATA TS, CASTRO DP, CASTRO LC, DE MORAES CG, MATTOX C, ROSEN RB, LIEBMANN JM, RITCH R, Acta Ophthalmol, 89 (2011) 274. DOI: 10.1111/j.1755-3768.2009.01719.x. — 27. ARCIERI ES, SANTANA A, ROCHA FN, GUAPO GL, COSTA VP, Arch Ophthalmol, 123 (2005) 186. — 28. AYDIN A, WOLLSTEIN G, PRICE LL, FUJIMOTO JG, SCHUMAN JS, Ophthalmology, 110 (2003) 1506. DOI: 10.1016/S0161-6420(03)00493-7. — 29. GREENFIELD DS, BAGGA H, KNIGHTON RW, Arch Ophthalmol, 121 (2003) 41. DOI: 10.1001/archopth.121.1.41. — 30. WOLLSTEIN G, SCHUMAN JS, PRICE LL, AYDIN A, BEATON SA, STARK PC, FUJIMOTO JG, ISHIKAWA H, Am J Ophthalmol, 138 (2004) 218. DOI: 10.1016/j.ajo.2004.03.019. — 31. LEE YC, CHUNG FL, CHEN CC, Am J Ophthalmol, 144 (2007) 203. — 32. GUYTON AC, HALL JE, Medical Physiology (Saunders Elsevier, Philadelphia, 2012). — 33. LEDERER DE, SCHUMAN JS, HERTZMARK E, HELTZER J, VELAZQUES LJ, FUJIMOTO JG, MATTOX C, Am J Ophthalmol, 135 (2003) 838. DOI: 10.1016/S0002-9394(02)02277-8. — 34. BARIŠIĆ F, SIČAJA AJ, RAVLIĆ MM, NOVAK-LAUŠ K, IVEKOVIĆ R, MANDIĆ Z, Coll Antropol, 36 (2012) 441. — 35. ZEIMER R, ASRANI S, ZOU S, QUIGLEY H, JAMPEL H, Ophthalmology, 105 (1998) 224. DOI: 10.1016/S0161-6420(98)92743-9.

A. Sesar

Department of Ophthalmology, Clinical Hospital Mostar, Bijeli brijeg b.b., 88000 Mostar, Bosnia and Herzegovina
e-mail: antoniosesar@yahoo.com

DEBLJINA MAKULE POSLIJE FILTRACIJSKE KIRURGIJE GLAUKOMA

S A Ž E T A K

Cilj ovog istraživanja bio je analizirati rane poslijeoperativne promjene makularnog područja koristeći optičku koherentnu tomografiju nakon nekompliciranih filtracijskih operacija glaukoma. U ovoj prospektivnoj studiji sudjelovala su 32 pacijenta (34 oka) s glaukomom otvorenog kuta, kojima je učinjena trabekulektomija sa ili bez primjene Mitomicina C. Isključujući kriteriji bili su: edem makule, uveitis, senilna makularna degeneracija, zamućeni optički mediji, sekundarni glaukom i glaukom zatvorenog kuta. Svim ispitanicima učinjen je kompletan oftalmološki pregled prije operativnog zahvata, drugi dan, tjedan dana i mjesec dana nakon operacije. Tijekom svakog pregleda učinjena je tomografija makule, koristeći Cirrus HD OCT, za analizu centralne fovealne debljine. Naši rezultati pokazuju blago zadebljanje makule tjedan dana i mjesec dana nakon operativnog zahvata u odnosu na debljinu makule preoperativno i drugog dana poslijeoperativno. Nije bilo statistički značajne promjene makularne debljine u pacijenata koji su koristili prostaglandine u odnosu na pacijente koji su koristili drugu lokalnu terapiju. Također nije bilo promjene u debljini makule u pacijenata u kojih je tijekom operacije bio primijenjen Mitomicin C u odnosu na pacijente, koji su operirani bez primjene Mitomicina C. Zaključno, pronašli smo blago subkliničko zadebljanje makule nakon nekompliciranе trabekulektomije, za koje smatramo da je rezultat smanjenja intraokularnog tlaka nakon operativnog zahvata. Zadebljanje makule nakon filtracijske operacije glaukoma moglo bi predstavljati fiziološki odgovor mrežnice na stres uzrokovan smanjenjem intraokularnog tlaka, što je posljedica izmijenjenih odnosa između kapilarnog tlaka i tlaka međustanične tekućine.