Does the use of Ultrafiltration in Open Heart Surgery Reduce Eye Complications?

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ABSTRACT

Introduction: The effects of cardiopulmonary bypass on human eyes are one of the least researched subjects. In our study, we investigated the effects of cardiopulmonary bypass and ultrafiltration on the eyes.

Patients and Methods: Patients undergoing elective coronary artery surgery using cardiopulmonary bypass were evaluated. The study was conducted with 40 patients. Patients were divided into two groups. In Group I (n= 20) ultrafiltration was applied during cardiopulmonary bypass, whereas in Group II (n= 20) ultrafiltration was not applied. Intraocular pressure, central corneal thickness and retinal nerve fiber layer thickness were measured in all patients

Results: We found non-statistically significant intraocular pressure increase in Group I (p= 0.586) and non-statistically significant intraocular pressure decrease in Group II (p= 0.133). There was a minimal increase in the central corneal thickness in both groups (p= 0.323), and there was a statistically significant increase in the retinal nerve fiber layer thickness in both groups but there was no statistically significant difference between the both groups (p= 0.908).

Conclusion: We did not detect any difference in ophthalmologic findings between both patient groups with and without ultrafiltration.

Key Words: Cardiopulmonary bypass; central corneal thickness; intraocular pressure; retinal nerve fiber layer thicknessess; ultrafiltration

Açık Kalp Cerrahisinde Ultrafiltrasyon Kullanımı Göz Komplikasyonlarını Azaltır mı?

ÖZET

Giriş: Kardiyopulmoner baypasın insan gözü üzerindeki etkileri en az araştırılan konulardan biridir. Çalışmamızda kardiyopulmoner baypas ve ultrafiltrasyonun göz üzerindeki etkilerini araştırdık.

Hastalar ve Yöntem: Kardiyopulmoner baypas kullanılarak elektif koroner arter cerrahisi yapılan hastalar değerlendirildi. Çalışma 40 hasta ile yapıldı. Hastalar iki gruba ayrıldı. Grup I'e (n= 20) kardiyopulmoner baypas sırasında ultrafiltrasyon uygulanırken, Grup II'ye (n= 20) ultrafiltrasyon uygulanmadı. Tüm hastalarda göz içi basıncı, santral kornea kalınlığı ve retinal sinir lifi tabakası kalınlığı ölçüldü.

Bulgular: Grup I'de göz içi basıncında istatistiksel olarak anlamlı olmayan artış (p= 0.586) ve Grup II'de göz içi basınında istatistiksel olarak anlamlı olmayan azalma (p= 0.133) saptadık. Her iki grupta da santral kornea kalınlığında minimal artış vardı (p= 0.323). Her iki grupta da retinal sinir lifi tabakası kalınlığında istatistiksel olarak anlamlı artış vardı ancak her iki grup arasında istatistiksel olarak anlamlı fark yoktu (p= 0.908).

Sonuç: Ultrafiltrasyon yapılan ve yapılmayan her iki grup arasında oftalmolojik bulgu farkı tespit etmedik.

Anahtar Kelimeler: Kardiyopulmoner baypas; ultrafiltrasyon; göz içi basıncı; santral kornea kalınlığı; retinal sinir lifi tabakası kalınlığı

INTRODUCTION

Cardiopulmonary bypass (CPB) is an indispensable but non-physiological process for cardiac surgery. Blood contact with extraneous surfaces causes cytokine and complement activation. This condition implies two important complications such as hemodilution and systemic inflammatory response syndrome. Capillary leakage may cause diffuse edema, abnormal coagulation due to platelet dysfunction and may cause low cardiac output syndrome, multisystem organ failure and mortality due to reperfusion injury[1]. The use of ultrafiltration (UF) during CPB allows removal of excess fluid and inflammatory mediators from the body. It is similar to

Cite this article as: Buğra O, Dağlar B, Ulaş F. Does the use of ultrafiltration in open heart surgery reduce eye complications? Koşuyolu Heart J 2020;23(3):183-90.

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Submitted: 23.10.2020
Accepted: 26.10.2020
Available Online Date: 29.12.2020

the system used in hemodialysis patients. It is performed with a filter placed between the arterial and venous lines in CPB circuits. It is based on passing the blood through a semipermeable membrane with hydrostatic pressure[1,2].

Patients with pathological ocular findings and sudden vision loss after CPB have been reported in the literature; however, the mechanism has not been fully elucidated. Ocular complications are usually severe after open heart surgery. Systemic hypotension, cerebral hypoperfusion, arterial embolism and hypothermia are the envisaged results during CPB[3,4].

In our study, we investigated the effects of CPB and UF on the eyes. In patients undergoing elective coronary artery surgery using CPB, the effects of CPB on the eyes due to fluid load in the body and the changes in the anterior and posterior segment structures of the eyes between patients with and without UF were evaluated using optical coherence tomography (OCT).

PATIENTS and METHODS

The study was conducted between January 2013 and December 2016 in a prospective, randomized study plan. Local Ethics Committee approval was obtained (AIBU 2012/95). All patients signed a procedure-oriented informed consent.

Participation and Exclusion Criteria of the Study

Patients undergoing elective coronary artery surgery using CPB were evaluated. Patients who required urgent surgery or underwent an additional surgery, those with comorbid additional disease, and those with an ejection fraction of 30% or less were excluded from the study. Patients with no more than 5 dioptric spheric and 3 dioptric cylindrical refraction defects, no intravitreal medication, no laser on the retina, no eye surgery other than uncomplicated cataract surgery and no ocular pathology to prevent visualization with OCT were included into the study.

Patient Groups

The study was conducted with 40 patients. Patients were divided into two groups. In Group I (n= 20), UF was applied during CPP, whereas in Group II (n= 20), UF was not applied. Intraocular pressure (IOP), central corneal thickness (CCT) and retinal nerve fiber layer thickness (RNFL) were measured in all patients preoperatively and on the second postoperative day by using the Fourier domain OCT. All examinations were performed by the same ophthalmologist. Patients included in the study were selected among the patients who did not develop complications during intensive care unit. Eye control examinations were planned to be performed as early as possible. The controls were performed on the second postoperative day when the patients were discharged from the intensive care unit. The patients who were unable to leave the intensive care unit on the second postoperative day were excluded from the study in order to ensure standardization.

Sampling Size

At least 18 patients were required in order to test the statistical significance at 80% power and 5% error level of difference. Sampling width calculations were performed through NCSS & PASS 2000 statistical package program.

Anesthesia

Routine cardiac anesthesia monitorization was performed with 5-arm electrogram, radial artery catheterization, central venous catheterization, pulse oximetry, bladder catheter and esophageal heat probe.

For standard anesthesia induction, 0.2 mg/kg midazolam (Roche, Basel, Switzerland), 5-10/g/kg fentanyl (Janssen-Cilag, Beerse, Belgium) and 0.1 mg/kg rocuronium bromide (Organon, Netherlands) were applied intravenously. Maintenance was provided with sevoflurane. Midazolam and fentanyl were repeated every half hour.

Operation

All patients were applied median sternotomy. The operations were performed under cardiopulmonary bypass (Biomedicus, Germany) using membrane oxygenator (Jostra, Herrlingen, Germany) and non-pulsatile flow. Activated coagulation time (ACT) was maintained for more than 480 seconds. Moderate hypothermia (32ºC) was applied. Myocardial protection was provided by antegrade and retrograde isothermic blood cardioplegia. During CPB, systemic blood flow was kept between 2-2.5 l/min/m^2 and systemic pressure was between 50-80 mm/Hg. After coronary anastomosis was completed, the patient was warmed to 37°C and the cross clamp was removed. All surgical procedures were performed by the same team.

Ultrafiltration

UF was used to achieve volume load, metabolites, inflammatory mediators, and adequate hemoconcentration in patients. The inlet portion of the filter (Capiox, Terumo Corporation, Tokyo, Japan) was connected to the arterial line and the outlet portion to the venous line. UF was initiated following cross clamping. The cross-clamp was operated at a rate of 10-20 ml/kg during the clamp period and 50-100 ml/kg during the warm-up period.

Statistical Analysis

Data analysis was performed using SPSS for Windows 11.5 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were shown as mean ± standard deviation or median (minimum-maximum) for continuous variables, and categorical variables as number of cases and percentages. The significance of the difference between the groups was examined by Spearman test and the significance of the difference in terms of median values was examined by Mann Whitney U test. Results were considered statistically significant for $p< 0.05$.

RESULTS

Preoperative Data

In the preoperative period, demographic and clinical characteristics were similar in both groups (p> 0.05) (Table 1). Group I consisted of 13 males and 7 females, and Group II consisted of 14 males and 6 females. Mean age was 63.0 ± 10.7 years (41-80 years) in Group I and 63.9 ± 7.4 years (53-78 years) in Group II. Eight patients in Group I and 6 patients in Group II had a history of diabetes mellitus (DM). There were 11 patients in Group I and 9 patients in Group II. Mean arterial blood pressure was 128 ± 14 mm/Hg in Group I and 134 ± 20 mm / Hg in Group II. Mean hemoglobin level was 36.8 ± 3.7 mg / dl in Group I and 37.4 ± 4.3 mg/dl in Group II. Body surface area (BSA) was calculated as 1.84 ± 0.1 m^2 in Group I and 1.81 ± 0.1 m^2 in Group II. The average ejection fraction (EF) in Group I was 35% (30-40) and the average EF in Group II was 37.5% (30-45).

Intraoperative Data

No significant difference was found between the two postoperative groups in terms of cardiopulmonary bypass time (p= 0.506), cross-clamp time (p= 0.392), number of distal anastomoses (p= 0.060), arterial pressure (p= 0.391) and hemoglobin values (p= 0.131) during CPB.

In Group I, an average of 1786 ± 566 cc UF was applied. UF was not applied in Group II (Table 2).

Postoperative Data

Mortality and morbidity were not observed in 40 patients evaluated in the study. No ocular complications were detected in the controls in whom OCT was performed. In Group I, preoperative IOP was measured as 13.45 ± 2.36 and postoperative IOP was 13.71 ± 2.71 (p= 0.586), and preoperative IOP was 15.52 ± 3.26 and postoperative IOP was 14.75 ± 3.71 (p= 0.133) in Group II. We found non-statistically significant IOP increase in

Table 1. Demographic and clinical characteristics of patients in Group I and Group II

Variables	Group I (n= 20)	Group II (n= 20)	p
Age (year)	63.0 ± 10.7	63.9 ± 7.4	0.761
Gender (M/F)	13/7	14/6	0.852
BSA (m^2)	1.84 ± 0.1	1.81 ± 0.1	0.469
Diabetes mellitus	8 (%40)	6 (%30)	0.327
Hypertension	11 (%55)	9 (%45)	0.194
EF (%)	35 (30-40)	37.5 (30-45)	0.293

BSA: Body surface area, EF: Ejection fraction, NA: Not analyzed.

Table 2. The intraoperative and postoperative characteristics of patients in Group I and Group II

Variables	Group I (n= 20)	Group II (n= 20)	p
CPB time (min)	85.8 ± 14.2	90.0 ± 18.9	0.506
Cross clamp time (min)	63.1 ± 12.6	69.6 ± 16.6	0.392
Number of grafts (mean)	3.01 ± 0.6	3.43 ± 0.8	0.060
UF (cc)	1786 ± 566	-	NA
Arterial pressure (mm/Hg)			
Pre-CBP	128 ± 14	134 ± 20	0.213
During-CPB	58 ± 5	59 ± 5	0.391
Post-CPB	113 ± 18	120 ± 13	0.087
Haemoglobin (mg/dl)			
Pre-CBP	36.8 ± 3.7	37.4 ± 4.3	0.647
During-CPB	25.1 ± 2.2	24.9 ± 2.7	0.134
Post-CPB	30.4 ± 1.8	28.5 ± 2.1	0.039

CPB: Cardiopulmonary bypass, UF: Ultrafiltration

Table 3. The comparison of preoperative and postoperative IOP, CCT and RNFL thickness

Variables	Group I (n= 20)	Group II (n= 20)	p
IOP			0.098
Pre-op	13.45 ± 2.36	15.52 ± 3.26	
Post-op	13.71 ± 2.71	14.75 ± 3.71	
CCT			0.332
Pre-op	529.39 ± 30.23	546.43 ± 23.89	
Post-op	532.44 ± 29.27	549.14 ± 25.05	
RNFL			0.908
Pre-op	98.67 ± 9.64	98.21 ± 9.68	
Post-op	100.44 ± 9.10	100.07 ± 8.69	

IOP: Intraocular pressure, CCT: Central corneal thickness, RNFL: Retinal nerve fiber layer thickness.

Group I and non-statistically significant IOP decrease in Group II. We could not find any statistically significant difference in terms of IOP changes in both groups (p= 0.098) (Table 3).

In Group I, preoperative CCT was measured as 529.39 ± 30.23, postoperative CCT was 532.44 ± 29.27 (p= 0.517), and preoperative CCT was 546.43 ± 23.89, and postoperative CCT 549.14 ± 25.05 (p= 0.530) in Group II. There was a minimal increase in CCT in both groups, but no statistically significant difference was found between the two groups (p= 0.323) (Table 3).

In Group I, preoperative RNFL was measured as 98.67 ± 9.64 and postoperative RNFL as 100.44 ± 9.10 (p= 0.006), and preoperative RNFL was 98.21 ± 9.68 and postoperative RNFL was 100.07 ± 8.69 (p= 0.048) in Group II. There was a statistically significant increase in RNFL in both groups, but there was no statistically significant difference between both groups (p= 0.908) (Table 3).

DISCUSSION

In this study, we evaluated the effects of CPB on the eye, and whether there was a difference in ocular findings between patients with and without UF. In the literature, we have not encountered any other study examining the effects of CPB on retinal and choroidal layers by OCT.

Hemodilution and volume load due to CPB after cardiac surgery increases morbidity and mortality. Hemodilution increases colloid oncotic pressure and causes total body fluid, interstitial edema, hypoxia, hypotension, hypo-coagulation, myocardial, cerebral, and renal dysfunction[5].

UF removes volume load and inflammatory mediators from the circulation due to capillary leak syndrome[6]. Higher postoperative hematocrit values and lower blood product transfusion requirements, better lung function, decrease in mechanical respiratory support, less inotropic use and shorter duration of intensive care have been reported in patients who received UF, compared to patients who did not[7]. Ugaki et al.[8] have observed better cardiac index and mix venous saturation values in the postoperative period of patients in undergoing UF process.

Ocular complications after cardiac surgery have been reported between 0.06-25.6%[9,10]. Non-pulsatile flow during CPP, prolonged CPB time (>180 min), hypotension, hypothermia (< 25ºC), IOP elevation, embolization, low hematocrit level (< 8.5 mg/dl), and epinephrine use are the most common causes of ocular complications[11].

Orihashi et al.[12] have found a decrease in central retinal artery blood flow during coronary bypass. The most important complications of CPB on the eyes are retinal embolism, occipital infarction and ischemic optic neuropathy. Hemodynamic changes during cardiac surgery can lead to retinal hypoperfusion, ischemia, infarction, nerve fiber damage, optic neuropathy and vision loss. Visual loss has been reported in the literature between 0.1-1%. It is mostly irreversible[13-15].

As the duration of CPB increases, the risk of retinal embolism increases due to blood, calcium, cholesterol, fat and air particles[16]. Rainio et al.[17] have shown that the rate of retinal infarction decreases significantly in operations without CPB. Roth et al.[14] have reported that systemic inflammatory response syndrome may also lead to ischemic optic neuropathy. Trethovan et al.[18] have reported that preoperative diabetes, hyperlipidemia, hyperfibrinogenemia and smoking history increase the risk of optic neuropathy due to hypotension, inflammatory response, embolism, anemia and inotropic use during CPB. The combination of these factors disrupts ocular blood flow and autoregulation.

Shaw et al.[19] have examined 312 patients undergoing coronary artery surgery and found ocular complications in 80 (25.6%) of these patients. Complications have been reported

as retinal infarction (17.3%), visual field defect (2.6%), retinal embolism (2.3%), and Horner syndrome (1.3%). Williams et al.[20] have examined 92 patients with postoperative visual loss and reported that 81 of these patients received open heart surgery. Holy et al.[15] have reported loss of vision in 9 (0.33%) of 2749 CABG patients. They have reported that risk factors such as coronary artery disease, diabetes, hypertension are seen in patients with complications but vision loss also occurs in healthy patients without any risk factors. In our study, no ocular complications were detected in 40 patients.

In our study, we detected IOP decline in the group without ultrafiltration, despite not statistically significant, and we also found minimal IOP increase in the group with ultrafiltration which is also not statistically significant. We could not find any statistically significant difference in terms of IOP changes in both groups (p= 0.098).

Decrease in plasma proteins and in colloid osmotic pressure due to hemodilution during CPB causes an increase in IOP. It has been reported that the increase in IOP during CPB potentiates ocular complications[21]. Roth et al.[15] have reported that IOP increased significantly during CPB, which also increased the incidence of ocular complications. There are also publications showing that IOP does not change[13]. In our study, we found minimal increase in one group and minimal decrease in the other group. In both groups, we did not see any complications due to an increase or a decrease in IOP.

In our study, we found insignificant increase in CCT in both groups (p= 0.332) (Figures 1,2). According to the ocular hyper-

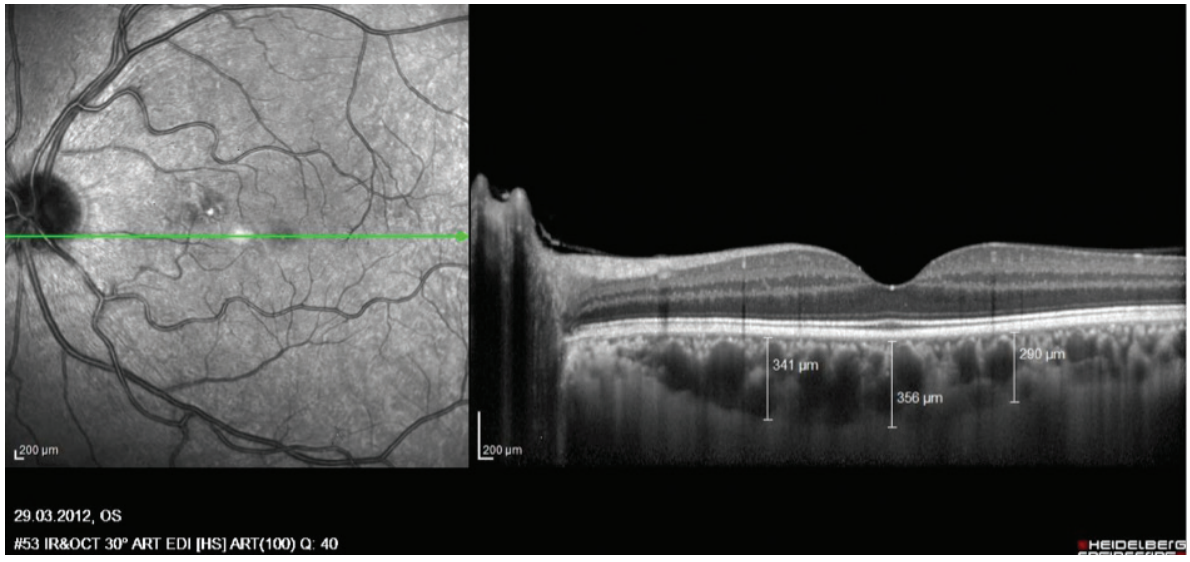

Figure 1. Preoperative central corneal layer thickness measurement image of a patient.

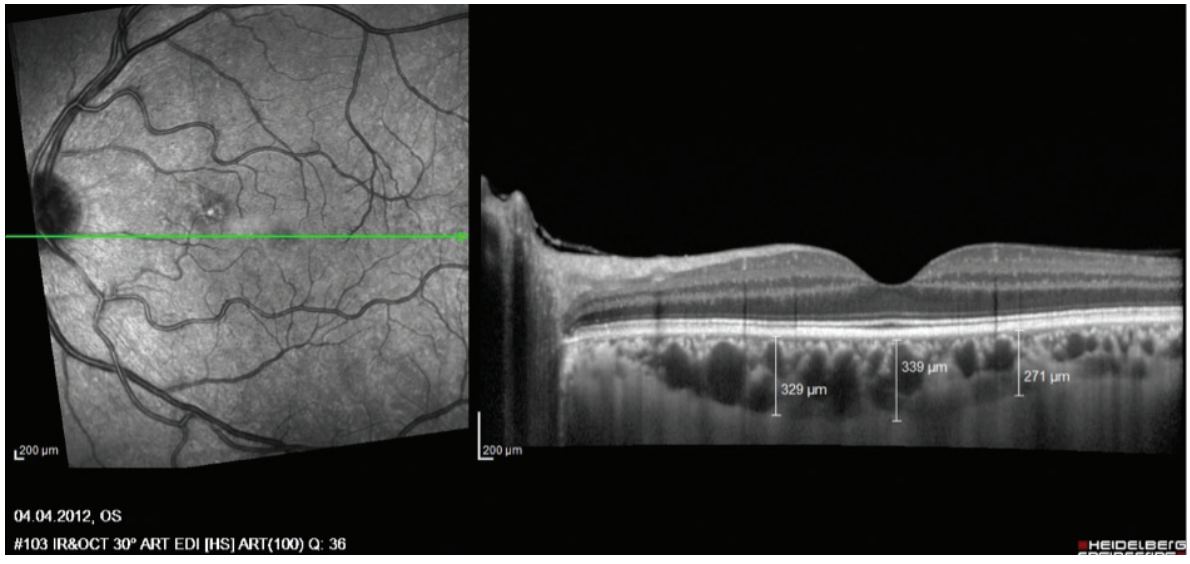

Figure 2. Postoperative central corneal layer thickness measurement image of the same patient.

tension treatment study (OHTS), increase in CCT thickness in ocular hypertensive patients has been reported as a risk factor for glaucoma development[22].

In healthy eyes, there are structural changes in optic nerve heads and optic disc area with CCT ignition[23]. The increase in CCT, which was not statistically significant in both groups, showed that IOP evaluation should be performed carefully in patients undergoing open heart surgery using CPB due to early CCT change.

In our study, we found a statistically significant increase for RNFL in both groups, but there was a statistically insignificant difference between two groups in the evaluation (p= 0.908) (Figures 3,4). In a study in which RNFL thickness was evaluated by scanning laser polarimeter device in hemodialysis patients, it has been reported that there is no change in RNFL thickness after hemodialysis[24]. In the literature, we found a study evaluating RNFL thickness in patients undergoing open heart surgery. In the study of Buyukates et al.,[25] they have found a decrease in RFNL by measuring with GDx Nerve Fiber Analyzer in 20 patients who underwent CABG. They have stated that hypoxia or vascular dysregulation may have caused this. RNFL thickness can be determined by scanning laser polarimeter, confocal scanning laser ophthalmoscope, retina thickness analyzer and OCT devices operating with different optical principles.

In our study, RNFL measurements after CPB were evaluated with reference to the measurement of RNFL before KBP with OCT device operating on the Fourier principle. Previous generation OCT devices do not have the ability to take follow-up shots from the same area with reference to the first shot. They are able to provide lower speed and resolution imaging. The Fourier domain OCT device used in our study measures the effect of KPB on RNFL thickness with a higher sensitivity than both the scanning laser polarimeter and the previous generation OCT devices. In the literature, we did not find any other studies showing increase of RFNL thickness. We attributed the statistically significant increase in RNFL thickness in both UF-treated and non-UF treated groups to the protection of patients from hypoperfusion during CPB and improving postoperative cardiac performance and to the improve of cardiac performance postoperatively.

Although there was a statistically significant difference between the two groups in terms of hemoglobin levels, which were evaluated as risk factors for ocular complications, we did not detect ocular complications in both groups.

Limitations

The limitations of the study were the small number of patients and the lack of late evaluation.

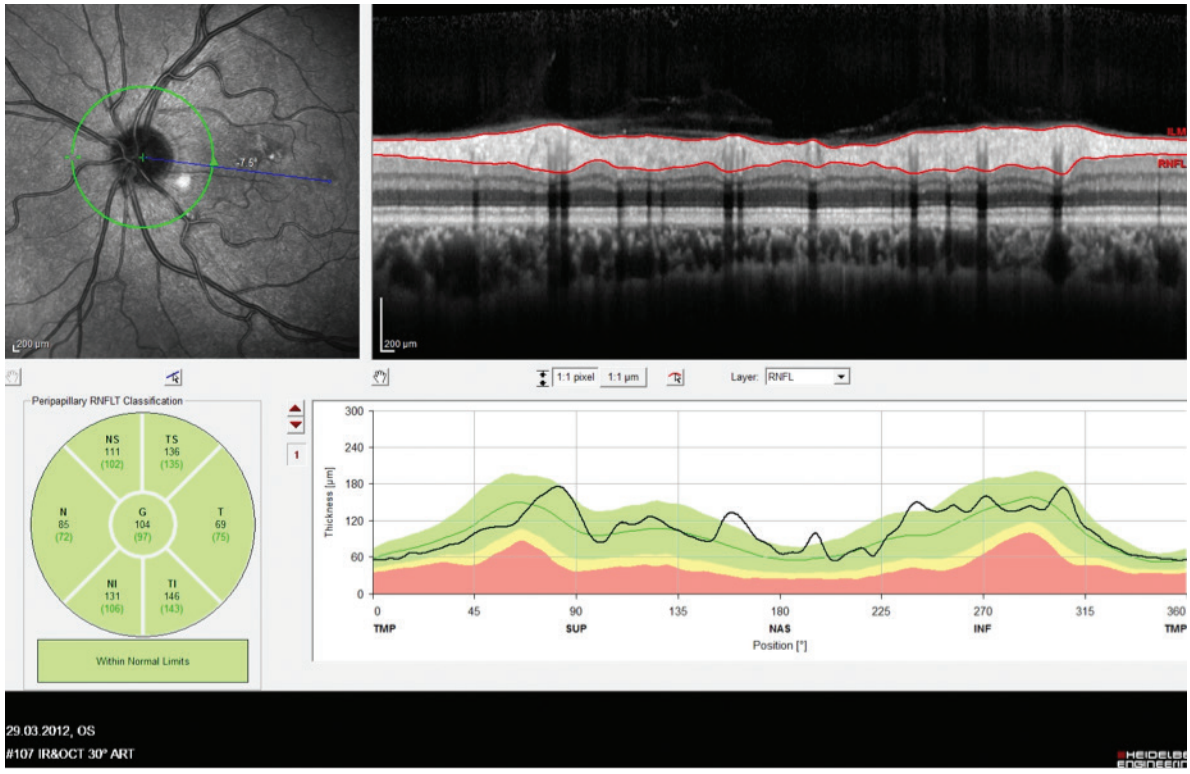

Figure 3. Preoperative retinal nerve fiber layer measurement image of a patient.

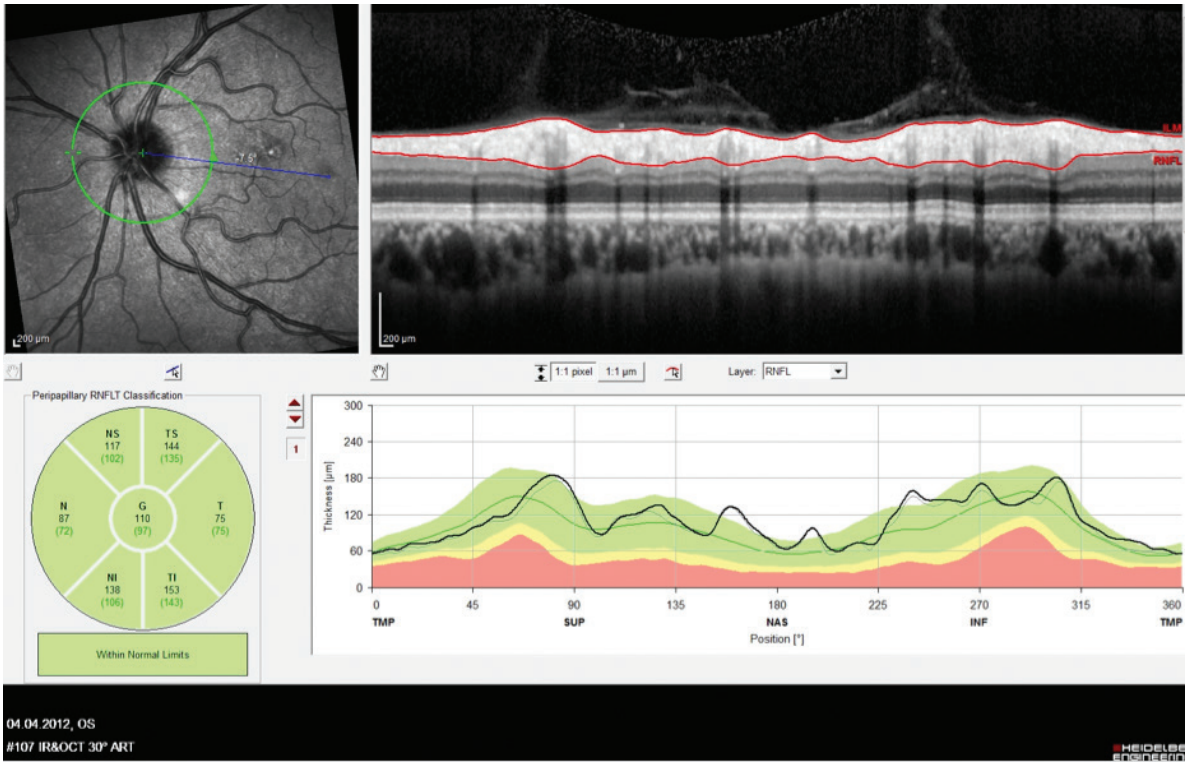

Figure 4. Postoperative retinal nerve fiber layer measurement image of the same patient.

CONCLUSION

We did not detect any difference in ophthalmologic findings between both patient groups with and without UF. We think that the eyes are not affected by systemic changes due to retinal autoregulatory mechanisms in patients with blood retinal barrier intact. New studies are needed with more patient groups, including late results.

Ethics Committee Approval: The approval for this study obtained from Abant İzzet Baysal University Clinical Researches Ethics Committee (Decision No: B.30.2.ABÜ.0.20.05.05.050.01.04-288 Date: 21.06.2012).

Informed Consent: Written informed consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - OB; Analysis/Interpretation - OB, BD; Data Collection - OB, FU; Writing - OB; Critical Revision - OB, FU; Final Approval - OB, BD; Statistical Analysis - OB; Overall Responsibility - OB, BD.

Conflict of Interest: The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Financial Disclosure: The authors declared that this study has received no financial support.

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