STRUCTURAL AND FUNCTIONAL MACULAR CHANGES AFTER CATARACT SURGERY IN DIABETIC PATIENTS

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Summary

Introduction. In recent years, the number of diabetic patients requiring cataract surgery has been on the rise. The aim of this study was to examine the effects of cataract surgery on visual acuity and changes in the central retinal thickness in diabetic patients with and without retinopathy, in relation to the duration of the disease, type of therapy, and the level of glycated hemoglobin and serum lipids.

Material and Methods. The prospective study included 51 eyes of 34 patients divided into three groups. Preoperatively, all patients underwent best-corrected visual acuity evaluation with Snellen chart, cataract grading using lens opacities classification system III, as well as fundus examination and optical coherence tomography. Postoperative follow-up visits were scheduled after the first, fourth, sixth, eighth, and twelfth weeks after which the patients underwent best-corrected visual acuity evaluation and optical coherence tomography. The obtained values were statistically processed and analyzed in relation to the duration of the disease, the type of therapy, and the level of glycated hemoglobin and serum lipids.

Results. Of 51 eyes, 5.9% developed macular edema during the fourth postoperative week with central retinal thickness > 310 μm. Subclinical central retinal thickness changes were registered in all groups with the highest values in group I (diabetics with retinopathy) in the sixth postoperative week. The average value of central retinal thickness in group I was 256 ± 11 μm at baseline and 273 ± 11 μm in week 6. The best-corrected visual acuity improved in all groups, without retinopathy, in relation to the duration of the disease, type of therapy, and the level of glycated hemoglobin and serum lipids.

Conclusion. Good visual acuity and absence of significant changes in macular thickness are helpful when making the decision to perform cataract surgery in patients with diabetes. Postoperative follow-up visits should include optical coherence tomography in addition to standard procedures.

Key words: Cataract; Macular Edema; Diabetes Complications; Cataract Extraction; Diabetic Retinopathy; Tomography, Optical Coherence; Visual Acuity; Glycated Hemoglobin A

Introduction

Diabetes mellitus (DM) is one of the most prevalent chronic metabolic diseases affecting millions of people in the world [1]. Diabetic macular edema (DME) is defined as retinal thickening within 1 disc diameter of the foveal center, along with microaneurysms and/or retinal hemorrhages. Recently, the most
The OCT is a non-contact, non-invasive ophthalmic diagnostic technique for retinal imaging and therefore has a significant place in detection of retinal thickness changes in diabetic patients after cataract surgery [10]. This technique provides high resolution and allows close study of retinal layers and cells in different diseases [11].

This clinical study was designed to compare visual functions and structural retinal changes between a group of diabetic patients with diabetic retinopathy and a group of diabetic patients without diabetic retinopathy in comparison to non-diabetic population, before and after cataract surgery, taking into consideration the following parameters: diabetestype and duration, type of treatment, HbA 1c levels, serum lipids, cataract type and phacoemulsification (PHACO) ultrasound time.

**Material and Methods**

This prospective study was conducted at the Eye Clinic of the University Clinical Center of Republic of Srpska from January to December 2019. The study was approved by the Ethics Committee of the University Clinical Center of Republic of Srpska, Bosnia and Herzegovina, and it was conducted in accordance with the Declaration of Helsinki (1964). A fully informed written consent was obtained from all patients prior to the study.

The inclusion criteria were as follows:
- Patients with cataract best corrected visual acuity (BCVA) ≤ 0.5 due to cataract
- Patients with type 2 DM.
- The exclusion criteria were:
  - Patients with severe diabetic retinopathy
  - Patients with preoperative macular edema history
  - Patients with previous panretinal photocoagulation treatment
  - Patients with previous intravitreal drug injection
  - Patients with epiretinal membrane or vitreoretinal traction
  - Patients with glaucoma, uveitis and any other ocular pathology except cataract
  - Patients with intraocular surgery within 6 months prior to the study
  - Patients with intraoperative cataract complications (capsular tear, iris lesions).

A total of 51 eyes of 34 participants were included in this study and divided into 3 groups:
- Group I: Diabetic patients with diabetic retinopathy (mild, moderate) (17 eyes)
- Group II: Diabetic patients without diabetic retinopathy (17 eyes)
- Group III: Healthy patients undergoing cataract surgery (17 eyes).

**Abbreviations**

| Abbreviation | Description |
|--------------|-------------|
| DM           | diabetes mellitus |
| DME          | diabetic macular edema |
| DR           | diabetic retinopathy |
| OCT          | optical coherence tomography |
| CRT          | central retinal thickness |
| BCVA         | best corrected visual acuity |
| HbA 1c       | serum glycosylated hemoglobin |
| VEGF         | vascular endothelial growth factor |
| ICAM-1       | intercellular adhesion molecule-1 activation |
| LOCS III     | lens opacities classification system |
| NSAID        | nonsteroidal anti-inflammatory drug |
| ANOVA        | analysis of variance |

Surgical trauma and subsequent inflammation following cataract surgery may increase the levels of VEGF and other cytokines more in diabetic patients than patients without diabetes. These factors can compromise the retinal vasculature and can lead to macular changes [9, 10].

Important characteristic of DME has become whether it involves the fovea or not. Central DME involves the center of the macula, with a central subfield thickening of at least 310 μm on optical coherence tomography (OCT) using a time domain device [2]. As diabetic patients are at increased risk of developing cataract and losing visual acuity, they are likely to need surgery. Unfortunately, surgery may lead to macular edema as well as to long term deterioration of visual functions. Furthermore, it can exacerbate diabetic retinopathy in patients with long term type 2 DM, patients with insulin dependence, patients with high level of glycated hemoglobin (HbA 1c) and serum lipids, patients with hypertension, poor nuclear transparency and longer ultrasound exposure, as well as patients with kidney dysfunction. These are important risk factors for DME [3–6].

Hyperglycemia induces several biochemical processes which contribute to the pathogenesis of diabetic retinopathy. Retinal neurons and glial cells increase their production of vascular endothelial growing factor (VEGF), even with no ophthalmoscopic evidence of diabetic retinopathy. Increased inflammation, characterized by leukostasis, accumulation of macrophages, and intercellular adhesion molecule-1 (ICAM-1) activation are associated with capillary nonperfusion and damage of the blood-retinal barrier. Patients with DME have elevated vitreous levels of VEGF, ICAM-1, interleukin-6 (IL-6), and monocyte chemoattractant protein-1 compared with non-diabetic patients.

High lipid levels may cause endothelial dysfunction and increased vascular permeability through a local inflammatory response. Decrease in subfoveal choroidal blood flow in type 2 diabetic patients with retinopathy may be relevant in the pathophysiology of macular edema. Eyes with macular edema have been reported to have a greater decrease in choroidal blood flow than eyes without macular edema, suggesting relative hypoxia of the retinal pigment epithelium (RPE) and outer retina which can worsen during the surgery [7, 8].

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All patients underwent a thorough preoperative ophthalmological examination including BCVA evaluation using Snellen chart, Goldmann applanation tomometry, slit lamp and fully dilated fundus examination. Posterior segment diagnostic procedures were performed including color fundus photography and autofluorescence (Zeiss Visucam 500) and OCT of the macula (Zeiss Cirrus HD-OCT). The scanning protocol for OCT used in this study was Macular Cube 512 x 128 A-scan pattern with the centre of 6 x 6 mm scanning area at the centre of the macula, creating 3 annular rings further divided into 9 zones: central circular zone of fovea with 1 mm diameter, 4 parafoveal zones with 3 mm diameter, and 4 parafoveal zones with 6 mm diameter. Presence of macular edema was defined as central retinal thickness (CRT) > 310 μm in central foveal pit assessed by OCT. In some patients both eyes were examined.

Lens opacities classification system III (LOCS III) was used for cataract classification. Early Treatment Diabetic Retinopathy Study (ETDRS) and International Clinical Diabetic Retinopathy Disease Severity Scale were used for diabetic retinopathy classification.

The following parameters were preoperatively examined: age, gender, diabetes type and duration, type of treatment, levels of HbA1c and serum lipids.

All patients underwent cataract surgery by the same trained surgeon (S. S.) using topical anesthesia. A 2.75 mm clear corneal (small) incision was made followed by capsulorhexis and phacoemulsification (Bausch & Lomb Stellaris 2016) after which a foldable one-piece hydrophilic acrylic intraocular lens (AKREOS ADAPT AO) was implanted. Intracameral antibiotic was injected at the end of the surgery. Postoperatively, topical corticosteroid was administered to all patients while topical nonsteroidal anti-inflammatory drug (NSAID) was not prescribed due to the intraoperative complications.

A standard phaco surgery was performed in all eyes. According to LOCS III system, 25 eyes had N2 grade of nuclear density, 10 eyes N1 grade, and 16 eyes P2 grade. The average phacoemulsification time was 5.13 seconds without statistically significant difference between the groups. Two eyes (3.9%) were excluded due to the intraoperative complications.

### Results

This study included 51 eyes of 34 patients of which 13 (38%) were men and 21 (62%) women. The average age was 65 ± 6 years with no difference between the groups. All participants had a clinical diagnosis of cataract. Twenty-three participants (68%) had type 2 DM; of these, 29.4% had DM for more than 10 years with average duration of 11 ± 1.6 years; at baseline, 22% of participants received insulin treatment. Regarding the diabetic retinopathy, 35.3% of diabetic patients had non-proliferative diabetic retinopathy, out of whom 20.6% had a mild and 14.7% moderate form. In regard to the HbA1c status, in the group of patients with HbA1c > 7%, the mean HbA1c levels were 7.75 ± 0.64%. Patient characteristics at the time of surgery, as well as the parameters of accompanying systemic diseases are presented and summarized in Table 1.

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### Visual acuity-functional outcomes

**Graph 1** and **Table 2** show mean BCVA in all 3 study groups at baseline, 1 week, 4 weeks, 6 weeks, 8 weeks, and 12 weeks after the cataract surgery. Postoperative BCVA was increased in all groups with its maximum 6 weeks after surgery, and no change was reported during further follow-up. There was a statistically significant difference in BCVA within groups at baseline and 4 weeks after the surgery (p = 0.00, Student’s t-test). BCVA changes did not follow CRT changes in the postoperative period (Graphs 1 and 2).

### Structural outcomes - optical coherence tomography measurements

**Graph 2** and **Table 2** show the results of OCT examination, average retinal thickness in central field at baseline, 1 week, 4 weeks, 6 weeks, 8 weeks, and 12 weeks after the cataract surgery.
Three eyes (5.9%) developed CRT > 310 μm after 4 weeks and they were excluded according to study protocol due to presence of intraretinal cysts on OCT scans. The other eyes had subclinical changes in OCT measurements after the surgery with the largest deviations after 6 weeks in comparison to baseline OCT values. Before statistical data processing, the number of eyes in groups was matched in order to get valid statistical results.

Table 1. Demographic characteristics at baseline

| Number (n) | Percentage (%) | Mean ± Standard Deviation (SD) |
|------------|----------------|---------------------------------|
| Gender/Pol | Male/Muški | 13/11 | 38/41 |
|            | Female/Ženski | 21/16 | 62/59 |
| Age/Starost | 34/27 | 65 ± 5/67 ± 5 |
| Diabetes mellitus/Diabetes mellitus (DM) | Yes/Da | 23/20 | 68/74 |
|            | No/Ne | 11/7 | 32/26 |
| DM duration | >10 years/10 godina | 10/9 | 44/45 |
|            | <10 years/10 godina | 13/11 | 56/55 |
| Treatment type | Oral antidiabetic drugs | 18/15 | 78/75 |
| Vrsta terapije | Insulin/Insulin | 5/5 | 22/25 |
| HbA 1c/Glukozilirani hemoglobin | >7% | 13/11 | 38/41 |
|            | <7% | 21/16 | 62/59 |
| Cholesterol | >5.2 mmol/l | 10/7 | 29/26 |
| Holesterol | <5.2 mmol/l | 24/20 | 71/74 |
| High-density lipoprotein | >1.55 mmol/l | 17/11 | 50/41 |
| Lipoprotein visoke gustine | <1.55 mmol/l | 17/16 | 50/59 |
| Low-density lipoprotein | >2.6 mmol/l | 14/10 | 41/37 |
| Lipoprotein niske gustine | <2.6 mmol/l | 20/17 | 59/63 |
| Triglycerides | <1.7 mmol/l | 23/19 | 68/70 |
| Trigliceridi | >1.7 mmol/l | 11/8 | 32/30 |

Legend: DM – Diabetes mellitus/Diabetes mellitus

Table 2. Central retinal thickness (CRT) changes

| Number of eyes (n)/Broj očiju (n) | Day 0 0. dan | 1 week 1. nedelja | 4 week 4. nedelja | 6 week 6. nedelja | 8 week 8. nedelja | 12 week 12. nedelja |
|-----------------------------------|-------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Group I (DM with DR) Grupa I (DM sa DR) | 13 | 256 ± 11 | 258 ± 9 | 268 ± 8 | 273 ± 11 | 273 ± 11 | 269 ± 14 |
| Group II (DM without DR) Grupa II (DM bez DR) | 13 | 252 ± 13 | 252 ± 13 | 254 ± 14 | 256 ± 13 | 256 ± 13 | 255 ± 14 |
| Group III (Healthy population) Grupa III (Zdravi) | 13 | 246 ± 8 | 246 ± 8 | 250 ± 8 | 251 ± 8 | 251 ± 7 | 249 ± 8 |
| ANOVA | F = 2.66 (p = 0.084) | F = 4.39 (p = 0.02) | F = 10.91 (p = 0.000) | F = 13.36 (p = 0.000) | F = 13.36 (p = 0.000) |
| P < 0.05 | F = 2.66, ANOVA |

Legend: CRT – Centralna retinalna debljina; DM sa DR – Dijabetes mellitus sa dijabetesnom retinopatijom; DM bez DR – Dijabetes melitus bez dijabetesne retinopatije; ANOVA – Analiza varijanse
was no statistically significant difference in mean CRT in the 6th postoperative week between diabetic subgroups in regard to duration of diabetes, type of treatment, HbA1c and lipid serums levels (Table 3).

Discussion

Diabetes can adversely affect all ocular tissues, including the natural crystalline lens. Diabetic patients develop cataract earlier and it matures to visual significance more quickly due to hyperglycemia. Beside the loss of visual acuity, cataract formation can mask the level of retinopathy and makes adequate treatment of retinopathy with laser photocoagulation difficult. Such patients require cataract surgery at an earlier age than nondiabetic patients [12, 13]. Phacoemulsification is a common surgical procedure applied in diabetic patients.

In this prospective study we demonstrated the influence of cataract surgery on visual acuity and macular changes in diabetic patients with and without DR and nondiabetic patients. The BCVA increased in all groups postoperatively and showed that cataract was the main reason of visual acuity loss at the time of surgery.

In previous studies, the prevalence of postoperative macular edema varied from 0.2% to 20.4%. Advance of modern phacoemulsification as well as application of NSAID drops in combination with steroids postoperatively, has reduced the rates of macular edema which was between 0.2% and 2.35%. In diabetic patients it may be as high as 22% [14, 15]. The prevalence of subclinical macular edema in diabetic patients varies from 31% to 81% due to many confounding factors [9].

In our study, 3.8% (3 eyes of 51) developed central involved macular edema (CRT > 310 μm, SD OCT) in the 4th postoperative week. According to Kown et al. [17] macular edema occurs one month after surgery. The prevalence of macular edema among the diabetic patients was lower than expected and found in the literature. The reason could be a higher rate of diabetic patients without retinopathy or mild form of retinopathy. Several authors reported CRT changes in patients with diabetic retinopathy after uncomplicated cataract surgery. The risk for macular thickening after cataract surgery depends on the severity of retinopathy and/or preexisting diabetic macular edema [16–18]. At our clinic, patients with severe diabetic retinopathy and/or diabetic macular edema undergoing cataract surgery were considered for anti-VEGF treatment preoperatively to avoid worsening of DR, development of DME, and improvement of visual function.

In our study, CRT measurement by OCT was the same in the three groups. Comparing the average CRT values, we found a statistically significant difference between the groups. Subclinical CRT changes (CRT < 300 μm) were detected postoperatively with the maximum value in group I (diabetics with DR) 6 weeks after surgery. Sarao et al. [10] found that the peak of CRT changes or development of macular edema was 5–6 weeks after uncomplicated cataract surgery. Dia-

![Graph 2. Postoperative optical coherence tomography (OCT) changes](image1)

**Graph 2.** Postoperative optical coherence tomography (OCT) changes

| Table 3. Subgroup analysis of CRT correlated with systematic parameters 6 weeks after surgery |
|-----------------------------------------------|
|       | Group I (DM with DR) | Group II (DM without DR) |
|       | Mean/Srednja vrednost ± SD | T | p | Mean/Srednja vrednost ± SD | T | p |
| DM > 10 years/DM > 10 godina | 274 ± 12.3 μm | -0.442 | 0.667 | 262 ± 2.2 μm | -1.202 | 0.255 |
| DM < 10 years/DM < 10 godina | 271 ± 10.4 μm | -0.075 | 0.941 | 253 ± 16.4 μm | -2.41 | 0.035 |
| Insulin/Insulin | 273 ± 11.0 μm | -0.075 | 0.941 | 250 ± 12.3 μm | -2.41 | 0.035 |
| OAD/Oralni antidiabetici | 272 ± 11.9 μm | 0.427 | 0.678 | 259 ± 13.6 μm | 1.079 | 0.304 |
| HbA1c > 7%/Glikozilirani hemoglobin | 271 ± 12.4 μm | -0.075 | 0.941 | 258 ± 9.3 μm | -0.534 | 0.604 |
| HbA1c < 7%/Glikozilirani hemoglobin | 274 ± 10.2 μm | -0.075 | 0.941 | 254 ± 16.6 μm | -2.41 | 0.035 |
| LDL > 2.6 mmol/L/Lipoprotein niske gustine | 274 ± 8.3 μm | -0.673 | 0.515 | 260 ± 12.4 μm | -2.41 | 0.035 |
| LDL < 2.6 mmol/L/Lipoprotein niske gustine | 269 ± 17 μm | -0.673 | 0.515 | 242 ± 2.3 μm | -2.41 | 0.035 |

**Legenda:** DM – Dijabetes mellitus, DR – Dijabetesna retinopatija
betics without DR and nondiabetic patients showed minimal CRT changes postoperatively. This was also confirmed by the study of Kim et al. [19] reporting changes in central point thickness on OCT after cataract surgery in patients with different status of retina due to DM.

In 25% to 50% of diabetic eyes, subclinical macular changes can progress to DME and compromised visual acuity during one year, according to the DCRC protocol G [20].

In this study, analysis of subgroups did not show that hyperglycemia affected CRT changes. There was a difference in mean CRT value between the group with HbA1c > 7% and group with HbA1c < 7%, but it was not statistically significant. In a study including 1,002 participants, Yang et al. [5] reported > HbA1c as a risk factor for developing macular edema in diabetic patients after cataract surgery. This was not established in our study, and the only reason could be the small number of patients included in the study without previous episodes of macular edema.

Our study did not show that the duration of diabetes and insulin dependence was a risk factor for macular edema after cataract surgery in diabetic patients. Although Kim et al. [19] showed that the group of patients with diabetes duration longer than 10 years had a postoperative increase of center point thickness of 83 μm, Flesner et al. [20] concluded that duration of diabetes longer than 10 years was not a risk factor for CRT changes after cataract surgery. In our population fewer patients receive insulin treatment and diabetic patients, particularly those who visit internal medicine specialist rarely, present with fear from insulin therapy.

We concluded that high level of low-density lipoprotein cholesterol was not a risk factor for postoperative CRT changes in diabetic patients and it is in contrast with previous studies [21]. There are, unfortunately, some limitations in this study. It included a small number of patients compared to large-scaled studies. Among the diabetic patients more than 50% had DM < 10 years and in groups with HbA1c > 7% mean HbA1c value was 7.75 which showed good metabolic control. Twenty-two percent of patients received insulin therapy. The study needs more patients and longer follow-up period to identify predictive factors of postoperative macular edema in diabetic population in order to be useful for prevention, diagnosis and adequate treatment of this condition.

**Conclusion**

In conclusion, we found that cataract surgery had a good impact on visual function in diabetic and nondiabetic patients. The impact on central retinal thickness in diabetic population without previous macular edema was mild and it was not connected with hyperglycemia, hyperlipidemia, insulin treatment and duration of diabetes.

Good visual function and improvement of the best visual acuity with minimal structural macular changes are helpful when making the decision to perform cataract surgery in diabetic patients. However, these patients should postoperatively be treated with topical nonsteroidal anti-inflammatory drugs in combination with steroids. Follow-up visits should include routine procedures to measure macular morphology and function.

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