Diabetes Alone Does Not Impair Recovery From Uneventful Cataract Surgery

REETA DANNI, CLAUDIA TAIPALE, LOTTA ILVESKOSKI, AND RAIMO TUUMINEN

• PURPOSE: To study the outcomes of uneventful cataract surgery in diabetic patients without retinal complications.

• DESIGN: A post hoc treatment analysis using data from 2 double-masked randomized clinical trials.

• METHODS: Setting: Conducted at Kymenlaakso Central Hospital, Kotka, Finland. Procedure: A total of 276 eyes of 266 patients undergoing routine cataract surgery were included in the study. Patients with type I or II diabetes (n = 56 eyes) were compared to nondiabetic patients (n = 220 eyes). Clinical evaluation was conducted by the operating physician, and outcome measures taken before surgery and day 28 were recorded by a research technician.

• RESULTS: Patient age, sex distribution, and all baseline ophthalmic and surgical parameters were comparable for the nondiabetic and diabetic patient groups. Increase in aqueous flare 6.3 ± 16.4 photon units (pu)/ms vs 3.7 ± 8.9 pu/ms (mean ± standard deviation; $P = .282$), central retinal thickness (CRT) 12.0 ± 38.2 μm vs 5.9 ± 15.8 μm ($P = .256$), corrected distance visual acuity 0.57 ± 0.31 decimals vs 0.53 ± 0.35 decimals ($P = .259$), and patient satisfaction 9.3 ± 0.9 vs 9.2 ± 1.1 ($P = .644$) were comparable for nondiabetic and diabetic patients. In eyes with steroid monotherapy (n = 64), CRT increased 38.1 ± 72.8 μm in nondiabetic patients compared to 7.8 ± 6.6 μm in diabetic ones ($P = .010$). In eyes with nonsteroidal anti-inflammatory drug (NSAID) monotherapy (n = 157), CRT increased 5.7 ± 18.4 μm in nondiabetic patients compared to 6.2 ± 20.5 μm in diabetic ones ($P = .897$). Among eyes with steroid and NSAID combination therapy (n = 55), CRT increased 3.6 ± 4.1 μm in nondiabetic patients compared to 2.9 ± 3.2 μm in diabetic ones ($P = .606$). At 28 days postsurgery, pseudophakic cystoid macular edema (PCME) was reported in 8 eyes, of which 7 were in nondiabetic patients ($P = 1.000$).

• CONCLUSIONS: Diabetic patients showed less change in CRT when compared to controls in steroid monotherapy. Other outcome measurements shows no statistical differences. (Am J Ophthalmol 2019;198:37–44. © 2018 Elsevier Inc. All rights reserved.)

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From the Helsinki Retina Research Group, University of Helsinki, Helsinki, Finland (R.D., C.T., L.I., R.T.); Department of Ophthalmology, Helsinki University Hospital, Helsinki, Finland (R.D., C.T., L.I.); and Unit of Ophthalmology, Kymenlaakso Central Hospital, Kotka, Finland (R.T.).

Inquiries to Raimo Tuuminen, Associate Professor, Chief Physician, Unit of Ophthalmology, Kymenlaakso Central Hospital, Kotkantie 41, FI-48210 Kotka, Finland; e-mail: raimo.tuuminen@helsinki.fi

DIABETES IS A RISK FACTOR FOR RETINAL COMPLICATIONS of the eye. Several registry-based studies have established that the incidence of pseudophakic cystoid macular edema (PCME) after routine cataract surgery is higher among diabetic patients compared to those without diabetes.[1,2] The level of macular edema after cataract surgery as well as the prevalence of PCME correlate well with the stage of diabetic retinopathy (DR).[2,3] Moreover, eyes with previous presence of diabetic macular edema (DME) undergoing cataract surgery were found to be at risk of developing macular edema after surgery.[4,5]

Tight glycemic control is associated with lower intravitreal levels of vascular permeability factors,[6,7] and is protective against the development of macular edema after cataract surgery.[8] Also, managing a diabetic patient's cardiovascular risk factors with medications such as systemic vasoactive agents may further decrease the risk of PCME.[9]

The necessity of ophthalmic check-up following a standard cataract surgery on a patient with no ocular comorbidities has been questioned.[10,11] Diabetic patients, on the other hand, with a risk to develop PCME are encouraged to be systematically followed by ophthalmologists. Clinical practice protocols may involve optical coherence tomography (OCT) imaging as it is highly sensitive in revealing macular cystoid structures.[3] Large register-based studies, discounting the data on baseline clinical measures, may misleadingly fail to distinguish pre-existing DME or its progression from PCME at postoperative screening. Furthermore, no unambiguous diagnostic definition exists to differentiate between asymptomatic nonrefractory and clinically relevant cases of PCME.[12,13] These biases raise concern of overestimating the risk of diabetes for PCME,[14] which in turn may mistarget effective allocation of public eye care services and cause unnecessary worry for the patients.[15,16]

The purpose of this study was to assess whether diabetes itself has any effect on the recovery from uneventful cataract surgery. Furthermore, we aimed to evaluate whether the relative risk of postoperative PCME in diabetic patients depends on the selected anti-inflammatory medication. These results may supplement our knowledge in planning

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the optimal follow-up and anti-inflammatory medication for diabetic patients without posterior segment complications.

METHODS

• **STUDY DESIGN:** This study is a post hoc treatment analysis using data from 2 double-masked RCTs conducted at the Kymenlaakso Central Hospital, Kotka, Finland.[17,18] Patients were enrolled between January 2016 and December 2016. In the first study conducted between January 2016 and October 2016,[17] we compared the efficacy of different anti-inflammatory eye drops, and their combination in 189 eyes of 180 patients undergoing routine cataract surgery. In the second study conducted between October 2016 and December 2016,[18] we compared the tolerability of 2 potent nonsteroidal anti-inflammatory drugs (NSAIDs) in 96 eyes of 95 patients also undergoing routine cataract surgery. Patients were postoperatively treated with either steroids, NSAIDs, or their combination. The outcomes were analyzed according to the presence of diabetes. The study was conducted according to the tenets of the Declaration of Helsinki and was approved by the Research Director and Chief Medical Officer of the Kymenlaakso Central Hospital, the Finnish Medicines Agency Fimea, and the Institutional Review Board of Helsinki University Hospital (EU Clinical Trials Register Numbers: 2015-003296-30, 2015-005313-79).

• **PATIENTS:** A total of 320 eyes of 309 patients were admitted according to the national guidelines for the management of cataract. Seventeen patients withdrew from the study before their 28-day control visits (Supplemental Figure; Supplemental Material available at AJO.com). They either withdrew at own request or could not attend their scheduled control visit. Moreover, 12 patients were excluded from the study because of medication misuse, 7 because of medication intolerance, 2 because of drug inefficacy or adverse effects, and 6 for other reasons (Supplemental Figure).

After the drop-outs in randomized clinical trials, 276 eyes of 266 patients remained to be included in the protocol analysis. No immediate sequential bilateral cataract surgeries were performed. Ten patients were operated for both eyes and the surgeries were performed independently of each other. The treatment group was randomized before each surgery, independent of prior contralateral eye surgeries. The minimum time between surgeries was 1 month, assuring the patient sufficient time to recover from the first operation.

Sixty-four eyes were treated with steroid monotherapy, 157 eyes with NSAID monotherapy, and 55 eyes with steroid and NSAID combination therapy.

The eyes of nondiabetic patients (n = 220 eyes) were compared to those with diabetes (n = 56 eyes). Of the 56 eyes, 15 belonged to insulin-dependent diabetic patients. Only 1 eye represented type I, and the remaining 55 eyes represented II diabetes. The duration of diabetes was 11.8 ± 7.2 years on average. Serum glycosylated hemoglobin (HbA1c) was available for 48 diabetic patients. The average level of HbA1c was 47.9 ± 12.9 mmol/mol (6.53% ± 1.18%), median 44 mmol/mol (6.2%), range 28-82 mmol/mol (4.7%–9.7%), representing recommended glycemic control of diabetic patients.

Diabetic patients belonged to our regular screening system for diabetic retinopathy according to the Current Care Guideline for Diabetic Retinopathy of the Finnish Medical Society, Duodecim (updated in 2015). DR was graded on a five-stage severity classification as none, background, moderate nonproliferative, severe nonproliferative, or proliferative DR according to international clinical classification systems for DR. Two eyes were evaluated with background DR at some point during their history based on a fundus photography as a screening method. These eyes were not subjected to any treatment. None of the eyes showed DR at the preoperative examination.

Based on the information of electronic prescriptions at the pharmaceutical database Kanta (The National Archive of Health Information in Finland), the most common concomitant systemic medications of the diabetic patients were statins (n = 35; 63% of diabetic patients), angiotensin-converting-enzyme (ACE) inhibitors or angiotensin II receptor (AT2) antagonists (n = 28; 50% of diabetic patients), β-blockers (selective or unselective; n = 23; 41% of diabetic patients), diuretics (loop or thiazide and potassium-sparing; n = 16; 29% of diabetic patients), and calcium channel blockers (vascular or cardioselective; n = 15; 27% of diabetic patients). It is noteworthy that acetylsalicylic acid is also available without a prescription.

• **INCLUSION CRITERIA:** The study subjects were aged 60-90 years and were eligible for cataract surgery according to the Current Care Guidelines for Cataract Surgery of the Finnish Medical Society, Duodecim (updated in 2013).

• **EXCLUSION CRITERIA:** The exclusion criteria, similar for both trials, were any form of DR at the preoperative examination, prior or active wet age-related macular degeneration, retinal vein/artery occlusion, retinal detachment, retinal necrosis, vitritis/endophthalmitis, vitreous hemorrhage, retinal phlebitis, optic neuritis, previous intraocular procedures (including fundus laser photocoagulation), prior or scheduled anti–vascular endothelial growth factor (anti-VEGF) treatment, and myopia above -6.0 diopters. Alcohol abuse, thyroid disease with abnormal thyroid-stimulating hormone (TSH) levels, continuous use of anti-inflammatory drugs, and sensitivity to any of the medications used during or after the operation were also considered exclusion criteria. Other criteria for exclusion were intraoperative complications such as iris prolapse, use of

sutures or posterior capsule tear, and failure to use the postoperative anti-inflammatory medications as prescribed.

• **RANDOMIZATION:** Both studies were conducted as randomized, double-masked, prospective, single-center trials (hrrg.fi/en/clinicaltrials/cataract/). Patients were randomized by a research technician for different anti-inflammatory medication protocols. The drug labels were covered with our hospital pharmacy's labels, and the bottles were then put into marked envelopes. The research technician randomized the patients after their cataract surgeries, and then distributed the marked envelopes accordingly. The drugs were unmasked after the data were analyzed.

• **ANTI-INFLAMMATORY MEDICATION:** Steroid treatment was carried out with dexamethasone (Monopex, 1mg/mL; Laboratoires Théa, Clermont-Ferrand, France) 3 times a day (t.i.d.) for 3 weeks. The study design of the 2 trials included 3 different NSAID regimens in different drug dispensers, either single-use drug pipettes or a bottle, depending on the study. NSAID treatment was carried out with preservative-free diclofenac sodium (Voltaren Ophtha, 1 mg/mL; Laboratoires Théa; or Dicloabak, 1 mg/mL, Laboratoires Théa) or nepafenac (Nevanac, 1 mg/mL; Novartis, Basel, Switzerland) t.i.d. for 3 weeks. Combination treatment with both steroid (Monopex, 1 mg/mL, Laboratoires Théa) and NSAID (Voltaren Ophtha, 1 mg/mL; Laboratoires Théa) was prescribed t.i.d. for 3 weeks.

• **SURGERY:** Prior to surgery, all eyes were prepared with a combination of tropicamide (Oftan Tropicamid, 5 mg/mL), phenylephrine hydrochloride (Oftan Metaoksedrin, 100 mg/mL), levofloxacin (Oftaquix, 5 mg/mL), and oxybuprocaine hydrochloride (Oftan Obucain, 4 mg/mL), all from Santen Pharmaceutical Co Ltd, Osaka, Japan.

A standardized phacoemulsification technique was used for all cataract operations (http://www.hrrg.fi/en/videos/). A 2.75-mm clear corneal incision was followed by capsulorrhexis, phacoemulsification (divide and conquer), and intraocular lens (IOL) placement into the capsular bag. An Ozil phacoemulsification handpiece and a 0.9-mm 30-degree beveled Kelman tip were used with the phacoemulsification system (Infiniti; Alcon, Fort Worth, Texas, USA). In all cases anesthesia was topical. Hyaluronic acid 1.6%–chondroitin sulfate 4.0% (DisCoVisc; Alcon) was used as the ophthalmic viscosurgical device. Preloaded aspheric, hydrophobic single-piece monofocal IOLs were used (AU00T0, AcrySof IQ, SN60WF in UltraSert delivery system; Alcon; PCB00, Tecnis IOL in iTec delivery system; Abbott Medical Optics Inc./Johnson & Johnson Vision, Jacksonville, Florida, USA). The antimicrobial medication used was intraoperative intracameral cefuroxime (Aprokam; Laboratoires Théa). Levofloxacin (Oftaquix; 5 mg/mL; Santen Pharmaceutical) eye drops were used postoperatively, t.i.d. for 1 week only in the trial EudraCT: 2015-003296-30.[17] Duration of operation and phaco energy (cumulative dissipated energy [CDE]) were recorded. Use of intraocular surgical aids (StabilEyes capsular tension ring; Abbott Medical Optics Inc/Johnson & Johnson Vision; 6.25 mm Malyugin Ring pupil extension device; MicroSurgical Technology, Redmond, Washington, USA) was not considered as an exclusion criterion, as currently their effect on aqueous flare and macular thickness changes remains ill-defined. As diabetes may affect pupillary dynamics,[19] the incidence of surgical aids was recorded.

• **CLINICAL EVALUATION:** The patients were examined preoperatively by an ophthalmologist on the day of the operation, and they visited a research technician at the 28th postoperative day (±2 days). A postoperative control at 28 days was set to follow clinical practices in government-based units that are recommended to stick to the Current Care Guidelines of Cataract Surgery of the Finnish Medical Society, Duodecim (updated in 2013), which state that 1-month follow-up is sufficient after uncomplicated cataract surgery.

Corrected distance visual acuity (CDVA) was evaluated preoperatively by the referring ophthalmologist and postoperatively with an autorefractometer by the research technician (ARK-1s; NIDEK Co Ltd, Aichi, Japan). Intraocular pressure (IOP) was measured by rebound tonometry (iCare tonometer; Revenio Group, Vantaa, Finland).

To pick up prolonged inflammation after the course of topical anti-inflammatory treatment, aqueous flare was recorded with a laser flare meter (FM-600; Kowa Company, Ltd, Nagoya, Japan). The mean of 5 reliable aqueous flare measurements was used in the analysis.

Central retinal thickness (CRT; here defined as mean thickness in the central 1000-μm-diameter area) was recorded by spectral-domain optical coherence tomography (SD-OCT; Heidelberg Eye Explorer Version 1.9.10.0 and HRA/SPECTRALIS Viewing Module Version 6.0.9.0; Heidelberg Engineering GmbH, Heidelberg, Germany). Follow-up 30-frame SD-OCT scans were performed using AutoRescan software.

When defining a certain cut-off for CRT that correlated with loss of vision, we have previously found in diabetic eyes that even smaller changes in CRT (smaller than previously defined 30% increase in central thickness on OCT as a diagnostic sign for PCME) seemed to present a trend for CDVA at 1 month.[8] Thus, incidences of CRT increase (≥10%, ≥20%, and ≥30% from the baseline) were represented. The diagnosis of PCME was made by a physician based on OCT findings and clinical evaluation. The diagnostic criteria for PCME were defined as CME (CRT ≥ 10% from baseline and foveal cysts) and expected CDVA deterioration.

At the 28-day control visit, the overall satisfaction of the participants was documented by an interview with the research technician.

• **STATISTICAL ANALYSES:** Data are given as mean ± standard deviation, except for the absolute numbers and proportions for the nominal scale. IBM SPSS Statistics 24 (SPSS Inc, Somers, New York, USA) was used for statistical analysis. For 2-group comparisons data were analyzed with the 2-factor χ^2 test for categorical variables (or with Fisher exact test when the value in any of the cells of a contingency table was 5 or less), the Student *t* test for continuous variables, and the Mann-Whitney *U* test for nonparametric variables. CDVA values were converted to logarithm of the minimum angle of resolution (logMAR) for statistical purposes. The very low visual acuity measurements have been converted as follows: counting fingers (CF) to 1.9 and hand motion (HM) to 2.3 logMAR units.[20] Primary outcome measures of the 2 prospective randomized double-masked trials were assessing the role in macular edema prevention and tolerability of the topical steroids, NSAIDs, or the combination of the 2. In that the present paper has an explorative nature and because there is no predicted outcome defined or statistical hypothesis given substantiating the sample size concerning patients with diabetes, $P \leq .05$ was considered statistically significant.

RESULTS

• **BASELINE VARIABLES:** Baseline variables for age and sex distribution, ophthalmic characteristics (aqueous flare, CDVA, CRT, IOP, pseudoexfoliation syndrome), and surgical characteristics (operation time, phaco energy [CDE], aid of pupil expansion device and capsular tension ring) were comparable for nondiabetic and diabetic patients (P = NS, nonsignificant Table 1).

After stratification for postoperative anti-inflammatory medication (steroids, NSAIDs, or their combination) all patient, ophthalmic, and surgical baseline variables remained comparable for the nondiabetic and diabetic groups, except for patient age for eyes treated with NSAID monotherapy (75.4 ± 6.1 years in nondiabetic patients vs 78.0 ± 5.9 years in diabetic patients, P = .029, Supplemental Table; Supplemental Material available at AJO.com).

• **AQUEOUS FLARE AND CENTRAL RETINAL THICKNESS IN THE EYES OF DIABETIC PATIENTS WITHOUT POSTERIOR SEGMENT COMPLICATIONS:** The change in aqueous flare was +6.3 ± 16.4 photon units (pu)/ms for the eyes of nondiabetic patients and +3.7 ± 8.9 pu/ms for the eyes of diabetic patients (P = .282, Table 2). At 28 days postsurgery, aqueous flare was 15.5 ± 16.9 pu/ms and 13.6 ± 8.8 pu/ms, respectively (P = .279, Table 2).

The change in CRT was +12.0 ± 38.2 μm in the eyes of nondiabetic patients and +5.9 ± 15.8 μm in the eyes of diabetic patients (P = .256, Table 2). Incidences of eyes having CRT increase over 10%, 20%, and 30% from the preoperative situation were nonsignificant between nondiabetic and diabetic patients (Table 2). At 28 days postsurgery, CRT was 284.6 ± 50.2 μm and 276.8 ± 31.6 μm, respectively (P = .275, Table 2).

We stratified the patients according to their postoperative anti-inflammatory medications and evaluated the effects of diabetes in these subgroups. In the steroid monotherapy group, change in aqueous flare was +12.5 ± 21.5 pu/ms for the eyes of nondiabetic patients and +6.5 ± 7.7 pu/ms for the eyes of diabetic patients (P = .373, Table 3). In the NSAID monotherapy group, the change was +4.3 ± 13.0 pu/ms in the eyes of nondiabetic patients and +4.5 ± 33.2 pu/ms in the eyes of diabetic patients (P = .957, Table 3). In the steroid and NSAID combination therapy group, the respective values were +4.5 ± 17.3 pu/ms and -0.8 ± 9.8 pu/ms (P = .309, Table 3).

In the steroid monotherapy group, the change in CRT was +38.1 ± 72.8 μm in the eyes of nondiabetic patients and +7.8 ± 6.6 μm in the eyes of diabetic patients (P = .010, Table 3). In the NSAID monotherapy group, CRT change was +5.7 ± 18.4 μm in the eyes of nondiabetic patients and +6.2 ± 20.5 μm in the eyes of diabetic patients (P = .897, Table 3). In the steroid and NSAID

TABLE 1. Baseline Variables in the Nondiabetic Patients and Diabetic Patients Without Posterior Segment Complications

	DM– (N = 220)	DM+ (N = 56)	*P*
Age (y)	75.8 ± 6.7	77.3 ± 6.6	.132
Sex (M:F), n (%)	81:139 (37:63)	26:30 (46:54)	.188
Aqueous flare (pu/ms)	8.7 ± 7.7	9.5 ± 6.6	.510
CDVA (logMAR)	0.53 ± 0.33	0.52 ± 0.37	.597
CRT mean (μm)	271.6 ± 27.6	270.3 ± 24.2	.756
IOP (mm Hg)	16.0 ± 3.9	16.1 ± 3.2	.941
PXF, n (%)	41 (19)	8 (14)	.447
Operation time (min)	20.6 ± 10.3	20.0 ± 11.8	.725
Phaco energy (CDE)	19.8 ± 10.7	18.6 ± 8.5	.438
Pupil extension device, n (%)	18 (8)	3 (5)	.584
CTR, n (%)	4 (2)	2 (4)	.352

CDE = cumulative dissipated energy; CDVA = corrected distance visual acuity; CRT = mean central retinal thickness; CTR = capsular tension ring; DM = diabetes mellitus; IOP = intraocular pressure; logMAR = logarithm of the minimum angle of resolution; pu = photon units; PXF = pseudoexfoliation syndrome.

Baseline variables regarding (1) patient, (2) ophthalmic, and (3) surgical parameters. Data are given as mean ± SD or absolute numbers and proportions. For 2-group comparisons, 2-factor χ^2 test (or Fisher exact test when values in any of the cells of a contingency table were 5 or below) was used for qualitative data, Student *t* test for continuous variables, and Mann-Whitney *U* test for ordinal measurement scale in CDVA.

TABLE 2. Aqueous Flare, Corrected Distance Visual Acuity, Central Retinal Thickness, and Intraocular Pressure 28 Days After Cataract Surgery in the Eyes of Nondiabetic Patients and Diabetic Patients Without Posterior Segment Complications

	DM−	DM+	*P*
Aqueous flare (pu/ms)			
Change	+6.3 ± 16.4	+3.7 ± 8.9	.282
At 28 days post	15.5 ± 16.9	13.6 ± 8.8	.279
CDVA (logMAR)			
Change	−0.47 ± 0.34	−0.45 ± 0.43	.126
At 28 days post	0.06 ± 0.17	0.07 ± 0.16	.771
CRT (μm)			
Change	+12.0 ± 38.2	+5.9 ± 15.8	.256
Increase > 10%, n (%)	14 (6)	1 (2)	.319
Increase > 20%, n (%)	7 (3)	1 (2)	1.000
Increase > 30%, n (%)	5 (2)	1 (2)	1.000
At 28 days post	284.6 ± 50.2	276.8 ± 31.6	.275
IOP (mm Hg)			
Change	−5.5 ± 3.8	−4.8 ± 3.1	.258
At 28 days post	10.6 ± 3.0	10.9 ± 3.1	.428

CDVA = corrected distance visual acuity; CRT = central retinal thickness; DM = diabetes mellitus; IOP = intraocular pressure; logMAR = logarithm of the minimum angle of resolution; post = after cataract surgery; pu = photon units.

Data are given as mean (±SD) or absolute numbers and proportions. For 2-group comparisons, Fisher exact test was used for qualitative data, Student *t* test for continuous variables, and Mann-Whitney *U* test for ordinal measurement scale in CDVA.

combination therapy group, the respective values were +3.6 ± 4.1 μm and +2.9 ± 3.2 μm ($P = .606$, Table 3).

• **INTRAOCULAR PRESSURE AND VISUAL ACUITY IN THE EYES OF DIABETIC PATIENTS WITHOUT POSTERIOR SEGMENT COMPLICATIONS:** The change in IOP was -5.5 ± 3.8 mm Hg in the eyes of nondiabetic patients and -4.8 ± 3.1 mm Hg in the eyes of diabetic patients ($P = .258$, Table 2). At 28 days postsurgery, IOP was 10.6 ± 3.0 mm Hg in the eyes of nondiabetic patients and 10.9 ± 3.1 mm Hg in the eyes of diabetic patients ($P = .428$, Table 2). In the steroid monotherapy, NSAID monotherapy, and combination therapy subgroups, IOP remained comparable for eyes of nondiabetic and diabetic patients (data not shown).

The CDVA gain was 0.47 ± 0.34 logMAR units in the eyes of nondiabetic patients and 0.45 ± 0.43 logMAR units in the eyes of diabetic patients ($P = .126$, Table 2). At 28 days postsurgery, CDVA was 0.06 ± 0.17 logMAR units in the eyes of nondiabetic patients and 0.07 ± 0.16 logMAR in the eyes of diabetic patients ($P = .771$, Table 2). CDVA gain was comparable for the eyes of nondiabetic and diabetic patients in the steroid monotherapy, NSAID monotherapy, and steroid and NSAID combination therapy groups (Table 3).

TABLE 3. Aqueous Flare, Corrected Distance Visual Acuity, and Central Retinal Thickness 28 Days After Cataract Surgery in the Eyes of Nondiabetic Patients and Diabetic Patients Without Posterior Segment Complications Stratified by Topical Anti-inflammatory Medication

	DM−	DM+	*P*
Steroid monotherapy			
Aqueous flare change (pu/ms)	+12.5 ± 21.5	+6.5 ± 7.7	.373
Aqueous flare at 28 days post (pu/ms)	23.3 ± 24.8	16.4 ± 12.4	.375
CDVA change (logMAR)	−0.49 ± 0.41	−0.39 ± 0.23	.367
CDVA at 28 days post (logMAR)	0.10 ± 0.19	0.06 ± 0.14	.495
CRT change (μm)	+38.1 ± 72.8	+7.8 ± 6.6	.010*
CRT at 28 days post (μm)	307.5 ± 85.1	283.8 ± 25.2	.102
NSAID monotherapy			
Aqueous flare change (pu/ms)	+4.4 ± 13.0	+4.4 ± 8.6	.998
Aqueous flare at 28 days post (pu/ms)	12.8 ± 12.8	14.0 ± 7.8	.631
CDVA change (logMAR)	−0.45 ± 0.25	−0.56 ± 0.62	.530
CDVA at 28 days post (logMAR)	0.03 ± 0.14	0.10 ± 0.19	.136
CRT change (μm)	+5.7 ± 18.4	+6.2 ± 20.5	.897
CRT at 28 days post (μm)	281.5 ± 34.5	280.6 ± 34.0	.895
Steroid and NSAID combination therapy			
Aqueous flare change (pu/ms)	+4.8 ± 17.4	−0.8 ± 9.8	.314
Aqueous flare at 28 days post (pu/ms)	13.9 ± 12.8	9.8 ± 5.5	.326
CDVA change (logMAR)	−0.47 ± 0.36	−0.40 ± 0.16	.590
CDVA at 28 days post (logMAR)	0.06 ± 0.18	0.02 ± 0.11	.646
CRT change (μm)	+3.6 ± 4.1	+2.9 ± 3.2	.606
CRT at 28 days post (μm)	268.6 ± 21.7	258.1 ± 25.8	.173

CDVA = corrected distance visual acuity; CRT = central retinal thickness; DM = diabetes mellitus; logMAR = logarithm of the minimum angle of resolution; NSAID = nonsteroidal anti-inflammatory drug; post = after cataract surgery; pu = photon units.

Data are given as mean (±SD). For 2-group comparisons, continuous variables (CRT) were analyzed with the Student *t* test and ordinal measurement scale (CDVA) with the Mann-Whitney *U* test.

*$P < .05$ was considered statistically significant.

• **PRESENCE OF PSEUDOPHAKIC CYSTOID MACULAR EDEMA IN THE EYES OF DIABETIC PATIENTS WITHOUT POSTERIOR SEGMENT COMPLICATIONS:** Overall, 8 cases of PCME were documented, 7 (incidence 3.2%) in the eyes of nondiabetic patients and 1 (1.8%) in a diabetic patient ($P = 1.000$, Table 4).

TABLE 4. Presence of Pseudophakic Cystoid Macular Edema at 28 Days in the Eyes of Nondiabetic Patients and Diabetic Patients Without Posterior Segment Complications

	DM−	DM+
All	7 of 220 (3.2%)	1 of 56 (1.8%)
Steroid monotherapy	7 of 51	0 of 13
NSAID monotherapy	0 of 125	1 of 32
Steroid and NSAID combination	0 of 44	0 of 11

DM = diabetes mellitus; NSAID = nonsteroidal anti-inflammatory drug.

Data are given as absolute numbers.

DISCUSSION

HERE, OUR RESULTS EMPHASIZE THAT DIABETES ITSELF, without posterior segment complications and having optimal glycemic target, does not impair the outcomes of uneventful cataract surgery. Interestingly, the relative risk for PCME among diabetic patients did not increase with any of the anti-inflammatory medications used.

A multitude of data exists showing that diabetes disturbs retinal microvascular function.[21] Hyperglycemia increases the circulating cytokine levels associated with oxidative stress and immune activation.[22] Further, activation of pro-apoptotic pathways, angiopoietin-2 signaling, and consecutive vasoregression evidenced by pericyte loss have been identified as early pathologic features of diabetic posterior segment complications and blood-retinal barrier breakdown.[23–26] High HbA1c levels, a sign of poor glycemic control, correlated with systemic and intravitreal levels of VEGF-A.[6,27,28] Moreover, high levels of VEGF in the aqueous humor were found to be a risk factor for macular edema after cataract surgery on diabetic patients with nonproliferative retinopathy.[29] Consequently, diabetic patients with retinopathy were far less likely to achieve the same postoperative visual acuity as those without retinopathy.[30]

Vitreous levels of proinflammatory cytokines were higher in the eyes that had previously undergone cataract surgery.[31] Interestingly, baseline variables of diabetic patients showed higher prevalence of cardiovascular medications than among nondiabetic patients.[9] Remarkably, macular swelling was less pronounced among diabetic patients than among nondiabetic patients on steroid monotherapy. One might assume that systemic vasoactive medications in diabetic patients without posterior segment manifestations would counteract the risk of PCME. Protective mechanisms include improvement of vascular endothelial and pericyte functions and inhibition of oxidative stress and inflammatory pathways. For diabetic patients, administration of preoperative statins decreased vitreous levels of permeability and profibrotic factors and improved outcome of vitreoretinal surgery.[32,33] Systemic vasoactive medications were also found to improve recovery after cataract surgery.[9]

As compared to steroid monotherapy, a combination of steroids and NSAIDs seems to better reduce the macular edema induced by cataract surgery in patients with diabetic retinopathy.[8,34,35] Interestingly, it has been shown that the incidence of PCME in diabetic patients treated postoperatively with a combination of steroids and NSAIDs was comparable to those not at risk for PCME.[36] Here, independent of the selected anti-inflammatory medication, diabetes itself did not impair recovery from uneventful surgery and did not increase the relative risk of PCME when compared to nondiabetic controls. Considering the relatively small sample size, caution is needed in drawing conclusions in this clinically important question. Furthermore, late-phase follow-ups could render evaluation of macular edema kinetics between diabetic and nondiabetic control patients. Our data, however, emphasize that diabetic patients with optimal management of the disease may not be subjected to increased risk of PCME.

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