Diabetes alone does not impair recovery from uneventful cataract surgery

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**Running title:** Diabetes in cataract surgery

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**Conflict of Interest:** No conflicting relationships exist for any author

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Abstract

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

**Setting:** Conducted at Kymenlaakso Central Hospital, Kotka, Finland.

**Design:** A post-hoc treatment analysis using data from 2 double-blind RCTs.

**Methods:** 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 non-diabetic 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, gender distribution and all baseline ophthalmic and surgical parameters were comparable for the non-diabetic and diabetic patient groups. Increase in aqueous flare 6.3±16.4pu/msec vs. 3.7±8.9pu/msec (mean±SD; P=0.282), CRT 12.0±38.2µm vs. 5.9±15.8µm (P=0.256), corrected distance visual acuity 0.57±0.31decimals vs. 0.53±0.35decimals (P=0.259), and patient satisfaction 9.3±0.9 vs. 9.2±1.1 (P=0.644) were comparable for non-diabetic and diabetic patients. In eyes with steroid monotherapy (N=64), CRT increased 38.1±72.8µm in non-diabetic patients compared to 7.8±6.6µm in diabetic ones (P=0.010). In eyes with nonsteroidal anti-inflammatory drug (NSAID) monotherapy (N=157), CRT increased 5.7±18.4µm in non-diabetic patients compared to 6.2±20.5µm in diabetic ones (P=0.897). Among eyes with steroid and NSAID combination therapy (N=55), CRT increased 3.6±4.1µm in non-diabetic patients compared to 2.9±3.2µm in diabetic ones (P=0.606). At 28 days, pseudophakic cystoid macular edema (PCME) was reported in eight eyes, of which seven in non-diabetic patients (P=1.000).

**Conclusions:** Diabetic patients showed less changes in CRT when compared to controls in steroid monotherapy. Other outcome measurement shows no statistical differences.

**Key words:** cataract surgery; diabetes; NSAID; steroid; pseudophakic cystoid macular edema.
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Abbreviations:

BRB: blood-retinal barrier
CDE: cumulative dissipated energy
CDVA: corrected distance visual acuity
CRT: central retinal thickness
DM: diabetes mellitus type I or II
DME: diabetic macular edema
DR: diabetic retinopathy
IOP: intraocular pressure
NSAID: nonsteroidal anti-inflammatory drug
PCME: pseudophakic cystoid macular edema
pu: photon units
PXF: pseudoexfoliation syndrome
OCT: optical coherence tomography
RCT: randomized clinical trial
Statin: HMG-CoA reductase inhibitor
t.i.d.: three times a day
VEGF: vascular endothelial growth factor
Introduction

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.\textsuperscript{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).\textsuperscript{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.\textsuperscript{4,5}

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

The necessity of ophthalmic check-up following a standard cataract surgery on a patient with no ocular comorbidities has been questioned.\textsuperscript{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.\textsuperscript{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 non-refractory and clinically relevant cases of PCME.\textsuperscript{12,13} These biases raise concern of overestimating the risk of diabetes for PCME,\textsuperscript{14} which in turn may mistarget effective allocation of public eye care services and cause unnecessary worry for the patients.\textsuperscript{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 the optimal follow-up and anti-inflammatory medication for diabetic patients without posterior segment complications.
Materials and Methods

Study design
This study is a post-hoc treatment analysis using data from 2 double-blind RCTs conducted at the Kymenlaakso Central Hospital, Kotka, Finland. Patients were enrolled between January 2016 and December 2016. In the first study, 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, we compared the tolerability of two potent NSAIDs in 96 eyes of 95 patients also undergoing routine cataract surgery. Patients were postoperatively treated either with steroids, NSAID 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 (Supplement Figure 1). They either withdrew at own request or could not attend their scheduled control visit. Moreover, twelve patients were excluded from the study because of medication misuse, seven because of medication intolerance, two because of drug inefficacy or adverse effects, and six for other reasons (Supplement Figure 1).

After the drop-outs in RCTs, 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 one 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 non-diabetic 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 one eye represented type I, and the rest 55 eyes represented II diabetes. The duration of diabetes was 11.8 ± 7.2 years on the 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 (hrg.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 unblinded after the data was analyzed.

**Anti-inflammatory medication**
Steroid treatment was carried out with dexamethasone (Monopex®, 1mg/ml, Laboratoires Théa, Clermont-Ferrand, France) three times a day (t.i.d.) for three weeks. The study design of the two trials included three 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®, 1mg/ml, Laboratoires Théa; or Dicloabak®, 1mg/ml, Laboratoires Théa) or nepafenac (Nevanac®, 1mg/ml, Novartis, Basel, Switzerland) t.i.d. for three weeks. Combination treatment with both steroid (Monopex®, 1mg/ml, Laboratoires Théa) and NSAID (Voltaren Ophtha®, 1mg/ml, Laboratoires Théa) was prescribed t.i.d. for three weeks.

**Surgery**
Prior to surgery, all eyes were prepared with a combination of tropicamide (Oftan Tropicamid®, 5mg/ml), phenylephrine hydrochloride (Oftan Metaoksedrin®, 100mg/ml), levofloxacin (Oftaquix®, 5mg/ml) and oxybuprocaine hydrochloride (Oftan Obucain®, 4mg/ml) all from Santen Pharmaceutical Co. Ltd, Osaka, Japan
A standardized phacoemulsification technique was used for all cataract operations at http://www.hrrg.fi/en/videos/. A 2.75 mm clear corneal incision was followed by capsulorrhexis, phacoemulsification (divide and conquer), and intraocular lens 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, TX). 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 intraocular lenses were used (AU00T0, AcrySof® IQ, SN60WF in UltraSertTM delivery system, Alcon; PCB00, Tecnis® IOL in iTec® delivery system, Abbott Medical Optics Inc. / Johnson & Johnson Vision, Jacksonville, FL). The antimicrobial medication used was intraoperative intracameral cefuroxime (Aprokam®, Laboratoires Thea, Clermont-Ferrand, France). Levofloxacin (Oftaquix®, 5 mg/ml, Santen Pharmaceutical) eye drops were used postoperatively, t.i.d. for one week only in the trial EudraCT: 2015-003296-30. Duration of operation and phaco energy (cumulative dissipated energy; C.D.E) 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, WA) was not considered as exclusion criteria as currently their effect on aqueous flare and macular thickness changes remains ill-defined. As diabetes may affect pupillary dynamics, 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 governmental 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 one-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 auto-refractometer 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 five 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, 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. 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 is given as mean ± SD, except for the absolute numbers and proportions for the nominal scale. IBM SPSS Statistics 24 (SPSS Inc., Somers, NY) was used for statistical analysis. For two-group comparisons data was analysed with the two-factor $\chi^2$ test for categorical variables (or with Fisher’s exact test when the value in any of the cells of a contingency table was five or less), the Student’s 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. Primary outcome measures of the two prospective randomized double-blind trials were assessing the role in macular edema prevention and tolerability of the topical steroids, NSAIDs or the combination of the two. In that, the present paper has an explorative nature and for the reasons, there is no predicted outcome defined or statistical hypothesis given substantiating the sample size concerning patients with diabetes. $P \leq 0.05$ was considered statistically significant.
Results

Baseline variables

Baseline variables for age and gender distribution, ophthalmic (aqueous flare, CDVA, CRT, IOP, pseudoexfoliation syndrome) and surgical characteristics (operation time, phaco energy [cumulative dissipated energy; CDE], aid of pupil expansion device and capsular tension ring) were comparable for non-diabetic and diabetic patients ($P = \text{NS}$, Table 1).

After stratification for postoperative anti-inflammatory medication (steroids, NSAID, or their combination) all patient, ophthalmic and surgical baseline variables remained comparable for the non-diabetic and diabetic groups, except for patient age for eyes treated with NSAID monotherapy (75.4 ± 6.1 years in non-diabetic patients vs. 78.0 ± 5.9 years in diabetic patients, $P = 0.029$, Supplement Table 1).

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 pu/msec for the eyes of non-diabetic patients and +3.7 ± 8.9 pu/msec for the eyes of diabetic patients ($P = 0.282$, Table 2). At 28 days, aqueous flare was 15.5 ± 16.9 pu/msec and 13.6 ± 8.8 pu/msec, respectively ($P = 0.279$, Table 2).

The change in CRT was +12.0 ± 38.2 µm in the eyes of non-diabetic patients and +5.9 ± 15.8 µm in the eyes of diabetic patients ($P = 0.256$, Table 2). Incidences of eyes having CRT increase over 10 %, 20 %, and 30 % from the preoperative situation were non-significant between non-diabetic and diabetic patients (Table 2). At 28 days, CRT was 284.6 ± 50.2 µm and 276.8 ± 31.6 µm, respectively ($P = 0.275$, 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/msec for the eyes of non-diabetic patients, and +6.5 ± 7.7 pu/msec for the eyes of diabetic patients ($P = 0.373$, Table 3). In the NSAID monotherapy group, the change was +4.3 ± 13.0 pu/msec in the eyes of non-diabetic patients, and +4.5 ± 33.2 pu/msec in the eyes of diabetic patients ($P = 0.957$, Table 3). In the steroid and NSAID combination therapy group, the respective values were +4.5 ± 17.3 pu/msec and -0.8 ± 9.8 pu/msec ($P = 0.309$, Table 3).

In the steroid monotherapy group, the change in CRT was +38.1 ± 72.8 µm in the eyes of non-diabetic patients, and +7.8 ± 6.6 µm in the eyes of diabetic patients ($P = 0.010$, Table 3). In the NSAID monotherapy group, CRT change was +5.7 ± 18.4 µm in the eyes of non-diabetic patients, and +6.2 ± 20.5 µm in the eyes of diabetic patients ($P = 0.897$, Table 3). In the steroid and NSAID combination therapy group, the respective values were +3.6 ± 4.1 µm and +2.9 ± 3.2 µm ($P = 0.606$, 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 mmHg in the eyes of non-diabetic patients, and -4.8 ± 3.1 mmHg in the eyes of diabetic patients ($P = 0.258$, Table 2). At 28 days, IOP was 10.6 ± 3.0 mmHg in the eyes of non-diabetic patients, and 10.9 ± 3.1 mmHg in the eyes of diabetic patients ($P = 0.428$, Table 2). In the steroid monotherapy, NSAID monotherapy, and combination therapy subgroups, IOP remained comparable for eyes of non-diabetic and diabetic patients (data not shown).

The CDVA gain was 0.47 ± 0.34 logMAR units in the eyes of non-diabetic patients, and 0.45 ± 0.43 logMAR units in the eyes of diabetic patients ($P = 0.126$, Table 2). At 28 days, CDVA was 0.06 ± 0.17 logMAR units in the eyes of non-diabetic patients, and 0.07 ± 0.16 logMAR in the eyes of diabetic patients ($P = 0.771$, Table 2). CDVA gain was comparable for the eyes of non-diabetic and diabetic patients in the steroid monotherapy, NSAID monotherapy, and steroid and NSAID combination therapy groups (Table 3).

**Presence of pseudophakic cystoid macular edema in the eyes of diabetic patients without posterior segment complications**

Overall, eight cases of PCME were documented, seven (incidence 3.2 %) in the eyes of non-diabetic patients and one (1.8 %) in diabetic patient ($P = 1.000$, Table 4).
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. Hyperglycemia increases the circulating cytokine levels associated with oxidative stress and immune activation. 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. High HbA1c levels, a sign of poor glycemic control, correlated with systemic and intravitreal levels of VEGF-A. Moreover, high levels of VEGF in the aqueous humor were to be a risk factor for macular edema after cataract surgery on diabetic patients with nonproliferative retinopathy. Consequently, diabetic patients with retinopathy were far less likely to achieve the same postoperative visual acuity as those without retinopathy.

Vitreous levels of proinflammatory cytokines were higher in the eyes that had previously undergone cataract surgery. Interestingly, baseline variables of diabetic patients showed higher prevalence of cardiovascular medications than among non-diabetic patients. Remarkably, macular swelling was less pronounced among diabetic patients than non-diabetic 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 pro-fibrotic factors and improved outcome of vitreoretinal surgery. Systemic vasoactive medications were also found to improve recovery after cataract surgery.

As compared to steroid monotherapy, a combination of steroids and NSAID seems to better reduce the macular edema induced by cataract surgery in patients with diabetic retinopathy. Interestingly, it has been shown that the incidence of PCME in diabetic patients treated postoperatively with a combination of steroids and NSAID was comparable to those not at risk for PCME. 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 non-diabetic 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 non-diabetic control patients. Our data, however, emphasizes that diabetic patients with optimal management of the disease may not be subjected to increased risk of PCME.
Acknowledgments

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References


Table 1. Baseline variables in the non-diabetic patients and diabetic patients without posterior segment complications.

<table>
<thead>
<tr>
<th>Variable</th>
<th>DM – (n = 220)</th>
<th>DM + (n = 56)</th>
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<tr>
<td>Age (y)</td>
<td>75.8 ± 6.7</td>
<td>77.3 ± 6.6</td>
<td>0.132</td>
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<tr>
<td>Gender M:F (n/%)</td>
<td>81:139 (37:63)</td>
<td>26:30 (46:54)</td>
<td>0.188</td>
</tr>
<tr>
<td>Aqueous flare (pu/ms)</td>
<td>8.7 ± 7.7</td>
<td>9.5 ± 6.6</td>
<td>0.510</td>
</tr>
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<td>CDVA (logMAR)</td>
<td>0.53 ± 0.33</td>
<td>0.52 ± 0.37</td>
<td>0.597</td>
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<tr>
<td>CRT mean (µm)</td>
<td>271.6 ± 27.6</td>
<td>270.3 ± 24.2</td>
<td>0.756</td>
</tr>
<tr>
<td>IOP (mmHg)</td>
<td>16.0 ± 3.9</td>
<td>16.1 ± 3.2</td>
<td>0.941</td>
</tr>
<tr>
<td>PXF (n/%)</td>
<td>41 (19)</td>
<td>8 (14)</td>
<td>0.447</td>
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<tr>
<td>Operation time (min)</td>
<td>20.6 ± 10.3</td>
<td>20.0 ± 11.8</td>
<td>0.725</td>
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<tr>
<td>Phaco energy (CDE)</td>
<td>19.8 ± 10.7</td>
<td>18.6 ± 8.5</td>
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<td>Pupil extension device (n/%)</td>
<td>18 (8)</td>
<td>3 (5)</td>
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<tr>
<td>CTR (n/%)</td>
<td>4 (2)</td>
<td>2 (4)</td>
<td>0.352</td>
</tr>
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</table>

Baseline variables regarding i) patient ii) ophthalmic and iii) surgical parameters. Data are given as mean (±SD) or absolute numbers and proportions. For two-group comparisons, two-factor χ² test (or Fisher’s exact test when values in any of the cells of a contingency table were five or below) was used for qualitative data. Student’s T-test for continuous variables and Mann-Whitney U test for ordinal measurement scale in CDVA. 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; log of the minimum angle of resolution, pu; photon units, PXF; pseudoexfoliation syndrome.
Table 2. Aqueous flare, corrected distance visual acuity, central retinal thickness and intraocular pressure 28 days after cataract surgery in the eyes of non-diabetic patients and diabetic patients without posterior segment complications.

<table>
<thead>
<tr>
<th></th>
<th>DM -</th>
<th>DM +</th>
<th>P =</th>
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</thead>
<tbody>
<tr>
<td><strong>Aqueous flare (pu/msec)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>+6.3 ± 16.4</td>
<td>+3.7 ± 8.9</td>
<td>0.282</td>
</tr>
<tr>
<td>At 28-day</td>
<td>15.5 ± 16.9</td>
<td>13.6 ± 8.8</td>
<td>0.279</td>
</tr>
<tr>
<td><strong>CDVA (logMAR)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>-0.47 ± 0.34</td>
<td>-0.45 ± 0.43</td>
<td>0.126</td>
</tr>
<tr>
<td>At 28-day</td>
<td>0.06 ± 0.17</td>
<td>0.07 ± 0.16</td>
<td>0.771</td>
</tr>
<tr>
<td><strong>CRT (µm)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>+12.0 ± 38.2</td>
<td>+5.9 ± 15.8</td>
<td>0.256</td>
</tr>
<tr>
<td>Increase &gt; 10% (n/%)</td>
<td>14 (6)</td>
<td>1 (2)</td>
<td>0.319</td>
</tr>
<tr>
<td>Increase &gt; 20% (n/%)</td>
<td>7 (3)</td>
<td>1 (2)</td>
<td>1.000</td>
</tr>
<tr>
<td>Increase &gt; 30% (n/%)</td>
<td>5 (2)</td>
<td>1 (2)</td>
<td>1.000</td>
</tr>
<tr>
<td>At 28-day</td>
<td>284.6 ± 50.2</td>
<td>276.8 ± 31.6</td>
<td>0.275</td>
</tr>
<tr>
<td><strong>IOP (mmHg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>-5.5 ± 3.8</td>
<td>-4.8 ± 3.1</td>
<td>0.258</td>
</tr>
<tr>
<td>At 28-day</td>
<td>10.6 ± 3.0</td>
<td>10.9 ± 3.1</td>
<td>0.428</td>
</tr>
</tbody>
</table>

Data are given as mean (±SD) or absolute numbers and proportions. For two-group comparisons, Fisher’s exact test was used for qualitative data, Student’s T test for continuous variables and Mann-Whitney U test for ordinal measurement scale in CDVA. CDVA; corrected distance visual acuity, CRT; central retinal thickness, DM; diabetes mellitus, IOP; intraocular pressure, logMAR; log of the minimum angle of resolution, pu; photon units.
Table 3. Aqueous flare, corrected distance visual acuity and central retinal thickness 28 days after cataract surgery in the eyes of non-diabetic patients and diabetic patients without posterior segment complications stratified by topical anti-inflammatory medication.

<table>
<thead>
<tr>
<th></th>
<th>DM -</th>
<th>DM +</th>
<th>P =</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Steroid monotherapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aqueous flare change (pu/msec)</td>
<td>+12.5 ± 21.5</td>
<td>+6.5 ± 7.7</td>
<td>0.373</td>
</tr>
<tr>
<td>Aqueous flare at 28-day (pu/msec)</td>
<td>23.3 ± 24.8</td>
<td>16.4 ± 12.4</td>
<td>0.375</td>
</tr>
<tr>
<td>CDVA change (logMAR)</td>
<td>-0.49 ± 0.41</td>
<td>-0.39 ± 0.23</td>
<td>0.367</td>
</tr>
<tr>
<td>CDVA at 28-day (logMAR)</td>
<td>0.10 ± 0.19</td>
<td>0.06 ± 0.14</td>
<td>0.495</td>
</tr>
<tr>
<td>CRT change (µm)</td>
<td>+38.1 ± 72.8</td>
<td>+7.8 ± 6.6</td>
<td><strong>0.010</strong></td>
</tr>
<tr>
<td>CRT at 28-day (µm)</td>
<td>307.5 ± 85.1</td>
<td>283.8 ± 25.2</td>
<td>0.102</td>
</tr>
<tr>
<td><strong>NSAID monotherapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aqueous flare change (pu/msec)</td>
<td>+4.4 ± 13.0</td>
<td>+4.4 ± 8.6</td>
<td>0.998</td>
</tr>
<tr>
<td>Aqueous flare at 28-day (pu/msec)</td>
<td>12.8 ± 12.8</td>
<td>14.0 ± 7.8</td>
<td>0.631</td>
</tr>
<tr>
<td>CDVA change (logMAR)</td>
<td>-0.45 ± 0.25</td>
<td>-0.56 ± 0.62</td>
<td>0.530</td>
</tr>
<tr>
<td>CDVA at 28-day (logMAR)</td>
<td>0.03 ± 0.14</td>
<td>0.10 ± 0.19</td>
<td>0.136</td>
</tr>
<tr>
<td>CRT change (µm)</td>
<td>+5.7 ± 18.4</td>
<td>+6.2 ± 20.5</td>
<td>0.897</td>
</tr>
<tr>
<td>CRT at 28-day (µm)</td>
<td>281.5 ± 34.5</td>
<td>280.6 ± 34.0</td>
<td>0.895</td>
</tr>
<tr>
<td><strong>Steroid and NSAID combination therapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aqueous flare change (pu/msec)</td>
<td>+4.8 ± 17.4</td>
<td>-0.8 ± 9.8</td>
<td>0.314</td>
</tr>
<tr>
<td>Aqueous flare at 28-day (pu/msec)</td>
<td>13.9 ± 12.8</td>
<td>9.8 ± 5.5</td>
<td>0.326</td>
</tr>
<tr>
<td>CDVA change (logMAR)</td>
<td>-0.47 ± 0.36</td>
<td>-0.40 ± 0.16</td>
<td>0.590</td>
</tr>
<tr>
<td>CDVA at 28-day (logMAR)</td>
<td>0.06 ± 0.18</td>
<td>0.02 ± 0.11</td>
<td>0.646</td>
</tr>
<tr>
<td>CRT change (µm)</td>
<td>+3.6 ± 4.1</td>
<td>+2.9 ± 3.2</td>
<td>0.606</td>
</tr>
<tr>
<td>CRT at 28-day (µm)</td>
<td>268.6 ± 21.7</td>
<td>258.1 ± 25.8</td>
<td>0.173</td>
</tr>
</tbody>
</table>

Data are given as mean (±SD). For two-group comparisons, continuous variables (CRT) were analyzed with the Student’s T test and ordinal measurement scale (CDVA) with the Mann-Whitney U test. CDVA; corrected distance visual acuity, CRT; central retinal thickness, DM; diabetes mellitus, logMAR; log of the minimum angle of resolution, NSAID; nonsteroidal anti-inflammatory drug, pu; photon units.
Table 4. Presence of pseudophakic cystoid macular edema at 28 days in the eyes of non-diabetic patients and diabetic patients without posterior segment complications.

<table>
<thead>
<tr>
<th></th>
<th>DM -</th>
<th>DM +</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>7 of 220 (3.2%)</td>
<td>1 of 56 (1.8%)</td>
</tr>
<tr>
<td>Steroid monotherapy</td>
<td>7 of 51</td>
<td>0 of 13</td>
</tr>
<tr>
<td>NSAID monotherapy</td>
<td>0 of 125</td>
<td>1 of 32</td>
</tr>
<tr>
<td>Steroid and NSAID combination</td>
<td>0 of 44</td>
<td>0 of 11</td>
</tr>
</tbody>
</table>

Data are given as absolute numbers. DM; diabetes mellitus, NSAID; nonsteroidal anti-inflammatory drug.
Raimo Tuuminen, MD, PhD, FEBO completed his military service in the Paratrooper and Military Diving units of the Finnish Armed Forces, studied medicine and specialized in Ophthalmology at the University of Helsinki. He completed his doctoral dissertation, entitled *Microvascular dysfunction in ischemia-reperfusion in cardiac and kidney allografts*, at the University of Helsinki with distinction. He was appointed as Associate Professor in Ophthalmology at the University of Helsinki, and his inaugural lecture, titled *The pathogenesis of, and treatment options for, wet age-related macular degeneration*, was graded as outstanding. Currently he is a Chief Physician at the Department of Ophthalmology in Kymenlaakso Central Hospital in the Hospital District of Helsinki and Uusimaa (HUS) Specific Catchment Area, the Principal Investigator for the Helsinki Retina Research Group at the University of Helsinki, and Responsible Director for clinical trials, which aim at optimizing medication connected with cataract surgery and retinal vascular diseases.
Table of Contents Statement

Diabetes itself, insulin-dependence, poor glycemic control, and diabetic ocular manifestations are all considered risk factors for PCME. Register-based studies may overestimate the risk of PCME in diabetic patients. When diabetes is appropriately managed, in eyes without posterior segment manifestations clinical outcomes after uneventful cataract surgery may be comparable to non-diabetic controls.