·Clinical Research·

# Macular edema after cataract surgery in diabetic eyes evaluated by optical coherence tomography

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## Abstract

**• AIM: To assess quantitative changes of the macula in diabetic eyes after cataract surgery using optical coherence tomography (OCT) and to estimate the incidence of development or worsening of macular edema (ME) in diabetic eyes with or without pre-existing ME.**

**• METHODS: In this prospective, observational study, 92 eyes of 60 diabetic patients who underwent cataract surgery were evaluated before surgery and 1, 3mo after surgery using OCT. Macular thickness was measured with OCT at nine macular subfields defined by the 9 zones early treatment of diabetic retinopathy study (ETDRS), as well as total macular volume obtained by OCT at 1, 3mo after surgery were compared with baseline features obtained before surgery. In addition, the incidence of development or worsening of ME was analyzed in diabetic eyes with or without pre-existing ME.**

**• RESULTS: The central subfield mean thickness increased 21.0 μm and 25.5 μm at 1, 3mo follow-up, respectively ($P$<0.01). The average thickness of inner ring and outer ring increased 14.2 μm and 9.5 μm at 1mo, 18.2 μm and 12.9 μm at 3mo. Central-involved ME developed in 12 eyes at 3mo, including 4 eyes with pre-existing central-involved and 8 eyes with pre-existing non-central involved ME. Pre-existing diabetic macular edema (DME) was significantly associated with central-involved ME development ($P$ <0.001).**

**• CONCLUSION: A statistically significant increase could be detected in the central subfield as well as perifoveal and parafoveal sectors though the increase was mild. And eyes with pre-operative DME prior to cataract surgery are at higher risk for developing central-involved ME.**

• **KEYWORDS:** macular edema; diabetes; optical coherence tomography; cataract surgery
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## INTRODUCTION

Macular edema (ME) is one of the most common causes of visual loss after uncomplicated cataract surgery nowadays[1-3]. A higher incidence of ME after cataract surgery is reported to occur in eyes with diabetic retinopathy (DR), and worsening of ME often occur after surgery in eyes with pre-operative diabetic macular edema (DME) [1,4-5]. Several studies made attempts to identify the risk factors of post-operative ME in diabetic eyes, though the exact cause of this phenomenon is still undetermined. Baker *et al* [6] indicated that pre-operative macular status and history of DME treatment might be associated with the increased risk. Despite these efforts, the accurate prediction of post-operative macular status before surgery is still no easy task [7-8]. However, with the availability of the optical coherence tomography (OCT), we can obtain qualitative and quantitative parameters of macula better than ever and explore the relationship of macular status before and after cataract surgery in diabetic patients[9-12].

In this study, we assessed the changes of macular thickness in diabetic patients after cataract surgery using OCT and also examined the influence of preoperative laser treatment and severity of DR on macular thickness [7]. We also analyzed the incidence of both central-involved ME and non-central-involved ME following cataract surgery regarding preoperative status of macula[1]. Through our study, we aimed to assess the quantitative changes of macula in diabetic eyes after cataract surgery and help to estimate the incidence of ME after surgery in diabetic eyes.

## SUBJECTS AND METHODS

The study was conducted with the approval of ethics committee of Peking University Third Hospital in China and in accordance with ethical requirements of Declaration of Helsinki. Patients with diabetes mellitus who underwent phacoemulsification with intraocular lens insertion at our hospital between January 2012 and July 2013 were enrolled

**Table 1 Baseline and outcome DME definitions**

| Baseline DME category | Definition |
|---|---|
| No central DME and no non-central DME | CSMT <310 μm, all ISF thickness <356 μm, and all OSF thickness <303 μm |
| No central DME and non-central DME | CSMT <310 μm, and ≥1 ISF thickness ≥356 μm or OSF thickness ≥303 μm |
| Central DME and no non-central DME | CSMT≥310 μm, all ISF thickness <356 μm, and all OSF thickness <303μm |
| Central DME and non-central DME | CSMT≥310 μm, and ≥1 ISF thickness ≥356 μm or OSF thickness≥303 μm |
| DME at follow-up | |
| New development or progression central-involved ME | 1) CSMT ≥310 μm and CSMT increased ≥1 logOCT unit from baseline; 2) CSMT increased ≥2 logOCT units from baseline. |
| New development or progression non-central-involved ME | 1) ≥1 ISF thickness ≥356μm and the corresponding ISF thickness increased ≥1 logOCT unit from baseline, or ≥1 OSF thickness ≥303 μm and the corresponding OSF thickness increased ≥1 logOCT unit from baseline; 2) ≥1 ISF thickness increased ≥2 logOCT units from baseline or ≥1 OSF thickness increased ≥2 logOCT units from baseline. |

DME: Diabetic macular edema; ME: Macular edema; CSMT: Central subfield macular thickness; ISF: Inner subfields; OSF: Outer subfields; OCT: Optical coherence tomography.

in this study. Patients with pre-operative DME were also included in the study. Patients were excluded from the study if they had any of the following conditions: prior or concomitant surgery such as vitreoretinal surgery or glaucoma surgery in the operated eye, intraoperative complications, a history of ocular and systemic conditions associated with potentially irreversible significant vision loss, presence of any retinal or choroidal disease other than diabetes that could affect retinal thickness and history of treatment for DME or proliferative DR (PDR) within six months prior to surgery.

Cataract surgeries were performed by an experienced surgeon. A clear corneal incision was made, and continuous curvilinear capsulorrhexis was performed. For cataract surgery, phacoemulsification equipment (Legacy; Alcon Laboratories Inc., Fort Worth, TX, USA) was used. The nucleus was divided and phacoemulsification and aspiration were performed after cortical aspiration, an acrylic foldable intraocular lens was inserted in the capsular bag.

Preoperative and postoperative examinations including best-corrected visual acuity using standard visual acuity chart, which was translated into a logarithm of the minimal angle of resolution (logMAR) scale for analysis purposes, slit-lamp examination, fundus photography were checked at every follow-up visit. All patients were followed at 1wk, 1 and 3mo after surgery. OCT was performed at 1 and 3mo follow-up, using commercially available equipment (Cirrus HD-OCT, Carl Zeiss Meditec, Dublin, CA, USA). After pupil dilation, a macular thickness map was generated. This standard OCT protocol uses six radially oriented scan lines to produce a topographical map of the macula and the mean value of 128 thickness values obtained in the central subfield, which is circular area of diameter 1 mm centered around the center point [central subfield mean thickness (CSMT)], was measured. The thicknesses of inner and outer four quadrants of the nine early treatment of DR study (ETDRS) grid as well as total macular volume were also measured. We used the absolute change of thickness, relative change of thickness as well as absolute change of macular volume to analyze the development or worsening of ME. The definition of central-involved and non-central involved ME at baseline and follow-up were shown in Table 1, as modified from criteria offered by DR clinical research network (DRCR.net)[1]. In addition, the influence of prior laser treatment and pre-operative ME was also analyzed.

Statistical analysis was performed by SPSS ver. 13.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics, including mean and standard deviation were calculated for each group. Group comparisons were performed using the student *t* test. Fisher's exact, two-tailed test was used for analysis of data on a nominal scale. A *P*-value less than 0.05 was considered statistically significant.

## RESULTS

In this prospective study, 104 eyes of 70 diabetic patients were enrolled initially. And 4 eyes of 4 patients were excluded because of loss to follow up at 1mo after surgery. Also 8 eyes of 6 patients were excluded with low quality of pre-operative OCT image for subsequent macular thickness analysis because of advanced cataract. As a result, 92 eyes of 60 diabetic patients were evaluated in the final study.

The 60 subjects in this series were 32 males and 28 females with mean age of 70.2 ±9.1y. Mean preoperative best-corrected visual acuity in logMAR units was 0.57±0.47 and mean preoperative CSMT was 246.6±30.8 μm. The mean preoperative thicknesses of inner and outer four quadrants as well as macular volume are shown in Table 2.

According to definition of DME at baseline, twenty eyes presented with DME before surgery. In these twenty eyes, two eyes had central-involved DME without non-central involved DME. Four eyes presented with both central-involved and non-central involved DME. Another fourteen eyes had only non-central involved DME. The remaining 72 eyes showed no sign of pre-operative ME according to the criteria in Table 1.

DR severity was also assessed on clinical examination on a scale that included following: no DR, mild to moderate

**Table 2 Demographics**

| Demographics | Data |
|---|---|
| Eyes/patients | 92/60 |
| Sex (M:F) | 32:28 |
| Age (a) | 70.2±9.1 |
| Preoperative BCVA (logMAR) | 0.57±0.47 |
| Baseline CSMT (μm) | 246.6±30.8 |
| Baseline average inner ring thickness (μm) | 314.0±23.5 |
| Baseline average outer ring thickness (μm) | 276.5±24.3 |
| Baseline macular volume ($mm^3$) | 10.5±0.6 |
| DR stage | |
| No DR | 72/92 |
| Mild to moderate NPDR | 8/92 |
| Severe NPDR or PDR | 12/92 |
| History of photocoagulation | |
| Yes | 4/92 |
| No | 88/92 |

BCVA: Best corrected visual acuity; CSMT: Central subfield macular thickness; DR: Diabetic retinopathy; NPDR: Non-proliferative diabetic retinopathy; PDR: Proliferative diabetic retinopathy.

non-PDR (NPDR), severe NPDR or PDR. The DR severity was identified according to International Clinical DR Disease Severity Scale published in 2002. During pre-operative examinations, seventy-two eyes included in the study did not show any sign of DR during preoperative examination. Another eight eyes had mild to moderate NPDR while twelve eyes had severe NPDR or PDR.

During the follow-up at 1wk, anterior segment examination was unremarkable except mild anterior segment inflammation in six eyes (6.5%). And this inflammation subsided at 1-month follow-up. Mean best corrected visual acuity (logMAR) improved from 0.57 to 0.35 at 1mo and 0.26 at 3mo.

There was a significant increase of central subfield thickness and average inner ring and outer ring thickness at 1, 3mo compared with baseline measurements ($P$<0.01). Mean central subfield foveal thickness (CSFT) increased from 246.6 μm to 267.6 μm at 1-month follow-up and to 272.1 μm at 3mo. The average inner ring thickness increased from 314.0 μm preoperatively to 328.2 μm (post-op 1mo) to 332.2 μm (post-op 3mo). And the average outer ring thickness increased from 276.5 μm preoperatively to 286.0 μm (post-op 1mo) to 289.4 μm (post-op 3mo). However, the absolute changes in thickness were mild in all measurements as shown in Table 3. In eyes with central-involved and no non-central involved DME at 1mo, the mean change of CSMT was 118.6 μm, which was much higher than the average change of all eyes. In eyes with both pre-operative central-involved and non-central involved DME, the mean change of CSMT was 92.4 μm. In eyes with pre-operative non-central involved DME at 1mo, the mean change of CSMT was 32.2 μm ($P$<0.01) while mean change of CSMT of remaining eyes was 12.1 μm. Similarly, the mean changes of CSMT in eyes at 3mo were shown in Table 4.

**Table 3 Absolute change in thickness of CSMT, average thickness of inner and outer ring at 1, 3mo after surgery compared with baseline**

| Measurements | 1mo | $P$ | 3mo | $P$ |
|---|---|---|---|---|
| CSMT (μm) | 21.0 (5.4-36.6) | 0.009 | 25.5 (12.1-39.0) | 0.007 |
| Average inner ring thickness (μm) | 14.2 (7.6-20.8) | 0.005 | 18.2 (9.5-26.6) | 0.008 |
| Average outer ring thickness (μm) | 9.5 (5.2-13.7) | 0.009 | 12.9 (7.9-18.0) | 0.015 |
| Macular volume ($mm^3$) | 0.2 (0.1-0.8) | 0.003 | 0.4 (0.1-0.9) | 0.007 |

CSMT: Central subfield macular thickness. $P$<0.01.

**Table 4 CSMT before surgery and at 1, 3mo follow-up regarding pre-operative macular status**

| Pre-op macular status | Pre-operation | 1mo follow-up | 3mo follow-up |
|---|---|---|---|
| Central DME (+) | 328.0 | 446.6 | 452.2 |
| Non-central DME (-) ($P$) | - | 0.015 | 0.039 |
| Central DME (+) | 331.3 | 423.4 | 421.3 |
| Non-central DME (+) ($P$) | - | 0.037 | 0.023 |
| Central DME(-) | 243.5 | 275.7 | 282.1 |
| Non-central DME (+) ($P$) | - | 0.008 | 0.017 |
| Central DME(-) | 240.2 | 252.3 | 256.6 |
| Non-central DME (-) ($P$) | - | 0.428 | 0.342 |

At 1-month follow-up, 15 eyes met the criteria of new development or worsening of central-involved DME, including 4 eyes with pre-existing central-involved ME. Fifteen eyes met the criteria of new development or worsening of non-central-involved DME, including 6 eyes with pre-existing non-central-involved ME. Respective values at 3mo were 20 eyes for central-involved DME progression and 19 eyes for non-central involved DME progression. The details of these incidences can be seen in Table 5.

Severity of DR was not significantly correlated to ME ($P$=0.46). Since the laser treatment could affect macular thickness and confuse the interpretation of the results, we re-evaluated the correlation between severity of DR and changes of macular thickness after patients who had prior laser treatment were excluded. Still no statistical difference in macular thickness was revealed through severity of DR after exclusion of these patients ($P$=0.39).

## DISCUSSION

This prospective, observational study demonstrates that in diabetic eyes, macular thickness of the central subfield as well as the inner and outer rings increase statistically up to three months after surgery, though the mean increase may be too small to reveal any clinical significance. In addition, pre-operative macular status is associated with progression or worsening of ME after surgery. In this study, eyes with pre-operative DME had a higher mean CSMT change than eyes without at 1, 3mo after surgery, and eyes with pre-operative central-involved DME had the highest mean change of CSMT. Besides, eyes with pre-operative DME suffered a higher incidence of central or non-central involved ME progression.

One unique feature of our study was the definition of ME. In the pre-OCT era, ME was diagnosed with fundus photography or fluorescein angiography. With the availability

**Table 5 Incidence of development or worsening of ME at 1, 3mo regarding pre-operative macula status**

| Measurements | Central-involved ME progression | | Non-central-involved ME progression | |
|---|---|---|---|---|
| | 1mo | 3mo | 1mo | 3mo |
| Pre-op macular status | | | | |
| Central DME and no non-central DME | 1/2 | 1/2 | 1/2 | 1/2 |
| Central DME and non-central DME | 3/4 | 4/4 | 3/4 | 4/4 |
| No central DME and non-central DME | 6/14 | 8/14 | 6/14 | 6/14 |
| No central DME and no non-central DME | 5/72 | 7/72 | 5/72 | 8/72 |

The incidence is shown in absolute number.

of OCT, clinicians attempted to detect more subtle macular changes using qualitative and quantitative measurements obtained by OCT. However, there was still no consensus when it comes to the OCT definition of ME[13-15]. We adapted and modified the concepts provided by DRCR.net and defined ME based on macular thickness. And we categorized ME into four subgroups in regard to involvement of central subfield and we evaluated progression or worsening of ME based on the log change in OCT CSFT from baseline, which takes into account baseline thickness and requires OCT change beyond variability of the OCT machine itself.

The incidence of ME after cataract surgery was 21/92 (22.8% ) in our study, similar to results from reports of post-surgical ME in diabetic eyes, which confirmed the feasibility of our definition of ME. In a single center study of 50 eyes, Kim *et al* [16] reported an incidence rate of 22% (95% CI, 13%-35%) for DME exacerbation (defined as ⩾30% increase in OCT center-point thickness compared with pre-surgical OCT) 1mo after cataract surgery.

The further analysis based on pre-operative macular status revealed that eyes with central-involved ME had a higher CSMT increase, and still suffered central-involved ME after surgery. And these eyes also revealed a higher incidence in developing non-central involved ME, though the clinical significance remains to be explored. In addition, among eyes without central-involved ME, eyes with non-central involved ME before surgery had a higher chance of developing central-involved ME after surgery. The result was consistent with reports of DRCR.net[1].

However, the incidence of progression of ME in this very group was almost 50% in our study, which was much higher than incidence of 10% (10 of 97 eyes) in Baker *et al*'s [6] study. The unusually high incidence may be contributed to small sample included in our study, as only 14 eyes were included in this group. In addition, previous study suggested that history of photocoagulation correlated with the incidence of ME after surgery [7]. However, this correlation was not observed in our study, possibly due to the small number of eyes who had photocoagulation before surgery.

Our study also found a mild increase of the central subfield and inner and outer ring retinal thickness in diabetic eyes after uncomplicated cataract surgery. Similar results have been reported by Biro and Balla [17], which indicated an around 5% percent increase in CPT and perifoveal retinal thickness in eyes of non-diabetic patients. Though the extent of increase was pretty much the same extent as the accuracy of OCT measurement, the definite trend of increase in thickness in all quadrants makes the probability of measurement variation unlikely. However, the clinical meaning of this increase in macular thickness remains to be explored, as most patients with this subclinical increase maintain good vision after surgery[18-19].

One limitation of our study is that we did not differentiate DME from Irvine-Gass cystoid macular edema (CME). As previous studies revealed, both types of ME can occur in diabetic eyes undergoing cataract surgery. However, in our study, we did not differentiate these two types. It is difficult to tell these two forms apart just assessing OCT measurements, obtaining parallel results of fundus fluorescence angiography may help to differentiate as petaloid accumulation of fluorescein around the fovea with staining of the optic disc characteristic of Irvine-Gass CME[20].

Follow-up time of only three months may be another limitation of study. Though studies suggested that more than 60% ME occur at 1-month follow-up, there are reports that ME occur at 6mo or even 1y after surgery. Longer follow-up in the future is needed to derive a more accurate incidence of ME in diabetic eyes after cataract surgery.

This study shows an increase in central and perifoveal thickness in diabetic eyes after cataract surgery regardless of stages of DR. Our study also shows that pre-operative macular status is a risk factor for post-operative ME. Clinicians should continue to maintain vigilance in diabetic patients after cataract extraction, and obtaining an OCT before surgery can establish baseline measurements as well as help assess the risk of ME development. Further studies with large sample size are needed to assess the risk of DME progression after cataract surgery.

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