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Original Article

# Changes in Central Macular Thickness after Uncomplicated Phacoemulsification Surgery in Diabetic and Non-Diabetic Patients

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**Abstract**

**Objectives:** The aim of this study was to assess changes in central macular thickness following uncomplicated phacoemulsification surgery in diabetic patients with and without retinopathy and in a control group.

**Methods:** The records of 43 eyes of patients with mild non-proliferative diabetic retinopathy (NPDR), 43 eyes of diabetic patients without diabetic retinopathy (no-DR), and 43 eyes of a control group that also underwent phacoemulsification surgery were prospectively reviewed. Foveal thickness was measured using optical coherence tomography preoperatively and at 1 week and 1, 3, 6, and 12 months postoperatively.

**Results:** No clinically significant differences in foveal thickness were observed preoperatively between groups. Foveal thickness had increased in the NPDR group at 1 week and 1 and 3 months after surgery, in the no-DR group at 1 week and 1 month, and in the control group at 1 week after surgery. Foveal thickness decreased gradually in the NPDR group after 3 months. When comparing the groups, foveal thickness was significantly greater in the NPDR group than in the no-DR group and the control group at postoperative months 1 and 3; however, at month 6, the differences had decreased, and there were no clinically significant differences between groups.

**Conclusion:** Foveal thickness increased until 3 months after cataract surgery and decreased gradually thereafter in NPDR patients. Foveal thickness had also increased during the first month in the no-DR group. Foveal thickness increased only in the first week in the control group. These changes were more prominent in eyes with NPDR than in eyes with no-DR and those of the control group.

**Keywords:** Diabetic retinopathy, macular thickness, uncomplicated phacoemulsification surgery.

## Introduction

Cataract is a common cause of decreased vision worldwide, and the treatment for cataracts is surgical removal (1). Cataracts occur more often in patients with diabetes than in those without diabetes. The worldwide prevalence of diabetes is on the rise; thus increasing the importance of the relationship between diabetes and cataracts (2). Cystoid macular edema (CME) is one of the potential complications following uncomplicated cataract surgery in patients that can cause unwanted visual outcomes (3).

Some processes may underlie pathogenic mechanisms of macular thickening, such as postoperative inflammation caused by surgically damaged tissue, the breakdown of the blood-retinal and blood-aqueous barriers, and the release of prostaglandins and vascular endothelial growth factor (VEGF) (3, 4).

Cataract surgery initiates an inflammatory process in the eye. The risk of macular thickening after uncomplicated phaco surgery may increase in the presence of ocular or systemic inflammatory diseases like uveitis or diabetes (5).

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Primarily, the status of macular thickness before the cataract surgery determines the visual outcome after surgery (6-8). Previous studies have described many diabetic patients who developed severe maculopathy, progression of retinopathy, and/or neovascular glaucoma following cataract surgery (9, 10). Progression of diabetic retinopathy (DR) has been demonstrated in approximately 10% to 30% of patients after uncomplicated cataract surgery (11, 12). Some surgeons think that the progression of DR after cataract surgery is due to the natural course of the condition, and that the progression is independent of the surgery (5, 12-14). According to previous studies, the most significant predictive factor for progression of DR is the status of DR before the cataract surgery (15, 16).

Two mechanisms may lead to macular edema after surgery. One is Irvine–Gass syndrome (transient pseudophakic edema), which usually resolves spontaneously, and the other is actual progression of diabetic maculopathy (17-19). A study reported by Kim et al. (20) revealed a short-term increase in macular thickness after cataract surgery in diabetic patients.

The purpose of this study was to demonstrate changes in macular edema that occurred after uncomplicated phacoemulsification surgery in eyes with and without DR in diabetic patients and in a control group. The foveal thickness was periodically measured using optical coherence tomography (OCT) to quantitatively compare the degree of macular edema before and after surgery. If there was a difference in foveal thickness between the measurements taken before and after surgery of 100 μm or greater, the patient was treated with intravitreal anti-VEGF or micropulse laser.

## Methods

All diabetic patients scheduled for phacoemulsification surgery and intraocular lens (IOL) implantation between May 2013 and July 2015 were consecutively screened for inclusion in this study. No statistically significant differences were observed between the 3 working groups with respect to average age, gender distribution, cataract grade, or mean phaco time and phaco power. The exclusion criteria were the presence of additional underlying disease other than diabetes and cataract that could affect macular thickness (e.g., uveitis, glaucoma, or epiretinal membrane), uncontrolled blood sugar level (glycated hemoglobin >6%), proliferative DR or preexisting macular edema, incomplete or missing baseline or follow-up data, no aggregate results, unrelated outcome measurements, and any operative complication.

Screening was continued until 43 eyes with DR, 43 eyes without DR, and 43 control eyes could be included in this study. At the time of cataract surgery, all of the patients underwent implantation of a hydrophobic acrylic IOL performed by 2 surgeons. The study protocol was approved by the hospital's institutional review board, and informed consent was obtained from each patient.

All of the surgeries were performed using the same technique. No significant differences were found between the 3 groups in the grade of the nucleus, ultrasound time, or ultrasound power emitted. Following a side port incision, a 3.0-mm superior incision was performed, and the continuous curvilinear capsulorhexis technique was used. Hydrodissection with balanced salt solution and cataract extraction using the bimanual "divide-and-conquer" endocapsular phacoemulsification technique was performed. Sodium hyaluronate 1.4% was injected into the capsular bag. A foldable intraocular lens was implanted (Eyecryl Plus, Biotech Vision Care Pvt. Ltd., Ahmedabad, India) using an injector. After insertion, the viscoelastic material was thoroughly evacuated. All surgeries included in the analysis were uneventful and the IOLs were implanted accurately within the capsular bag. All patients used the same steroid and antibiotic 4x1 per day for 1 month after the surgery. We did not use a non-steroid anti-inflammatory drug in any patient to avoid any potential effect on the macular thickness.

The central retinal (foveal) thickness of all patients was measured with OCT (RS-3000 Advance; Nidek Co. Ltd., Gamagori, Japan) a day before surgery and 1 week and 1, 3, 6, and 12 months after surgery.

A fundus examination with full pupil dilation was performed before surgery and during each scheduled examination.

### Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA) software. The distribution parameters were evaluated using the Shapiro-Wilks test and found to be in accordance with the parameters of normal distribution. Analysis of variance and Tukey's Honest Significant Difference test were used for inter-group comparisons. For intra-group comparison, a paired sample t-test was used. $P<0.05$ was considered statistically significant.

## Results

The mean preoperative foveal thickness in each group is provided in Table 1. The mean foveal thickness of the DR group was significantly lower than that of the control group ($p=0.009$). However, this small difference was not clinically significant. There were no statistically significant differences between other groups in preoperative mean macular thickness.

No statistically significant differences were observed between the groups in the first week after surgery. Differences

**Table 1.** Distribution of foveal thickness by group

| Foveal thickness | Control group Mean±SD | No-DR group Mean±SD | NPDR group Mean±SD | 1p |
|---|---|---|---|---|
| Preoperative | 236.28±14.71 | 233.6±15.53 | 227.56±8.42 | 0.009* |
| Postoperative | | | | |
| 1 week | 239.4±15.19 | 236.37±14.52 | 238.53±13.57 | 0.608 |
| 1 month | 235.65±13.59 | 237.49±14 | 256.33±13.64 | 0.001* |
| 3 months | 237.4±9.95 | 236.93±11.5 | 257.74±14.01 | 0.001* |
| 6 months | 235.58±11.79 | 233.49±13.86 | 224.42±7.14 | 0.001* |
| 1 year | 234.37±12.7 | 231.77±11.06 | 225.4±7.39 | 0.001* |
| Preoperative 1 week2p | 0.001*(increased) | 0.030*(increased) | 0.001*(increased) | |
| Postoperative1 month2p | 0.844 | 0.009*(increased) | 0.001*(increased) | |
| 3 months2p | 0.510 | 0.061 | 0.001*(increased) | |
| 6 months2p | 0.471 | 0.938 | 0.002*(decreased) | |
| 1 year2p | 0.024* | 0.163 | 0.041*(decreased) | |
| One-way ANOVA Test | 2Paired-sample t-test | *p<0.05 | | |

ANOVA: Analysis of variance; No-DPR: No diabetic retinopathy; NPDR: Non-proliferative diabetic retinopathy.

in the mean central foveal thickness were observed between the groups at months 1 and 3 (p=0.001). Binary comparisons were performed: the mean foveal thickness level of the NPDR group after 1 and 3 months was significantly higher than that of the control and the no-DR group (p=0.001), and there were no statistically significant differences between the control and no-DR groups at months 1 and 3.

In the control group, a statistically significant increase was seen in the mean foveal thickness in the first week after surgery compared with the preoperative value (p=0.001); however, no significant changes were observed in the first, third, and sixth months. The decline observed in the mean macular thickness in the first year, in comparison with the preoperative value, was statistically significant (p=0.024).

In the no-DR group, in comparison with the mean preoperative foveal thickness, there was a statistically significant increase in the first week (p=0.030) and in the first month (p=0.009), but no statistically significant differences were observed at the third and sixth months or the first year.

In a comparison with the mean preoperative foveal thickness in the DR group, there were statistically significant increases in the first week (p=0.001) and the first (p=0.001) and third months (p=0.001). A statistically significant reduction was observed after 6 months (p=0.002) and 1 year (p=0.041).

The percent of change in foveal thickness by group over time from baseline can be seen in Table 2.

A statistically significant difference in the mean foveal thickness was observed at week 1 and months 1 and 3 in comparison with the baseline (p=0.001). Binary comparisons

**Table 2.** Percent change in foveal thickness by group at the first week; first, third, and sixth months; and first year postoperatively, in comparison with the mean preoperative foveal thickness

| Foveal thickness (% change) | Control group Mean±SD | No-DR group Mean±SD | NPDR group Mean±SD | p |
|---|---|---|---|---|
| 1 week | 1.33±1.92 | 1.27±3.42 | 4.83±4.63 | 0.001* |
| 1 month | 0.12±8.4 | 1.78±3.93 | 12.76±6.83 | 0.001* |
| 3 months | 0.67±4.65 | 1.64±4.83 | 13.41±7.3 | 0.001* |
| 6 months | -0.2±2.67 | 0.08±4.29 | -1.33±2.59 | 0.112 |
| 1 year | -0.74±2.24 | -0.63±3.57 | -0.89±2.92 | 0.914 |
| One-way ANOVA test | | *p<0.05 | | |

ANOVA: Analysis of variance; No-DPR: No diabetic retinopathy; NPDR: Non-proliferative diabetic retinopathy.

**Table 3.** Percent of patients by group with increased foveal thickness in the first week; first, third, and sixth months; and first year postoperatively

| | 1st week | 1st month | 3rd month | 6th month | 1st year |
|---|---|---|---|---|---|
| Control | 69.8% | 46.5% | 41.9% | 39.5% | 32.6% |
| No-DR | 65.1% | 55.8% | 67.4% | 34.9% | 32.6% |
| NPDR | 83.7% | 93% | 97.7% | 30.2% | 32.6% |

No-DPR: No diabetic retinopathy; NPDR: Non-proliferative diabetic retinopathy.

were performed. The NPDR group had significantly higher macular thickness measurement results in the first week and at the first and third months than the control and no-DR groups (p=0.001).

No statistically significant differences were observed in the first week and first and third months after surgery between the control and no-DR groups.

There was no statistically significant difference between the groups at the sixth month and first year after surgery. When comparing group results 3 months after surgery, the percent increase in the DR group was significantly higher than those of the no-DR and control groups. Foveal thickness decreased 6 months after surgery.

Table 3 illustrates the percent of patients with increased postoperative foveal thickness. Values for the NPDR group in the first and third months were greater than those of the other groups; however, that difference was no longer observed at the sixth month and first year after surgery.

Figures 1 and 2 show changes in foveal thickness over time and the percent of change in foveal thickness in the groups.

## Discussion

Following phacoemulsification surgery, no visual impairment accompanied the subclinical thickening of the central macula, which could now be visualized using OCT and angiographic examination with fundus fluorescein (21). The application of phacoemulsification can lead to inflammation due to the release of inflammatory substances directly involved in the thickening of macula, including prostaglandins (22). It has been reported that after phacoemulsification without complication, an inflammation response triggered by the surgery led to early edema in the macula (23, 24). Measurement of central macula thickness (CMT) at week 1 and months 1 and 3 indicated a significant change following phacoemulsification surgery that was without complication. The CMT later

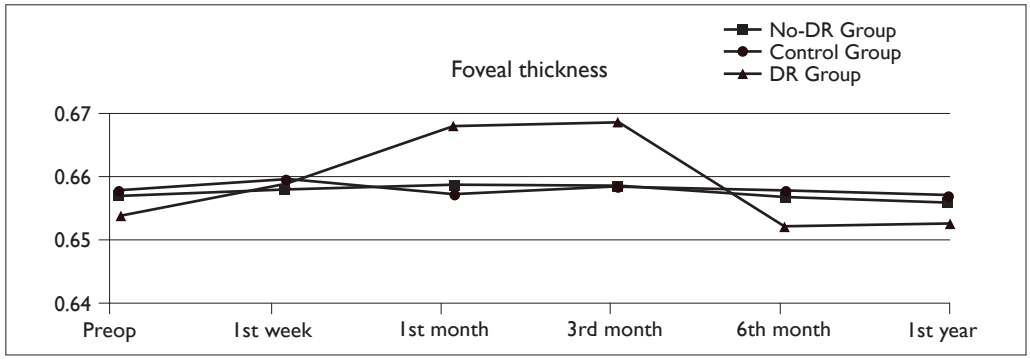


**Figure 1.** Changes in foveal thickness over time.

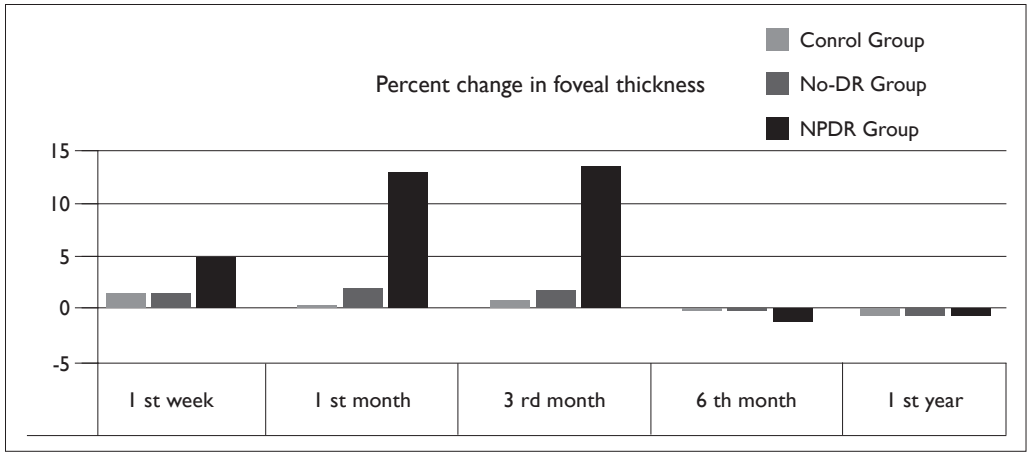


**Figure 2.** Percent change in foveal thickness by group.

showed a gradual decrease in diabetes patients who also had concomitant mild NPDR. This indicates that compared with the control group and with diabetes patients with no DR, the phacoemulsification surgery had a stronger effect on the blood-aqueous barrier of diabetes patients with mild NPDR. Pseudophakic CME that develops following the surgical treatment of cataracts differs in many respects from diabetic edema of the macula, particularly in the immediate postoperative period. Pseudophakic CME is known to show regression within a period of 1 month (when associated with Irvine-Gass syndrome), while diabetic edema can exhibit progression for a period of more than 3 months (25). It is important for physicians to recognize the distinction between surgical treatment-related pseudophakic CME and diabetic edema of the macula.

Following cataract surgery, patients with diabetes are more likely to experience subclinical thickening or edema in the macula (26). Due largely to its ability to increase blood vessel permeability, VEGF assumes a central role in the development of diabetes-related microangiopathies (27). It is also known that proliferative DR patients have considerably higher VEGF levels in the vitreous humor (28). A number of risk factors are also involved in changing the extent of DR progression following phacoemulsification, such as the administration of insulin treatment to the patient, uncontrolled blood sugar level, and younger age. Some researchers have demonstrated that such factors had no impact on the degree of retinopathy progression (29, 30). In patients both with and without diabetes, CME following surgery is generally caused by prostaglandin-induced intraocular inflammation (31).

A comparison of the control group and diabetes patients without DR with patients with mild NPDR revealed that the NPDR group exhibited a statistically greater likelihood of macular thickening or edema in week 1 and in months 1 and 3 following phacoemulsification surgery.

In the present study, preoperative and postoperative CMT levels in diabetes patients without DR were compared with the level observed in the control group and in diabetes patients with mild NPDR. These comparisons indicated that, relative to the control group, phacoemulsification surgery (without complications) could potentially have a greater impact on the CMT value of diabetes patients than on the CMT value of the control group.

At month 1 following the surgery, it was observed that diabetes patients with mild NPDR exhibited significantly greater CMT values, while diabetes patients without DR demonstrated an almost significant rise in CMT values ($p=0.054$). The greater CMT level might have been caused by the inflammatory response resulting from the phacoemulsification at 1 month after the surgery; however, it may equally have been associated with Irvine-Gass syndrome, which is induced by growth factors and cytokines (such as VEGF and prostaglandins) passing through the blood-aqueous barrier following phacoemulsification.

Certain researchers have suggested that in patients with a lengthy prior history of edema in the eye and maculopathy, the rapid rise in CMT level due to micro-injuries caused by the phacoemulsification surgery may result in a greater likelihood of postoperative CME (32, 33). The present study excluded patients with a history of severe proliferative or non-proliferative retinopathy, prior cataract surgery with complications, and prior CME. Such exclusion criteria can also be considered a limitation of the present study.

The present study revealed that, compared with the control group, diabetes patients without DR and with NPDR had a notably different CMT level 1 week and 1 and 3 months following phacoemulsification without complications. That is, a diabetes patient with mild NPDR had a greater CMT level at week 1 and months 1 and 3 after surgery. However, the CMT level began to gradually decrease starting from postoperative month 3, and completely returning to a normal level by postoperative month 6. Yet, it must also be noted that in all groups, any increase in CMT level was still subclinical. Neither the control group nor the diabetes patients without DR exhibited any statistically significantly greater CMT level in months 3 and 6 following surgery. The study findings revealed that phacoemulsification without complications had a minimal impact on the mechanisms and pathology of retinopathy in diabetes patients with mild NPDR – a group known to be associated with a greater occurrence of subclinical thickening in the macula following phacoemulsification relative to control groups and diabetes patients without retinopathy.

The present study demonstrated that in comparison with the control group and the no-DR group, phacoemulsification surgery without complications and accompanied by the implantation of an intraocular lens is associated with a significantly greater incidence of subclinical macular thickening in a mild NPDR group, specifically at week 1 and months 1 and 3 after surgery.

**Disclosures**

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Involved in design and conduct of the study (SA, YO); preparation and review of the study (SA, YO); data collection (SA); and statistical analysis (SA).

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