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Protecting the Corneal Endothelium during Cataract Surgery Using the Anterior Capsulorhexis Flap as a Corneal Protection Shield

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ABSTRACT

Purpose: *Classification and quantification of swirling lens fragments during phacoemulsification with or without using the capsulorhexis flap as an additional endothelial protective shield. Also, to determine the effects on endothelial cell count (ECC) and central corneal thickness (CCT) caused by fragments during cataract surgery.*

Methods: *Patients with dense cataracts scheduled for surgery were randomized into study and control groups (2:1). In the study group, the anterior capsule 'flap' from the capsulorhexis was used as an endothelial protection shield during phacoemulsification. The control group underwent standard surgery. During surgery, intra-operative optical coherence tomography was performed to score swirling lens fragments that hit the corneal endothelium. CCT and ECC were measured at several time points before and after surgery.*

Results: *In total, 176 fragments in 49 eyes of 49 patients came in contact with the corneal endothelium. The mean number of fragments was 2.8 in the study group and 4.8 in the control group. There was no statistically significant change of ECC between the groups. Mean CCT increased by 16.6 µm in the study group and by 42µm in the control group 1 day postoperatively. There was no significant difference between the groups regarding the increase in CCT.*

Conclusions: *No significant benefit concerning ECC or CCT was found in the study group compared to the control group, meaning that we were not able to prove that using the capsulorhexis flap as a protection shield is a sufficient method of protecting the corneal endothelium.*

Keywords

Endothelial cell loss, Phacoemulsification, Swirling lens fragments.

Introduction

Since phacoemulsification has become established as the main technique in cataract surgery, risks and complications decreased significantly [1]. One of the remaining serious complications that can arise is endothelial cell loss [2]. If the endothelial cell density falls below 1000 cells/mm^2, the physiological function of the corneal endothelium may no longer be sustained, resulting in corneal edema and decrease of visual function [3]. Usually, corneal edema occurs in the immediate postoperative period and may resolve completely within 4-6 weeks [4]. However, a significant loss in corneal endothelial cells can result in chronic bullous keratopathy and endothelial grafting may be required.

In a previous study, swirling lens fragments during cataract surgery and their impact on the endothelium were analyzed [5]. Continuous intraoperative OCT video recordings showed 104 swirling lens fragments in 40 eyes that came into contact

with the corneal endothelium. A mean of 2.6 lens fragments (range 0 to 6) that came into contact were observed per eye. Small fragments and fragments touching the center of the endothelium had a significantly greater effect on postoperative ECD than other fragment parameters.

The technique of using the rhexis flap during surgery as a shield was first mentioned by La Rocca et al. They showed a protective effect concerning endothelial cell count [6].

Aim of this study was to assess if the use of the anterior lens capsule flap from the capsulorhexis as a protection shield during cataract surgery leads to a significantly reduced loss of endothelial cells compared to standard cataract surgery in a randomized controlled design.

Patients and Methods

In this study, patients scheduled for cataract surgery were included. All the participants were selected by the clinical investigators at the Department of Ophthalmology in Hanusch Hospital. All the research and measurements were approved by the local ethics committee and followed the tenets of The Declaration of Helsinki and the study was registered (NCT03855293). Written informed consent was obtained from all patients in the study prior to surgery.

We included patients with moderate to hard nuclear cataract with a LOCS N (nuclear) grading of at least 2. Exclusion criteria were corneal pathologies, pregnancy and an increased surgical risk (e.g. patients with pseudo exfoliation syndrome, with the potential risk of intra-operative floppy iris syndrome).

On the day of the pre-operative examination, patients underwent a full ophthalmic assessment and routine optical biometry was performed (IOLMaster 700, Carl Zeiss Meditec AG, Jena, Germany). Patients were randomly allocated to the study group or the control group, in a 2:1 fashion. Randomization was performed using an online randomization software (randomizer.org).

Surgery was performed in topical anesthesia. The standard pre-operative therapy was tropicamide 1% gtt, phenylephrine 2.5% gtt, cyclopentolate 1% gtt. A self-sealing incision, injection of ophthalmic viscoelastic device (OVD), capsulorhexis, phacoemulsification, irrigation/aspiration of cortical material were performed as standard procedure by one experienced surgeon (OF). A dispersive OVD of Hydroxypropylmethylcellulose 2.0% (HPMC, Eye fill HD, Bausch+Lomb, Rochester, New York, USA) was used in all eyes. The Stellaris phacoemulsification platform (Bausch+Lomb, Rochester, New York, USA) was used in both groups. At the time of phacoemulsification, phacopower was 50%, vacuum was 300mmHg and bottle height was 100cm H_20. Intra-operative OCT (Rescan 700, Carl Zeiss Meditec AG, Jena, Germany) measurements were taken continuously as a video during the operation. The surgeon was masked to allocation until the beginning of surgery.

In the study group, the anterior capsule, which was gained by capsulorhexis, was placed in the anterior chamber close to the endothelium prior to phacoemulsification (Figure 1). The anterior capsulorhexis-flap was positioned under the corneal endothelium using the OVD (Eye fill HD, 2% HPMC). Intraoperative OCT was used to verify the position of the flap (Figure 1). Before IOL implantation, either the rhexis-shield was with the irrigation/aspiration tip or OVD positioned peripheral to the flap. The IOL was implanted using a dedicated injector system. Postoperatively patients received bromfenac eye drops (Yellox 0,9 mg/ml Bausch + Lomb/ Dr. Mann Pharma), twice daily for 4 weeks, as standard medication.

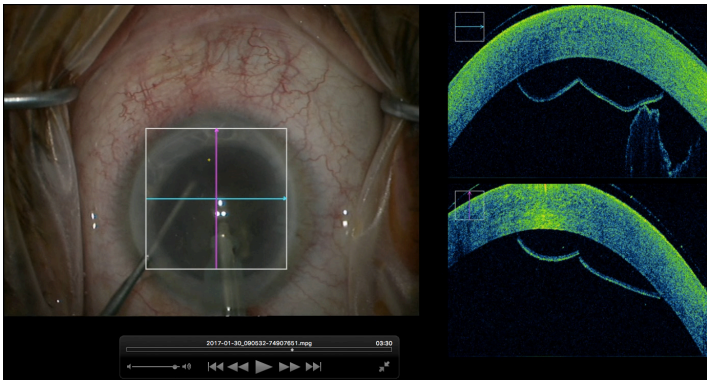

Figure 1: Intraoperative OCT image of a correctly positioned rhexis flap and a fragment colliding with it.

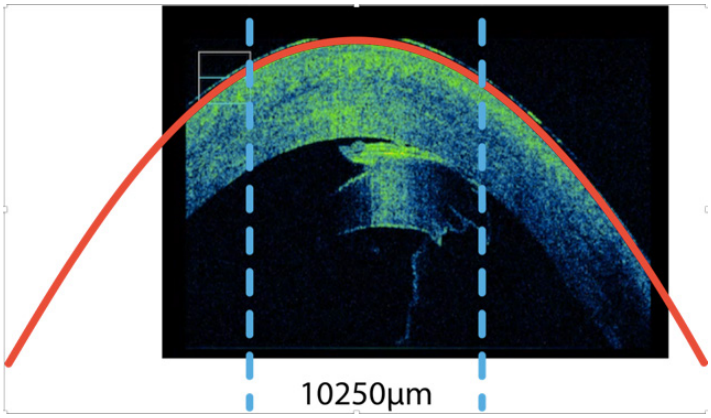

Figure 2: Large fragment hits the centre of the cornea during phacoemulsification.

Follow-ups were performed one hour, one day and two months after surgery. The examiners were masked to allocation.

Endothelial cell count was measured before and two months after surgery (Konan NSP-9900, KOWA, Japan). Corneal thickness was measured before, one hour, one day and two months after phacoemulsification using partial coherence laser interferometry (AC-Master Carl Zeiss Meditec AG) [7]. Three measurements were taken, and the median was used for further analysis.

All the data was recorded on a case report form specifically designed for this investigation. This data was then transferred into Apple Numbers Version 4.0.5 and SPSS Statistics 22 (IBM Corporation).

Fragment analysis

All OCT videos were analyzed after screenshots were taken whenever a fragment hit the cornea. The method of fragment analysis was explained previously [5]. In short, the position of the cornea-fragment hits (central zone defined as 3.4 mm diameter), the size of the fragment, size of the contact area and the duration of the contact with the cornea were analyzed.

Statistical analysis

For statistical analysis Apple Numbers Version 4.0.5 and SPSS Statistics Version 22 (IBM Corporation) were used. When follow-up data was missing, observations were excluded from analysis. The main outcome was assessed using the t-test for paired samples. For nonmetric data the chi-square test was used. Descriptive data was always shown as mean, with standard deviation (SD) and range.

Results

Seventy eyes of 70 patients were included in the study. Twenty-one patients (16-study group, 5-control group) had to be excluded. In 8 (11,4%) patients the rhexis flap dislocated and was flushed out before or at the beginning of phacoemulsification. Another 10 patients were excluded due to organizational issues on the day of surgery because the surgeon was not available, or the patient changed their mind concerning study participation. In one case a technical problem with the intra-operative OCT prevented us from measuring intra-operatively. There was a rupture of the posterior capsule in one of the patients. One patient passed away due to a previously known pulmonary disease.

Of the remaining 49 patients, 24 (49%) were male and 25 (51%) were female, the mean age was 74.9 years (range: 59-87). Overall, there were 19 eyes of 19 patients assessed in the control group, and 30 eyes of 30 patients in the study group. To assess the level of severity of the cataract we used the LOCS II score to determine the nuclear density. Twenty patients had a score of 2, and 29 patients had a score of 3.

In this cohort, mean phaco time was 4.4 seconds (SD: ± 3.5, range: 0.6–20.2) and mean phaco energy was 20.3% (SD: ± 9.5, range: 6–50). There was no significant difference between groups and no significant influence of phaco time or energy on ECC loss or increase of CCT.

Normal distribution was tested positive for all assessed data using the Kolmogorow-Smirnow Test.

Endothelial Cell Count (ECC)

The loss in endothelial cells was higher in the control group, but this difference was not found to be statistically significant (p=0.39). (Table 1, Figure 3). There was no significant effect of fragment size (r^2=0.018; p=0.20) on postoperative ECC loss using linear regression analysis. However, there was a significant positive correlation between the number of fragments and postoperative ECC loss (r^2=0.101; p=0.03). Furthermore, fragments with a short contact time (r^2=0.083; p=0.05) and with a contact area equal to or greater than pinpoint size (r^2=0.118; p=0.018) showed a significant positive correlation with postoperative ECC. There was no correlation between postoperative loss of ECC and LOCS score (r^2=-0.240; p= 0.11). There was also no correlation between the number of fragments and LOCS score (r^2=0.261; p=0.070).

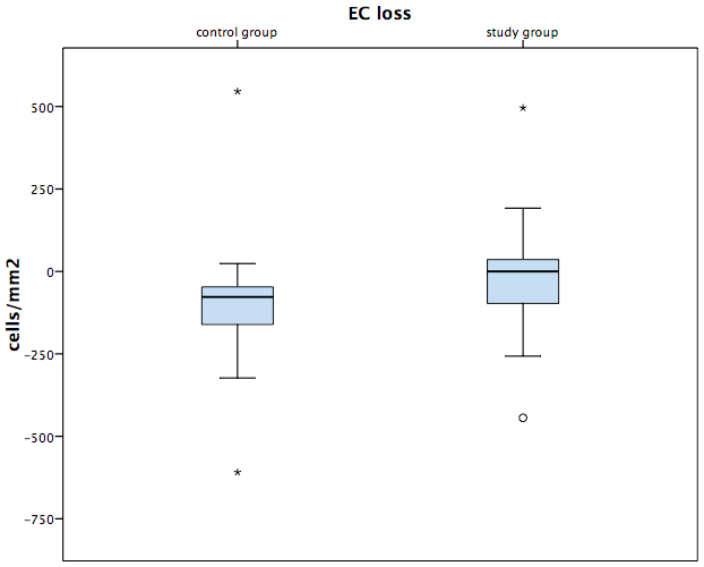

Figure 3: EC (endothelial cell) loss (/mm²) in the control and study group from pre-operatively to 2 months post-operatively.

Table 1: (ECC = endothelial cell count).

ECC (cells/mm²)	Control	Study	Total
Pre-operatively	2634.3 (SD: ± 328, range: 1866-3115)	2586.7 (SD: ± 263, range: 2096-3086)	2604.9 (SD: ± 287, range: 1866-3115)
2 months post-operatively	2538.1 (SD: ± 337, range: 1874-3049)	2553.1 (SD: ± 250, range: 2016-3115)	2547.34 (SD: ± 283, range: 1874-3115)
Decrease	-89 (SD: ± 214, range: -609 - 546)	-21 (SD: ± 168, range: -444 - 496)	-47 (SD: ± 187, range: -609 - 546)

Central Corneal Thickness

There was no statistically significant difference between study and control group regarding the central corneal thickness pre, 1h, 1d, and 2m post-operatively (Table 2, Figure 4). There was no significant effect of fragment number (r^2=0.001; p=0.63), fragment size (r^2=0.001; p=0.92) duration of impact (r^2=0.004; p=0.65) or impact area (r^2=0.002; p= 0.76) on CCT one hour postoperatively using linear regression analysis. There was no correlation between postoperative loss of ECC and increase of CCT (r^2=0.202; p= 0.22).

Fragments

In total, 176 fragments hit the cornea, 85 in the study and 91 fragments in the control group (p= 0.34). The mean number of fragments was 3.6 (SD: ± 3.8, range: 0-13), 2.8 (SD: ± 3.8, range:

0-12) in the study group and 4.8 (SD: ± 4.2, range: 0-13) in the control group (p= 0.34). While 100 of all fragments hit the centre of the cornea, 76 hit the periphery. In the study group, 47 fragments hit the rhexis flap, which covered the center of the cornea, and 38 hit the periphery. In the control group, 53 fragments hit the central cornea and 38 fragments hit the periphery (p= 0.37). There was no correlation between number of fragments and LOCS score (p= 0.09).

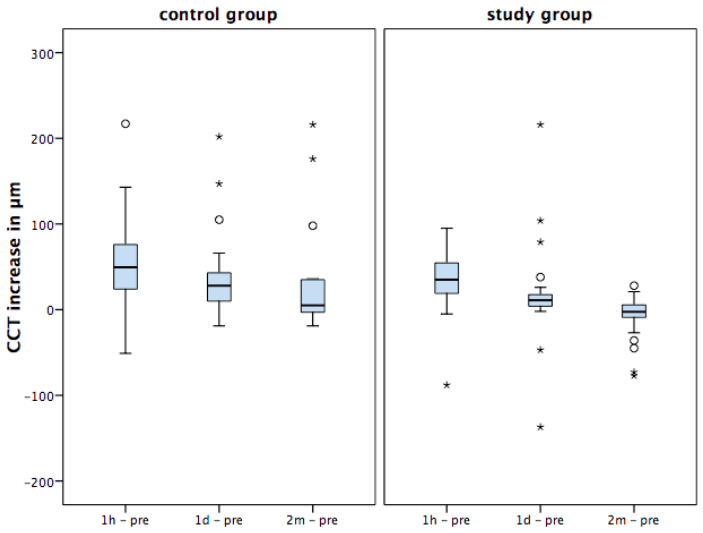

Figure 4: CCT (central corneal thickness) increase (in microns) in the control and study group from pre-operatively to 1 hour, 1 day and 2 months post-operatively

Table 2: (CCT = central corneal thickness).

CCT (µm)	Control	Study
Pre-operatively	499.7 (SD: ± 56.9, range: 381– 576)	529.7 (SD: ± 32.1, range: 472 – 608)
1h post-operatively	556.5 (SD: ± 43.7, range: 487– 641)	556.3 (SD: ± 64.9, range: 295 – 657)
1d post-operatively	541.7 (SD: ± 41.7, range: 491– 625)	546.3 (SD: ± 57.6, range: 438 – 766)
2m post-operatively	531.3 (SD: ± 40.0, range: 475– 599)	522.8 (SD: ± 40.3, range: 399 – 605)

The mean fragment area was 337 µm² (SD: ± 199, range 51-920), in the study group 327µm² (SD: ± 219, range: 83-920, p =0.34) and in the control group 351µm² (SD: ± 171, range: 51-647).

One hundred-one fragments that hit the cornea had a contact area that was equal or bigger than pinpoint size. Of those, 44 (43.6%) were in the study group and 57 (56.4%) were in the control group (p=0.47). Of the 76 fragments with a contact area smaller than pinpoint size, 42 (55.3%) were in the study group and 34 (44.7%) were in the control group (p= 0.52).

128 fragments had a contact time less than one second. Sixty-two (48.4%) of them were in the study group and 66 (51.6%) in the control group. (p=0.28) The number of fragments with a contact time of more than 1 second was 49, 24 (49.0%) of them being in the study group and 25 (51.0%) in the control group (p=0.56).

Discussion

Using a corneal protection shield during cataract surgery potentially has a protective effect on the corneal endothelium. However, endothelial cell loss was low and differences between groups were not found to be significant. In previous studies it was shown that the endothelial cell loss in modern cataract surgery is low (40 – 70 cells/mm² 1 month after surgery) [5,8,9]. Contrary, results of statistically significant endothelial cell loss were compiled by Teoh et al. [10], Ventura et al. [11] and Faramarzi et al. [12]. As cataract density has a relevant influence on endothelial cell loss, direct comparison between studies is difficult. Chamorro et al. found that there was no significant difference of endothelial cell loss between surgeons with more or less than five years of experience [13].

We found a significant increase in central corneal thickness throughout the follow-up measurements compared to baseline. Other studies measuring the pre- and postoperative central corneal thickness in a similar way were conducted by Assaf et al., Bamdad et al. and Perone et al. [2,3,9]. Their findings also showed statistically significant changes between the baseline and the measurement 1 month post-operatively. Other, similar findings show significant increases of the central corneal thickness during their follow-ups, but the intervals of post-operative measurements differed greatly [11,14]. This complicates the interpretation of the cause behind the increased corneal thickness. However, most of the more recent results, including the data presented in this paper, suggest that the peak of central corneal thickness is shortly after surgery, which indicates that corneal edema is indeed a direct reaction to stressful factors during phacoemulsification and will decrease until it approximates baseline values after a certain amount of time. This opinion was likewise stated by Kohlhaas et al. [4], who also pointed out the opposing opinion built up on less recent surveys, which says that CCT change is more or less independent of ECC change, because long-term follow-up data has shown that CCT values would have increased even 1 year after surgery when ECC values were stable.

There are several suggestions to possibly get more conclusive results. A similar phaco time and energy were used, and the resulting lens fragments should have a similar force when colliding with the corneal endothelium. However, some of the patients that were included had cortical cataracts and less nuclear cataracts. In these cases, phacoemulsification was performed with little energy use and in relatively short surgical time which results in little trauma to the corneal endothelium. This resulted in less harmful impact of the resulting lens fragments. Therefore, including only patients with hard nuclear cataract might result in more conclusive data since the difference between shielded endothelium and the control group may have been much larger.

Another possible approach may be to refine the surgical technique to find a way to prevent the flushing out of the capsulorhexis flap. Maybe additional use of different kinds of OVDs could improve handling and placement of the rhexis flap and therefore provide

better protection of the corneal endothelium. The thickness of the capsulorhexis flap may also be crucial for the protecting effect. To further investigate this question, techniques with a hydrophilic acrylic shield device introduced into the anterior chamber instead of the thin rhexis flap may be an alternative. This technique was described by Levy et al. [15]. However, we have found this device to tilt during the phacoemulsification procedure which caused touch of the acrylate disc with the endothelium in the mid periphery potentially causing trauma. For this reason, we have not continued to investigate that device.

A subsequent question would be to explore if the process of pressing the capsulorhexis against the peripheral endothelium while placing it may also induce damage. However, as mainly central corneal damage seems to be responsible for complications such as corneal edema other improvements of procedures and technique should have priority in further investigations.

Alterations of the technique of phacoemulsification may also yield further insight in how to prevent endothelial cell loss. Li et al. found, that using cystotome-assisted prechop phacoemulsification in contrast to conventional phacoemulsification lead to significantly reduced endothelial cell damage and therefore a faster regression of central corneal thickness in the follow-ups, as there was less phaco time and energy used [16]. Another prechopping method, using a reverse chopper in contrast to routine stop-and-chop phacoemulsification was like wise found to reduce phaco time and therefore endothelial cell loss and corneal edema significantly by Zhao et al. [17]. In this trial we used a horizontal chop technique which appears to cause little endothelial cell loss as seen in this and previous trials. Taking into account femtosecond laser-assisted cataract surgery, Kaur et al. showed that lens fragmentation with a femtosecond laser before actual phacoemulsification reduced side effects of cataract surgery such as loss of endothelial cells, even more so using a matrix pattern than a chop pattern [18]. Obviously, the technique of producing an absolutely round and standardized capsulotomy flap which is already unfolded using a femtosecond laser may make this technique of positioning the flap under the endothelium more simple and reproducible and possibly show less loss of the flap at the beginning of surgery, which we experienced in 11,4% of the study group.

There are also several technical issues that should be tackled to make data in this field of research more reliable. Although the frame rate and resolution of OCTs have greatly improved in the last years, there is still room for improvement. Even if a more precise analysis of fragments seemed to be possible compared to former studies conducted at our institute, a better frame rate would enable better identification of fragments and allow a more accurate assessment of the duration of the fragments impact. Furthermore, it is of utmost importance to automatize the process of gathering fragment-related data. The subjective scoring that is currently done to gain results is exceedingly time consuming and vulnerable for human error. An automated, objective scoring of each fragment and its moment of collision with the corneal endothelium, maybe already included in the OCT-device would certainly decrease this source of error significantly.

In conclusion, usage of an endothelial protection shield seems to be a good approach to reduce endothelial cell damage during phacoemulsification. Although in this study only a positive trend of reduced ECC loss and increase of CCT in the protection shield group was found, measures like only including hard nuclear cataract and improving the surgical technique to prevent irrigation of the capsulorhexis may lead to more conclusive results. Furthermore, technical improvements such as an intraoperative OCT with higher resolution and frame rate combined with automated fragment assessment would improve data quality and reproducibility greatly.

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