(17)

The effect of the selected factors on corneal endothelial cell loss following phacoemulsification

Wpływ wybranych czynników na utratę komórek śródbłonka rogówki po fakoemulsyfikacji

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Abstract: Introduction: Corneal endothelium is a single layer of cells, which do not regenerate. Damage to the endothelium can take place in the course of certain diseases and after intraocular operations. When the number of endothelial cells decreases, corneal decompensation can occur. Pre- and postoperative measurement of the number of the corneal endothelial cells can help assess the degree of corneal damage during the surgery.

Purpose: To compare the effect of various factors, such as: sex, age, corneal incision, intraocular pressure, cataract density, visual acuity and surgeon's experience on corneal endothelial cell loss following uneventful phacoemulsification.

Material and methods: 365 patients (114 men and 251 women aged 19 to 91 years) undergoing phacoemulsification were examined preoperatively and postoperatively at 4 weeks. 68 eyes underwent phacoemulsification through a 1.8 mm microincision and 297 eyes through a standard 2.75 mm incision. Patients were operated on by four surgeons.

Results: There was a significant difference in the postoperative endothelial cell loss relative to the degree of cataract hardness ($p<0.001$). Endothelial cell loss was significantly higher in patients aged 71 and above than in the remaining age groups. Significant differences in the postoperative endothelial cell loss were observed in relation to the clear corneal incision size ($p<0.01$). Preoperative best corrected visual acuity influenced the postoperative endothelial cell loss in a statistically significant way ($p< 0.05$). Endothelial cell loss was strongly influenced by the surgeon's experience.

Conclusions: Surgeon's experience, hardness of cataract, type of corneal incision, age and preoperative visual acuity influenced endothelial cell loss at 4 weeks following uneventful phacoemulsification, however such factors as sex and intraocular pressure showed no statistically significant influence on corneal endothelial cell loss.

Key words: corneal endothelium, postoperative cell loss, phacoemulsification.

Abstrakt: Wstęp: Śródbłonek rogówki to pojedyncza warstwa nieregenerujących się komórek wielobocznych. W przebiegu niektórych chorób oraz po operacjach wewnątrzgałkowych może dojść do uszkodzenia śródbłonka. Kiedy liczba komórek śródbłonka rogówki ulega zmniejszeniu, może dojść do dekompensacji rogówki. Przed- i pooperacyjne obliczenie liczby komórek śródbłonka rogówki może pomóc w oszacowaniu stopnia uszkodzenia rogówki podczas zabiegu operacyjnego.

Cel: ocena wpływu czynników takich jak płeć pacjenta, wiek pacjenta, doświadczenie operatora, przedoperacyjna ostrość wzroku, ciśnienie wewnątrzgałkowe, twardość zaćmy wg skali LOCS oraz wielkość cięcia w przeziernej rogówce na ubytek liczby komórek śródbłonka rogówki u pacjentów poddanych niepowikłanej fakoemulsyfikacji.

Materiały i metody: Badaniom poddano 365 pacjentów (114 mężczyzn i 251 kobiet, w wieku od 19 do 91 lat) przed operacją zaćmy metodą fakoemulsyfikacji i 4 tygodnie po niej. U 68 pacjentów wykonano cięcie skroniowe szerokości 1,8 mm w przeziernej rogówce, natomiast u 297 pacjentów wykonano cięcie skroniowe szerokości 2,75 mm w przeziernej rogówce. Zabiegi zostały przeprowadzone przez 4 różnych operatorów.

Wyniki: Stwierdzono istotną różnicę w ubytku śródbłonka po zabiegu, w zależności od stopnia twardości soczewki ($p<0,001$). Stopień utraty śródbłonka rogówki był istotnie większy u pacjentów powyżej 71. roku życia niż u pozostałych chorych. Stwierdzono istotną zależność między wielkością cięcia chirurgicznego a stopniem utraty śródbłonka komórek rogówki po operacji ($p<0,01$). Stwierdzono istnienie związku między przedoperacyjną wartością najlepiej skorygowanej ostrości wzroku a stopniem utraty śródbłonka komórek rogówki ($p<0,05$). Skala ubytku komórek śródbłonka rogówki po operacji była mocno uzależniona od doświadczenia operatora.

Wnioski: Stwierdzono, że istotny wpływ na ubytek komórek śródbłonka rogówki miały: doświadczenie operatora, twardość zaćmy wg skali LOCS, wielkość cięcia w przeziernej rogówce, wiek pacjenta oraz przedoperacyjna ostrość wzroku. Czynniki takie jak płeć pacjenta oraz wysokość ciśnienia wewnątrzgałkowego nie miały wpływu na gęstość komórek śródbłonka rogówki.

Słowa kluczowe: śródbłonek rogówki, pooperacyjny ubytek komórek śródbłonka rogówki, fakoemulsyfikacja.

Introduction

Corneal endothelium is a single layer of polyhedral cells which adjoin one another tightly and are not exchanged during the lifetime. Their number decreases physiologically with age from 3500–4000 per mm^2 in new-born babies to 1500–2000 per mm^2 in elderly persons. Substantial damage to the endothe-

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lium can take place in the course of certain diseases and after intraocular operations. Corneal transparency depends on a low level of hydration of the corneal stroma, which depends on special pumping qualities of the corneal endothelial cells. When the number of endothelial cells decreases, a so-called corneal decompensation can occur (corneal edema causing a substantial decrease in visual acuity). Pre- and postoperative measurement of the corneal endothelial cell count is a vital factor to determine corneal integrity which can help assess the degree of corneal damage during the surgery.

Purpose

The aim of the study was to determine the effect of various factors, such as patient's sex, age, the surgeon's experience, preoperative visual acuity, intraocular pressure, the hardness of the cataract according to the LOCS III scale, and the size of clear corneal incision, on the corneal endothelial cell loss, in patients undergoing phacoemulsification.

Material and methods

365 patients who underwent routine scheduled phacoemulsification between 2009 and 2010 were examined pre-operatively and at 1 month postoperatively. These were 114 men (31.2%) and 251 women (68.8%) whose age ranged from 19 to 91 years, mean 72.7 $\pm$ 10.5 years.

In 68 patients (18.6%) a temporal 1.8 mm clear corneal microincision was created, whereas in 297 patients (81.4%) a temporal 2.8 mm clear corneal incision was made. The operations were performed by 4 different surgeons: 116 operations by surgeon A (31.8%), 146 operations by surgeon B (40%), 65 operations by surgeon C (17.8%) and 38 operations by surgeon D (10.4%).

All procedures were performed under local, topical proxymetacaine hydrochloride (Alcaine) drops, Lidocaine gel 2% and intracameral (Lidocaine 1% solution) anaesthesia. Before the surgery, pupils were dilated using a solution of Tropicamide and phenylephrine (NeoSynephrine). Hydroxypropyl methylcellulose 2% (Celoftal, Alcon) was used as an ophthalmic viscosurgical device (OVD) and balanced salt solution (BSS) was used as the infusion fluid.

All procedures were performed using the burst mode of phacoemulsification and "stop and chop" technique for dividing the nucleus. Surgical settings were the same in all patients from both groups – the aspiration flow was set at 25 cm^3/min and the vacuum at 400 mmHg. In all eyes from the same group, the same type of metal keratome was used; all incisions were self-sealing and sutureless. The exclusion criteria were: corneal disorders, previous intraocular surgery and a history of ocular trauma.

In the C-MICS subgroup a trapezoidal 1.8 mm metal keratome (E7600, Bausch & Lomb) was used to create a self-sealing temporal 1.8 mm clear corneal incision. Capsulorrhexis was performed with micro-forceps under an OVD. A 20-gauge MVR blade was used to create two side-ports in the clear cornea, 90 degrees away from the main incision, for bimanual aspiration and irrigation tips. Phacoemulsification and aspiration were performed and a single-piece acrylic foldable lens (MI60®, Bausch & Lomb) was implanted through the main incision using an injector in a wound-assisted manner.

In the standard phacoemulsification subgroup, a self-sealing 2.75 mm temporal clear corneal incision was created with a 2.75 mm ClearCut™ Dual Bevel (Alcon) metal slit knife. Capsulorrhexis was done with Utrata forceps under an OVD. Two side-ports were created with a 20-gauge (microvitreoretinal – MVR) blade in the clear cornea, 90 degrees away from the main incision. Phacoemulsification and aspiration were then performed and a single-piece acrylic foldable lens was implanted with an injector through the main incision.

All patients underwent uneventful surgery. They were examined preoperatively and at two weeks to one month postoperatively.

In both groups postoperative treatment was the same and included topical dexamethasone and tobramycin combination eyedrops (Tobradex), instilled 4 times daily for 4 weeks.

In all patients the corneal endothelial cell count was measured with a TOPCON SP-2000P specular microscope. The hardness of the cataract was evaluated preoperatively according to the LOCS III scale.

For the purposes of statistical analysis, the mean, standard deviation (SD), median (Me), minimum (Min) and maximum (Max) were calculated.

Prior to comparing the results in two or more subgroups, the distribution of the analysed factors was checked against the standard distribution. For this purpose the λ-Kołmogorow–Smirnow test with Lilliefors's adjustment was used. Since the distribution of the analysed features was significantly different from the standard distribution, the non-parametric tests were used for further analysis.

In order to determine statistical significance of the differences in the distribution of best corrected visual acuity (BCVA), a Chi^2 independence test was calculated for the contingency table pre- and postoperatively. In order to compare the preoperative and postoperative results (interdependent tests), Wilcoxon's test of pair order was used.

In case of comparisons of age subgroups (in reference to cataract hardness or the surgeon), a non-parametric test of Kruscal-Wallis was calculated, and for multiple comparisons a post-hoc non-parametric Mann-Whitney test was used. In order to compare the loss of endothelial cells relative to preoperative BCVA, a non-parametric test of the median was used. In order to test the interdependence between the measurable features, the ratio of rectilinear correlation was calculated, and in order to test its relevance t-Student's test was used. Calculations were performed for the significance level $\alpha = 0.05$. A P value less than 0.05 was considered statistically significant.

Results

The mean preoperative endothelial cell density was 2463 ± 410 cells/mm^2 and it decreased to 2237 ± 529 cells/mm^2 postoperatively. The difference between the endothelial cell count preoperatively and at 4 weeks following the surgery was statistically significant ($p < 0.001$). Figure 1 shows the postoperative corneal endothelial cell loss.

A statistically significant corneal endothelial cell density (ECD) loss was observed postoperatively in the entire group ($p < 0.001$). The mean ECD loss was 321.4 $\pm$ 431 cells/mm^2.

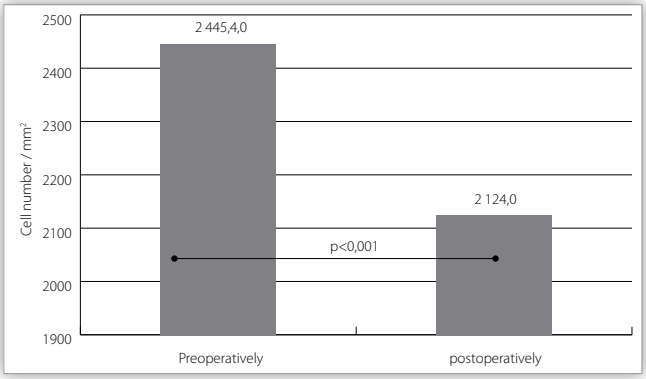

Fig. 1. The mean pre- and postoperative endothelial cell count (cells/mm²).
Ryc. 1. Średnia liczba komórek śródbłonka rogówki przed zabiegiem i po zabiegu (komórki/mm²).

A statistically significant improvement in BCVA was observed postoperatively ($p<0.001$). The preoperative BCVA ranged between 0.5 and 0.9 in 153 patients (41.9%), whereas postoperatively this number increased to 296 patients (81.1%) (Table I, Fig. 2).

BCVA	Preoperatively/ Przedoperacyjnie		Postoperatively/ Pooperacyjnie	
	n	%	n	%
0.5–0.9	153	41.9	296	81.1
0.2–0.4	113	31.0	40	11.0
<= 0.1	99	27.1	29	7.9
All/ Razem	365	100.0	365	100.0

Tab. I. Pre- and postoperative best corrected visual acuity (BCVA) ($Chi^2 = 118.655$, $p<0.001$).
Tab. I. Ostrość wzroku z najlepszą korekcją (BCVA) przed zabiegiem i po zabiegu ($Chi^2 = 118.655$, $p<0.001$).

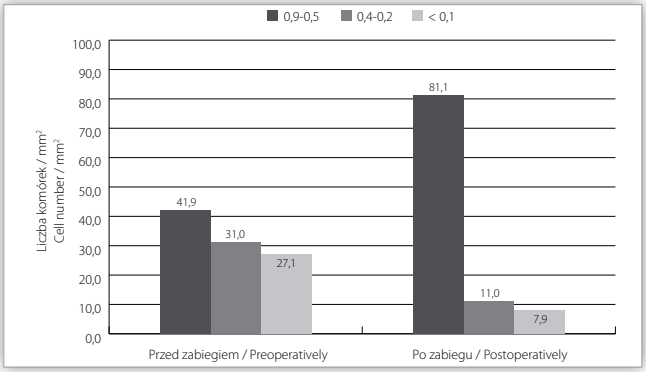

Fig. 2. Comparison of pre- and postoperative visual acuity.
Ryc. 2. Porównanie ostrości wzroku przed zabiegiem i po zabiegu.

The effect of preoperative BCVA on the postoperative endothelial cell loss was statistically significant ($p<0.05$). The highest loss was observed in patients with the lowest preoperative BCVA. Patients with visual acuity of 0.1 and less had the mean loss of 363.2 ± 447 cells/mm², whereas the average endothelial cell loss (ECD) in patients with the best preoperative BCVA (above 0.5) was 261.8 ± 386 cells/mm² (Fig. 3).

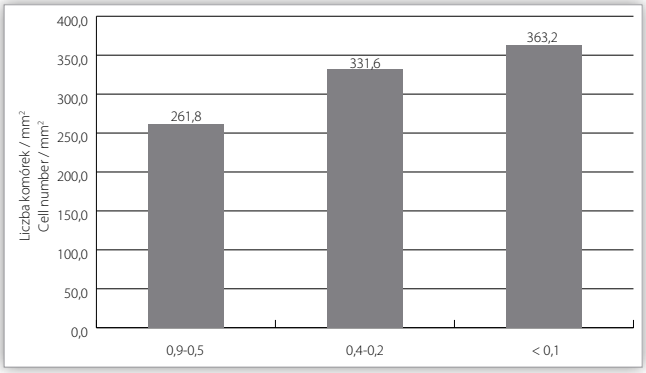

Fig. 3. Endothelial cell loss (cells/mm²) in reference to preoperative visual acuity.
Ryc. 3. Ubytek komórek śródbłonka rogówki w stosunku do przedoperacyjnej ostrości wzroku.

The degree of nuclear sclerosis according to LOCS III scale was evaluated in 235 patients. LOCS stage 1–2 of nuclear opacification was present in 38 patients (16.1%), stage 3 – in 96 patients (40.9%), stage 4 – in 62 patients (26.4%), stage 5 – in 31 patients (13.2%) and stage 6 – in 8 patients (3.4%). The majority of patients had stage 3 cataract (40.9%).

The association between the postoperative ECD loss and the degree of nuclear sclerosis was statistically significant ($p<0.001$). It turned out that the relation was proportional – the higher the degree of cataract hardness, the higher the endothelial cell loss was observed (Table II).

Endothelial cell loss gradually increased, from 152.3 ± 245 cells/mm² in patients with stages 1–2 LOCS cataract, up to 801.2 ± 493 cells/mm² in patients with stage 6 LOCS cataract.

A detailed comparison of mean postoperative ECD loss between the subgroups classified according to the LOCS scale revealed a significantly higher ECD loss in eyes with harder cataracts in comparison with eyes with softer lenses.

LOCS	Endothelial cell loss/ mm² Utrata komórek śródbłonka rogówki/ mm²			
	X Średnia	Mean loss %/ Śr. ubytek %	Me Mediana	SD Odch. stand.
1–2	152.3	6.41	33.8	245.6
3	265.5	10.63	124.7	385.6
4	281.8	12.03	172.3	314.6
5	455.6	18.13	385.9	412.4
6	801.2	31.60	708.70	493.9
Comparison/ Porównanie	$H = 24.501$, **$p<0.001$**			

Tab. II. Postoperative ECD loss in reference to cataract hardness according to LOCS III scale.
Tab. II. Pooperacyjny ubytek komórek śródbłonka rogówki w stosunku do stopnia twardości zaćmy w skali LOCS III.

The postoperative ECD loss also depends on the age of patients ($p<0.01$). The highest ECD loss was observed in patients aged 71 and more, (mean of 363.0 ± 443 cells/mm², 14.7%)

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which was significantly higher than the loss in the remaining age groups. The mean ECD loss in patients aged 61–70 years old was 245.7±379.6 cells/mm² and 196.8 ± 387.0 cells/mm² in patients under 60 years of age. The differences in the ECD loss between the two age groups were not statistically significant ($p>0.05$). Nevertheless, it should be noted that regardless of statistical significance, there is a tendency towards higher ECD loss in elderly persons.

There was no statistically significant difference in the postoperative ECD loss between the sex groups ($p>0.05$).

Statistically significant differences in the postoperative ECD loss were observed between the groups classified according to the clear corneal incision size ($p<0.01$). The mean endothelial cell loss in a standard phaco group was 355.0 ± 459.3 cells/mm² (13.63%) and 174.6 ± 233.4 cells/mm² in the MICS group (6.90%). It turned out that the mean endothelial cell loss associated with MICS technique was significantly lower as compared to the standard incision ($p<0.01$).

The mean ECD loss in patients after standard phaco expressed as absolute values was almost twice as high as in patients after MICS.

In order to determine the effect of the surgeon on endothelial cell loss after phacoemulsification, patients were divided into subgroups according to the operating doctor.

Surgeon A has been practicing phacoemulsification surgery for 16 years, performing approximately 700 operations a year; surgeon B also has a 16-year experience (700 operations a year), surgeon C has a 10-year experience (400 operations a year) and surgeon D has a 2-year experience (200 operations a year).

The mean ECD loss after phacoemulsification performed by particular surgeons is presented in Table III.

Surgeon/ Chirurg	Changes in the endothelial cell count (cells/ mm²)			
	X Średnia	Mean loss %/ Śr. ubytek %	Me Mediana	SD Odch. stand.
A	224.9	9.29	93.0	325.5
B	265.6	10.87	135.0	341.5
C	431.0	15.89	228.2	531.8
D	643.1	15.19	399.7	624.8
Comparison/ Porównanie	H = 23.711, **p<0.001**			

Tab. III. The effect of the surgeon's experience on the postoperative ECD loss.
Tab. III. Wpływ doświadczenia chirurga na pooperacyjną utratę komórek śródbłonka rogówki.

The ECD loss was significantly higher in patients operated by surgeon D as compared to patients operated by surgeons A or B ($p<0.001$). Moreover, there is no significant difference between the results of the surgeons A and B ($p>0.05$) (Table IV).

We have also measured the effect of the analysed features on the endothelial cell loss, calculating the correlation ratio, as illustrated in table V.

Based on these calculations, we have found that the endothelial cell loss was primarily affected by the surgeon's experience (the strength of the association was great). A significant and moderately strong effect of cataract hardness was also observed. The next factor in terms of significance was the incision size. Age and visual acuity were the least to affect the ECD loss.

Surgeons compared/ Porównanie chirurgów	Postoperative values/ Wartości pooperacyjne	
	Value of the Z test/ Wartość testu Z	p
A and B	1.125	ns
A and C	2.174	ns
A and D	**4.494**	**p<0.001**
B and C	1.492	ns
B and D	**3.985**	**p<0.001**
C and D	2.464	ns

Tab. IV. Z and P values for multiple comparisons (surgeons) (ns – not significant).
Tab. IV. Wartości Z i P dla porównań wielokrotnych (chirurdzy) (ns – statystycznie nieistotne).

Factors influencing ECD loss/ Czynniki wpływające na utratę ECD	The correlation ratio/ Współczynnik korelacji
Surgeon/ Chirurg	0.303
Cataract hardness/ Twardość zaćmy	0.292
Incision size/ Wielkość cięcia	0.163
Age/ Wiek	0.153
Preoperative visual acuity/ przedoperacyjna ostrość wzroku	0.121

Tab. V. The effect size of particular factors on the endothelial cell loss at 4 weeks postoperatively.
Tab. V. Ocena siły wpływu poszczególnych czynników na ubytek komórek śródbłonka rogówki 4 tygodnie po zabiegu.

Discussion

In our research, the following factors influenced the endothelial cell loss after uncomplicated phacoemulsification: the surgeon, cataract hardness according to the LOCS scale, the incision size, the patient's age, and the preoperative visual acuity. However, neither patients' gender nor intraocular pressure had any effect on the ECD loss.

There have been research papers investigating into the problem of ECD loss after phacoemulsification.

Wilczynski et al. (1) compared the ECD loss after two microincision techniques (namely: bimanual microincision B-MICS and coaxial microincision C-MICS) and found no statistically significant difference.

Beltrame et al. (2) confirmed that less corneal damage during the operation results in smaller ECD loss. However, the effect of corneal incision on ECD loss compared with the scleral incision is much higher, since the corneal incision causes more surgical trauma to the cornea than when the scleral incision is used.

We observed a similar difference comparing a standard clear corneal incision and a microincision, as the standard one causes larger surgical trauma to the cornea than the microincision.

The results published by Dick et al. (3) confirmed higher ECD loss in wider corneal incisions. However, the ECD loss was compared for corneal incision of 3.5 mm and 5.0 mm in this analysis.

Kohlhaas et al. (4) confirmed the influence of the phacoemulsification technique on the ECD loss. They found that surgical results of the so-called "Reversed Tip and Snip" technique lead to a smaller ECD loss than "Divide and Conquer" technique. Kosrirukvongs et al. (5) also showed that the surgical technique of phacoemulsification has an influence on the ECD loss. They observed that "Divide and Conquer" technique leads to a smaller ECD loss than „chip and flip" technique.

Sobottka Ventura et al. (6) found a similar corneal endothelial cell loss in patients who underwent cataract surgery through a standard clear corneal incision to our results.

The results reported by Wirbelauer (7), Milla (8), Durovic (9), Xie (10), Beiko (11), and Lesiewska-Junk (12) also confirm the influence of the surgical incision on the ECD loss.

Kim et al. (13) found that cataract hardness affected the ECD loss, which confirms our results. The authors found that the ECD loss after cataract surgery was significantly higher in patients with LOCS stages 4 or more, in comparison with patients with lower LOCS stages.

Similar results were obtained by Bourne et al. (14) and Hayashi et al. (15) – both authors found that patients with a higher stage of nuclear sclerosis had a higher ECD loss after phacoemulsification.

O'Brien et al. (16) also found that both cataract density and the surgeon's experience play contribute to the increased ECD loss, which is probably connected with increased procedure duration when performed by less experienced surgeons.

Walkow et al. (17) point to the prolonged phacoemulsification time as the factor which increases ECD loss. Our research also shows that the longer the surgeon has practiced phacoemulsification and the more experienced he/ she is, the smaller the loss of endothelial cells after phacoemulsification will be.

Laudańska-Olszewska et al. (18) examined 45 patients with LOCS stages 1–2 (group 1), and 3–4 (group 2) cataracts undergoing phacoemulsification and found no statistically significant difference in ECD loss between the groups, although the ECD loss in the second group was slightly higher than in the first group. They also noted that there was no significant association between the magnitude of ECD loss and the duration of phacoemulsification.

Roszkowska et al. (19) observed that patients' age influences the number of corneal endothelial cells. In their study, patients were not subjected to any surgery, however, the analyses showed a statistically significant association between patient's age and the corneal ECD loss, whereas no statistically significant association was shown between the patient's sex and the latter parameter.

The results by Hayashi et al. (15) confirm the influence of patients' elderly age on the increased ECD loss after phacoemulsification. In contrast, Kohlhaas et al. (20) drew opposite conclusions – having examined 48 patients after phacoemulsification, they found no correlation between patients' age and the ECD loss.

The lack of influence of intraocular pressure on the ECD loss after phacoemulsification was confirmed by Yachimori et al. (21), which complies with our results.

The variability of factors which influence the corneal endothelial cell loss as well as varying and not always conclusive published results, suggest the need for further analysis and more thorough research of the influence of different factors on the corneal endothelial cell loss after phacoemulsification.

Conclusions

Different factors impact the corneal endothelial cell loss after phacoemulsification. We found that the surgeon, cataract density, clear corneal incision size, patient's age and preoperative visual acuity had a significant influence on the postoperative corneal endothelial cell loss, whereas patient's sex, intraocular pressure and the preoperative number of corneal endothelial cells did not significantly affect the ECD loss.

Factors which influence the endothelial cell loss after phacoemulsification have different strenght of influence. The experience of the surgeon influenced the endothelial cell loss most significantly. The effect of cataract density and the corneal incision size on corneal cell loss was moderately strong, whereas age and preoperative visual acuity had the lowest effect on the endothelial cell loss.

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