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# ENDOTHELIAL CELL LOSS AFTER PARS PLANA VITRECTOMY

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## SUMMARY

**Aims:** To analyse the changes in endothelial cell density (ECD) after pars plana vitrectomy (PPV) and to identify the factors implicated.
**Patients and Methods:** This was a prospective, consecutive, and non-randomised, case-control study. All 23-gauge vitrectomies were performed by a single surgeon at a tertiary centre. ECD was measured at baseline before surgery and on postoperative Days 30, 90, and 180. The fellow eye was used as the control eye. The primary outcome was a change in ECD after PPV.
**Results:** Seventeen patients were included in this study. The mean age of the patients was 65 years. The mean ECD count at baseline was 2340 cells/mm$^2$. The median ECD loss in the vitrectomised eye was 3.6 %, 4.0 %, and 4.7 % at Days 30, 90, and 180, respectively, compared to +1.94 %, +0.75 %, +1.01 %, respectively, in the control eye. The relative risk of ECD loss after PPV was 2.48 (C.I. 1.05–5.85, p = 0.0247). The pseudophakic eyes lost more ECD than the phakic eyes, but this was not statistically significant. There were no significant differences in diagnosis, age, surgical time, or tamponade used after surgery.
**Conclusions:** Routine pars plana vitrectomy had an impact on the corneal endothelial cells until Day 180 post-op. The phakic status was slightly protective against ECD loss after PPV, although it was not statistically significant. The pathophysiology of corneal cell damage after routine PPV remains unclear. Further studies are required to confirm these findings.
**Keywords:** corneal endothelial cells, pars plana vitrectomy, specular microscopy

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## INTRODUCTION

A healthy cornea with a good endothelial cell population is important for maintaining its transparency and function. Loss of corneal endothelial cell density (ECD) is a well-known complication after intraocular surgery, such as routine phacoemulsification [1]. Other factors unrelated to surgery might have an impact on ECD changes, such as age, sex, or intraocular diseases [2,3]. Early studies have observed the impact of pars plana vitrectomy (PPV) on ECD loss [4,5]. At that time, lensectomy was often associated with retinal surgery. The amount of ECD loss associated with these early PPVs was significantly higher when no lens or capsule was present in the eye. Reports showed an ECD loss after PPV of 1.3 % in phakic eyes versus 27.5 % in aphakic eyes [4,6]. The direct contact of the tamponade, gas, or silicone oil (S.O.) with the corneal endothelial cells has an impact on the ECD [7,8]. Therefore, aphakia is a risk factor for ECD loss after PPV. However, we might assume that the introduction of innovative technology and better fluidic control during surgery improve surgical outcomes and reduce collateral damage. Published data suggest that there is no significant difference in ECD loss after combined cataract vitrectomy or deferred surgery. In one study, the ECD decreased significantly at 12 months by 15.3 %, 20.0 % and 19.3 % in the cataract alone, vitrectomy alone and combined cataract/vitrectomy group, respectively [9]. In another study, the ECD was decreased slightly more in the combined cataract/vitrectomy group compared with the vitrectomy alone group (13.9 % vs 9.0 %), although this was not statistically significant [10]. However, later studies have found contradictory results in ECD loss after PPV when performed in phakic eyes or pseudophakic eyes with a posterior chamber intraocular lens (PCIOL) [9,11,12].

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The goal of this study was to assess ECD changes after vitrectomy alone, compared with the fellow healthy eye. Other factors include age, lens status, retinal diagnosis, surgical time, and tamponade use.

## PATIENTS AND METHODS

This was a prospective, consecutive, and non-randomised, case-control observational study of patients requiring routine uncomplicated PPV for the first time. Only phakic and pseudophakic eyes previously implanted with a posterior chamber intraocular lens (PCIOL) were included in this study. The exclusion criteria were previous PPV or retinal surgery, previous complicated cataract surgery, aphakia, eye trauma, corneal pathology, and history of uveitis or glaucoma. The study was conducted in accordance with the principles of the Declaration of Helsinki. Protocols were approved by an independent Ethics Committee/institutional review board to confirm that the study met national and international guidelines for research on humans. Informed consent was obtained from each patient prior to inclusion in the study. All patient information was anonymised for the publication of this dataset.

A total of 20 patients were recruited in this study. Seventeen patients completed the 6-month follow-up period, and three patients left the study protocol due to early re-intervention (1x re-PPV, 2x cataract surgery). The study comprised 4 males and 13 females. The mean age was 65 years (range, 27–82 years). The indications for vitrectomy were as follows: epiretinal membrane (2 patients), full-thickness macular hole (5 patients), vitreomacular traction syndrome (2 patients), rhegmatogenous retinal detachment (4 patients), and tractional diabetic retinopathy (4 patients). The tamponade used at the end of surgery was no-tamponade (6 patients), gas (9 patients), and silicone oil (2 patients). The surgical intervention time range was from 30 minutes as the shortest to 120 minutes as the longest. For the purpose of statistical analyses, a cut at 1-hour duration was given to classify the surgery as short (less than 1 hour, including 15 patients) and long (more than 1 hour, including 2 patients). (Table 1, Supplemental Material).

During the therapeutic routine protocol, all patients underwent a baseline preoperative examination, including best-corrected visual acuity (BCVA), tonometry, and slit-lamp examination. ECD scanning was performed in both eyes, using specular microscopy (Nidek CEM-530, Nidek Co. Ltd., Japan). ECD measurements were performed automatically, using the manufacturer's software at the central cornea. These examinations were repeated on Days 30, 90, and 180 post-operatively.

### Surgical procedure

All vitreoretinal surgeries were performed by the same experienced surgeon (D.S.C.) at a tertiary centre. The 23-gauge pars plana vitrectomies were performed under local anaesthesia, using the Constellation system (Alcon, Fort Worth, TX, USA). After three EdgePlus® (Alcon, Fort Worth, TX, USA) valved cannulas were inserted, core and peripheral vitrectomy was performed. Detachment of the posterior hyaloid was performed if it was not present. During PPV, an ophthalmic balanced salt solution (BSS Plus, Alcon Laboratories, Fort Worth, TX, USA) was used as the intraocular irrigating solution. Should epiretinal membrane (ERM) or internal limiting membrane (ILM) peeling have been necessary, it was performed with the assistance of MEMBRANEBLUE-DUAL® dye (D.O.R.C., The Netherlands). Laser photocoagulation and/or cryo-coagulation was performed as required. Three types of vitreous substitutes were used: no tamponade, gas (Perfluoropropane (C3F8) 12 %) or SO (RS OIL 1000 centistokes, AL.CHI.MI.A. SRL, Italy).

### Statistical analysis

Statistical aid was provided by the Department of Public Health and Biostatistics. Statistical analysis was performed using SPSS software (ver.16, SPSS Inc., Chicago, IL, USA). Since the Shapiro-Wilk test showed that our population was not normally distributed, the quantitative variables were calculated using the median and interquartile range. To determine the differences in ECD loss given in percentages in the operated eye between Days 30, 90, and 180, Friedman's nonparametric test for related samples was used. The risk of ECD loss between the operated and control eyes was analysed, using the relative risk RR (95 % CI, $p < 0.05$). To study the association between ECD loss and other factors, the Mann-Whitney test and the nonparametric Pearson's chi-squared test were used. Statistical significance was set at $P < 0.05$.

## RESULTS

The mean BCVA in the operated eye was 0.38LogMar (range 0.01–1.6) at baseline and 0.39LogMar (range 0.05–1.0) at Day 180. The mean ECD count at baseline was 2340 cells/mm$^2$ in the operated eye and 2324 cells/mm$^2$ in the fellow control eye. The median ECD loss in the vitrectomised eye was -3.60 %, -4.00 %, and -4.70 % at Days 30, 90, and 180, respectively. The median ECD changes in the control fellow eyes were +1.94 %, +0.75 %, +1.01 % at Days 30, 90, and 180, respectively (Graph 1). The relative risk of ECD loss after PPV was 2.48 (95 % CI 1.05–5.85, $p = 0.0247$). Approximately 75 % of the vitrectomised eyes lost ECD, compared to 23 % of the fellow control eyes.

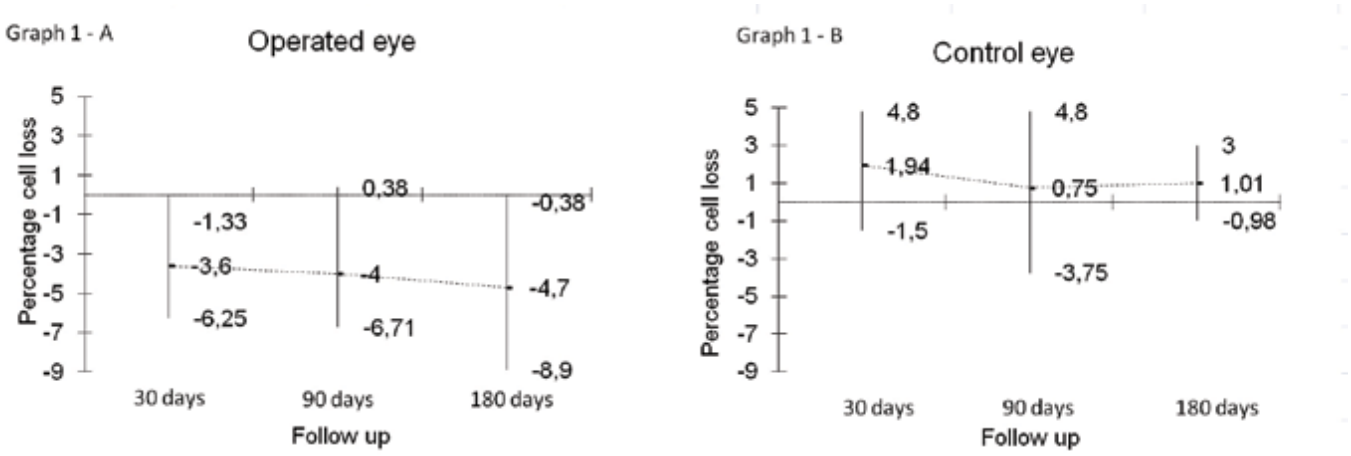
In the studied population, 75 % of the eyes were phakic and 25 % pseudophakic. The percentage of ECD loss in pseudophakic eyes was -3.56 %, -7.04 %, and –7.65 % at Days 30, 90, and 180, respectively, compared to -4.31 %, -3.55 %, and -4.53 %, respectively, in the phakic eyes (Graph 2). However, these differences were not statistically significant (Pearson's chi-squared test, $p = 0.195$).

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**Table 1.** The Table describes the baseline characteristics of the studied population including age, diagnosis and lens status. Details include the tamponade used at the end of vitrectomy and the surgical duration of vitrectomy: "0" being less than 1-hour duration and "1" more than 1-hour duration. The net ECD counts of the operated eye and the control fellow eye are shown in every clinical visit. In the follow-up visits are shown the percentages of ECD loss, compared to baseline in the operated and the fellow control eyes; a negative value being considered ECD loss and a positive value considered ECD gain

| Table 1 | Age | Dg. | Tamponade | Long surgery | Lens | Baseline | |
|---|---|---|---|---|---|---|---|
| | | | | | | operated | fellow |
| 1 | 64 | FTMH | Gas | 0 | PCIOL | 2901 | 2846 |
| 2 | 27 | RD | Gas | 0 | PCIOL | 2771 | 2741 |
| 3 | 68 | FTMH | Gas | 0 | Phakic | 2008 | 1997 |
| 4 | 49 | RD | Gas | 0 | Phakic | 3012 | 2810 |
| 5 | 63 | TDR | none | 1 | Phakic | 2319 | 2289 |
| 6 | 56 | RD | Gas | 0 | Phakic | 2251 | 2566 |
| 7 | 72 | TDR | none | 0 | Phakic | 2059 | 1978 |
| 8 | 73 | VMT | none | 0 | Phakic | 2637 | 2200 |
| 9 | 66 | ERM | none | 0 | Phakic | 1823 | 2065 |
| 10 | 60 | FTMH | Oil | 0 | Phakic | 2446 | 2470 |
| 11 | 64 | FTMH | Gas | 0 | Phakic | 2909 | 2135 |
| 12 | 76 | ERM | Gas | 0 | Phakic | 3028 | 2902 |
| 13 | 63 | TDR | Oil | 1 | Phakic | 1873 | 1790 |
| 14 | 81 | VMT | none | 0 | Phakic | 1962 | 1600 |
| 15 | 82 | FTMH | Gas | 0 | PCIOL | 928 | 1030 |
| 16 | 59 | RD | Gas | 0 | Phakic | 2615 | 2433 |
| 17 | 58 | TRD | none | 0 | Phakic | 2360 | 2407 |

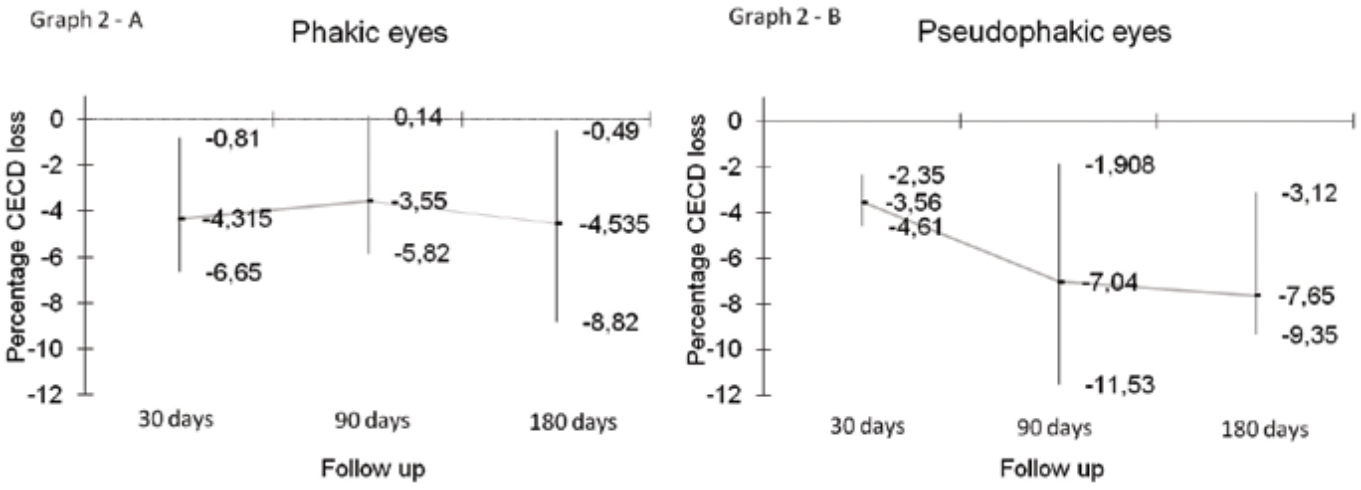
*ERM: epiretinal membrane, FTMH: full thickness macular hole, VMT: vitreomacular traction syndrome, RRD: rhegmatogenous retinal detachment, TDR: tractional diabetic retinopathy. PCIOL: posterior chamber intraocular lens. (% change): percentage of ECD change from baseline*




**Graph 1.** The percentage ECD loss in the vitrectomised eye (**A**) compared to the fellow control eye (**B**) at Days 30, 90, and 180 respectively. The median ECD loss in the vitrectomised eye (**A**) shows a statistically significant loss of ECD compared to the control fellow eyes (**B**), with a RR of 2.48 (95 % CI 1.05–5.85, p = 0.0247)

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| | 1 month | | | | 3 months | | | | 6 months | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | operated (% change) | | fellow (% change) | | operated (% change) | | fellow (% change) | | operated (% change) | | fellow (% change) | |
| | 2890 | -0.38 | 2796 | -1.75 | 2933 | 1.10 | 2716 | -4.56 | 2908 | 0.24 | 2875 | 1.01 |
| | 2671 | -3.61 | 2801 | 2.18 | 2576 | -7.04 | 2746 | 0.18 | 2512 | -9.35 | 2754 | 0.47 |
| | 1962 | -2.29 | 1987 | -0.50 | 1895 | -5.63 | 2012 | 0.75 | 1974 | -1.69 | 1964 | -1.65 |
| | 2780 | -7.70 | 2799 | -0.39 | 2693 | -10.59 | 2697 | -4.02 | 2820 | -6.37 | 2739 | -2.52 |
| | 2191 | -5.52 | 2320 | 1.44 | 2317 | -0.10 | 1827 | -20.18 | 2296 | -1.00 | 2728 | 19.17 |
| | 2148 | -4.60 | 2518 | -1.87 | 2161 | -4.00 | 2476 | -3.5 | 2029 | -9.90 | 2558 | -0.31 |
| | 1931 | -6.20 | 2336 | 18.09 | 1972 | -4.23 | 2261 | 14.30 | 1939 | -5.83 | 2039 | 3.08 |
| | 2472 | -6.30 | 2077 | -6.04 | 2555 | -3.10 | 2289 | 4.04 | 2363 | -10.40 | 2233 | 1.50 |
| | 1778 | -2.50 | 2265 | 9.68 | 1818 | -0.30 | 2108 | 2.08 | 1842 | 1.04 | 2067 | 0.09 |
| | 2248 | -8.10 | 2267 | -8.21 | 2467 | 0.86 | 2612 | 5.74 | 2339 | -4.37 | 2295 | -7.08 |
| | 2251 | -22.62 | 2205 | 3.27 | 2036 | -30.00 | 2137 | 0.09 | 2178 | -25.20 | 2167 | 1.49 |
| | 2924 | -3.43 | 3052 | 5.16 | 2949 | -2.60 | 2945 | 1.48 | 2886 | -4.70 | 2921 | 0.65 |
| | 2009 | 7.26 | 1861 | 3.96 | 1969 | 5.13 | 1732 | -3.24 | 1854 | -1.01 | 1832 | 2.34 |
| | 1883 | -4.03 | 1656 | 3.50 | 1878 | -4.28 | 1792 | 12.00 | 1796 | -8.46 | 1832 | 14.50 |
| | 895 | -3.56 | 1050 | 1.94 | 821 | -11.53 | 925 | -10.00 | 857 | -7.65 | 1040 | 0.97 |
| | 2710 | 3.63 | 2608 | 9.24 | 2448 | -6.39 | 2513 | 3.28 | 2643 | 1.07 | 2506 | 3.00 |
| | 2582 | 9.40 | 2387 | -0.83 | 2580 | 9.32 | 2502 | 3.94 | 2463 | 6.90 | 2447 | 1.66 |




**Graph 2.** The percentage of ECD loss after vitrectomy in phakic (**A**) and pseudophakic eyes (**B**) at Days 30, 90, and 180 respectively. The percentage of ECD loss in pseudophakic eyes (**B**) was higher compared to the phakic eyes (**A**). However, these differences were not statistically significant (p = 0.195)

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There were no statistically significant differences observed among diagnosis, age, surgical time, or tamponade used, regardless of lens status. No postoperative complications or high intraocular pressure (IOP) were observed. All corneas remained clear throughout the study and at the end of the follow-up period.

## DISCUSSION

In our cohort, a significant ECD loss of 4.70 % was maintained up to 6 months of routine PPV alone, compared with no change in the fellow control eye. The PPV had an impact on the corneal endothelial cells in our patients, with a relative risk of ECD loss of 2.48 (95 % CI 1.05–5.85, $p = 0.0247$). After vitrectomy, approx. 75 % of the eyes presented ECD loss, while only 23 % in the control group. The ECD loss observed after vitrectomy alone in our study was proximate to the loss reported after phacoemulsification alone [1]. In previous reports, the ECD loss related to PPV returned to normal levels after time [11], but this was not observed in our study.

The ECD loss, when performing combined phaco-vitrectomy versus cataract or vitrectomy deferred surgery, was reported in previous studies without statistically significant differences [9,10]. However, there is no consensus on whether PPV is safer in phakic or pseudophakic eyes. In this regard, some studies praise PPV as being slightly safer in phakic eyes [4,10,12], while others have shown it to be modestly safer in pseudophakic eyes [9,11]. In our study group, the percentage of ECD loss after 6 months of routine PPV was 7.65 % in pseudophakic eyes compared to 4.53 % in phakic eyes (Graph 2). Although this difference was not statistically significant, we observed some protective effects of the crystalline lens.

Currently, the pathophysiology of endothelial cell damage after PPV remains unclear, whether it is due to inflammation alone or due to some other physical damage during surgery. In our study, we were not able to identify any specific cause of ECD loss, apart from the vitrectomy itself. The age was not determinant, regardless of the significant age range in the study group. The reason for this is that the fellow eye was used as the control eye, removing this potential bias. No intraoperative factors were identified as a cause for ECD loss. The vitrectomies were performed using the same Constellation Vision system settings (IOP control system) and a valved trocars system that minimise the chances of hypotony or IOP fluctuations during surgery [15].

The surgical time range ranged from 30 minutes to 120 minutes, and this might be considered as a risk factor for ECD loss. The statistical analysis of the different time ranges was not possible in our study group, due to the small number of patients. However, the cut at 1-hour surgical duration time did not show any statistical impact on ECD loss, but only 2 of 17 patients had a long surgical intervention. Hence, no conclusion can be drawn regarding the impact of surgical time on ECD loss in this study.

Furthermore, no manipulation was performed in any case at the anterior chamber, removing any potential bias of direct physical endothelial cell damage or anterior chamber depth fluctuations. In terms of prevention, the use of protective ophthalmic viscoelastic devices (OVDs) has shown to be protective during phacoemulsification [13,14]. Therefore, intraocular OVDs as a preventive measure during routine PPV may be the subject for future studies.

This study has several limitations. This was a small cohort with many asymmetries among the study population. The study was confined to one centre and a single surgeon. Although the fellow eye was used as the control eye, no randomisation was applied to the patients. The aim of the study was not to compare the outcomes of different vitrectomy systems or specular microscopy techniques. The ECD measurements were performed in an automated manner, using the manufacturer's software to minimise operator biases. However, the ECD measurements were taken only at the central cornea. Inaccuracy of ECD measurement might represent a confounding factor, but this would have equally affected the control group, where a small negligible gain was observed. In our study, the impact of surgical time on ECD loss was not conclusive. Furthermore, several retinal pathologies were included in this study, adding more confounding factors.

## CONCLUSION

Routine pars plana vitrectomy alone causes damage to the corneal endothelial cells, with an RR of 2.48 (95 % CI 1.05–5.85, p = 0.0247). The percentage of ECD loss seems to be maintained up to 6 months postoperatively. The phakic status is slightly protective against ECD loss after PPV, although it is not statistically significant. Further studies are required to confirm these findings.

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Pro naše kliniky v Praze a Brně hledáme oftalmology.

CANADIAN MEDICAL

CANADIAN MEDICAL je síť prémiových klinik, která poskytuje klientům vysokou úroveň lékařské péče. Našim lékařům kromě zajímavého finančního ohodnocení nabízíme možnost věnovat se moderní ambulantní medicíně v nadstandardních podmínkách a s klienty, kteří jsou motivováni se o své zdraví starat. Do našeho týmu hledáme zkušené lékaře (i sestry) se zájmem o moderní medicínu, s výbornými komunikačními dovednostmi, empatií a plynulou angličtinou. Jsme leadrem v oblasti online služeb, digitalizace péče a distanční medicíny, budete tedy v kontaktu s moderními medicínskými trendy. Lékařům ponecháváme velkou míru autonomie, redukujeme administrativní zátěž a podporujeme je ve vzdělávání. Samozřejmostí je moderní technické vybavení, hezké pracovní prostředí, 5 týdnů dovolené i extra „sick days“.

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