

# Impact of Combined Phaco-PPV and Tamponades on Corneal Endothelial Cell Health in Rhegmatogenous Retinal Detachment

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## ABSTRACT

**Objective:** To evaluate the impact of different tamponade agents on corneal endothelial morphology following combined phacoemulsification and pars plana vitrectomy (Phaco-PPV) for rhegmatogenous retinal detachment (RRD).

**Methods:** This prospective, single-center study included 65 eyes with RRD and cataract that underwent combined Phaco-PPV with either silicone oil or perfluoropropane (C3F8) tamponade. Patients with prior intraocular procedures, corneal pathologies, or intraoperative complications were excluded. Best-corrected visual acuity (BCVA) and specular microscopy parameters—endothelial cell density (ECD), hexagonality (HEX), and coefficient of variation (CV)—were assessed preoperatively and at 3 months postoperatively. Percentage changes in specular parameters were analyzed between the two tamponade groups.

**Results:** BCVA improved significantly in both tamponade groups at 3 months ( $p < 0.001$ ). Both groups showed significant reductions in ECD and HEX, while CV remained stable. Percentage ECD loss was significantly greater in the C3F8 group compared to the silicone oil group ( $p = 0.043$ ), whereas changes in HEX and CV did not differ significantly between tamponades. Early postoperative complications included fibrin exudation (4 eyes silicone oil vs. 11 eyes C3F8), IOP elevation (4 eyes silicone oil vs. 9 eyes C3F8), and posterior synechiae (4 eyes, C3F8 only).

**Conclusions:** Combined Phaco-PPV with C3F8 tamponade is associated with greater corneal endothelial cell loss compared to silicone oil, while HEX and CV remain unaffected by tamponade choice. Given the risk of future intraocular interventions, preservation of endothelial integrity is critical. Silicone oil tamponade was associated with relatively lower endothelial cell loss than C3F8 gas in patients undergoing combined phaco-PPV for rhegmatogenous retinal detachment.

**Keywords:** Combined phaco-PPV, rhegmatogenous retinal detachment, silicone oil, C3F8, specular microscopy

## INTRODUCTION

Retinal detachment (RD) occurs when subretinal fluid accumulates between the neurosensory retina and the retinal pigment epithelium<sup>[1]</sup>. Once considered untreatable, advancements in surgical interventions have significantly improved outcomes<sup>[2]</sup>. Optimal management for rhegmatogenous retinal detachment (RRD) remains a subject of debate. Pneumatic retinopexy, scleral buckling, and pars

plana vitrectomy (PPV) are viable options, though the choice among these methods depends on the surgeon's expertise, patient-specific factors (such as positional compliance), and case complexity. Currently, PPV is the most commonly preferred method, with gas or silicone oil tamponades effectively enhancing anatomical success.

In modern practice, corneal transparency is one of the most critical parameters for successful PPV outcomes. Any cor-

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neal pathology can obstruct the visualization required for managing coexisting posterior segment diseases. When corneal and vitreoretinal pathologies coexist, combined PPV surgeries, such as those involving penetrating keratoplasty (PKP) with temporary or permanent keratoprotheses, may be considered. However, outcomes are generally less favorable than in uncombined cases due to the high risk of graft failure. Additionally, these methods cannot fully replicate the clarity of the patient's native cornea, limiting the achievement of optimal results<sup>[3]</sup>.

The corneal endothelial cell (CEC) layer plays a vital role in maintaining corneal health and transparency by regulating stromal hydration through dynamic fluid transport mechanisms. The CEC layer lacks regenerative capability, leading to a constant, age-related decline in cell density. This cell loss can be further exacerbated by trauma or surgeries, such as vitrectomy or phacoemulsification (phaco), eventually resulting in corneal edema and reduced transparency<sup>[4, 5]</sup>.

In phakic eyes with RRD, determining the optimal order of surgeries is essential, as PPV accelerates cataract development, making future cataract surgery inevitable in vitrectomized eyes<sup>[6, 7]</sup>. Limited studies have examined the impact of Phaco-PPV procedures or the effects of different endotamponades on CEC morphology<sup>[8, 9]</sup>. Given the critical role of corneal transparency in visual outcomes and the irreversible nature of corneal endothelial cell loss, preserving the CEC layer is essential for long-term success in surgical management. Postoperative complications such as recurrent RRD, glaucoma, endophthalmitis, or the need for additional surgeries can further challenge corneal health. Even in cases without complications or re-detachment, maintaining a clear cornea during routine follow-up is vital for both anatomical and functional success. This study aimed to assess the impact of combined Phaco-PPV procedures using different tamponades on corneal health by analyzing specular microscopy results, with the goal of informing strategies to optimize endothelial cell preservation postoperatively.

## **METHODS**

This single-center, prospective study was conducted on eyes with RRD and cataracts that underwent combined Phaco and PPV between March 2023 and June 2024 at the

ophthalmology department of a tertiary care hospital in Turkey. The study was approved by the Clinical Research Ethics Committee prior to its initiation (IRB Approval No: E-96317027-514.10-231669444). It was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Exclusion criteria included patients with a history of prior intraocular or refractive surgery, intravitreal injections, or retinal laser treatments; zonular instability; pseudoexfoliation syndrome (PEX); contact lens use; corneal pathology; or a high refractive error exceeding  $\pm 6.00$  diopters or; any intraoperative complications during phaco that could potentially increase postoperative inflammation. The decision for cataract surgery was made only in patients with a nuclear grade of at least 4, according to the LOCS III classification. Silicone oil tamponade was preferentially used in eyes with inferior retinal breaks located between the 4 and 8 o'clock meridians, whereas C3F8 gas tamponade was used in eyes without inferior breaks in this range. Eyes with advanced PVR (grade C), in which silicone oil is routinely preferred in our clinical practice, were excluded to minimize indication-related bias. All patients underwent a comprehensive ophthalmological assessment at each follow-up visit, which included best-corrected visual acuity (BCVA) measurement using a Snellen chart, biomicroscopic examination, intraocular pressure (IOP) measurement with Goldmann applanation tonometry, detailed fundus examination, and optical coherence tomography (OCT). Evaluations were conducted one day before surgery, on postoperative day 1, on day 7, and at 1 and 3 months postoperatively. Endothelial cell function was evaluated using non-contact specular microscopy (EM-4000, Tomey Corporation, Nagoya, Japan). This method offers a non-invasive and highly reproducible assessment of endothelial cell density (ECD), size, shape, and morphology. Specular microscopy was performed one day prior to surgery and repeated at the 3-month postoperative follow-up.

BCVA values recorded on the Snellen chart were converted to the logarithm of the minimal angle of resolution (LogMAR) for statistical analysis. Counting fingers (CF), hand motion (HM), and light perception (LP) were assigned LogMAR values of 2.0, 2.4, and 2.7, respectively.

## SURGERY

All cataract surgeries were performed by an experienced surgeon, who used phaco techniques with intraocular lens (IOL) implantation within the lens capsule. A dispersive viscoelastic was used to protect the corneal endothelium. All PPV procedures were conducted by an experienced retinal surgeon under general anesthesia, using the Constellation vitrectomy system (Alcon Laboratories, Fort Worth, Texas, USA) with the Eibos 2 noncontact wide-viewing system. Cannulas were placed in the inferotemporal, superotemporal, superonasal, and superior quadrants (the latter for chandelier illumination). A 25-gauge core vitrectomy was performed, and posterior vitreous detachment was induced with triamcinolone assistance via the vitreous cutter's vacuum probe, followed by peripheral vitreous shaving. Perfluorocarbon liquid was applied to flatten the retina and displace subretinal fluid via the original retinal break, after which a fluid-air exchange was conducted. Retinopexy around the retinal breaks was performed with photocoagulation. Finally, either gas perfluoropropane (C3F8) or silicone oil was used as a tamponade. Trocars were removed at the conclusion of the procedure, and any scleral wounds with leakage were closed with 8-0 vicryl sutures. Patients received topical antibiotics (0.5% moxifloxacin), 1% prednisolone acetate, and 0.5% tropicamide for six weeks postoperatively, with additional systemic steroids, antibiotics, or topical antiglaucoma drops administered as necessary.

## STATISTICS

Statistical analyses were performed using SPSS Version 22.0 (IBM Corp., Armonk, NY, USA). A *p*-value of <0.05 was considered statistically significant. The Shapiro–Wilk test was used to assess the normality of data distribution. Descriptive statistics were presented as mean ± standard deviation for continuous variables and as counts and percentages for categorical variables. Group comparisons were performed using the independent samples *t*-test for normally distributed data and the Mann–Whitney *U* test for nonparametric data. For preoperative and postoperative comparisons of the same parameters, either the paired samples *t*-test or the Wilcoxon signed-rank test was applied, depending on the data distribution. The chi-square test with Yates correction was used to assess differences in gender distribution, and Pearson correlation analysis was

used to evaluate relationships between continuous variables. Linear regression analyses were conducted to identify predictors of percentage change in ECD loss, hexagonality (HEX), coefficient of variation (CV) following surgical management of rhegmatogenous retinal detachment.

## RESULTS

A total of 65 age- and gender-matched patients were included in the study. The mean age of participants was  $59.7 \pm 12.3$  years, with no significant difference between the silicone oil and C3F8 groups. The mean cataract grade was  $4.38 \pm 0.99$  in the silicone oil group and  $4.52 \pm 0.89$  in the C3F8 group, with no statistically significant difference between the two tamponade groups (Mann–Whitney *U* test, *p* = 0.52). Similarly, age, gender, duration of disease, and baseline ECD, HEX, and CV were comparable across groups (Table 1).

The mean operation time was  $91.5 \pm 22.9$  minutes in the silicone oil group and  $87.7 \pm 22.3$  minutes in the C3F8 group (*p* = 0.191). No significant difference in operation time was observed between the silicone oil and C3F8 groups (*p* = 0.155) (Table 1). Additionally, no correlation was found between operation time and CEC parameters in either group.

The mean preoperative BCVA was  $1.5 \pm 0.6$  logMAR overall,  $1.7 \pm 0.5$  in the silicone oil group, and  $1.4 \pm 0.6$  in the C3F8 group. Postoperatively, BCVA improved significantly in all groups (*p* < 0.001 for each). The mean percentage change in BCVA was  $-29.4 \pm 28.2\%$  overall,  $-20.7 \pm 29.7\%$  in the silicone oil group, and  $-39.0 \pm 23.2\%$  in the C3F8 group (*P* < 0.05).

In both the silicone oil and C3F8 tamponade groups, a significant decrease in ECD was observed in the total patient population (*p* < 0.001) (Table 2). A significant reduction in HEX was also noted in both groups at the 3-month postoperative assessment. However, no significant change was found in CV in either group (Table 2).

When percentage changes were analyzed, ECD loss was found to be significantly greater in the C3F8 group compared with the silicone oil group. In contrast, no significant differences were observed between the two tamponade groups regarding percentage changes in HEX and CV (Table 3).

**Table 1.** Comparison of Demographics, Specular Parameters, and Surgical Metrics Between Silicone oil and C3F8 Groups

	Silicone (n=34)	C3F8 (n=31)	p
Age (years)	58.5± 12.9	61± 11.7	0.757m
Gender (F/M)	20/14	18/13	0.951m
Duration of disease (days)	10± 2.4	11.1± 19	0.053t
Operation time (minute)	91.5±22.9	87.7± 22.3	0.191t
ECD	2263.9± 343.5	2336.9± 285.2	0.354t
HEX	44.1±5.7	45.5±7.8	0.443t
CV	41.2±5.9	40.3±5.6	0.797m

C3F8: Gas perfluoropropane, F: Female, M: Male, ECD: Endothelial cell density, HEX: Hexagonality, CV: Coefficient of variation, p: p-value for the comparison between Silicone Oil and C3F8 tamponade groups, m: Mann–Whitney U test, t: Independent samples t-test

**Table 2.** Comparison of Preoperative and 3-Month Postoperative Specular Parameters by Endotamponade Type

	total	Silicone oil	C3F8	pt
ECD preoperative	2298.7±316.7	2263.9± 343.5	2336.9± 285.2	0.354t
ECD postoperative	1890.1± 374.8	1938± 377	1837.7± 371.5	0.214m
p <sup>preop-postop</sup>	<0.001w	<0.001w	<0.001w	
HEX preoperative	44.8±6.7	44.1±5.7	45.5±7.8	0.443t
HEX postoperative	40.6±6	41.3±6.6	39.8±5.2	0.325m
p <sup>preop-postop</sup>	<0.001w	0.050w	<0.001w	
CV preoperative	40.8±5.7	41.2±5.9	40.3±5.6	0.301m
CV postoperative	42.3±7	43±7.8	41.5±6	0.797m
p <sup>preop-postop</sup>	0.146w	0.338w	0.273w	

C3F8: Gas perfluoropropane, ECD: Endothelial cell density, HEX: Hexagonality, CV: Coefficient of variation, p preop-postop: p-value between preoperative and postoperative parameters, pt: p-value for the comparison of preoperative baseline parameters between Silicone oil and C3F8 tamponade groups, m: Mann–Whitney U test, w: Wilcoxon signed-rank test, t: Independent samples t-test

**Table 3.** Analysis of Percentage Changes in Specular Parameters Between Preoperative and 3-Month Postoperative

	Total (% mean±SD)	Silicone oil (% mean±SD)	C3F8 (% mean±SD)	p
ECD loss %	-16.5±19.8	-12.5±22.5	-20.8± 15.6	0.043m
Change(Reduction) of HEX %	-7.7±15.8	-5.6±15.8	-10.5±15.8	0.256m
CV changes %	4.7±17.7	5.6±21.4	3.7±12.9	0.823m

C3F8: Gas perfluoropropane, ECD: Endothelial cell density, HEX: Hexagonality, CV: Coefficient of variation, p: p-value for the comparison between Silicone Oil and C3F8 tamponade groups, m: Mann–Whitney U test

A non-significant decrease in central corneal thickness (CCT) was observed in both groups during the postoperative period. As an early postoperative complication, fibrin exudation was observed in four eyes in the silicone oil group and eleven eyes in the C3F8 group. Early postoperative IOP elevation was detected in 9 eyes in the C3F8 group and 4 eyes in the silicone oil group. All cases were successfully managed with antiglaucomatous drops within the first postoperative week. Preoperative and postoperative 3-month intraocular pressure values were comparable (16.55 vs. 16.58 mmHg), with no statistically significant difference observed (Wilcoxon signed-rank test,  $p = 0.98$ ), indicating the absence of sustained postoperative IOP elevation. In our cohort, no significant correlation was found between changes in intraocular pressure and percentage endothelial cell loss (Spearman  $\rho = 0.058$ ,  $p = 0.65$ ), further supporting the notion that transient postoperative IOP fluctuations below clinically critical thresholds are unlikely to be a primary driver of endothelial damage. Posterior synechiae developed in 4 eyes in the C3F8 group.

## DISCUSSION

In healthy adults, ECD typically ranges from 2500 to 3000 cells/mm<sup>2</sup>. When ECD falls below 400 to 700 cells/mm<sup>2</sup>, the cornea can no longer maintain its deturgescence, resulting in corneal edema and visual deterioration. A decline in endothelial cell count can be attributed to several factors, including aging, ocular trauma, inflammation, and surgical interventions<sup>[11]</sup>. Cataract surgery is recognized as one of the most common iatrogenic causes of corneal endothelial cell loss<sup>[12]</sup>. Although filtering procedures for glaucoma generally result in less endothelial loss compared to cataract extraction, significant cell loss may still occur, particularly when performed in combination with cataract surgery<sup>[13]</sup>. In addition, PPV surgeries are known to have also a negative impact on CEC function due to the inflammatory response they induce. Numerous studies in the literature have shown CEC loss following PPV and phaco procedures<sup>[4, 8, 10, 14, 15]</sup>. However, within the same indication group, there is limited research evaluating the effects of different surgical methods with various tamponades on specular parameters, which is an essential aspect of maintaining corneal health.

It is well-established that PPV can accelerate cataract formation or progression, leading to potential challenges in performing cataract surgery on vitrectomized eyes. These

challenges arise from factors such as fluctuating anterior chamber depth, zonular weakness, increased lens-iris diaphragm mobility, and lack of vitreous support<sup>[16]</sup>. Consequently, performing cataract surgery during PPV has become common practice, depending on factors such as the patient's age, lens condition, and surgeon's preferences. In our study, we exclusively included patients who underwent combined phaco-PPV procedures. Previous investigations evaluating phaco-PPV independently of tamponade choice have already demonstrated that the sequence of surgery does not exert a significant effect on ECD.<sup>[9]</sup> Based on this evidence, we designed our methodology to specifically assess the impact of different tamponade agents within a single surgical indication. By excluding other indications and surgical variations, our aim was to isolate and clearly delineate the effect of tamponade choice on corneal endothelial morphology.

The earliest studies investigating the impact of lens status on CEC parameters in PPV consistently concluded that the absence of lens support significantly increases corneal endothelial vulnerability, regardless of the tamponade agent or other surgical variables. Rosenfeld et al. reported a reduction in ECD at 6 months postoperatively in both aphakic eyes (13%) and eyes undergoing lensectomy combined with PPV (17%), compared with only 0.4% in phakic eyes<sup>[19]</sup>. In a separate study, no endothelial cell loss was observed in phakic eyes undergoing PPV without lens removal<sup>[20]</sup>. In a study evaluating 22 patients, Mittl et al. reported that the most significant change in corneal ECD occurred in the aphakic group, with a mean loss of 7.6%.<sup>[21]</sup> Similarly, Takkar et al. assessed patients with various indications and observed an overall 10% reduction in ECD and did note greater endothelial damage in aphakic eyes<sup>[14]</sup>. Moreover, Mitamura et al. had previously shown that combining vitrectomy with lensectomy and anterior capsule removal led to significantly greater CEC loss<sup>[22]</sup>. However, these studies were conducted two to three decades ago and did not involve cataract surgery or anterior chamber procedures, limiting the direct comparability of their findings with those of the present study.

There are studies investigated the impact of tamponade agents other than lens status in vitrectomized eyes. For instance, Yang et al. demonstrated increased apoptosis in endothelial cells and reduced endothelial proliferation when

using silicone oil as a tamponade, indicating its potentially damaging effect on CEC health<sup>[23]</sup>. Early removal of silicone oil is suggested once the therapeutic goal of tamponade has been met. Another study utilizing in vivo confocal microscopy reported decreased ECD, reduced HEX, and increased CV in eyes with silicone oil in the anterior chamber, even when slit lamp examinations appeared normal<sup>[24]</sup>. This suggests that silicone oil may impact CEC morphology subtly, with changes undetectable through routine slit-lamp exams. In contrast to our study, these two investigations evaluated only silicone oil and did not include other tamponade agents. In our analysis, demonstrated that C3F8 tamponade showed a statistically higher significant effect on endothelial outcomes compared to silicone oil.

Farrahi et al. revealed no significant difference in ECD at six months between vitrectomized eyes with and without silicone oil ( a mean ECD loss of 6.08%). No differences were observed also between phakic and pseudophakic subgroups<sup>[10]</sup>. Cinar et al. also reported no significant differences in CEC parameters between SF6 and silicone oil in 25 phakic eyes (a mean ECD loss of 3.8% in phakic eyes)<sup>[25]</sup>. These two studies included cases beyond RRD, which may limit their applicability to pure RRD populations. Additionally, both used 20 and 23-gauge vitrectomy systems, which are associated with greater postoperative inflammation compared to smaller-gauge systems such as 25-gauge. This elevated inflammatory response may have diminished the observable impact of tamponade type on specular microscopy parameters. The differences in both surgical technique and case selection therefore limit the direct comparability of their findings with our study. RRD surgeries typically involve extensive intraoperative manipulations, such as vitreous base shaving, endophotocoagulation, and chandelier-assisted illumination. In addition, scleral indentation increases the risk of subclinical trauma to the lens capsule and zonular apparatus, thereby promoting intraocular inflammation. We hypothesize that when these manipulations are combined with C3F8 tamponade, the resulting inflammatory response is amplified. Moreover, C3F8 may contribute to postoperative IOL tilt and anterior chamber narrowing, increasing the likelihood of iris–cornea contact. Collectively, these factors may exacerbate mechanical trauma to the corneal endothelium, resulting in greater ECD loss compared with silicone oil. Consistent with this hypothesis, early postoperative fibrin exudation and intraocular

pressure elevation were observed more frequently in the C3F8 group, supporting the notion that tamponade-related inflammatory responses may contribute to the greater endothelial cell loss seen in these eyes.

Coman Cernat et al. examined only RRD patients and found no significant difference in CEC parameters between early postoperative and third-month measurements in eyes treated with either silicone oil or gas tamponade<sup>[26]</sup>. Nonetheless, their study included only 20 patients, which may reduce the statistical power and limit the generalizability of the results. Most importantly, a key difference in their protocols is the absence of phaco, which further limits direct comparison. Anterior segment surgeries are known to have a greater impact on corneal endothelial health compared to PPV alone<sup>[15, 20]</sup>.

On the other hand, Koushan et al. compared combined phaco-PPV (13.9% ECD loss) to PPV alone (9.0% ECD loss) and found no statistically significant difference between the two groups<sup>[8]</sup>. However, they used gas tamponade exclusively in RRD and macular hole cases, and no detailed information was provided regarding other tamponade choices or the full range of surgical indications. Goezinne et al. also reported that silicone oil in the anterior chamber was associated with a greater ECD loss (32%), compared to 13% in eyes without silicon oil in the AC. In contrast, our study excluded patients with silicone oil in the anterior chamber to eliminate any additional impact on CEC beyond that caused by the surgical procedure and tamponade type. This highlights a key methodological difference between the two studies.

In the current study, no correlation was found between operation time and CEC parameters in either group. In the literature, some studies highlight a significant correlation between prolonged phaco time and endothelial cell loss in cataract surgery, but this association does not appear as prominently for PPV<sup>[15, 27]</sup>. This variability suggests that further large-scale studies examining cumulative surgical durations are needed to achieve a more definitive understanding of how combined surgical procedures impact CEC morphology and overall corneal health.

Similar to previous literature, our study found a non-significant decrease in CCT postoperatively in both surgical groups<sup>[5]</sup>. There are also some reports in the literature sug-

gesting an increase in CCT.<sup>[9]</sup> Although CCT has been proposed as an indirect marker of endothelial cell function, recent studies suggest that specular microscopy parameters are more reliable for assessing corneal health following intraocular surgery. For instance, Watanabe et al. and Calik et al. reported that while CCT tends to increase initially after vitreoretinal procedures, a slight, non-significant decrease is often observed in the later postoperative period<sup>[28, 29]</sup>. These chronic-phase changes may reflect adaptive mechanisms of the corneal endothelium over time. Despite measurable endothelial cell loss, the remaining endothelial cells can maintain corneal transparency by enlarging and changing shape to cover denuded areas, thereby helping to prevent corneal decompensation.

A large-scale study by Feng et al. evaluated corneal endothelial cell loss following pars plana vitrectomy with silicone oil tamponade and reported significantly greater endothelial loss in tractional retinal detachment compared to rhegmatogenous retinal detachment<sup>[30]</sup>. The authors identified combined anterior–posterior segment surgery, advanced age, and the absence of a natural lens as major risk factors for endothelial damage, while transient postoperative intraocular pressure elevations below 40 mmHg were not independently associated with endothelial cell loss. The greater endothelial vulnerability observed in tractional retinal detachment may be explained, at least in part, by the underlying diabetic status of these patients and the associated chronic inflammatory milieu. Diabetes-related microvascular dysfunction and elevated intraocular inflammatory cytokines have been shown to increase endothelial susceptibility to surgical stress, potentially accounting for the more pronounced endothelial loss observed in tractional retinal detachment compared with rhegmatogenous retinal detachment. In contrast, the present study focused on a homogeneous cohort of rhegmatogenous retinal detachment cases undergoing combined phacoemulsification and pars plana vitrectomy, allowing a direct comparison of tamponade-related effects under similar surgical conditions. Consistent with the findings of Feng et al., our analysis demonstrated no significant association between changes in intraocular pressure and percentage endothelial cell loss (Spearman  $\rho = 0.058$ ,  $p = 0.65$ ), suggesting that transient postoperative intraocular pressure fluctuations below clinically critical thresholds are unlikely to be a primary driver of endothelial damage. These findings further support the

hypothesis that tamponade-related inflammatory and mechanical factors, rather than short-term intraocular pressure changes, may play a more prominent role in postoperative corneal endothelial cell loss.

Recent comparative studies have addressed the influence of tamponade agents on endothelial health. Zhou et al. reported a higher ECD loss with silicone oil (16.38%) versus C3F8 gas (9.39%) at one year; however, their analysis included different surgical indications, and silicone was preferentially used in more complex eyes, including those with PVR<sup>[31]</sup>. In contrast, our study excluded PVR-C cases and included only pseudophakic eyes, helping reduce confounding by lens status and disease severity. Rani et al. similarly noted greater endothelial loss in the silicone group, yet their study was limited by unequal group sizes ( $n=4$  for C3F8 vs.  $n=11$  for silicone) and a bias toward shorter surgeries and simpler macular hole cases in the gas group<sup>[32]</sup>. Jiang et al. further demonstrated that prolonged silicone tamponade leads to sustained intraocular inflammation, characterized by elevated IL-8 and TNF- $\alpha$  levels, which are known to drive neutrophil recruitment, cytokine amplification, and endothelial stress<sup>[33]</sup>. These cytokines enhance leukocyte adhesion and prolong neutrophil survival, thereby amplifying tissue-level inflammation. Importantly, Jiang's findings showed that a shorter tamponade duration significantly mitigated this inflammatory cascade and reduced endothelial loss, emphasizing the time-dependent nature of silicone-related damage. While our silicone duration was longer than theirs, none of our patients showed emulsification at 3 months, possibly explaining the moderate endothelial loss. Shimmura-Tomita also emphasized that prolonged oil retention is a key risk factor, whereas the presence of oil droplets in the anterior chamber alone did not predict higher loss<sup>[34]</sup>. Our finding that endothelial decline in the silicone group remained relatively limited may be partly due to the presence of a pseudophakic barrier, minimizing oil-cornea contact. This aligns with the foundational observations of Gurelik et al., who noted that anterior migration of silicone not its presence in the posterior segment is the primary driver of accelerated endothelial damage<sup>[35]</sup>.

The limitations of this study include the relatively small patient group and the short follow-up period. However, as clearly demonstrated in the literature, no significant changes in specular morphology are observed beyond the third

postoperative month[4]. Another limitation of this study is that intraoperative phacoemulsification parameters, such as effective phaco time and cumulative ultrasound energy, were not directly measured, although cataract severity was comparable between the tamponade groups. To the best of our knowledge, there is no existing prospective study evaluating the effect of tamponade agents in combined phaco-PPV on corneal endothelial morphology in RRD. Importantly, all surgeries were performed by the same surgeon, and the study focused on a single surgical indication group, which we consider key strengths of our work.

In this prospective study evaluating endothelial changes after combined Phaco-PPV for rhegmatogenous retinal detachment, both silicone oil and C3F8 gas tamponades were associated with a significant reduction in endothelial cell density at 3 months postoperatively. However, endothelial cell loss was more pronounced in eyes receiving C3F8 gas tamponade, whereas changes in HEX and CV were comparable between the two tamponade groups. Although tamponade selection was indication-based and the observational design warrants cautious interpretation, the present findings suggest that silicone oil tamponade was associated with relatively less endothelial cell loss in this cohort. Given that patients undergoing vitreoretinal surgery may require additional intraocular procedures during follow-up, preservation of corneal endothelial integrity remains clinically relevant. Further prospective, controlled studies are needed to confirm these observations and to better elucidate the impact of tamponade choice on long-term corneal endothelial health in eyes with coexisting cataract.

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### Conflicts of Interest

The authors declare that they have no conflict of interest.

### Ethical Approval

The study was approved by the Clinical Research Ethics Committee (IRB Approval No: E-96317027-514.10-

231669444) and conducted in accordance with the principles of the Declaration of Helsinki.

### Informed Consent

Written informed consent was obtained from all participants.

### Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

### Authors' role in this study was as follows:

Design of the study : Yusuf Cem Yilmaz, Serife Ciloglu Hayat, Merve Uran, Sadik Altan Ozal

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