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The role of surgical experience in posterior capsule rupture in eyes with prior intravitreal injections

 **Figen Bezci Aygun,¹**  **Hilal Toprak Tellioglu,²**  **Sibel Kadayifcilar¹**

¹Department of Ophthalmology, Hacettepe University Faculty of Medicine, Ankara, Türkiye

²Department of Ophthalmology, Elbistan State Hospital, Kahramanmaraş, Türkiye

Abstract

Purpose: The aim of the study is to explore intraoperative challenges and complications during cataract surgery in patients with an intravitreal injection (IVI) history.

Methods: This retrospective study included 119 eyes of patients who underwent cataract surgery following a history of IVIs at a tertiary center between January 2015 and October 2022. Data on demographics, number and type of injections, surgical technique, and intraoperative challenges and complications were collected. Surgeries were performed by either experienced surgeons or ophthalmology residents, and outcomes were compared accordingly.

Results: Experienced surgeons exhibited lower complication rates compared to resident surgeons (odds ratio [OR], 5.68 $p=0.06$), highlighting the role of surgical expertise in minimizing complications during cataract surgery in patients with an IVI history. A moderate correlation was observed between the total number of prior IVIs and the complications during cataract surgery, suggesting a cumulative effect with multiple injections (> 10 IVIs, OR, 1.81). Dexamethasone injections were associated with higher rate of intraoperative difficulties (OR, 1.29, $p=0.033$). Posterior capsule rupture occurred in 9.2% of cases, with a higher incidence in cases performed by resident surgeons.

Conclusion: Cataract surgery in patients with a history of IVIs may present specific challenges, emphasizing the importance of surgical experience and individualized preoperative assessment. This study provides valuable insights for surgical decision-making and patient management in this specific population. Larger cohorts and further research are recommended to validate and extend these observations.

Keywords: Cataract surgery; complication; intravitreal injection; posterior capsule rupture; resident surgeon.

Cataract and retinal diseases are known to be co-existent conditions in ophthalmology, and their incidence tends to rise with increasing age.^[1] Age-related cataract, in particular, is considered a major cause of visual impairment worldwide. Retinal diseases such as age-related macular degeneration (AMD) and diabetic retinopathy (DRP) also contribute significantly to visual morbidity and pose

significant challenges in ophthalmic practice.^[2] Given the frequency of these conditions, intravitreal injection (IVI) and cataract surgery have emerged as commonly preferred treatment modalities. The rate of cataract extraction, which is the most frequently performed surgical procedure globally, has shown a significant increase among medicare beneficiaries, rising from 13.4 to 61.8 individuals per 1000



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Correspondence: Figen Bezci Aygun, M.D. Department of Ophthalmology, Hacettepe University Faculty of Medicine, Ankara, Türkiye

E-mail: bezcifigen@gmail.com

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person-years between 1980 and 2003.^[3,4] In addition, approximately 3.7 million cataract surgeries, including both phacoemulsification (phaco) and manual planned extracapsular cataract extraction (PECCE), were performed in the United States in 2015.^[5] While cataract surgery remains the most frequently performed surgical procedure, recent studies suggest that IVI is gaining momentum and surpassing it in certain aspects.^[6]

While cataract surgery is generally considered a safe procedure with low complication rates, there are potential intraoperative challenges, including posterior capsule rupture (PCR), vitreous loss, and lens fragment dislocation into the vitreous cavity.^[7] The occurrence of PCR during surgery can lead to an increased risk of post-operative endophthalmitis^[8] and retinal detachment.^[9] The development of complications during cataract surgery is influenced by various individual factors, including age, gender, and the type of cataract. In addition, a history of previous IVI has been identified as a significant risk factor.^[10] Studies have reported that each previous intravitreal injection increases the risk of PCR development by 1.4 times.^[11] In addition, the choice of injector tip length, its path, and distance from limbus in phakic patients during IVIs can impact the likelihood of lens trauma and complications.^[12,13] Furthermore, the surgeon's experience and skill in performing both IVIs and cataract surgery are significant factors in minimizing complications and achieving favorable outcomes.^[14]

The study aims to examine the potential associations between variables related to previous IVIs and the occurrence of intraoperative challenges and complications in the context of cataract surgery. In addition, this study aims to evaluate whether surgeon experience plays a role in complication rates by comparing outcomes between experienced surgeons and ophthalmology residents.

Materials and Methods

This retrospective, single-center, cohort study aimed to collect data on patients who underwent cataract surgery after IVIs at a single tertiary clinic between January 2015 and October 2022. The study adhered to the principles of the Declaration of Helsinki and was conducted with institutional review board approval from the Non-Invasive Human Research Ethics Committee (GO 22/1080). The study focused on collecting demographic data, pre-operative characteristics, and intraoperative details.

The medical records of patients who underwent cataract surgery and had previous IVI were retrospectively

reviewed. Age and gender of each patient were collected. Indications for injection were noted as AMD, diabetic macular edema (DME), retinal vein occlusion (RVO), uveitic macular edema (UME), and Coats disease. The condition of the posterior capsule (defect or intact) and specific triangular posterior subcapsular cataract (PSC) localization compatible with previous injection site (suspicious posterior capsule defect [PCD]) were noted during slit-lamp examination before cataract surgery. In addition, the number of IVIs and the type of injection (anti-vascular endothelial growth factor [VEGF] agents or dexamethasone [DEX] implant) were recorded. In this study, informed consent was not required as it is a retrospective analysis. IVIs were performed by a vitreoretinal specialist or by residents under supervision using standard techniques. This included proparacaine for analgesia, betadine for antisepsis, and injection placement 3.5–4 mm behind the limbus based on the status of the lens. Cataract surgeons were graded based on their experience level. Specialists with more than 10 years of experience in cataract surgery were classified as "experienced surgeons," while last-year residents (3–5 years experience) were categorized "resident surgeons."

According to the definition used in the Royal College of Ophthalmologists' National Ophthalmology Database study^[15] on cataract surgery, PCR or vitreous loss was identified as unintended communication with the posterior segment. This definition covered a range of events, including intraoperative PCR with or without vitreous loss, zonular rupture with associated vitreous loss, dislodgment of nuclear or epinuclear fragments into the vitreous, intraocular lens (IOL) displacement into the vitreous, vitreous involvement observed at the conclusion of the surgery, or instances of vitreous loss not specifically classified otherwise.

In cases of PCR during phacoemulsification, surgical decisions were made based on the size and location of the defect. When the defect was small, well-circumscribed, and adequate capsular support remained, the IOL was placed in the capsular bag. If the defect was larger but the anterior capsule was intact, a three-piece monoblock IOL was implanted in the ciliary sulcus. In PECCE cases with PCR, a rigid PMMA lens was positioned in the sulcus. For eyes lacking sufficient capsular support, secondary IOL implantation – either anterior chamber or scleral-fixated – was deferred to same second session, with the choice guided by patient age and corneal endothelial status.

Surgical technique (phaco or PECCE), intraoperative

difficulties encountered (inability to separate epinucleus from nucleus, difficulty in nucleus fragmentation), PCR with or without vitreous loss during cataract surgery, and loss of nuclear or epi-nuclear fragments into the vitreous were collected from the dataset of the system. Patients with a history of injection at another center, a history of trauma, lack of follow-up data, or unclear indication for injection were excluded from the study.

Statistical Analysis

The statistical analysis was performed using IBM SPSS Statistics for Windows Version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean±standard deviation (range), while categorical variables were reported as frequencies and percentages. To compare groups, the independent samples t-test and Mann–Whitney U test were used for normally and non-normally distributed parameters, respectively. We used logistic regression to calculate the odds ratio (OR) for identifying risk factors. Correlation analysis was conducted using the Eta (η) correlation ratio.

Results

Demographic Characteristics

A total of 102 patients, corresponding 119 eyes, were included in the study, comprising 58 males (48.7%) and 61 females (51.3%). The average age of the participants was 68.1±13.2 years. Among these patients, 65 eyes underwent Phaco, while 54 eyes underwent PECCE surgery (Table 1). A total of 55 eyes with AMD, 40 patients with DME, 14 patients with retinal RVO, 7 patients with UME, and 3 patients with Coats' disease were included. No significant difference was found between the diagnoses and types of surgeries ($p=0.272$). The surgeries were performed by experienced surgeons in 97 cases (81.5%), while the remaining 22 cases (18.5%) were performed by resident surgeons. There was no significant difference in the distribution of surgical

Table 1. Case demographics

Eyes, n	119
Age, years	68.1±13.2
Male, %	48.7 (58)
Female, %	51.3 (61)
Phacoemulsification, %	54.5 (65)
PECCE, %	45.5 (54)
Experienced surgeons' surgery, %	81.5 (97)
Resident surgeons' surgery, %	18.5 (22)

PECCE: Planned extracapsular cataract extraction.

types and the experience level of the operating surgeons ($p=1.00$). The distribution was as follows: 54.5% Phaco and 45.5% PECCE for both groups. Among patients with RVO compared to other diagnoses, a significantly higher risk of encountering intraoperative challenges was identified (OR, 7.22, 95% CI: 1.0–1.6, $p=0.042$). No significant relationship was found between the diagnosis and the type of complications ($p=0.091$).

Pre-operative Findings

PCDs were identified in six eyes. Among all cases, five eyes exhibited a triangular-shaped PSC formation in the upper temporal or temporal quadrant, corresponding to the previous injection site during the pre-operative examination. Due to the uncertain nature of the defects associated with the observed PSC formation, these eyes were managed with the suspicion of PCDSs. Of the patients with identified PCD, five underwent PECCE (experienced physicians have more expertise in PECCE surgeries), and one underwent Phaco surgery, and in the cases with PCDS, all patients underwent Phaco, performed by experienced surgeons. Notably, no additional intraoperative difficulties or complications (anterior vitrectomy), enlarging the defect during surgery, were encountered, and IOLs were placed in the capsular bag. Furthermore, intraoperatively, fibrotic characteristics were observed at the margins of the capsular defect. In patients with PCDS, it was observed that the posterior capsule was intact, with only a localized PSC area. Patients with pre-operative capsular defects and suspicion were not included in the assessment of intraoperatively developed complications.

In cases where PCR occurred, 3 instances were observed during Phaco, and 8 cases occurred during PECCE. While PCRs were noted during the phacoemulsification step in Phaco, the defects in PECCE were identified after nucleus extraction. The decision to perform PECCE was made specifically for advanced cataracts and patients with PCD (except one case). There was no identified relationship between the pre-operative findings and the types of previous agents administered (bevacizumab, $p=1.00$; ranibizumab, $p=0.417$; aflibercept, $p=0.454$; DEX, $p=1.00$).

Intraoperative Challenges

During the Phaco operation, no intraoperative difficulties were encountered in 54 eyes (83.0%), while 5 eyes (7.6%) experienced challenges in nucleus fragmentation, and 6 eyes (9.2%) faced difficulties in hydrodissection for separating epinucleus from the nucleus. Although not

statistically significant, it was found that the intraoperative challenges increased by 2.85 times in cases performed by the resident surgeons ($p=0.121$) (Table 2). When examining injected agents, there was no association between the administration of anti-VEGF injections (bevacizumab, ranibizumab, aflibercept) and intraoperative difficulties ($p=0.629$, $p=0.872$, $p=0.920$, respectively). However, it was observed that difficulties were encountered in 63.6% of eyes who received DEX implant ($p=0.012$). Having received DEX implant at least once increased the intraoperative difficulties risk by 1.29 times ($p=0.033$). In patients who underwent DEX implantation before Phaco and faced intraoperative challenges, 57.1% reported issues in separating the epinucleus from the nucleus, and 42.8% encountered complications during nucleus fragmentation.

Posterior Capsule Rupture

Posterior capsule rupture was observed during the operation in 11 (9.2%) eyes without any pre-operative findings suggestive of PCD, one (0.8 %) of these cases resulting in the dislocation of a lens fragment into the vitreous. No noticeable zonular weakness was observed in any of the patients. Among patients with detected PCR, 54.5% were operated on by residents, and there was a significant difference between PCR and experience of the surgeon (OR, 5.68, 95% confidence interval [CI]: 1.6–19.8, $p=0.006$). No significant relationship was identified

between the occurrence of PCR and anti-VEGF injections (bevacizumab, ranibizumab, and aflibercept) ($p=0.107$, $p=0.326$, $p=0.850$) or DEX implants ($p=0.648$). There was no relation between PCR risk and age or gender ($p=0.801$, $p=0.606$, respectively). While the risk increased by 2.65 times with advanced cataract level and 1.81 times with a history of more than 10 injections, these associations were not found to be statistically significant ($p=0.126$, $p=0.782$, respectively) (Table 3).

Injection History and Intraoperative Impact

The mean number of anti-VEGF injections was 10.1 ± 9.7 (range: 1–42), and the mean number of DEX implants was 1.06 ± 2.0 (range: 1–9) per eye before cataract surgery. A moderate correlation was observed between the total number of IVIs administered and the total number of pre and intraoperative surgical difficulties and complications ($\eta=0.406$). A history of more than 10 injections did not statistically significant impact intraoperative challenges (OR, 0.96, 95% CI: 0.2–3.3, $p=0.957$) or the risk of PCR (OR, 1.81, 95% CI: 0.3–3.9, $p=0.782$).

As a retrospective study, follow-up duration varied across patients. However, the minimum follow-up period was 6 months. No cases of post-operative endophthalmitis or IOL dislocation were observed during the available follow-up period.

Table 2. Determinants of intraoperative challenges during cataract surgery in patients with a history of previous intravitreal injections (univariate logistic regression)

	OR	95 % CI	P
Age	0.967	0.928–1.007	0.105
Sex			
Female	(Reference)		
Male	1.750	0.484–6.326	0.393
Indication for IV injection			
AMD	(Reference)		
Diabetes	3.786	0.695–20.609	0.124
RVO	7.227	1.077–48.485	0.042
Uveitic	3.786	0.303–47.360	0.302
Surgeon type			
Experienced	(Reference)		
Resident	2.857	0.757–10.788	0.121
Injection type			
Anti-VEGF	0.962	0.887–1.043	0.348
Dexamethasone	1.298	1.021–1.650	0.033
No. of prior intravitreal injection			
>5 injections	0.434	0.124–1.518	0.191
>10 injections	0.967	0.278–3.359	0.957

OR: Odds ratio; CI: Confidence interval; AMD: Age-related macular degeneration; RVO: Retinal vein occlusion; VEGF: Vascular endothelial growth factor.

Table 3. Determinants of posterior capsule rupture during cataract surgery in patients with a history of previous intravitreal injections (univariate logistic regression)

		OR	95 % CI	P
Age		1.006	0.960–1.054	0.801
Sex				
Female	(Reference)			
Male		1.374	0.410–4.601	0.606
Indication for IV injection				
AMD	(Reference)			
Diabetes		0.762	0.207–2.802	0.682
RVO		0.527	0.059–4.468	0.566
Surgeon type				
Experienced	(Reference)			
Resident		5.68	1.629–19.854	0.006
Injection type				
Anti-VEGF		0.997	0.934–1.064	0.919
Dexamethasone		0.703	0.400–1.235	0.220
No. of prior intravitreal injection				
>5 injections		0.529	0.159–1.754	0.298
>10 injections		1.814	0.359–3.906	0.782
Advanced cataract		2.652	0.752–9.348	0.129

OR: Odds ratio; CI: Confidence interval; AMD: Age-related macular degeneration; RVO: Retinal vein occlusion; VEGF: Vascular endothelial growth factor.

Discussion

The results of this retrospective study highlight the challenges and potential complications encountered during cataract surgery in patients with a history of IVIs. Experienced surgeons demonstrated lower complication rates compared to resident surgeons, emphasizing the importance of surgical expertise in managing these cases. In addition, there was a moderate correlation between the number of IVIs administered and the occurrence of complications during cataract surgery, suggesting that the cumulative effect of multiple injections may increase the likelihood of encountering difficulties. Moreover, this study suggests that the administration of DEX injections may result in notable changes in the structure of the lens, potentially impeding the surgical procedure.

A comprehensive study, reported in the United Kingdom through a collaborative effort led by Lee et al.,^[14] incorporated 10 years of data from 20 centers to investigate factors contributing to the increased risk of PCR during phacoemulsification surgery. In this study encompassing 65,836 cataract surgeries, a subset of 1,935 cases with a history of prior IVIs was analyzed. The factors identified as risk factors for PCR during phacoemulsification surgery included patient age, advanced cataract, surgeon experience, and the number of IVIs administered. The study included various IVIs, including different anti-VEGF and

corticosteroid injections, applied for different diagnoses such as AMD and DRP, similar to our study. In patients with a history of prior injections, the overall rate of PCR was reported as 2.22%. When considering all surgical methods, the overall rate of PCR in our study was 9.24%, only involving individuals undergoing Phaco; this rate was found to be 4.61% (3/65). However, in cases of advanced cataracts treated with PECCE, the incidence of PCR was notably higher, reaching 14.8% (8/119). While advanced cataract has been identified as an increased risk factor for PCR,^[14] the preference for the PECCE method in this study prevents us from conclusively determining whether this elevated risk is solely related to the previous injection history, surgical technique, or if it is associated with the degree of cataract severity. The risk of PCR appeared to increase by 2.65 times in patients with advanced cataracts, although a statistically significant difference could not be identified ($p=0.126$). Our Phaco-related PCR rate (4.61%) is quite comparable with the findings of Nagar et al. (6.67%), supporting the consistency of our results with existing literature. The higher overall PCR rate in our study can be partially attributed to the inclusion of PECCE cases, which typically involve more advanced cataracts and greater surgical complexity. Therefore, differences in surgical technique and cataract severity may explain the variation in reported PCR rates.^[16] In patients who received 10 or more injections, this study did not observe a statistically

significant increase in intraoperative challenges (OR: 0.967, 95% CI: 0.2–3.3, $p=0.957$), although there might be a minimal, statistically non-significant increase in PCR risk (OR: 1.81, 95% CI: 0.3–3.9, $p=0.782$). However, the risk of PCR was reported to increase by 2.59^[14] and 2.36^[16] times in the studies mentioned above. The limited number of patients in the study may be the main reason for the lack of a significant difference in the observed trend. Similar to our study (102 patients), another investigation with a limited number of patients (197 patients) found 3% prevalence of PCR in individuals with a history of intravitreal injections. Notably, patients with PCR were observed to have a higher frequency of prior injections compared to the control group, although this difference did not achieve statistical significance.^[17] These collectively suggest that while prior injection number may influence complication risk, its significance might only emerge in larger datasets. Our findings are therefore directionally consistent with larger studies but limited by sample size.

Another study, involving a broad participant base, was reported from the United States.^[18] This study specifically focused on surgical and post-operative complications in patients with a history of prior anti-VEGF IVIs undergoing cataract surgery. The removal of residual lens fragments (RLF) after the initial surgery within 28 days was associated with intraoperative complications and was identified in 0.43% of individuals with a prior history of injections, who had a 126% higher risk of requiring such procedures (Hazard ratio [HR], 2.26). In addition, on the contrary, in our study, they found a significant association between male gender and age with RLF removal (HR 1.38, 1.03).^[18] However, the specific type of cataract surgery performed in this study and the diagnoses of patients were not specified, and the reasons for the persistence of RLF remain unclear. Furthermore, it should be noted that not every intraoperative complication necessarily requires a second surgery, and the reported rate may be underestimated compared to the actual occurrence. This discrepancy might be a reason for the apparent contradiction with the higher rates reported in this study.

Although the exact cause of capsular damage is not yet understood, it is hypothesized that such damage could result from either inadvertent posterior microtrauma caused by the injection or unspecified biochemical damage.^[19] The development of a subcapsular cataract, shaped like a triangle and localized to the injection site as observed in this study, might be attributed to these factors. The trauma effect on the capsule may have been induced by the jet stream during the drug administration toward

the vitreous. Furthermore, while defects were detected in some patients during pre-operative examination, and complications developed despite the absence of such findings in others, microtraumas or unnoticed zonular weaknesses could potentially account for this discrepancy. A more thorough pre-operative evaluation may provide valuable guidance.

In the analysis comparing residents at the senior level with experienced cataract surgeons (>10 years), experience level was identified as a significant criterion for PCR (OR, 5.68, 95% CI: 1.6–19.8, $p=0.006$). Despite the preference for experienced surgeons in cases with preoperatively identified risk factors (PCD or PCDS) and the absence of PCR in these cases, this significant positive association emphasizes the importance of surgical experience. A similar study in the literature, involving surgeons with approximately the same level of experience, also observed an increased risk (OR, 1.79)^[14] and the other study reported that there was an increasing trend in the risk of PCR among inexperienced surgeons but statistical significance was not reached.^[19] Cataract surgery in patients without a history of IVIs reported a complication rate of 13.7% in previous studies conducted by residents.^[20] However, in this study, the rate was concluded at 27.2%, indicating that the involvement of resident surgeons in cases with an IVI history poses a higher risk. Our data not only reinforce existing findings regarding the learning curve in cataract surgery but also highlight that prior IVI history further compounds this risk in less experienced hands. This suggests that resident involvement in such cases should be accompanied by greater caution, case selection, and supervision. In addition, in the risk model conducted by af Segerstad,^[10] surgeons performing fewer than 600 cataract surgeries were reported to have a 2.77 times increased risk.

In cases included in the study, univariate regression analysis demonstrated an increase in intraoperative challenges in the group that underwent DEX implant and was diagnosed with RVO. While the development of cataracts after the use of DEX is known,^[21] there is no consensus on the specific mechanism involved.^[22] The effects of glucocorticoid receptor activation in cells are the suppression of proliferation, differentiation, and decreased susceptibility to apoptosis, and also may indirectly affect the growth factors that regulate lens development and maintain lens homeostasis.^[22] The difficulties encountered during hydrodissection and nucleus fragmentation stages suggest that structural alterations in the lens may result in a more adhesive and compact state. The correlation

with the diagnosis of RVO is attributed to the observation that nearly all these patients (13/14) have undergone DEX implant at least once. Unlike many studies focusing solely on PCR, our results provide insight into intraoperative handling difficulties possibly related to DEX-associated lens changes. This adds a novel dimension to the understanding of DEX-related risks and may inform surgical planning.

Study Limitations

The study has several limitations, the most significant being the small size of the included patient population. This limitation poses challenges, especially in subgroup analyses. In addition, the use of two different surgical methods reduced the analyzed sample size and limited the attainment of statistically significant data. The study's long duration made it difficult to access complete and clear data.

Conclusion

This retrospective study sheds light on the challenges and potential complications encountered during cataract surgery in patients with a history of IVIs. Notably, experienced surgeons demonstrated lower complication rates compared to resident surgeons, emphasizing the crucial role of surgical expertise in managing these cases. The study identified a moderate correlation between the number of IVIs administered and the occurrence of complications during cataract surgery, suggesting that the cumulative effect of multiple injections may increase the likelihood of encountering difficulties. Furthermore, the study indicates that the use of DEX injections may lead to alterations in the lens structure, potentially hindering certain steps of the surgical procedure. Patients who received DEX injections were more likely to experience intraoperative challenges, particularly during the stages of separating epinucleus from nucleus and nucleus fragmentation.

In summary, cataract surgery in patients with prior IVIs poses unique challenges, and surgical decision-making should consider the patient's IVI history, the surgeon's experience, and potential complications associated with specific injection types.

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