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A Large-Scale Cohort Analysis of Topical Prostaglandin Analog Use and Pseudophakic Cystoid Macular Edema Following Cataract Surgery

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Purpose: To evaluate whether perioperative topical prostaglandin analog (PGA) use alters the risk of pseudophakic cystoid macular edema (PCME) following routine cataract surgery.

Design: A retrospective cohort study.

Participants: Patients undergoing cataract surgery, without pre-existing high-risk factors for PCME (such as prior cystoid macular edema, uveitis, or retinal vascular diseases), categorized into three perioperative PGA exposure groups: (1) PGA prescribed within 3 months prior to surgery ("PGA Before"), (2) PGA prescribed within 1 month after surgery ("PGA After"), and (3) PGA prescribed both before and after surgery ("PGA Before & After"). The control group included patients with no PGA prescriptions any time before and 3 months after surgery.

Methods: The data were collected from the TriNetX United States Collaborative Network. Propensity score matching was conducted to balance demographics, cataract type and surgical complexity, glaucoma type and severity, comorbidities, and concomitant topical and long-term systemic anti-inflammatory medication use between groups. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated to assess the 3-month risk of PCME following cataract surgery.

Main Outcome Measures: Three-month incidence of diagnostically significant PCME following cataract surgery.

Results: After matching, 9457 patients were included in the "PGA Before" group and its control, 1993 patients in the "PGA After" group and its control, and 2367 patients in the "PGA Before & After" group and its control. No significant difference in the risk of PCME was observed among those prescribed PGA prior to surgery (HR 1.08, 95% CI: 0.89–1.31), after surgery (HR 1.08, 95% CI: 0.68–1.70), or both before and after surgery (HR 0.86, 95% CI: 0.61–1.23), compared to matched controls.

Conclusions: Perioperative PGA use before or after cataract surgery was not associated with an increased risk of PCME. These findings provide evidence that PGA use in the perioperative period may not significantly impact the risk of PCME within 3 months postsurgery.

Financial Disclosure(s): Proprietary or commercial disclosure may be found in the Footnotes and Disclosures at the end of this article. *Ophthalmology Glaucoma 2026;9:295-301 © 2025 by the American Academy of Ophthalmology*

Supplemental material available at www.ophthalmologyglaucoma.org.

Pseudophakic cystoid macular edema (PCME) is a condition characterized by the accumulation of fluid in the macula, resulting in cystic spaces within the retina.[1] It is a postoperative complication of cataract surgery, primarily caused by postoperative inflammation.[1,2] Clinically significant PCME is commonly defined by a combination of anatomical changes, such as a 40% or greater increase in foveal thickness, and functional impairments, such as reduced visual acuity or macular sensitivity.[3–5] The American Academy of Ophthalmology estimates its incidence at 1% to 3% following routine, uncomplicated cataract surgery.[6–9] Pseudophakic cystoid macular edema can range from mild, subclinical cases that resolve spontaneously to severe forms that may lead to persistently impaired visual acuity. Patients with PCME generally have worse visual outcomes compared to those without, with a greater likelihood of achieving a best-recorded visual acuity worse than 20/40 at 12 months postoperatively.[10] Persistent or refractory cases, though rare (0.02%), can lead to permanent visual impairment.[6]

Ophthalmic risk factors for PCME[6] include a history of PCME in the fellow eye, uveitis, diabetic retinopathy, retinal vein occlusion, epiretinal membrane, prior vitreoretinal surgery, and retinitis pigmentosa.[6] Demographic risk factors, such as male gender and older age, also contribute.[6] Additionally, systemic conditions

https://doi.org/10.1016/j.ogla.2025.12.010
ISSN 2589-4196/26

like diabetes mellitus, hypertension, and inflammatory diseases have been implicated.[6,11] By identifying at-risk populations and modifiable risk factors, earlier diagnosis and mitigation of perioperative risk factors may be possible to optimize visual outcomes.

A theoretical association between prostaglandin analogs (PGAs) and PCME has been proposed due to the ability of prostaglandins to increase vascular permeability, potentially leading to the breakdown of the blood−retinal barrier and fluid accumulation in the macula.[12,13] Some studies suggest that PGA use may increase the risk of PCME due to this mechanism, while others report no significant association, particularly in uncomplicated cases.[14,15] The lack of consensus in existing literature highlights the need for further investigation into the association between perioperative PGA use and PCME pathogenesis.

In this study, we aim to clarify the association between PGA use and the risk of PCME using the TriNetX database. By analyzing a large cohort and employing robust propensity score matching (PSM), we seek to contribute to the existing body of evidence regarding the potential impact of PGAs on PCME risk.

Methods

The data used in this study were collected on August 20, 2025, from the TriNetX United States Collaborative Network, which provided access to electronic medical records (diagnoses, procedures, medications, laboratory values, and genomic information) from approximately 120 million patients from 69 health care organizations across the country. Diagnoses are represented in TriNetX by the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) code set, which is a modification of the World Health Organization ICD-10 standard. This retrospective study is exempt from informed consent. The data reviewed are a secondary analysis of existing data, do not involve intervention or interaction with human subjects, and are deidentified per the deidentification standard defined in Section §164.514(a) of the Health Insurance Portability and Accountability Act Privacy Rule. The process of data deidentification was confirmed through a formal determination by a qualified expert, as outlined in Section §164.514(b) (1) of the Health Insurance Portability and Accountability Act Privacy Rule, and a waiver was obtained from the Western Institutional Review Board. This study was conducted in compliance with the principles of the Declaration of Helsinki.

Cohorts

We conducted a retrospective cohort study to examine the risk of PCME following cataract surgery. Patients were included if they underwent cataract extraction and intraocular lens implantation, identified by Current Procedural Terminology codes 66984 and 66982. Patients were excluded if they had a history of infantile or juvenile cataract, traumatic cataract, complicated cataract, or drug-induced cataract. Additional exclusion criteria included ophthalmic diabetic complications, such as type 1 or type 2 diabetes with nonproliferative or proliferative diabetic retinopathy or diabetic macular edema. Patients with a history of prior cystoid macular edema (CME), eye surgeries (including yttrium aluminum garnet laser capsulotomy and cyclophotocoagulation), eye injuries, retinal vascular occlusions, hypertensive retinopathy, retinal edema, pigmentary retinal dystrophy, macular degeneration, epiretinal membrane, uveitis, or microphthalmos were also excluded. The study group included all patients who had a prescription for PGAs within 3 months prior to cataract surgery. The control group consisted of patients who were never prescribed PGAs before or up to 3 months after cataract surgery. Detailed coding data are provided in Table S1 (available at www.ophthalmologyglaucoma.org).

Sensitivity Analysis

In some cases, ophthalmologists may recommend discontinuing or holding PGAs perioperatively without formally discontinuing the prescription to mitigate perceived PCME risks. To account for database-related limitations in accounting for this, we performed 2 sensitivity analyses. The first sensitivity analysis evaluated PCME risk in patients who had a PGA prescription within 1 month after cataract surgery. The second sensitivity analysis evaluated PCME risk in patients who had a prescription for PGAs both within 3 months prior to cataract surgery and again within 1 month after cataract surgery.

Covariates

We utilized the TriNetX integrated analytics platform to perform 1:1 PSM to ensure balance in baseline characteristics and comorbidities between all study and control groups. Matching was conducted using a nearest-neighbor greedy matching algorithm with a caliper of 0.1 standard deviations. Patients were matched based on comorbid conditions including hypertension, hyperlipidemia, type 2 diabetes mellitus, chronic kidney disease, and a detailed assessment of glaucoma type and severity (including unspecified, mild, moderate, severe, or indeterminate primary open-angle glaucoma, ocular hypertension, normal tension glaucoma, pigmentary glaucoma, and pseudoexfoliation glaucoma). To account for surgical complexity and cataract morphology, we also matched on cataract type (age-related incipient, including cortical, anterior and posterior subcapsular polar, nuclear, Morgagnian, or combined forms) and complex cataract surgery (Current Procedural Terminology 66982). Finally, to account for other medications that influence PCME risk, we matched for the use of topical ophthalmic anti-inflammatories (nonsteroidal anti-inflammatory drugs and corticosteroids) and the long-term use of systemic anti-inflammatories (nonsteroidal anti-inflammatory drugs and corticosteroids).

Statistical Analyses

For the primary outcome, we evaluated the risk of PCME, identified by ICD-10-CM codes H35.35 and H59, within 3 months of cataract surgery. For all analyses, each exposure group was independently matched to its own control group using PSM. The control patients were those who were never prescribed PGAs before or up to 3 months after cataract surgery. Time-to-event analyses were conducted using Kaplan−Meier survival analysis to calculate hazard ratios (HRs) with 95% confidence intervals (CIs), which were generated using univariate analyses after PSM. Baseline characteristics were summarized as averages with standard deviations for continuous variables and as counts with proportions for categorical variables. The outcomes of the PSM were evaluated at each time point to ensure covariate balance between groups using standardized mean differences. A standardized mean difference of less than 0.1 was considered indicative of a well-matched cohort. The threshold for statistical significance was set at $P < 0.05$ using 2-sided tests.

Table 2. Baseline Characteristics of the PGA before the Group and Matched Control Group: Before and after Propensity Score Matching

Characteristics	Before Matching			After Matching		
	PGA Use (n = 9637)	*No PGA Use (n = 465 135)*	*Standardized Difference*	*PGA Use (n = 9457)*	*No PGA Use (n = 9457)*	*Standardized Difference*
Age, mean ± SD	71.8 ± 9.67	69.7 ± 9.99	0.2114	71.8 ± 9.69	72.1 ± 9.10	0.0364
Gender, No. (%)						
Male	4136 (42.92%)	187 444 (40.30%)	0.0532	4050 (42.83%)	4161 (44.00%)	0.0237
Female	4967 (51.54%)	262 541 (56.44%)	0.0985	4873 (51.53%)	4743 (50.15%)	0.0275
Unknown	534 (5.54%)	15 150 (3.26%)	0.1115	534 (5.65%)	553 (5.85%)	0.0086
Race, No. (%)						
White	4989 (51.77%)	338 410 (72.76%)	0.4435	4946 (52.30%)	4874 (51.54%)	0.0152
Black or African American	2436 (25.28%)	51 849 (11.15%)	0.3724	2340 (24.74%)	2421 (25.60%)	0.0197
Asian	424 (4.40%)	19 756 (4.25%)	0.0075	423 (4.47%)	402 (4.25%)	0.0109
American Indian or Alaska Native	30 (0.31%)	2058 (0.44%)	0.0214	30 (0.32%)	20 (0.21%)	0.0206
Native Hawaiian or Other Pacific Islander	13 (0.14%)	2176 (0.47%)	0.0608	13 (0.14%)	12 (0.13%)	0.0029
Other race	511 (5.30%)	13 088 (2.81%)	0.1264	488 (5.16%)	489 (5.17%)	0.0005
Unknown race	1234 (12.81%)	37 798 (8.13%)	0.1533	1217 (12.87%)	1239 (13.10%)	0.0069
Ethnicity, No. (%)						
Hispanic/LatinX	753 (7.81%)	34 790 (7.48%)	0.0126	727 (7.69%)	733 (7.75%)	0.0024
Non-Hispanic/LatinX	7046 (73.11%)	343 176 (73.78%)	0.0151	6920 (73.17%)	6975 (73.76%)	0.0132
Unknown	1838 (19.07%)	87 169 (18.74%)	0.0085	1810 (19.14%)	1749 (18.49%)	0.0165
Comorbidities, No. (%)						
Hypertension	5395 (55.98%)	249 159 (53.57%)	0.0485	5275 (55.78%)	5079 (53.71%)	0.0416
Hyperlipidemia	3515 (36.47%)	167 071 (35.92%)	0.0116	3457 (36.56%)	3259 (34.46%)	0.0438
Type 2 diabetes mellitus	2508 (26.03%)	115 404 (24.81%)	0.0279	2459 (26.00%)	2280 (24.11%)	0.0437
Chronic kidney disease	1045 (10.84%)	45 809 (9.85%)	0.0327	1034 (10.93%)	959 (10.14%)	0.0258
Glaucoma, No. (%)	7897 (81.95%)	47 629 (10.24%)	2.0705	7717 (81.60%)	7701 (81.43%)	0.0044
Primary open-angle glaucoma (stage unspecified)	1323 (13.73%)	2048 (0.44%)	0.5362	1162 (12.29%)	1101 (11.64%)	0.0199
Primary open-angle glaucoma (mild stage)	1306 (13.55%)	1945 (0.42%)	0.5333	1145 (12.11%)	1084 (11.46%)	0.0200
Primary open-angle glaucoma (moderate stage)	1318 (13.68%)	1955 (0.42%)	0.5362	1153 (12.19%)	1096 (11.59%)	0.0186
Primary open-angle glaucoma (severe stage)	1318 (13.68%)	1937 (0.42%)	0.5364	1153 (12.19%)	1092 (11.55%)	0.0199
Primary open-angle glaucoma (indeterminate stage)	1281 (13.29%)	1890 (0.41%)	0.5276	1121 (11.85%)	1070 (11.31%)	0.0169
Ocular hypertension	1048 (10.88%)	4955 (1.07%)	0.4232	1028 (10.87%)	1008 (10.66%)	0.0068
Low-tension glaucoma	414 (4.30%)	647 (0.14%)	0.2851	377 (3.99%)	361 (3.82%)	0.0087
Pseudoexfoliation glaucoma	327 (3.39%)	711 (0.15%)	0.2474	307 (3.25%)	315 (3.33%)	0.0047
Pigmentary glaucoma	120 (1.25%)	217 (0.05%)	0.1500	114 (1.21%)	115 (1.22%)	0.0010
Age-related cataract type, No. (%)						
Cortical age-related cataract	961 (9.97%)	43 730 (9.40%)	0.0193	925 (9.78%)	1134 (11.99%)	0.0710
Anterior subcapsular polar age-related cataract	16 (0.17%)	1582 (0.34%)	0.0347	16 (0.17%)	24 (0.25%)	0.0184
Posterior subcapsular polar age-related cataract	425 (4.41%)	29 677 (6.38%)	0.0873	409 (4.33%)	546 (5.77%)	0.0662
Age-related nuclear cataract	6763 (70.18%)	264 468 (56.86%)	0.2794	6604 (69.83%)	6384 (67.51%)	0.0502
Age-related cataract, morgagnian type	80 (0.83%)	2888 (0.62%)	0.0247	79 (0.84%)	64 (0.68%)	0.0183
Combined forms of age-related cataract	3235 (33.57%)	148 767 (31.98%)	0.0338	3191 (33.74%)	3531 (37.34%)	0.0752
Cataract surgery complexity, No. (%)						
Complex cataract surgery (CPT 66982)	1961 (20.35%)	62 319 (13.40%)	0.1864	1915 (20.25%)	1834 (19.39%)	0.0215
Medications, No. (%)						
Topical anti-inflammatories	8621 (89.46%)	353 854 (76.08%)	0.3600	8448 (89.33%)	8321 (87.99%)	0.0424
Long-term use of steroids	272 (2.82%)	14 721 (3.17%)	0.0201	269 (2.84%)	208 (2.20%)	0.0411
Long-term use of NSAIDs	130 (1.35%)	8754 (1.88%)	0.0423	129 (1.36%)	116 (1.23%)	0.0122

CPT = Current Procedural Terminology; No. = number of patients; NSAID = nonsteroidal anti-inflammatory drug; PGA = prostaglandin analog; SD = standard deviation.

Table 3. Risk of Pseudophakic Cystoid Macular Edema in Patients Using PGAs Compared to Nonusers Following Cataract Surgery

Group	PGA Cohort		Control Cohort		Hazard Ratio	95% Confidence Interval
	Total	*Events, No. (%)*	*Total*	*Events, No. (%)*		
PGA before	9457	219 (2.32%)	9457	197 (2.08%)	1.08	(0.89−1.31)
PGA after	1993	39 (1.96%)	1993	35 (1.76%)	1.08	(0.68−1.70)
PGA before and after	2367	58 (2.45%)	2367	64 (2.70%)	0.86	(0.61−1.23)

PGA = prostaglandin analog.

Results

Primary Analysis

Before matching, the PGA use group included 9637 patients, while the control group had 465 135 patients. After PSM, both the PGA use and control groups included 9457 patients. The mean age after matching was comparable between the PGA group (71.8 ± 9.69 years) and the control group (72.1 ± 9.10 years). Gender distribution was also balanced, with females comprising 51.53% of the PGA group and 50.15% of the control group. Racial distribution showed close alignment post-matching, with White patients representing 52.30% of the PGA group and 51.54% of the control group, while Black or African American patients accounted for 24.74% and 25.60%, respectively. Comorbid conditions were similarly distributed, with hypertension present in 55.78% of the PGA group and 53.71% of the control group, and hyperlipidemia noted in 36.56% and 34.46%, respectively. Chronic kidney disease occurred in 10.93% of the PGA group and 10.14% of the control group. Surgical complexity was also well-balanced; complex cataract surgery (Current Procedural Terminology 66982) accounted for 1915 (20.25%) cases in the PGA group and 1834 (19.39%) cases in the control group after matching. The PSM process effectively resulted in well-matched groups across key demographic and clinical variables, as shown in Table 2.

Table 3 shows the incidence of PCME across all cohorts. In the "PGA Before" group, the incidence of PCME was 2.32% (219 events) compared to 2.08% (197 events) in the control group. This yielded a HR of 1.08 (95% CI: 0.89−1.31).

Sensitivity Analysis

In the "PGA After" group, which included 1993 patients per cohort, the incidence of PCME was 1.96% (39 events) in the PGA group compared to 1.76% (35 events) in the control group, yielding a HR of 1.08 (95% CI: 0.68−1.70). In the "PGA Before & After" group, which included 2367 patients per cohort, the incidence of PCME was 2.45% (58 events) in the PGA group and 2.70% (64 events) in the control group, resulting in a HR of 0.86 (95% CI: 0.61−1.23). These findings are summarized in the forest plot shown in Figure.

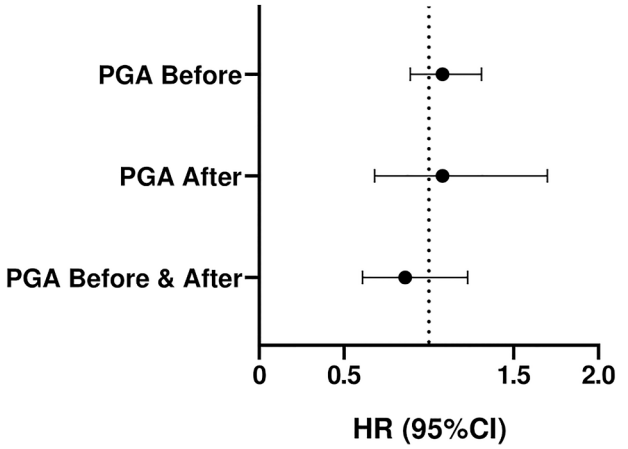

Figure. Hazard ratios for the risk of PCME across PGA exposure groups. This forest plot illustrates the HRs and 95% CIs for the risk of PCME in patients using PGAs compared to matched controls. None of these associations were statistically significant. This plot visually represents the findings of our study and underscores the lack of a significant association between PGA use, regardless of timing, and the development of PCME. CI = confidence interval; HR = hazard ratio; PCME = pseudophakic cystoid macular edema; PGA = prostaglandin analog.

Discussion

This retrospective cohort study investigated the association between perioperative PGA use and the risk of PCME following cataract surgery. Our findings did not reveal a statistically significant association between PGA use, regardless of timing (before, after, or both), and the incidence of PCME within 3 months.

Lack of consensus on risk of PCME in patients with topical prostaglandin use exists in prior literature; herein, we provide meaningful contribution to the existing body of literature by exploring this issue using data derived from routine clinical practice. Our findings align with those of many prior studies. A meta-analysis by Hu et al reviewed 214 studies (28 232 patients) encompassing all reported instances of CME associated with PGA use.[16] The meta-analysis found no significant association between PGA use and CME or uveitis. It suggested that cases of CME or uveitis observed in patients using PGAs may have been confounded by the effects of ocular surgeries, such as cataract extraction, rather than being directly caused by the medication itself. This analysis suggests that PGA use in nonsurgical settings may not pose a significant risk of PCME.[16] This suggests that the surgical procedure itself, rather than PGA use, may be a more significant contributing factor to the development of CME.

Furthermore, a retrospective cohort study by Chu et al analyzed a total of over 80 000 cataract surgeries from 8 independent United Kingdom clinical sites, also found no statistically significant association between PGA use and PCME (relative risk, 1.11; 95% CI, 0.82−1.51).[17] A randomized controlled trial by Niyadurupola et al focused on patients with glaucoma and demonstrated no cases of clinically significant PCME in their cohort.[18] Importantly, this study highlighted that patients who continued PGAs postoperatively maintained significantly lower intraocular pressures compared to those who discontinued them.[18] This emphasizes the crucial role of PGAs in managing glaucoma and raises the clinical concern that discontinuing PGAs perioperatively could compromise intraocular pressure control, particularly in patients with pre-existing glaucoma.

In contrast, Wendel et al, in a nested case-control study of 508 cases and 5080 controls, found an increased risk of PCME associated with postoperative PGA use, with a relative risk of 1.86 (95% CI, 1.04-3.32) for current use and 2.06 (95% CI, 1.37−3.11) for PGA use within 1 year prior to PCME diagnosis.[19] The discordance in findings may be explained by several factors. The only covariables accounted for in their analysis were age and sex, whereas we performed a more comprehensive PSM of demographic, ophthalmic, and systemic factors. Furthermore, we assessed HRs, which allow incorporation of censored data and account for time to event. Additional important strengths of our study design include 1:1 study to control ratio, larger study design, and focus on narrower perioperative windows, allowing for a more precise assessment of the temporal relationship between PGA use and PCME risk.

The prevalence of PCME observed in our study aligns closely with rates reported in other large-scale studies. In a comprehensive registry of 3.1 million cataract surgeries, PCME was diagnosed in 25 595 eyes, reflecting a prevalence of 0.8%, with an average onset approximately 6 weeks postoperatively.[10] Additionally, a multicenter study by Shakarchi et al involving nearly 55 000 patients reported a 0.9% risk of PCME in the second eye among those without first-eye PCME, closely aligning with the rates observed in our study.[20] While PCME was identified via ICD-10-CM coding, these diagnoses typically represent cases requiring intervention or formal clinical reporting, suggesting that the outcomes assessed here likely correspond to clinically significant PCME, which is the most relevant outcome for visual prognosis. These findings collectively underscore the generalizability of our study's results within the broader context of PCME prevalence.

Our study provides valuable insights into the association between PGAs and PCME, leveraging the strengths of a large, multi-institutional database through the TriNetX platform. Building on prior research with a larger cohort and well-defined exposure groups, we accounted for potential biases related to medication. recommendations, enhancing the precision of our findings. The use of PSM allowed us to balance key confounders, including demographics, comorbidities, and surgical complexity factors such as cataract type, thereby ensuring robust comparability between groups. Additionally, the inclusion of distinct PGA groups, including those initiating therapy postoperatively, provides a nuanced analysis of timing and its potential impact on PCME risk.

Despite these strengths, there are inherent limitations to our study. As with any observational study, residual confounding from unmeasured or misclassified variables remains a possibility. Our reliance on ICD-10 coding for both exposure and outcome may introduce inaccuracies in patient selection and PCME diagnosis. Additionally, the lack of clinical data, such as the precise timing of PCME diagnosis or adherence to PGA therapy, limits our ability to assess more granular patient-specific factors. As with many administrative database studies, we lacked access to granular surgical metrics such as phacoemulsification energy and precise nuclear density grading. While we matched for cataract surgery complexity and cataract type to balance the cohorts, we could not fully account for specific nuclear hardness or intraoperative energy parameters. It is also possible there may have been undiagnosed or subclinical PCME that is not represented in our findings. Furthermore, while PSM minimizes bias from observed variables, it cannot account for unmeasured confounders or differences in ophthalmic care access, which may influence PCME diagnosis rates. It is critical to note that the study design excluded patients with pre-existing high-risk factors for PCME, including prior CME, uveitis, and various retinal pathologies (as detailed in the Methods). Consequently, the findings presented here apply to a relatively lower-risk cohort undergoing cataract surgery. Therefore, these results do not apply to the high-risk patient population, and the clinical significance of these findings for complex cases, often managed by glaucoma specialists, should be interpreted with caution, as these patients may have additional, unmeasured risk factors. Nevertheless, our study builds upon prior literature by providing a large-scale, rigorously matched analysis, offering important evidence on the relationship between PGAs and PCME.

An important consideration in interpreting our findings is whether the study was sufficiently powered to detect clinically meaningful differences in PCME risk. Unlike prospective randomized trials, retrospective cohort studies cannot predefine sample size calculations. Instead, precision is best judged by the width of the CIs around effect estimates. In our analysis, the HRs for all PGA exposure groups were close to unity, with relatively narrow 95% CIs (e.g., 0.89−1.31 in the primary cohort). These intervals exclude large increases in risk, such as the twofold elevations reported in some prior observational studies, but do not completely rule out more modest differences. However, such modest relative risks would translate into very small absolute differences in PCME incidence given the low baseline risk. Our results therefore suggest that if any effect of perioperative PGA use exists, it is likely to be minimal and of limited clinical significance. This interpretation is supported by prior randomized controlled trials and meta-analyses, which similarly report no significant increase in PCME with perioperative PGA use.

In conclusion, we found no significant difference in PCME risk with perioperative PGA use. Our results highlight the importance of accounting for timing and potential confounders, such as surgical complexity and comorbidities, when evaluating PCME risk. While our findings suggest that PGA use does not substantially alter PCME risk, clinicians should remain vigilant in monitoring for PCME in higher-risk patients and consider individualizing perioperative care to optimize outcomes. Future research should focus on prospective studies to further clarify these relationships and guide evidence-based perioperative management strategies.

Footnotes and Disclosures

Originally received: July 4, 2025.
Final revision: December 10, 2025.
Accepted: December 24, 2025.
Available online: January 2, 2026. Manuscript no. OGLA-D-25-00368.

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Disclosures:

All authors have completed and submitted the ICMJE disclosures form.

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I.I.K.A.: Consultant — AbbVie, Ace Vision, Alcon, Aliph Medical, Aquea Health, Inc., ArcScan, Avellino Lab USA, Inc., Avisi, Balance Ophthalmics, Bausch and Lomb, Beaver Visitec, Belkin Vision, Bionode, Carl Zeiss, Centricity Vision, Inc., CorNeat Vision, Custom Surgical, Elios Vision, ElutiMed, eyeFlow, Inc., EyeMed, EyeQ Technologies, Exhaura Limited, Glaukos, Gore, Hexiris Pharma, Iantrek, InjectSense, Iridex, iCare, iStar, Johnson & Johnson Vision, LayerBio, Liqid Medical, Long Bridge Medical, Inc., MST Surgical, Myra Vision, New World Medical, Nova Eye, Ocular Instruments, Ocular Therapeutix, Oculus Surgical, OcuSciences, Omega Ophthalmics, Peripherex, PolyActiva, PulseMedica, Radiance Therapeutics, Inc., Radius XR, Rheon Medical SA, Ripple Therapeutics, Sanoculis, Santen, Singapore Biodesign, Shifamed, LLC, Sight Sciences, Smartlens, Inc., Stroma, Thea Pharma, TFS Health Science, ViaLase, Visci Ltd, Visus Therapeutics, Vizzario, Zilia, Inc.; Research support — AbbVie, Alcon, Bionode, Carl Zeiss, CorNeat Vision, Elios Vision, Glaukos, Gore, iCare, iStar, Johnson & Johnson Vision, Myra Vision, New World Medical, Santen, Nova Eye.

T.D.F.: Speaker — Allergan and Nova Eye; Consultant — Zeiss, Glaukos, Elios, Iantrek, Sight Sciences, ViaLase, Myra, Nova Eye.

C.Y.W.: Consultant — Allergan/AbbVie, Alcon, Apellis Pharmaceuticals, Alimera Sciences, Zeiss/DORC, Ocular Therapeutix, Genentech, Regeneron, REGENXBIO, Iveric Bio/Astellas, EyePoint; Research support — DRCR Retina Network, Alimera Sciences, EyePoint; Royalties — Springer Publishers.

Iqbal Ike K. Ahmed, MD, an editorial board member of this journal, was recused from the peer-review process of this article and had no access to information regarding its peer review.

HUMAN SUBJECTS: No human subjects were included in this study. The study did not meet the criteria for human subjects research, as this was an analysis of an existing anonymized dataset. As a federated network, TriNetX received a waiver from Western IRB since only aggregated counts and statistical summaries of deidentified information, but no protected health information, are received, and no study-specific activities are performed in retrospective analyses. This retrospective study is exempt from informed consent. This study was conducted in compliance with the principles of the Declaration of Helsinki.

No animal subjects were used in this study.

Author Contributions:

Conception and design: Muayad, Mukhtar, Bordbar, Loya, Alsoudi, Weng, De Francesco, Ahmed

Analysis and interpretation: Muayad, Mukhtar, Bordbar, Loya, Alsoudi, Weng, De Francesco, Ahmed

Data collection: Muayad, Mukhtar, Bordbar, Loya, Alsoudi, Weng, De Francesco, Ahmed

Obtained funding: N/A

Overall responsibility: Muayad, Mukhtar, Bordbar, Loya, Alsoudi, Weng, De Francesco, Ahmed

Abbreviations and Acronyms:
CI = confidence interval; **CME** = cystoid macular edema; **HR** = hazard ratio; **ICD-10-CM** = International Classification of Disease, Tenth Revision, Clinical Modificatios; **PCME** = pseudophakic cystoid macular edema; **PGA** = prostaglandin analog; **PSM** = propensity score matching.

Keywords:
Pseudophakic cystoid macular edema, Prostaglandin analogs, Cataract surgery, Postoperative complications.

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References

1. Fouad YA, Karimaghaei S, Elhusseiny AM, et al. Pseudophakic cystoid macular edema. *Curr Opin Ophthalmol*. 2025;36:62–69.
2. Guo S, Patel S, Baumrind B, et al. Management of pseudophakic cystoid macular edema. *Surv Ophthalmol*. 2015;60:123–137.
3. Aaronson A, Achiron A, Tuuminen R. Clinical course of pseudophakic cystoid macular edema treated with nepafenac. *J Clin Med*. 2020;9:3034.
4. Scheers D, Rens J, Van Os L, et al. Safety of the bag-in-the-lens implantation regarding the development of clinically significant pseudophakic cystoid macular edema: a retrospective case series study. *Plos one*. 2023;18, e0278861.
5. Yang J, Cai L, Sun Z, et al. Risk factors for and diagnosis of pseudophakic cystoid macular edema after cataract surgery in diabetic patients. *J Cataract Refractive Surg*. 2017;43:207–214.
6. Miller KM, Oetting TA, Tweeten JP, et al. Cataract in the adult eye preferred practice pattern. *Ophthalmology*. 2022;129:P1–P126.
7. Jaycock P, Johnston R, Taylor H, et al. The Cataract National Dataset electronic multi-centre audit of 55 567 operations:

updating benchmark standards of care in the United Kingdom and internationally. *Eye*. 2009;23:38–49.
8. Greenberg PB, Tseng VL, Wu W-C, et al. Prevalence and predictors of ocular complications associated with cataract surgery in United States veterans. *Ophthalmology*. 2011;118:507–514.
9. Zaidi FH, Corbett MC, Burton BJ, Bloom PA. Raising the benchmark for the 21st century—the 1000 cataract operations audit and survey: outcomes, consultant-supervised training and sourcing NHS choice. *Br J Ophthalmol*. 2007;91:731–736.
10. Iftikhar M, Dun C, Schein OD, et al. Cystoid macular edema after cataract surgery in the United States: IRIS registry (Intelligent Research in Sight) analysis. *Ophthalmology*. 2023;130:1005–1014.
11. Rotsos TG, Moschos MM. Cystoid macular edema. *Clin Ophthalmol*. 2008;2:919–930.
12. Miyake K, Ibaraki N. Prostaglandins and cystoid macular edema. *Surv Ophthalmol*. 2002;47:S203–S218.
13. Holló G, Aung T, Cantor LB, Aihara M. Cystoid macular edema related to cataract surgery and topical prostaglandin analogs: mechanism, diagnosis, and management. *Surv Ophthalmol*. 2020;65(5):496–512.
14. Lee KM, Lee EJ, Kim T-W, Kim H. Pseudophakic macular edema in primary open-angle glaucoma: a prospective study using spectral-domain optical coherence tomography. *Am J Ophthalmol*. 2017;179:97–109.
15. Walkden A, Porter LF, Morarji J, et al. Pseudophakic cystoid macular edema and spectral-domain optical coherence tomography–detectable central macular thickness changes with perioperative prostaglandin analogs. *J Cataract Refractive Surg*. 2017;43:1027–1030.
16. Hu J, Vu JT, Hong B, Gottlieb C. Uveitis and cystoid macular oedema secondary to topical prostaglandin analogue use in ocular hypertension and open angle glaucoma. *Br J Ophthalmol*. 2020;104:1040–1044.
17. Chu CJ, Johnston RL, Buscombe C, et al. Risk factors and incidence of macular edema after cataract surgery: a database study of 81984 eyes. *Ophthalmology*. 2016;123:316–323.
18. Niyadurupola N, Brodie J, Patel T, et al. Topical prostaglandin analogue use and cystoid macular oedema following uneventful cataract surgery: a randomised control trial. *Br J Ophthalmol*. 2022;106:1662–1666.
19. Wendel C, Zakrzewski H, Carleton B, et al. Association of postoperative topical prostaglandin analog or beta-blocker use and incidence of pseudophakic cystoid macular edema. *J Glaucoma*. 2018;27:402–406.
20. Shakarchi AF, Soliman MK, Yang YC, Sallam AB. Risk of pseudophakic cystoid macular edema in fellow-eye cataract surgeries: a multicenter database study. *Ophthalmology*. 2023;130:640–645.