Cataract Surgery and Rate of Visual Field Progression in Primary Open-Angle Glaucoma

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• PURPOSE: To test the hypothesis that cataract surgery slows the apparent rate of visual field (VF) decay in primary open-angle glaucoma patients compared with rates measured during cataract progression.

• DESIGN: Retrospective cohort study.

• METHODS: Consecutive open-angle glaucoma patients who underwent cataract surgery and who had ≥4 VFs and ≥3 years of follow-up before and after surgery were retrospectively reviewed. Mean deviation (MD) rate, visual field index (VFI) rate, pointwise linear regression (PLR), pointwise rate of change (PRC), and the Glaucoma Rate Index (GRI) were compared before and after cataract surgery.

• RESULTS: A total of 134 eyes of 99 patients were included. Median (interquartile range) follow-up was 6.5 (4.7-8.1) and 5.3 (4.0-7.3) years before and after cataract surgery, respectively. All intraocular pressure (IOP) parameters (mean IOP, standard deviation of IOP, and peak IOP) significantly improved ($P < .001$) after cataract surgery. All VF indices indicated an accelerated VF decay rate after cataract surgery: MD rate (-0.18 ± 0.40 dB/year vs -0.40 ± 0.62 dB/year, $P < .001$), VFI rate (-0.44% ± 1.09%/year vs -1.19% ± 1.85%/year, $P < .001$), GRI (-5.5 ± 10.8 vs -13.5 ± 21.5; $P < .001$), and PRC (-0.62% ± 2.47%/year before and -1.35% ± 3.71%/year after surgery; $P < .001$) and PLR (-0.20 ± 0.82 dB/year before and -0.42 ± 1.16 dB/year after surgery; $P < .001$) for all VF locations. Worse baseline MD and postoperative peak IOP were significantly associated with the postoperative VF decay rate and the change in the decay rate after cataract surgery.

• CONCLUSION: Although all IOP parameters improved after cataract surgery, VFs continued to progress. Cataract surgery does not slow the apparent rate of glaucomatous VF decay as compared to rates measured during the progression of the cataract. (Am J Ophthalmol 2019;201:19–30. © 2019 Elsevier Inc. All rights reserved.)

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CATARACT AND GLAUCOMA FREQUENTLY COEXIST, as the prevalence of both diseases increases with age.[1,2] Moreover, glaucoma treatment, including medication in addition to surgery, increases the rate of cataract development.[3,4] The presence of cataract causes diffuse visual field (VF) loss in patients with glaucoma, and differentiating perimetric deterioration caused by cataract from deterioration that is caused by worsening glaucoma is an important but challenging clinical task.[5]

A number of studies have investigated changes in VF after cataract surgery in glaucoma patients. Most studies have shown that cataract surgery results in improvement of mean deviation (MD) in normal and glaucomatous eyes,[5,6] although changes in indicators of localized field loss such as pattern standard deviation (PSD) in glaucomatous eyes after cataract surgery have been more variable.[5–7]

We have developed a technique based on trend analysis that uses a pointwise exponential model to fit the behavior of individual test locations in visual field series.[8–12] This technique separates slow components and fast components of visual field decay, and operates without discontinuities across a wide range of disease severity. A previous study from our group found that cataract progression is the main determinant of the slow visual field rate component and does not change the fast visual field rate component.[13] We suggested that the method used in that study could help reduce the confounding effects of cataract progression and cataract extraction on measured perimetric progression in glaucoma. Based on a similar strategy, we recently presented a new algorithm to define a rate index for serial glaucomatous visual fields. The algorithm is able to provide a standardized estimate of the rate of change of the entire VF, identified as Glaucoma Rate Index (GRI), for which regional specificity is maintained in a graphical representation.[12]

The purpose of this study is to test the hypothesis that cataract surgery would slow the apparent rate of glaucomatous visual field decay in open-angle glaucoma patients, as compared to rates measured during the progression of the cataract.

METHODS

• PARTICIPANTS: A retrospective review of medical records of patients with open-angle glaucoma who underwent cataract surgery with intraocular lens implantation at the Stein Eye Institute, David Geffen School of Medicine at

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UCLA, between July 1, 2000 and June 30, 2012 was performed. This study was approved by the UCLA Human Research Protection Program, was conducted in accordance with tenets set forth in the Declaration of Helsinki, and complied with the Health Insurance Portability and Accountability Act regulations. Inclusion criteria were as follows: diagnosis of primary open-angle glaucoma; uncomplicated cataract surgery performed with small-incision phacoemulsification; ≥4 reliable VFs before and after cataract surgery; ≥3 years of follow-up before and after cataract surgery; last visit before cataract extraction within 1 year from surgery; and first visit after cataract extraction within 1 year after surgery. Exclusion criteria were presence of other ocular diseases other than glaucoma and cataract, performance of cataract surgery combined with and any form of glaucoma surgery (eg, trabeculectomy, glaucoma drainage device, or minimally invasive glaucoma surgery), and previous major ocular surgery other than uncomplicated glaucoma surgery.

All cataract surgery was performed by an experienced anterior segment surgeon with temporal, clear-corneal, small-incision phacoemulsification. The patients received a silicone intraocular lens (STAAR Surgical) or an acrylic foldable intraocular lens (Alcon Laboratories Inc) implanted in the capsular bag; all intraocular lenses were monofocal. All VF examinations were performed with the Humphrey Field Analyzer (Carl Zeiss Meditec, Inc, Dublin, California, USA) with a 24-2 or 30-2 test pattern, size III white stimulus Swedish Interactive Threshold Algorithm standard strategy. For the 30-2 test pattern, only the 54 locations corresponding to the 24-2 test pattern were included in the pointwise analysis. Reliability criteria were set as follows: fixation losses <30%, false-positive rates <15%, and false-negative rates <30%. Entire VF examinations were excluded if they did not meet the reliability criteria. VF test locations were excluded from the analysis if they were part of the physiologic blind spot or if any 2 of the initial 3 measurements at a test location had threshold sensitivities of 0 decibels dB. The total number of locations included in the preoperative and postoperative periods was calculated by multiplying the number of test locations for VF (n = 52) for the number of VF series included (n = 134), and excluding locations with 0 dB sensitivity in 2 of the first 3 VFs of the series, or having fewer than 4 measurements after the applications of Cook's distance and the Studentized residual test. The last visual field before surgery and the first visual field after surgery were required to have both been measured within 1 year of cataract surgery.

• **GLAUCOMA RATE INDEX:** The GRI method has been detailed elsewhere.[12] All calculations were performed on raw threshold sensitivity values. Each pointwise series was categorized a priori as either decaying or improving based on its linear trend (negative or positive, respectively). Pointwise exponential regression (PER) of each series was performed. The technique for this process varied, depending on the a priori categorization of a location as having a negative or positive trend. For locations with a negative trend, the following formula was used: $y = e^{(a+bt)}$, where y = threshold sensitivity (dB), a = constant, b = slope, and t = time (years). For locations with a positive trend, the following formula was applied: $Y\text{-}y = e^{(a+bt)}$, where Y = the normal age-matched threshold sensitivity + 2 standard deviation (SD), y=threshold sensitivity (dB), a = constant, b = slope, and t = time (years). Outliers were removed from pointwise series on the basis of their Cook's distance[14] and the Studentized residual test.[15] The former method removes high-leverage points at the tails of each pointwise series, which can significantly change the slope of the regression line; the latter method removes points with high root mean square error, which can significantly enlarge the confidence interval (CI) of the slope. As suggested by Weisberg,[16] we removed points with Cook's distance >1 and |Studentized residual| >3. After the outliers' removal, the PER was recalculated and was used to generate 2 values: pointwise rate of change (PRC) and 90% CI of the slope. PRC was defined as the difference between the first and final PER values divided by the age and test location-matched dynamic range.[17,18] Therefore, PRC is expressed as a percentage of the entire normal perimetric range corrected for age and test location, and indicates the rate of change of each pointwise sequence. The 90% CI was used to categorize a series as decaying, improving, or no change. For decay, 2 criteria have to be met: (1) the slope of the upper (least negative) 90th percentile of all possible PER fits must be negative, and (2) the median slope must be more negative than the 95th percentile for the normal age-matched slope for that particular location and the patient's age. Decay PRC locations were further divided into slow and fast decay based on a cutoff PRC of -5%/year, which is the fastest quartile of decaying locations.[12] Similarly, improving series must have a positive slope for the lower (least positive) 90th percentile. If a test location did not meet these criteria, it was defined as no change.[12]

The PRCs are displayed in a color-coded map, which retains spatial information, and are used to calculate the GRI score, which is generated from the sum of the PRC values of the significant locations across the entire VF. This value is then normalized from a maximum rate of decay (-100) to a maximum rate of improvement (+100). Decaying eyes were defined as GRI ≤ -6, stable eyes as those with GRI between -6 and +10, improving eyes as eyes with GRI ≥ +10, and fast progressors as eyes with GRI ≤ -37.[12]

• **STATISTICAL ANALYSIS:** Preoperative best-corrected visual acuity (BCVA) was recorded from the visit immediately before cataract surgery. All eyes were refracted within 1 month after cataract surgery and postoperative BCVA was compared with the preoperative BCVA. Snellen visual acuities were converted to the logMAR scale before statistical analyses. Eyes were stratified according to glaucoma severity as early and moderate-to-severe with MD ≥ -5 dB

TABLE 1. Demographic and Clinical Characteristics of Study Sample

Variable	All	Mild	Moderate to Severe	*P* Value
Eyes/patients, n	134/99	98/76	36/31	-
Age (years)	65.8 ± 7.5	66.5 ± 7.5	63.4 ± 8.8	.14
Female sex, n (%)	54 (54.5%)	41 (53.4%)	21 (67.7%)	.27
Race, n (%)				-
White	76 (76.7%)	58 (76.3%)	26 (83.9%)	.55
Hispanic	6 (6.1%)	6 (7.9%)	0 (0%)	-
Asian	8 (8.1%)	6 (7.9%)	2 (6.5%)	-
Others or unknown	9 (9.1%)	6 (7.9%)	3 (9.7%)	-
Baseline MD, dB	−3.7 ± 4.0	−1.7 ± 1.7	−9.2 ± 3.4	<.001*
Baseline PSD, dB	4.6 ± 3.9	2.9 ± 2.1	9.3 ± 3.8	<.001*
Baseline VFI, %	91.1 ± 11.1	96.1 ± 4.3	77.5 ± 12.4	<.001*
Number of visual fields, n				-
Before surgery	9.9 ± 4.2	9.6 ± 4.0	10.8 ± 4.6	.82
After surgery	9.3 ± 4.1	9.2 ± 4.1	9.8 ± 3.9	.04*
Follow up period, years				-
Before surgery	6.6 ± 2.3	6.6 ± 2.3	6.6 ± 2.4	.42
After surgery	6.0 ± 2.5	6.0 ± 2.5	5.8 ± 2.5	.80
Baseline IOP, mm Hg	16.3 ± 4.2	16.3 ± 4.2	16.3 ± 4.1	.41
Number of medications	1.2 ± 1.2	1.2 ± 1.1	1.3 ± 1.4	.34
Refractive error, diopter	−2.0 ± 4.0	−1.8 ± 3.4	−2.4± 5.3	.90
Central corneal thickness, μm	555.4 ± 43.1	551.9 ± 45.0	564.3 ± 37.0	.47
Previous glaucoma surgery, n (%)	23 (17.2 %)	12 (12.2 %)	11 (30.6 %)	.58

IOP = intraocular pressure; MD = mean deviation; PSD = pattern standard deviation; VFI = visual field index.
Statistically significant *P* values are indicated by an asterisk (*).

and < -5 dB, respectively.[19] Demographic and clinical characteristics of the 2 severity groups were compared. Continuous and factorial variables related to the patient (and not to the eye) were compared with unpaired *t* test (ie, age) and χ^2 test (ie, sex, ethnicity), respectively. Continuous and binary variables related to the eye (and not to the patient) were compared with a linear or logistic mixed model, respectively, where the inclusion of the fellow eye was the random factor to account for intereye correlations.

Mean intraocular pressure (IOP), SD of IOP, peak IOP, and the number of medications were compared for the preoperative and postoperative periods with a linear mixed model, where the random factor was nested in 2 levels to account for within-subject (2 eyes of the same patient) and within-eye (paired design with the same eye considered before and after cataract extraction) correlations. Postoperative mean IOP, SD of IOP, and IOP did not include readings within 1 month from cataract surgery. Similarly, the MD, PSD, and visual field index (VFI) values of the last visual field before surgery and the first visual field after surgery were also compared with a linear mixed model.

For each eye, GRI was calculated for the preoperative and postoperative periods separately. The MD and VFI rates of change for the preoperative and postoperative periods were also calculated with univariate linear regression analyses of these indices against time, and the corresponding regression slopes (in decibels per year for MD and in percentages per year for VFI) were compared before and after cataract extraction. The changes in VF decay rates after cataract surgery were stratified according to glaucoma severity and previous trabeculectomy history. To compare rates before and after cataract extraction, a linear mixed model was employed to take into account the within-subject and within-eye correlations. Differences between preoperative and postoperative rates between eyes with or without previous trabeculectomy were assessed with a linear mixed model, where the inclusion of the fellow eye was the random factor.

For each location, the mean preoperative and postoperative pointwise rates were calculated with both PRC and pointwise linear regression (PLR). The PLR for the preoperative and postoperative periods were calculated with univariate linear regression analyses of raw threshold sensitivities over time. For PLR, locations were categorized as follows: fast decaying, defined as a significant ($P < .05$) regression slope equal to -2 dB/year or faster; slow decaying, defined as a significant regression slope slower than -2 dB/year and equal to -1 dB/year or slower; improvement, defined as a significant regression slope equal to +1 dB/year or more positive; no change, if none of the above criteria was met. Locations with a sensitivity of 0 dB in 2 of the first 3 VF examinations were excluded. PRCs and PLR values for fast- and slow-decay components, improvement, or

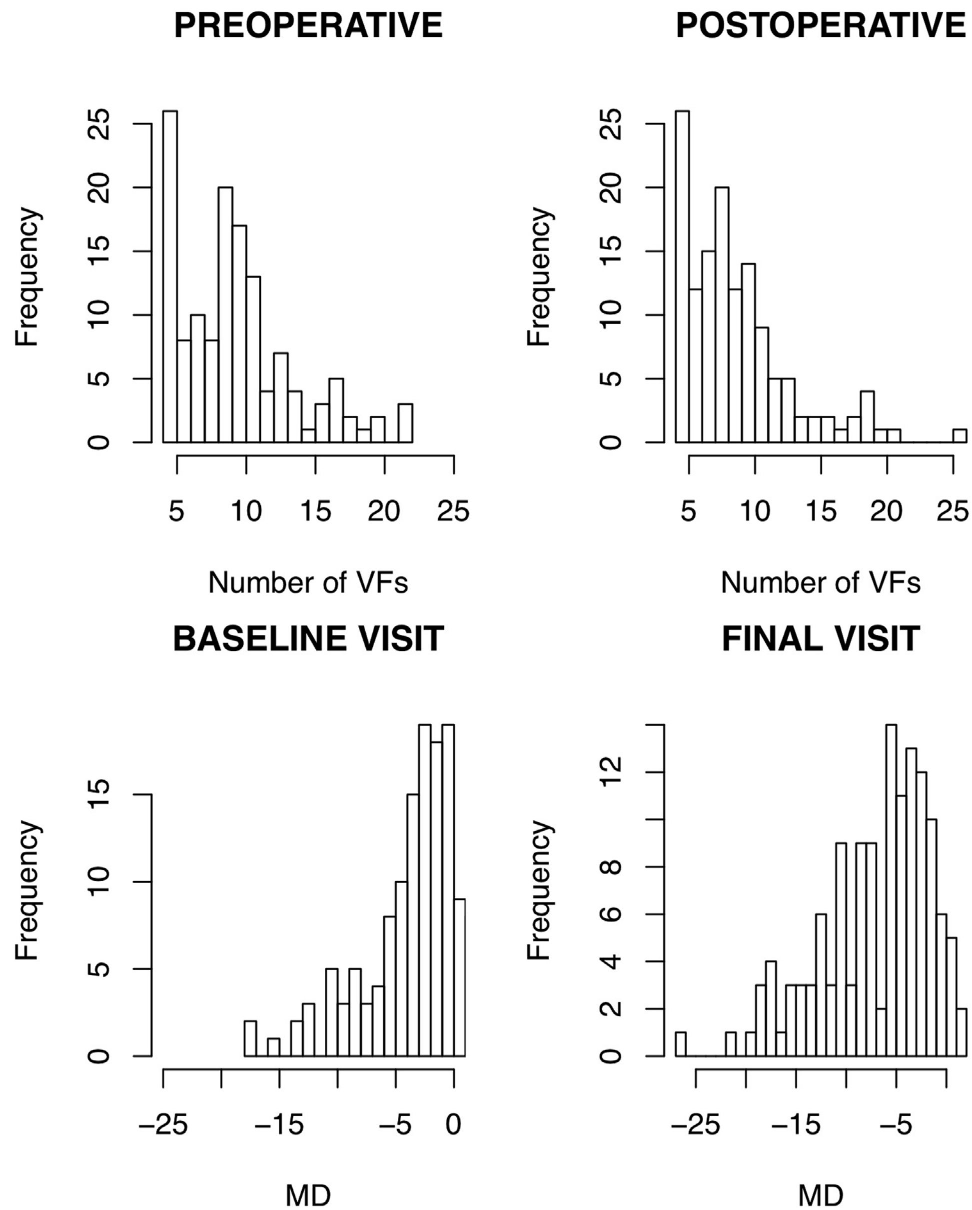

FIGURE 1. (Top) Frequency distribution of series length in the preoperative (Top left) and postoperative (Top right) periods. VF = visual field. (Bottom) Frequency distribution of mean deviation (MD) values at baseline (Bottom left) and final (Bottom right) visits.

no change were calculated, and the mean PRC and PLR value of all locations was compared before and after surgery with a linear mixed model, where the random factor was nested in 3 levels (patient, eye, test location) to account for the within-subject (2 eyes of the same patients), within-eye (52 test locations of the same eye), and within-VF (paired design with same location tested before and after cataract surgery) correlations. Similarly, a logistic mixed model with the same nested random effects was used to determine whether the frequencies of locations with preoperative decay, fast decay, or improvement were different from those with postoperative decay, fast decay, and improvement. For each pointwise series, the root mean squared error for both PRC and PLR was calculated as a measure of goodness of fit.

Associations between clinical variables and visual field decay rates (measured with MD rate, VFI rate, or GRI) after cataract surgery were explored with a linear mixed model with variables (baseline age, baseline MD, central corneal thickness, postoperative mean IOP, postoperative SD of IOP, postoperative peak IOP, and previous trabeculectomy) as fixed factors and the inclusion of the fellow eye as a random factor to account for within-subject correlations. Multivariable linear mixed models were used to identify parameters that may explain the change in visual field decay rates after cataract surgery measured with GRI, MD rate, or VFI rate. The same models were used to test associations between the aforementioned variables and changes in VF rates, defined as the difference between postoperative

TABLE 2. Changes in Visual Acuity, Intraocular Pressure, and Global Visual Field Parameters After Cataract Extraction

	All			Mild			Moderate to Severe		
	Preop	Postop	*P* Value	Preop	Postop	*P* Value	Preop	Postop	*P* Value
logMAR BCVA	0.27 ± 0.18	0.12 ± 0.11	<.001*	0.25 ± 0.18	0.11 ± 0.10	<.001*	0.33 ± 0.19	0.15 ± 0.13	<.001*
IOP, mm Hg									
Mean	13.9 ± 3.1	12.9 ± 3.0	<.001*	14.3 ± 3.0	13.1 ± 3.2	<.001*	12.9 ± 3.1	12.3 ± 2.5	.19
SD	2.7 ± 1.4	2.3 ± 1.2	<.001*	2.7 ± 1.4	2.2 ± 1.1	<.001*	2.8 ± 1.4	2.5 ± 1.5	.24
Peak	19.5 ± 5.5	17.8 ± 5.4	.002*	19.8 ± 5.5	17.8 ± 5.0	<.001*	18.8 ± 5.4	18.0 ± 6.6	.53
No. of meds	1.3 ± 1.0	1.1 ± 0.9	<.001*	1.4 ± 1.0	1.2 ± 0.9	.003*	1.2 ± 1.0	0.9 ± 0.9	.009*
MD, dB	−4.8 ± 4.3	−5.0 ± 4.5	.48	−2.9 ± 2.4	−2.9 ± 2.4	.98	−10.0 ± 4.1	−10.5 ± 4.2	.12
PSD, dB	5.3 ± 3.9	5.5 ± 4.2	.038*	3.8 ± 2.5	3.9 ± 2.8	.47	9.5 ± 3.8	10.2 ± 3.9	.004*
VFI, %	88.0 ± 12.2	87.1 ± 13.2	.022*	93.3 ± 6.3	92.9 ± 6.3	.39	73.7 ± 13.2	71.0 ± 13.9	.011*

BCVA = best-corrected visual acuity; IOP = intraocular pressure; logMAR = logarithm of the minimum angle of resolution; MD = mean deviation; Meds = medications; Postop = postoperative; Preop = preoperative; PSD = pattern standard deviation; VFI = visual field index.

Statistically significant *P* values are indicated by an asterisk (*).

TABLE 3. Mean Pointwise Rate of Change, Pointwise Linear Regression Rates, and Proportion of Various Outcomes Before and After Cataract Surgery

	PRC (%/Year)			No. of Locations (%)		
	Preoperative	Postoperative	*P* Value	Preoperative	Postoperative	*P* Value
Total	−0.62 ± 2.47	−1.35 ± 3.71	<.001*	6437 (100 %)	6454 (100 %)	
No change	−0.41 ± 2.02	−0.80 ± 2.88	<.001*	5479 (85.1 %)	5227 (81.0 %)	<.001*
Decay	−3.36 ± 3.13	−4.94 ± 4.84	<.001*	720 (11.2 %)	1044 (16.2 %)	<.001*
Slow decay	−2.24 ± 1.05	−2.50 ± 1.10	<.001*	595 (9.2 %)	737 (11.4 %)	<.001*
Fast decay	−8.73 ± 4.04	−10.79 ± 5.30	<.001*	125 (1.9 %)	307 (4.8 %)	<.001*
Improvement	2.75 ± 2.52	3.50 ± 3.36	<.001*	238 (3.7 %)	183 (2.8 %)	<.001*
	PLR (dB/Year)			**No. of Locations (%)**		
	Preoperative	Postoperative	*P* Value	Preoperative	Postoperative	*P* Value
Total	−0.20 ± 0.82	−0.42 ± 1.16	<.001*	6437 (100%)	6454 (100%)	
No change	−0.15 ± 0.67	−0.28 ± 0.89	<.001*	6109 (94.9%)	5858 (90.7%)	<.001*
Decay	−1.99 ± 1.18	−2.38 ± 1.51	.003*	265 (4.1%)	534 (8.3%)	<.001*
Slow decay	−1.37 ± 0.26	−1.39 ± 0.26	.44	174 (2.7%)	303 (4.7%)	<.001*
Fast decay	−3.18 ± 1.33	−3.67 ± 1.50	.01*	91 (1.4%)	231 (3.6%)	<.001*
Improvement	1.84 ± 1.11	2.25 ± 1.30	.04*	63 (1.0%)	62 (1.0%)	.34

PLR = pointwise linear regression; PRC = pointwise rate of change.

Statistically significant *P* values are indicated by an asterisk (*).

and preoperative rates measured with MD rate, VFI rate, and GRI.

We compared IOP and number of glaucoma medications preoperatively and at specific postoperative time points (1 day; 1 week; 1, 3, and 6 months; and 1, 2, 3, 4, and 5 years after cataract surgery) with a linear mixed model, where the IOP was the outcome variable, the time was the independent variable, and the patient and eye were the random factors to account for the inclusion of both eyes of the same patient and the presence of multiple observations from the same eye. Pairwise difference between preoperative and postoperative values within the models were tested with the Tukey test. We also calculated the mean % IOP decrease as follows: (IOP − mean preoperative IOP)/mean preoperative IOP × 100 (%).

Data were presented as mean (± SD) unless specified otherwise. Calculations were performed with R software version 3.3.2 (Vienna, Austria).

• **COMPARISON GROUP:** To help evaluate the long-term effects of cataract surgery on VF decay rates, subgroup analysis for those eyes that had at least 10 years of follow-up and 10

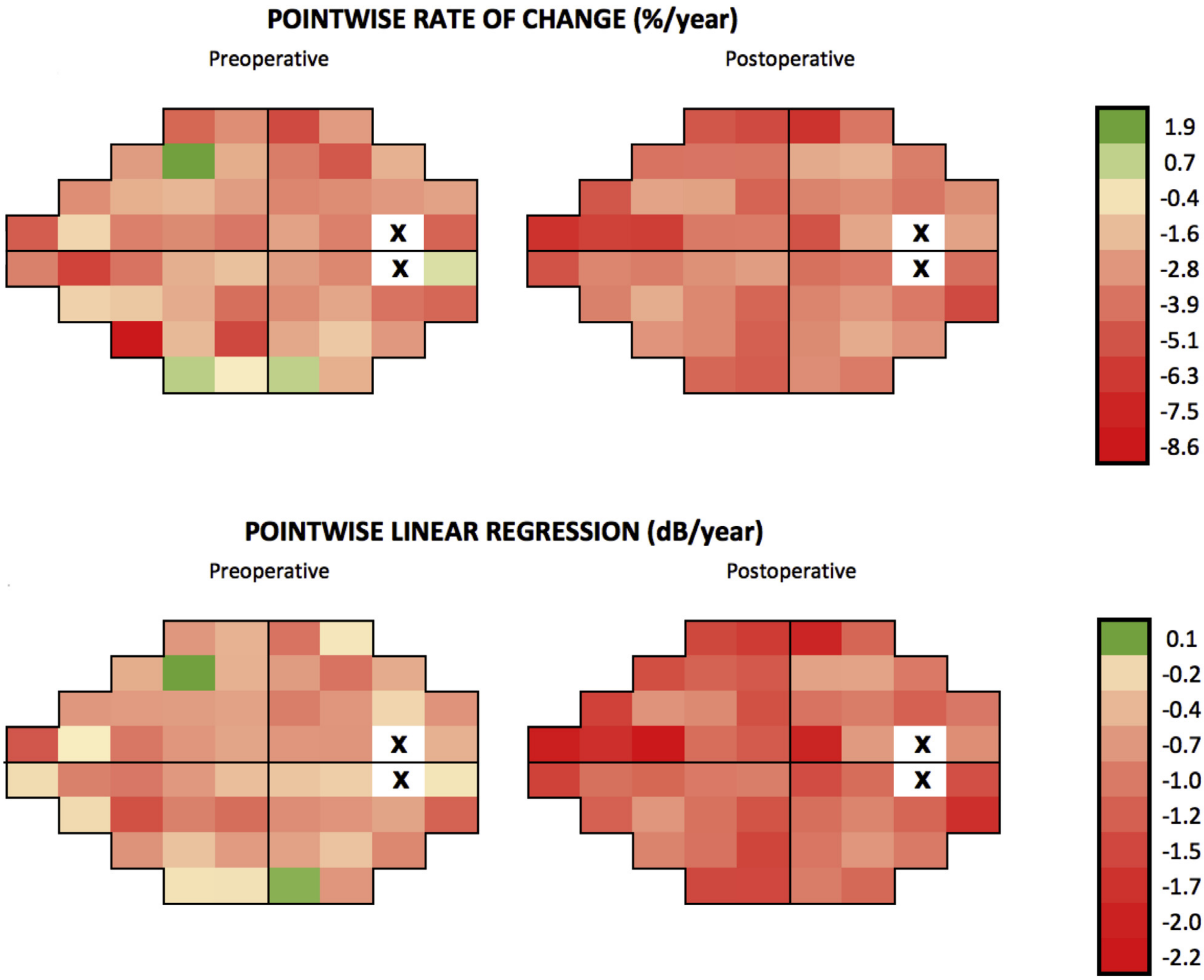

FIGURE 2. Spatial distributions of mean visual field (VF) pointwise rate of change (PRC) preoperatively (Left) and postoperatively (Right). Color scale indicates rates in unit of percentage of normal perimetric range per year (%/year), with negative values indicating decay and positive values denoting improvement.

VFs after cataract surgery was performed as a comparison group. After dividing their postoperative period in half, we compared the visual field decay rates between the first half and the second half of the follow-up period with a linear mixed model, where the patient and the eye were treated as random effects to account for the inclusion of both eyes of the same patient and the presence of multiple observations from the same eye.

RESULTS

ONE HUNDRED THIRTY-FOUR EYES OF 99 PATIENTS WERE included in this study. Of the 134 eyes, 98 (73.1%) and 36 (26.9%) eyes were classified as early and moderate-to-advanced glaucoma, respectively. Demographic characteristics of the study participants are presented in Table 1.

The median (interquartile range) follow-up was 6.5 (4.7-8.1) and 5.3 (4.0-7.3) years before and after surgery, respectively. The frequency distribution of VFs in the preoperative and postoperative period is shown in Figure 1. The mean number of VFs was 9.9 (± 4.2) and 9.3 (± 4.1) before and after surgery, respectively. Distribution of MD values at the baseline and final visits are shown in Figure 1. Baseline visual field global indices were worse in the moderate-to-advanced group than in the mild glaucoma group ($P < .001$ for all). The number of VFs in the postoperative period was slightly higher in the moderate-to-advanced group than in the mild glaucoma group ($P = .04$). None of the other demographic and main clinical data were significantly different between the 2 severity groups.

The mean BCVA significantly improved from 0.27 (± 0.18) before surgery to 0.12 (± 0.11) after cataract extraction ($P < .001$) (Table 2). All IOP parameters significantly decreased in the postoperative period ($P < .01$). The mean

TABLE 4. Visual Field Decay Rates Measured by Glaucoma Rate Index, Mean Deviation Rate, and Visual Field Index Rate Before and After Cataract Surgery

	Total				Mild				Moderate to Advanced			
	Preop	Postop	Delta	*P* Value	Preop	Postop	Delta	*P* Value	Preop	Postop	Delta	*P* Value
MD slope (dB/year)	−0.18 ±0.40	−0.40 ±0.62	−0.22 ±0.70	<.001*	−0.19 ±0.39	−0.39 ±0.61	−0.20 ±0.69	.003*	−0.15 ±0.43	−0.43 ±0.65	−0.28 ±0.75	.023*
VFI slope (%/year)	−0.44 ±1.09	−1.19 ±1.85	−0.74 ±1.92	<.001*	−0.40 ±0.95	−1.06 ±1.75	−0.66 ±1.76	<.001*	−0.57 ±1.41	−1.54 ±2.08	−0.96 ±2.32	.010*
GRI	−5.5 ±10.8	−13.5 ±21.5	−8.0 ±22.8	<.001*	−5.2 ±10.7	−12.9 ±21.0	−7.7 ±22.2	<.001*	−6.3 ±11.2	−15.1 ±22.8	−8.8 ±24.8	.036*

GRI = glaucoma rate index; MD = mean deviation; Postop = postoperative; Preop = preoperative; VFI = visual field index.
Statistically significant *P* values are indicated by an asterisk (*).

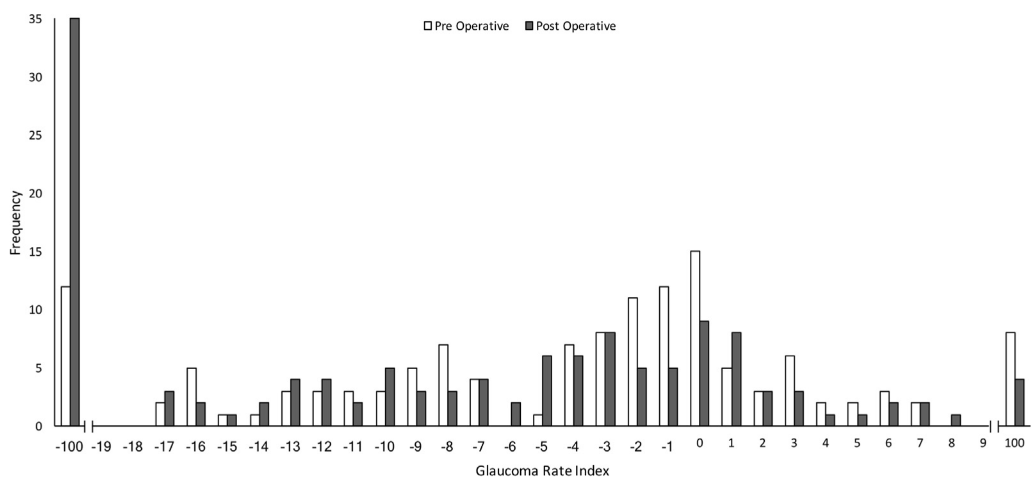

FIGURE 3. Frequency distributions of Glaucoma Rate Index before and after cataract surgery.

number of glaucoma medications was also reduced after cataract extraction ($P < .001$). As shown in Supplementary Figure 1 (Supplemental Material available at AJO.com), IOP decreased significantly 3 months after surgery ($P = .04$), and this effect persisted through 5 years after cataract surgery, although the difference was significant only at the 1-year time point ($P = .009$). The IOP peaked the day following the cataract extraction, and the difference was significant when compared with the baseline preoperative IOP ($P < .001$). As shown in Supplementary Figure 1, the number of medications significantly ($P < .05$) decreased from baseline at every time point except the 5-year follow-up ($P = .58$).

No significant change after cataract extraction was observed for MD ($P = .5$), while PSD ($P = .04$) and VFI ($P = .02$) significantly increased and decreased, respectively. PSD slightly increased after cataract surgery in the moderate-to-advanced glaucoma group ($P = .004$), but not in the early group ($P = .5$). VFI slightly decreased after cataract surgery in the moderate-to-advanced glaucoma group ($P = .011$), but not in the early glaucoma group ($P = .4$) (Table 2).

• **POINTWISE VISUAL FIELD DECAY RATES:** The mean PRC values and the proportion of test locations status (improving, stable, slow decay, and fast decay) before and after the cataract extraction are shown in Table 3. Overall, the mean PRC (%/year) of all test locations worsened from -0.62 (± 2.47) preoperatively to -1.35 (± 3.71) postoperatively ($P < .001$). Both the number of decaying locations ($P < .001$) and their PRC ($P < .001$) worsened in the postoperative period. When worsening locations were divided into slow and fast decay, both groups experienced significant worsening in terms of number of locations ($P < .001$) and PRC values ($P < .001$). Although the number of stable locations significantly decreased in the postoperative period ($P < .001$), the mean PRC value slightly accelerated after cataract extraction ($P < .001$).

TABLE 5. Comparison of the Change in Visual Field Decay Rates After Cataract Surgery According to Previous Trabeculectomy History

	No Previous Trabeculectomy (N = 111)				Previous Trabeculectomy (N = 23)			
	Before	After	Delta	*P* Value	Before	After	Delta	*P* Value
MD slope (dB/year)	−0.18 ±0.39	−0.42 ±0.63	−0.24 ±0.74	<.001*	−0.18 ±0.47	−0.31 ±0.58	−0.13 ±0.52	.22
VFI slope (%/year)	−0.42 ±1.05	−1.23 ±1.86	−0.81 ±1.97	<.001*	−0.54 ±1.27	−0.97 ±1.80	−0.42 ±1.67	.21
GRI	−5.4 ±11.1	−14.3 ±22.2	−8.8 ±24.4	<.001*	−5.9 ±9.1	−9.8 ±17.2	−3.9 ±13.0	.15

GRI = Glaucoma Rate Index; MD = mean deviation; VFI = visual field index.
Statistically significant *P* values are indicated by an asterisk (*).

TABLE 6. Variables Associated With Postoperative Visual Field Rates and Their Change After Cataract Surgery at the Multivariate Analysis

	Postoperative Rates						Delta Rates (Postoperative Rate–Preoperative Rate)					
	MD Rate		VFI Rate		GRI		MD Rate		VFI Rate		GRI	
Variable[a]	Coeff	*P* Value	Coeff	*P* Value	Coeff	*P* Value	Coeff	*P* Value	Coeff	*P* Value	Coeff	*P* Value
Age	0.064	.80	0.003	.92	0.007	.98	−0.001	.96	0.008	.76	0.270	.38
Baseline MD	2.434	.12	0.126	.007*	0.833	.11	0.030	.09	0.106	.02*	0.824	.15
CCT	0.001	.98	−0.003	.47	0.080	.08	0.000	.81	0.001	.86	0.056	.27
Postoperative peak IOP	0.272	.60	−0.014	.63	−0.276	.41	−0.025	.02*	−0.045	.12	−0.387	.30
Previous trabeculectomy	0.898	.34	−0.348	.48	−3.950	.47	−0.180	.33	−0.223	.65	−2.671	.66

CCT = central corneal thickness; Coeff = coefficient; GRI = Glaucoma Rate Index; IOP = intraocular pressure; MD = mean deviation; SE = spherical equivalent; VFI = visual field index.
Statistically significant *P* values are indicated by an asterisk (*).
[a]For increase in 1 unit of measurement.

Similar results were observed when pointwise decay rates were analyzed with PLR analysis (Table 3). Although the number of slowing decay locations significantly increased after surgery ($P < .001$), linear slow decaying rates did not significantly differ ($P = .44$). As shown in Supplementary Figure 2 (Supplemental Material available at AJO.com), the 2 models exhibited similar fits.

Figure 2 shows the spatial distribution of mean PRC and PLR before and after surgery. Overall, all the locations accelerated their rates of progression in the postoperative period compared to the preoperative period, and locations in the superior nasal area experienced the fastest decay. None of the test locations exhibited an improving trend postoperatively.

• **GLOBAL VISUAL FIELD DECAY RATES:** As shown in Table 4, VF rates significantly worsened according to all the methods ($P < .001$). Figure 3 represents the frequency distribution of the preoperative and postoperative GRI values. The number of eyes with decaying GRI significantly increased from 43 (23.6%) preoperatively to 79 (43.4%) postoperatively ($P < .001$). The increase in the number of progressing eyes was seen both for the slow (43 to 73, $P = .001$) and fast (0 to 6, $P = .041$) progressors. The number of stable eyes significantly decreased from 137 to 102 ($P < .001$), while the numbers of improving eyes did not significantly change before (n = 2) and after (n = 1) cataract surgery ($P > .99$).

Twenty-three eyes (17.2%) had trabeculectomy before cataract surgery. In eyes with no previous trabeculectomy, all visual field decay rates based on MD rate, VFI slope, or GRI worsened after cataract surgery ($P < .001$, $P < .001$, $P < .001$, respectively). However, in eyes with previous trabeculectomy, there was no significant change in the visual field decay rates after cataract surgery ($P > .05$ for all) (Table 5). The difference between delta MD rate ($P = .65$), VFI rate ($P = .66$), or GRI rate ($P = .46$) between eyes without and with previous trabeculectomy was not statistically significant.

• **FACTORS PREDICTIVE OF POSTOPERATIVE RATES:** Table 6 and the Supplementary Table (Supplemental Material available at AJO.com) show the factors associated with the rates of VF decay and their changes after cataract surgery in the univariable and multivariable analyses, respectively. Worse baseline MD was significantly associated with the rates of postoperative VF decay as measured by VFI rate ($P = .007$) and with accelerated rates of progression after surgery, measured as the difference between postoperative and preoperative VFI rate ($P = .02$). The postoperative peak IOP was associated with the difference between postoperative and preoperative rates of MD ($P = .02$). Trabeculectomy prior to cataract surgery was not associated with VF rates regardless of the method used.

• **COMPARISON GROUP:** Thirty-six eyes of 29 patients were included in the comparison group (pseudophakic throughout the entire VF follow-up). We compared the VF decay rates between the first and second halves of follow-up. The mean GRI was -0.36 (± 10.85) during the first half and -9.71 (± 14.78) during the second half ($P < .001$). The VF decay rates measured with MD slope were also worse in the second half compared to the first half (-0.29 [± 1.63] dB/year and -1.27 [± 1.79] dB/year, respectively; $P < .001$), as was VFI slope (-0.66 [± 1.19]%/year and -0.77 [± 1.07]%/year, respectively; $P = .003$).

DISCUSSION

IN THIS STUDY, WE FOUND THAT GLAUCOMATOUS VF decay rates measured with the MD rate, VFI rate, and GRI rate all worsened after cataract surgery, except for eyes that underwent prior trabeculectomy. Although all IOP parameters changed favorably after cataract surgery, these modifications did not slow VF decay rates. Among the studied parameters, higher postoperative peak IOP and worse baseline MD were significantly correlated with faster postoperative VF decay rates, suggesting that these variables are risk factors for further glaucoma deterioration.

Cataract causes a generally diffuse visual field loss in patients with glaucoma, and several studies have dissected the impact of cataract progression and cataract surgery on global visual field indices (ie, MD, PSD, VFI), with discordant results.[5–7,13,20–25] The degree of postoperative change in global indices varies according to the severity of both glaucoma and cataract.[6,24] In our study, we did not observe any significant change in these indices after cataract extraction.

A number of studies have reported changes in visual field global indices after cataract surgery, but studies of visual field decay rates after cataract surgery are few. Bengtsson and Heijl[25] evaluated the MD and VFI rates of change in patients undergoing cataract surgery. They found that VFI rates were smaller than MD rates, especially before cataract surgery, and with a narrower CI, which is indicative of higher precision. In a previous study, we evaluated the effect of cataract extraction on the visual field decay rates in patients with glaucoma measured with regression of both global indices and of single locations.[13] In that study, we did not find any significant difference in the rates of progression after cataract surgery with regard to the MD or VFI rates.[13] When test locations were classified into slow and fast decay, we found that the slow component rate of visual field decay is significantly slowed after cataract extraction, while the fast component rate did not change after surgery.[13] Those results suggested that cataract development is the main contributing factor for the deterioration of the slow component, which represents more diffuse and nonspecific decline related to aging and media opacity.[13] In contrast, the fast component reflects more focal, rapidly deteriorating test locations from glaucoma, and was not affected by cataract surgery.[13]

In the present study, we applied a novel method called GRI to further characterize the rates of VF decay.[12] This technique is based on exponential fits of pointwise threshold sensitivities in serial visual field tests, and provides a graphical presentation of spatially conserved, standardized pointwise rates in which test locations are partitioned into the following categories: immeasurable, no change, slow decay, fast decay, and improving.[12] Since it is based on exponential regression, GRI does not assume a VF decay constant over time; the decay rate, termed PRC, is expressed as a percentage of the entire normal perimetric dynamic range corrected for age and location. The method uses 2 tests (Cook's distance and the Studentized residual test) to remove outliers that can affect the model fit and to improve the signal-to-noise ratio. To provide a global measure that reflects the status of the entire visual field, a GRI score is calculated from the normalized sum of the PRC values of the significant locations across the entire VF. In contrast to other global measures of rates of progression (eg, MD rate, VFI rate), GRI score is calculated only on test locations with a significant change, and excludes those locations with a stable trend, which can mask the focal, but clinically important, VF changes. Also, the method allows the distinction between fast- and slow-progressing locations and eyes, and it is able to detect improvement, despite that its main application relies on individuation and quantification of VF decay.

In this study, the PRC and PLR decay rates of all test locations deteriorated after cataract surgery and the proportion of decaying locations was significantly increased after cataract surgery. The changes in MD rates, VFI rates, and GRI after surgery all showed similar trends. Visual field decay rates measured with MD rate, VFI rate, and GRI all showed that the VF decay rates worsened after cataract surgery. To better clarify the unexpected worsening of VF decay after cataract surgery, despite significant IOP reduction, we performed a subgroup analysis for pseudophakic eyes with sufficient follow-up periods and VFs. After dividing the postoperative cataract period into 2 halves, we compared the first half and second half. The VF decay rates measured with MD rate, VFI rate, and GRI were all worse in the second half than in the first half.

We have previously reported that the loss of visual sensitivity from glaucoma is nonlinear over time and different phases of the disease are associated with different measured perimetric rates of deterioration.[9,11] The course of perimetric decay is best described by a logistic function (Supplementary Figure 3; Supplemental Material available at AJO.com), with asymptotes corresponding to normal sensitivity values and perimetric blindness; an inflection point, which is the steepest part of the curve; and a drop-off and level-off point for the beginning and end of the decaying period, respectively. The faster rate of decay in the second part of the follow-up in both the cataract and comparison groups may be related to the natural history of the glaucomatous disease, which is nonlinear over time.[11] Our study has a long follow-up, and it is more likely to show the effects of progressive glaucoma, even under treatment. Since the rate of deterioration after cataract surgery was always later in the course of glaucoma than was the rate of deterioration before cataract surgery, at least some of the failure of cataract surgery to reduce or maintain the rate of deterioration (compared to the rate of deterioration before cataract surgery) could be explained by this evidence, which suggests the possibility that the rate of deterioration may increase over time. Supplementary Figure 4 (Supplemental Material available at AJO.com) shows the case of a patient with progressive nonlinear VF decay over the course of 19 years, which accelerated following cataract extraction.

The occurrence of early postoperative IOP spikes could be another possible explanation to the worsening in the VF rates following cataract surgery. Although IOP spikes could have contributed to the worsening of glaucomatous damage, it is unlikely that they played a pivotal role, since the accelerated VF decay took place over the course of many years and a similar decay was also observed in the comparison group.

Our results indicate that cataract surgery alone does not seem to slow progression of the disease or play a role in slowing visual field progression with long-term exposition of the glaucoma as compared to rates measured during the progression of the cataract. All patients enrolled in this study, even those with advanced baseline damage, had stable glaucoma with medical therapy or previous filtering surgery. In our practice, we usually do not combine minimally invasive glaucoma surgery (MIGS) or other, more aggressive surgical options with cataract extraction in patients unless glaucoma is advancing or the IOP is consistently above baseline. Also, the minimum follow-up required post cataract extraction (>3 years) dictated that the surgery was performed before or at the dawn of the MIGS era. It remains still unknown whether the combination of cataract extraction and MIGS can modify the course of glaucomatous decay in the long run.

It must be noted that this study does not provide any information about how the visual field progression might have been different had cataract surgery not occurred at that point in the course of the glaucoma, as we have neither gathered any data nor performed any analyses in this regard. This study only shows that VF rates accelerate following uncomplicated cataract extraction, but the reader should not reach the erroneous conclusion that patients would not have experienced an increase of the VF progression rate if they had not had cataract surgery at that point in the course of the glaucoma. In other words, it is likely that worsening of VF rates occurred despite cataract extraction and not because of it. As discussed above, VF rates are not constant over the course of the glaucomatous disease and tend to increase over time.[11,26]

To investigate the factors that may affect changes in VF decay rates after cataract surgery, we divided eyes based on baseline glaucoma severity and history of prior trabeculectomy. The trend was also similar to the entire cohort of patients when we divided the patients into 2 groups based on their baseline MD. The worsening of the rate of deterioration after cataract surgery in the group with mild glaucoma was more prominent, but the difference between the 2 groups was not statistically significant. When we divided eyes into groups by whether trabeculectomy was performed before cataract surgery or not, the VF decay rates did not change significantly after cataract surgery in the group that had prior trabeculectomy. In contrast, the VF decay rates with all 3 methods were significantly worse after cataract surgery in the eyes without previous trabeculectomy. Trabeculectomy is known to slow the rate of perimetric decay and can improve visual function in some patients with glaucoma.[27,28] Postoperative mean IOP and peak IOP were statistically lower in the group with prior trabeculectomy than in the nontrabeculectomy group. We hypothesize that trabeculectomy minimizes IOP peaks after cataract surgery and helps to decrease VF decay rates after cataract surgery.

IOP is a well-recognized risk factor for the development and progression of glaucoma and remains the only modifiable risk factor in glaucoma treatment.[3,29–31] In agreement with previous studies,[32–35] all IOP parameters had a significant and sustained improvement after cataract surgery; however, the measured rate of glaucoma progression surprisingly did not slow. In the present study, postoperative peak IOP was significantly associated with postoperative rates and the change in rates compared with the preoperative period. The importance of IOP peaks in glaucoma progression has been previously reported.[36,37] The results presented here are consistent with risk factor analyses of open-angle glaucoma patients in larger glaucoma cohorts. De Moraes and associates[38] reported that peak IOP, more so than mean IOP, was a significant risk factor for glaucoma progression. Furthermore, the presence of a filtering bleb may prevent early postoperative IOP spikes, which could be 1 of the factors promoting VF worsening in the postoperative period.

Our study also identified worse baseline VF damage as a risk factor for VF worsening after cataract surgery. We believe that this finding is related not to the cataract extraction itself, but rather to the progression of the glaucomatous disease. The association between disease severity at baseline and glaucoma progression has been previously illustrated.[39]

There are several limitations to this study. One limitation is its retrospective design, which prevents homogeneity in the data. The effect of lens opacities on visual field test results may be influenced by lens opacity location and severity,[21] which was not addressed in this study. Most of the patients included in the current study were white and had primary open-angle glaucoma, so we cannot comment on the effects of race and different types of glaucoma. Subanalyses in eyes with moderate-to-advanced glaucoma or with previous trabeculectomy were conducted on a small subset of patients, so these and other analyses, such as the comparison of the rate of deterioration after cataract surgery between the group with mild glaucoma and the group with moderate/advanced glaucoma, are likely underpowered. Additionally, this study reviewed the results of patients in a tertiary glaucoma clinic, and results may not be generalizable to glaucoma patients in other clinical settings. The results must be interpreted prudently, since they do not substantiate a causal relationship, but rather demonstrate variables associated with VF decay rates after cataract surgery.

In conclusion, VF decay rates measured with MD rates, VFI rates, and GRI worsened after cataract surgery, and postoperative peak IOP seems to be a main risk factor for further deterioration after cataract surgery. The sustained reduction of IOP associated with cataract surgery does not slow the rate of glaucomatous VF decay in patients with treated open-angle glaucoma.

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