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The Impact of Surgical Intraocular Pressure Reduction on Visual Function Using Various Criteria to Define Visual Field Progression

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Abstract

Purpose—To examine the impact of surgical Intraocular pressure (IOP) reduction on visual function using various methods to define visual field (VF) progression.

Methods—A retrospective chart review was conducted on consecutive glaucoma patients who underwent surgical IOP reduction between January 1, 2002 and December 31, 2007. All subjects had glaucomatous optic neuropathy, a minimum of 5 preoperative and 5 postoperative visual fields, and were followed for a minimum of 2 years both before and after surgery. VF progression was determined using Guided Progression Analysis (GPA), linear regression analysis of the visual-field index (VFI), and individual sensitivity values using Progressor™ software.

Results—Seventeen eyes of 17 patients (mean age 77.9 ± 9.9 years) were enrolled. Subjects were followed for a mean 5.8 ± 2.4 years prior to surgery and 4.5 ± 1.5 years following surgery. Mean postoperative IOP (11.3 ± 4.2mmHg) and medications (1.3 ± 1.3) were significantly ($p<0.001$ and $p=0.01$) reduced compared with prior to surgery (18.0 ± 3.9mmHg, 2.4 ± 0.9 respectively). The number of eyes judged to have VF progression using any method during the postoperative period (3 of 17, 17.6%) was significantly ($p=0.03$) reduced compared to the preoperative period (9 of 17 eyes, 52.9%). Using VFI criteria, 8 eyes were judged to have preoperative VF progression and 1 eye had persistent VF progression during the postoperative period. None of the eyes judged to have preoperative VF progression using EMGT (n=4) and Progressor criteria (n=1) demonstrated persistent VF progression during the postoperative period. Among eyes with preoperative VF progression, the postoperative slope of mean deviation (−0.21 ± 0.23 db/yr) was significantly ($p=0.03$) reduced compared with prior to surgery (−1.01 ± 0.23 db/yr).

Conclusions—Despite differences in the criteria used to define visual field progression, glaucoma surgical IOP reduction significantly reduces the incidence and rate of visual field progression.

Keywords

glaucoma; visual field progression; intraocular pressure; optic nerve

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INTRODUCTION

Elevated intraocular pressure (IOP) is a major risk factor for development and progression of glaucomatous optic neuropathy. The Early Manifest Glaucoma Trial (EMGT) showed that non-surgical IOP reduction resulted in a significant delay in glaucoma progression in patients with open-angle glaucoma.[1] Furthermore, the Advanced Glaucoma Intervention Study demonstrated reduced progression of visual field (VF) defects with surgical IOP reduction.[2]

Limited information exists regarding the impact of surgical IOP reduction on visual function in glaucomatous eyes. In the Collaborative Initial Glaucoma Treatment Study, surgery as initial treatment was more effective than medical therapy in reducing IOP and preventing VF progression in subjects with more advanced visual field loss at baseline.[3] Folgar and colleagues[4] examined the impact of surgical IOP reduction on the rate of VF progression among a cohort of 28 glaucomatous eyes. The global rate of progression was reduced by more than two thirds and there was a significant reduction in the rate of localized progression of the most rapidly progressing points as judged using pointwise linear regression (PLR). Recently, Sehi et al demonstrated that reversal of retinal ganglion cell dysfunction occurs following surgical reduction of IOP and may be quantified using pattern electroretinogram optimized for glaucoma screening (PERGLA).[5]

Accurate methods for detecting disease progression are essential to monitor glaucoma patients and evaluate the efficacy of therapy. Statistical methods for evaluating glaucomatous visual field progression have evolved considerably, yet criteria for defining progression remains inconsistent in the absence of established standards. [6–12] There are limited data comparing these analysis methods for progression detection following glaucoma surgery. We hypothesized that the incidence and rate of visual field progression was significantly reduced in glaucomatous eyes following surgical IOP reduction, irrespective of the criterion used to define visual field progression. The purpose of this study was to examine the impact of surgical IOP reduction on visual function using various methods to define visual field progression.

METHODS

Study Population

A retrospective chart review was conducted on consecutive glaucoma patients who underwent surgical IOP reduction between January 1, 2002 and December 31, 2007. All subjects had a minimum of 5 preoperative and 5 postoperative visual fields performed using a Swedish Interactive Threshold Algorithm (SITA) standard 24-2 strategy (Humphrey Field Analyzer II; Carl Zeiss Meditec, Dublin, CA). Only reliable test results (≤ 33% fixation losses, false-negative results and false-positive results) were included. Glaucoma surgery was performed by two glaucoma specialists (DSG, DLB) and was indicated when there was suspected VF progression, or if the IOP was considered unsatisfactory relative to the stage of glaucomatous damage.

Glaucoma patients had glaucomatous optic nerve damage and a corresponding repeatable abnormal VF defined as an abnormal glaucoma hemifield test or pattern standard deviation (PSD) outside 95% normal limits. Glaucomatous optic neuropathy was defined as neuroretinal rim narrowing to the optic disc margin, notching, excavation, or RNFL defect. Exclusion criteria consisted of age less than 18 years old, prior intraocular surgery except for uncomplicated cataract extraction, eyes with ocular disease that could affect the VF (corneal pathology, uveitis, vitreoretinal pathology, or non-glaucomatous optic nerve disease), and eyes with less than 5 VF examinations prior to or following glaucoma surgery.

Data Collection Procedures

We reviewed the medical records of patients satisfying enrollment criteria and data was abstracted concerning patient demographics, type of glaucoma, method of surgical intervention, and postoperative complications. VF indices used to evaluate the rate of progression consisted of mean deviation (MD), pattern standard deviation (PSD), and visual field index (VFI). We also examined the number of progressing VF points and the global rate of progression, which were automatically generated using Progressor™ software. Preoperative and postoperative IOP measurements were obtained using Goldmann applanation tonometry and recorded at each visit. Data was collected concerning the number of glaucoma medications used at each visit. IOP measurements from all visits before surgery were averaged to calculate the mean and SD prior to surgery, maximum IOP, and range of IOP measurements. IOP measurements from all visits starting 8 weeks after the date of surgery were averaged to provide the mean and SD after surgery, maximum IOP and range of IOP measurements. Visits within 2 months after surgery were excluded to eliminate outliers caused by the large variability in IOP that characteristically occur in the immediate postoperative period.

Assessment of Visual Field Progression

Visual field progression was defined using 3 analysis methods. Eyes were classified as preoperative and postoperative progressors or non-progressors based upon the presence or absence of VF progression using any of the 3 analysis methods. The first method employed Guided Progression Analysis (GPA; Humphrey Field Analyzer; Version 4.2). GPA uses statistical criteria designed for the Early Manifest Glaucoma Trial[13] and compares the locations on pattern deviation change probability map on follow-up visual fields to the average of 2 baseline exams. An automated analysis identifies test locations that show change greater than the expected variability in pattern deviation (at the 95% significance level). Progression was defined as a significant change detected in ≥3 points, and repeated in the same locations in 3 consecutive follow-up tests, categorized by the GPA software as “Likely Progression”.

The second method was based upon linear regression analysis of sequential fields to measure the slope of the Visual Field Index (VFI; Humphrey Field Analyzer; software version 4.2 Carl Zeiss Meditec Inc, Dublin, CA). Progression was defined as a significant ($p<0.05$) decline in the slope of the VFI, an age-corrected index with a range from 0 to 100 calculated based on the pattern deviation probability map and the total deviation plot.[14] The final analysis method employed automated pointwise linear regression (PLR) analysis of VF sensitivity values using Progressor™ software (version 3.3; Medisoft Inc, Leeds, UK) which generates slopes to analyze the rate of global and local sensitivity change and the associated level of statistical significance (p-values).[7] Progression was defined as a significant ($p<0.01$) sensitivity loss >1dB/year detected in ≥ 2 adjacent test locations in the same hemifield.[15]

Statistical Analysis

Statistical analysis was performed using JMP software version 8.0 (SAS Inc., Cary, NC) and SPSS 18 (SPSS, Chicago, IL). Clinical characteristics of the study population were compared using one-way analysis of variance (ANOVA), and independent samples T-test. Categorical variables were compared using the chi-square and McNemar tests. Mean slopes of MD, PSD, and VFI were calculated using linear regression analysis. Rates of progression before and after surgery were compared within the same subject (Analysis of Variance). The same approach was used to evaluate the IOP mean, maximum and range. All tests were two-sided and p-value of < 0.05 was considered significant.

RESULTS

A retrospective review was conducted on consecutive glaucoma patients who underwent surgical IOP reduction between January 1, 2002 and December 31, 2007. The charts of 806 patients were evaluated for enrollment. 789 patients were excluded from the analysis (755 had <10 reliable VF examinations, 34 had co-morbid ocular disease that could impact VF assessment). Seventeen eyes of 17 patients (mean age 77.9 ± 10.1 years) were enrolled (Table 1). Eleven eyes (65%) underwent trabeculectomy with mitomycin C (MMC), 5 eyes (29%) underwent combined phacoemulsification and trabeculectomy with MMC, and 1 eye (6%) underwent glaucoma drainage device implantation. The mean numbers of preoperative and postoperative VF examinations were 7.0 ± 2.4 and 6.5 ± 1.9, respectively. Subjects were followed for a mean of 5.8 ± 2.4 years prior to surgery and 4.5 ± 1.5 years following surgery.

All eyes were phakic at baseline. Eleven of 17 eyes (65%) underwent cataract surgery during the study (5 at the time of initial glaucoma surgery, and 6 during the postoperative period). In order to determine the potential impact of cataract on visual function, we compared the change in vision over time of phakic eyes (n=6) to pseudophakic eyes (n=11). Compared to baseline, the change in vision among pseudophakic eyes (−0.043 +/− 0.16 logMAR) was similar (p=0.16, one way ANOVA) to the change in vision among phakic eyes (0.061 +/− 0.056 logMAR). Presence or absence of cataract surgery during the study period was not significantly associated with VF progression status using GPA, VFI, PLR or any analysis method (p=0.86, logistic regression analysis).

Table 2 demonstrates the incidence of VF progression among the study population based upon the three criteria used to assess progression. The number of eyes judged to have VF progression using any method during the post-operative period (3 of 17, 17.6%) was significantly (p=0.03) reduced compared to the pre-operative period (9 of 17 eyes, 52.9%). Using VFI criteria, 8 eyes were judged to have pre-operative VF progression and 2 eyes had persistent VF progression during the post-operative period. None of the eyes judged to have pre-operative VF progression using EMGT (n=3) and Progressor criteria (n=1) demonstrated persistent VF progression during the postoperative period.

Among the entire cohort, mean postoperative IOP (11.3 ± 4.2mmHg) and medications (1.3 ± 1.3) were significantly (p<0.001 and p=0.01) reduced compared with prior to surgery (18.0 ± 3.9mmHg, 2.4 ± 0.9 respectively). Significant reduction in mean postoperative IOP (Tables 3 and 4) was seen in eyes with preoperative VF progression (17.9 ± 3.5 mmHg prior to surgery, 12.0 ± 4.0 mm Hg following surgery, p<0.001) and non-progressors (18.0 ± 4.5 mm Hg prior to surgery, 10.5 ± 4.6 mmHg after surgery, p=0.005). Reduction in maximum IOP was seen in eyes with preoperative VF progression (22.2 ± 4.4 mmHg prior to surgery, 16.4 ± 4.8 mmHg after surgery, p=0.004) and non-progressors (23.1 ± 7.0 mmHg prior to surgery, 13.1 ± 5.6 mmHg after surgery, p=0.007). Although not significant, postoperative progressors tended to have greater maximum IOP and higher range of IOP (p=0.06 and 0.09, respectively) compared with non-progressors. The magnitude of IOP reduction was associated with the change in PSD slope (R = −0.64, p=0.06), but not correlated with the change in slope of MD, VFI or global progression rate (R=0.52, p=0.15; R=0.14, p=0.7; R=0.44, p=0.2, respectively).

Eyes with preoperative VF progression demonstrated a significant (p=0.018) decrease in the slope of VF mean deviation (−1.0 ± 0.9 dB/yr prior to surgery, −0.2 ± 0.38 dB/yr postoperatively). They also demonstrated a significant (p=0.048) reduction in the global VF sensitivity as judged by Progressor from −0.6 ± 0.7 dB/year prior to surgery to −0.2 ± 0.34 dB/year postoperatively. The number of significantly progressing points (1.4 ± 2.0 prior to

surgery, 0.2 ± 0.34 postoperatively) decreased after surgery, but did not reach statistical significance (p=0.08).

We compared the clinical characteristics of progressing and non-progressing eyes (Table 5). Although not significant (p=0.09, 0.06 and 0.09, respectively), postoperative progressors tended to have greater mean (15.0 ± 3.2 vs 10.4 ± 4.1 mmHg), maximum (20.0 ± 2.8 vs 13.8 ± 5.0 mmHg), and a higher range of IOP (9.7 ± 1.5 vs 5.2 ± 3.2 mmHg) compared with non-progressors. Table 6 demonstrates the results of progression evaluation for each patient during the preoperative and postoperative periods.

DISCUSSION

In the present study, we conducted an analysis to compare the impact of surgical IOP reduction on visual function using various methods to define visual field progression. Although event and trend analysis are complementary, there are significant differences in their approach for detection of progression.[9,16] Event-based analyses identify a repeatable and significant change as compared to baseline VF sensitivity measures, while trend-based analyses quantify the rate or velocity of sensitivity change over serial VF examinations. Previous studies[17,18] have shown that different progression criteria do not always identify the same eyes as progressing and have at best only fair to moderate agreement among different algorithms. There is presently no consensus among clinicians or investigators as to the best method for defining glaucomatous visual field progression.

There are few studies that assess the effect of incisional glaucoma surgery on visual field change over time. In the Collaborative Initial Glaucoma Treatment Study,[19] the incidence of optic disc progression was higher in the medicine group (10%) than in the surgical group (3%), and there was less VF progression (as judged using MD values) observed in eyes with advanced VF loss at presentation treated with initial surgery.[3] Nouri-Mahdavi et al[20] compared the performance of PLR, Glaucoma Change Probability Analysis (Carl Zeiss Meditec, Dublin, CA), and the AGIS method for detecting progression among glaucoma patients with 8 years of follow-up and reported high specificity for all methods but limited concordance. Folgar et al[4] studied the efficacy of glaucoma surgery in decreasing the rate of VF progression using PLR in a cohort of 28 patients. The authors found a 70% reduction in the mean global rate of progression after surgery as well as a significant reduction in the number of progressing points after surgery. Koseki and associates[21] reported a significant decrease in global VF progression among 21 eyes using the regression coefficients of the MD in a postoperative period of up to 3 years. Our study differs from prior studies by comparing PLR with criteria commonly employed by clinicians for classification of progression (GPA) and characterization of the rate of progression (VFI). Despite differences in criteria for visual field progression, eyes with preoperative VF progression eyes had a significantly reduced overall incidence of progression and slower rate of VF decline following surgical reduction in IOP compared with non-progressing eyes. These findings emphasize the importance of re-establishing a new baseline following surgical intervention allowing serial comparison of postoperative fields with preoperative examinations for assessment of further progression, and measurement of subsequent changes in the rate of functional loss.

We classified patients as progressors or non-progressors based upon the presence of absence of preoperative VF progression. Non-progressors had preoperative IOP that was considered unsatisfactory relative to the stage of glaucomatous damage and were considered at high risk for future progression. Such patients did not manifest preoperative VF progression, and would therefore not be expected to achieve a significant postoperative change in the incidence or rate of VF progression. In contrast, progressors achieved a significant reduction

in the incidence and rate of VF progression (judged using MD and PLR global rate of progression) with a mean postoperative IOP of 12.0 mmHg. Although not significant, we observed a trend such that eyes with postoperative progression had greater mean, maximum and range in postoperative IOP. Although 24-hour IOP measurements were not assessed in this study, we hypothesize that more successful surgical IOP lowering was not only associated with lower mean IOP but also with reduced IOP fluctuation over time.[22,23]

Various methods for assessment of glaucomatous visual field progression are available including event and trend-based approaches. In this study, we compared several analysis methods commonly employed to judge visual field progression. We found that no single analysis method is ideal for identifying progression and may be influenced by several variables including disease severity, the velocity and magnitude of sensitivity loss over time, and whether the loss in visual sensitivity is localized or generalized. Some methods may be more suitable for identifying localized change such as PLR or GPA, and other methods may be more appropriate for identifying generalized sensitivity loss such as the rate of change in VFI or MD. Our data demonstrates that analysis methods often disagree, which is consistent with other studies[24–26]; and may be complementary to each other.

Our study has limitations that include a retrospective study design and small sample size. Despite an extensive chart review of over 800 patients, only 17 met criteria. As our institution represents a tertiary care facility, patients are often referred for surgical management and subsequently followed elsewhere. Another limitation is the absence of a control population, such as medically treated population, with which to judge the incidence of VF progression. Although fellow eyes of patients enrolled in this study could potentially have served as a useful comparator, such eyes did not satisfy entry criteria precluding their use as controls.

The presence or absence of cataract surgery during the study period had no significant impact on the VF progression status using SAP-GPA, slope of VFI or PLR method. This is not surprising since SAP-GPA uses Early Manifest Glaucoma Trial (EMGT) criteria, which are based on a significant change in 3 or more test locations on the pattern deviation change probability map, and therefore is designed to be robust against bias produced by cataract progression. In addition, the impact of cataract on VFI has been removed by calculating age-corrected defect depth at test locations identified as significantly depressed on the pattern deviation probability map. It is important to note that our analysis was neither designed, nor was it statistically powered, to examine the impact of lens extraction on visual field progression independent of the effect of IOP reduction

In conclusion, despite differences in the criteria used to define VF progression, surgical IOP reduction significantly reduces the incidence of postoperative VF progression. Our data demonstrate that glaucoma surgery reduces the rate of VF progression in patients who demonstrate preoperative progression, and can prevent subsequent VF progression in eyes with unsatisfactory IOP control prior to manifest VF progression.

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Table 1

Baseline clinical characteristics of the study population (n=17)

Clinical Characteristics	Mean (SD)
Age (yrs)	66 (10.1)
Intraocular pressure (mmHg)	19.5 (5.7)
Gender (M/F)	5/12
Diabetes mellitus, n (%)	2 (12%)
Diagnosis, n (%)	
Primary open-angle glaucoma	10 (59%)
Chronic angle-closure glaucoma	2 (12%)
Exfoliation glaucoma	1 (6%)
Normal-tension glaucoma	3 (18%)
Mixed mechanism glaucoma	1 (6%)
Type of glaucoma surgery, n (%)	
Trabeculectomy	11 (65%)
Phacoemulsification and trabeculectomy	5 (29%)
Glaucoma drainage device implantation	1 (6%)
Visual field (VF)	
Mean deviation (dB)	−5.3 (6.0)
Pattern standard deviation (dB)	5.7 (4.5)
Number of preoperative VF exams	7.0 (2.4)
Number of postoperative VF exams	6.5 (1.9)
Follow-up	
Preoperative follow-up (mos)	5.8 (2.4)
Postoperative follow-up (mos)	4.5 (1.5)
Lens status, n phakic (%)	17 (100%)

Table 2

Incidence of visual field progression among the study population based upon three different criteria used to assess progression (n=17).

VF criteria	Progression				p-value*
	No Preop No Postop	Yes Preop No Postop	No Preop Yes Postop	Yes Preop Yes Postop	
VFI	7 (44%)	6 (38%)	1 (6%)	2 (13%)	0.059
GPA	12 (75%)	3 (19%)	1 (6%)	0	0.317
PLR	16 (94%)	1 (6%)	0	0	NA
Any	7 (41%)	7 (41%)	1 (6%)	2 (12%)	0.034

* McNemar's test (comparison of preoperative progression and no postoperative progression to eyes with postoperative progression and no preoperative progression)

VF = visual field; VFI = visual field index; GPA = guided progression analysis; PLR = pointwise linear regression

Table 3

Clinical and visual field (VF) parameters before and after glaucoma surgery among eyes with preoperative visual field progression (n=9).

Parameters	Before Surgery†	After Surgery†	p-value††
Number of medications	2.6 (0.9)	1.6 (1.5)	0.17
Visual acuity (logMAR)	0.12 (0.08)	0.14 (0.08)	0.43
Mean IOP (mmHg)	17.9 (3.5)	12.0 (4.0)	<0.001
Maximum IOP (mmHg)	22.2 (4.4)	16.4 (4.8)	0.004
Range of IOP (mmHg)	8.7 (4.0)	7.2 (2.4)	0.41
Slope of mean deviation (dB/yr)	−1.0 (0.9)	−0.2 (0.38)	0.018
Slope of pattern standard deviation (dB/yr)	0.36 (1.01)	0.32 (0.34)	0.93
Slope of VFI (%/yr)	−3.0 (2.9)	−1.6 (2.3)	0.13
Number of significantly progressing VF points*	1.4 (2.0)	0.2 (0.4)	0.084
Global rate of progression* (db/yr)	−0.6 (0.7)	−0.2 (0.34)	0.048

*Values determined by Progressor™ software

†Values presented as mean (standard deviation)

††One-way ANOVA

IOP = intraocular pressure; VFI = visual field index

Table 4

Clinical and visual field (VF) parameters before and after glaucoma surgery among eyes without preoperative visual field progression (n=8).

Parameters	Before Surgery†	After Surgery†	p-value††
Number of medications	2.1 (1.0)	0.9 (0.9)	0.046
Visual acuity (logMAR)	0.23 (0.18)	0.19 (0.14)	0.62
Mean IOP (mmHg)	18.0 (4.5)	10.5 (4.6)	0.005
Maximum IOP (mmHg)	23.1 (7.0)	13.1 (5.6)	0.007
Range of IOP (mmHg)	8.5 (3.7)	6.4 (4.0)	0.23
Slope of mean deviation (dB/yr)	0.1 (0.8)	−0.2 (0.4)	0.40
Slope of pattern standard deviation (dB/yr)	−0.06 (0.3)	0.2 (0.6)	0.20
Slope of VFI (%/yr)	−0.5 (0.7)	−0.9 (1.4)	0.54
Number of significantly progressing points*	0.4 (0.7)	0.4 (0.5)	1.00
Global rate of progression* (db/yr)	0.2 (0.7)	−0.2 (0.4)	0.21

*Values determined by Progressor™ software

†Values presented as mean (standard deviation)

††One-way ANOVA

IOP = intraocular pressure; VFI = visual field index

Table 5

Clinical and visual field parameters in postoperative progressors and non-progressors.

Parameters mean (SD)	Postoperative Progressors (N=3)	Postoperative Non-Progressors (N=14)	p-value
Postoperative IOP (mmHg)			
Mean (mmHg)	15.0 (3.2)	10.4 (4.1)	0.09
Maximum (mmHg)	20.0 (3.6)	13.8 (5.0)	0.06
Range (mmHg)	9.7 (1.5)	5.2 (3.2)	0.08
Baseline age (yrs)	74.7 (5.5)	64.6 (10.4)	0.13
Baseline visual field			
PSD (dB)	8.2 (3.5)	6.6 (3.7)	0.48
Mean deviation (dB)	−9.8 (7.7)	−7.1 (6.6)	0.53
Exfoliation (n)	1	1	0.33

IOP = intraocular pressure; SD = standard deviation; PSD = pattern standard deviation

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Table 6

Demonstrates the progression status for each patient during the preoperative and postoperative periods using three criteria for assessment of visual field progression.

	Preoperative period			Postoperative period		
Patient	**PLR**	**VFI**	**GPA**	**PLR**	**VFI**	**GPA**
1	No	No	Yes	No	No	No
2	Yes	Yes	Yes	No	No	No
3	No	No	No	No	No	No
4	No	Yes	Yes	No	No	No
5	No	Yes	No	No	No	No
6	No	No	No	No	No	No
7	No	Yes	No	No	Yes	No
8	No	No	No	No	No	No
9	No	Yes	No	No	No	No
10	No	No	No	No	Yes	Yes
11	No	Yes	No	No	No	No
12	No	No	No	No	No	No
13	No	Yes	No	No	No	No
14	No	No	No	No	No	No
15	No	No	No	No	No	No
16	No	Yes	Yes	No	Yes	No
17	No	No	No	No	No	No

PLR = Pointwise Linear Regression; VFI = Visual Field Index; GPA = Guided Progression Analysis