Canadian Glaucoma Study

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3. Impact of Risk Factors and Intraocular Pressure Reduction on the Rates of Visual Field Change

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Objectives: To determine rates of visual field change associated with risk factors for progression in the Canadian Glaucoma Study (abnormal anticardiolipin antibody level, age, female sex, and mean follow-up intraocular pressure [IOP]), and to evaluate the effect of IOP reduction on subsequent rates of visual field change in progressing patients.

Methods: Two hundred sixteen patients (median age, 65.2 years) were followed up at 4-month intervals with perimetry and were monitored for progression. Patients reaching an end point based on total deviation analysis underwent 20% or greater reduction in IOP. Rates of mean deviation (MD) change were calculated.

Results: Patients with 0, 1, and 2 end points had a median of 18, 23, and 25 examinations, respectively. The median MD rate in progressing patients prior to the first end point was significantly worse compared with those with no progression (–0.35 and 0.05 dB/y, respectively). An abnormal anticardiolipin antibody level was associated with a significantly worse MD rate compared with a normal anticardiolipin antibody level (–0.57 and –0.03 dB/y, respectively). Increasing age was associated with a worse MD rate, but female sex and mean follow-up IOP were not. After the first end point, the median IOP decreased from 18.0 to 14.8 mm Hg (20% in individual patients), resulting in a significant MD rate change from –0.36 to –0.11 dB/y.

Conclusions: Patients with abnormal anticardiolipin antibody levels and increasing age had faster visual field change. Modest IOP reduction in progressing patients significantly ameliorated the rate of visual field decline.

Trial Registration: clinicaltrials.gov Identifier: NCT00262626

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RECENT CLINICAL STUDIES AND trials in glaucoma have advanced knowledge on risk factors for the disease.[1-8] A recurring finding from these investigations is the importance of intraocular pressure (IOP) for both the development of the disease in glaucoma suspects and progression in patients with established glaucoma. Lowering IOP reduces the overall incidence of glaucoma in ocular hypertensive subjects[9] and the incidence of progression of established glaucoma across the spectrum of IOP.[10,11]

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Evidence pertaining to risk factors and the effect of IOP reduction is derived almost exclusively from event-based or binary (progression vs no progression) outcomes. In practical terms, it may be more beneficial to determine the effect of a risk factor or its modification on the rate of change such that the clinician can gauge the likelihood of lifetime visual disability with consideration of factors such as age, stage of the disease, and life expectancy.

While there are numerous reports on the rate of visual field change in patients with established glaucomatous visual field loss, most of this evidence is derived from clinical observational studies where the effect of different treatment modalities, frequency of follow-up, and stage of disease have a significant impact on the results. The published rates of mean deviation (MD) change from such studies range from approximately 0 to –2.5 dB/y.[12-14] Estimates of rates of visual field change in controlled studies and trials where treatment interventions and follow-up schedules are standardized are sparse in comparison.[11] The mean rate of visual field change in patients with untreated glaucoma was –0.41 dB/y in the Collaborative Normal Tension Glaucoma Study[15] and –1.08 dB/y in the Early Manifest Glaucoma Trial,[16] although the interpatient variability was large in both trials.

The Canadian Glaucoma Study (CGS) is a prospective multicenter interventional cohort study.[17] Its primary objective was to determine demographic, ocular, and systemic risk factors for glaucomatous visual field progression under an interventional protocol for IOP control. Patients with an end point based on visual field progression underwent additional IOP reduction. In an earlier article, we identified 4 independent risk factors for progression, namely abnormal baseline anticardiolipin antibody (ACA) level, higher baseline age, female sex, and higher mean follow-up IOP.[7] The purpose of this article is 2-fold: first, to provide the rates of visual field change associated with these risk factors; and second, to determine the effect of additional IOP reduction on subsequent rates of visual field change in those patients with progression.

METHODS

The CGS is a multicentered study involving 5 Canadian hospital-based university departments. The study participants, procedures, and baseline data have been detailed elsewhere[17] and are described here briefly. In summary, after enrollment and documentation of several baseline demographic, systemic, and ocular parameters, patients with open-angle glaucoma were followed up with a standardized protocol for IOP control and were examined every 4 months with standard automated perimetry (SAP), short-wavelength automated perimetry, and confocal scanning laser tomography. Optic disc stereophotographs were obtained at baseline and at intervals of 28 months. Patients with confirmed visual field progression received an additional 20% or greater IOP reduction using the treatment protocol.

The CGS is registered with the ClinicalTrials.gov Protocol Registration System (identifier NCT00262626) and was approved by the research ethics committee of each participating center. Written informed consent was obtained from each study patient.

INCLUSION AND EXCLUSION CRITERIA

Patients with either newly or previously diagnosed open-angle glaucoma were enrolled. Inclusion criteria were the following: (1) best-corrected visual acuity of 6/10 or better with the Early Treatment Diabetic Retinopathy Study chart; (2) photographically documented glaucomatous optic disc changes; (3) glaucomatous visual field changes including localized visual field defects, MD better than –10 dB, and a positive glaucoma hemifield test; and (4) nonoccludable anterior chamber angles. Exclusion criteria were the following: (1) significant nonglaucomatous ocular disease; (2) long-term nonglaucomatous ocular medication use; (3) systemic disease with known effects on the visual field; (4) distance refraction greater than 6.00 diopters (D) (equivalent sphere) or greater than 2.50 D of astigmatism; and (5) previous incisional glaucoma surgery. Patients developing other ocular or systemic disease affecting the visual field during the study were excluded.

BASELINE AND FOLLOW-UP EXAMINATIONS

Baseline examinations (separated by 7-10 days) consisted of 2 SAP and short-wavelength automated perimetry examinations, a confocal scanning laser tomographic examination and disc photography, an eye examination, refraction, a blood sample collection, and an objective measurement of peripheral vasospasm. Pertinent to this article, SAP examinations were repeated at 4-month intervals. The full-threshold 30-2 program of the Humphrey Field Analyzer (Carl Zeiss Meditec, Dublin, California) was used with the appropriate refractive correction.

VISUAL FIELD PROGRESSION

Event-based SAP progression criteria based on the glaucoma change probability analyses[18] were used to define an end point.[17] Progression was suspected when 8 or more locations in the total deviation change probability map, with 4 or more clustered locations in a single hemifield, were flagged. Patients with suspected progression underwent another SAP examination within 7 to 10 days and progression was confirmed if there was an overlap of 4 or more locations with 2 or more locations clustered within a single hemifield. If progression was not confirmed at this second examination, a third confirmation examination was conducted within 7 to 10 days. Hence, 2 of 3 examinations had to demonstrate visual field progression. We selected this criterion to ensure a high specificity to minimize the false-positive rate. In a previous study, we estimated the specificity of this progression criterion to be around 95%.[19] When progression was confirmed, the end point occurred at the visit at which visual field progression was first suspected. The visual fields were read by a committee that also had the perimetrist's notes, clinical data, and the ophthalmologist's notes.

IOP AND TREATMENT STEPS

Patients were entered into the study with a baseline target IOP (based on a ≥30% reduction in newly diagnosed patients or a physician-defined reduction based on history and rate of visual field change prior to entering the study). Patients who reached an end point underwent an additional 20% or greater reduction from the baseline target IOP, defined as the new (second) target IOP after progression. The same procedure was repeated for subsequent end points. A stepwise treatment protocol of monotherapy, adjunct topical therapy, argon laser trabeculoplasty, and/or systemic carbonic anhydrase inhibitors and trabeculectomy was used to achieve the target IOP.[17]

STATISTICAL ANALYSIS

The raw SAP data were exported with third-party software (PeriData version 2.2.3; PeriData Software GmbH, Huerth, Germany) and analyzed with standard statistical software (PASW version 18; SPSS Inc, Chicago, Illinois). Pointwise threshold deviations were derived with published normative values and the normal age-related decline in sensitivity.[20] Unweighted MD values were then calculated for each examination.

Rates of MD change, computed with regression analysis, associated with the 4 previously identified independent risk factors for progression[7] (ie, abnormal baseline ACA level, higher baseline age, female sex, and higher mean follow-up IOP) were examined. In patients with at least 1 end point, only data up to the first end point were used to compute MD rates associated with progression and attributed to the risk factors. For patients who had not reached an end point, all visual field data were used.

The effect of IOP reduction on MD rates was evaluated in patients with at least 1 end point. For patients with 1 end point, all visual field examinations prior to and including the end point were used to compute the preprogression MD rate and all subsequent examinations were used to calculate the postprogression MD rate. For patients with 2 end points, the preprogression MD rate was computed with examinations after the first end point up to the second end point, while the postprogression MD rate was computed with all examinations after the sec-

ond end point. This procedure was repeated for subsequent end points.

After the first end point, reduction in IOP was the difference between target IOP and the mean IOP subsequent to the first end point (and mandated IOP reduction) up to the end of the follow-up or second end point. After the second end point, reduction in IOP was the difference between the mean of the last 3 IOP measurements before the second end point and the mean IOP subsequent to the second end point (and mandated further IOP reduction) up to the end of the follow-up or the third end point. This procedure was repeated for subsequent end points.

To ensure that MD rates were based on a reasonable number of visual field examinations, in patients with no end point, only those with 5 or more visual field examinations were included in the analysis. Similarly, in patients with at least 1 end point, only those with 5 or more examinations before and 5 or more examinations after the end point were included in the analysis.

Parametric or nonparametric statistical tests were used where appropriate after examination of the distributions and variance characteristics of the variables analyzed. The analysis was based on the study eye, which was chosen by a random selection technique at the beginning of the study if both eyes were eligible.

RESULTS

The CGS enrolled 258 patients with open-angle glaucoma. The study population,[17] baseline characteristics,[17] and risk factors for visual field progression[7] have been detailed elsewhere. Of the original population, 216 patients (83.7%) had a sufficient number of visual field examinations to be included in the present analysis. There were 113 men (52.3%) and 103 women (47.7%), with a median age of 65.2 years (interquartile range [IQR], 55.2-71.5 years) at baseline.

There were 153 patients (70.8%) with no end point, 45 (20.1%) with 1 end point, 16 (7.4%) with 2 end points, and 2 (0.9%) with 3 end points. Owing to the small number of patients with 3 end points, these data were not analyzed further.

The median MD rates in patients with at least 1 end point (derived with data only up to the first end point) and those with no end point were –0.35 dB/y (IQR, –0.76 to –0.12 dB/y) and 0.05 dB/y (IQR, –0.14 to 0.35 dB/y), respectively (**Figure 1**). The respective mean (SD) values were –0.54 (1.10) dB/y and 0.06 (0.47) dB/y. The difference in MD rates between these 2 groups of patients was statistically significant ($P<.001$, Mann-Whitney U test).

There were no differences in the sex ratio among patients with 0, 1, or 2 end points ($P=.16$, χ^2 test) (**Table 1**). Baseline age was statistically different among these 3 groups, with higher age associated with 1 or 2 end points ($P=.01$, Kruskal-Wallis test). Neither baseline visual acuity nor baseline target IOP was related to the number of end points ($P>.65$). The mean IOP during the follow-up (only up to the first end point in progressing patients) was not significantly related to the number of end points ($P=.15$). However, MD rates (only up to the first end point in progressing patients) were significantly different among patients with 0, 1, and 2 end points ($P<.001$), indicating that patients with a worse initial MD rate were more likely to have more end points (Table 1). The median MD rate worsened by approximately –0.3 dB/y per end point. There was a significant relationship between the number of end points and both the total number of visual field examinations and follow-up duration ($P<.001$, Table 1).

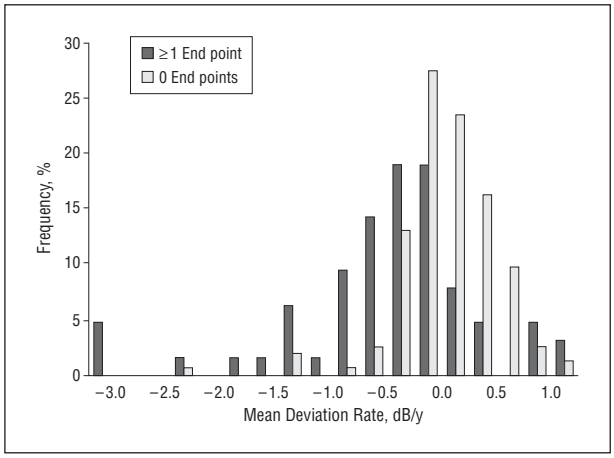

Figure 1. Frequency distribution of the mean deviation rate in progressing patients (≥1 end point) and nonprogressing patients (0 end points).

There were 181 patients (83.8%) with available baseline ACA results. The MD rates for the 10 patients (5.5%) with abnormal ACA levels were significantly worse than the 171 patients (94.4%) with normal ACA levels (median, –0.57 dB/y [IQR, –2.37 to –0.09 dB/y] and median, –0.03 dB/y [IQR, –0.33 to 0.33 dB/y], respectively; $P=.004$) (eFigure, http://www.archophthalmol.com). The MD rates were not statistically different among men and women (median, –0.04 dB/y [IQR, –0.30 to 0.22 dB/y] and median, –0.04 dB/y [IQR, –0.42 to 0.34 dB/y], respectively; $P=.85$) (eFigure). Worse MD rates were weakly but statistically significantly associated with increasing baseline age (Spearman $\rho=-0.190$; $P=.005$) but not with mean IOP during follow-up (measurements only up to the first end point in progressing patients; Spearman $\rho=0.021$; $P=.76$).

There were 49 patients with at least 1 end point with 5 or more visual field examinations before and 5 or more visual field examinations after the first end point. The median numbers of examinations before and after the first end point were 10 (IQR, 7 to 14) and 9 (IQR, 8 to 13), respectively. The median IOP decreased from the baseline target IOP of 18.0 mm Hg to 14.8 mm Hg after the first end point ($P<.001$, Wilcoxon test) (**Table 2**), representing a 20% median decrease in individual patients. The median MD rate became less negative, by a factor of around 3 (from a median of –0.36 dB/y to –0.11 dB/y; $P<.02$) (Table 2), after IOP reduction. A less negative MD rate was observed in 33 patients (67.3%) and a more negative MD rate was observed in 16 patients (32.7%) (**Figure 2**). There was no relationship between the change in MD rate and the magnitude or percentage of IOP reduction ($P>.31$).

The median MDs at the first end point and the 5 preceding and 5 subsequent examinations are shown in **Figure 3**. The median MDs at the confirmation examination and subsequent examination were –5.70 dB (IQR, –8.16 to –3.34 dB) and –5.86 dB (IQR, –7.74 to –3.52 dB), respectively, indicating that there was no apparent regression to the mean of MD after the end point. To estimate a potential regression to the mean of the MD rates, the latter were calculated with and without the 1 or 2 confirmation examinations af-

Table 1. Baseline and Follow-up Characteristics of Patients With 0, 1, and 2 End Points

Characteristic	End Point 0 (n=153)	1 (n=45)	2 (n=16)
Baseline variables			
Sex, No. (%)			
Male	84 (54.9)	19 (42.2)	10 (62.5)
Female	69 (45.1)	26 (57.8)	6 (37.5)
Age, median (IQR), y	62.4 (53.0 to 70.8)	68.2 (63.5 to 75.1)	65.8 (62.2 to 72.7)
Visual acuity, median (IQR), logMAR	0.10 (0.00 to 0.10)	0.10 (0.00 to 0.10)	0.10 (0.00 to 0.20)
Baseline target IOP, median (IQR), mm Hg	17.0 (15.5 to 19.5)	17.5 (15.0 to 19.5)	18.0 (15.8 to 21.9)
Follow-up variables			
Visual field examinations, median (IQR), No.	18 (14 to 22)	23 (18 to 28)	25 (19 to 32)
Follow-up duration, median (IQR), y	6.0 (4.7 to 7.2)	7.2 (5.8 to 8.4)	7.1 (6.0 to 8.7)
Mean IOP, median (IQR), mm Hg[a]	16.3 (14.7 to 17.8)	16.1 (15.3 to 17.7)	17.4 (15.7 to 19.0)
Rate of MD change, median (IQR), dB/y[a]	0.05 (–0.14 to 0.35)	–0.30 (–0.67 to –0.03)	–0.67 (–1.66 to –0.20)

Abbreviations: IOP, intraocular pressure; IQR, interquartile range; MD, mean deviation.
[a]Prior to the first end point.

Table 2. Intraocular Pressure and Rates of Mean Deviation Change

IOP or MD Change	Median (IQR) Before First End Point	After First End Point	Before Second End Point	After Second End Point
Target IOP, mm Hg	18.0 (15.3 to 19.8)		16.3 (13.3 to 17.3)	
Mean IOP, mm Hg		14.8 (13.2 to 16.6)		14.5 (11.3 to 16.1)
IOP reduction, mm Hg		3.1 (0.0 to 5.5)		3.0 (0.4 to 4.8)
IOP reduction, %		20 (0 to 28)		18 (0 to 25)
Rate of MD change, dB/y	–0.36 (–0.81 to –0.11)	–0.11 (–0.93 to 0.52)	–1.07 (–2.20 to –0.40)	–0.83 (–1.51 to –0.19)

Abbreviations: IOP, intraocular pressure; IQR, interquartile range; MD, mean deviation.

ter the first end point. In this subset of 42 patients with 5 or more examinations available before and 5 or more examinations available after the first end point, the median MD rate before the end point was –0.41 dB/y (IQR, –0.88 to –0.12 dB/y). The median MD rate after the end point excluding the confirmation examinations was –0.26 dB/y (IQR, –0.76 to 0.18 dB/y), while with their inclusion it was –0.10 dB/y (IQR, –0.76 to 0.45 dB/y).

Nine patients had 2 or more end points and met the criteria for sufficient visual field examinations to measure MD rates before and after the second end point. The median numbers of examinations before and after the second end point were 10 (IQR, 7 to 11) and 9 (IQR, 6 to 13), respectively. The median IOP decreased from 16.3 mm Hg to 14.5 mm Hg after the second end point ($P = .04$, Wilcoxon test) (Table 2), representing an 18% median decrease in individual patients. The median MD rate changed from –1.07 dB/y to –0.83 dB/y after further IOP reduction; this was not statistically different ($P = .44$). A less negative MD rate was observed in 5 patients (55.6%) and a more negative MD rate was observed in 4 patients (44.4%) (Figure 2). Because of the small sample size, the power to detect a 0.30-dB/y difference in MD rate after IOP reduction was only 12%.

COMMENT

Identification of risk factors for glaucomatous visual field progression in the CGS was achieved with a binary event-based definition of progression, that is, whether and when progression occurred.[7] Although event-based definitions of progression are useful for elucidating risk factors, accommodating patients with different lengths of follow-up, and data censoring, they do not provide information on how risk factors affect the rate of visual field change, which was the focus of the present analyses. We also evaluated the effect of IOP reduction on the rate of visual field change.

In attributing rates of visual field change to risk factors for progression, we deliberately included data only up to the first end point in patients with progression. As the CGS mandated further IOP reduction in these patients, rate estimates from the inclusion of all visual field data would have been influenced by the effects of the treatment intervention. Patients without an end point had stable MD values during the study period, with a median or mean MD rate of approximately 0 dB/y. On the other hand, patients with at least 1 end point had significantly worse MD rates prior to reaching the first end point. The median and mean rates in these patients were –0.35 dB/y and –0.54 dB/y, respectively; however, it is important to note the large interindividual variation (Figure 1). The mean MD rate in the CGS falls between the values reported in the Early Manifest Glaucoma Trial for treated (–0.36 dB/y) and untreated (–0.60 dB/y) patients prior to reaching the end point.[11]

The initial rate of visual field change was related to the number of end points. The median MD rate worsened by approximately –0.3 dB/y per end point. This find-

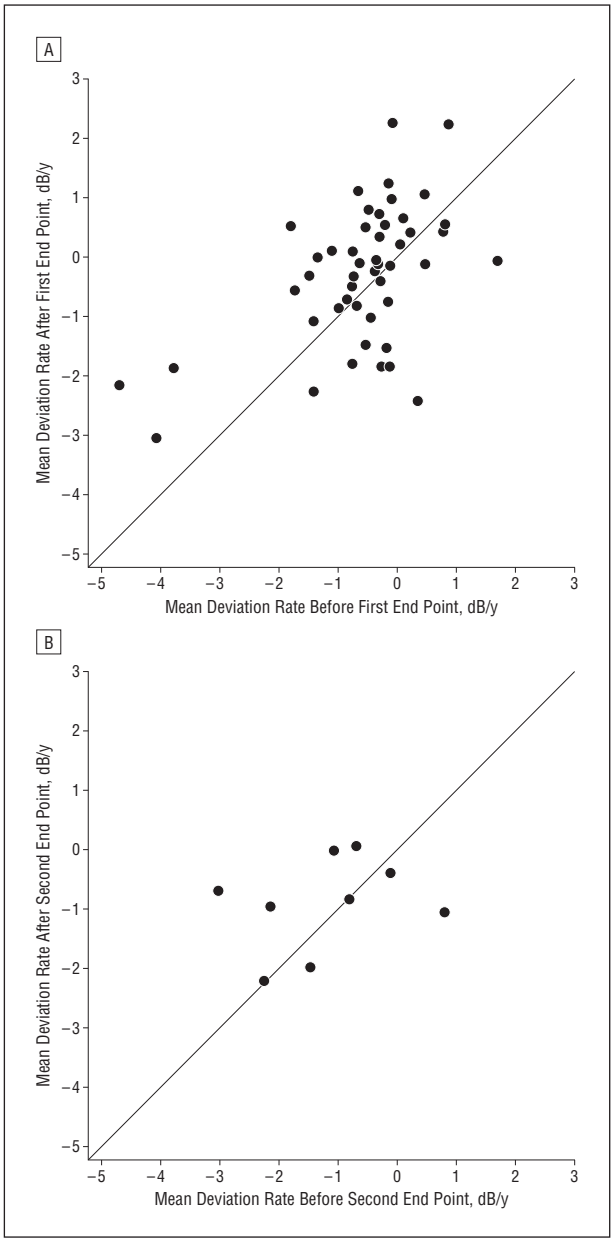

Figure 2. Effect of intraocular pressure reduction on the mean deviation rate, showing the mean deviation rate before and after the first end point (A) and before and after the second end point (B). A diagonal line indicates equal rates before and after the end point.

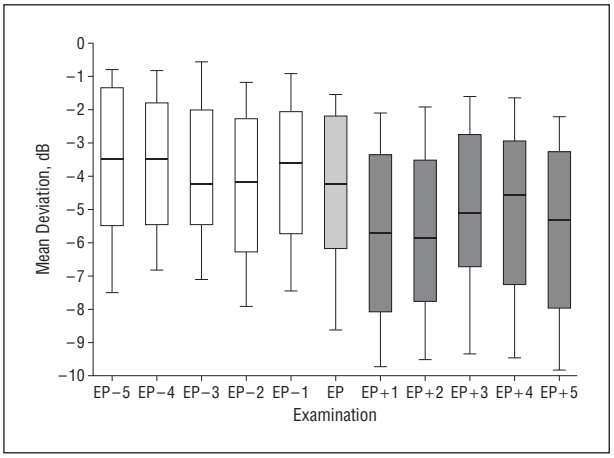

Figure 3. Mean deviation in progressing patients in 5 examinations leading up to the first end point (EP) (shown as EP –5 to EP –1), at the EP (shown as EP), and 5 examinations after the EP (shown as EP +1 to EP+5). EP +1 is the confirmation examination. Horizontal lines in each box indicate the median; box boundaries, 25th and 75th percentiles; and tails, 10th and 90th percentiles.

ing is of significance as it indicates that a worse initial rate of visual field change is related to subsequent progression despite additional IOP reduction after an end point. Further research is necessary to determine whether such patients may benefit from greater IOP lowering than that in the CGS protocol. As expected, the number of end points was related to the total number of visual field examinations as the chance of detecting progression increases with follow-up time. Furthermore, because end points required confirmation, these patients had additional visual field examinations. Besides older age, none of the other baseline or follow-up parameters investigated were related to the number of end points.

Previously we showed that patients with glaucoma and abnormal baseline ACA levels were 4 times more likely to have visual field progression.[7] The present analyses demonstrate that they have a notably more rapid rate of visual field deterioration compared with patients with normal ACA levels. While this finding is significant, its practical implications are unclear as only 5.5% of the tested patients had abnormal ACA levels. Whether instituting greater IOP reduction in these patients might be beneficial remains to be determined. It is well established that the incidence of glaucomatous progression increases with age,[1] and in accordance we found an association between the rate of visual field change and age. Female sex and mean IOP during the follow-up were independent risk factors for progression[7]; however, no association was found with MD rates. There are at least 2 potential explanations for these findings. First, risk factors were previously identified using multivariate survival models that accounted for the interaction between several variables and differences in follow-up times, whereas in this study we performed a univariate analysis without accounting for the differences in follow-up. Second, end points were defined with event-based criteria of the number of points in the visual field with significant total deviation change and not MD rate.

A significant finding in this study was the effect of additional IOP reduction on MD rate in patients with 1 end point. In these patients, a median reduction of 3.1 mm Hg (or 20%) resulted in the median slope changing significantly from –0.36 dB/y to –0.11 dB/y. In some patients, this amelioration may not be clinically meaningful; however, over 20 years, the difference in total MD change resulting from these 2 rates is 5 dB. In younger patients with more advanced damage, this difference is likely to be important.

Previous retrospective studies have examined the effect of a larger IOP reduction by trabeculectomy on the rate of visual field change.[21-23] Interestingly, even though the initial MD rate was considerably worse, the magnitude of the change in MD rate after trabeculectomy in 2 of the studies[22,23] was similar to that in the CGS. The CGS treatment protocol required an IOP reduction of at least 20% from the target IOP prior to progression. There was, however, provision for the IOP to be 1 mm Hg higher than

Canadian Glaucoma Study Group

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the target.[17] Furthermore, the IOP could be 2 mm Hg higher than the target for a maximum of 2 consecutive visits before additional intervention was required.[17] This treatment protocol largely explains why the median IOP reduction was only 20% in patients after the first end point and 18% after the second end point. Because of the study and treatment protocols, the IOP reduction in the CGS was modest compared with those using trabeculectomy.[21-23] While there are several studies and trials reporting the effect of IOP reduction on the incidence of visual field progression in glaucoma, we are not aware of additional studies reporting changes in the rate of visual field change after IOP reduction instituted following visual field progression.

There was no demonstrable effect of further IOP reduction on the rate of visual field progression in patients with 2 or more end points. There are several potential reasons, either in isolation or in combination, to explain this finding. These patients had a considerably worse MD rate prior to the second end point compared with patients prior to the first end point (median, –1.07 vs –0.36 dB/y, respectively). They may therefore represent a subset of fast progressors who have a poorer prognosis or those who require greater IOP reduction. The magnitude of IOP reduction after the second end point was comparable to that after the first end point (18% and 20%, respectively). Furthermore, the mean IOPs after the first and second end points were similar (14.8 mm Hg and 14.5 mm Hg, respectively). Hence, a higher degree of IOP reduction may have had a more favorable effect on the MD rate after the second end point. Finally, only 9 patients with 2 or more end points met the criteria for inclusion in this analysis. The power to detect a 0.3-dB/y difference in the MD rate was only 12%; therefore, clinically important changes in the rate of visual field change after IOP reduction may not have been detected because of the limited sample size.

Although we demonstrate the positive effect of additional IOP reduction on the rate of visual field change in patients reaching an end point, the CGS is limited by the lack of a control group of patients who did not receive additional treatment after an end point. Consequently, other factors may have potentially been responsible for the observed amelioration of MD rates. Regression to the mean of the MD rates is one of these factors; however, in the absence of a control group, its effect cannot be measured directly. We investigated the possibility of 2 related factors that may have potentially overestimated the treatment effect. First, if the visual field examination at the end point resulted in a spuriously worse MD, then the preprogression MD rate may have been erroneously worse. We ruled out this possibility because there was a large and sustained reduction in the median MD from the end point to the first and second examinations after the end point. Second, the inclusion of confirmation examinations to calculate MD rates after the end point may have artificially biased the estimates toward less negative values. Excluding these examinations unsurpris-

ingly resulted in a more negative median postprogression MD rate, although it was still almost less than half of the preprogression rate. Because errors in regression (for example, from a reduced number of observations) decrease the precision of the slope estimate,[24] we elected to use all available examinations.

The CGS used visual field change as the sole criterion for progression. There are limitations of this approach as patients with optic disc changes may also have had significant glaucomatous progression without affecting the visual field to trigger an end point. Nonetheless, there is convincing evidence from glaucoma trials indicating that an end point is triggered frequently by either visual field change or optic disc change but infrequently by both.[9-11] Clinical studies indicate a significant decoupling between visual field and optic disc changes in glaucoma[25,26] and question whether end points derived from these 2 modalities are actually related.[25] There are also potentially different interpretations of functional and structural change in glaucoma. For these reasons, an end point derived from 1 testing modality is a feasible alternative in clinical trials and studies, particularly those with treatment interventions.

The results of the CGS have some practical implications for clinical practice. They indicate that patients with early to moderate visual field damage who do not reach a visual field end point based on localized visual field change and maintain an average IOP of around 16 mm Hg have notably stable visual fields. A modest additional IOP reduction in patients with an end point has a significant effect on the subsequent MD rate. We cannot speculate whether a greater IOP reduction would have had an even more beneficial effect on the visual field or whether these findings can be extended to those patients with more visual field damage at baseline.

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Intraocular Triamcinolone for Giant Cell Arteritis?

Giant cell arteritis (GCA) is a focal, segmental, granulomatous arteritis characterized by disruption of the internal elastic lamina and vascular occlusion in medium to large vessels. Involvement of the ophthalmic artery and its branches typically results in irreversible vision loss from arteritic anterior ischemic optic neuropathy (91%), central retinal artery occlusion (10.5%), cilioretinal artery occlusion (10%), or arteritic posterior ischemic optic neuropathy (4%), either alone or in combinations.[1] Prompt, aggressive systemic corticosteroid is the mainstay of treatment to prevent bilateral blindness. A proportion of patients with initial visual impairment also continue to deteriorate despite adequate treatment.[2]

New intraocular formulae of triamcinolone acetonide injection are approved by the US Food and Drug Administration to treat several ocular inflammatory conditions, including temporal arteritis.[3] We are puzzled by this specific indication. Based on our knowledge of the affected vasculatures and the systemic nature of GCA (arteries with internal elastic lamina only and potential aortic involvement), intraocular steroid as a sole or adjuvant therapy should not be effective.

We conducted a literature review on Medline and PubMed for the efficacy of intravitreal triamcinolone acetonide (IVTA) in GCA. We found no articles on the efficacy of IVTA in arteritic-anterior or posterior ischemic optic neuropathy associated with GCA. Nor did we identify any reports of IVTA for central retinal artery occlusion. Use of IVTA has been studied as a treatment for nonarteritic anterior ischemic optic neuropathy (not typically caused by GCA) but no marked visual acuity improvement was demonstrated.[4]

Why are the new intraocular formulae of triamcinolone acetonide indicated specifically for temporal arteritis, then? Perhaps this indication is based on the initial Drug Efficacy Study Implementation reviews on triamcinolone acetonide in 1970, but the intended route of administration at the time was intramuscular only.[3] We are concerned that the current labeling for intraocular formulae of triamcinolone acetonide is misleading and may lead to inappropriate local treatment for a sight-threatening systemic disease.

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Correction

Error in Title. In the Clinical Sciences article titled "[Canadian Glaucoma Study:] 3. Impact of Risk Factors and Intraocular Pressure Reduction on the Rates of Visual Field Change" by Chauhan et al, published in the October issue of the *Archives* (2010;128[10]:1249-1255), the title was inadvertently omitted from the print version. It should have appeared as "Canadian Glaucoma Study: 3. Impact of Risk Factors and Intraocular Pressure Reduction on the Rates of Visual Field Change." The title appeared correctly in the online version.