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Long-term progression and risk factors in primary open-angle glaucoma in clinical care

Crenguţa Feraru · Dorin Chiseliţă · Anca Pantalon ⓘD

Summary

Purpose The aim of the present study was to investigate the perimetric progression rate and associated risk factors in open-angle glaucoma in clinical practice.

Methods This was a retrospective study based on clinical chart reviews of patients with primary open-angle glaucoma (POAG) followed up for more than 5 years with ≥5 SITA standard visual fields. Demographics, visual acuity (VA), central corneal thickness (CCT), intraocular pressure values (IOP), treatment (number of medications), visual fields (VFs), and associated systemic pathologies were recorded. Patients were followed up every 3–6 months and identical tests were performed. The VF progression rate was calculated as slope of mean deviation (MD) over time using the Glaucoma Progression Analysis software.

Results In all, 69 eyes from 69 patients with POAG were included in the study and followed up for a mean period of 72.9 months (SD ± 31.7). The mean MD at the start was –4.4 dB (SD ± 6.0), with a mean number of VF tests of 8.3 (SD ± 2.9). The progression rate reached –0.18 ± 0.1 db/year. The mean IOP at all visits decreased over time from 18.2 mm Hg to 16.5 mm Hg ($p < 0.05$). A step-wise one-way ANOVA regression analysis concluded that for the MD slope the significant predictors were final MD level ($R^2 = 0.126$, $p = 0.003$) and a combination between baseline and final MD level ($R^2 = 0.656$, $p = 0.000$). Systemic factors such as sex, positive history of cardiovascular diseases, and hypertension reached no statistical relevance in terms of increased risk or significant association with glaucoma progression. Diabetes had a borderline significance ($p = 0.07$) as a "protective factor" against progression, as more "stable" cases were associated with diabetes than "progressing" ones.

Conclusion The rate of VF changes in POAG correlated with and dependent on the baseline/final MD level; additional risk factors reached no statistical significance in our clinical care glaucoma study.

Keywords Glaucoma progression · Risk factors · Glaucoma Progression Analysis · Clinical care

Langzeitprogression und Risikofaktoren beim primären Offenwinkelglaukom in der klinischen Versorgung

Zusammenfassung

Ziel Ziel war die Untersuchung der perimetrischen Progressionsrate und assoziierter Risikofaktoren bei primärem Offenwinkelglaukom (POWG) in der klinischen Versorgung.

Methoden Es handelt sich um eine retrospektive Studie, basierend auf Krankengeschichten von Patienten mit POWG, die einen Beobachtungszeitraum >5 Jahre mit ≥5 SITA-Standard-Gesichtsfelduntersuchungen aufwiesen. Demographische Daten, Sehschärfe, zentrale Hornhautdicke (CCT), Intraokulardruck (IOD), Therapie (Zahl der Medikamente), Gesichtsfelder und assoziierte Systemerkrankungen wurden dokumentiert. Die Patienten wurden alle 3–6 Monate untersucht, der Ablauf dieser Visiten war standardisiert. Die Progression des Gesichtsfeldschadens wurde als die Steigung der mittleren Abweichung („mean deviation", MD) über die Zeit mittels Glaucoma Progression Analysis Software bestimmt.

Ergebnisse In die Studie wurden 69 Augen von 69 Patienten mit POWG eingeschlossen. Die mittlere Beobachtungsdauer betrug 72,9 ± 31,7 Monate. Die

C. Feraru · D. Chiseliţă · A. Pantalon (✉)
Ophthalmology Department, Sf. Spiridon University Hospital, "Gr. T. Popa" University of Medicine and Pharmacy Iaşi, 16 Universităţii Str., 700115 Iaşi, Romania
anca.pantalon@gmail.com

MD zu Beginn war –4,4 ± 6,0 dB, im Mittel wurden 8,3 ± 2,9 Gesichtsfelduntersuchungen durchgeführt. Die Progressionsrate in der Studienpopulation wurde mit –0,18 ± 0,1 db/Jahr ermittelt. Der mittlere IOD aus allen Visiten reduzierte sich über die Zeit von 18,2 mmHg auf 16,5 mmHg ($p < 0,05$). Eine schrittweise durchgeführte Regressionsanalyse mittels einfaktorieller ANOVA zeigte, dass für die MD-Steigung der finale MD-Wert ($R^2 = 0,126$; $p = 0,003$) und eine Kombination aus MD-Wert zu Beginn und am Ende der Beobachtungsdauer ($R^2 = 0,656$, $p = 0,000$) prädiktiv waren. Sowohl der IOD als auch systemische Faktoren wie Geschlecht, Anamnese kardiovaskulärer Erkrankungen und Bluthochdruck waren nicht mit der Rate der Glaukomprogression verknüpft. Es war eine Tendenz zu beobachten, dass Diabetes mit einer geringeren Progressionsrate assoziiert ist, aber dieser protektive Faktor war grenzwertig nicht signifikant ($p = 0,07$).

Schlussfolgerung Die Rate der Gesichtsfeldverlusts bei POWG war in dieser Studie assoziiert mit der MD am Ende des Beobachtungszeitraums. Weitere Risikofaktoren waren in der vorliegenden Studie zur klinischen Versorgung nicht mit der Progression des Gesichtsfeldschadens assoziiert.

Schlüsselwörter Glaukomprogression · Risikofaktoren · Glaukomprogressionsanalyse · Klinische Versorgung

Introduction

Glaucoma is an optic neuropathy that can lead to irreversible damage of the optic nerve and blindness. Among all glaucoma types, primary open-angle glaucoma (POAG) is the most common form and a leading cause of visual loss worldwide [1].

Treatment might stop or slow down progression in glaucoma, but the individual evolution is variable [2]. Consequently, visual field changes and progression rates differ greatly among patients [3].

Many randomized control trials investigated different risk factors in glaucoma progression [2–7]. These trials reported that older age, decreased central corneal thickness (CCT), pseudoexfoliation, lower ocular perfusion pressure, disk hemorrhage, baseline visual field (VF) status, and optic nerve anatomy were variables associated with glaucoma progression. Most reports had a very specific study protocol, with strict research requirements, and there are scarce recent data in the literature about glaucoma patients followed in clinical care context [2, 3]. Although retrospective, these types of studies collected relevant information for clinical practice [2–5]. Thus, the aim of our study was to assess progression rate and risk factors in POAG in the context of clinical care of South-Eastern Romania.

Materials and methods

The study was a retrospective review of patient charts. We studied the records of patients with a diagnosis of POAG followed up in our Glaucoma Unit at "Sf. Spiridon" University Hospital, Iasi, Romania, between January 2003 and September 2010. Our study was performed in accordance with the Declaration of Helsinki. The Ethical Review Board of "Gr. T. Popa" University of Medicine and Pharmacy approved the study and informed consent was signed by each patient.

Records were selected only for the patients followed up more than 5 years during the study period. POAG was defined in the presence of open anterior chamber angle on gonioscopy, glaucomatous optic disc damage on clinical examination (focal or diffuse neuroretinal rim thinning, localized notching or nerve fiber layer defect), and corresponding visual field (VF) defects. Glaucoma severity was graded according to the Hodapp criteria [8].

Using standard automated perimetry (24–2 SITA Standard SAP, Humphrey Field Analyzer II, Carl Zeiss Meditec Inc., Dublin, Calif.) VF changes for glaucoma were defined if at least two of the three Anderson criteria were fulfilled (three or more non-edged points in a cluster depressed to $p < 5\%$ and one of which depressed to $p < 1\%$, glaucoma hemifield test results outside normal limits and pattern standard deviation depressed to $p < 5\%$). The reliability of the tests was assessed. Tests with fixation losses and with false-positive or false-negative rates of $>20\%$ were considered unreliable and excluded from the analysis. A minimum number of 5 VF tests were required for each patient in our study.

All VF tests were analyzed for progression using the Glaucoma Progression Analysis (GPA) software, which provided both an event-based and a trend-based progression analysis. Both analyses took the first two reliable VF tests as baseline landmark.

In the event-based progression analysis, GPA used statistical criteria designed for the Early Manifest Glaucoma Trial to identify progression of VF defects [9]. When significant ($p < 0.05$) deterioration was evident on the pattern standard deviation (PSD) maps at the same three or more points on two consecutive follow-up tests, the GPA warned of "possible progression"; if significant deterioration was seen at the same three or more points in three consecutive follow-up tests, GPA warned of "likely progression." When both of these criteria were not met, the software flagged "no progression detected." When the VF was severely depressed (MD $\Leftarrow 20$ dB), GPA could not determine progression. For the purpose of this study, progression was quantitatively assessed by linear regression (trend) analysis of the mean deviation (MD) changes over time; slopes of progression (decibels/year) based on threshold maps and its level of significance (p values) were calculated.

During the study patients were followed up every 3–6 months and identical tests were performed. We excluded subjects with significant lens opacities, ocular comorbidities and refractive errors of >5D spherical and >3D cylinder.

If both eyes were eligible for the study, only one was chosen based on the worse MD level at baseline. At baseline, clinical parameters were collected from the charts and included in our study: age, gender, best corrected visual acuity (BCVA) by ETDRS chart, intraocular pressure (IOP) by Goldmann tonometer, central corneal thickness (CCT) by ultrasonic pachymetrer (DGH-550, DGH Technology Inc., Exton, Pa.) C/D ratio (Volk 78D lens), number of topical medications, and VF test parameters. Furthermore, systemic pathologies were assessed and noted with "yes" or "no" in the charts if present (diabetes, arterial hypertension, cardiovascular diseases); at each follow-up visit, VA, IOP, and VF tests were repeated. The majority of the patients required topical therapy, but no surgical intervention (laser or incisional procedures – trabeculectomy) was performed during the follow-up period. During monitoring, treatment was modified if the IOP was not efficiently controlled; the IOP level was individually set, according to glaucoma severity, risk factors and life span. The intermediary IOP was calculated by averaging all the IOPs taken during the follow-up interval. OCT evaluation was possible late during the study, therefore very few patients could be evaluated through this method. Because of this, the authors decided not to include any results in the statistical analysis and interpretation due to the small sample size and lack of adequate time for progression evaluation using OCT. Moreover, both Stratus (Carl Zeiss Meditec) and Cirrus OCT (Carl Zeiss Meditec) machines were used for our glaucoma patients and at the time this study was ongoing our conversion equation was not fully validated for comparing and translating data.

Statistical analysis

SPSS 18.0 statistical software (SPSS Inc., Chicago, Ill.) was used to process the data. Descriptive analysis was used on demographics, follow-up time MD, PSD and IOP. We also calculated the mean number of VFs per patient. Progression rate (MD slope) was calculated by linear regression analysis of MD values over time and expressed in dB/year.

Independent sample *t* tests were used for comparisons of continuous variables between groups. When paired groups were compared (baseline and final parameters) we used the Wilcoxon test. An association between various risk factors and glaucoma progression was tested using Pearson's chi-square test. Odds ratios (ORs) were also calculated. Spearman's correlation coefficients (*r*) were calculated to assess the relationship between age, BCVA, MD, PSD, IOP and MD slope. Statistical significance was defined at the *p* <

0.05 level. We used a logistic regression to evaluate the effect of each parameter on the progression outcome. Each parameter was tested independently in an univariate model and then retested after age adjustment. A multivariate model was analyzed for all parameters that achieved a level of $p < 0.2$ in univariate analysis. Analysis of variance (one-way ANOVA) was used for comparisons of continuous variables.

Results

We studied 69 eyes from 69 patients (53 females and 16 males) with POAG for a period of 72.8 months (SD ± 31.7). Mean age at the start was 62.3 years (SD ± 10.4). At baseline, subjects had a (decimal) visual acuity of 0.9 (SD ± 0.1) with limits 0.5–1.2. The mean calculated spherical equivalent showed a slight hyperopic tendency of +0.7 D (SD ±1.03), limits between ±4 D. IOP range was wide from 11 to 28 mm Hg, but the mean baseline IOP was 18.2 mm Hg (SD ± 3.6). In total, 14 eyes from 14 patients had a positive history for glaucoma surgery (trabeculectomy/trabeculoplasty) before the study started. After the surgical interventions, of these 14 patients, only four patients (5.8 %) required no further treatment, as the IOP was well controlled postoperatively for the entire study period. The remaining 65 patients needed a mean number of 1.8 (SD ± 0.9) topical substances to control the IOP: 22 patients (31.9 %) were treated with one substance, 23 patients (33.3 %) were treated with two substances and 20 patients (29 %) were treated with three substances. Mean central corneal thickness (CCT) was 537 µm (SD ± 40 µm), range = 428–608 µm.

Taking into account the Hodapp criteria [5], visual field analysis revealed early defects in 54 patients (78.3 %), moderate defects in seven patients (10.1 %), and severe defects in eight patients (11.6 %). The mean MD level at baseline was –4.4 dB (SD ± 6.0 dB), range between –25.2 dB and 1.55 dB and median around –2.6 dB (see Fig. 1).

The calculated mean PSD at baseline was 4 dB (SD ± 3.0), limits 1.0–12.3 dB and median PSD of 2.7 dB. By averaging all the IOPs measured at each follow-up visit, we calculated the intermediary IOP: 16.6 mm Hg (SD ± 2.8). A mean number of 8.3 VFs/eye (SD ± 2.9) were recorded in our study (range = 5–19 tests/eye).

Systemic comorbidities, according to the patient's personal history in the medical charts, were arterial hypertension in 56.5 % patients, diabetes in 15.9 % patients, and cardiovascular diseases in 23.2 % patients.

Final analysis showed a significant decline in BCVA over time and also in the IOP level (see Table 1). The IOP changes in time are shown in Fig. 2.

Final VF parameters changed significantly only in terms of MD (see Fig. 3; Table 1), but not in terms of PSD values (see Table 1).

We used the Wilcoxon test to compared the baseline with the final parameters for our study; statistical

Fig. 1 Mean deviation (*MD*) distribution in all 69 patients with primary open-angle glaucoma
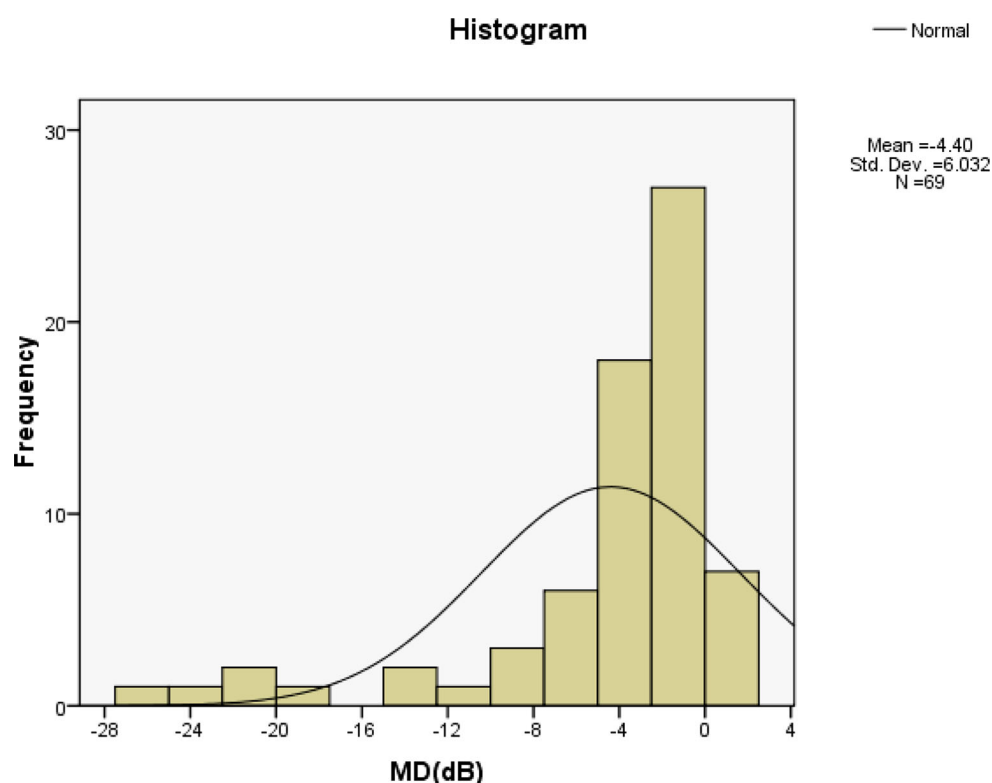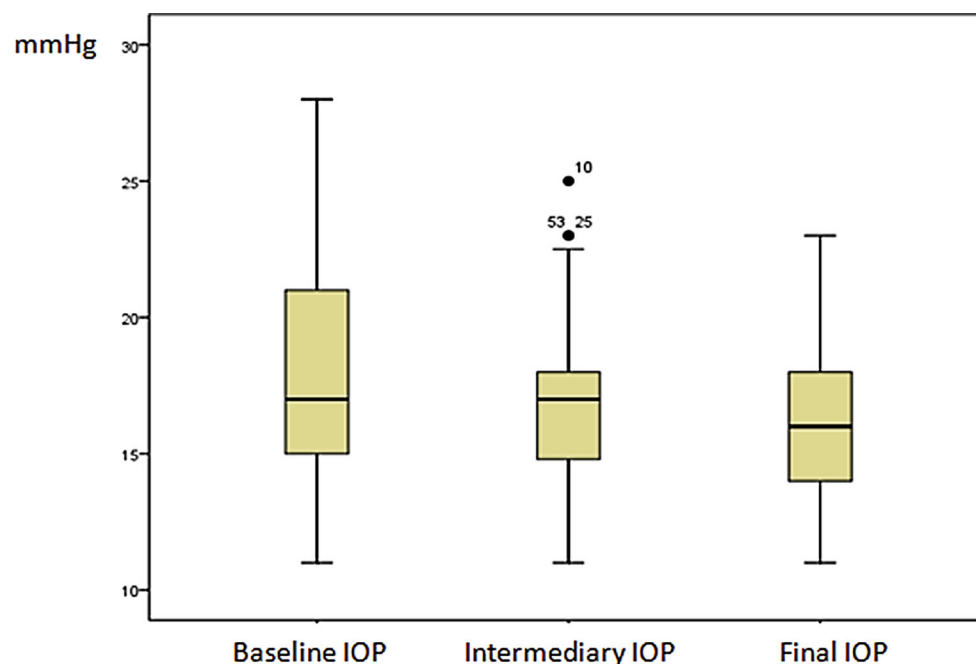

Fig. 2 Intraocular pressure (*IOP*) dynamics (baseline vs. intermediary vs. final level, measured in mm Hg)

significance was attributed to values of $p < 0.05$ (see Table 1).

Overall, the mean rate of VF change in our study was –0.18 dB/year (SD ± 0.78). The progression rate histogram is shown in Fig. 4, with a negatively skewed distribution; 98 % of the MD slope values are within one standard deviation range, with 59.7 % negative slopes, but no statistical significance could be attributed to this aspect ($p = 0.142$) in binomial tests.

Six patients (8.70 %) progressed at a rate higher than –0.5 dB/year, while four patients (5.80 %) progressed at rates higher than –1 dB/year; we recorded a progression rate higher than –2 dB/year in only one patient (1.44 %).

As expected, based on Spearman's correlation coefficient, there was a strong negative correlation between VF parameters at baseline (MD/PSD): $r = -0.740$, $p = 0.000$, but the MD slope was only weakly

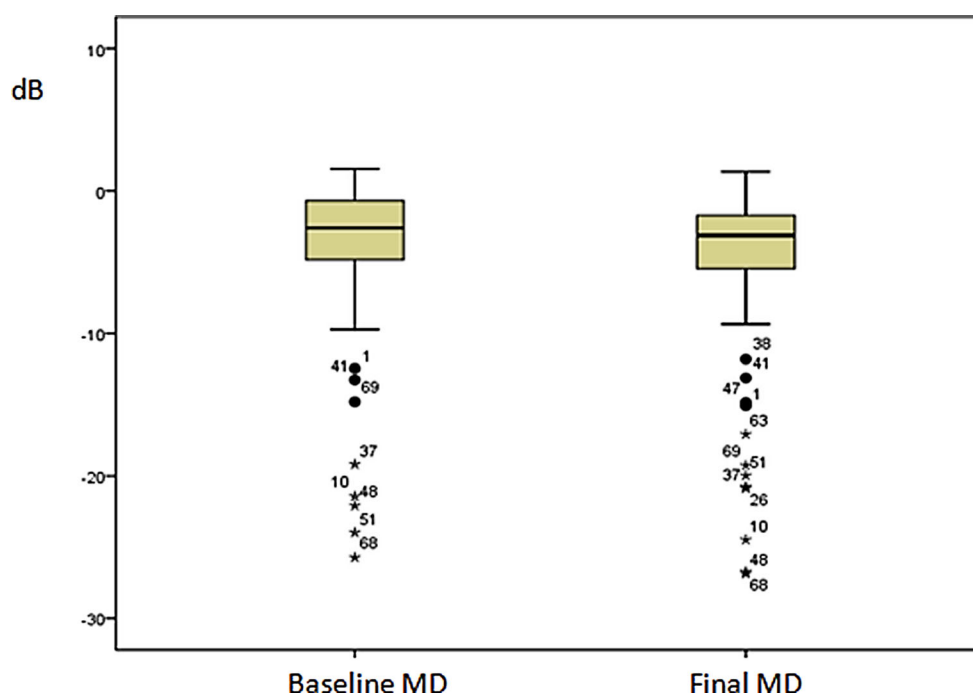**Fig. 3** Mean deviation (*MD*) levels at baseline vs. final measurement (in dB)

Table 1 Baseline vs. final levels in the main study parameters

Parameter	Baseline level (mean)	Final level (mean)	Wilcoxon test ($p < 0.05$)
BCVA (ETDRS)	0.9 ± 0.1	0.85 ± 0.2	*p = 0.01*
IOP (mm Hg)	18.2 ± 3.5	16.4 ± 2.8	*p = 0.000*
MD (dB)	−4.4 ± 6.0	−5.6 ± 6.9	*p = 0.008*
PSD (dB)	4.0 ± 3.0	4.4 ± 3.5	*p = 0.418*

BCVA best corrected visual acuity, *IOP* intraocular pressure, *MD* mean deviation, *PSD* pattern standard deviation

correlated with baseline MD level ($r = -0.245$, $p = 0.046$). The same type of correlation was found between MD slope and the number of topical medications ($r = -0.248$, $p = 0.043$), but when age was controlled for, the correlation was no longer significant ($p > 0.05$).

We found no other statistically significant correlation between the VF decay rate (dB/year) and other baseline parameters (VA, IOP, CCT, PSD level). In our study we found that at enrollment, age was inversely correlated with the number of topical medications ($r = -0.306$, $p = 0.01$), an indirect sign of a more aggressive treatment in cases where younger patients were to be treated and followed up. We also observed that the higher the VA was at baseline, the better the MD level at the end of our study ($r = 0.237$, $p = 0.05$).

A step-wise one-way ANOVA regression analysis could include only a few predictors for the MD slope: mean final MD ($r^2 = 0.126$, $p = 0.003$) and a combination between baseline and final MD level ($R^2 = 0.656$, $p = 0.000$; see Table 2).

For a better understanding of which variables might have influenced glaucoma progression in our study and to have an exact estimate of the progression risk associated with each parameter in our population, we used logistic regression in a univariable model. Both systemic and local risk factors were tested for this as-

sociation. Using predefined cut-off values, based on the calculated means of different variables, we evaluated whether patients older than 62 years with baseline IOP > 18 mm Hg, CCT < 537 µm, baseline MD <−4 dB, and a history of diabetes, arterial hypertension, or cardiovascular events exhibited a higher risk for glaucoma progression. Associations between the same parameters and glaucoma progression were assessed by Pearson's chi-square test. The results are summarized in Table 3.

In our study we observed that local parameters such as baseline IOP higher than the calculated average, baseline MD lower than −4 dB, or thinner than average corneas exhibited a pattern of increased risk for glaucoma progression, but owing to the small sample size, no statistical significance could be attributed to these findings.

Regarding systemic factors, male sex had no relevance as a risk factor in glaucoma progression, and progression rate between sexes showed no statistical significance in the Wilcoxon test ($p = 0.28$).

A positive history of cardiovascular diseases and hypertension reached no statistical relevance in terms of increased risk or significant association with glaucoma progression. Interestingly we found a borderline significance ($p = 0.07$) for diabetes as a "protective factor" against progression, since more "stable"

Fig. 4 Mean deviation (*MD*) slope distribution in the study (db/year). Calculation was possible in 67 out of 69 eyes
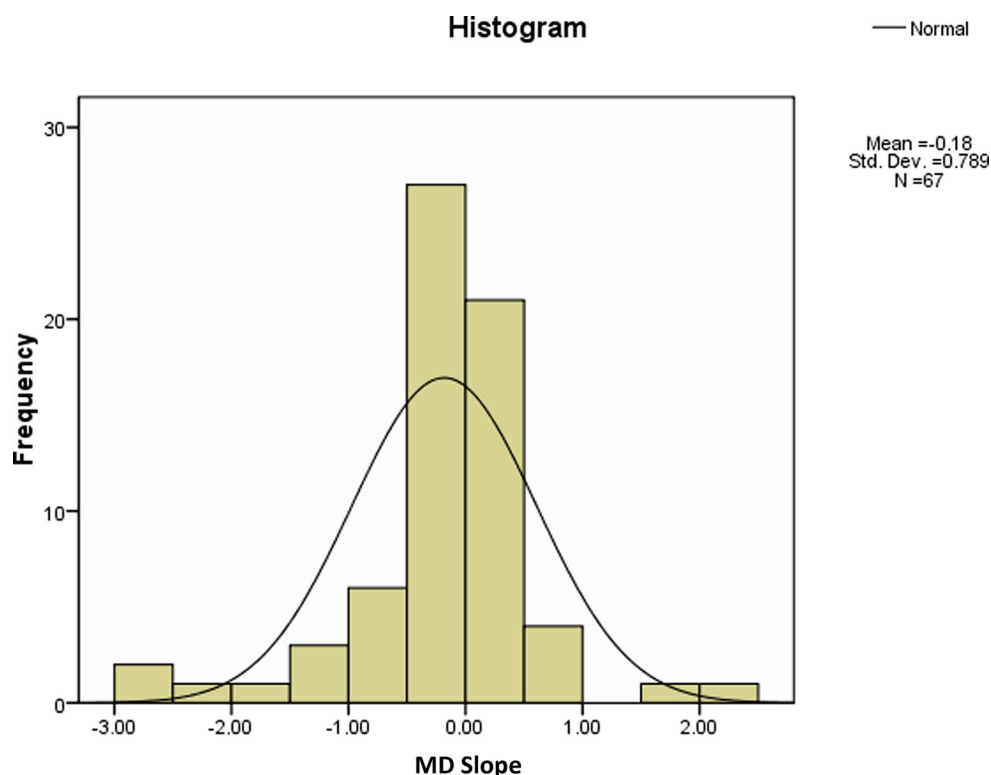

Histogram

— Normal

Mean =-0.18
Std. Dev. =0.789
N =67

Table 2 Mean deviation (MD) slope model summary[a]

| Model | R | R^2 | Adjusted R^2 | SE of the estimate | Change statistics | | | | |
					R^2 change	F change	df1	df2	Sig. F change
1	0.355[b]	0.126	0.113	0.74283	0.126	9,385	1	65	0.003
2	0.810[c]	0.656	0.645	0.46956	0.530	98,671	1	64	0.000

[a]Dependent variable: MD slope
[b]Predictors: (constant), final MD
[c]Predictors: (constant), final MD, baseline MD

cases were associated with diabetes than "progressing" ones. Further, all parameters with a $p < 0.2$ in the univariate model were introduced in a multivariate model, but this analysis could not validate any additional information as statistically significant for our study ($p > 0.05$).

Discussion

Progression rate and risk factors are among the most important aspects in glaucoma care because of their impact on visual decay. Although several guidelines for glaucoma management recommended the assessment of progression rate in routine care [8], information has been scarce to date. According to these studies, older age, baseline IOP, decreased CCT, pseudoexfoliation, baseline VF status, and systemic diseases (hypertension, diabetes, cardiovascular events) were risk factors associated with VF progression.

Our study aimed to prove that on clinical care grounds, progression in POAG and its risk factors might be different than in standard clinical trials pos-

sibly due to standardized inclusion/exclusion criteria, strict treatment plans, and clear follow-up schedules.

During a 6-year period we followed up 69 eyes from 69 patients with POAG in clinical care. Overall in our study, VF decreased at a rate of –0.18 dB/year. This is much lower than other reported results, regardless of whether randomized control trials or clinical care studies were evaluated [2, 10–16]. Still, the mean age of our patients was younger than in all other studies and, because of this, we decided to treat the patients more aggressively from the start, assuming a longer life span.

In our study there was no standard IOP-lowering strategy, meaning each doctor involved in the study decided how/when to adjust the IOP according to their own experience until the desired level was reached. No additional surgical procedure was recorded in any patient during the follow-up period, but only changes in topical treatment. Treatment intensity was correlated with VF progression rate up to the point where age was controlled for ($p < 0.05$);

Table 3 Risk of glaucoma progression associated with different variables in univariable model

Parameter	Progression OR (95 % CI)	Significance ($p < 0.05$)	Association with progression Pearson's chi-square test ($p < 0.05$)
Sex, male	0.5 (0.17–1.46)	0.2	0.51
Age >62 years	0.89 (0.45–1.74)	0.74	0.73
Baseline IOP >18 mm Hg	1.66 (0.78–3.5)	0.18	0.16
Baseline MD <–4 dB	1.47 (0.76–2.85)	0.25	0.27
CCT <537 µm	1.17 (0.65–2.1)	0.61	0.73
Diabetes	0.54 (0.27–1.05)	0.07	0.1
Cardiovascular diseases	1.43 (0.57–33.6)	0.74	0.42
Arterial hypertension	0.84 (0.42–1.66)	0.63	0.6

OR odds ratio, *IOP* intraocular pressure, *MD* mean deviation, *CCT* central corneal thickness

after this correction, Spearman's correlation was no longer significant ($p > 0.05$).

Our study analyzed progression in glaucoma based on trend analysis. Although MD itself could not discriminate central from peripheral VF loss, its variations still evaluated the overall visual disability [17].

Our results showed that progression rate in glaucoma (MD slope) was only correlated and influenced by the initial ($p = 0.04$) and final ($p = 0.001$) MD level. In this respect, our results were similar to the OHTS [18, 19] or EMGT [20]. study, where the initial MD level predicted progression rate in hypertensive glaucoma forms. Also for any patient with a baseline MD level lower than –4 dB, we observed an OR > 1, but no statistical significance could be attributed ($p > 0.05$).

EMGT results showed that, by reducing the IOP by 25 %, progression occurred later than in nontreated patients. This could also be the reason for our patients progressing at such a low rate compared with other studies, since medication was constantly changed/added to lower the IOP according to the concept of "target pressure." When a cut-off value was established (baseline IOP > 18 mm Hg), we found OR > 1, but again statistics could not validate this result as significant or reliable ($p > 0.05$). Age as a risk factor for glaucoma progression has been confirmed by many clinical trials [19–24], but disregarded by others [25, 26]. Our study revealed that MD slope was not correlated with age in univariate analysis for the entire study group; also when a cut-off value was established (62 years old), no difference in glaucoma progression (MD slope) was found in older patients (Wilcoxon test, $p > 0.05$), and no increased risk for this parameter could be validated (OR = 0.88, $p > 0.05$).

Most randomized control trials failed to show any association between sex [20] and glaucoma progression. In the OHTS trial [27] men were more likely to convert to glaucoma than women were, whereas CNGTS [26] reported that the risk of glaucomatous progression on women was 1.85 times higher relative to that in men; in our study we found no differences in the progression rates by Wilcoxon test ($p > 0.05$); also we could not prove if male sex was a risk factor in glaucoma progression owing to no statistical significance ($p > 0.05$).

Regarding CCT, De Moraes [6] calculated an OR of 1.38 per 40 mm Hg thinner CCT. In our study we found no significant correlation between MD slope and CCT ($p > 0.05$). The OR calculation for the chosen cut-off value, although >1, could not be taken into account owing to a lack of statistical support ($p > 0.05$).

A recent meta-analysis presented data on systemic hypertension [28], cardiovascular diseases [28], and diabetes [29] as risk factors in glaucoma. For OAG progression, older studies (AGIS [30] and CIGTS [22]) reported a positive association with diabetes while others (CNGTS [26] and EMGT [22]) reported no influence. A systolic pressure lower than 125 mm Hg was a risk factor for progression in the EMGT study [19], whereas there was no association between systemic hypertension and OAG progression as reported by Kang [31], AGIS [30] or CNGTS [26]. Recently, Choi and Kook [28] (2015) offered a more balanced opinion, stating that systemic hypertension had different effects on the development/progression in glaucoma in different age groups.

In our study, although we found an increased incidence of these clinical factors in glaucoma patients, we could not prove any significant association (Pearson chi-square test, $p > 0.05$) or an increased risk of progression (OR, $p > 0.05$). Interestingly, and with borderline statistical significance ($p = 0.07$), we noted diabetes as a "protective" factor in our study group. However, large-scale epidemiological studies reported an association between diabetes and glaucoma [32–34], while others reported this finding as inconclusive and contradictory [35]. Having in mind the "vascular theory" and the complex interaction between blood pressure/IOP or blood pressure/glaucoma [36, 37], we could have calculated the ocular perfusion pressure for our patients, but no blood pressure values were available from the patients' charts. As such, no information could be established in our study whether glaucoma incidence or progression were related in any aspect to the perfusion parameters. Other limitations are the retrospective nature of our study, small number of patients and the clinical care approach; thus our results cannot be generalized or applied to other clinical settings.

Due to logistic limitations (no VFI), we used trend analysis to define and measure progression rates (db/year) in the same manner as Nouri-Mahdavi [38] evaluated some of the patients in AGIS. We acknowledge that the progression rate might not have been linear in glaucoma patients, especially those followed up in the long term, but this approach allowed the clinician to evaluate the patient's behavior when certain treatment was applied. Moreover, it is true that the precision of determining the MD slope is related to several factors, including the length of the follow-up period and the number of examinations. Yet in our study both the follow-up period and the number of VF were comparable to other studies and thus the calculated MD slope could be considered reliable.

Conclusion

Our study aimed to assess whether the risk factors in glaucoma progression based on normal clinical care were the same as those described in other major clinical trials. What we concluded was that the progression rate (db/year) depended on the baseline/final MD levels. Additional risk factors for glaucoma progression reached no statistical significance in our study, therefore larger studies are needed to examine this aspect.

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