Comparison of Visual Field Progression Rates Among the High Tension Glaucoma, Primary Angle Closure Glaucoma, and Normal Tension Glaucoma

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PURPOSE. To compare the visual field (VF) progression among high tension glaucoma (HTG), primary angle closure glaucoma (PACG), and normal tension glaucoma (NTG) subjects in routine clinical care.

METHODS. All patients had ≥5 VF tests using HFA, 24-2, SITA-standard strategy. We compared the progression between glaucoma subtypes after matching the VFs for baseline severity (mean deviation [MD]) and the age at presentation. Global VF progression was evaluated by linear regression analysis (LRA) of MD. For local VF progression, scotoma expansion (SE) and scotoma deepening (SD) were defined as appearance of new scotoma and scotoma deepening (SD) defined by pointwise LRA were calculated. SE and SD were analyzed in three VF zones: superior arcuate (SA), inferior arcuate (IA), and central (C).

RESULTS. A total of 310 HTG, 304 PACG, and 165 NTG eyes were included. When VFs were matched by baseline MD, a greater number (n = 20/76) of eyes with HTG showed significant progression compared to PACG (n = 9/76; P = 0.04). The number of progressing eyes were not significantly different between HTG and NTG (n = 11/76; P = 0.10) and between NTG and PACG (P = 0.65). When the baseline VFs were matched by age, the number of eyes showing significant progression were similar in all the subtypes. SA zone in HTG and NTG showed greater SE and SD compared to other zones (P < 0.05), whereas IA zone in PACG showed greater SE and SD compared to other zones (P < 0.05).

CONCLUSIONS. In our cohort of treated primary glaucoma with matched baseline severity, a greater proportion of HTG eyes progressed faster compared to PACG. SA zone in HTG and NTG and IA zone in PACG showed greater VF progression.

Keywords: visual field, progression, glaucoma

Visual field (VF) progression is the main outcome measure for the majority of glaucoma clinical trials. 1–6 The mean VF progression rates for the patients enrolled in these clinical trials ranged from 0.00 to −1.1 dB/year. 3,6–9 Clinical trials usually have a strict protocol to monitor IOP control, compliance, and follow-up. However, in regular clinical care, patient’s compliance and follow-up are important determinants for treatment outcomes. Therefore, the progression rates obtained from clinical trials may not always reflect the disease course or progression seen in patients under regular clinical care.

Studies comparing VF progression rates in primary open angle glaucoma (POAG) patients enrolled in clinical trials and those under routine clinical care have reported conflicting results. Chauhan et al. 10 reported lower VF progression rate in clinical care, while Heijl et al. 11 reported highly variable VF progression rates in clinical care. Henson et al. 12 reported faster VF progression in routine clinical care patients compared to clinical trials.

Majority of these clinical trials had POAG patients, which was due to a higher prevalence of POAG compared to primary angle closure glaucoma (PACG) in these study populations. However, in the South Asian population, the prevalence of PACG is high and is estimated to contribute to 86% of the world’s angle closure glaucoma population. 13 PACG in the south Indian population is reported to be as high as POAG. 14–18

The existing sparse literature comparing VF progression rates in different glaucoma subtypes in patients under standard clinical care has reported similar mean progression rates among the glaucoma subtypes, without adjusting for baseline severity and age at presentation. 19 However, the progression rates can be affected by age at presentation and baseline severity. 20 Hence evaluating rates of progression by subtypes matched for baseline severity and age at presentation is important.

Studies have shown different spatial pattern of VF defects among various glaucoma subtypes; in normal tension glaucoma (NTG), the VF locations closer to fixation are involved early, whereas in high tension glaucoma (HTG), the field defects are
noted in the arcuate areas. From a clinical perspective, it is important to study the pattern of VF defects in glaucoma as different areas of VF loss would have a different impact on the vision-related quality of life.

In this study, we analyzed the longitudinal VF data collected at a tertiary eye care center, with an aim to study the (1) global VF progression rate in different glaucoma subtypes matched for baseline severity and age; and (2) to evaluate patterns of VF progression in different glaucoma subtypes. We choose to study this in the three primary glaucoma subtypes: the POAG referred as HTG, PACG, and NTG.

**METHODS**

This retrospective study was approved by the institutional review board and followed the tenets of the Declaration of Helsinki. Patients with a clinical diagnosis of HTG, PACG, and NTG with five or more VF examinations performed from January 2000 to December 2012 were included in this study.

Participants in this study were under standard clinical care by glaucoma specialists. Unlike clinical trials where the protocol was standardized and the VF examinations were carried out at regular intervals, the frequencies of VF examinations were different for different participants. The frequency with which VF examinations were conducted in our study varied from 3 months to 2 years. To standardize and for meaningful comparison, we included VFs that were at least 1 year apart but not more than 2 years apart. Data from both eyes were included.

All patients underwent comprehensive eye examination that included IOP measurements using Goldmann applanation tonometry, four mirror gonioscopy in dark room using Sussman lens, dilated fundus examination using 90D lens, VF examination using HFA, and Swedish Interactive Threshold Algorithm (SITA) standard test strategy using the 24-2 grid. VF overview reports were saved in PDF format from Zeiss Forum software. Using custom written computer program in R software, we extracted the reliability parameters, raw threshold values, mean deviation (MD), and pattern standard deviation (PSD) values from the overview reports. VFs that had false positive, false negative, and fixation loss greater than 33% were excluded from the analyses. Any patient with a follow-up period of <5 years or any other ocular diseases other than cataract were excluded from the study. Patients who underwent any intraocular surgery (including cataract and glaucoma filtration surgery) either prior to their presentation to our institute or during the follow-up period were excluded from the study. Eyes with with acute angle closure attack were also excluded. All those included had a minimum number of five VFs per eye after fulfilling the exclusion criteria.

HTG, PACG, and NTG diagnoses required the presence of optic nerve head changes characteristic of glaucoma (focal or diffuse neuroretinal rim thinning, localized notching, or nerve fiber layer defects) with correlating VF defects. Angle closure was diagnosed in the presence of occludable angle or closed angle (posterior trabecular meshwork was not visible in ≥180° on gonioscopy) with synechiae or elevated IOP > 21 mm Hg with glaucomatous disc damage. HTG was diagnosed in the presence of open angles on gonioscopy and IOP greater than 21 mm Hg without treatment. NTG was diagnosed with features similar to HTG, but with IOP <21 mm Hg on more than two clinic visits or on diurnal IOP measurements prior to treatment (of the 212 NTG eyes, 156 eyes had 24-hour diurnal IOP measurements prior to initiation of treatment and the rest were diagnosed based on IOP < 21 mm Hg on more than two clinic visits).

**Table 1.** Baseline Parameters, Follow-Up Years, and Median Time Between Follow-up in HTG, PACG, and NTG Subgroups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>HTG (N = 310 eyes)</th>
<th>PACG (N = 304 eyes)</th>
<th>NTG (N = 165 eyes)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline age, y</td>
<td>58 (49 to 65)</td>
<td>54 (48 to 60)</td>
<td>57 (50 to 63)</td>
<td>0.22</td>
</tr>
<tr>
<td>Baseline MD, dB</td>
<td>−8.4 (−3.6 to −18.9)</td>
<td>−4.6 (−2.2 to −13.0)</td>
<td>−7.2 (−3.5 to −14.1)</td>
<td>0.003</td>
</tr>
<tr>
<td>Follow-up, y</td>
<td>10.5 (8.5 to 13.1)</td>
<td>11.3 (9.1 to 13.4)</td>
<td>9.5 (7.5 to 11.9)</td>
<td>0.05</td>
</tr>
<tr>
<td>Median time between follow-up, y</td>
<td>1.6 (1.3 to 2.0)</td>
<td>1.6 (1.3 to 2.0)</td>
<td>1.6 (1.3 to 1.8)</td>
<td>0.49</td>
</tr>
</tbody>
</table>
### Table 2. Showing Baseline MD, Age, and Rate of MD Progression for Baseline MD Matched Triplets and Age Matched Triplets

<table>
<thead>
<tr>
<th>Parameters</th>
<th>HTG (N = 106)</th>
<th>PACG (N = 106)</th>
<th>NTG (N = 106)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline MD Matched (N = 76)</td>
<td>Baseline Age Matched (N = 106)</td>
<td>Baseline Age Matched (N = 106)</td>
<td>Baseline Age Matched (N = 106)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
</tr>
<tr>
<td><strong>Baseline MD, dB</strong></td>
<td>3.7 (2.4 to 6.2)</td>
<td>3.7 (2.4 to 6.2)</td>
<td>3.7 (2.4 to 6.2)</td>
</tr>
<tr>
<td><strong>Baseline age, y</strong></td>
<td>58 (50 to 65)</td>
<td>50 (47 to 59)</td>
<td>52 (44 to 61)</td>
</tr>
<tr>
<td><strong>Rate of MD progression, in dB/y</strong></td>
<td>0.5 (−1.2 to 0)</td>
<td>0.4 (−0.8 to 0)</td>
<td>0.4 (−0.8 to 0)</td>
</tr>
</tbody>
</table>

Our treatment protocol for PACG is to perform laser peripheral iridotomy (LPI) for all eyes. Following LPI, based on the post PI IOP, disc damage, and angle opening/ocludability, we initiate treatment. One to 2 weeks post-LPI, the VFs are performed. We have excluded eyes with acute angle closure attack.

Since we extracted only raw threshold values from “overview” HFA printouts, the total deviation values, and pattern deviation values were calculated from “visualField” packages available in R. The “visualField” package contains normative data of 24-2 SITA test strategy. The details of the normative database are described elsewhere. Marín-Franch et al. have shown that the MD values calculated from this normative data set showed good agreement with HFA normative data set.

### Definition of Progression

**Global VF Progression.** To calculate the global VF progression, we regressed MD values over time. Chauhan et al. used a robust linear regression analysis (robust to the outliers) to calculate VF progression in large clinic populations. We also adopted robust linear regression to calculate the slopes. We matched VFs for age and glaucoma severity (MD) at presentation. A custom built computer program automatically selected the VF triplet. Each triplet contained either baseline MD or age matched VF from HTG, PACG, and NTG cohorts. The computer program chooses a triplet when the MD difference between groups was ≤ 0.1 dB or age difference between groups was ≤ 11 months. If there were multiple combinations of matched triplets, then we chose the triplet that had least MD or age difference. The computer program selected triplets with the condition that each patient’s VF data was used only once.

**Fast VF Progression.** We defined fast VF progression as the rate of worsening of MD greater than 1 dB/year with a P value ≤ 0.05. The P value for robust linear regression was obtained using Wald test for multiple coefficients of robust linear regression. We chose this rate of progression (ROP) cut off value because eyes with early glaucomatous VF damage progressing at this rate will reach an end stage glaucoma in 10 to 15 years. We determined the fast progressing subtype in a triplet by calculating the differences in the ROP between eyes. In a triplet, if a particular subtype had a ROP greater than 1 dB/year compared to other two subtypes then that particular subtype was labelled as fast progressing subtype in the triplet. Figure 1 shows an example of a fast progressing subtype in baseline MD matched triplet (Fig. 1A) and baseline age matched triplet (Fig. 1B). In both of these triplets, the HTG was a fast progressing subtype.

**Local VF Progression.** For local VF progression, we studied the (a) enlargement of scotoma, and (b) deepening of scotoma in all the three glaucoma subtypes. We defined scotoma enlargement as an appearance of new scotoma at last visit, that is, VF locations that were normal at baseline visit but showed pattern deviation probability (PDP) < 0.5% at last visit. To estimate the scotoma deepening we used the point-wise linear regression (PLR) technique. The PLR technique has been described in detail elsewhere. Briefly, PLR fits a linear regression to VF pattern deviation sensitivity values against the patient’s visit. In this study, we used robust linear regression to calculate slopes and locations. They were considered as significantly progressing when the slope was greater than −1 dB/year and had a P value ≤ 0.01. For the outermost points in 24-2 VF slope greater than −2 dB/year with P value ≤ 0.01 was used. The VF locations with significant PLR progression were determined for scotoma deepening analysis. For all local analysis, VF locations (X = 15, Y = ±3 degrees)
above and below the blind spot were eliminated from the analysis and VF locations with PDP < 0.5% at baseline were excluded from the analysis. 
VF defects were shown to have an impact on the vision-related quality of life. Different areas/zones of VF loss would have a different impact on the vision-related quality of life. To estimate which VF zone was more prone to scotoma enlargement and/or deepening in each subtype, we divided VFs into three zones: central, superior arcuate, and inferior arcuate (shown in Fig. 2).

Statistical Methods
A generalized estimate equation (GEE) was used to compare the parameters between groups as we used data from both eyes. A \( \chi^2 \) test was used to compare the proportion of eyes with a subtype of glaucoma that had fast progressing eye in the triplet analysis. One-way ANOVA was used to calculate the significant difference between zones and 2-way ANOVA was used to find the interaction between zones and groups. Statistical significance was set at \( P \leq 0.05 \). All statistical analysis was performed using “R” software.\(^{33}\)

RESULTS
In total, 2065 patients had clinical diagnosis of glaucoma and had five or more VFs between January 2000 to December 2012. Among these, 213 HTG (310 eyes), 206 PACG (304 eyes), and 108 NTG (165 eyes) were included in the study. The remaining eyes were excluded and the reasons were unreliable follow-up VFs or irregular follow-up (\( n = 784 \)), cataract or glaucoma filtration surgery (\( n = 111 \)), other ocular diseases such as age-related macular degeneration (ARMD) (\( n = 285 \)), pseudoexfoliation (\( n = 42 \)), diabetic retinopathy (\( n = 81 \) patients), hypertensive retinopathy (\( n = 36 \)), anterior ischemic optic neuropathy (AION) (\( n = 18 \)), papilledema (\( n = 14 \)), optic neuritis (\( n = 8 \)), and retinal vein occlusion (\( n = 159 \)), which could affect the VFs.

Visual Field Progression in Subtypes of Glaucoma

Table 1 shows the median and interquartile range (IQR) of the baseline age, baseline MD, and years of follow-up for HTG, PACG, and NTG eyes.

Figure 3 shows the distribution of MD progression rate in the three subtypes of glaucoma. The median progression rate (in dB/year) and IQR in HTG was \(-0.3 (-1.0 to 0.0)\), PACG was \(-0.3 (-0.8 to 0.0)\), and NTG was \(-0.3 (-0.7 to -0.1)\). The global median progression rates between groups did not show a statistically significant difference (\( P = 0.44 \)). However, the proportion of eyes showing fast progression (MD worsening greater than 1 dB/year) between groups showed a statistically significant difference (\( \chi^2 \) test: \( P = 0.03 \)). In our cohort, 45 out of 310 eyes (14.5%) in HTG, 39 out of 204 eyes (12.8%) in
PACG, and 24 out of 165 eyes (14.5%) in NTG showed fast progression.

A total of 76 triplets were matched based on their baseline MD (severity matched) and 106 triplets were matched based on their age at presentation. The baseline parameters of the subtypes of glaucoma cohorts among these triplets matched for MD and age are given in Table 2.

In 36 out of 76 baseline MD matched triplets, none of the subtypes had ROP differences greater than 1 dB/year between them. In the remaining 40 triplets, HTG had the greatest proportion of progressing eyes (n = 20 of 40 eyes; 50%), followed by NTG (n = 11 of 40 eyes; 28%), and PACG (n = 9 out of 40 eyes; 22%) (Fig. 4A). A $\chi^2$ test showed a statistically significant difference in the proportion of progressing eyes between HTG and PACG ($P = 0.04$). The differences between HTG versus NTG and PACG versus NTG were not significant.

Similarly, in 58 out of 106 baseline age matched triplets, none of the subtypes had ROP differences greater than 1 dB/year between them. In the remaining 48 triplets, both HTG eyes (n = 17 out of 48 eyes; 35%) and NTG eyes (n = 17 out of 48 eyes; 35%) had similar proportion of progressing eyes followed by PACG (n = 14 out of 29 eyes; 29%) (Fig. 4B). A $\chi^2$ test showed no statistically significant difference in the number of progressing eyes between the subtypes of glaucoma (Fig. 4B).

IOP is known to influence the VF progression. We collected the IOP values of all eyes from triplet analysis. Figure 5 compares the baseline IOP (IOP value measured on first visit), peak IOP (maximum recorded IOP during follow-up visits), and follow-up IOP (average IOP values of all visits) for the fast progressing eye in triplets versus other two eyes in the triplet. The mean follow-up IOP was higher ($P = 0.001$) in the fast progressing eye in MD matched and in the age matched triplet ($P = 0.04$) compared to the other two eyes in the triplet. The baseline IOP and maximum IOP were not statistically significantly different between the fast progressing eye and other two eyes in the triplet.

In the triplet analyses, we defined fast progressing subtype as the difference in the rate of MD progression greater than 1 dB/year compared with other subtypes. To check the robustness of our results, we repeated analyses with different rates of progression (ROP) cut off values. Figure 6 shows the number of progressing eyes for each subtype with different ROP cut offs for both MD and age matched triplets. A similar trend was noted with HTG showing a greater number of eyes progressing compared to NTG and PACG at all five different ROP cut offs.

**Local VF Progression**

In moderate and advanced glaucoma, VF locations might have already reached the floor effect at $P < 0.5%$. Because these defects are so deep, they are unlikely to change and if they do so, they tend to be unreliable. Therefore, for local VF progression analysis we included only early glaucoma, that is, MD equal to or better than $-6$ dB at baseline. In total 406 eyes were included. Out of which, 135 eyes in HTG, 183 eyes in PACG, and 88 eyes in NTG had MD equal or better than $-6$ dB at baseline. The median (IQR) of the baseline MD for the three subgroups were HTG: $-3.17$ ($-2.25, -4.13$) dB, PACG: $-2.65$ ($-1.38, -4.02$) dB, and NTG: $-3.54$ ($-1.99, -4.33$) dB ($P = 0.81$). The number of VF visits between groups was not
Figure 7 shows (A) baseline threshold values, (B) percentage of eyes showing scotoma enlargement at each VF location, and (C) percentage of eyes showing scotoma deepening at each VF location in HTG, PACG, and NTG. The dB values and percentages were pseudo-color coded according to the color bar shown in Figure 7.

Figure 8A shows the percentage of eyes with scotoma enlargement in the three different zones among the glaucoma subtypes. Each dot in the box plot represents one VF location in the corresponding zone. One-way ANOVA showed significant difference between zones in all three subtypes: HTG $F(2, 29) = 4.87, P = 0.015$; PACG: $F(2, 29) = 5.387, P = 0.01$; and NTG $F(2, 29) = 22.05, P < 0.001$. Post-hoc analysis using Tukey HSD test revealed greater scotoma enlargement in the superior arcuate zone in HTG and NTG and inferior arcuate zone in PACG. Two-way ANOVA showed significant interaction between zones and subtype: $F(4, 87) = 6.23, P < 0.001$.

Figure 8B shows the percentage of eyes with scotoma deepening at superior arcuate, inferior arcuate, and central zones in three subtypes of glaucoma. Each dot in the box plot represents one VF location in the corresponding zone. One-way ANOVA showed significant difference between zones in all three subtypes: HTG $F(2, 29) = 11.69, P < 0.001$; PACG: $F(2, 29) = 7.46, P = 0.002$; and NTG: $F(2, 29) = 4.93, P = 0.014$. Post-hoc analysis using Tukey HSD test showed superior arcuate zone in POAG and NTG and inferior arcuate zone in PACG with greater scotoma deepening. Two-way ANOVA showed a significant difference $F(4, 87) = 6.039, P < 0.001$, suggesting scotoma deepening zone were not similar between subtypes.

Figure 9 shows the progression rate in each zone for all three subtypes (dots in the boxplot represents the progression rate for each VF location in that zone). As seen only in NTG, the progression rates were significantly different between zones. Two-way ANOVA showed significant interaction between zones and subtype: $F(4, 87) = 6.23, P < 0.001$.

**Discussion**

This study aimed to assess VF progression in the three subtypes of primary glaucoma—in HTG, PACG, and NTG subjects under clinical care of glaucoma specialists. The median VF progression rate found in this study is similar to the VF progression rates reported in clinical trials, which ranged from 0.0 dB/year to −1.1 dB/year.3,6,8–10 The median ROP among all three subtypes was similar (−0.3 dB/year). The mean progression rates in the study by De Moraes et al.19 for HTG, PACG, and NTG were −0.48 dB/year, −0.39 dB/year, and −0.33 dB/year, respectively. Majority of HTG (53.9%), PACG (54.3%), and NTG (65%) eyes had slope value between 0 and −1. Approximately, 22.3% of eyes in HTG, 28.3% of eyes in PACG, and 20% of eyes in NTG had slope value greater than zero. Similar positive slope values in VFs have been reported in major randomized controlled trials (RCTs) and clinic-based studies.3,6,8–10 The positive slopes are attributed to the learning effect, measurement variability,40,41 and true improvement beyond the measurement variability related to clinical parameters.42

For global VF progression, we matched VFs based on baseline severity and age. The result as shown in Figure 4A suggests that even though all three subtypes of glaucoma had the same level of disease severity at baseline, HTG subtype had greater proportion of eyes progressing compared to NTG and PACG. However, when subtypes were matched based on age at presentation (Fig. 4B), all three subtypes had a similar proportion of progressing eyes.

Various studies have reported that PACG eyes to be at two times higher risk of blindness compared to the
FIGURE 5. Baseline IOP, peak IOP, and follow-up IOP for fast progressing eye and other two eyes in the triplets.
This was also noted in the Andhra Pradesh Eye Disease Study (APEDS), which reported 20% bilateral blindness in PACG compared to 11% in POAG.45,46 However, in the current clinic based study, we noted lower progression rates in PACG compared to HTG when baseline severity was matched. The reason for this discrepancy could be due to the study type and the level of clinical care. Studies that concluded higher risk of blindness in PACG eyes were cross-sectional population-based prevalence studies13,14,16,17,43,44 whereas the current study is a clinic-based study.

The level of clinical care available for patients in population-based estimate studies cannot be commented on. In our study, patients were under the clinical care of glaucoma specialist and had a regular follow-up. The possible reasons for the higher risk of blindness in PACG in population-based studies may be due to lack of awareness of the disease, poor access to health care, disease diagnosis at advanced stages, and including patients with acute angle closure attack. In our study, we excluded patients with a history of acute angle closure attack. In our study, all eyes in the PACG group had LPI as primary procedure in the management and later treated with appropriate medical treatment. This study suggests that diligent clinical care of PACG eyes, which includes an LPI as initial treatment and standard treatment thereafter, can lower VF progression rates in PACG.

Clinical parameters such as pseudoexfoliation, poor IOP control, number of glaucoma medications, and surgical interventions are known to affect the rate of VF progression.3,6,37,38,47,48 In our study, we excluded all eyes with pseudoexfoliation and eyes that underwent surgical intervention. When we compared the IOP between the fast progressing eye and the other two eyes in the triplet (both age and MD matched), the median follow-up IOP was higher in the fast progressing eye compared to the other two eyes in the triplet. This suggests that the difference in the progression rates between subtypes could be due to higher mean follow-up IOPs.

Learning effect is shown to influence VF progression.40,41 To rule out the suspicion of learning effect influencing our VF progression between groups, we compared the slope of the first three VFs between groups. The median slope (IQR) for first three VFs in HTG, PACG, and NTG were 0.2 (0.5 : −1.1), 0.2 (0.6 : −1), and 0.1 (0.5 : −0.9), respectively ($P=0.918$). This suggests that the learning effect between groups was not different and hence may not have influenced the VF progression rate between groups.

It is well-known that VFs in glaucomatous eyes progress in one or a combination of the following: new defects, deepening, or expansion of an existing defect. The findings in our study were consistent with it. HTG and NTG showed scotoma enlargement and deepening in superior arcuate zone, whereas PACG showed scotoma enlargement and deepening in inferior arcuate zone. Although, in HTG and PACG, the number of locations that show progression (both enlargement and deepening) were different, the rate at which these zones progress, that is, the average dB loss per year for each zone were not significantly different between zones in HTG and PACG (Fig. 9).

Our study agrees with previous studies that the nasal region and the superior arcuate region is the most common location for VF defects in HTG.21,22,24,49 Similarly, the paracentral region and VF locations close to fixation are more prone to VF defects in NTG. An interesting finding in our study was that in PACG the inferior arcuate locations were more prone to scotoma enlargement compared to superior arcuate locations.

Cross-sectional studies comparing the total deviation values of the superior hemifield with that of the inferior hemifield at various stages (mild, moderate, and severe) of PACG reported greater total deviation values in the superior than in the inferior hemifield.25,50 Verma et al.51 have shown that in early PACG, greater number of locations progressed in superior temporal Garway-Heath (GH) VF sector compared to inferior temporal GH VF sector. The reason for this discrepancy between Verma et al.51 and our study results may be due to the difference in the criteria for progression used in these studies.

**Figure 6.** Number of eyes that showed progression in the three glaucoma subtypes at different rates of progression cut off values. (A) Baseline MD matched triplet and (B) baseline age matched triplet.
We defined significant pointwise VF progression as slope was greater than $-1$ dB/year with $P < 0.01$ and for edge/peripheral locations slope greater than $-2$ dB/year with $P < 0.01$. However, in their study, the rapid progression was defined as slope $<-1.5$ with no criterion set on $P$ value.

Most studies divide VF into GH VF sectors. We choose to divide VF into three zones: central, superior arcuate, and inferior arcuate because of the functional implications of VF defects in these zones and on vision-related quality of life. We ran the same analysis dividing into GH VF sectors (results not shown) and the conclusion remained the same; the superior temporal sector in HTG and NTG and inferior temporal GH sector in PACG showed greater scotoma enlargement and deepening.

Various studies have shown patients with superior VF defects have difficulty in driving and reading task, whereas patients with inferior VF defects have difficulty in mobility and increased rates of falls. In our study, HTG and NTG showed significant scotoma deepening in superior arcuate zone, whereas in PACG the inferior zone showed significant scotoma deepening. Therefore, the vision related quality of life would be differently affected in the PACG group compared to HTG and NTG groups.

Our study has its limitations, many confounders that would influence the disease progression such as between visit IOPs, compliance to medications, regularity of follow-up, and persistence to treatment cannot be commented on since these data were not evaluated. Also, because of the retrospective nature of this study, the effects of systemic and hemodynamic factors on progression have not been looked at. Other factors could be that in the baseline MD matched cohort, the HTG cohort was on average 4 years older compared to PACG; therefore, the increase in age and the effect of possible cataractous changes on MD cannot be ruled out.

We used MD to calculate global VF progression. The MD was calculated using total deviation values, which were shown to be affected by media opacities. Since cataract grading data were not available in our retrospective data, the effect of cataract in our data set cannot be commented. We made an assumption that the cataract effect on MD in all three subtypes.
would be similar because the age group in three subtypes were similar. The VF index (VFI) calculated from PDP plots could have been less prone to cataract changes. However, we avoided using VFI because at both early and late stages of glaucoma VFI can be unreliable. Rao et al. have shown that when MD crosses −20 dB the decrease in VFI can be highly variable. Artes et al. have shown that in early glaucoma when MD was better than −5 dB, the ceiling effect on VFI would influence progression analysis.

Years of follow-up and time between follow-up was shown to influence the MD regression analysis. To detect a change of −1 dB/year for a moderately variable VF with a power of 80% requires 9 years of follow-up period. Although the median follow-up period was greater than 9 years in this study, the frequency of VF testing was longer 1.6 years (Table 1). A limitation of PLR analysis in our study was few of the VF in PLR analysis have only five visits. The PLR analysis have poor specificity for VF with only five visits (series). Since a greater proportion of eyes in NTG had lesser VF visits compared to the other two groups, the specificity of PLR analysis in NTG maybe poorer compared to HTG and PACG. Hence, PLR analysis in NTG should be interpreted with caution while comparing with other subtypes.

Another limitation of our study was that all patients in our study underwent SITA test strategy that uses a “growth pattern” to estimate the VF defects. Briefly, growth pattern

FIGURE 8. Boxplot showing the percentage of eyes showing scotoma enlargement (A) and scotoma deepening (B) at superior arcuate (SA), inferior arcuate (IA), and central zones in the three glaucoma subtypes. Each dot in the boxplot represents one VF location in the corresponding zone. An asterisk indicates the group responsible for significance in the post-hoc analysis.

FIGURE 9. Boxplot showing the ROP (dB/year) at superior arcuate (SA), inferior arcuate (IA), and central zones in the three subtypes of glaucoma. An asterisk indicates the group responsible for significance in the post-hoc analysis.
estimates threshold at four fixed primary locations (in case of SITA they are 12.7° from fixation in each quadrant) and the starting intensity for the secondary location is borrowed from the primary location.62 Studies have shown that the defect at the primary location will have an effect on secondary locations,63 a false or incorrect response at the primary location may give rise to a false increase in the spread of VF defects. This type of artefact arises when the patient was not attentive or learning to do the test in the first few minutes of testing. Since primary locations were tested first, an incorrect response at these locations may result in a false spread of VF defects. Finally, the 6° grid used by the 24-2 SITA program may not be adequate to pick up subtle scotoma,64 as a result, the spatial spread of progression measured using a 6° grid may be undersampled.

In this study, we have shown that the global rates of VF progression were less in PACG than HTG when the baseline severity were matched, and the pattern of progression for PACG was different from HTG. Several studies have shown that the pattern of structural damage is also different between HTG and PACG,24,64,65 which may suggest different disease mechanisms. In conclusion, in patients under clinical care by glaucoma specialists, VF progressed faster in HTG compared to PACG and NTG.

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References

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