Rates of Visual Field Loss in Primary Open-Angle Glaucoma and Primary Angle-Closure Glaucoma: Asymmetric Patterns

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Purpose. The purpose of this study was to evaluate the rate of visual field (VF) loss in primary open-angle glaucoma (POAG) and primary angle-closure glaucoma (PACG).

Methods. Four hundred forty eyes of 282 patients with POAG (aged 53.4 ± 12.0: mean ± standard deviation, years) and 79 eyes of 49 patients with PACG (aged 62.7 ± 9.0 years) with at least six or more reliable VF tests were studied. Point-wise, region-wise, and global rates of VF change were assessed for POAG and PACG eyes. Only the VF records prior to laser iridotomy or cataract surgery were included in PACG eyes. The global and superior-inferior asymmetric rates of VF loss were compared between POAG and PACG eyes.

Results. The mean total deviation (mTD) values at baseline were −6.4 ± 5.7 dB in POAG patients and −6.4 ± 7.3 dB in PACG patients. There was not a significant difference in the progression rates of mTD between POAG eyes (−0.23 ± 0.38 dB/y) and PACG eyes (−0.29 ± 0.45 dB/y). In POAG eyes, the VF progression rate was significantly asymmetric across the horizontal line; the central, paracentral, and peripheral arcuate 2 regions in the superior hemifield had a significantly faster rate of VF loss than their inferior counterparts. In contrast, this asymmetry was not observed in the rate of VF loss in PACG eyes.

Conclusions. POAG eyes showed a faster rate of VF loss in the superior hemifield compared to in the inferior hemifield, particularly in central and paracentral regions. This difference was not observed in PACG eyes.

Keywords: primary angle-closure glaucoma, primary open-angle glaucoma, visual field, progression rate

Glaucoma is one of the leading causes of blindness worldwide.[1–3] There are two types of primary glaucoma: primary open-angle glaucoma (POAG) and primary angle-closure glaucoma (PACG). POAG is characterized by an open iridocorneal angle, and in contrast, PACG is characterized by a narrow or closed iridocorneal angle that hampers the aqueous efflux, which can lead to increased IOP.

POAG predominates over PACG in most populations, with a prevalence of 3.54% in those between 40 and 80 years old.[4] The prevalence is approximately 0.92% in PACG.[2] In contrast to the higher prevalence of POAG, PACG has a threefold greater risk of developing blindness compared to POAG.[4–8] As a result, it is estimated that 4.5 million people worldwide are bilaterally blind due to POAG, whereas that number is 3.9 million people with PACG.[2] This is problematic, particularly in areas where there is a high prevalence of PACG such as in in Alaska (among those of Eskimo descent[9]), Asia,[4,9] Myanmar,[10] and Mongolia.[11,12]

The clinical courses of POAG and PACG are very different. It has been well documented that IOP is the major risk factor for POAG. However, there are other risk factors, including older age, disc hemorrhage, large cup-to-disc ratio, beta-zone parapapillary atrophy, and lower systemic blood pressure.[13–24] On the other hand, in PACG, the elevation of IOP due to angle closure is usually the exclusive disease mechanism.[12] This difference in disease mechanisms is also supported by genetic findings of different single nucleotide polymorphism associations in PACG and POAG.[25,26]

Previous studies have reported that POAG and PACG have different patterns in visual field (VF) damage.[27–31] The VF damage is more pronounced in the superior hemifield than in the inferior hemifield in both POAG and PACG groups[32–35]; however, this tendency is more obvious in POAG eyes.[27–30]

Without doubt, the assessment of the rate of VF loss is very important in the management of glaucoma.Nonetheless, most of the previous studies have investigated the cross-sectional

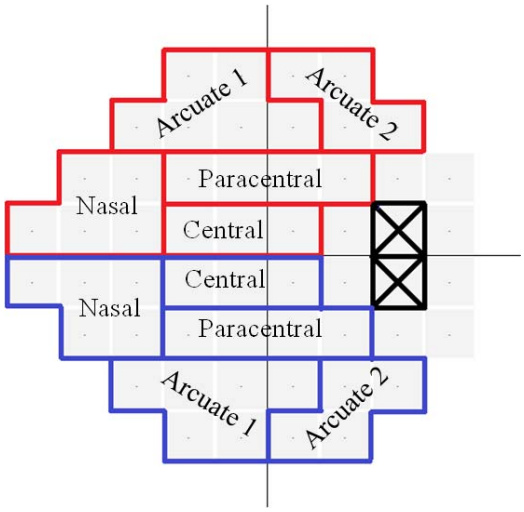

FIGURE 1. GHT VF regions. Five GHT regions were allocated both in the superior and inferior hemifields.

spatial patterns of VF loss. However, a recent study has investigated the rates of VF loss in eyes with PACG.[36] It has been reported in some of the population-based studies that the rate of glaucoma-induced blindness is greater in eyes with PACG compared to eyes with POAG. This might suggest that the progression course in eyes with PACG is more aggressive than eyes with POAG. To the best of our knowledge, there has been no study comparing the progression rates and the hemifield asymmetry of the rate of VF loss in POAG and PACG eyes.

The purpose of the current study was to determine and compare global, region-wise, and point-wise rates of VF loss in POAG and PACG eyes to identify whether POAG and PACG eyes progress at different rates and or with different patterns.

METHODS

Subjects

The review board of both institutes of Tokyo University Hospital and Ryukyus University Hospital reviewed and approved the study protocol. This study complied with the tenets of the Declaration of Helsinki. Written consent was given by each patient for their information to be stored in the hospital database and used for research based on the regulations of the Japanese Guidelines for Epidemiologic Study 2008 from the Ministry of Education, C., Sports, Science and Technology.

VF tests were retrospectively acquired from the electronic medical records of patients who visited either the Tokyo University Hospital or Ryukyus University Hospital between 1998 and 2016. All patients with POAG and PACG who met the criteria below were included: (1) glaucoma was the only disease causing VF damage, (2) at least six VF measurements were taken with 24-2 or 30-2 Humphrey Field Analyzer II (HFA) (Carl Zeiss Meditec, Inc., Dublin, CA, USA) using the Swedish Interactive Threshold Algorithm standard program, (3) an abnormal VF defined with the Anderson-Patella criteria,[37] (4) 20 years or older, and (5) secondary ocular hypertension in either eye other than angle closure.

POAG was defined as (1) presence of typical glaucomatous changes in the optic nerve head, including a rim notch with rim width $\leq$0.1 disc diameters or a vertical cup-to-disc ratio greater than 0.7 and/or a retinal nerve fiber layer defect with its width at the optic nerve head margin greater than a major retinal vessel, diverging in an arcuate or wedge shape, and (2) wide open angle with gonioscopy. POAG eyes with significant cataract were carefully excluded, except for clinically insignificant senile cataract on biomicroscopy.

PACG was defined as (1) presence of angle closure defined as at least 180° of the posterior pigmented trabecular meshwork not visible on gonioscopy in the primary position of gaze without indentation and (2) existence of glaucomatous optic neuropathy defined as neuroretinal rim loss with a vertical cup-to-disc ratio of greater than 0.7 or between eye vertical cup-to-disc ratio asymmetry of greater than 0.2, focal notching of the neuroretinal rim with a VF defect suggestive of glaucoma, or both.[38] Eyes with significant cataract were carefully excluded, except for clinically insignificant senile cataract on biomicroscopy. Those with a history of an acute primary angle closure attack were excluded. Only the VF records prior to laser iridotomy or cataract surgery were included for analysis with the PACG eyes. This is because VF progression rate would be different between before and after laser iridotomy (LI)/cataract surgery, whereas the principal purpose of the current study was to investigate whether the difference of disease mechanisms between POAG and PACG yields difference in the VF progression rates between POAG and PACG eyes.

Visual Fields

Reliable VF tests with less than 33% fixation losses and less than 15% false-positive results were included, as recommended by the manufacturer. The first VF records were excluded to reduce learning effects. VFs with a 30-2 test pattern were matched to 24-2 test patterns by using only the 52 overlapping test locations. The mean of the 52 total deviation (TD; mTD) values was calculated.

For both POAG and PACG groups, longitudinal VFs were stratified into groups of six (first six VFs) to 10 visits (first 10 VFs). The entire VF was divided into 10 spatial regions by allocating five regions both in the superior and inferior hemifields following the Glaucoma Hemifield Test (GHT)[28,39]: central, paracentral, nasal, arcuate 1, and arcuate 2 regions (Fig. 1).

The mean values of TD in each of the 10 regions was calculated by averaging the TD values of all test locations included in the region.

Statistical Analysis

Processes. We first investigated the overall rate of VF loss in POAG and PACG eyes. We then assessed the superior-inferior asymmetry in the rate of VF loss in POAG and PACG eyes. This was performed by comparing the rates of VF loss of the superior and inferior hemifields in both a point-wise and a region-wise manner. The rate of VF loss was calculated based on various VF sequences lengths (from 6 to 10 VFs) using a linear regression model. Subsequently, the asymmetry in the rate of VF loss between superior and inferior hemifields was investigated for each sequence length (Fig. 2).

Within-Group Comparisons. This comparison was performed for POAG and PACG groups region-wise and point-wise, separately. The analyses were conducted using (1) the rates of VF loss calculated from VF sequences of 6 to 10 visits (as shown in Fig. 2) and also (2) the rate of VF loss calculated from VF sequences with all visits. The significance of the superior-inferior asymmetry in the rate of VF loss was compared using the Generalized Estimating Equation (GEE)[40] to account for the nested structure of the analyzed data, since the current study included both left and right eyes of patients. More specifically,

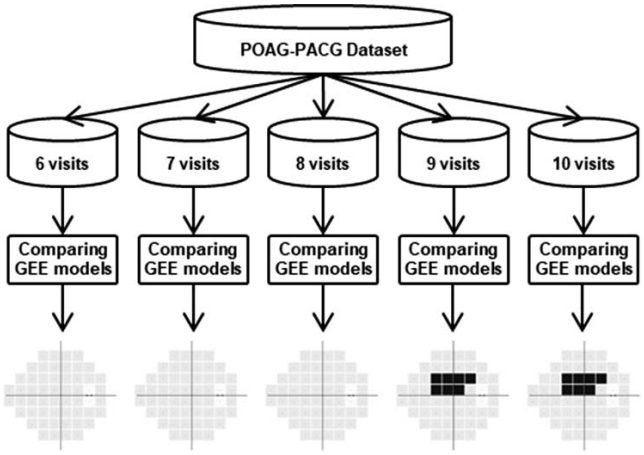

FIGURE 2. A flowchart showing the investigation of the superior-inferior asymmetry in the rate of VF loss. The superior-inferior asymmetry in the rate of VF loss was calculated by comparing the GHT regions in the superior and inferior hemifields using rates calculated from VF sequences of 6 to 10 visits. The *black* areas indicate a statistically significant difference ($P < 0.05$) between the rate of VF loss in the superior and inferior hemifields in that region.

for POAG (alternatively, PACG) eyes, the rates of VF loss were calculated from VF sequences, and GEE models were fitted to the rates of VF loss in the superior and inferior hemifields. The outcome variables (rates of VF loss) were then compared between the superior and inferior hemifields. Thus, we conducted eight separate analyses: (1) POAG group at GHT regions using VF sequences of 6 to 10 visits, (2) POAG group at GHT regions using VF sequences with all visits, (3) POAG group at each VF test point using VF sequences of 6 to 10 visits, (4) POAG group at each VF test point using VF sequences with all visits, (5) PACG group at GHT regions using VF sequences of 6 to 10 visits, (6) PACG group at GHT regions using VF sequences with all visits, (7) PACG group at each VF test point using VF sequences of 6 to 10 visits, and (8) PACG group at each VF test point using VF sequences with all visits.

Between-Group Comparisons. This comparison was performed in GHT regions and test points using the asymmetry in the rates of VF loss calculated from VF sequences of 6 to 10 visits (as shown in Fig. 2) and as well as the asymmetry in the rate of VF loss calculated from VF sequences with all visits. More specifically, the statistical difference between the extent of asymmetry in the rates of VF loss (the difference between the rates of VF loss in the superior and inferior hemifields) between POAG and PACG groups was carried out by constructing region-wise GEE models (alternatively, point-wise models) where the outcome variable was the asymmetry in the rate of VF loss and the primary independent variable was diagnosis (POAG or PACG) controlling for gender, visual acuity, length of follow-up, maximum IOP, and refractive error. Thus we carried out two separate analyses: (1) extent of asymmetry in the rates of VF loss at GHT regions using VF sequences with of 6 to 10 visits and (2) extent of asymmetry in the rates of VF loss at GHT regions using VF sequences with all visits.

Between-Group Comparison Subanalyses. As the number of eyes, the length of follow-up, and age were significantly different between the POAG and PACG groups, we resampled the eyes in each of POAG and PACG groups, requiring that the difference between the length of follow-up and age be less than 2 and 9 years, respectively. Using this new subset, the between-group comparisons were repeated to confirm the reproducibility of the outcome.

The demographics of the groups were compared using the GEE model with the Gaussian function for continuous variables and the binomial function for categorical variables, except for age and gender, where the comparisons were made in patient level. All statistical analyses were performed using the statistical programming language R (R version 3.3.1; available free of charge from The Foundation for Statistical Computing, Vienna, Austria, https://www.r-project.org/).

RESULTS

Demographic characteristics of POAG and PACG eyes are shown in the Table.

The POAG and PACG patients were similar in baseline mTD values ($P = 0.88$, GEE model), but the PACG patients were significantly older than POAG patients (62.7 vs. 53.4 years, $P < 0.001$, GEE model) and had a higher proportion of females compared to the POAG group (61.0% versus 50.0%, $P = 0.067$, GEE model). The POAG patients had a greater maximum IOP

TABLE. Demographic Information of Patients

Characteristics	POAG	PACG	*P*
Subjects	282	49	–
Number of eyes total	440	79	–
Number of eyes at various VF series length, follow-up:			
6 visits, y (mean ± SD)	440 (2.4 ± 0.7)	79 (3.7 ± 1.7)	<0.001*
7 visits, y (mean ± SD)	439 (3.0 ± 0.9)	61 (4.3 ± 1.7)	<0.001*
8 visits, y (mean ± SD)	432 (3.6 ± 1.0)	47 (5.1 ± 1.9)	<0.001*
9 visits, y (mean ± SD)	430 (4.3 ± 1.0)	41 (6.0 ± 2.1)	<0.001*
10 visits, y (mean ± SD)	424 (4.9 ± 11)	33 (6.7 ± 1.6)	<0.001*
Age, y	53.4 (12.0)	62.7 (9.0)	<0.001*
Sex, %female	50.0%	61.0%	0.052
BCVA, logMAR	−0.07 (0.08)	−0.01 (0.09)	<0.001*
Follow-up of all visits, y	7.6 (1.8)	7.1 (3.5)	0.13
mTD at the baseline, dB	−6.4 (5.7)	−6.4 (7.3)	0.88
mTD at the superior hemifield, baseline, dB	−7.9 (8.5)	−6.6 (8.1)	0.20
mTD at the inferior hemifield, baseline, dB	−5.1 (5.7)	−6.4 (8.0)	0.25
Max IOP, mm Hg	16.0 (2.8)	14.0 (3.2)	0.03*
Refractive error, diopters	−4.4 (3.9)	−0.38 (1.7)	<0.001*

BCVA, best-corrected visual acuity.
* *P* values for the comparisons of follow-up length.

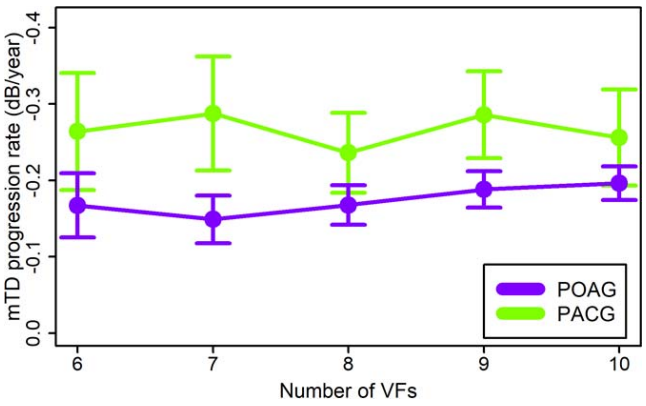

FIGURE 3. Global rates of VF (mTD) loss in POAG and PACG eyes at various VF series lengths. PACG eyes had a consistently faster progression rate of mTD compared to POAG eyes; however, this difference was not statistically significant in any VF series length. The overal mTD progression rate was –0.29 (SD = 0.45) dB/y in PACG eyes and –0.23 (SD = 0.38) dB/y in POAG group.

compared to the PACG eyes (16.0 compared to 14.0, $P = 0.038$, GEE model) and had a significantly better visual acuity than PACG eyes ($P < 0.001$, GEE model). The refractive error of the POAG eyes was significantly more myopic than PACG eyes ($P < 0.001$, GEE model). The length of follow-up was similar in POAG and PACG patients (7.6 vs. 7.1 years, respectively, $P = 0.13$, GEE model).

Figure 3 shows the global rate of VF (mTD) loss in POAG and PACG eyes with different number of VF sequences (from 6 to 10). PACG eyes had a consistenly faster global rate of VF loss compared to POAG eyes; however, this difference was not statistically significant in any number of VF sequences ($P = 0.39$, 0.13, 0.29, 0.17, and 0.48, with 6, 7, 8, 9, and 10 VFs, respectively, GEE model). The global rate of VF (mTD) loss was –0.29 (SD = 0.45) dB/y in the PACG group and –0.23 (SD = 0.38) dB/y in POAG group, calculated using VF sequences with all available visits for each eye.

Figure 4 represents the cumulative density function of the global rate of VF (mTD) loss in POAG and PACG eyes; approximately 40% of the POAG eyes and 60% of the PACG eyes had an mTD progression rate equal to or faster than –0.25 dB/y, and approximately 20% of the eyes, in both PAOG and PACG groups, had an mTD progression rate equal to or faster than –0.50 dB/y.

Within-Group Analyses

Region-wise. Figure 5 demonstrates the region-wise superior-inferior asymmetry in the rate of VF loss in POAG (top panels) and PACG eyes (bottom panels) using VF sequences of 6 to 10 visits. In eyes with POAG, there was a significant asymmetry in the GHT central and paracentral regions; that is, GHT central and paracentral regions in the superior hemifield had significantly faster rates of VF loss compared to their counterparts in the inferior hemifield ($P = 0.01$ and $P = 0.03$, respectively). However, only GHT central region in the superior hemifield had significantly faster rates of VF loss than inferior hemifield after adjusting for multiple observations using Bonferroni correction. In contrast, in eyes with PACG, there was no significant asymmetry in the rate of VF loss in any GHT region.

Figure 6 shows the region-wise superior-inferior asymmetry in the rate of VF loss in eyes with POAG (left panel) and PACG (right panel) using VF sequences with all visits. In POAG, significant superior-inferior asymmetry in the rate of VF loss (faster rate of VF loss in the superior hemifield than in the inferior hemifield) was observed in the central and peripheral arcuate 2 regions ($P = 0.04$ and $P = 0.01$ in the GEE model, respectively). On the other hand, there was no asymmetry in the rates of VF loss in PACG eyes.

Point-wise. Figure 7 shows the point-wise superior-inferior asymmetry in the rate of VF loss in eyes with POAG (top panel) and PACG (bottom panel) using VF sequences of 6 to 10 visits. In POAG, significant superior-inferior asymmetry in the rate of VF loss (faster progression rate in the superior hemifield than the inferior hemifield) was observed more frequently in test points located in the central, paracentral, temporal, and

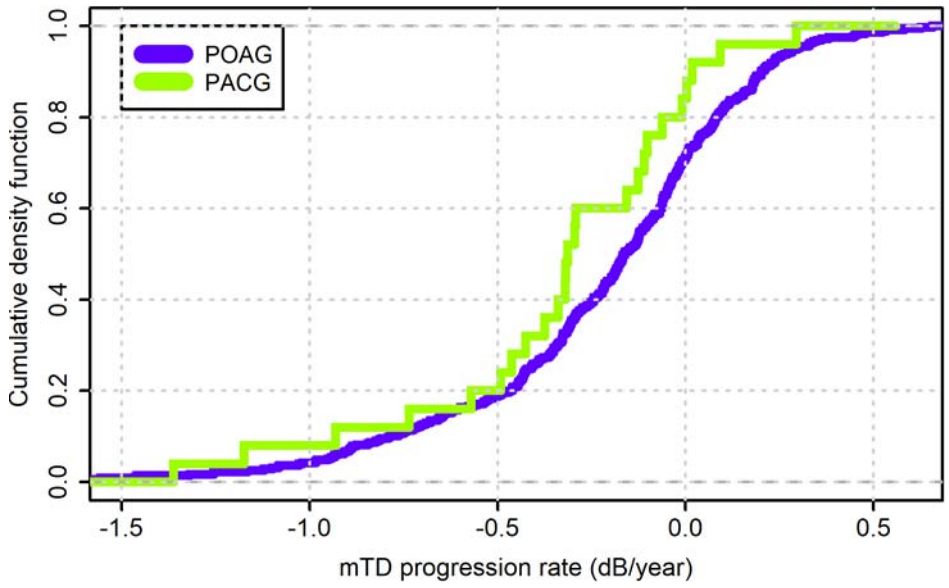

FIGURE 4. Cumulative density function of the progression rate of mTD in POAG and PACG eyes. Approximately 40% of the POAG eyes and 60% of the PACG eyes had a mTD progression rate equal to or faster than –0.25 dB/y, and approximately 20% of the eyes both in POAG and PACG groups had a mTD progression rate equal to or faster than –0.50 dB/y.

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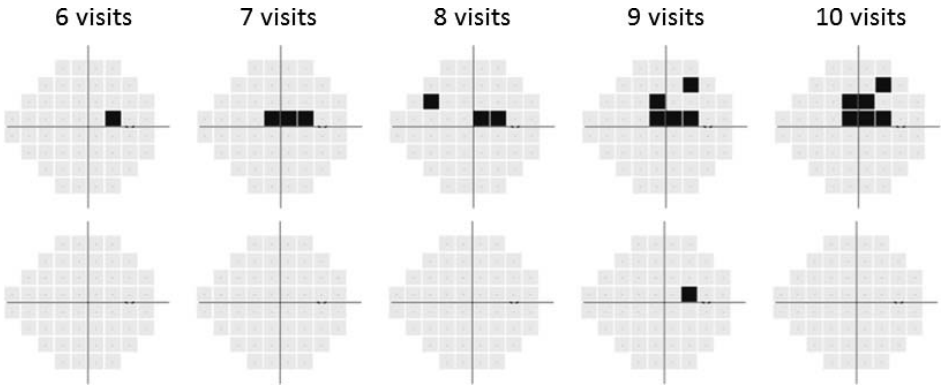

FIGURE 5. Superior-inferior asymmetry in the rate of VF loss in eyes with POAG (*top panel*) and PACG (*bottom panel*) at VF sequences of length 6 to 10. In eyes with POAG (*top panel*), GHT central and paracentral regions in the superior hemifield had frequently significantly faster rates of VF loss compared to their counterparts in the inferior hemifield. To the contrary, in eyes with PACG (*bottom panel*), there was no significant asymmetry in the rate of VF loss in any region of any VF sequence.

arcuate 2 regions. This asymmetry remained significant for the test points in central, paracentral, and arcuate 2 regions in the superior hemifield after adjusting for multiple observations using Bonferroni correction. On the other hand, there was no test point with significant superior-inferior asymmetry in the rate of VF loss in PACG eyes.

Figure 8 shows the point-wise superior-inferior asymmetry in the rate of VF loss in eyes with POAG (left panel) and PACG (right panel) using VF sequences with all visits. In POAG, significant superior-inferior asymmetry in the rate of VF loss (faster rate of VF loss in the superior hemifield than the inferior hemifield) was observed in the central, and peripheral arcuate 2 regions. On the other hand, there was no asymmetry in the rates of VF loss in PACG eyes.

Between-Group Comparison (Extent of Asymmetry in POAG Versus PACG)

Using VF Sequences of Length 6 to 10. To identify the extent of the asymmetry in the rate of VF loss of eyes with POAG and PACG, we compared these two groups using the GEE model. Figure 9 shows the comparisons of superior-inferior asymmetry in the rate of VF loss between eyes with POAG and PACG, with VF sequences of length 6 to 10, in all GHT regions (each curve represents rate of VF loss in the superior region minus that in the inferior region). In eyes with POAG, the rate of VF loss was always faster in the superior hemifield than in the inferior hemifield (suggested by negative values, purple curve). In contrast, eyes with PACG had a faster rate of VF loss in the inferior hemifield than the superior hemifield, except in the central region (green curve) when analyzing VF sequences of length 6 to 10.

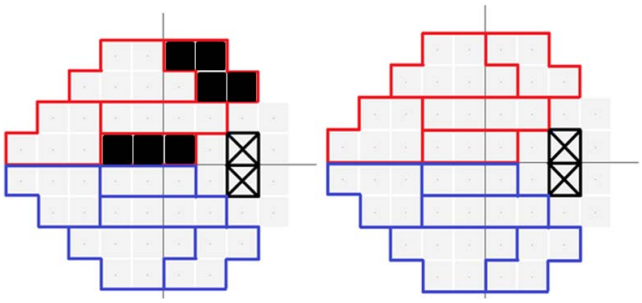

FIGURE 6. Superior-inferior asymmetry in the rate of VF loss in eyes with POAG (*left panel*) and PACG (*right panel*) using VF sequences with all visits. In eyes with POAG (*left panel*), GHT central and peripheral arcuate 2 regions in the superior hemifield had significantly faster rates of VF loss compared to their counterparts in the inferior hemifield. However, in eyes with PACG (*right panel*), there was no significant asymmetry in the rate of VF loss in any region of any VF sequence.

To investigate the significance of these differences, we accounted for gender, maximum IOP, visual acuity, length of follow-up, and refractive error covariates in the GEE model and determined that the difference between the asymmetry in the rates of VF loss between POAG and PACG eyes was statistically significant in the paracentral region ($P = 0.03$, GEE model) and peripheral arcuate 2 region ($P = 0.04$, GEE model). However, in none of the regions was the extent of asymmetry in the rate of VF loss different between eyes with POAG and PACG after adjusting for multiple observations using Bonferroni correction.

Using VF Sequences With All Visits. To identify the extent of the asymmetry in the rate of VF loss of eyes with POAG and PACG, we compared these two groups using GEE model of the rates of VF loss using sequences with all visits. We observed that eyes with POAG had significantly faster rate of VF loss in the paracentral regions of the superior hemifield than inferior hemifield ($P = 0.04$, GEE model). However, there was no significant asymmetry in the rate of VF loss in the GHT regions of eyes with PACG.

We also observed that there was a significant difference between the extent of asymmetry in the rate of VF loss in eyes with POAG and PACG in only the paracentral region of GHT ($P = 0.03$, GEE model).

Between-Group Comparison (Extent of Asymmetry in POAG Versus PACG) Using Matched Groups

We repeated the between-group comparison using 75 eyes with POAG and 75 eyes with PACG in the resampled dataset (matched for length of follow-up and age). The *P* values of the difference between the parameters of eyes with POAG and PACG for the length of follow-up, age, gender, visual accuity, maximum IOP, and refractive error were 0.47, 0.30. 0.62, 0.17, 0.93, and <0.001, respectively (using GEE models). Similar to the initial analysis above, we observed that there was a significant difference between the extent of asymmetry in the rate of VF loss of eyes with POAG and PACG in the paracentral region of GHT ($P = 0.04$, GEE model).

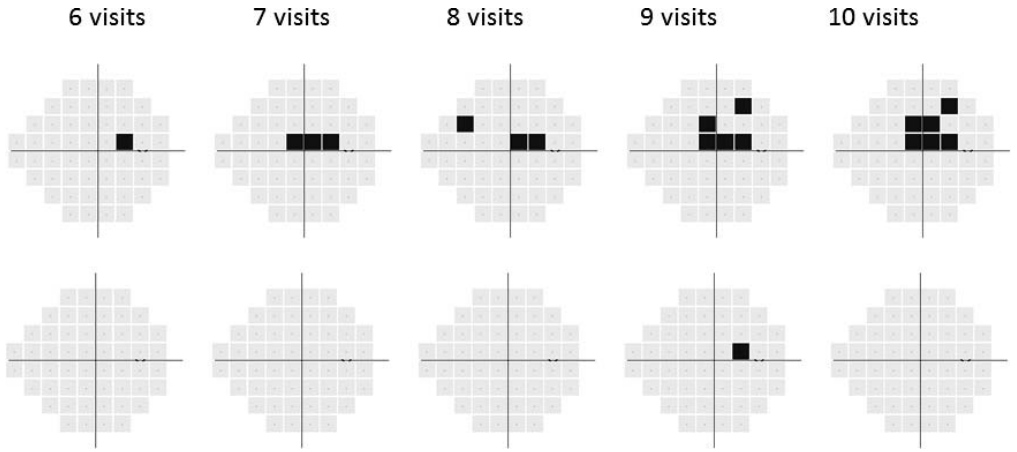

FIGURE 7. Point-wise comparison of the asymmetry in the rate of VF loss in eyes with POAG and PACG at VF sequences of length 6 to 10. In eyes with POAG (*top panel*), significant superior-inferior asymmetry in the rate of VF loss (faster progression rate in the superior hemifield than inferior hemifield) was observed more frequently in the test locations located in the central and paracentral regions. In eyes with PACG (*bottom panel*), there was no test location that frequently appeared with significant superior-inferior asymmetry in the rate of VF loss.

DISCUSSION

In the current study, VF records were collected from 440 eyes with POAG and 79 eyes with PACG, with at least six reliable VFs, and global and the superior-inferior asymmetry in the rates of VF loss were examined region-wise and point-wise. There was no significant difference in the mTD progression rates between POAG and PACG eyes. Despite the similar mTD values at baseline for POAG and PACG eyes, there was a significant superior-inferior asymmetry in the rate of VF loss in the GHT central, paracentral, and arcuate 2 regions (faster rate of VF loss in the superior hemifield than in the inferior hemifield) of eyes with POAG. In contrast, asymmetry was not observed in eyes with PACG. Therefore, an asymmetric rate of VF loss in central, paracentral, and arcuate 2 regions seems to be a feature of POAG and not PACG.

While the rate of VF loss in POAG eyes,[41–52] as well as differences between the patterns of VF loss in POAG and PACG eyes,[27,30,34,53] has been reported previously, this is, to our knowledge, the first study directly investigating the differences in the rate of VF loss as well as the superior-inferior asymmetry between POAG and PACG eyes with automated perimetry. Lee and colleauges compared the rate of VF loss using the Goldmann perimetry; however, their relatively small number of eyes (25 POAG eyes and 23 PACG eyes) makes the comparison challenging.[54] In the current study, comparison was made using a larger number of eyes (440 POAG eyes and 79 PACG eyes).

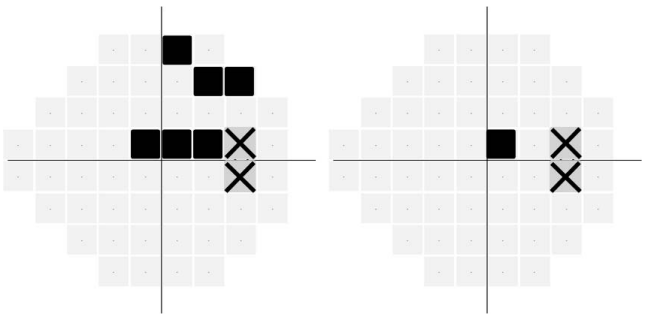

FIGURE 8. Point-wise comparison of the asymmetry in the rate of VF loss in eyes with POAG and PACG using VF sequences with all visits. In POAG (*left*), significant superior-inferior asymmetry in the rate of VF loss (faster progression rate in the superior hemifield than inferior hemifield) was observed in the test locations located in the central and peripheral arcuate 2 regions. In PACG (*right*), only one test location in the central region had significant superior-inferior asymmetry in the rate of VF loss.

We observed a greater number of females in the PACG group than in the POAG group (see the Table), which is in agreement with previous studies suggesting that females are more likely to develop PACG,[8,29,55,30] and gender is even an independent risk factor for developing PACG.[12]

In the current study, VFs were collected only prior to laser iridotomy or cataract surgery in the eyes with PACG, excluding those with prior acute-angle closure attack; nonetheless, the progression rates were slow both in POAG (–0.23 dB/y) and PACG eyes (–0.29 dB/y) without a significant difference between the two groups (Fig. 3). Similar slow progression rates were reported in the study by De Moraes and colleagues[56]: the mean rate of VF loss of –0.48 and –0.39 dB/y in POAG and PACG eyes, respectively. Verma and colleagues[36] reported even slower progression rate in PACG eyes (–0.12 dB/y).[56] There are other previous studies that reported faster rates of progression in PACG eyes compared to POAG eyes, and hence PACG has a threefold greater risk of developing blindness compared to POAG.[2,4,6,25,26] The slow rate of progression in PACG eyes in the current study could be due to the fact that these subjects were patients with controlled glaucoma under treatment in a hospital setting. Thus, different results could be obtained if eyes with a history of an angle-closure attack are analyzed. Also, active chronic PACG eyes, in which intermittent high IOP is observed, is also problematic, but it is unlikely the current study included these eyes because the VF data were collected at hospital settings, and such eyes were treated with laser iridotomy or cataract surgery without delay. Indeed, low maximum IOP value was observed in eyes with PACG (14.0 mm Hg on average), which was lower than that in POAG eyes (16.0 mm Hg on average; see the Table).

In the current study, several VF sequence lengths, from 6 to 10 visits, were analyzed (see Fig. 2). As can be seen in Figure 5, the superior-inferior asymmetry in the rate of VF loss (faster in the superior hemifield than in the inferior hemifield) was not observed in POAG eyes when short series of VFs (up to seven) were used. In contrast, the superior-inferior asymmetry in the rate of VF loss became obvious when longer series of VFs were used. This is probably due to VF variability and measurement noise leading to undetectable progression information in

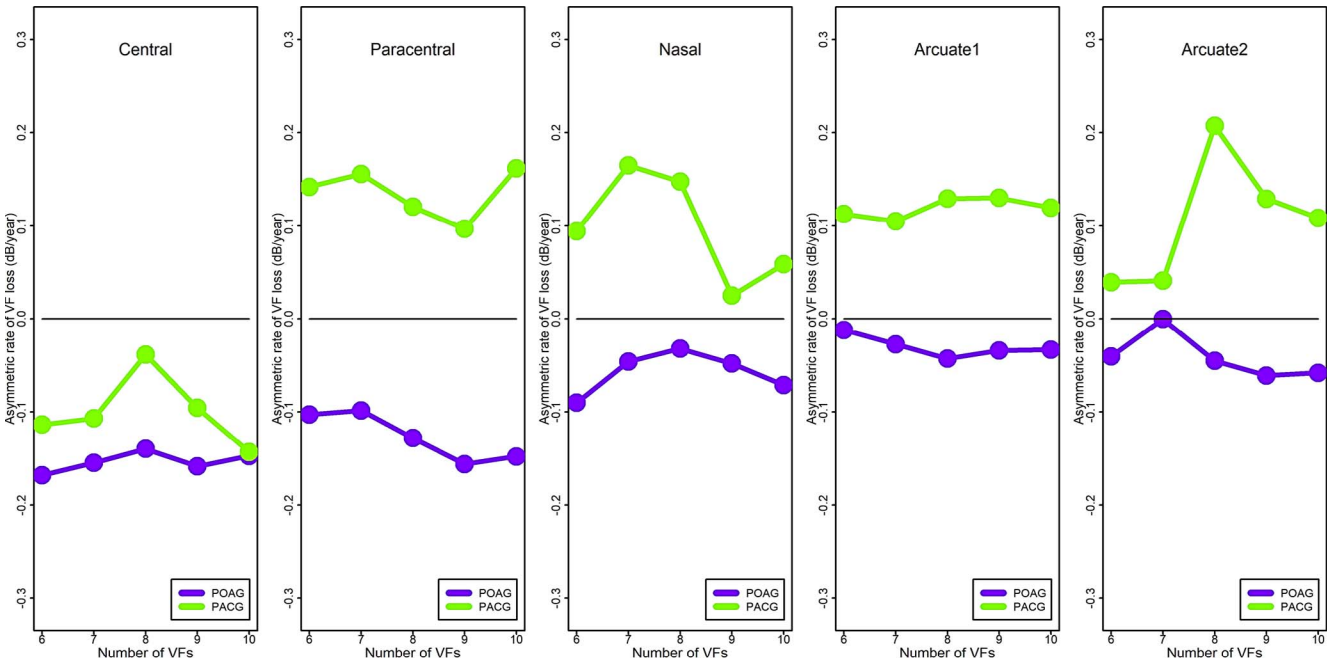

FIGURE 9. The extent of asymmetry in the rate of VF loss in eyes with POAG and PACG in each GHT region. The difference was calculated by subtracting the regional rate of TD values in the inferior hemifield from that in the superior hemifield. Panels from *left* to *right* correspond to central, paracentral, nasal, peripheral arcuate 1, and peripheral arcuate 2 regions of GHT. While eyes with POAG had a faster rate of VF loss in the superior hemifield than in the inferior hemifield, eyes with PACG had a faster rate of VF loss in the inferior hemifield than in the superior hemifield (except in the central region).

analyses with small numbers of VFs. This is in agreement with previous studies that suggested obtaining a considerable number of VF tests (e.g., eight VF tests) when assessing progression.[57–60] Moreover, it has been reported that VF sequence length affects the sensitivity to the progression rate changes in the trend analysis.[61]

In the current study, a significant superior-inferior asymmetry in the rate of VF loss was observed in POAG in both analyses, whereas this finding was not observed in PACG eyes; more specifically, in POAG eyes, the superior central and paracentral had a faster rate of VF loss compared to corresponding inferior regions based on the analysis with different numbers of VF sequences (Figs. 5, 6). When we repeated the analysis using all VF sequences with all visits from eyes with POAG and PACG, we observed that the superior central and peripheral arcuate 2 had a faster rate of VF loss compared to corresponding inferior regions. This was consistent with our point-wise analysis (see Fig. 6). Supporting this, the comparison between POAG and PACG eyes, using all VF sequences, revealed a significantly faster progression in the paracentral region in the superior hemiflield than that in the inferior hemifield. A possible caveat was that including VF sequences with larger numbers of visits results in smaller subject population, which may affect the power of statistical analysis, in particular for eyes with PACG. To address this possible concern, we resampled both POAG and PACG eyes so that the number and other backgrounds were matched between the two groups. As a result, the superior-inferior asymmetry in the rate of VF loss was confirmed in the paracentral region of GHT.

Several studies have shown a significant difference in the spatial patterns of VF defects between eyes with POAG and PACG using cross-sectional VF data.[27–30] For instance, Gazzard et al.[28] reported that the superior hemifield was more depressed than in the inferior hemifield in eyes with POAG and PACG; however, this tendency was much more obvious in eyes with POAG. This fact corroborates our findings of the faster rate of VF loss in eyes with POAG than in eyes with PACG in multiple regions in the superior hemifield. We also found that only the central region of the superior hemifield of eyes with PACG had a faster progression rate than that in the inferior hemifield (although not statistically significant; see Fig. 7). This may also corroborate the results by Gazzard et al.,[28] indicating the central region in the superior hemifield is more pronounced than the inferior hemifield in eyes with PACG. These results are also supported by many previous studies that have suggested that VF damage at baseline is a risk factor for progression.[20,62,63]

As a limitation of the current study, the follow-up length of PACG eyes was shorter than that of POAG eyes for given number of VFs, which may have biased the current results. Also, the number of PACG eyes (79 eyes) was smaller than the number of POAG eyes (440 eyes). Therefore, not observing a significant superior-inferior asymmetry in PACG eyes (Figs. 5, 6) may be biased in this aspect. However, this effect would be marginal because a similar result was obtained in the comparison between POAG and PACG eyes. Moreover, there is a slight trend to asymmetry in the opposite direction of the PACG eyes (the inferior hemifield faster than the superior hemifield; Fig. 7). Nevertheless, our supplemental analysis of selecting a subset of POAG eyes matched with PACG eye confirmed that the extent of asymmetry in the rate of VF loss in the paracentral region is statistically significantly different between eyes with POAG and PACG. Also, in the current study, only the VF records prior to laser iridotomy or cataract surgery were included for analysis with the PACG eyes. Different results may be observed in eyes with PACG after laser iridotomy or cataract surgery, which should be investigated in a separate study.

In conclusion, in eyes with POAG, the rate of VF loss was faster in superior hemifield than in inferior hemifield, particularly in central, paracentral, and peripheral arcuate 2 regions. This finding was not observed in PACG eyes. This

novel finding could further promote our understanding of mechanisms underlying both glaucoma types.

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