Concordance of 24-h intraocular pressure curve in patients with untreated unilateral primary open-angle glaucoma

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Abstract. The present study aimed to assess the concordance of 24-h intraocular pressure (IOP) curves between glaucomatous and contralateral eyes for patients with untreated unilateral primary open-angle glaucoma (POAG). A total of 32 patients with unilateral POAG and 32 age-matched normal subjects were enrolled. The IOP measurements were performed every 2 h over a 24-h period. The concordance of the 24-h IOP curves was assessed via the correlation coefficient (r), intraclass correlation coefficient (ICC) and repeated-measures analysis of variance (ANOVA). No significant difference was identified between all IOPs, as well as the mean, peak and trough IOP or IOP fluctuations of the paired eyes in the two groups. The strength of association of all IOPs was moderate in the glaucoma group (r, 0.752-0.867) and the normal controls (r, 0.625-0.873). IOP readings at each time-point indicated a high agreement in the glaucoma group (ICC, 0.857-0.929) and the normal controls (ICC, 0.768-0.932). Repeated-measures ANOVA indicated that the 24-h IOP curves of the paired eyes had parallel profiles in the two study groups (P=0.837 and P=0.897, respectively). The glaucoma patients had significantly higher proportions of all IOPs displaying absolute differences of ≥2 and ≥3 mmHg (46.09 vs. 35.68%, P<0.001; 29.69 vs. 12.50%, P<0.001, respectively). In conclusion, the 24-h IOP curves of the paired eyes had parallel profiles in unilateral glaucoma patients and normal subjects. However, unilateral glaucoma patients had a significantly larger proportion of IOP differences of ≥2 and ≥3 mmHg.

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Introduction

Primary open-angle glaucoma (POAG) is a chronic optic neuropathy that is progressive and generally bilateral, but frequently asymmetric. It is estimated that ~80 million individuals aged 40-80 years will have developed POAG by 2040 (1). Although the precise pathogenesis remains to be elucidated, intraocular pressure (IOP) is considered to be the most significant risk factor contributing to the development and progression of the disease (2,3). As an assumption of symmetrical variation of IOP between the right eye and the left eye in healthy individuals was previously made (4), a significant interocular difference in IOP, also known as IOP asymmetry, has been recognized as an additional risk factor for glaucoma (5,6). A 1-mmHg increase in IOP asymmetry between a pair of eyes is correlated with a 17% increase in the risk for the development of POAG (7).

Previous studies have explored the concordance of IOP curves in glaucoma patients, only to obtain inconsistent results (8-10). However, in these studies, the enrolment criteria for the study populations of glaucoma patients were not strict, as there was no limitation regarding the degree of retinal nerve fiber layer (RNFL) defect or visual field defect. Therefore, whether asymmetric glaucomatous damage is attributed to asymmetric IOP curves remains elusive. A clinical evaluation of symmetry in unilateral glaucoma may be able to demonstrate this hypothesis. In addition, the IOP in an individual is not stable as expected, and fluctuation in IOP is a well-known phenomenon. It changes over short and long periods ranging from days to months (11,12). Therefore, repeated IOP measurements, particularly 24-h IOP readings, are an important factor to evaluate the clinical course.

In the present study, glaucoma patients who had RNFL defects and visual field defects in only one eye and a normal fellow eye on examination were selected, which allowed for better investigation of the association between the onset of glaucomatous changes and potential disturbances in IOP. The

fellow eyes were compared to the corresponding glaucomatous eyes and the eyes of healthy control subjects to test for any evidence of asymmetry in 24-h IOP curves. To the best of our knowledge, the present study was the first to assess the concordance of 24-h IOP curves in patients with untreated unilateral glaucoma.

Materials and methods

Study population. In the present observational study, all of the participants who visited the Ophthalmology Clinic at Ruijin Hospital between May 2016 and May 2017 were considered.

POAG patients enrolled in the present study had to meet the following inclusion criteria: A typical glaucomatous optic disc abnormality (diffuse or localized thinning of the neuro-retinal rim, rim notching or inter-eye asymmetry of vertical cup-to-disc ratio >0.2), corresponding glaucomatous visual field loss and an open angle on gonioscopic examination (13). Unilateral POAG was defined as POAG patients with a characteristic RNFL defect (Fig. 1A and B) and corresponding visual field defect (Fig. 1C) in only one eye and the other eye appearing normal on ophthalmic examination. The eye with visual field defect was designated as the affected eye and the other eye was designated as the fellow eye. All participants were newly diagnosed POAG patients who had not received any previous anti-glaucoma treatments. The population of normal subjects, recruited from healthy individuals seeking physical examination in the outpatient department, was comprised of subjects without any evidence of RNFL defect and with normal visual field test results. IOP measurements were >21 mmHg on different days. Subjects with concomitant ocular diseases, severe systemic disease, previous ocular surgery or any medical treatment for glaucoma were excluded. Those whose central corneal thickness (CCT) measured >650 or <450 μm were also excluded from the study.

Ophthalmologic examination. All participants underwent a comprehensive ophthalmologic examination, including best-corrected visual acuity, slit-lamp examination, gonioscopy and fundus examination. CCT was measured three times using an ocular biometer (IOL Master; Carl Zeiss Meditec, Dublin, CA, USA), and the mean value of three consecutive readings within a range of 5 μm was calculated for each eye. A Humphrey Field Analyzer II (Carl Zeiss Meditec) was used for visual field examinations, with the Swedish Interactive Threshold Algorithm Fast strategy and the 30-2 test pattern (14). All participants had been subjected to at least two prior visual field tests. Visual fields were defined as normal if the Glaucoma Hemifield Test was within normal limits, and the pattern deviation plots indicated no sign of one or more clusters of three or more neighboring test points with a sensitivity loss of >5 dB, or two adjacent test points with a sensitivity loss of >10 dB. Two qualifying visual field tests were performed to confirm the glaucomatous visual field loss. Furthermore, all of the participants were tested by the same operator with extensive experience in optical coherence tomography (OCT) imaging (Cirrus HD-OCT; Carl Zeiss Meditec). The optic disc cube 200x200 scan protocol was used to assess RNFL thickness.

24-h IOP measurements. All of the subjects were hospitalized to perform 24-h IOP measurements. The procedure began at 0:00 a.m. on the next day after a quick adaption to the hospital environment. The IOP measurements were performed every 2 h for the next 24 h by resident ophthalmologists using an auto non-contact tonometer (NCT) (TX-F; Canon, Tokyo, Japan). The IOP measurement was taken in the sitting position and first obtained from the right eye at all time-points. Repeated measurements of IOP were performed three times and the mean values were calculated for further analysis. If one of the IOP values was 3 mmHg higher than the other two, it was discarded and repeated measurements were performed. Specifically, the IOP was measured following resting of the patients in a horizontal position during their sleeping hours. In order to obtain the routine IOP curves, the patients were encouraged to remain active within the hospital unit. In addition, their bedtime was not specified and they were permitted to have naps as desired. Systemic anti-hypertensive medications were not prohibited. Food and drink were not restricted, including alcohol and caffeine.

Statistical analysis. SPSS 20.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The Chi-squared test and the independent-samples t-test were used for comparisons between the two groups. The paired-samples t-test was used for comparison of basic ophthalmologic parameters and all IOP values in the two study groups. The Pearson's correlation coefficient (r) was used to evaluate the strength of association in the paired IOP data. Intra-class correlation coefficients (ICC) were calculated and Bland-Altman plots were generated to determine the agreement of IOP values between paired eyes. The interpretation of ICC values has been described as follows: A value of <0.4 represents poor agreement beyond chance, a value of 0.4-0.75 represents a moderate agreement and a value of >0.75 represents excellent agreement (15). A repeated-measures analysis of variance (ANOVA) was performed to examine the bilateral symmetry of the IOP over time. In addition, the frequency of the time difference for peak IOP time-points between the two paired eyes was analyzed using Fisher's Exact Test in the two study groups. The frequency distribution of IOP differences between bilateral eyes was calculated for all IOP values. The percentage of asymmetries of ≥2 and ≥3 mmHg was also calculated. When the minimum value was less than 5, the Yate's continuity corrected Chi-square test was used. In other circumstances, the Chi-square test was used. $P<0.05$ was considered to indicate a statistically significant difference for all comparisons.

Results

Patient characteristics. A total of 64 subjects comprising 32 newly diagnosed POAG patients (15 males and 17 females) and 32 age-matched normal subjects (13 males and 19 females) were enrolled in the final analysis. All of the included subjects were native Han Chinese. The average age was 47.69±15.22 (range, 26-74 years) for the glaucoma patients and 47.41±15.47 (range, 23-77 years) for the normal controls, respectively ($t=0.073$, $P=0.942$). There was also no significant intergroup difference in the gender distribution ($\chi^2=1.890$, $P=0.169$). In the glaucoma group, 14 right eyes and 18 left eyes had visual

Table I. Basic ophthalmologic data of the study groups.

	POAG			Normal		
Variable	Affected eye	Fellow eye	P-value	Right eye	Left eye	P-value
CCT (μm)	542.91±33.37	541.22±34.67	0.472	551.84±38.30	549.91±35.38	0.162
MD (dB)	-5.41±4.67	-1.05±1.11	<0.001	-0.79±0.90	-0.96±1.00	0.299
PSD (dB)	5.95±3.93	1.82±0.40	<0.001	1.59±0.29	1.68±0.30	0.098
RNFL (μm)	73.59±6.49	90.81±7.36	<0.001	94.72±7.35	93.66±7.09	0.059

Values are expressed as the mean ± standard deviation. POAG, primary open-angle glaucoma; CCT, central cornea thickness; MD, mean deviation; PSD, pattern standard deviation; RNFL, retinal nerve fiber layer.

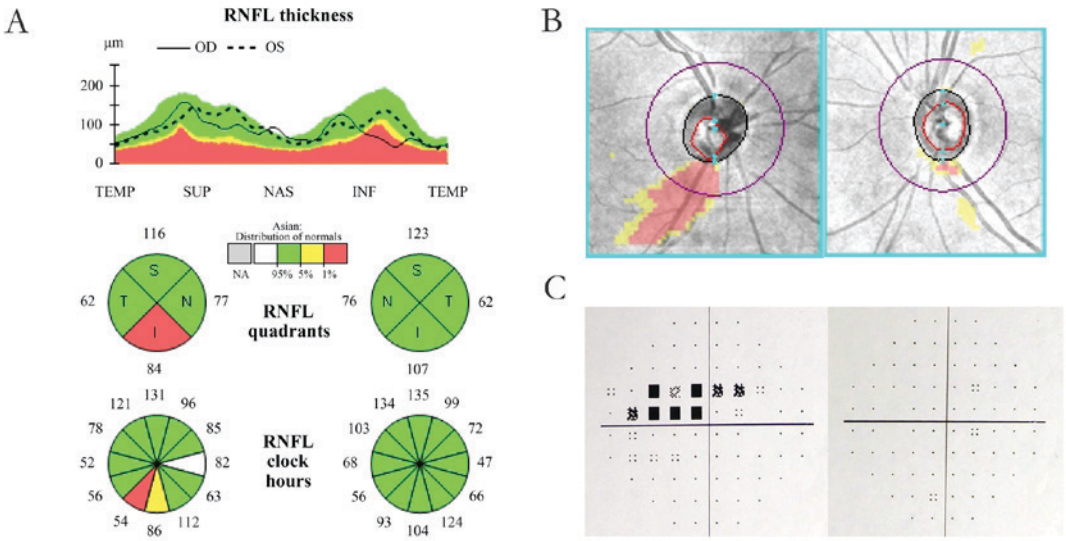

Figure 1. (A) Example of unilateral primary open-angle glaucoma exhibiting unilateral RNFL defect in quadrants and clock hour map displaying unilateral RNFL defect. (B) Deviation map indicating a unilateral RNFL defect. The right eye, also termed as the affected eye, is on the left-hand side. The left eye, also termed as the fellow eye, is on the right-hand side. (C) Test of a Humphrey Field Analyzer presenting unilateral visual field defect. The right eye, also termed as the affected eye, is on the left-hand side. The left eye, also termed as the fellow eye, is on the right-hand side. RNFL, retinal nerve fiber layer. The green areas represent normal thickness of RNFL, the yellow areas represent borderline thickness of RNFL and the red areas represent abnormal thinning of RNFL. OD, right eye; OS, left eye; TEMP, temporal; SUP, superior; NAS, nasal; INF, inferior.

field defects and abnormal RNFL thickness. According to the peak IOP value throughout the 24-h period, 22 cases were hypertension glaucoma and 10 were normal tension glaucoma.

Opthalmologic data. The basic ophthalmologic data of the study groups are summarized in Table I. No inter-eye difference in CCT was present in either glaucoma subjects (P=0.472) or normal subjects (P=0.162). As expected, the affected eyes in the POAG group had worse visual field indices than the fellow eyes [P<0.001 for mean deviation (MD) and pattern standard deviation (PSD)], whereas no significant differences were observed between the paired eyes in the normal group (P=0.299 for MD, P=0.098 for PSD). Comparison of RNFL thickness in paired eyes revealed similar results in the two groups.

IOP profiles. Fig. 2 indicates the 24-h IOP rhythms in POAG patients and normal subjects. In the POAG group, the minimum IOP was at 20:00 pm, exhibited a marked increase at night and peaked at 4:00 a.m. In normal subjects, the lowest mean IOP was observed at 8:00 p.m. and the highest mean IOP at 10:00 a.m. The detailed IOP profiles of paired eyes at each time-point in each of the two study groups are listed in Tables II and III. There was no statistically significant difference between paired eyes at any of the time-points examined in the two groups (all P>0.05). The correlation coefficients for paired IOP readings indicated that the strength of association was moderate in the glaucoma group (r, 0.752-0.867) and the normal controls (r, 0.625-0.873). IOP readings at each time-point exhibited high agreements in the glaucoma group (ICC, 0.857-0.929) and the normal controls (ICC, 0.768-0.932).

Differences in IOP between paired eyes. The mean IOP, peak IOP, trough IOP and IOP fluctuation were not significantly different between the paired eyes in unilateral glaucoma patients (P=0.492, P=0.338, P=0.318, P=0.883, respectively; Table IV). Furthermore, the mean IOP, peak IOP and trough IOP were in high agreement between paired eyes in glaucoma

Table II. Comparison of intraocular pressure between paired eyes in glaucoma patients.

Time-point (h)	Affected eye	Fellow eye	Inter-eye difference (affected vs. unaffected)	P-value	r	ICC	95% CI of ICC
0:00	18.34±5.55	17.62±5.36	0.72±3.49	0.252	0.796	0.886	(0.767,0.944)
2:00	19.22±5.98	19.83±5.82	-0.62±3.04	0.261	0.867	0.929	(0.854,0.965)
4:00	20.19±6.97	19.69±6.06	0.50±3.68	0.448	0.849	0.914	(0.823,0.958)
6:00	19.17±5.86	18.83±5.47	0.34±3.36	0.567	0.827	0.904	(0.803,0.953)
8:00	18.55±6.04	18.55±5.70	0.00±3.53	0.996	0.821	0.901	(0.797,0.952)
10:00	19.41±5.46	19.14±4.92	0.27±3.33	0.651	0.799	0.886	(0.766,0.944)
12:00	18.34±5.44	17.33±5.88	1.01±4.01	0.163	0.752	0.857	(0.707,0.930)
14:00	17.51±4.86	17.68±5.06	-0.17±3.05	0.761	0.812	0.896	(0.787,0.949)
16:00	17.77±4.90	17.79±4.94	-0.03±3.05	0.963	0.807	0.893	(0.782,0.948)
18:00	17.48±4.87	17.32±5.13	0.17±2.78	0.738	0.847	0.916	(0.829,0.959)
20:00	17.30±4.85	16.56±5.07	0.74±3.08	0.184	0.808	0.893	(0.782,0.948)
22:00	17.49±4.43	17.06±4.45	0.43±2.87	0.402	0.791	0.883	(0.761,0.943)

Values are expressed as the mean ± standard deviation. ICC, intraclass correlation coefficient; CI, confidence interval.

Table III. Comparison of intraocular pressure between paired eyes in normal subjects.

Time-point (h)	Right eye	Left eye	Inter-eye difference (right vs. left)	P-value	r	ICC	95% CI of ICC
0:00	14.63±3.02	14.65±3.28	-0.02±2.07	0.966	0.786	0.879	(0.752,0.941)
2:00	15.18±3.26	14.98±3.57	0.20±2.39	0.640	0.758	0.861	(0.714,0.932)
4:00	15.39±2.68	15.60±3.19	-0.21±2.51	0.645	0.648	0.779	(0.547,0.892)
6:00	15.79±2.73	15.30±3.18	0.49±2.35	0.251	0.692	0.813	(0.616,0.909)
8:00	15.52±2.95	16.01±2.90	-0.49±1.48	0.070	0.873	0.932	(0.860,0.967)
10:00	15.87±2.61	16.46±2.93	-0.59±1.89	0.087	0.774	0.869	(0.732,0.936)
12:00	15.27±3.17	15.33±3.21	-0.07±1.97	0.845	0.808	0.894	(0.783,0.948)
14:00	14.74±3.03	14.97±2.69	-0.23±1.85	0.490	0.798	0.884	(0.762,0.943)
16:00	15.23±2.53	15.48±2.88	-0.25±1.81	0.434	0.784	0.875	(0.744,0.939)
18:00	15.56±2.63	15.83±2.85	-0.28±2.38	0.518	0.625	0.768	(0.525,0.887)
20:00	14.42±2.36	14.70±2.63	-0.28±1.84	0.404	0.733	0.843	(0.678,0.923)
22:00	14.90±2.73	14.86±2.64	0.04±1.98	0.908	0.729	0.843	(0.678,0.923)

Values are expressed as the mean ± standard deviation. ICC, intraclass correlation coefficient; CI, confidence interval.

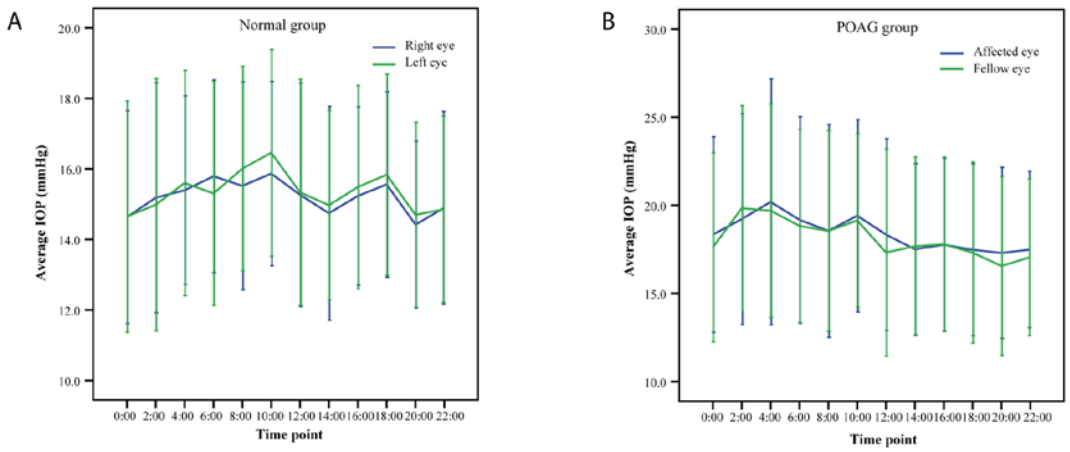

Figure 2. 24-h IOP curves for (A) patients with unilateral POAG and (B) normal subjects. IOP, intraocular pressure; POAG, primary open-angle glaucoma.

Table IV. Comparison of the 24-h IOP curves between paired eyes in the study groups.

Parameter	Affected eye or right eye	Fellow eye or left eye	Inter-eye difference[a]	P-value	r	ICC	95% CI of ICC
Average IOP							
POAG	18.40±4.91	18.12±4.72	0.28±2.30	0.492	0.887	0.940	(0.877,0.971)
Normal	15.21±2.26	15.36±2.47	-0.14±1.24	0.518	0.865	0.926	(0.848,0.964)
Peak IOP							
POAG	22.92±6.43	22.39±5.75	0.53±3.05	0.338	0.880	0.933	(0.863,0.967)
Normal	18.02±2.37	18.52±2.45	-0.50±1.58	0.083	0.785	0.880	(0.753,0.941)
Trough IOP							
POAG	14.54±4.32	13.92±4.37	0.62±3.43	0.318	0.689	0.816	(0.622,0.910)
Normal	12.35±2.22	12.59±2.55	-0.24±1.56	0.389	0.795	0.881	(0.757,0.942)
IOP fluctuation							
POAG	8.38±3.19	8.47±3.99	-0.09±3.47	0.883	0.553	0.701	(0.388,0.854)
Normal	5.68±1.55	5.93±1.57	-0.26±1.86	0.435	0.293	0.454	(-0.119,0.733)

[a]Inter-eye difference refers to affected-fellow in glaucoma subjects and right-left in normal controls. Values are expressed as the mean ± standard deviation. ICC, intraclass correlation coefficient; CI, confidence interval; IOP, intraocular pressure; POAG, primary open-angle glaucoma.

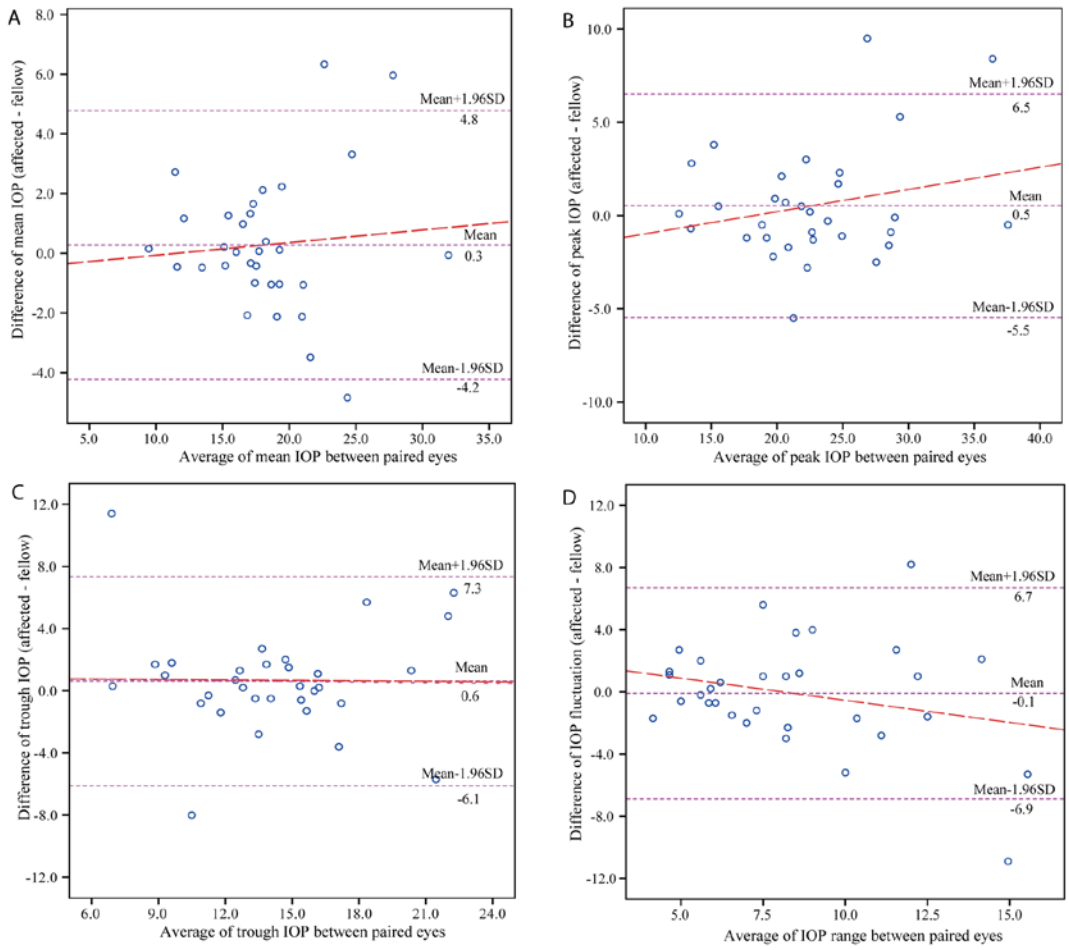

Figure 3. Bland-Altman plots for the 24-h IOP curve parameters in the unilateral glaucoma group. (A) Mean IOP, (B) peak IOP, (C) trough IOP and (D) IOP fluctuation are presented. IOP, intraocular pressure; SD, standard deviation.

patients (ICC, 0.816-0.940). Similar results were observed in the normal controls. Figs. 3 and 4 display the Bland-Altman plots comparing the parameters of 24-h IOP profiles between the paired eyes in the POAG and normal group, respectively.

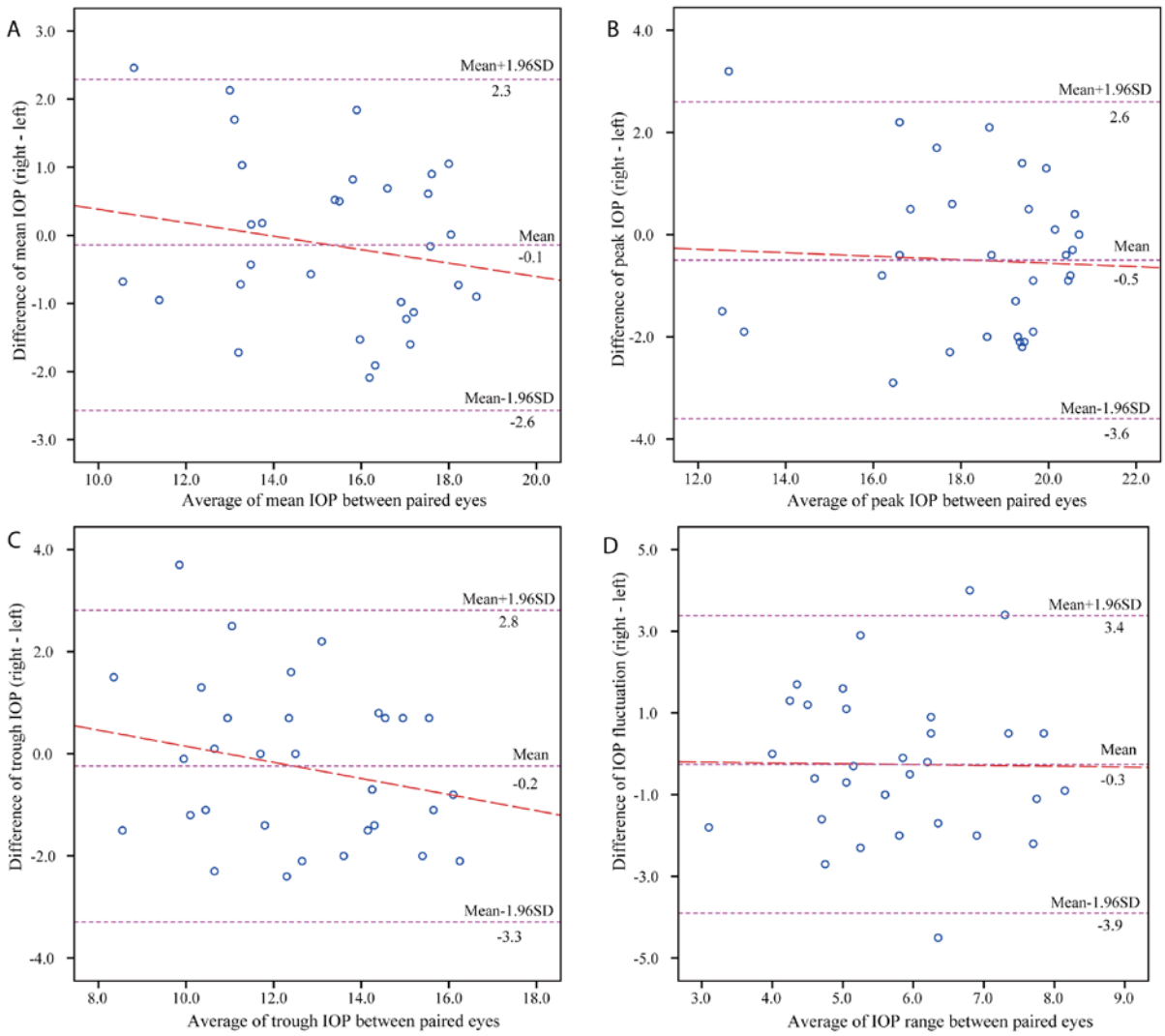

Figure 4. Bland-Altman plots for the 24-h IOP curve parameters in the normal group. (A) Mean IOP, (B) peak IOP, (C) trough IOP and (D) IOP fluctuation are presented. IOP, intraocular pressure; SD, standard deviation.

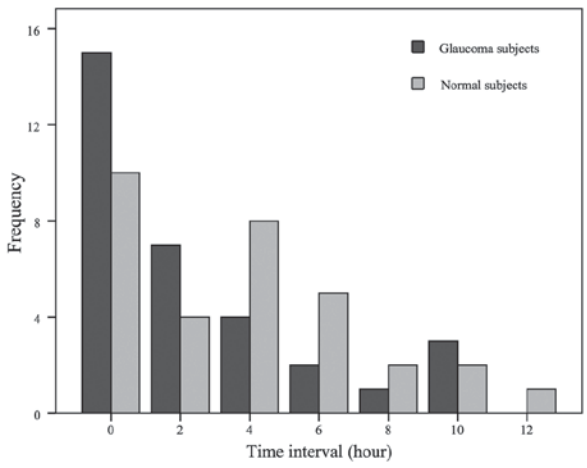

Figure 5. Frequency of the time difference for peak IOP time-points between paired eyes in patients with unilateral primary open-angle glaucoma and normal subjects. IOP, intraocular pressure.

In patients with unilateral glaucoma, the mean difference between paired eyes was 0.28 mmHg for the mean IOP, 0.53 mmHg for the peak IOP, 0.62 mmHg for the trough IOP and -0.09 mmHg for IOP fluctuations, while that in normal controls was -0.14 mmHg for the mean IOP, -0.50 mmHg for the peak IOP, -0.24 mmHg for the trough IOP and -0.26 mmHg for IOP fluctuations.

24-h IOP patterns in the two groups. To further characterize the concordance between the two paired eyes, repeated-measures ANOVA was performed. The results indicated that IOPs changed significantly over time in the two study groups (both P<0.001), and there was no significant eye-time interaction in either POAG patients (P=0.837) or normal subjects (P=0.897). This suggested that the 24-h IOP pattern of the paired eyes had parallel profiles in the two study groups.

IOP peak-interval timing and distribution of differences between pairs of eyes. Fig. 5 presents the distribution of eyes at different time intervals for peak IOP time-points between the paired eyes in the two groups. There was no significant difference in peak-interval timing between the two groups (Fisher's exact test, P=0.434), indicating that the intervals of peak IOP time-points were similar. Fig. 6 illustrates the frequency

Table V. Proportions of subjects with absolute IOP differences of ≥2 and ≥3 mmHg between paired eyes in the POAG and normal groups (%).

	Unilateral POAG		Normal subjects	
Parameter	≥2 mmHg	≥3 mmHg	≥2 mmHg	≥3 mmHg
All IOPs	46.09[a]	29.69[a]	35.68	12.50
Mean IOP	34.38[b]	15.63	9.38	0.00
Peak IOP	37.50	18.75	34.38	0.03
Trough IOP	31.25	21.88	28.13	0.03
IOP fluctuation	46.88	25.00	28.13	0.09

[a]Significant difference from the normal control group according to the Chi-squared test. [b]Significant difference from the normal control group according to Yate's continuity-corrected Chi-squared test. POAG, primary open-angle glaucoma; IOP, intraocular pressure.

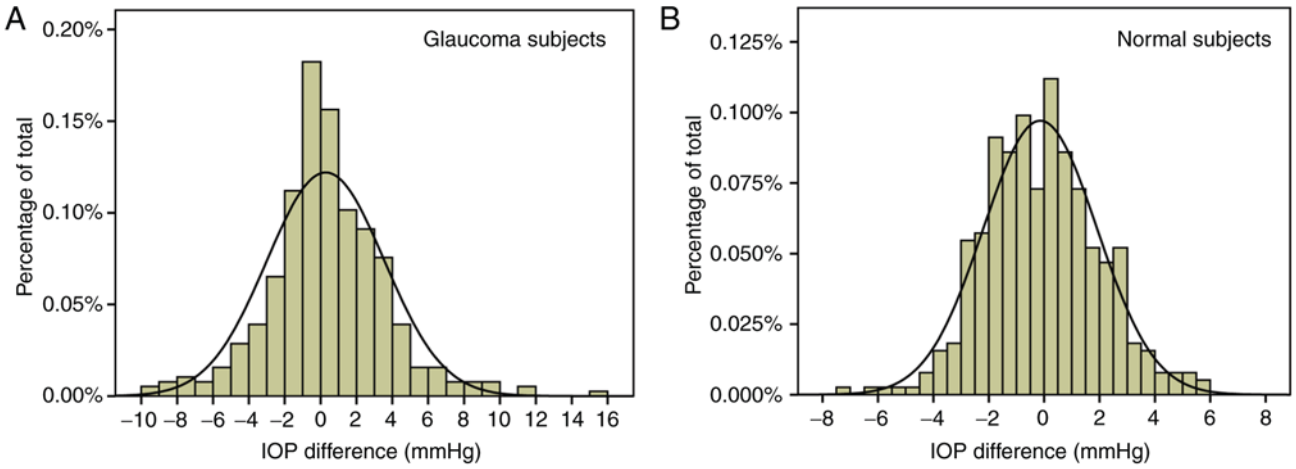

Figure 6. Comparison of frequency distributions of IOP differences in (A) patients with open-angle glaucoma and (B) normal subjects. IOP, intraocular pressure.

distributions of IOP differences for all IOPs in patients with unilateral POAG and normal subjects. The distribution in the unilateral POAG group was wider than that in the normal controls, suggesting greater asymmetry of a single pair of IOP measurements in unilateral glaucoma patients.

POAG patients have an increased frequency of absolute IOP differences of ≥2 and ≥3 mmHg between paired eyes. The proportions of cases with absolute differences of ≥2 and ≥3 mmHg between paired eyes in the different study groups are presented in Table V. It should be noted that the proportion of mean IOPs with absolute differences of ≥2 mmHg between paired eyes in the unilateral POAG group was significantly higher than that in the healthy individuals (χ^2=4.480, P=0.034). In addition, there were significantly higher proportions of all IOPs with absolute differences of ≥2 and ≥3 mmHg in the unilateral POAG group compared with those in the normal control group (χ^2=21.960, P<0.001; χ^2=56.403, P<0.001, respectively). With regard to peak IOPs, trough IOPs and IOP fluctuations, the POAG group had higher proportions of cases with absolute IOP differences of ≥2 and ≥3 mmHg, but the differences were not statistically significant (all P>0.05).

Discussion

It is generally thought that IOPs between right and left eyes in healthy individuals are symmetric, and this hypothesis is commonly based on clinical experience and research studies. Asymmetric IOP results between the paired eyes have been considered as a hallmark of glaucoma (16). However, most of the early studies that analyzed the symmetry of the IOP focused on diurnal IOP curves of bilateral glaucoma patients. The correlation between asymmetric IOP and asymmetric visual field defects remains to be elucidated. To further characterize the symmetry and concordance of IOP variations between paired eyes in glaucoma, the 24-h IOP curves of untreated unilateral glaucoma patients were recorded in the present study.

The present results indicated no statistically significant differences between all IOPs, as well as the mean, peak, trough IOPs or IOP fluctuations of the paired eyes within a 24-h period in the two groups. The strength of association of all IOPs was moderate and IOP readings at each time-point were in high agreement in each study group. The repeated-measures ANOVA indicated that the 24-h IOP curves of the paired eyes had parallel profiles in the two groups. Based on the above

results, a preliminary conclusion may be drawn that the 24-h IOP curves were similar and concordant between paired eyes in unilateral open-angle glaucoma. However, certain subtle differences between the 24-h IOP curves of glaucoma patients and normal subjects were noted. The frequency distribution of differences in all IOPs in unilateral POAG patients was wider than that in normal subjects, and unilateral glaucoma patients had a significantly higher proportion of all IOPs with absolute differences of ≥2 and ≥3 mmHg.

Previous studies have also examined the concordance of 24-h IOP curves between paired eyes of glaucoma patients. Chiseliţă *et al* (17) reported that the nictemeral variation of IOP between paired eyes in glaucoma patients were largely concordant and the 24-h IOP curves of bilateral eyes exhibited parallel changes. The study also concluded that IOP differences of ≥3 mmHg were present in 20.53% glaucoma patients with therapeutically uncontrolled IOP, which was in accordance with the present results. Dinn *et al* (8) reported that the diurnal IOP variations were largely concordant in untreated POAG patients as well as in POAG patients treated with the same IOP-lowering medications on each of their eyes, which was compatible with the present results. Sit *et al* (9) also indicated that the strength of association between right and left IOPs for untreated glaucoma patients was moderate. However, Liu and Weinreb (10) indicated that the strength of association in untreated POAG patients was significantly weaker than that in healthy individuals. One possible reason for this inconsistent result may be that the glaucoma patients in their study were part of an older population.

The results of the present study supported a presumed symmetry in the 24-h IOP curves between the paired eyes in newly diagnosed untreated POAG patients with monocular visual field defects, suggesting that an asymmetric IOP curve may not be a prerequisite for asymmetric visual field loss in the development of the disease. However, throughout the entire 24 h, the IOP in general was slightly higher in the affected eyes than in the fellow eyes, which means that an increased IOP may be a major risk factor in the development and progression of POAG. However, there is no means of determining the IOPs at the time-point at which the damage occurred. Furthermore, other factors may contribute to the asymmetric visual field loss, including vascular disorders. For instance, Plange *et al* (18) reported that POAG patients with asymmetric glaucomatous visual field defects exhibited asymmetric flow velocities of the central retinal artery and the ophthalmic artery.

In the present study, patients with unilateral glaucoma exhibited a wide variation in the frequency distribution of IOP differences and had significantly higher proportions of all IOPs with absolute differences of ≥2 and ≥3 mmHg, suggesting that the prevalence of IOP asymmetry in a single pair of right and left IOP measurements was increased in patients with unilateral glaucoma compared with that in normal control subjects. The increase is most probably a result of the impairment of the aqueous outflow facility in glaucoma patients (19,20). This also emphasizes the viewpoint that IOP asymmetry is more damaging than an equal increase in IOP in both eyes. Variations in IOP occur continuously and the IOPs of bilateral eyes may exhibit differential fluctuations. Therefore, caution is required when interpreting this limitation of the 24-h IOP concordance of fellow eyes in clinical practice. Further study may identify whether variations in IOP symmetry between each eye correlate with the prevalence of glaucoma.

Of note, the present study had several limitations. First, all IOP measurements were obtained using an auto non-contact tonometer. However, recent studies reported that IOPs measured by NCT were not significantly different from those measured by Goldmann applanation tonometry (21,22). Furthermore, it is well-known that IOP interpretation is affected by the CCT. However, IOP fluctuation within a 24-h cycle was assumed to be independent from CCT values in POAG patients (23). In addition, evidence indicated that the CCT changed slightly over the day and a close symmetry between the fellow eyes was observed (24,25). Second, one important variable that may affect the 24-h IOP curves is the body position. Recent studies indicated that the eye on the lower side in the lateral decubitus position had a higher IOP in glaucoma patients and healthy individuals (26-29), which may be attributed to the IOP difference during the nocturnal period. Since all participants were hospitalized instead of being monitored in the sleep laboratory, the sleeping posture was not controlled. Third, the IOP values were measured every 2 h over a 24-h period rather than continuous 24-h IOP monitoring, which may have missed certain maximal and minimal IOP values. The newly developed contact lens sensor (CLS), recording the data every 5 min, may provide more detailed information (30). Previous studies have demonstrated good tolerability and high reproducibility for 24-h recording with the CLS (31,32), but the clinical applications of the CLS require to be further investigated.

The 24-h IOP curves of the paired eyes had parallel profiles in unilateral glaucoma patients and normal subjects. However, the group of unilateral glaucoma patients had a significantly larger proportion of IOP differences of ≥2 and ≥3 mmHg.

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Availability of data and materials

The data sets analysed or generated during the study are available from the corresponding author on reasonable request.

Authors' contributions

ZL, ZC and YZ were involved in the study design. ZL and SH performed ophthalmologic examinations. PH, SH and CL performed measurement and data analysis. ZL drafted the manuscript. ZC and YZ reviewed the manuscript.

Ethical approval and consent to participate

The design of the study was in compliance with the principles of the Declaration of Helsinki and the study was approved by

the Ethics Committee of Ruijin Hospital, affiliated to Shanghai Jiao Tong University School of Medicine (Shanghai, China). Consent forms were signed by all of the participants prior to the examination.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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