

Increased 24-Hour Variation of Human Intraocular Pressure with Short Axial Length

Nils A. Loewen, John H. K. Liu, and Robert N. Weinreb

PURPOSE. To characterize 24-hour variation of intraocular pressure (IOP) in healthy young adults based on the axial length of the eye.

METHODS. Twenty-four-hour IOP data were collected from nine healthy young adults with hyperopia, age range 18 to 25 years, in a sleep laboratory. Every 2 hours, measurements of IOP were taken in the participants after 5 minutes in the supine position and 5 minutes in the sitting position during the 16-hour diurnal/wake period as well when supine in bed during the 8-hour nocturnal/sleep period. Variations in 24-hour IOP in this hyperopia group were analyzed, together with previously collected data under the same laboratory conditions from 32 age-matched subjects with emmetropia or mild myopia (emmetropia group) and 34 subjects with moderate to severe myopia (myopia group).

RESULTS. Average diurnal sitting IOP was lower in the hyperopia group than in the other two groups. The difference between the diurnal sitting and diurnal supine IOP was larger in the hyperopia group than in the myopia group. In all three groups, the nocturnal supine IOP was higher than the diurnal sitting IOP. This elevation in habitual IOP was most significant in the hyperopia group. The hyperopia group also presented a significant IOP elevation within the nocturnal period. Simulated 24-hour rhythms of supine IOP were detected in all groups with different phase timings, but simulated 24-hour IOP variations were not different. The 24-hour habitual IOP fluctuation (peak minus trough) was inversely correlated to axial length.

CONCLUSIONS. Shorter eyes had a larger 24-hour IOP variation than longer eyes in healthy young adults. (*Invest Ophthalmol Vis Sci.* 2010;51:933–937) DOI:10.1167/iops.09-4218

Elevated intraocular pressure (IOP) is a major risk factor for glaucoma. There are other known risk factors that include the refractive state of the eye. Axial myopia is a risk factor for open-angle glaucoma,^{1,2} and hyperopia accompanied by short axial length and shallow anterior chamber depth is a risk factor for angle-closure glaucoma.^{3–5} During office hours, levels of IOP measured in patients while sitting are correlated to the refractive state. A longer myopic eye has relatively higher IOP and a shorter hyperopic eye has relatively lower IOP than do emmetropic eyes.^{6–11} In a study performed in our sleep laboratory, sitting IOP during the diurnal/wake period in healthy

young adults with moderate to severe myopia (myopia group) was higher than in individuals with emmetropia and mild myopia (emmetropia group).¹² A similar difference was not observed when supine IOP was measured during the nocturnal/sleep period.

Based on the observation that the myopia group showed a smaller 24-hour IOP variation than the emmetropia group, one may hypothesize that basal 24-hour IOP variation correlates with axial length or eye size.¹² To test this hypothesis over the entire spectrum of healthy young adults, hyperopic individuals with a shorter axial length should be included. However, no IOP data in hyperopic individuals during the nocturnal period is available in the literature. Thus, we collected 24-hour IOP data from a group of hyperopic young adults in the sleep laboratory and analyzed their 24-hour IOP variations along with those young adults with emmetropia and myopia, to evaluate the hypothesis.

METHODS

The study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board. Experimental subjects were recruited from university students as previously described,¹² and informed consents were obtained. Selected volunteers were healthy nonsmokers, age range 18 to 25 years, of either sex, of diverse ethnicity, and with a regular sleep cycle of approximately 11 PM to 7 AM. Refractive surgery was an exclusion criterion. After a complete eye examination that included gonioscopy to confirm absence of any eye disease and absence of a narrow angle, cycloplegic refraction was determined. Subjects with an interocular difference of 1 D were excluded. Enrolled subjects were categorized as hyperopic with a spherical equivalent equal to or greater than 1 D. Axial length and its components were determined using an A-scan biometer (model 5100; DGH, Exton, PA). Data for the emmetropia group and the myopia group were retrieved from all age-matched subjects available in the laboratory record, bringing the number to 32 and 34, respectively, from 17 and 19, as previously reported in part.¹² The emmetropia group had a refractive state between 0 and –2 D and the myopia group had –3 D or higher in each eye.

The study participants maintained a consistent 8-hour sleep period for 7 days before the laboratory experiment, which was confirmed with a wrist monitor for physical activity and light exposure (Mini Mitter; Actiwatch, Sunriver, OR). They were instructed to keep a wake-sleep log and to avoid alcohol for 3 days and caffeine for 1 day. Contact lens use was discontinued for at least 24 hours before the laboratory recording. After arriving at approximately 2 PM, the subjects stayed in individual rooms for 24 hours, where light intensity was held constant at 500 to 1000 lux during the diurnal/wake period. The darkness period of 8 hours was adjusted to the individual sleep time. For data presentation, corresponding clock times were normalized as a sleep period from 11 PM to 7 AM. Measurements of IOP with a pneumatonometer (model 30 Classic; Reichert Ophthalmic, Depew, NY) and blood pressure and heart rate with an automated monitor (model HEM-608; Omron, Vernon Hills, IL) were taken every 2 hours. Experienced researchers performed these measurements in three ran-

From the Hamilton Glaucoma Center and Department of Ophthalmology, University of California, San Diego, La Jolla, California.

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Corresponding author: John H. K. Liu, University of California, San Diego, Department of Ophthalmology, 9500 Gilman Drive, La Jolla, CA 92093-0946; joliu@ucsd.edu.

TABLE 1. Demographic and Biometric Information of the Study Groups

	Hyperopia	Emmetropia	Myopia	<i>P</i> *
<i>n</i>	9	32	34	
Sex/ethnicity	7 Women, 2 Men	16 Women, 16 Men	19 Women, 15 Men	0.333
Race	5 White, 2 Asian, 2 Hispanic	19 White, 9 Asian, 2 Hispanic, 2 Black	15 White, 16 Asian, 3 Hispanic	0.271
Age, y	22.0 ± 2.7	21.5 ± 1.9	21.8 ± 1.8	0.750
Height, in	65.2 ± 4.5	67.5 ± 4.2	66.5 ± 3.9	0.295
Weight, lb	133.2 ± 17.7	155.1 ± 27.4	145.8 ± 29.9	0.096
Body mass index	22.2 ± 3.4	23.8 ± 2.8	23.1 ± 3.5	0.367
Central corneal thickness, μm	557.5 ± 9.9	542.2 ± 37.0	546.3 ± 28.3	0.704
Refractive state, D (range)	3.2 ± 2.2 (+1to+7)	-0.5 ± 0.7 (0to-2)	-7.1 ± 2.0 (-3to-12)	H/E/M < 0.01
Axial length, mm	21.7 ± 1.0	23.4 ± 0.9	25.9 ± 1.0	H/E/M < 0.01
Anterior chamber depth, mm	3.0 ± 0.3	3.5 ± 0.3	3.6 ± 0.4	H/M < 0.01, H/E < 0.05
Lens thickness, mm	3.7 ± 0.2	3.6 ± 0.3	3.7 ± 0.7	0.704
Vitreous chamber depth, mm	15.0 ± 1.0	16.4 ± 1.0	18.5 ± 1.2	H/E/M < 0.01

Calculated data are the mean ± SD. H, hyperopia; E, emmetropia; M, myopia.

* χ^2 test for sex and race/ethnicity. All others, one-way ANOVA and post hoc Bonferroni test.

dom shifts. Their interindividual variations of prestudy measurements were confirmed as insignificant.

Measurements before the sleep period were obtained at 3:30, 5:30, 7:30, and 9:30 PM. Subjects lay in bed for 5 minutes before blood pressure, heart rate, and bilateral IOPs were measured. Measurements of IOP were taken from the right eyes first. A second set of measurements were followed after sitting for 5 minutes. Readings of IOP were accepted when the recorded tonograph pattern was normal and the SD less than 1 mm Hg. Subjects were allowed to continue normal indoor activities and food and water intake were not regulated. Lights were turned off at 11 PM followed by nocturnal measurements of blood pressure, heart rate, and IOP only in the supine position at 11:30 PM and 1:30, 3:30, and 5:30 AM. Subjects were woken up for the measurements. A dim room light (<10 lux) was used to assist the measurements.¹² Nocturnal measurements were then followed by diurnal measurements at 7:30, 9:30, and 11:30 AM and 1:30 PM.

Mean blood pressure was calculated as the diastolic blood pressure plus one third of the difference between the systolic and diastolic pressures. Data from one eye in each individual was used for analysis. The right eye was selected unless its data were not available in the laboratory record. The average IOP at each time point and during the diurnal and nocturnal periods were calculated. Fluctuation of 24-hour IOP was defined as the IOP peak minus trough. χ^2 test and one-way ANOVA with post hoc Bonferroni test were used to compare study parameters among the three groups. Linear regression was used to examine the correlation between the axial length and 24-hour IOP fluctuation. Results were considered significant at $P < 0.05$.

The best fitting cosine curve was determined for each subject's 24-hour supine IOP data assuming that the rhythm resembled a cosine profile. The peak of the fitted cosine curve (acrophase) was defined as the phase timing of the 24-hour rhythm.¹³ The null hypothesis that phase timings were distributed randomly in 24 hours was tested with the Rayleigh test.¹⁴ Significant difference ($P < 0.05$) would indicate a synchronized 24-hour rhythm for the group. The magnitude of the 24-hour IOP rhythm was estimated by the amplitude of the fitted cosine curve. Phase timings and amplitudes of the three study groups were compared using the nonparametric Kruskal-Wallis test with the post hoc Dunn multiple comparisons.

RESULTS

The demographics of the hyperopia, emmetropia, and myopia groups are summarized in Table 1. No significant difference was apparent in the demographic and biometric data among the three groups except their refractive states and ocular dimensional parameters. The differences in refractive state re-

flected the differences in axial length and vitreous chamber depth. Anterior chamber depth was shorter in the hyperopia group than in the emmetropia and myopia groups.

Figure 1 shows the 24-hour IOP profiles in habitual body positions consisting of sitting during the diurnal/wake period and supine during the nocturnal/sleep period. In all three groups, IOP decreased continuously in general during the diurnal period and experienced a sharp elevation at the beginning of the nocturnal period. Nocturnal IOP continued to increase toward awakening, especially in the hyperopia group, followed by a sharp drop after awakening. The highest IOP occurred at 5:30 AM and the lowest at 9:30 PM. The 24-hour IOP profiles in the supine body position are shown in Figure 2. The lowest IOP occurred at 9:30 PM, and the highest IOP occurred at 5:30 AM for the hyperopia and emmetropia groups and at 11:30 AM for the myopia group. The most notable IOP variation occurred at 3:30 and 5:30 AM for the hyperopia group.

The hyperopia group had a lower average diurnal sitting IOP than both the emmetropia and myopia groups (Table 2). Average postural IOP changes (supine versus sitting) during the diurnal period were in a descending order for the hyperopia, the emmetropia, and the myopia groups. A similar descending order for the IOP difference between the nocturnal and diurnal periods was observed for either the habitual body positions or the supine position. Most notably, the hyperopia group experienced a nocturnal IOP elevation that surpassed the myopia group (Table 2). The largest 24-hour habitual IOP fluctuation of 12.8 ± 3.4 (mean ± SD) mm Hg was observed in the hyperopia group, significantly larger than ($P < 0.01$) the fluctuation of 9.1 ± 3.0 mm Hg in the emmetropia group and the 8.3 ± 2.8 mm Hg in the myopia group (Table 2). After eliminating the postural IOP influence by comparing the 24-hour IOP fluctuations in the supine position, no statistically significant difference was observed. There was no significant difference in the diurnal and nocturnal mean blood pressures or heart rate between the three study groups.

To further examine the posture-independent IOP variation, we applied the cosine fits of 24-hour supine IOP and computed the phase timing and amplitude for each individual. The Rayleigh test showed that all three study groups had a synchronized 24-hour IOP rhythm. The phase timings occurred at $6:46 \text{ AM} \pm 4 \text{ hours, 17 minutes}$; $8:04 \text{ AM} \pm 5 \text{ hours, 24 minutes}$; and $11:32 \text{ AM} \pm 5 \text{ hours, 8 minutes}$ in the hyperopia, emmetropia, and myopia groups, respectively. The phase timing in the myopia group was significantly later than that in the other two

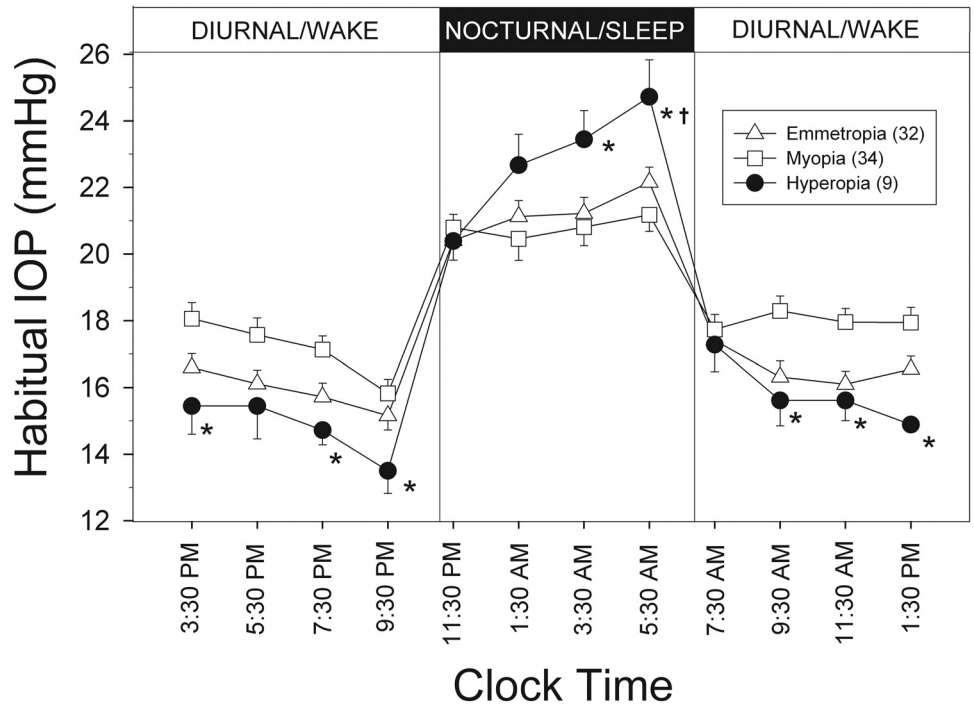


FIGURE 1. Twenty-four-hour IOP profiles of hyperopia, emmetropia, and myopia groups in habitual body positions, sitting during the diurnal/wake period and supine during the nocturnal/sleep period. Error bars, SEM. * $P < 0.05$, different from the myopia group; † $P < 0.05$, different from the emmetropia group using one-way ANOVA and post hoc Bonferroni test.

groups ($P < 0.05$). However, the amplitudes of 24-hour rhythm in supine IOP were not different in the three groups (1.9 ± 1.0 mm Hg in the hyperopia group, 1.3 ± 0.7 mm Hg in the emmetropia group, and 1.6 ± 0.8 mm Hg in the myopia group).

The 24-hour IOP fluctuation in habitual body positions was inversely correlated with axial length: the shorter the eye, the larger the fluctuation (Fig. 3). In contrast, there was no correlation between axial length and the fluctuation in 24-hour supine IOP (Fig. 4). When considering the posture-related IOP fluctuation (calculated as the difference between the 24-hour habitual IOP fluctuation and the 24-hour supine IOP fluctua-

tion), a significant correlation with the axial length appeared ($P < 0.01$, $r = -0.45$).

DISCUSSION

In this systematic analysis of 24-hour IOP variation over a wide range of refractive state and axial length, we found that the 24-hour habitual IOP fluctuation correlated negatively with axial length (Fig. 3). Hyperopic eyes with a shorter axial length had a larger 24-hour IOP variation with the highest IOP occurring in the early morning before awakening and the lowest in

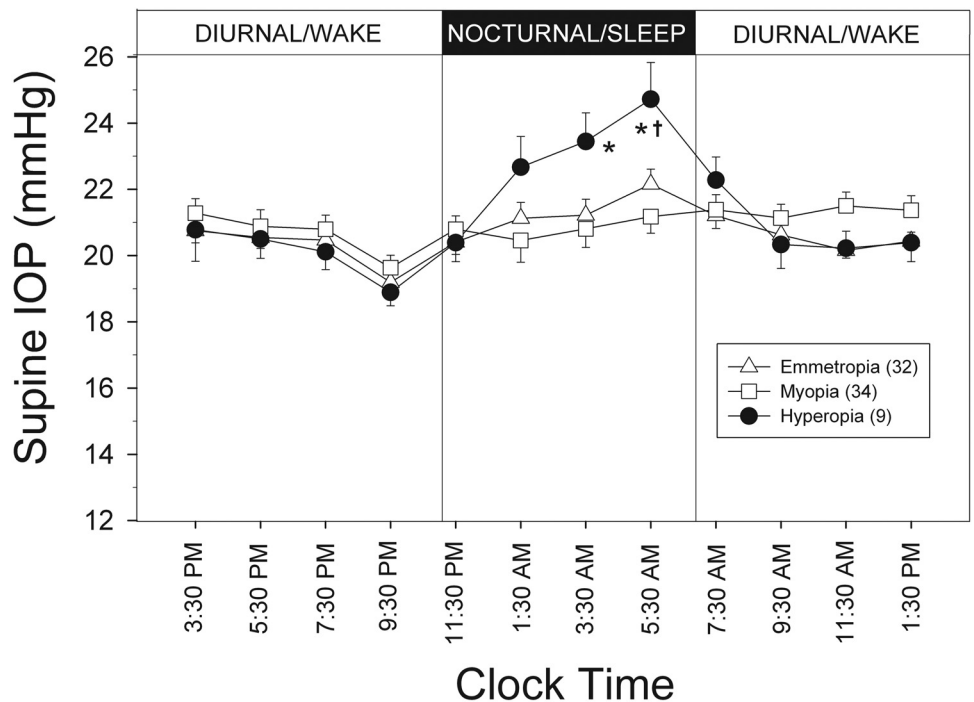


FIGURE 2. Twenty-four-hour supine IOP profiles of hyperopia, emmetropia, and myopia groups. Error bars, SEM. * $P < 0.05$, different from the myopia group; † $P < 0.05$, different from the emmetropia group; one-way ANOVA and post hoc Bonferroni test.

TABLE 2. Variations in 24-Hour IOP of the Study Groups

Group	Hyperopia	Emmetropia	Myopia	P*
<i>n</i>	9	32	34	
Average diurnal sitting IOP	15.3 ± 1.2	16.2 ± 1.8	17.6 ± 2.1	H/E, H/M < 0.05
Average diurnal supine IOP	20.4 ± 0.8	20.4 ± 1.3	21.0 ± 2.0	0.303
Average nocturnal supine IOP	22.8 ± 1.8	21.2 ± 2.0	20.8 ± 2.5	0.062
Average diurnal IOP difference Supine/sitting	5.1 ± 1.3	4.2 ± 1.4	3.4 ± 1.4	H/M < 0.05
Average IOP difference between the nocturnal and diurnal periods				
Habitual	7.5 ± 1.7	5.0 ± 2.6	3.2 ± 2.5	H/M < 0.01
Supine	2.4 ± 1.7	0.8 ± 1.9	-0.2 ± 2.1	H/E, E/M < 0.05 H/M < 0.01
24-hour IOP fluctuation (peak minus trough)				
Habitual	12.8 ± 3.4	9.1 ± 3.0	8.3 ± 2.8	H/E, H/M < 0.01
Supine	8.0 ± 3.1	6.2 ± 2.3	6.6 ± 2.4	0.151

Data are expressed as the mean ± SD. H, hyperopia; E, emmetropia; M, myopia.
* One-way ANOVA and post hoc Bonferroni test.

the late evening (Fig. 1). Therefore, the hypothesis that basal 24-hour IOP change is correlated with axial length¹² is applicable to the entire spectrum of healthy young adults including the hyperopic individuals with a shorter axial length.

The results indicate that there are posture-dependent and posture-independent mechanisms for the 24-hour habitual IOP fluctuation. The posture-dependent mechanism can be examined using the IOP readings during the diurnal period; IOP in the sitting position was lower than that in the supine position.¹⁵ The posture-dependent IOP change was significantly larger in eyes with shorter axial length compared with eyes with longer axial length (Table 2). This IOP change was detected 5 minutes after the participants sat up from the supine body position. It is unlikely that a slow physiological process in aqueous humor dynamics, such as aqueous humor formation or pressure-independent uveoscleral flow, caused the relatively fast IOP response. In contrast, a hydrostatic change due to different postures can lead to a fast change of episcleral venous pressure without a significant effect on anterior chamber depth.^{16,17} A reduction of episcleral venous pressure from supine to sitting should set IOP to a lower level for the experimental subjects according to the Goldmann equation. In ad-

dition, filling status of choroidal vasculature should change rapidly after a new posture. Because of a shorter axial length and thus smaller ocular volume, hyperopic eyes may be affected more by the removal or redistribution of blood from the choroid to the vascular beds in the lower body.¹⁸ Therefore, a larger IOP difference between the sitting and supine positions appeared in the hyperopia group.

We also identified a posture-independent mechanism that caused additional IOP elevation in the hyperopia group within the nocturnal period (Fig. 2). This mechanism was less significant in the emmetropic and myopic eyes. For the hyperopic eyes, IOP increased between the first and second nocturnal IOP measurements and continued to rise within the nocturnal period. However, this nocturnal-only effect had a limited impact on the amplitude in the simulated 24-hour rhythm of supine IOP. A well-known nocturnal reduction in aqueous humor flow cannot be a contributing factor for this posture-independent IOP elevation in the hyperopic eyes.¹⁹ It is unclear whether a nocturnal change in the axial length or its choroidal component was involved. If such a change occurred, it would have to be very substantial to have an impact. An expected 0.1% to 0.2% change in the axial length during the

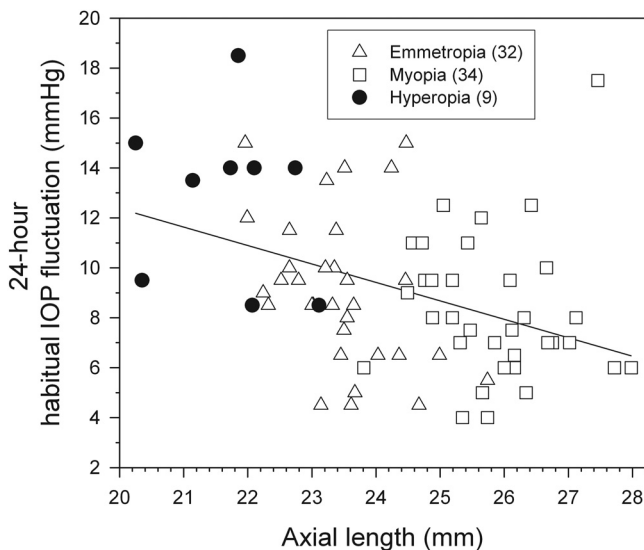


FIGURE 3. Linear regression showing a correlation between axial length and 24-hour habitual IOP fluctuation, peak minus trough ($P < 0.01$, $r = -0.40$).

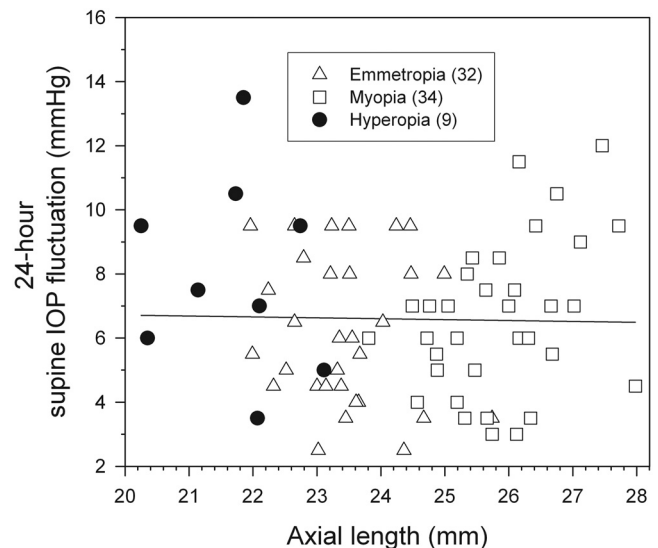


FIGURE 4. Linear regression showing no correlation between axial length and 24-hour supine IOP fluctuation ($P = 0.866$).

diurnal period did not translate to a noticeable IOP variation in the present study.²⁰⁻²³

The shallower anterior chamber of the hyperopia group is likely to be associated with this posture-independent and time-limited mechanism, which has not been reported in the literature. A shorter anterior chamber depth is an established risk factor for angle-closure glaucoma, and pupillary dilation is known to trigger angle closure in such eyes.²⁴ Although office-hour gonioscopy indicated an open angle, it is possible that a relative pupillary block occurred during the nocturnal/sleep period in eyes with a shallow anterior chamber, gradually increasing nocturnal IOP in healthy young adults by reduced outflow facility. It was also noted that any pupillary change during the nocturnal IOP measurements under the dim light condition did not immediately lead to a different IOP for the hyperopia group when examining the IOP values at 11:30 PM. The young adults who participated in the present study were all at an age when refractive states may continue to evolve. Our findings that hyperopic individuals have an increased 24-hour IOP variation provide no support for the hypothesis that an elevated IOP or an IOP spike is associated with the development of myopia.^{25,26}

In summary, basal 24-hour fluctuation of habitual IOP correlated inversely with axial length in healthy young adults. Eyes with a shorter axial length had a significantly larger IOP elevation from the diurnal/wake period to the nocturnal/sleep period. The 24-hour habitual IOP fluctuation had a significant posture-dependent mechanism and, for a shorter eye, a posture-independent mechanism within the nocturnal/sleep period.

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