

Time Spent in Lateral Sleep Position and Asymmetry in Glaucoma

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PURPOSE. To explore sleep position in asymmetric primary open-angle glaucoma (POAG) with a focus on low pressure glaucoma (LPG).

METHODS. Sleep laboratory videos of 54 POAG patients were examined for lateral sleep. Then, 29 LPG patients (intraocular pressure [IOP] < 22 mm Hg) with an intereye visual field index (VFI) asymmetry of more than 5% continuously recorded their sleep position at home for 2 nights by using a portable device. Correlations were sought between sleep position, visual field (VF), and retinal nerve fiber layer (RNFL) symmetry as well as ocular biometric data and positional IOP changes. Finally, an expanded data set of 178 POAG patients (63 LPG and 115 high pressure glaucoma [HPG; IOP ≥ 22 mm Hg]) was used to correlate VF and the RNFL symmetry to the self-assessed sleep position collected in a survey.

RESULTS. In the video analysis, patients spent 19% ± 2% (mean ± SEM) more time sleeping on one side than on the other. Right-sided sleep was preferred. Right-sided sleep was 1.6 times more common in continuously recorded home data and correlated to an asymmetric VF that was worse in the left eye ($b = -0.422$, $P = 0.002$). Pulse amplitude of left eyes was lower in the right decubitus position ($P = 0.02$). In the expanded survey, 73% of LPG and 58% of HPG patients slept asymmetrically. Right-sided sleepers had a worse RNFL symmetry score.

CONCLUSIONS. Asymmetric sleep behavior is common. Right-sided sleep was preferred and correlated with a lower VFI on the left.

Keywords: sleep position, asymmetry, visual field

Low pressure glaucoma (LPG) optic nerve damage and visual field loss often shows considerable intereye asymmetry despite symmetric IOP in the sitting position.^{1,2} Around the age of 65 years, the mean age of LPG patients in this study, a more asymmetric, preferentially right-sided sleep behavior can be observed.³ Interestingly, position, perfusion, and protective goggles are routinely considered in longer procedures in nonophthalmologic specialties owing to complications that range from increased IOP to central retinal artery occlusion (particularly in spinal surgery where a prone position has to be maintained and head positioning can increase orbital pressure).^{4,5} Lateral sleep is now recognized as a disease mechanism in floppy eyelid syndrome.⁶ In addition to external pressure, IOP varies by body position as do intracranial and perfusion pressures.⁷⁻⁹ Recent surveys that investigated sleep position in glaucoma have used the self-assessed, presumed sleep position as a surrogate for objective sleep behavior and concluded that the dependent eye correlates with worse glaucoma damage.^{10,11} To address the paucity of objective

sleep position data in glaucoma patients, several methods were used to generate data on true sleep behavior in this population.

Since humans spend nearly one-third of their life sleeping, we hypothesized that the predominant sleep position may contribute to asymmetric glaucoma damage. The higher prevalence of asymmetric visual fields in LPG² could result from a mechanism that is independent of office-hour IOP. If sleep position were a contributing mechanism in glaucoma, inexpensive treatment could be readily made available, for instance, in the form of sleep position trainers.^{12,13}

METHODS

Subject Selection

All investigations adhered to the Declaration of Helsinki and were approved by the Institutional Review Board at Yale University and the University California San Diego. Participants were identified consecutively between January 2009 and February 2012 as diagnosed with open-angle glaucoma by a

glaucoma specialist on the basis of glaucomatous optic nerve changes on slit lamp examination, retinal nerve fiber analysis (Cirrus HD OCT; Carl Zeiss Meditec, Dublin, CA, USA), and glaucomatous visual fields (Humphrey Visual Field II-i; Carl Zeiss Meditec, Jena, Germany) in addition to a comprehensive examination that included gonioscopy. Patients were categorized as LPG if baseline IOP was below or equal to 21 mm Hg without medications, or as high pressure glaucoma (HPG) if IOP was above 21 mm Hg during office hours. The study consisted of three parts. A first analysis examined sleep laboratory videos of primary open-angle glaucoma (POAG) patients. In the second part, LPG patients underwent sleep position monitoring with portable devices and postural pneumatonometry and ocular response analysis measurements. Finally, both LPG and HPG patients took a sleep survey to look for a correlation of sleep position and visual field index (VFI)¹⁴ or retinal nerve fiber layer (RNFL) parameters. High pressure glaucoma patients were included to expand the study population and because recent data indicate that POAG may be a continuum of HPG and LPG.^{15,16}

Sleep Laboratory Video Analysis

An initial sleep laboratory video analysis investigated whether asymmetric sleep behavior was present in glaucoma patients who were seen in a sleep laboratory. This study group consisted of POAG patients, regardless of IOP. The asymmetry of visual fields was not analyzed in this group. Patients with nonglaucomatous visual field loss, smoking, irregular sleep habits, sleep apnea, or video recordings of insufficient quality were excluded. All subjects were asked to avoid caffeine on the day of the study and keep a regular sleep/wake cycle for the week before the study. Patients were instructed to relax into their normal sleep routines and positions. In this labor-intensive process, the initial sleep position was determined first and footage was then advanced in fast-forward continuous view until a movement occurred. Time stamps were documented and the number of minutes spent in the right lateral decubitus, left lateral decubitus, supine, and prone positions were computed. The time spent in the left and right lateral position was expressed as a percentage of total sleep time.

At-Home Continuous Sleep Position Monitoring

A different group of patients who had asymmetric LPG was equipped with continuously worn sleep position monitors. To qualify, these patients had to have an untreated Goldmann tonometry IOP of less than 22 mm Hg, reliable visual fields with less than 15% false-positive responses, and 20% fixation losses and an interocular VFI difference of more than 5% (Humphrey Visual Field II-i). One hundred ninety-five charts with ICD 9 code 365.12 were reviewed and 112 were eligible for the study by the response to the survey question and fulfillment of the study criteria. Twenty-nine LPG patients were successfully recruited. Exclusion criteria included self-reported supine sleep position, sleep apnea, IOP 22 mm Hg or greater except during the immediate postoperative period after cataract surgery, diagnosis of secondary glaucoma, or evidence of retinal pathology that could affect the visual field.

Pneumatometric IOP (Model 30 pneumatonometer; Reichert, Inc., Depew, NY, USA) was measured after sitting in a standard examination room chair for 5 minutes and compared to the IOP in the left and right lateral decubitus position after maintaining each for 5 minutes. For the decubitus positions, the IOP was measured while maintaining that position. All measurements were taken with a deviation of less than 1 mm Hg in the pulse IOP mode. Four measurements were taken for each eye with the ocular response analyzer

(version 2.0; Reichert, Inc.)¹⁷ to determine corneal hysteresis, corneal resistance factor, and corrected IOP. The highest waveform score was selected for each eye.

Patients received training to wear the Embletta X10 sleep monitor (Embla, Broomfield, CO, USA)¹⁸ on an adjustable cloth belt around their abdomen for two nights. Sleep position data were recorded on a 360° scale with 10-Hz resolution (Remlogic; Embla¹⁹) and analyzed (Matlab version 7.8; The MathWorks, Inc., Natick, MA, USA) by mean sleep position in degrees and the percentage of total sleep time spent in each of the four sectors. We used the following cutoffs: Time spent with the chest monitor facing 30° to 150° were counted as left-sided sleep (i.e., left lateral recumbent position), 150° to 210° were counted as prone, 210° to 330° were counted as right-sided sleep, and 330° to 30° were counted as supine. The degree cutoffs were chosen on the basis of our pilot data, which showed good correlation between these numerical values and patient's perception of position.

Average RNFL thickness in micrometers and symmetry scores were obtained for all patients from the most recent (131 ± 68 days prior) optical coherence tomography (OCT) Cirrus examination using the Cirrus HD OCT.

Expanded Sleep Position Survey

To extrapolate the continuous sleep-monitoring results, 178 POAG patients (63 LPG and 115 HPG patients) with a reliable visual field²⁰ were prospectively enrolled to assess self-reported sleep position in a survey. Patients were asked to choose to characterize their predominant sleep position as "side," "prone," "supine," or "unknown." Those who chose side as their primary position were further asked to specify whether they were sleeping "mostly on the right," "mostly on the left," or "both sides equal." Patients who could not select a primary sleep position or had sleep apnea were excluded. Demographic information, such as sex and ethnicity, was also included. Visual field index and RNFL data were obtained as described.

Statistical Analysis

All analyses were performed by using nonparametric analyses with JMP version 9.0 (SAS Institute, Inc., Cary, NC, USA). The primary variable of interest was VFI and its relationship to percentage of time spent in a specific sleeping position. Continuous variables such as VFI and average sleep position angle were also compared with type of glaucoma, a categorical variable, by using a Wilcoxon rank sum test. For continuous variables, analysis of variance test based on a linear fit was used. Categorical variables were compared with a Pearson's χ^2 test. Based on a postulated effect size of a correlation of 0.6 of sleep position and ocular pathology (VFI being significantly worse) from the limited data available at inception of this study ($\alpha = 0.05$, sample size = 20),²¹ there was an approximately 82% chance of discovery. All results were considered significant with a *P* value less than or equal to 0.05.

RESULTS

Sleep Surveillance Video Analysis

There were sleep videos of 54 patients. The average age was 70 ± 12 years, 57% were female, 72% Caucasian, 12% Asian, 9% African American, and 7% Hispanic. On average, glaucoma patients spent $19\% \pm 2\%$ (mean \pm SEM) more time sleeping on one side compared to the other (Fig. 1A). Right-sided sleep was slightly preferred (Fig. 1B).

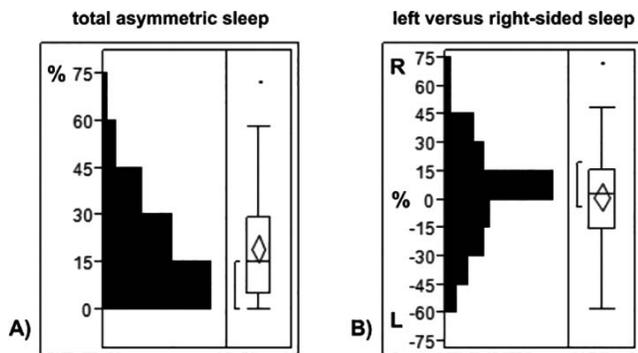


FIGURE 1. Sleep position analysis of video-recorded sleep laboratory glaucoma patients ($n = 54$) with asymmetric sleep. (A) Percentage of time spent sleeping on preferred side. (B) Preferred lateral sleep position. Box and whisker plots with (from top to bottom): 1st percentile (dot), 5th percentile (bar), 25th percentile (box), median (bar), confidence diamond, and shortest half (bracket) (most dense 50% of observations).

Continuous Sleep Position Monitoring

Home Sleep Position Monitoring and Correlation With VFI. Twenty-nine LPG patients participated and successfully recorded their sleep position. The average age was 63 ± 14 years, 62% were female, 70% Caucasian, 23% African American, 4% Hispanic, and 3% Asian. Sleep behavior was visualized by using circle graphs. Figure 2 shows an example from a predominantly right-sleeping patient. The size of each wedge indicates the time spent at the angle shown, while each circle represents 33 minutes.

Right and supine sleep was more common. Similar to the video analysis, patients wearing sleep position monitors also spent the greatest amount of time in the right decubitus position, followed by the supine position, the left decubitus position, and the prone position (Fig. 3). Right-sided sleep was significantly more common than all other positions ($P = 0.03$) and supine sleep was more common than prone sleep ($P = 0.01$).

The mean right VFI was 87 ± 14 and the mean left VFI was 81 ± 20 ($P = 0.197$), while the average absolute difference was 18 ± 11 . Seventeen patients were categorized as right sleepers and 12 patients were left sleepers (Fig. 4). Right sleepers had a right VFI (90 ± 10) that was not significantly different from the left VFI (88 ± 11 ; $P = 0.725$), while left sleepers had an average

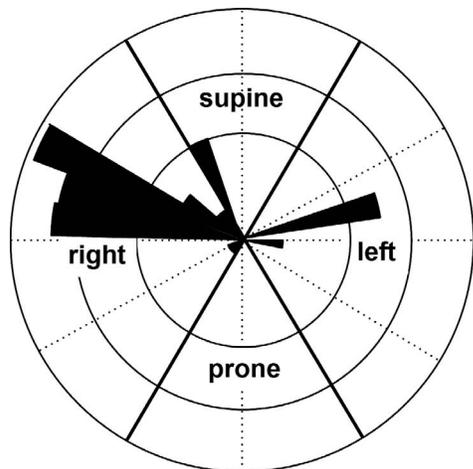


FIGURE 2. Sleep position sectors by cardinal sleep position. Right refers to right side facing and left to left side facing.

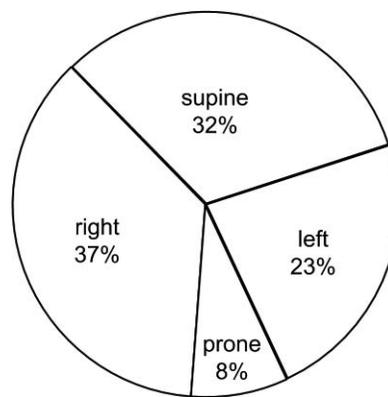


FIGURE 3. Graphic representation of sleep position in continuously monitored patients. Time spent in the four cardinal sleep positions by patients who underwent home sleep monitoring.

left VFI of 81 ± 13 and an average right VFI of 83 ± 20 ($P = 0.795$).

However, in the regression analysis, sleep laterality (Fig. 4) had a significant negative association with relative VFI difference of left VFI – right VFI ($b = -0.422$, $P = 0.002$), indicating patients with increasing preference for right-sided sleep had a proportionally more decreased VFI in the left or nondependent eye. Time spent in the prone position was also found to have a significant negative association with relative VFI difference ($b = -0.79$, $P = 0.006$).

There was no significant association between average RNFL thickness of the dependent eye and sleep position (right sleepers: right eye 70 ± 13 , left eye 72 ± 17 , $P = 0.597$; left sleepers: left eye 69 ± 18 , right eye 71 ± 12 , $P = 0.657$).

Postural Pneumatometry and Ocular Response Analysis. There were no pneumatometric IOP differences between right and left eyes for any given position (Table 1) and no significant difference between the corneal properties in the right and left eye (Table 2). In the right eye, the IOP increased

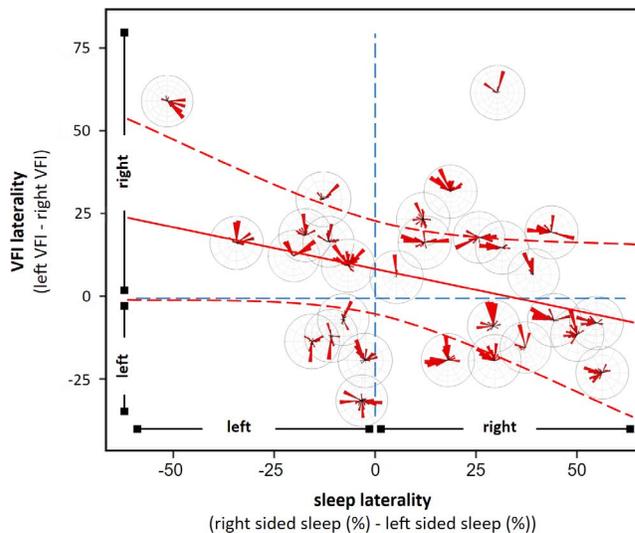


FIGURE 4. Scatterplot of interocular VFI difference by sleep position. Circle graphs depict continuously recorded sleep position as detailed in Figure 2. Supine and prone position segments are also shown. Sleep laterality is the difference between the percentage of time spent in the right and left sleep position and VFI laterality is expressed as left VFI – right VFI. Red line = linear fit model; blue dotted lines = left/right separation lines.

TABLE 1. Postural Pneumatometry

Position	R IOP, mm Hg	L IOP, mm Hg	P	R PA	L PA	P
Seated	19.7 ± 1.4	19.9 ± 1.4	0.84	4.7 ± 3.5	5.1 ± 2.8	0.36
Right decubitus	22.4 ± 1.5*	21.5 ± 1.3	0.17	6.3 ± 3.5	4.2 ± 3.0	0.02
Left decubitus	21.7 ± 1.5*	21.9 ± 1.4*	0.43	4.9 ± 3.7	5.0 ± 4.9	0.94

Mean ± standard deviation; *n* = 29. L, left eye; PA, pulse amplitude; R, right eye.

* *P* < 0.05 compared to the seated position.

significantly as compared to the seated position when the right or the left decubitus position was assumed. In the left eye, the IOP only increased in the left decubitus position. The pulse amplitude in the left eye was significantly lower than in the right eye when the right decubitus position was assumed (*P* = 0.02). There was no significant association between visual field asymmetry and IOP increase with either decubitus position for either eye (*P* = 0.05, 0.39 for both right and left eyes).

Expanded Sleep Position Survey

All 29 patients who underwent continuous sleep position monitoring also received a survey to assess their predominant sleep position. In those, the objective sleep position in degrees was significantly associated with the self-reported sleep position (*P* = 0.03). The primary sleep position matched the self-reported one in 77% of participants.

The demographic data of all 178 subjects who received the sleep survey (63 LPG and 115 HPG) are displayed in Table 3. Right and left were the most common self-reported positions, 33% and 26%, respectively. Supine position was reported by 16% of participants, while 6% reported a preference for the prone position. The remaining 19% of participants stated equal preference for both right and left sleep position. The mean left and right VFIs were approximately equal in the HPG and LPG subjects. Low pressure glaucoma patients had a greater degree of self-reported sleep position asymmetry than HPG patients (*P* = 0.02; Fig. 5).

The nonparametric testing of the survey data showed as the only significant findings for the subgroups that right-sleeping LPG patients had a lower RNFL spectral-domain OCT symmetry score than nonright sleepers (*P* = 0.03), but no significant difference or correlation was found between left and right RNFL in sided sleepers in either LPG or HPG. When LPG and HPG data were combined as a POAG continuum, right-sided sleepers did have a lower right RNFL thickness (*P* = 0.003) and a lower RNFL symmetry score (*P* = 0.039).

DISCUSSION

There is limited knowledge about the objective sleep behavior of glaucoma patients or whether a patient's self-assessed, presumed sleep position correlates with the true position. This study tried to fill this void by collecting pilot data by using three different methods to help properly estimate the sample

TABLE 2. Ocular Response Analyzer Results

	Right Eye	Left Eye	P Value
IOP, mm Hg	10.6 ± 4.3	11.0 ± 4.1	0.52
IOP, corrected	13.1 ± 4.5	14.1 ± 4.6	0.13
Corneal hysteresis	9.2 ± 1.6	8.6 ± 2.2	0.06
Corneal resistance factor	7.9 ± 1.6	7.5 ± 2.0	0.13

There was no significant difference between the corneal properties in the right and left eye.

size for future studies when correlating objective sleep position with glaucoma asymmetry and objective sleep position assessment with self-reporting. The initial analysis of sleep laboratory surveillance videos revealed that asymmetric sleep behavior was relatively common and present in more than 25% of glaucoma patients who spent between 30% to 75% of sleep in a lateral position, and more preferred right-sided sleep. Lateral sleep position training is now used to address obstructive sleep apnea or snoring.^{22,23} Although sleep laterality in adults without sleep pathology has not been studied well, the percentage observed here is consistent with a recent survey of sleep behavior in glaucoma.¹⁰

We hypothesized that analyzing sleep behavior in LPG would provide an opportunity to discover novel glaucoma mechanisms because of the lack of a significant relationship between IOP or other risk factors and visual field status.² The LPG visual field loss is often more asymmetric than HPG^{24,25} and may manifest earlier and be more pronounced in the left eye than the right eye.^{2,26–28} There was no significant asymmetry of other known risk factors noted, including low corneal hysteresis or corneal resistance.^{17,29–31} Exposure to an asymmetric risk factor that occurs at night has potential to be significant because we spend, on average, nearly 8 hours asleep,³² enough for lateral sleep to be a recognized disease mechanism in floppy eyelid syndrome.⁶ To increase the chance of discovery, LPG patients were selected who had an established asymmetric visual field damage. We took advantage of the increased statistical testing power from correlating the recently introduced continuous VFI¹⁴ with the continuous data from wearable sleep position monitors.¹⁸ We expected the correlation between sleep position and glaucomatous damage to be more pronounced in LPG patients than in HPG patients since LPG patients are more sensitive to positional changes³³ and may experience more pronounced translaminal pressure gradients³⁴ as ocular perfusion adjusts.³⁵

TABLE 3. Demographic and VFI Information of LPG and HPG Subjects (Mean ± SD)

	LPG, <i>n</i> = 63	HPG, <i>n</i> = 115	P Value
Age, y	64 ± 15	72 ± 12	0.01
Sex, %			0.41
Female	73	57	
Male	27	43	
Ethnicity, %			0.31
Caucasian	71	64	
African American	18	25	
Hispanic	7	9	
Asian	4	2	
VFI right eye, %	88.0 ± 22.3	80.2 ± 24.7	0.72
VFI left eye, %	83.2 ± 18.9	79.1 ± 23.0	0.35
Absolute VFI difference	15.4 ± 17.0	15.0 ± 19.1	0.85
IOP, mm Hg	14.1 ± 5.4	17.5 ± 4.1	<0.01

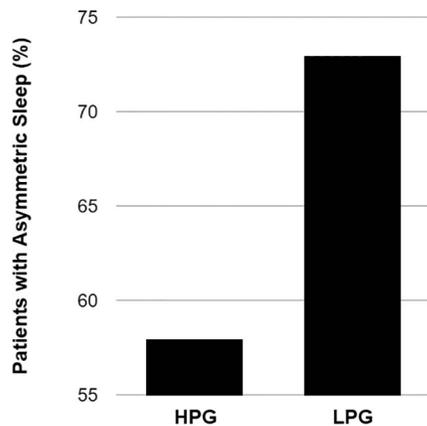


FIGURE 5. Glaucoma type versus percentage asymmetric. Low pressure glaucoma and HPG subjects were classified as asymmetric if interocular VFI difference was greater than 5%.

Continuously recorded sleep behavior of LPG patients showed that they tended to sleep more on the right side and had moderately correlated worse left visual fields. This result is different from recent survey results that used the presumed sleep position in lieu of objective sleep behavior.¹⁰ The survey by Kim et al.¹⁰ found that the dependent eye is correlated with a worse visual field. In our study, the mean IOP increased similarly to that found in other studies^{8,35,36} but not asymmetrically upon changing from the sitting to the lateral decubitus position. The only significant asymmetric finding that was higher in the right eye than the left was the pulse amplitude in the right lateral decubitus position. A limitation of our study was that we did not formally measure blood flow. Although it is tempting to speculate that the lower pulse amplitude we found in nondependent left eyes with worse visual fields may be related to a relatively decreased perfusion in these eyes, this cannot be concluded because the lower amplitude is a reflection of both blood flow and ocular rigidity.³⁷ Nevertheless, these individuals may be more susceptible to autonomic dysfunction that includes cardiac output.³⁸ Decreased sympathetic output and increased vagal tone can be demonstrated in the right decubitus position when compared to left decubitus and supine positions. In congestive heart failure patients, this preferential sleep pattern has been interpreted to be a mechanism to normalize the imbalance of increased cardiac sympathetic activity and decreased vagal tone.^{39,40}

The results from our expanded sleep position survey cast doubt on whether it is possible to deduct objective sleep behavior via self-assessed preferential sleep position. The only significant observation in the expanded component was that after combining LPG with HPG to a POAG continuum, presumed right-sided sleep was associated with a lower right-sided RNFL, contradicting the objective sleep-monitoring results.

Our study was explorative in nature and used three different methods to gather different aspects of sleep in glaucoma that will help to establish recruitment needs for future interventional studies. If causality can be demonstrated, sleep position training that is used in obstructive sleep apnea to modify risks^{12,13,22,23} could be used here as well. Any such study has to consider potential risk of modifying sleep position. For instance, while 30° head-up positioning lowers IOP,⁴¹ as little as 6° head-down positioning may cause peripapillary RNFL changes and even scotomas.⁴²

In conclusion, LPG patients often have objective, asymmetric sleep behavior and prefer right-sided sleep, which was

moderately correlated to lower VFI scores in the left eye. Additionally, asymmetric sleep was correlated with a lower symmetry RNFL score.

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