Fluctuations of the Intraocular Pressure in Medically Versus Surgically Treated Glaucoma Patients by a Contact Lens Sensor

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• PURPOSE: To compare fluctuations in intraocular pressure (IOP) in medically vs surgically treated glaucoma patients.
• DESIGN: Prospective, nonrandomized case series.
• METHODS: IOP-related fluctuations were measured for 24 hours using a contact lens sensor (CLS). SUBJECTS: We performed monitoring with CLS in 91 eyes of 77 patients; 59 eyes were receiving ocular hypotensive medication and had no previous history of glaucoma surgery (medical group), while 32 eyes with open-angle glaucoma (OAG) had previously undergone glaucoma surgery (surgical group). MAIN OUTCOME MEASURES: The amplitude, expressed as an indicator of the IOP-related fluctuation, and the presence of a nocturnal acrophase. We also identified maximum and minimum IOP-related values for each patient.
• RESULTS: The mean (standard deviation) amplitude of IOP-related CLS signal in the group of surgically treated eyes was 100 (41) mV eq, while in the medically treated group it was 131 (69) mV eq (difference: $P = .010$). We found that 42.9% of the surgically treated but only 13.8% of the medically treated glaucoma group exhibited an absence of nocturnal acrophase (difference: $P = .011$). The maximum and minimum IOP-related values for the medical group were statistically higher than the surgical group ($P = .001$ and $P = .006$, respectively).
• CONCLUSIONS: IOP-related fluctuations were larger in eyes with medically treated glaucoma than in those with surgically treated glaucoma. A significantly larger fraction of the surgical group exhibited an absence of nocturnal acrophase compared to the medically treated group. (Am J Ophthalmol 2019;203:1–11. © 2019 Elsevier Inc. All rights reserved.)

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GLAUCOMA IS THE LEADING CAUSE OF IRREVERSIBLE blindness worldwide. While elevated intraocular pressure (IOP) is no longer part of the definition of glaucoma, it is recognized as the only modifiable risk factor for the development and progression of the disease.[1] Reducing IOP below a clinically determined target level, whether through the daily application of eye drops, laser procedures, or surgical interventions, is therefore the mainstay of glaucoma therapy.

Goldmann applanation tonometry (GAT) is the most commonly used tonometric technique and is considered the "gold standard" for measuring IOP. GAT is influenced by several ocular factors, including central corneal thickness, corneal biomechanical properties, and scleral rigidity.[2] The most significant shortcoming of GAT is, however, the static nature of its measurements, which represent only a 1- to 2-second snapshot of an individual's IOP, taken in the sitting position.

IOP is a dynamic parameter with a circadian rhythm and is subject to spontaneous changes. IOP may fluctuate by as much as 4–5 mm Hg in healthy individuals, while substantially greater fluctuations have been reported in some glaucoma patients.[3] There is evidence that single IOP measurements taken in the sitting position and during normal office hours reflect neither the true range of an individual's IOP nor peak IOP, nor any other variation that could occur throughout the day. Studies that measure IOP several times over a whole day have found that approximately two thirds of glaucoma patients have their highest IOPs outside regular clinic hours; these are most frequently seen during the nocturnal/sleep period.[4–7]

One contributor to glaucoma development and progression may be the variability of IOP itself. Studies have suggested that fluctuations in IOP are an independent risk factor for glaucoma progression.[8–10] In addition, for simple IOP reduction, IOP "modulation"—involving a thorough assessment of a patient's IOP profile—and targeted IOP-lowering treatments have also been suggested as ways of reducing the progression of the disease.[11]

Intraocular pressure is known to fluctuate and, as such, it is essential that we understand these fluctuations over time in order to manage patients and take appropriate decisions related to their treatment. The dynamic nature of IOP underlies the need for a clinical tool that would allow its continuous assessment over a 24-hour period, and

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especially during the night, when the IOP often tends to increase. A major breakthrough was made when Leonardi and associates[12] updated the concept of a soft contact lens with an embedded wireless sensor and developed an approved commercial product. The contact lens sensor (CLS) is a recently developed device that records IOP-related patterns with no requirement of waking subjects up during the nocturnal sleep period. The CLS was developed to monitor ocular volume change habitually fluctuating along with IOP over a period of 24 hours by measuring changes in the circumference of their eyes and in the area of their corneoscleral junction.[13]

The purpose of this study was to compare the IOP-related fluctuations in medically vs surgically treated glaucoma patients under physiological conditions. We hypothesized that 24-hour ocular volume–related assessments could provide better information for the control of IOP in glaucoma patients with different treatment options, such as medical and surgical approaches.

METHODS

THIS STUDY WAS A PROSPECTIVE, NONRANDOMIZED CASE series that involved patients recruited from the Glaucoma Unit of the Department of Ophthalmology of the Arnau de Vilanova University Hospital in Lleida, Catalonia, Spain, from April 2016 to June 2017. Two glaucoma specialists (M.J.M. and J.E.) diagnosed and treated all the cases involving eyes affected by glaucoma. The protocol and informed consent procedures were approved by the Ethics Committee of the University Hospital Arnau de Vilanova, Lleida, Catalonia, Spain. Informed consent was obtained from all patients.

We obtained continuous IOP-related values using a CLS (Sensimed Triggerfish; Sensimed AG, Lausanne, Switzerland).

We performed monitoring with CLS in 91 eyes from 77 patients, of which 11 patients underwent monitoring of their right eye and left eye, and 3 patients underwent monitoring of the same eye, before and after glaucoma surgery. The medical group consisted of 59 eyes with either open-angle glaucoma (OAG) or ocular hypertension based on ocular hypotensive medications and with no history of previous glaucoma surgery. These eyes may have undergone cataract surgery at least 6 months prior to be included in this study, but may not have been involved in previous glaucoma surgery or laser trabeculoplasty. In the medical group, all patients were controlled using 2 or 3 topical hypotensive medications (including beta blockers, carbonic anhydrase inhibitors, alpha-2 adrenergic agonists, and prostaglandin analogs), but not acetazolamide.

The surgical group included 32 phakic or pseudophakic eyes with OAG and previous glaucoma surgery at least 3 months before entering the trial; 18 of the eyes had received deep nonpenetrating sclerectomy (56.15%), 12 trabeculectomy (37.5%), and 2 ExPress implants (6.2%). The bleb must have been well functioning. We included diffuse filtering blebs with subconjunctival fluid collection. We did not include patients with IOP <10 mm Hg.

All 77 patients underwent a comprehensive ophthalmic examination, which included visual acuity, with a recording of refractive correction; slit-lamp and funduscopy examinations; IOP by GAT; ultrasonic corneal pachimetry (Ocuscan RXP; Alcon Laboratorios, Fort Worth, Texas, USA); visual field analysis with a Humphrey Field Analyzer (Carl Zeiss Meditec, Dublin, California, USA; SITA-standard program, central 24-2 threshold test); and measurement of the thickness of the retinal fiber layer, using optical coherence tomography (Cirrus OCT; Zeiss Carl Ophthalmic Systems Inc, Dublin, California, USA).

The patients diagnosed with OAG included those with primary open-angle glaucoma (POAG), normal tension glaucoma (NTG), pseudoexfoliation syndrome, and pigmentary syndrome. Patients diagnosed with POAG and NTG were defined as those with open normal-appearing angles, typical glaucomatous optic atrophy (ie, neural rim thinning, notching, saucerization, or nerve fiber layer disc hemorrhage), and typical glaucomatous visual field damage (ie, arcuate, paracentral scotoma, or nasal step). An initial diagnosis of POAG required an indication from the patient chart of an untreated IOP of >21 mm Hg. Diagnosis of NTG required an untreated mean diurnal IOP of ≤21 mm Hg from diagnosis to enrollment, indicated by the patient chart. Patients with exfoliation glaucoma exhibited typical anterior chamber exfoliative material deposits. Pigmentary glaucoma was characterized by the deposition of pigment on the lens, zonules of the lens, trabecular meshwork, and corneal endothelium. Ocular hypertension was defined as a condition in which the IOP was greater than 21 mm Hg in the absence of glaucomatous defects in visual field testing, the normal appearance of the optic disc and nerve fiber layer, anatomic normality, open angles in gonioscopy, and the absence of ocular conditions contributing to the elevation of pressure, such as narrow angles, neovascular conditions, and uveitis.

The exclusion criteria were age <21 years, visual defects attributable to nonglaucomatous conditions, primary angle closure glaucoma, neovascular glaucoma, history of ocular trauma, retinal disease or ocular inflammation, and laser therapy. The patients had to meet best-corrected Snellen visual acuity of ≥0.3 and spherical equivalent of > -6 diopter.

• **MEASUREMENTS WITH CONTACT LENS SENSOR:** The baseline IOP with GAT was obtained by averaging the last 3 readings taken before the start of the measurements with the CLS. We measured the IOP of each subject at the same time of day as that used to obtain the baseline values for the same subject. The doctors who had been trained in CLS measurement (M.J.M., J.E.) placed and

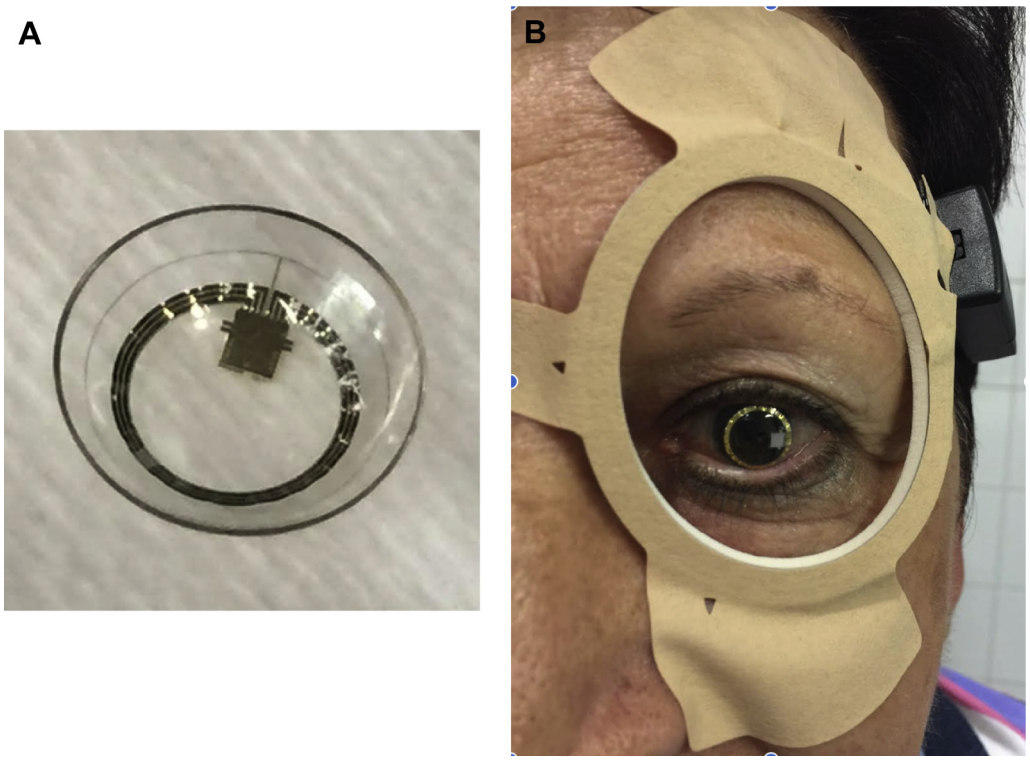

FIGURE 1. Images demonstrating the Sensimed Triggerfish contact lens sensor. (A) The sensor and the telemetry chip are embedded in the oxygen-permeable silicone contact lens. (B) The Sensimed Triggerfish antenna embedded in a soft patch is in place and is connected by wire to the recorder.

removed each subject's CLS at the hospital. If both eyes had received medical or surgical treatment for glaucoma, we measured the eye that had the worst visual field. All monitoring started between 1:00 PM and 3:00 PM.

The 24-hour IOP-related pattern ocular volume change was monitored using a CLS (Sensimed Triggerfish; Sensimed AG, Lausanne, Switzerland). The CLS is a highly oxygen-permeable soft contact lens whose key elements are 2 sensing-resistive strain gauges that are capable of registering circumferential changes in the area of the corneoscleral junction (Figure 1). The device is based on an approach to IOP pattern recording in which changes in corneal curvature and hence ocular volume are assumed to be related to changes in IOP.[13] The measurement unit of the CLS is millivolt equivalent (mV eq); this is unique to the Sensimed Triggerfish. The median values were monitored for 30 seconds, once every 5 minutes, providing 288 points over a 24-hour period. The CLS is available in 3 different sizes, based on the central corneal radius: steep (8.4 mm), medium (8.7 mm), and flat (9 mm). The appropriate size of the lens was determined using keratometry readings. The possible risks associated with the use of the lens were discussed with each patient; these include discomfort, dry eyes, blurred vision, foreign body sensation, itching, swelling, and irritation. A local anesthetic (oxybuprocaine hydrochloride 0.4%) was applied to improve comfort when fitting the lens and then, after its placement, its positioning was checked using a slit lamp. All patients were instructed to return 24 hours later for the removal of the lens and data collection. The subjects were instructed to record at what time they went to bed and woke up. The subjects did not have any restrictions on their posture during the monitoring process. The patients who had received medical treatment used their glaucoma medication at the usual times throughout the measurement period. Following removal of the CLS, the slit-lamp examination was repeated.

• **MEASUREMENT OF INTRAOCULAR PRESSURE FLUCTUATIONS AND CIRCADIAN INTRAOCULAR PRESSURE PATTERNS:** After 24 hours, the CLS was removed and the data were download and analyzed using proprietary software incorporating cosinor-based rhythmometry, a function commonly used to study circadian biological rhythms. The use of modified cosinor rhytmometry for the analysis of 24-hour IOP-related patterns obtained with the CLS[14] simplifies data interpretation by providing several key parameters relating to the circadian IOP rhythm: acrophase and bathyphase (the timing of CLS signal peaks and troughs) and also signal amplitude expressed as an indicator of fluctuations in IOP.[15] The amplitude of the cosine curve is a parameter based on the

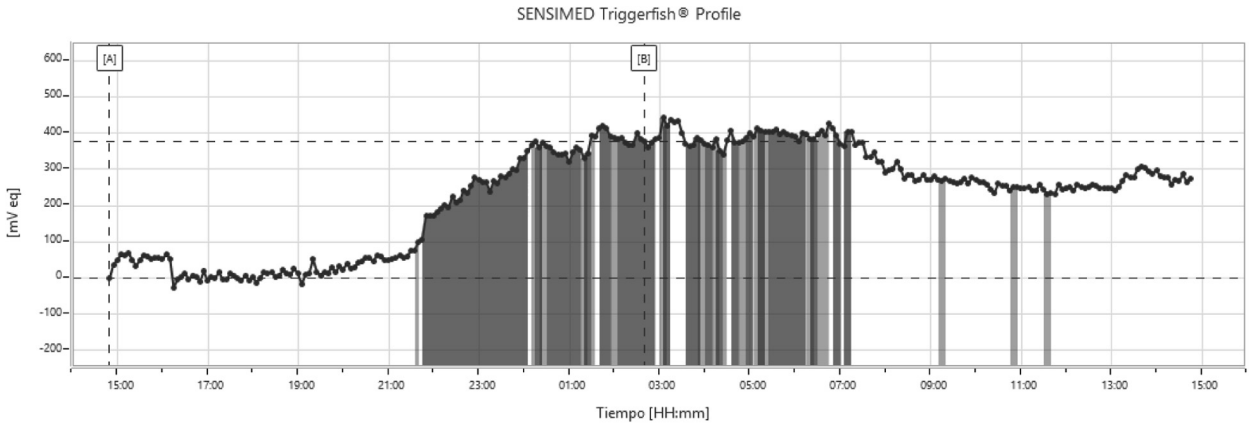

FIGURE 2. Twenty-four-hour intraocular pressure monitoring with contact lens sensor. Example obtained from the monitoring of the intraocular pressure during 24 hours with contact lens sensor. The shaded area represents the sleeping period assessed by analyzing blink patterns.

cosine model fitted to the CLS data. The amplitude is the difference between the maximum and minimum values of the cosine-fit curve divided by 2. This is an overall estimate of the magnitude of signal oscillation during the tested period. The software also automatically identifies the sleeping period by analyzing blink patterns, with blinks (which produce a transient spike in the electrical signal) being less frequent during sleep[16] (Figure 2).

The curves obtained from the monitoring were classified into 3 circadian IOP-related pattern groups depending on the night acrophase pattern (Figure 3): high nocturnal pattern, low nocturnal pattern, and absence of pattern. In the high nocturnal pattern group, the nocturnal acrophase was higher than the diurnal pattern (Figure 3A). In the low nocturnal pattern group, the nocturnal acrophase was only slightly higher than the diurnal pattern, with the maximum value being nocturnal (Figure 3B). In the group without any acrophase the average diurnal amplitude was similar to the average nocturnal amplitude without a nocturnal acrophase and with absence of pattern (Figure 3C).

The doctors who had been trained in CLS measurement (M.J.M., J.E.) independently evaluated the curves of each patient to define the circadian IOP patterns in a masked-side-by-side comparision, confirmed by an independent reader (I.B.).

• **STATISTICAL ANALYSIS:** Quantitative variables were described as mean and standard deviation (SD). Absolute and relative frequencies were used to describe qualitative variables. We performed a bivariate analysis of the baseline variables and CLS measures by treatment (medical or surgical). The *t* test or the Kruskal-Wallis test was used to compare quantitative variables (depending on the distribution of the data) and the χ^2 test for qualitative variables. Additionally, CLS measures were compared using a linear model adjusted by the baseline IOP measure by GAT. The individual IOP-related fluctuations for 24-hours were represented using nonparametric smoothed splines. Furthermore, an average distribution of the IOP fluctuation for 24 hours was calculated for each group and it was compared by Kolmogorov-Smirnov test. A *P* value of $<.05$ was considered statistically significant. All statistical analyses and data processing procedures were performed using R software, version 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

NINETY-ONE EYES OF 77 GLAUCOMA PATIENTS WERE consecutively included in the present study. We were able to successfully measure the 24-hour IOP-related fluctuations in all patients. CLS wearing resulted in good levels of tolerance and no serious complications. Some subjects did, however, experience minor complications: slight hyperemia, peripheral corneal edema, and superficial keratitis. These healed within a few days without the need for any eye drops.

The CLS accurately identified the sleeping periods in all the patients when these were compared to the self-reported diary entries.

The mean (SD) age was 67.2 (10.1) years and 50% of the patients were women. No significant differences were found between the medical and surgical groups for age, sex, study eye, diagnosis, or central corneal thickness. The mean IOP (mm Hg) values were significantly higher in the medical glaucoma group ($P = .02$) and the vertical cup-to-disc values were greatest in the surgical group ($P < .01$). The patient characteristics are detailed in Table 1.

The CLS cosinor analysis revealed a higher amplitude in the medical than in the surgical group. The maximum

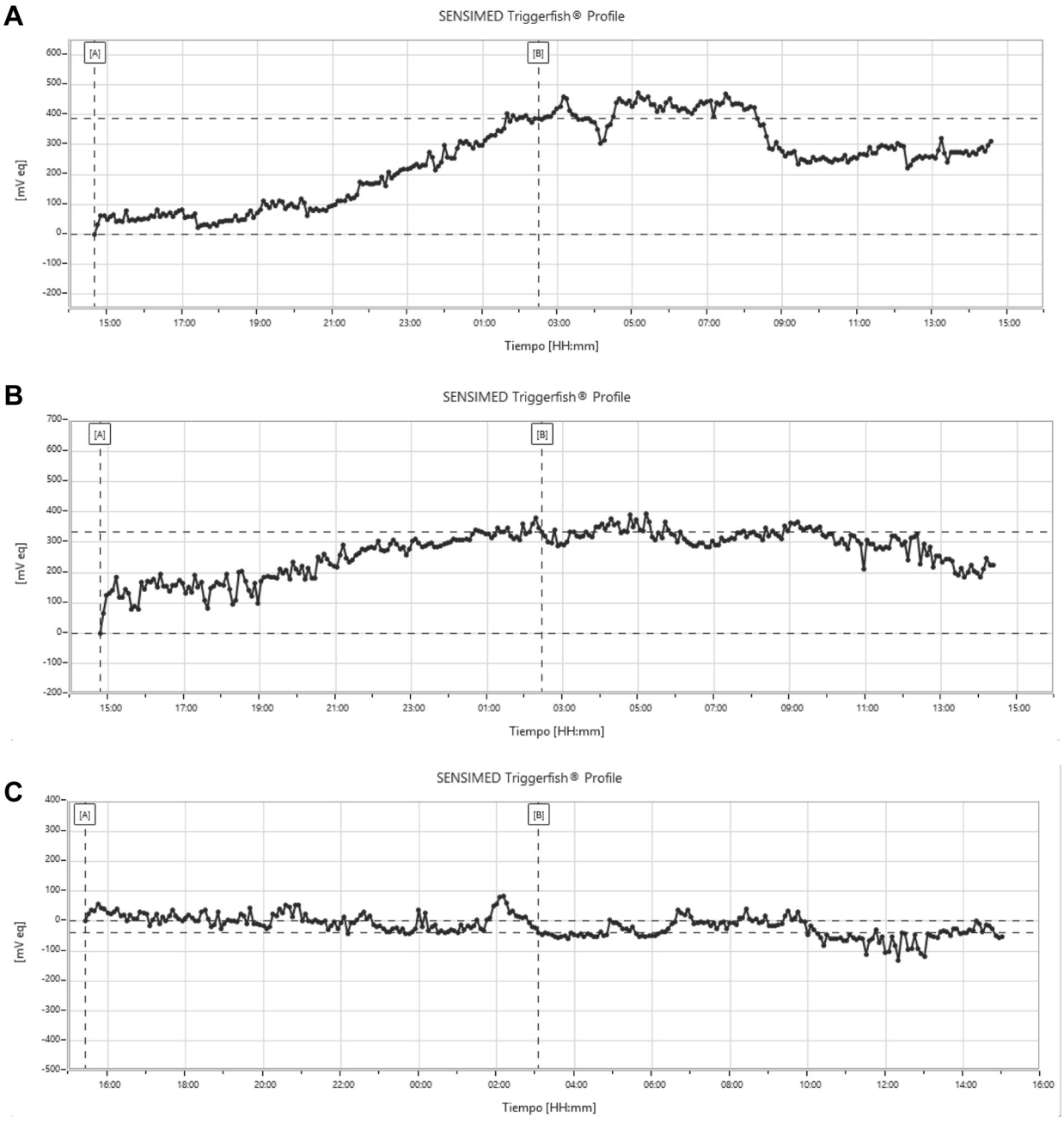

FIGURE 3. Classification of the curves. The curves were classified into 3 circadian intraocular pressure–related pattern groups depending on the night acrophase pattern. (A) High nocturnal pattern. (B) Low nocturnal pattern. (C) Absence of pattern.

(acrophase) and minimum (bathyphase) IOP-related values for the medical group were higher than for the surgical group. These results remained statistically significant after adjusting for baseline IOP (mm Hg). We found that 42.9% of surgically treated glaucoma eyes were associated with an absence of nocturnal acrophase, while only 13.8% of the medically treated eyes ($P = .011$) had absence of nocturnal pattern. In 5 patients, we could not classify the circadian pattern type of the curve obtained. Table 2 shows the measurements with CLS and the night acrophase pattern for all patients. Figure 4 shows the 24-hour IOP-related profiles with CLS in the medically vs surgically treated group. The IOP-related (mV eq) of each patient was smoothed and plotted (Figure 4A). An average distribution of IOP-related (mV eq) was calculated for each treatment group; when compared, statistical differences were found ($P < .001$) (Figure 4B). Figure 4A and B shows higher distribution values in the medical group.

TABLE 1. Characteristics of the Sample

	Medical Group (N = 59)	Surgical Group (N = 32)	*P* Value
Age (y)	66.6 (8.50)	68.3 (12.5)	.499
Sex (female)	32 (54.2%)	13 (40.6%)	.307
Study eye (right eye)	25 (42.4%)	17 (53.1%)	.446
IOP (mm Hg)	18.8 (3.90)	16.5 (3.06)	.002
Diagnosis			.071
Primary open-angle glaucoma	42 (71%)	27 (84.3%)	
Normotensive glaucoma	3 (5.2%)	1 (3.33%)	
Pseudoexfoliative glaucoma	2 (3.3%)	3 (9.37%)	
Pigmentary glaucoma	3 (5.2%)	1 (3.33%)	
Ocular hypertension	9 (15.8%)	0 (0%)	
Vertical cup-to-disc ratio	0.46 (0.23)	0.76 (0.21)	<.001
CCT (μm)	545.7 (42)	533.2 (32.86)	.16
Hypotensive drops (yes)	59 (100%)	11 (34.3%)	<.001

CCT = central corneal thickness; IOP = intraocular pressure.
Data are mean (SD) or n (%).

TABLE 2. Measurement of Intraocular Pressure–Related Fluctuations and Circadian Intraocular Pressure–Related Patterns With Contact Lens Sensor

	Medical Group (N = 59)	Surgical Group (N = 32)	*P* Value
Amplitude, mV eq	131 (69)	100 (41.3)	.011 (.011[a])
Acrophase mV eq	303 ± 176	160 (187)	.001 (<.001[a])
Bathyphase	52.8 ± 128	−39.25 ± 155	.006 (.004[a])
Night acrophase pattern			.011
Absence of pattern	8 (13.8%)	12 (42.9%)	
Low nocturnal pattern	25 (43.1%)	9 (32.1%)	
High nocturnal pattern	25 (43.1%)	7 (25%)	

Data are mean (SD) or n (%).
[a]*P* value adjusted: estimated *P* value using lineal model by intraocular pressure (mm Hg) baseline.

Figure 5 shows the curves with CLS for the same glaucoma patient with medical treatment in the right eye (Figure 5A) and glaucoma surgery in the left eye (Figure 5B). Figure 6 shows the curves with CLS for the same eye of another glaucoma patient before (Figure 6A) and after (Figure 6B) glaucoma surgery. We highlight the effectiveness of the CLS device to detect changes in the circadian IOP patterns and in the amplitude of the IOP-related profile over a 24-hour period.

DISCUSSION

IN THE PRESENT STUDY WE SHOWED THAT THE AMPLITUDE of the IOP-related fluctuations and nocturnal acrophase were significantly greater in the medical than in the surgical group. These results suggest that the IOP fluctuation is greater in patients with medically treated glaucoma than in surgically treated glaucoma patients. This effect could represent an additional benefit of the use of surgery to control IOP for a period of 24 hours. Furthermore, in our study, the maximum and minimum values of the CLS signal were higher in the medical than in the surgical group. To the best of our knowledge, the present study is the first to have compared IOP-related fluctuations over 24 hours and the circadian pattern in medically vs surgically treated glaucoma patients under physiological conditions.

Konstas and associates[17] reported that the patients with well-functioning trabeculectomies had statistically lower mean IOPs, but also lower peaks and ranges of IOP over 24 hours than advanced glaucoma patients on maximum tolerated medical therapy. Musch and associates[18] examined the variations in IOP in medically and surgically treated patients in the Collaborative Initial Glaucoma Treatment Study. Patients who had undergone surgery as their initial glaucoma treatment had a lower SD for intervisit IOP and also a better-preserved visual field than those

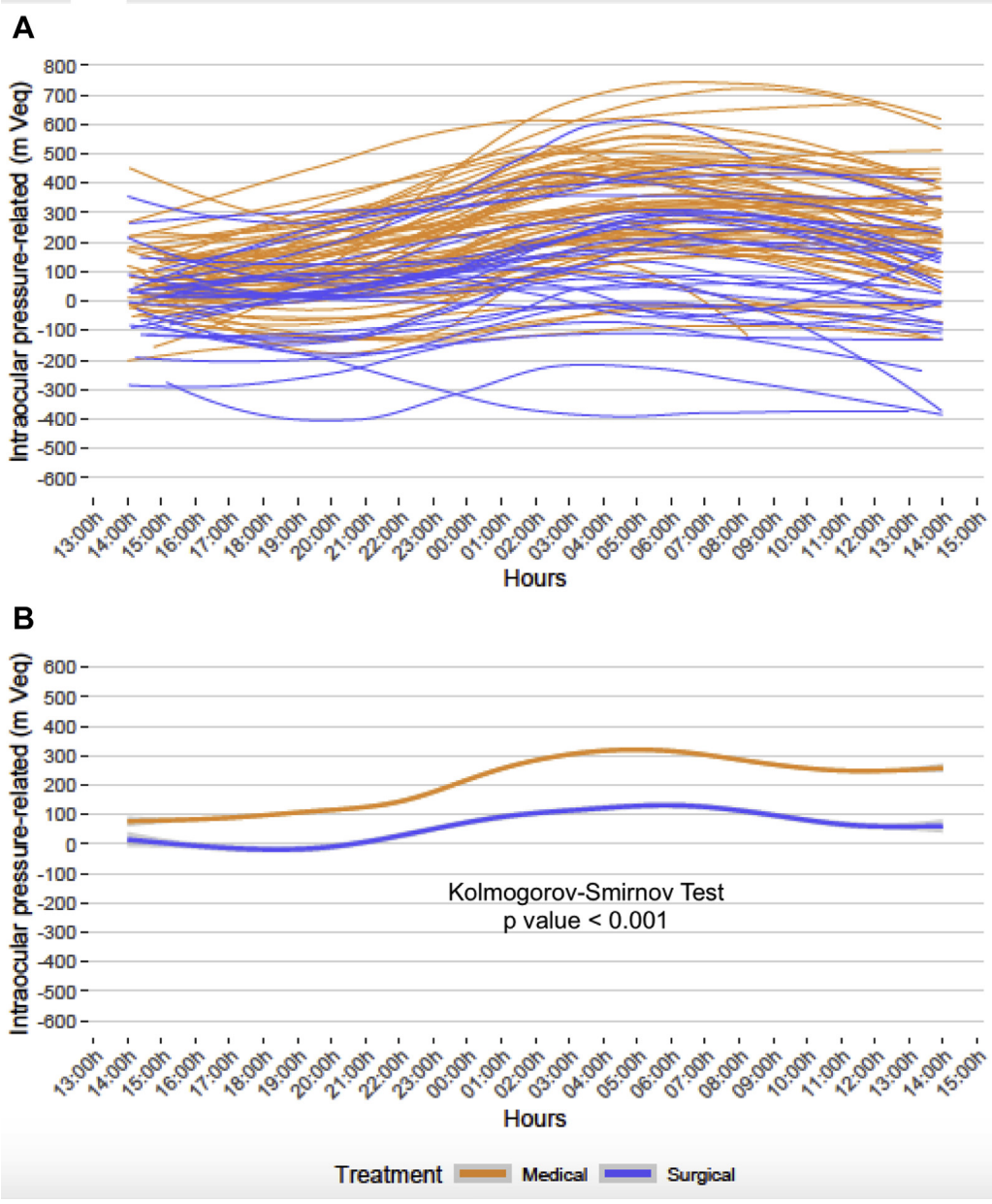

FIGURE 4. The 24-hour intraocular pressure–related profiles in medically vs surgically treated group. The measures of 24-hour continuous intraocular pressure measurement with the contact lens sensor are represented by nonparametric smoothed splines. (A) The curves for each patient. (B) An average curve for each treatment group.

who were treated with medication. A study by Mansouri and associates[8] found that the mean IOP during the diurnal period was significantly lower for the trabeculectomy and deep sclerectomy and collagen implant patients than for latanoprost patients, but that the IOP fluctuations were similar between the groups; this finding contrasted with the results reported by Konstas and associates[17] and Medeiros and associates,[19] who found that the mean, peak, and daytime diurnal IOP curves were greater for the medically treated patients than for the patients who had received a trabeculectomy.

Successful filtration surgery may provide greater 24-hour IOP control and less IOP fluctuation compared with medical therapy, even when the mean IOP is similar.[20] In our study, these differences persisted after adjustment for IOP (mm Hg), indicating that with similar IOP, surgical patients had less fluctuations in IOP for 24 hours than the medical group. Patients with medical treatment showed a more pronounced, and significantly different, nocturnal acrophase compared with patients of the surgical group. A high nocturnal acrophase was found in 43% of the medical group, whereas only 25% of patients with glaucoma

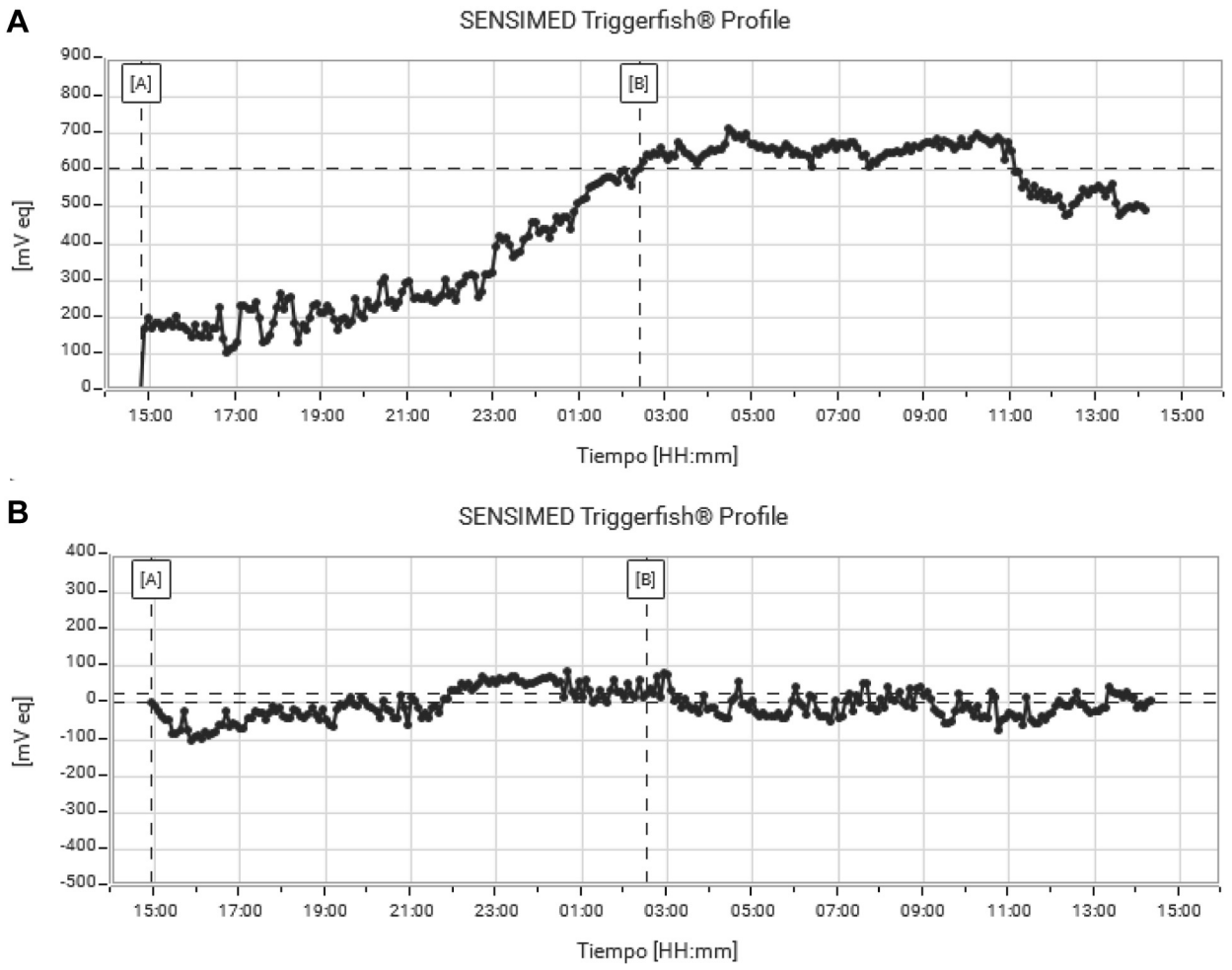

FIGURE 5. Example of the 24-hour intraocular pressure (IOP)–related measurement with contact lens sensor. Images show the curves with the contact lens sensor for the same glaucoma patient with medical treatment in the right eye and glaucoma surgery in the left eye. (A) Sixty-three-year-old woman with open-angle glaucoma and IOP of 20 mm Hg under treatment with a topical beta blocker and prostaglandin analogue in her right eye. We can observe that the patient has a high nocturnal pattern. Amplitude 261.84 mV eq. (B) The same patient after glaucoma surgery (deep nonpenetrating sclerectomy) in her left eye and IOP of 16 mm Hg without hypotensive drops. We can observe the absence of nocturnal pattern. Amplitude 30.91 mV eq.

surgery continued to present a marked nocturnal linear trend. The 42% of patients with glaucoma surgery have absence of nocturnal acrophase vs only 13% in the medical group. We hypothesize that medical therapy tends to reduce without eliminating the nocturnal acrophase. This may probably suggest that patients whose glaucoma is controlled with drops showed IOP behavior more similar to glaucoma patients without treatment than patients with glaucoma surgery. This hypothesis is compatible with the results reported by Holló and associates[21] and Mansouri and associates.[22] Hollo and associates[21] presented results from a case series of 9 glaucoma patients in whom 24-hour IOP-related patterns before and after the introduction of a prostaglandin analogue eye drop were compared using the CLS. They did not find any significant changes in the circadian CLS IOP-related patterns after treatment introduction. However, they did not evaluate the nocturnal IOP slope but rather absolute changes of the CLS signal. Mansouri and associates[22] studied the circadian IOP-related effects of ocular hypotensive medications using a CLS in 23 glaucoma patients. They concluded that prostaglandin analogues, but not other medications, seem to flatten the IOP-related increase at transition of the wake/sitting to the sleep/supine period, but do not seem to have an effect on acrophase and amplitude. This may also account for the high risk of natural progression in patients with medical treatment compared with surgical treatment.[23] The diurnal type of IOP circadian rhythm may be not normal[24]; in our study no patients had the diurnal type of IOP.

The role of IOP fluctuation as a predictor of glaucoma progression beyond that of mean IOP reduction is

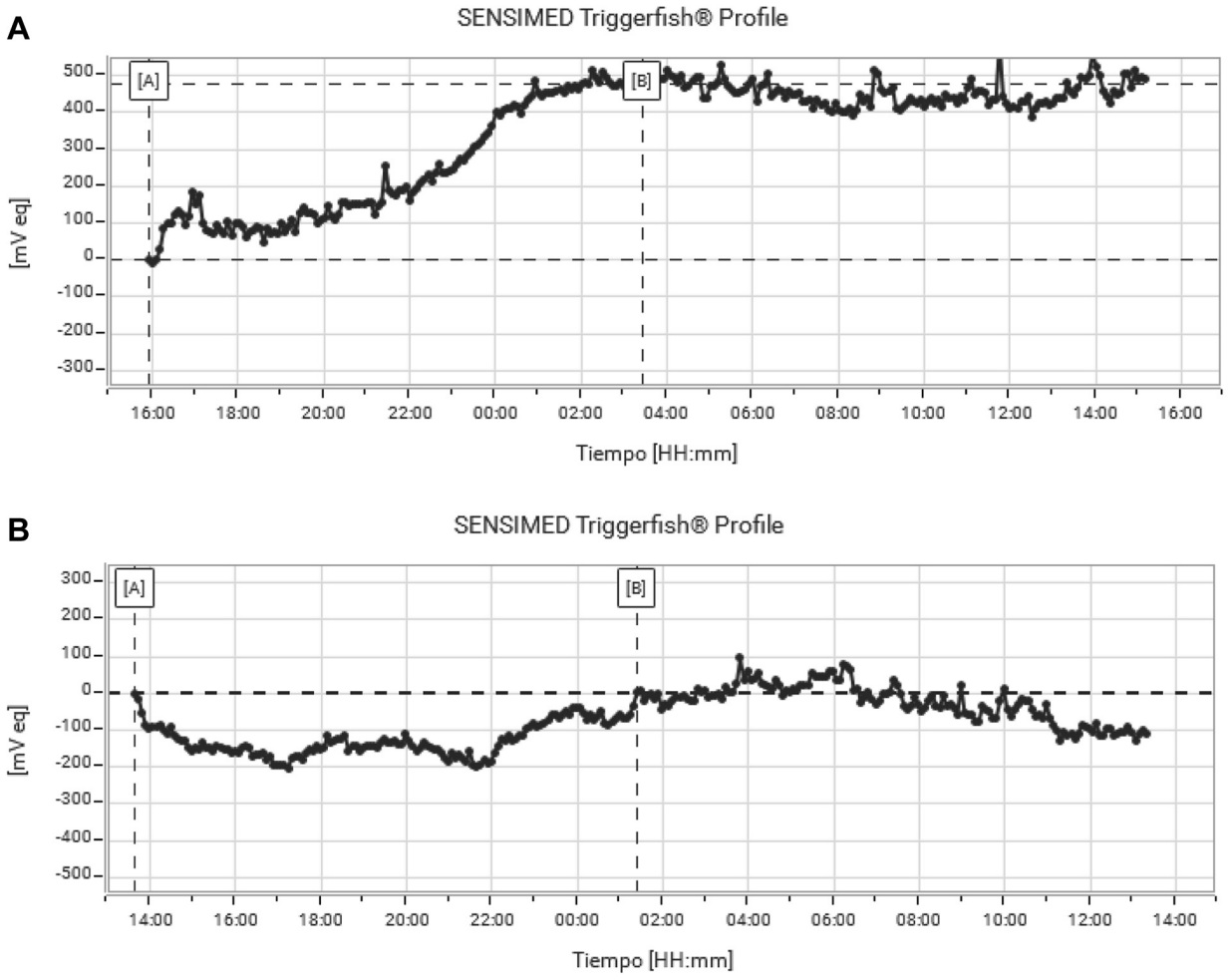

FIGURE 6. Example of the 24-hour intraocular pressure (IOP)-related measurement with contact lens sensor. Images show the curves with the contact lens sensor for the same eye of a glaucoma patient before and after glaucoma surgery. (A) Eighty-one-year-old man with open-angle glaucoma and IOP of 14 mm Hg under treatment with a topic beta blocker, a prostaglandin analogue, and dorzolamide. We can observe that the patient has a high nocturnal pattern. Amplitude 178.66 mV eq. (B) The same eye after glaucoma surgery (ExPress implant) and IOP of 14 mm Hg without hypotensive drops. Amplitude 90.46 mV eq. We can observe a low nocturnal pattern with a decrease in amplitude as an indicator of lower fluctuation of IOP.

controversial, but different studies have shown that glaucoma treatment is needed not only to reduce a temporary IOP, but also to lessen IOP fluctuation.[25–28] It has been difficult to determine the significance of these variations owing to the lack of standardization regarding the time between assessments, the methods of measurement, and the definition of fluctuation itself.[28] De Moraes and associates[29] recently reported that certain characteristics of the 24-hour IOP-related profile, measured using the CLS, may be useful markers of faster rates of disease progression. Their findings suggests the potential application of 24-hour IOP-related recordings with a CLS to correlate with the rates of visual field progression in treated glaucoma patients based on a specific time of treatment. According to the results of De Moraes and associates, the significant differences found in our study in the curves of glaucoma patients with medical or surgical treatment would support the usefulness of 24-hour CLS monitoring of IOP in those patients in whom we have made a change in treatment such as a filtering surgery, with the aim to correlate it with the rates of visual field progression. Prospective studies are now needed to evaluate whether the "flatter" IOP profiles translate into better long-term glaucoma control. Furthermore, future implications of the present study could be the use of the CLS to compare new surgical modalities such as microinvasive glaucoma surgery on 24-hour IOP-related patterns.

In line with previous reports,[13,30] our study confirmed the ability of the Sensimed Triggerfish sensor to describe the circadian IOP-related profile. Even though several studies have clearly shown that the highest IOP values occur at night[7,10] in most cases, clinical management of

glaucoma is based on a single IOP measurement, usually taken during hospital outpatient hours. Using GAT, the IOP during the interval period between the IOP measurement remains unknown. The new methods of measurement of IOP-related fluctuation with a CLS can avoid these burdens and provide clearer assessment of circadian patterns of IOP.[28] The present results suggested a trend toward a higher-amplitude IOP-related profile in patients with medical treatment of glaucoma than in patients with glaucoma surgery. We find that the majority of patients had a nocturnal pattern with a peak IOP-related profile during nocturnal hours, in agreement with previous studies showing that the majority of patients have a peak IOP at night.[7,10] The present study reflects that a single IOP measurement during regular clinic hours fails to reflect the true range of an individual's IOP. These results sustain the hypothesis that the daytime IOP profile may not reflect the nighttime profile and that therapeutic strategies are imprudent when based only on diurnal curves.

In our study, the CLS was found to accurately determine sleep patterns, with a good correlation between sleeping periods identified by the lens and patients' diary entries. The corneal thickness was not different between the medical and surgical group, so we can considerer that corneal thickness did not influence the CLS IOP-related profile between the medical and surgical group.

The CLS seems to be a well-tolerated device that may help determine patterns of IOP fluctuation without recourse to a sleep laboratory or the need to wake the patients or sit them up to obtain measurements.

A limitation of CLS is that it was not possible to convert the recorded units of mV eq to units of mm Hg. The CLS recorded a relative, IOP-related signal (not the absolute IOP). The relationship between the CLS device output and IOP as measured with a tonometer is unknown. Even though there are some limitations of the CLS, it is useful to measure the IOP-related peak value and the fluctuations with monitoring for 24 hours. Investigations using 24-hour IOP-related measurement with the CLS may help develop a test that can be used to decide on glaucoma treatment strategies. But it is also necessary to take into account the possible limitations of CLS in detecting changes on 24-hour IOP-related patterns with the introduction of glaucoma medications.[21,22] A recent study by Martin and associates[31] indicates that the CLS may be a new biomarker for POAG, but further investigations are mandatory to define the ocular parameters affecting CLS measurements.

In conclusion, the IOP-related fluctuation was larger in patients with medically treated glaucoma than in the surgically treated glaucomatous patients. A significant number of surgically treated patients had absence of nocturnal acrophase vs patients with medical glaucoma treatment. This effect could represent an additional benefit of surgery in controlling the IOP for 24 hours in physiological conditions. In this regard, surgical treatment of glaucoma is needed not only to reduce a temporary IOP, but also to lower the peak IOP and IOP fluctuation. Data from 24-hour IOP-related monitoring by a CLS might be one of the useful methods to evaluate the fluctuation of IOP and to evaluate the effect of the different glaucoma treatments on IOP.

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