Clinical Study on the Ocular Manifestations in Patients with Obstructive Sleep Apnea Syndrome—Preliminary Results

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Abstract: Obstructive sleep apnea syndrome is a multisystemic disorder associated with a series of side effects. Obstructive sleep apnea syndrome (OSAS) includes hypoxemia and is correlated with an increased incidence for various neuronal conditions, including glaucoma, strokes, reduced mental ability, depressive disorders, peripheral neuropathy, and non-arteritic ischemic optic neuropathy. This study’s aims are the evaluation of the degree of ocular surface damage in obstructive sleep apnea patients (in the absence of the continuous positive airway pressure treatment) and the structural changes in the optic nerve, and to establish correlation between the degree of damage to the ocular surface (eye dryness by Schirmer test) and corneal biomechanics by ocular response analyzer. The subjects included in the study will be grouped as follows: a group of patients with glaucoma and obstructive sleep apnea syndrome that will be compared to patients with glaucoma only as well as identifying the evolution of structural changes in patients with glaucoma and sleep apnea syndrome. A prospective study included 65 eyes from 65 subjects diagnosed with obstructive sleep apnea (45 eyes of 45 subjects with glaucoma and OSAS as well as 20 subjects, 20 eyes with dry-eye syndrome and OSAS) who did not follow the continuous positive airway pressure treatment. The control group consisted of 45 subjects (45 eyes) with (mild or moderate) primary open-angle treated glaucoma without obstructive sleep apnea. All patients had ophthalmologic evaluations according to a standardized protocol. Moreover, respiratory functional parameters (apnea–hypopnea index—AHI) and the body mass index were recorded. Within the studied group, patients with mild or moderate primary open-angle glaucoma, with moderate or severe dry-eye syndrome, patients with floppy-eyelid syndrome, with optical non-arteritis ischemic neuropathy, and a patient with retinal central vein occlusion were identified. The increased rate of the apnea syndrome during sleep produces a severe disorder of the ocular surface and a retinal neuro-degenerative disorder. The eyes of patients with sleep apnea syndrome (SAS) and glaucoma have lower mean intraocular pressure than eyes with glaucoma without SAS. However, the mean C/D ratio in eyes with glaucoma correlates with the severity of SAS. There is a positive correlation between the severity of the apnea and the ocular disorder’s degree similar to the studies in the literature review. The joint cooperation between the sleep specialists and ophthalmologists can lead to the improvement of the vascular and ocular status for the obstructive sleep apnea patients.

Keywords: obstructive sleep apnea syndrome (OSAS); continuous positive airway pressure (CPAP); schirmer test; ocular response analyzer (ORA)
1. Introduction

Sleep apnea is a common condition in the category of sleep disorders. The complexity and relevance of early diagnosis and treatment is motivated by several complications it can cause. Obstructive sleep apnea is one of the most common chronic respiratory diseases with a prevalence of 3–7% in the adult population, along with other obstructive pulmonary diseases such as asthma (7.7%) and chronic obstructive pulmonary disease (11.7%) [1,2]. As one of the characteristic mechanisms of sleep apnea syndrome, hypoxia is a condition that can progress with cardiovascular, neurological, or ophthalmic complications [1,2]. Sleep apnea syndrome is classified into three types depending on its production mechanism: obstructive, central, mixed. Obstructive sleep apnea syndrome (OSAS) is characterized by the collapse of the upper airways (CAS) that causes full or partial lapse of air flow, followed by a decrease in oxygen saturation of the arterial blood, and disruption of sleep stages by short awakenings. Mixed sleep apnea syndrome is characterized by episodes of central apnea and obstructive sleep apnea within the same episode [2]. In central SAS (SASC) disorders occur in the respiratory centers, so the impulse is transmitted to the respiratory muscles causing insufficient ventilation.

The severity of OSAS can be estimated using the apnea–hypopnea index (AHI), apnea being defined by a total obstruction of the upper airways, while hypopnea by a partial one. Thus, AHI highlights the number of episodes of apnea/hypopnea, being able to establish the lack of pathology (AHI < 5/h) or its presence (AHI ≥ 5/h), the latter being classified as mild (AHI: 5–15/h), moderate (AHI: 15–30/h) and severe (AHI > 30/h) SAS [3]. Investigations for OSAS diagnosis are drowsiness questionnaires, pulmonary function tests, ENT examination, printing cardio-respiratory polysonography or multichannel respiratory polygraphy called sleep study (gold standard in diagnosis), cardiac examination, vigilance tests, sleep latency tests [2,3]. Favoring factors in the onset or progression of SAS have been mentioned in the literature: obesity (the main risk factor), gender, alcohol (depression of the upper respiratory tract muscles selectively and negatively influences the response to awakening at the end of each apnea), physiological (short neck) or pathological structural anatomical defects (adenotonsillar hypertrophy, retrognation and macroglossia, size reduction of the upper respiratory tract that may be caused by obesity, and pathology in which there is an increase in adipose tissue deposition in the soft tissues of the pharynx), snoring determined by the pathways narrowing that occurs years before the onset of the pathology) and cardiovascular risk factors: essential hypertension, insulin resistance, pathological glucose tolerance test, dyslipidemia [4].

Among the most common eye events we mention are floppy-eyelid syndrome, glaucoma, central serous chorioiretinopathy, non-arteritic anterior ischemic optic neuropathy (NAION), central vein occlusion of the retina, diabetic retinopathy, macular disease, keratoconus, papillary conjunctivitis, corneal punctate epitheliopathy, recurrent corneal erosion, keratitis, dry-eye syndrome [3,5]. During episodes of apnea hypoxemia and transient hypotension occur, sometimes oxyhemoglobin desaturation drops below 30%, these being proposed as an etiological mechanism for the advancement of glaucoma and NAION complications after ischemic optic nerve injury [6].

2. Materials and Methods

A prospective, comparative clinical study took place in the Ophthalmology Clinic of St. Spiridon Hospital and Oftaprof Clinic, in Iasi, during October 2018 and December 2019. Patients were evaluated for a period of 6 months after enrollment. The study was approved by the Ethics Commission of University Hospital St. Spiridon Iasi, approval no.49/9.12.2018 in compliance with ethical and deontological rules for medical and research practice. The study was conducted in accordance with the Helsinki Declaration and with several published principles [7].
The patients were divided into two groups based on the following inclusion criteria: patients with sleep apnea syndrome at different stages, with associated glaucoma (primitive open-angle or normal tension glaucoma) and ocular surface disease representing the study group and the control group (patients with glaucoma but without SAS). The exclusion criteria were patients with SAS in whom full evaluations were not performed and patients in whom the diagnosis of SAS was denied, i.e., those who refused further evaluations. The study included 65 subjects (65 eyes) OSA-diagnosed subjects (45 subjects/eyes with glaucoma and SAS as well as 20 subjects, 20 eyes with dry-eye syndrome and SAS) who did not follow the CPAP (continuous positive airway pressure) treatment and a control group made up of 45 subjects (45 eyes) with primary open-angle glaucoma (mild or moderate), treated, without OSA. All patients underwent the following determinations, according to a standardized protocol: the best corrected visual acuity (Snellen optotype), the Schirmer I test (without anesthetics); intraocular pressure (with the Goldmann applanation tonometry), OCT (optical coherence tomography Cirrus HD OCT Zeiss) with the evaluation of the optic nerve, macula, and measurement of the retinal nerve fiber layer, determination of the visual field (Humphrey perimeter—C24-2 program), measurement of the central corneal thickness (Tomey ultrasonic pachymeter) and the corneal hysteresis with ORA (ocular response analyzer, Reichert technology). Moreover, the respiratory functional parameters (apnea–hypopnea index—AHI) and body mass index were recorded. The age of the patients, sex, background data, and associated general conditions (hypertension, obesity, diabetes, etc.) were also recorded.

Statistical analysis. The database was created in the EXCEL program and was statistically processed with the SPSS 18.0 program. The ANOVA (analysis of variance) test, student t test, χ² test, Kruskal-Wallis test, non-parametric test comparing 3 or more groups, the study of the correlation between different phenomena were performed using the “r” (Pearson) correlation coefficient, receiver operating characteristic (ROC) curve—highlighting the specificity/sensitivity balance as a prognostic factor and logistic regression (multivariate analysis) were used as analytical tests.

3. Results

Within the studied group, patients with mild or moderate primary open-angle glaucoma, with moderate or severe dry-eye syndrome, patients with floppy-eyelid syndrome, an optical non-arteritic ischemic neuropathy case, and a patient with retinal central vein occlusion were identified. No case of keratoconus or central serous chorioretinopathy was identified. Of all the patients with SAS (N = 65), 64.6% had mild airflow obstruction, and 7.7% severe mixed syndrome. Severe mixed apnea syndrome was found only in males, and 71.4% of the patients with average obstructive syndrome were male (p = 0.046). The age ranged from 28 to 88 years, registering a significantly lower average level in patients with severe mixed syndrome, compared to the highest average level recorded in patients with mild obstructive syndrome (53.40 vs. 67.52 years; p = 0.036). About 80% of patients with severe mixed apnea syndrome and 85.7% of patients with moderate obstructive syndrome came from urban areas, while 63.6% of patients with severe obstructive syndrome came from rural areas (p = 0.131). Among patients with sleep apnea, 32.3% were experiencing NTG (normal tension glaucoma), 23.1% POAG (primary open-angle glaucoma) and 30.8% dry-eye syndrome (Figure 1). Comparing the percentage distributions of sleep apnea syndrome by types of glaucoma, the following aspects were highlighted:

- 60% of total POAG cases and 61.9% of total NTG cases were associated with mild obstructive sleep apnea;
- 45.5% of patients with severe obstructive SAS were also experiencing NTG;
- 40% of patients with severe mixed syndrome were experiencing NTG while 40% POAG;
Body mass index (BMI) ranged from 27 to 44.26 kg/cm² with no statistically significant correlation to the type and severity of the apnea. The lowest mean level was recorded in patients with mild obstructive syndrome, and the highest in patients with moderate obstructive syndrome (33.05 vs. 34.57 kg/cm²; \( p = 0.875 \)). By types of glaucoma, BMI did not show any significant differences between mean scores. From the total group of glaucoma + SAS, 81.5% were obese (BMI index over 30 kg/cm²) and 60% hypertensive (arterial tension value over 129/70 mmHg).

The lowest mean level of AHI/h (apnea/hypopnea index/hour) was recorded in patients with moderate obstructive syndrome, while the highest was in patients with severe obstructive syndrome (\( p = 0.043 \)) (Figure 2 and Table 1). By types of glaucoma, AHI/ha recorded the highest average level in patients with other types of glaucoma and those with dry eyes (\( p = 0.05 \)).

**Figure 1.** Distribution of patients with SAS by types of glaucoma.

**Figure 2.** Distribution of the AHI/h ratio by types of SAS. Mean AHI/h +/- SD (standard deviation) is higher in patients with severe sleep apnea syndrome as shown in Table 1.

**Table 1.** Distribution of the AHI / h ratio by types of SAS.

| Sleep Apnea Syndrome | N  | Mean   | Std. Deviation | Std. Error | 95% Confidence Interval for Mean | Min  | Max  | FANOVA Test \( p \) |
|----------------------|----|--------|----------------|------------|---------------------------------|------|------|---------------------|
|                      |    |        |                |            | Lower Bound                     |      |      |                     |
| Mild obstructive     | 42 | 46.69  | 22.57          | 3.48       | 39.65                           | 53.72| 6.20 | 89.00               |
| Moderate obstructive | 7  | 30.03  | 30.13          | 11.39      | 2.16                            | 57.90| 14.00| 98.00               |
| Severe obstructive   | 11 | 54.07  | 18.34          | 5.53       | 41.75                           | 66.39| 35.20| 98.00               |
| Severe mixed         | 5  | 55.12  | 9.82           | 4.39       | 42.93                           | 67.31| 43.50| 65.20               |
| Total                | 65 | 46.79  | 22.70          | 2.82       | 41.17                           | 52.42| 6.20 | 98.00               |
The correlation between AHI/h and BMI was indirect (having a value minus, with a small value, r is a small indirect correlation, so when one variable is high, the other is low) and low in intensity, but the result could not be extrapolated to the general population (r = −0.111; p = 0.377), while AHI/h and age were apparently independent parameters (r = −0.072; p = 0.568).

Regarding the structural changes, at the level of RNFL (retinal nerve fiber layer), depending on the sleep apnea syndrome, the average level of disk area of the studied eye was lower in mild obstructive SAS and the highest in severe mixed SAS (1.98 vs. 2.45; p = 0.081). By tracing the ROC curve, it is emphasized that the area of the optical disk is a good predictor in determining the severe types of SAS (AUC = 0.842; IC95: 0.632–1.051; p = 0.012) (Figure 3): cut off score = 2.37; sensitivity = 80% and specificity = 80%.

![Figure 3. ROC Curve. Severe SAS dependent variable. Predictor of optic disk area. DISC RE and DISC LE represent the disc area measured by ocular computer tomography on each eye separately (right eye and left eye).](image)

Depending on the sleep apnea syndrome, the mean level of the central macular thickness of the studied eye was lower in severe OSAS and the highest in mild significant OSAS (249.60 vs. 274.05; p = 0.130), but the differences were not statistically significant. In the applied case study, the ROC curve validates that the macula thickness was not significantly associated with SAS severity (AUC < 0.600).

The multivariate analysis also highlighted the fact that the AHI in conjunction with the area of the optic disk are good predictors of the SAS severity: model 2 shows that approximately 24% of patients with severe SAS had higher scores of the optic disk size area associated with lower AHI scores (Table 2):

\[ y = 0.003 - 0.002 \text{AHI} + 2.819 \text{DISCRE} - 1.842 \text{DISCLE} \]
Table 2. Multivariate analysis of structural changes.

| Model | R      | R Square | Adjusted R Square | Std. Err. of the Estimate | Change Statistics |
|-------|--------|----------|-------------------|---------------------------|-------------------|
|       |        |          |                   |                           | R Square Change   |
| 1     | 0.115a | 0.013    | -0.004            | 1.25                      | 0.013             |
| 2     | 0.490b | 0.241    | 0.199             | 1.117                     | 0.227             |
| 3     | 0.557c | 0.311    | 0.246             | 1.084                     | 0.07              |
| 4     | 0.572d | 0.328    | 0.235             | 1.091                     | 0.017             |
| 5     | 0.589e | 0.347    | 0.227             | 1.097                     | 0.019             |

|       | F Change | df1 | df2 | Sig. F Change |
|-------|----------|-----|-----|---------------|
| 1     | 0.766    | 1   | 57  | 0.385         |
| 2     | 8.23     | 2   | 55  | 0.001         |
| 3     | 2.693    | 2   | 53  | 0.077         |
| 4     | 0.645    | 2   | 51  | 0.529         |
| 5     | 0.724    | 2   | 49  | 0.49          |

* Predictors: (Constant), AHI/h.  
** Predictors: (Constant), AHI/h, DISC RE, DISC LE.  
+ Predictors: (Constant), AHI/h, DISC RE, DISC LE, MACULAcentralLE, MACULAcentralRE.  
& Predictors: (Constant), AHI/h, DISC RE, DISC LE, MACULAcentralLE, MACULAcentralRE, MACULAvolLE, MACULAvolRE.

Depending on the sleep apnea syndrome, the average level of the C/D (cup/disc) ratio of the studied eye was higher in moderate obstructive SAS and the lowest in mild obstructive SAS (0.64 vs. 2.43; p = 0.001). The multivariate analysis did not show a significant change in the C/D ratio due to age and type of apnea (R square = 0.50; p = 0.127). All measurements of disc area and cup/disc ratio were performed automatically by ocular computer tomography. The regression line validates the indirect correlation of the C/D ratio with age and the direct correlation with the severity of SAS: y = 1.17 − 0.001 Age + 0.056 SAS.

Dry eye. Schirmer score was significantly lower in patients with glaucoma and SAS, a statistically significant score (12.64 vs. 14.18; p = 0.004). AHI/ha recorded an average level higher in patients with dry-eye syndrome and SAS (p = 0.05). The patients with dry eyes did not have topical antiglaucoma medication treatment what could influence.

Corneal biomechanics in SAS. Comparing the two groups of Glaucoma + SAS vs. Glaucoma—SAS, the following preliminary statistical results were found in both eyes: The IOP level was significantly lower in the Glaucoma + SAS group (16.58 vs. 18.19; p = 0.05) in the study eye. The PIOcc (Corneal Compensated Intraocular Pressure) level was significantly lower in the Glaucoma + SAS group in the study eye (17.40 vs. 20.48; p = 0.006). The PIOg (Goldmann correlated PIO value) level was significantly lower in Glaucoma + SAS group in both studied eyes (16.30 vs. 18.52; p = 0.014). The CH (Corneal Hysteresis) level was significantly higher in the Glaucoma + SAS group in the left eye (10.49 vs. 9.24; p = 0.004). The average levels of CRF (corneal resistance factor) did not significantly differ depending on the presence or absence of SAS in the study eye (10.13 vs. 10.65; p = 0.249). The mean levels of CCT (central corneal thickness) did not significantly differ depending on the presence or absence of SAS in the study eye (551 vs. 556; p = 0.554). However, the mean levels of the PIO, PIOcc, PIOg, CH, CRF, CCT parameters did not differ in the study eye, either in the groups with glaucoma and SAS, or in the groups of glaucoma without SAS (p > 0.05).

The multivariate analysis did not find any significant predictors among age, BMI, SAS, and AHI for the CH dependent variable. Thus, it was revealed that age and BMI were good predictors of CRF for the studied eyes: model 2 shows that approximately 15% of older patients with a higher level of BMI generate higher scores of CRF (R square = 15.1, p = 0.02) (Table 3).
Table 3. Multivariate analysis of corneal biomechanical parameters.

| Model | R    | R Square | Adjusted R Square | Std. Err. of the Estimate | Change Statistics | F Change | df1 | df2 | Sig. F Change |
|-------|------|----------|-------------------|---------------------------|-------------------|----------|-----|-----|---------------|
| 1     | 0.267 | 0.071    | 0.056             | 2.64734                   | 0.071             | 4.76     | 1   | 62  | 0.033         |
| 2     | 0.389 | 0.151    | 0.123             | 2.55145                   | 0.08              | 5.748    | 1   | 61  | 0.02          |
| 3     | 0.398 | 0.158    | 0.116             | 2.56184                   | 0.007             | 0.506    | 1   | 60  | 0.48          |
| 4     | 0.437 | 0.191    | 0.136             | 2.53294                   | 0.033             | 2.377    | 1   | 59  | 0.128         |

a Predictors: (Constant), age. b Predictors: (Constant), age, BMI. c Predictors: (Constant), age, BMI, SAS. d Predictors: (Constant), age, BMI, SAS, AHI/h.

4. Discussion

SAS is characterized by recurrent episodes of total or partial collapse of the upper airways. It is associated with daytime drowsiness that cannot be explained by other factors, or the patients “experience two or more of the following factors: episodes of suffocation during sleep, recurrent episodes of awakening during sleep, fatigue during the day, impaired ability to focus, restless sleep” [1,2,8]. Known as one of the characteristic mechanisms of SAS, hypoxia can progress with cardiovascular, neurological, ophthalmic complications [9]. Current evidence suggests that the inflammatory processes, oxidative stress, and endothelial dysfunction play a role in the pathogenesis of sleep apnea complications. Most ophthalmic connections with SAS show a vascular potential etiology [6]. Among the ocular manifestations, the most significantly evaluated ones by our study are the damage to the ocular surface (dry-eye syndrome and changes in corneal biomechanics) and lesions in the optic nerve (glaucoma, ischemic optic neuropathy), etc. In SAS, the levels of pro-inflammatory cytokines (TNF-alpha, IL-1, IL-6) are increased based on chronic intermittent hypoxia. As AHI increases, the mechanical stress of tissues, the hypoxia and inflammation of the ocular surface increase, which in turn lead to loss of meibomian and goblet cells function, and a decrease of corneal sensitivity and of tear production as a response to the stimulation of the lacrimal glands. The loss of these cells is clinically reflected as deterioration in the tear film quality [5]. An early complication of SAS is the dry-eye syndrome, especially the one associated with floppy eye syndrome, highlighted by the Schirmer 1 test and the Break-up time test. In 2019, Karaca et al. [9] conducted their first study aiming at evaluating the ocular surface and the morphological changes of meibomius glands by specific tests: the breaking of the tear film (break-up time), Schirmer 1 test and objectively by meibography in patients diagnosed with SAS to highlight the connection between SAS and dry-eye syndrome. The meibography showed significant loss of the meibomius glands, their morphological alterations including shortening of the ducts, dilation, and distortion. As a result, the hypothesis was validated, while in the case of patients with severe SAS a particularity was observed, namely: the association of SAS with a dry-eye syndrome by evaporation. In 2020 Vehof et al. conducted a cohort study where they confirmed the connection between the dry-eye syndrome and other factors, including ocular disease surface. High blood pressure and high BMI were strongly associated with fewer dry-eye symptoms or current smoking, while former smokers had drier eyes [10]. In our study, the Schirmer I test was performed, and according to statistical analysis the results were similar to Karaca’s study, i.e., it was significantly statistical lower in patients with glaucoma and SAS vs. those without SAS, thus demonstrating the effects of sleep apnea on the ocular surface. Karaca et al. [9] claim that the damage to the meibomius gland in the upper eyelids in patients with SAS is much more visible compared to healthy subjects, especially those with severe SAS.

The connection between SAS and glaucoma has been confirmed over time by several studies, which investigated several glaucoma-specific ocular parameters, including increased IOP, thinning of RNFL peripapillary, visual field impairment, glaucomatous changes of the optic nerve [3]. The prevalence of glaucoma in SAS patients has been investigated by numerous studies, the results ranging from 5.9% [3], 12.9%—Muniesa et al.
There are several types of glaucoma, but those associated with SAS are: normal pressure glaucoma and primary open-angle glaucoma [1,8,12]. The connection between SAS and glaucoma has been confirmed over time by several studies, which investigated several glaucoma-specific ocular parameters, including increased IOP, peripapillary RNFL thinning, visual field impairment, glaucomatous changes of the optic nerve [11] SP Hashim et al. stated that patients who do not have glaucoma but have SAS may develop glaucoma if SAS is not well controlled. Thus, strict control of this condition can contribute to a better management of glaucoma and stabilization of visual fields [11–14]. In 2019, Abdullayev et al. [13] conducted a study to evaluate the RNFL and complex in patients with SAS, which confirmed that 40% of retinal ganglion cells axons are already lost before the occurrence of visual field defects. In a study that included more than 800 subjects aged 19–22, of which 150 had different types of SAS vs. healthy subjects assessing the OCT RNFL, Samantha Lee et al. showed a preclinical thinning of RNFL in young subjects, suggesting an increased risk of glaucoma, which may already be present in young adults with OSA. Following this study, they concluded that patients diagnosed with SAS had an increase in RNFL of approximately 4 µm (especially in the infratemporal and supratemporal segments), compared to the control group [14]. The change in the thickness of RNFL was also highlighted by Ekinci et al. and Lin et al. [15,16] in patients who had a severe type of SAS compared to the control group. In their studies, the authors referred to an early thinning in the RNFL the supero lateral sectors being most severely affected in SAS. RNFL thinning is a change found in early glaucoma, which may indicate an increased risk of SAS-associated glaucoma at an early age. [1]. In our study, depending on the sleep apnea syndrome, the average level of disk area in the study eye was lower in mild obstructive SAS and the most increased in severe mixed SAS. The ROC curve highlights that the area of the optical disk is a good predictor in determining severe SAS. Although not statistically significant, the mean level of central macular thickness in the study eye was lower in severe SAS between the groups with and without glaucoma. More suggestive changes are achieved when evaluating the average level of C/D ratio in the study eye, which was higher in moderate obstructive SAS and lower in mild obstructive SAS. The regression line validates the indirect correlation of the C/D ratio with age and the direct correlation with the severity of SAS. Thus, we can say that there is a significant change in the retinal nerve fibers at the level of the optic nerve for the patients with moderate or severe SAS.

The evaluation of biomechanical properties in glaucoma patients is introduced by various studies [17–21]. By comparing 1200 patients with glaucoma vs. 1000 healthy subjects a recent meta-analysis by Gaspar et al. show that corneal properties seem to differ among the patients with glaucoma and healthy subjects. The results also underline the relevance of the biomechanical properties of the cornea in interpreting the intraocular pressure and it should support further studies on the influence of CH and CCT in glaucoma screening and diagnosis [22–26]. Changes in the properties of corneal biomechanics by associating sleep apnea syndrome with glaucoma are a starting point for further studies, as there are few studies in the literature that refer to these changes that may occur in patients with SAS. Hypoxia is associated with significant changes in central corneal thickness (CCT) and endothelial cell density (ECD) [27–31]. The severity of hypoxemia and the increase in AHI values reduce the CCT and endothelial cell density in patients [25,30–32]. In our study, the IOP level was significantly lower in Glaucoma + SAS group in the study eye. Among the biomechanical and corneal parameters, the PIOcc level, the PIOg level was significantly lower in Glaucoma + SAS in the study eye. The level of CH, the average levels of CRF and those of GCC were not significantly different according to the presence or lack of SAS in the study eye. The multivariate analysis reveals that age and BMI are good predictors of CRF in the study eye. Thus, it can be said that SAS worsens glaucoma through an independent pressure mechanism (hypoxia could be a plausible factor). However, our results are preliminary, a longer follow-up period and a more complex database could produce statistically significant results. The only study of Dikkaya et al. [27] which directly
refer to the change in the corneal biomechanics in patients with SAS compares a total of 54 patients with mild or moderate SAS vs. 20 healthy subjects. They concluded that the patients with severe SAS had lower CH and CRF scores compared to mild and moderate as well as controls. Lower scores of the CH and CRF within the severe group were possibly related to changes in the structural properties of the cornea. Further studies on large groups of patients with SAS during various stages may show significantly structural changes and can prevent glaucoma even in the early stages of the disease.

**Limitations.** They are mainly represented by the short follow-up period, the small number of enrolled cases and the lack of data on the BMI and AHI in the control group. The use of data from chronic patients with SAS, with a longer prevalence of the disease compared to another group would bring valuable information about the structural and corneal biomechanical changes of patients with SAS.

5. **Conclusions**

The increased development of the apnea syndrome during sleep produces a severe disorder of the ocular surface, a retinal neuro-degenerative disorder (manifested by the RNFL thickness reduction). There is a positive correlation between the severity of the apnea and the ocular disorder’s level, similar to the studies in the literature review. The eyes of patients with SAS and glaucoma have lower mean intraocular pressure than eyes with glaucoma, without SAS. However, the mean cup/disc ratio in eyes with glaucoma correlates with the severity of SAS. It can be said that SAS worsens glaucoma through an independent pressure mechanism (hypoxia could be a plausible factor). Body mass index is a risk factor associated with the moderate type of obstructive SAS. The joint cooperation between the sleep specialists and ophthalmologists can lead to the improvement of the vascular and ocular status for the obstructive sleep apnea syndrome patients.

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**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

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