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Prognostic Factors Related to Sleep Quality in Patients With Obstructive Sleep Apnea After Positive Airway Pressure Therapy

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Background and Objectives: This study aimed to evaluate the factors that influence deep sleep restoration in patients with obstructive sleep apnea (OSA) following positive airway pressure (PAP) therapy.

Methods: In total, 363 patients diagnosed with OSA who received PAP therapy over at least 3 months were enrolled in the study. Polysomnographic parameters, anatomical characteristics, and subjective sleep-related parameters were evaluated according to the presence of daytime sleepiness and morning headache before and after 3 months of PAP treatment.

Results: Age was significantly different according to whether excessive daytime sleepiness (EDS) was alleviated (average: 49.35 years) or persisted (average: 52.82 years) (p=0.001). Age was also significantly associated with morning headache (p=0.037). Body mass index (BMI) was higher in the alleviated EDS group (28.70 kg/m^2) than in the persistent EDS group (27.13 kg/m^2; p=0.002). The apnea-hypopnea index (AHI) was correlated with the EDS outcome (p=0.011). The group with alleviated EDS had a longer mandibular plane to hyoid distance (MPH) than the group with persistent EDS (17.95 mm vs. 15.38 mm; p<0.001). However, BMI, AHI, and MPH showed no significant associations with morning headache. Epworth Sleepiness Scale scores were higher in the alleviated EDS and alleviated morning headache groups (EDS: p<0.001, morning headache: p=0.001). Self-Efficacy Measure for Sleep Apnea (SEMSA) values differed significantly between the EDS groups (p<0.001), but not between the morning headache groups (p=0.122). After 3 months of PAP therapy, the MPH was negatively correlated with EDS in univariate (odds ratio [OR]=0.921, p<0.001) and multivariate analyses (OR=0.937, p=0.028). The SEMSA score was also negatively correlated with EDS in univariate (OR=0.961, p<0.001) and multivariate (OR=0.973, p=0.019) analyses.

Conclusion: Age, polysomnographic metrics, and anatomical considerations were important for sleep quality-associated daytime symptoms. In addition, anatomical characteristics and the patient's self-efficacy were significantly associated with the effect of PAP treatment on sleep quality.

Keywords: Sleep apnea; Obstructive; Continuous positive airway pressure; Sleep quality.

INTRODUCTION

Obstructive sleep apnea (OSA) is a prevalent sleep disorder characterized by recurrent interruptions in breathing during sleep, leading to disrupted sleep patterns and decreased oxygen levels [1]. One of the significant challenges in managing OSA is addressing its impact on the quality of sleep, specifically the attainment of deep sleep stages [2]. Deep sleep, also known as N3 or slow-wave sleep, is crucial for restorative functions, memory consolidation, and overall well-being [3]. However, patients with OSA often experience disturbances in achieving and maintaining deep sleep, which can contribute to daytime fatigue, morning headache, and cognitive impairments [4,5].

Positive airway pressure (PAP) therapy has emerged as a highly effective treatment for OSA. It involves the use of devices such as continuous positive airway pressure (CPAP) machines to keep the airways open during sleep, thus reducing the frequency of apneic and hypopneic episodes. While PAP therapy is known to alleviate the symptoms of OSA, there remains a significant variability in its impact on deep sleep among patients with OSA. Some patients may still ex-

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perience poor sleep quality with PAP therapy and complain about symptoms such as excessive daytime sleepiness (EDS) and morning headache [4,6]. Therefore, understanding the prognostic factors related to deep and good sleep quality in patients with OSA after PAP therapy is essential for optimizing treatment strategies and improving patient outcomes.

This study aimed to assess the various factors that influence the restoration of deep sleep in patients with OSA following PAP therapy. We divided patients into groups based on changes in EDS and morning headache symptoms, which are factors related to deep sleep before and after treatment. By identifying these prognostic factors, we can tailor treatment approaches, enhance sleep quality, and ultimately improve the overall health and well-being of individuals battling this sleep disorder. In this paper, we explore the current state of knowledge in this area, highlight potential variables affecting deep sleep in patients with OSA, and discuss the implications for clinical practice and future research. This study aimed to be another step towards confirming the implications for clinical practice.

METHODS

Subject recruitment

In this retrospective study, we reviewed the medical records of 433 adult patients (age >18 years) diagnosed with OSA who received PAP therapy between January 2017 and March 2020. After review of the medical records, 70 patients were excluded who did not use a CPAP device consistently for a minimum of 3 months. Finally, 363 patients were enrolled in the present study. All subjects in this study underwent endoscopic and computed tomographic examinations of the upper airway, as well as full-night polysomnography (PSG), to evaluate and diagnose OSA. In addition, participants completed subjective symptom questionnaires, including the Epworth Sleepiness Scale (ESS), to assess daytime sleepiness at the initial evaluation and the 3-month follow-up after commencing PAP therapy. Patients with neurological disorders or those regularly using analgesics were excluded during the initial data collection phase.

In clinical practice at our institution, patients diagnosed with OSA based on PSG findings receive PAP therapy as determined by physicians. PAP titration was conducted manually by well-trained sleep technicians at the sleep study center of our tertiary hospital and reviewed by certified sleep physicians. PAP therapy was scheduled according to a prescribed protocol [5]. A physician prescribed the auto CPAP device (DreamStation Auto CPAP, Philips Respironics, Murrysville, PA, USA) based on the optimal pressure range (optimal pressure ± 2 cm H_2O). Patients visited our outpatient clinic at 2 weeks, 5 weeks, and 3 months after PAP initiation. The CPAP device was adjusted as necessary for optimal treatment. Compliance with PAP therapy was assessed at the 3-month mark after PAP therapy initiation, with good compliance defined as using a CPAP device for ≥4 hours daily and on ≥70% of nights. This study received approval from the Institutional Ethics Committee of Korea University Ansan Hospital. Informed consent was waived due to the study's nature in accordance with the Institutional Review Board approval (2020AS0258). All research adhered to the principles outlined in the Declaration of Helsinki.

Polysomnography

Full-night PSG was conducted using an Alice 6 device (Respironics, Murrysville, PA, USA) at our tertiary hospital, utilizing the standard neurophysiological and respiratory signals recommended by the American Academy of Sleep Medicine (AASM). This included electroencephalography, electromyography, electrooculography, and electrocardiography. Oronasal airflow was detected using a thermistor to identify apnea and a pressure transducer to detect hypopnea. Chest and abdominal wall movements were recorded through plethysmography, and oxygen saturation was monitored using pulse oximetry. Polysomnographic data were meticulously scored by a highly trained sleep technician and reviewed by certified clinical physicians in accordance with AASM criteria. Apnea was defined as a >90% reduction in airflow, and hypopnea as a ≥30% reduction in airflow accompanied by a ≥4% decrease in SpO_2 or arousal lasting at least 10 seconds [7].

Assessment of data collection and scoring

We gathered a comprehensive set of data, encompassing demographic information, clinical and medical histories, medication specifics, and PSG results. These PSG results included key metrics such as the apnea-hypopnea index (AHI) with a 3% oxygen desaturation threshold (AHI 3%) and the arousal index (ArI) during both the diagnostic and therapeutic phases of PSG. We also examined factors such as respiratory effort-related arousals (RERAs), snoring prevalence, oxygen saturation levels, oxygen desaturation index (ODI), supine and lateral sleeping times, sleep efficiency, as well as sleep stages 1 to 3 and REM sleep, based on initial and titration PSG data.

Furthermore, all participants underwent a comprehensive physical examination, to evaluate Mallampati score and tonsil grade. Radiologic assessment and acoustic rhinometry were also performed to determine upper airway anatomy. Mandibular plane to hyoid (MPH) distance, posterior airway space, and palatal length were evaluated in cephalometric analysis. Bilateral nasal cavity volumes and minimal cross-sectional areas were evaluated in acoustic rhinometry. To evaluate sleep quality, the participants completed subjective questionnaires

that gauged the severity of EDS and morning headache over the preceding 3 months. This assessment employed a 7-point Likert scale (ranging from 0 to 6 points) both prior to and 3 months following the initiation of PAP therapy. Participants who had scores of 0 or 1 on the scale were categorized as not experiencing EDS or morning headache. In addition, we assessed pretreatment ESS scores, mouth breathing, and Self-Efficacy Measure for Sleep Apnea (SEMSA) scores [8].

Statistical analysis

Statistical analysis was conducted using SPSS version 21 (IBM Corp., Armonk, NY, USA). Comparisons of patient demographics and the associations between EDS, the presence of morning headache, and various PSG parameters were assessed using independent t-test or the Mann–Whitney U test, depending on data distribution. The data summaries are presented as mean±standard deviation for normally distributed data. The chi-square test or Fisher exact test was used to compare the prevalence of EDS and morning headache before PAP therapy and after 3 months of therapy. To identify predictors, we employed a stepwise linear regression model, adjusting for variables that were independently associated with persistent sleep apnea and exhibited a p-value <0.05 in the univariate analysis. Subsequent multivariate analysis was conducted on significant variables. All tests were two-sided, and a significance level of $p<0.05$ was considered statistically significant.

RESULTS

Subject demographics

In the comprehensive database, 363 patients undergoing PAP treatment for OSA were documented at the 3-month follow-up consultation. Although the preliminary cohort consisted of 582 participants, certain individuals were excluded for absence of follow-up data or lack of pertinent data in the online PAP prescription system (e.g., treatment refusal, engagement with alternative sleep centers). Of the included patients, 325 were male with an average age of 50.67±10.69 years and a body mass index (BMI) of 27.97±4.25 kg/m^2. Notably, prior to initiating PAP therapy, 87.6% (n=318) of the participants exhibited symptoms of EDS, while 55.9% (n=203) reported experiencing morning headache.

After grouping the data based on EDS and morning headache, age differences between those with alleviated EDS (average: 49.35 years) and those with persistent EDS (average: 52.82 years) were significant (p=0.001). Significant variations were also present for morning headache (p=0.037). BMI was significantly higher (p=0.002) in the group with alleviated EDS (28.70 kg/m^2) than in the group with persistent EDS (27.13 kg/m^2). However, no significant BMI differences (p=0.176) were found in the morning headache groups. The AHI showed notable variations between the EDS groups (p=0.011) but remained consistent for the morning headache groups (p=0.149). The RERA values were significantly lower in the group with alleviated EDS than in the group with persistent EDS (p=0.001) but were consistent for the morning headache groups (p=0.984). The lowest saturation during sleep (LSAT) levels differed significantly between EDS groups (p=0.002) but not between morning headache groups (p=0.623). The group with alleviated EDS had a higher MPH (17.95 mm vs. 15.38 mm, p<0.001), but this was not observed in the morning headache groups (p=0.056). ESS scores were higher in the groups with alleviated EDS and decreased morning headache (EDS, p<0.001; morning headache, p=0.001). The group with alleviated EDS had significantly higher ESS scores than those with persistent EDS (p<0.001); this was similar for morning headache groups (p=0.001). Finally, SEMSA values differed significantly between the EDS groups (p<0.001), but not between the morning headache groups (p=0.122) (Table 1).

Predictors of deep sleep in patients with OSA after 3 months of PAP treatment

In the univariate analysis, age showed a pronounced association with EDS (odds ratio [OR]=1.032, p=0.005); however, it was not significant in the multivariable analysis for EDS or any other results. Interestingly, for every unit increase in BMI, there appeared to be a reduced likelihood of EDS (OR=0.913, p=0.002) in the univariate evaluation but not in the multivariable context. Both AHI and apnea index (AI) scores showed an inverse relationship with EDS, signifying that as they increased, the EDS odds decreased. Notably, the AI was strongly correlated with EDS in the univariate context (OR=0.983, p=0.001). In addition, each unit increment in the RERA related to higher odds of EDS (OR=1.037, p=0.009) in univariate analysis but not in multivariable analysis.

Furthermore, the LSAT showed a positive link with EDS in the univariate analysis (OR=1.029, p=0.009), while the ODI (OR=0.987, p=0.007) and supine AHI (OR=0.989, p=0.014) both showed an inverse association with EDS. The MPH values (OR=0.921, p<0.001) also exhibited a marked negative correlation with EDS in the univariate analysis, with MPH values maintaining significance in the multivariable analysis. It is noteworthy that the ESS scores in univariate analysis had a robust negative relationship with EDS (OR=0.836, p<0.001) (Table 2).

DISCUSSION

The present study offered significant insights into the relationship between OSA and the achievement of deep sleep,

Table 1. Demographic data and characteristics of study subjects according to the severity and prevalence of EDS and MH after positive airway pressure therapy

Variable	EDS total (n=318)	EDS (+) (n=196)	EDS (−) (n=122)	p	MH total (n=203)	MH (+) (n=113)	MH (−) (n=90)	p
Age (yr)	50.68±10.70	49.35±10.17	52.82±11.21	0.001	49.90±10.86	48.73±10.58	51.37±11.08	0.037
BMI (kg/m^2)	28.10±4.35	28.70±4.50	27.13±3.93	0.002	28.15±4.40	28.48±4.53	27.74±4.23	0.176
AHI	42.67±25.34	45.41±25.71	38.27±24.19	0.011	41.45±24.23	43.75±25.15	38.56±22.85	0.149
AI	30.20±23.81	33.66±25.11	24.63±20.45	0.003	28.50±22.59	30.34±23.72	26.20±20.98	0.324
HI	12.49±12.12	11.75±11.40	13.69±13.15	0.056	12.95±12.06	13.42±11.29	12.36±13.00	0.114
RERA	9.40±8.64	8.38±8.10	11.04±9.25	0.001	10.15±8.54	10.33±8.94	9.92±8.05	0.984
LSAT (%)	71.78±11.75	70.40±11.38	74.00±12.03	0.002	71.61±12.20	71.69±10.99	71.51±13.63	0.623
ArI	51.86±20.02	53.74±20.10	48.85±19.61	0.012	51.68±18.46	53.61±18.91	49.26±17.69	0.095
ODI	39.50±25.34	42.58±25.80	34.56±23.86	0.005	38.40±24.13	40.75±25.18	35.43±22.55	0.140
Supine position AHI	54.86±26.68	57.78±27.06	50.16±25.46	0.005	53.59±26.13	55.75±26.85	50.88±25.09	0.206
MP score (0−4)	3.03±0.64	3.00±0.67	3.09±0.59	0.267	3.04±0.60	3.00±0.60	3.09±0.59	0.291
Tonsil grade (0−4)	1.26±0.61	1.28±0.62	1.23±0.59	0.568	1.24±0.59	1.25±0.61	1.22±0.58	0.776
Vol-R (cm^3)	7.17±2.70	7.15±2.85	7.22±2.46	0.386	7.25±2.48	7.43±2.69	7.02±2.19	0.506
Vol-L (cm^3)	7.14±2.86	7.28±3.07	6.90±2.47	0.525	7.23±2.82	7.37±2.87	7.06±2.77	0.337
MCA-R (cm^2)	0.57±0.21	0.57±0.21	0.57±0.20	0.772	0.58±0.20	0.59±0.19	0.57±0.21	0.490
MCA-L (cm^2)	0.54±0.22	0.55±0.23	0.53±0.21	0.588	0.54±0.21	0.55±0.21	0.53±0.21	0.476
MPH (mm)	16.97±5.76	17.95±5.69	15.38±5.54	<0.001	17.06±5.47	17.59±5.29	16.39±5.66	0.056
PAS (mm)	10.35±3.17	10.34±3.26	10.37±3.01	0.753	10.33±3.15	9.97±3.00	10.77±3.30	0.066
PAL (mm)	30.50±4.68	30.61±4.98	30.32±4.15	0.574	30.72±4.57	30.32±4.80	31.23±4.23	0.161
Optimal pressure (cm H_2O)	9.49±2.53	9.62±2.57	9.29±2.46	0.314	9.40±2.57	9.58±2.61	9.18±2.51	0.167
Sleep stage 1	38.23±16.33	39.69±17.01	35.89±14.95	0.054	38.12±16.21	39.31±16.06	36.62±16.36	0.154
Sleep stage 2	46.18±14.12	44.87±14.47	48.29±13.33	0.042	46.46±13.61	46.00±12.90	47.04±14.51	0.312
Sleep stage 3	0.47±1.83	0.47±1.96	0.45±1.60	0.735	0.55±1.96	0.60±2.19	0.48±1.63	0.767
Sleep stage REM	15.49±5.59	15.57±5.82	15.37±5.20	0.755	15.36±5.91	14.98±5.95	15.85±5.85	0.294
ESS score (0−24)	10.26±4.96	11.65±5.09	8.03±3.82	<0.001	10.65±5.30	11.70±5.45	9.32±4.82	0.001
EDS	3.87±1.41	4.49±1.21	2.87±1.10	<0.001	3.97±1.60	4.30±1.48	3.54±1.66	0.001
MH	2.17±1.66	2.41±1.75	1.79±1.44	0.003	3.18±1.30	3.81±1.24	2.38±0.84	<0.001
Mouth breathing	4.01±1.68	4.26±1.56	3.61±1.79	0.002	4.18±1.59	4.46±1.58	3.83±1.55	0.002
SEMSA	80.68±14.32	83.63±13.51	75.95±14.37	<0.001	83.14±12.90	84.32±13.00	81.67±12.69	0.122

Data are presented as mean±standard deviation. EDS, excessive daytime sleepiness; MH, morning headache; BMI, body mass index; AHI, apnea-hypopnea index; AI, apnea index; HI, hypopnea index; RERA, respiratory effort-related arousals; LSAT, lowest saturation during sleep; ArI, arousal index; ODI, oxygen desaturation index; MP, Mallampati; Vol, volume of nasal cavity (right and left); MCA, minimal cross-sectional area (right and left); MPH, mandibular plane to hyoid distance; PAS, posterior airway space; PAL, palatal length; REM, rapid eye movement sleep; ESS, Epworth Sleepiness Scale; SEMSA, Self-Efficacy Measure for Sleep Apnea

Table 2. Predictors for deep sleep in OSA patients after 3 months of PAP treatment

Factor	EDS								MH							
	Univariable logistic regression				Multivariable logistic regression				Univariable logistic regression				Multivariable logistic regression			
	Estimate	SE	OR	p	Estimate	SE	OR	p	Estimate	SE	OR	p	Estimate	SE	OR	p
Age (yr)	0.032	0.011	1.032	0.005	0.021	0.015	1.021	0.169	0.023	0.013	1.023	0.088				
BMI	-0.091	0.030	0.913	0.002	-0.053	0.047	0.948	0.252	-0.039	0.033	0.962	0.236				
AHI	-0.011	0.005	0.989	0.015					-0.009	0.006	0.991	0.130				
AI	-0.017	0.005	0.983	0.001	-0.019	0.015	0.982	0.200	-0.008	0.006	0.992	0.195				
HI	0.013	0.009	1.013	0.169					-0.007	0.012	0.993	0.536				
RERA	0.036	0.014	1.037	0.009	0.034	0.029	1.034	0.244	-0.006	0.017	0.994	0.729				
LSAT	0.028	0.011	1.029	0.009	-0.011	0.016	0.989	0.508	-0.001	0.012	0.999	0.917				
ArI	-0.013	0.006	0.988	0.035	0.017	0.023	1.018	0.452	-0.013	0.008	0.987	0.096				
ODI	-0.013	0.005	0.987	0.007	-0.004	0.020	0.996	0.846	-0.009	0.006	0.991	0.120				
Supine position AHI	-0.011	0.004	0.989	0.014	0.041	0.026	1.042	0.120	-0.007	0.006	0.993	0.187				
MP	0.223	0.184	1.250	0.224					0.255	0.242	1.290	0.292				
Tonsil	-0.126	0.192	0.881	0.511					-0.074	0.240	0.929	0.759				
Vol-R	0.000	0.043	1.010	0.820					-0.067	0.058	0.935	0.247				
Vol-L	-0.048	0.042	0.953	0.251					-0.041	0.051	0.960	0.426				
MCA-R	-0.163	0.560	0.850	0.771					-0.495	0.714	0.610	0.488				
MCA-L	-0.387	0.531	0.679	0.466					-0.485	0.678	0.615	0.474				
MPH	-0.082	0.022	0.921	<0.001	-0.065	0.030	0.937	0.028	-0.041	0.027	0.960	0.120				
PAS	0.003	0.037	1.003	0.930					0.081	0.046	1.084	0.078				
PAL	-0.013	0.025	0.987	0.589					0.044	0.031	1.045	0.161				
Optimal pressure	-0.052	0.047	0.949	0.260					-0.063	0.056	0.939	0.264				
Sleep stage 1	-0.015	0.007	0.985	0.045					-0.011	0.009	0.990	0.241				
Sleep stage 2	0.018	0.008	1.018	0.037	-0.003	0.019	0.997	0.885	0.006	0.010	1.006	0.585				
Sleep stage 3	-0.006	0.064	0.994	0.921					-0.034	0.075	0.967	0.650				
Sleep stage REM	-0.007	0.021	0.994	0.754					0.025	0.024	1.026	0.293				
ESS	-0.179	0.030	0.836	<0.001	0.026	0.043	1.027	0.543	-0.090	0.029	0.914	0.002	-0.011	0.045	0.989	0.806
EDS	-1.116	0.130	0.328	<0.001	-1.218	0.179	0.296	<0.001	-0.307	0.093	0.736	0.001	0.016	0.144	1.016	0.910
MHA	-0.239	0.075	0.788	0.001	0.102	0.109	1.108	0.345	-1.316	0.197	0.268	<0.001	-1.291	0.205	0.275	<0.001
Mouth breathing	-0.232	0.070	0.793	0.001	0.097	0.099	1.102	0.328	-0.253	0.092	0.776	0.006	-0.073	0.114	0.930	0.526
SEMSA	-0.040	0.009	0.961	<0.001	-0.028	0.018	0.973	0.019	-0.016	0.011	0.984	0.147				

OSA, obstructive sleep apnea; PAP, positive airway pressure; SE, standard error; OR, odds ratio; BMI, body mass index; AHI, apnea-hypopnea index; AI, apnea index; HI, hypopnea index; RERA, respiratory effort-related arousals; LSAT, lowest saturation during sleep; ArI, arousal index; ODI, oxygen desaturation index; MP, Mallampati; Vol, volume of nasal cavity; MCA, minimal cross-sectional area; MPH, mandibular plane to hyoid; PAS, posterior airway space; PAL, palatal length; REM, rapid eye movement sleep; ESS, Epworth Sleepiness Scale; EDS, excessive daytime sleepiness; MHA, morning headache; SEMSA, Self-Efficacy Measure for Sleep Apnea

particularly in patients using PAP therapy. It has already been established that OSA disrupts sleep cycles, predominantly the deep sleep stage, with cascading effects on daytime functioning [9]. Our research advances understanding of PAP therapy efficacy in improving deep sleep in patients with OSA and highlights potential factors that may influence treatment outcomes. Although PAP therapy has revolutionized the treatment regimen for OSA, ensuring improved quality of sleep remains a significant challenge, as reflected in the persistent symptoms of EDS and morning headache [4,6]. The nuances of the relationship between these symptoms and their prognostic relevance in determining the effectiveness of PAP therapy formed the backbone of this investigation.

Age appears to play a pivotal role, with significant differences noted between those with alleviated EDS and those with persistent EDS. The age gap became more pronounced when considering the prevalence of morning headache, indicating a potential vulnerability to diminished sleep quality among older individuals following PAP therapy. Further inquiries are needed into whether age-specific neural and physiological processes influence sleep quality. Such phenomena could potentially be linked to age-related alterations in sleep architecture, including changes in anatomical features such as decreased muscle function.

Anatomical parameters like the MPH turned out to be significant predictors of EDS and should be considered in OSA management. An intriguing observation was the correlation between ESS scores and both EDS and morning headache [10,11]. The prominence of this relationship points towards the possible value of ESS as a multifaceted tool, not just for assessing daytime sleepiness but also as a proxy for overall sleep quality.

Interestingly, metrics like the RERA and LSAT showed potential as indicators, given their significant variations between the EDS groups, but this pattern did not extrapolate to the morning headache groups. While certain indices like the AHI and AI demonstrated an inverse relationship with EDS, their correlation with morning headache remained consistent. This implied that while these indices can be reliable indicators of daytime sleepiness, they might not be as sensitive when gauging the quality of deep sleep.

While several studies have reported associations between morning headache and sleep apnea-related parameters [12,13], our data presents an intricate relationship between EDS and morning headache. It is intriguing to note that while a significant percentage of patients experienced alleviation in EDS after PAP therapy, a significant proportion still reported persistent morning headache. This bifurcation is crucial as it suggests that while PAP therapy might be addressing the mechanical challenges of sleep apnea, the holistic restoration of quality sleep might still be elusive for many. In a previous large population-based study by Kristiansen et al. [14], it was noted that the average and lowest oxygen saturation levels during sleep did not significantly differ based on the presence of morning headache. Similarly, Sand et al. [15] reported no relationship between headache and oxygen desaturation. Moreover, Lovati et al. [16] reported better respiratory parameters (higher mean oxygen saturation and lower time with oxygen saturation below 90%) among headache sufferers than those without headache. These observations suggest that hypoxia and respiratory events alone may not be sufficient factors to explain the mechanism of morning headache.

Within the broader group with alleviated EDS and morning headache, we have identified several statistically significant factors believed to hold medical utility in predicting clinical therapeutic outcomes, particularly concerning deep sleep. Notably, these groups exhibit strong correlations with well-established indicators of sleep quality, such as the ESS. Therefore, we believe that these factors can serve as valuable predictive markers for deep sleep, aligning with our original research objective. Furthermore, the MPH and SEMSA, which have established connections with EDS, demonstrated close associations that bolstered their potential as supplementary tools for clinical assessment.

Therefore, a more comprehensive evaluation is warranted to elucidate the pathophysiological mechanisms, including factors related to elevated intracranial pressure. We believe that further research is essential to identify causal relationships.

A limitation of this study was its retrospective nature. Although we established an association between EDS and morning headache, we could not establish a causal relationship, and delving into underlying pathophysiological mechanisms remained beyond the scope of this study.

Second, while we did evaluate morning headache in subjects with OSA, our findings indicated that morning headache was not consistently linked to OSA. Furthermore, in accordance with the International Classification of Headache Disorders, third edition, sleep apnea-related headache was categorized separately from morning headache. Due to the retrospective design of our study, we lacked sufficient data on the headache characteristics required for diagnosing sleep apnea-related headache. Had we applied the criteria for sleep apnea-related headache assessment, it is plausible that we might have uncovered associations with various PSG parameters. Thus, we intend to carry out an additional prospective study focusing on diverse PSG parameters and sleep apnea-related headache.

Third, our study was predominantly comprised of male participants, precluding us from conducting statistical analyses based on gender differences. However, prior studies have re-

ported that the incidence of morning headache is approximately twice as high in women than men. Therefore, it is imperative to take gender differences into account when interpreting the findings of this study.

Lastly, we did not evaluate other sleep related diseases such as restless leg syndrome, Parkinson's disease, and REM sleep behavior disorder, which could affect sleep quality and would likely increase in prevalence with age. Therefore, without analyzing these factors, we might have underestimated the effect of PAP therapy on older adults.

In conclusion, while PAP therapy offers a promising solution to the management of OSA, the road to achieving restorative deep sleep is multifaceted. Age, polysomnographic metrics, and anatomical considerations play crucial roles in OSA-associated daytime symptoms. In addition, anatomical characteristics and patient self-efficacy were significantly associated with the effect of PAP therapy on sleep quality. Personalized treatment plans, considering these prognostic factors, could be the way forward in improving the sleep quality and overall well-being of patients with OSA. This research offers valuable insights for clinicians and paves the way for future studies in this domain.

Availability of Data and Material

The datasets generated or analyzed during the study are not publicly available due to our institution's policy but are available from the corresponding author on reasonable request.

Conflicts of Interest

Min Young Seo who is on the editorial board of the *Journal of Rhinology* was not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

Author Contributions

Conceptualization: Dong Heun Park, Min Young Seo. **Formal analysis:** Dong Heun Park, Hangseok Choi, Kukjin Nam. **Investigation:** Kukjin Nam, Seung Hoon Lee. **Supervision:** Seung Hoon Lee, Min Young Seo. **Validation:** Seung Hoon Lee, Min Young Seo. **Writing—original draft:** Dong Heun Park. **Writing—review & editing:** Hangseok Choi, Min Young Seo.

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