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Sleep impairment in patients with empty nose syndrome*

Chien-Chia Huang[1,2,3], Cheng-Chi Lee[3,4,5], Pei-Wen Wu[1,3,6,†], Chi-Cheng Chuang[3,4], Yun-Shien Lee[7,8], Po-Hung Chang[1,2], Chi-Che Huang[1,2,3], Chia-Hsiang Fu[1,2,3], Ta-Jen Lee[1,3,9,†]

[1] Division of Rhinology, Department of Otolaryngology, Chang Gung Memorial Hospital and Chang Gung University, Taoyuan, Taiwan

[2] Graduate Institute of Clinical Medical Sciences, College of Medicine, Chang Gung University, Taiwan

[3] School of Medicine, Chang Gung University, Taoyuan, Taiwan

[4] Department of Neurosurgery, Chang Gung Memorial Hospital at Linkou and Chang Gung University, Taiwan

[5] Department of Biomedical Engineering, National Taiwan University, Taipei, Taiwan

[6] Department of Otolaryngology–Head and Neck Surgery, Chang Gung Memorial Hospital and Chang Gung University, Keelung, Taiwan

[7] Genomic Medicine Research Core Laboratory, Chang Gung Memorial Hospital, Taoyuan, Taiwan

[8] Department of Biotechnology, Ming Chuan University, Taoyuan, Taiwan

[9] Department of Otolaryngology, Xiamen Chang Gung Hospital, Xiamen, China

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[†] contributed equally

Abstract

Background: Empty nose syndrome (ENS) is characterized by paradoxical nasal obstruction that usually occurs after turbinate surgery. Patients with ENS may also experience significant psychiatric symptoms and sleep dysfunction, which negatively affect the quality of life of affected subjects. This study aimed to evaluate sleep impairment and sleepiness in patients with ENS.

Methods: Patients with ENS and control participants were recruited prospectively. The Sino-Nasal Outcome Test-25 (SNOT-25), Empty Nose Syndrome 6-item Questionnaire (ENS6Q), Epworth Sleepiness Scale (EpSS), and modified sleep quality index (MSQI) were used to evaluate the participants before and after nasal surgery.

Results: Forty-eight patients with ENS and forty-eight age- and sex-matched control subjects were enrolled. The SNOT-25, ENS6Q, EpSS, and MSQI scores in the ENS group were all significantly higher than those in the control group before and after surgery. After surgery, ENS patients all exhibited significant improvements in SNOT-25, ENS6Q, EpSS, and MSQI scores. Regression analysis revealed that SNOT-25 score was a significant predictor of EpSS and MSQI in preoperative evaluations. ENS patients experiencing daytime sleepiness suffered from significantly more "dryness of nose" and "suffocation" than those not experiencing daytime sleepiness.

Conclusions: Patients with ENS experienced significantly impaired sleep quality and sleepiness. Nasal reconstruction surgery improved the sleep quality of ENS patients. The severity of sleep dysfunction is associated with the severity of ENS symptoms. Recognizing individuals with significant sleep impairment and sleepiness and providing appropriate management are critical issues for ENS patients.

Key words: empty nose syndrome, Epworth Sleepiness Scale, Empty Nose Syndrome 6-item Questionnaire, Sino-Nasal Outcome Test-25, sleep quality

Introduction

Empty nose syndrome (ENS) was first described in 1994 by Kern and Stenkvist [1,2] as a syndrome of paradoxical nasal obstruction that usually occurs after turbinate surgery. The pathophysiology

of ENS is not fully understood, but studies have described the abnormal sensory input from nasal airflow due to the inappropriate recovery of mucosal healing and changes in the airflow of the nose after surgical intervention [3–9]. Disorder of communication between breathing and the brain may play a crucial role in ENS development.

The main symptom is a subjective sensation of nasal obstruction despite objectively wide nasal patency [3]. Other bothersome complaints include a sensation of suffocation, dryness, burning, crusting, and a lack of sense of airflow [10,11]. Patients with severe ENS may also experience significant psychiatric symptoms, including chronic fatigue, frustration, irritability, anger, anxiety, and depression [12-15]. These factors negatively impact the quality of life of affected patients.

Previous studies have demonstrated a high prevalence of anxiety and depression among patients [14,15]. The sleep dysfunction domain in the Sino-Nasal Outcome Test-25 (SNOT-25) evaluation was closely related to the severity of the empty nose symptom domain and was a good predictor of moderate-to-severe depression [15]. It is possible that empty nose symptoms, such as dryness, difficulty with nasal breathing, and suffocation, may negatively impact sleep quality in patients with ENS. Poor sleep quality can further lead to or aggravate the psychological burden in these patients [12]. Thus, awareness and appropriate management of sleep problems are some of the most critical issues in patients with ENS. In this study, we aimed to evaluate the sleep quality in patients with ENS and characterize severe cases for further intervention. These results would be beneficial for optimizing patient-centered care.

Methods

Patients

This was a prospective case series consisting of patients diagnosed with ENS who subsequently underwent submucosal Medpor implantation between 2016 and 2021. Patients were diagnosed with ENS according to paradoxical nasal obstruction, previous procedure of inferior turbinate reduction, loss of inferior turbinate tissue on nasal endoscopy and/or computed tomography examinations, and a positive cotton test. A cotton test was performed at enrolment as described in previous studies(3). The participant was asked to breathe through the nose before and after the placement of a moistened cotton ball in the widest area of the nasal cavity. Improvements in nasal symptoms indicated positive results. Patients with 1) a craniofacial anomaly, 2) other sinonasal diseases such as rhinosinusitis, or 3) psychiatric disorders managed by psychiatrists were excluded. To construct a control group, subjects who visited the otolaryngology outpatient clinic for a problem other than nasal symptoms were recruited after nasal evaluation with the nasal symptom questionnaire and endoscopic examination. Participants with allergic rhinitis received therapy as regular clinical practice before and after surgery. The clinical characteristics of the patients were collected. All patients provided informed consent to participate in the study. This study was approved by the Institutional Review Board of Chang Gung Medical Foundation (IRB numbers: 201601703A3, 201802147A3, 201902001A3, and 202201142B0).

Nasal reconstruction with submucosal Medpor implantation

Patients then underwent endoscopic-assisted submucosal Medpor implantation, as described previously [11,14]. A porous, high-density polyethylene implant (Medpor; Porex Surgical, Inc.), made of a nonreactive material that allows tissue and vascular in-growth, was utilized and resized into smaller pieces. In brief, the surgery was performed on patients under local anesthesia, and Medpor implantation was performed via a submucosal pocket created by an incision on the lateral wall. The reconstruction procedures were performed on the side of affected nose and could be unilateral or bilateral depending on the diagnostic criteria and evaluation. The size of Medpor implant inserted was based on the surgeon's experience and the capacity of the created mucosal pocket at inferior meatus. It was crucial to avoid injury to the valve of Hasner, maintain the integrity of the mucosal flap, and prevent protrusion of the implants.

Questionnaire evaluations

The Chinese versions of the SNOT-25 [10] (Table S1), Empty Nose Syndrome 6-item Questionnaire (ENS6Q) [16] (Table S2), Epworth Sleepiness Scale (EpSS) [17] (Table S3), and modified Sleep Quality Index (MSQI) (Table S4) were used to evaluate the symptoms and quality of life in patients with ENS before and after surgical reconstruction. During the SNOT-25 and ENS6Q evaluations, the patients were instructed to grade each symptom item from 0 (no symptoms) to 5 (indicating the most severe symptom). An ENS6Q score ≥ 10.5 suggests the possible presence of ENS [16,18].

The EpSS is the most commonly used instrument for assessing daytime sleepiness [17]. This self-administered questionnaire evaluates the frequency of sleepiness on a 4-point scale (0–3) in eight different situations in daily life. EpSS scores of >10 indicate extensive daytime sleepiness [19].

The MSQI is a 15-item questionnaire that measures sleep quality and disturbances over the previous month and has been used in our institute since 2015. Participants were asked to rate the frequency or severity using a 4-point scale (0–3). The evaluation was completed by participants and their bed partner, if they had one, under the assistance of our research assistant. If they did not have a bed partner, the participants could answer according to prior experience of sleeping with others.

Statistical analyses

The data were statistically analyzed using GraphPad Prism 5 (GraphPad Prism Software, Inc., San Diego, CA, USA) and are

Table 1. Clinical characteristics of participants.

	ENS	Control	P value†
Case number, n (%)	48	48	
Age (year)	47.7 ± 13.0	45.3 ± 14.5	0.788
Female : male, n	9 : 39	9 : 39	1.000
BMI (kg/m^2)	24.3 ± 3.7	23.5 ± 4.2	0.764
Smoker, n (%)	10 (20.8)	8 (16.7)	0.791
Serum IgE (IU/ml) [a]	113.5 (238.8)	-	
Previous nasal surgery:		-	
Inferior turbinate surgery, n (%)	48 (100)		
Nasal septal surgery, n (%)	32 (66.7)		
Endoscopic sinus surgery, n (%)	14 (29.2)		
Caldwell-Luc operation, n (%)	3 (6.3)		
Pre-op SNOT-25	73.3 ± 22.7	14.0 ± 10.3	<0.001***
Pre-op ENS6Q	16.8 ± 5.2	1.5 ± 2.0	<0.001***
Pre-op EpSS	11.3 ± 5.9	3.8 ± 3.5	<0.001***
Pre-op MSQI	28.1 ± 7.8	11.2 ± 6.2	<0.001***

Data are represented as mean ± SD. ENS, empty nose syndrome; Pre-op, pre-operative; SNOT-25, 25-Item Sino-Nasal Outcome Test; ENS6Q, Empty Nose Syndrome 6-item Questionnaire; EpSS, Epworth sleepiness scale; MSQI, modified sleep quality index. † Categorical variables were compared using the χ^2 test and continuous variables were analysed using the Mann-Whitney U test. *** p<0.001. [a] Data are represented as median (interquartile range).

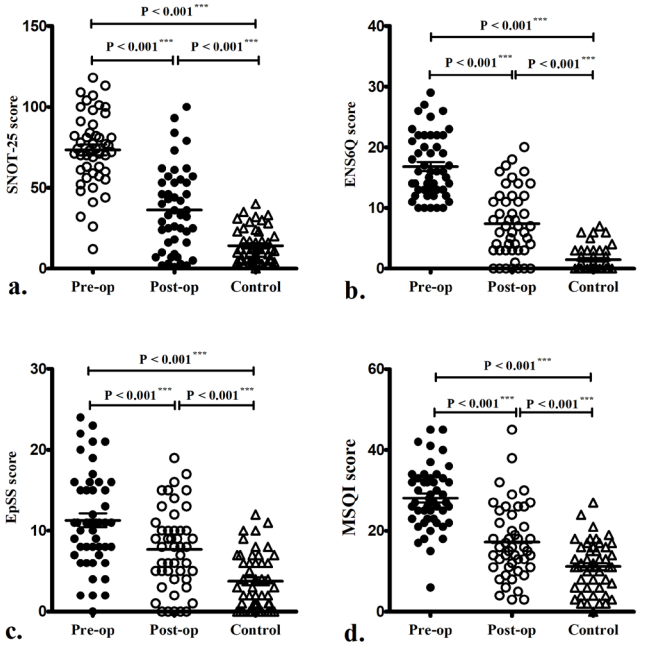

Figure 1. Preoperative (Pre-op) and postoperative (Post-op) 25-Item Sino-Nasal Outcome Test (SNOT-25)(a), Empty Nose Syndrome 6-item Questionnaire (ENS6Q)(b), Epworth sleepiness scale (EpSS)(c), and modified sleep quality index (MSQI)(d) in empty nose syndrome patients and control group. *** p<0.001.

presented as mean ± standard deviation (SD). The continuous variables were analyzed using the Mann–Whitney U test, Wilcoxon signed-rank test, or t-test between the groups according to the results of the D'Agostino–Pearson omnibus normality test. Univariate and multivariate linear regression analyses were used to assess the associations between sleep quality and other variables. To identify and characterize the sensitivity and specificity of clinical metrics for the detection of excessive sleepiness in ENS participants, the receiver operating characteristic (ROC) curves were analyzed and the area under the ROC curve (AUC) was calculated. Statistical significance was set at $P < 0.05$.

Results

Clinical characteristics of the study population

Forty-eight patients with ENS and forty-eight age- and sex-matched control subjects were enrolled. Table 1 summarizes the general characteristics of the patients with ENS. Most of the ENS patients underwent surgeries on the inferior turbinates previously, including partial or total inferior turbinectomy, bipolar electrocautery, microdebrider or radiofrequency assistance inferior turbinoplasty, according to the statements provided by the patients.

There were 43, 47, and 32 patients with ENS who completed postoperative (post-op) follow-up at 3 months, 6 months, and 1 year, respectively. Perioperative (peri-op) changes were evaluated by comparing the difference between the preoperative (pre-op) and 6 months post-op measurements.

Questionnaire evaluation

The pre-op SNOT-25, ENS6Q, EpSS, and MSQI scores in the ENS group were all significantly higher than those in the control group before and after surgery (Figure 1). Twenty-six patients (54.2%) experienced excessive sleepiness (EpSS > 10) before surgery. After surgery, SNOT-25, ENS6Q, EpSS, and MSQI all exhibited significant improvement in ENS patients but were still significantly higher than those in the control group (Figure 1). The pre-op and 3, 6, 12-month post-op scores for each item of the MSQI and EpSS in ENS patients are shown in Tables S3 and S4. Most items showed significant improvement 3 months after surgery in both evaluations.

Association analysis

Simple regression analysis was used to investigate the association of sleep quality, evaluated by the MSQI and EpSS, and other

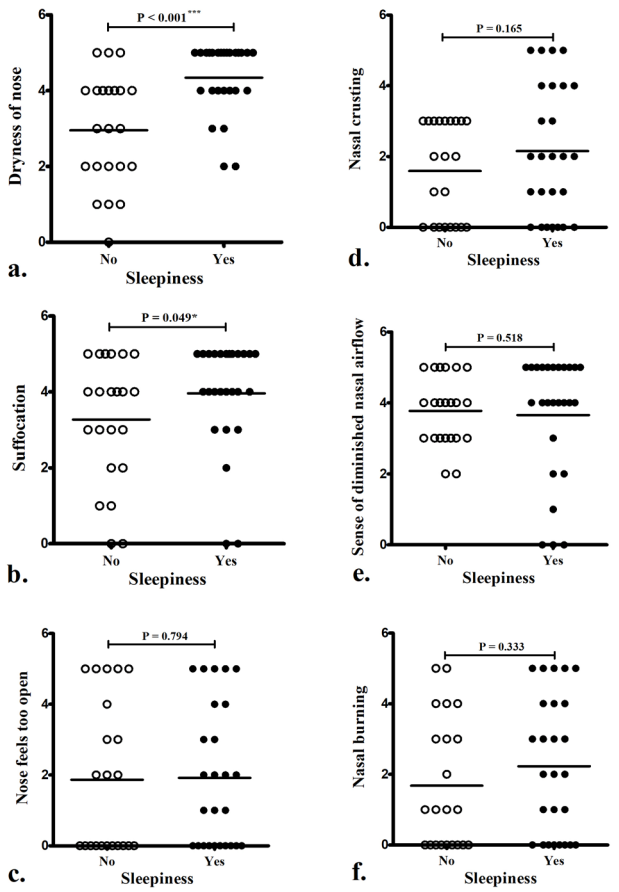

Figure 2. To determine which ENS symptom was associated to extensive daytime sleepiness (EpSS > 10) in ENS patients, we further compared symptom score in each ENS6Q item between ENS patients with and without experiencing daytime sleepiness. ENS patients with experiencing sleepiness suffered from significantly more "dryness of nose" (a) and "suffocation" (b). * $p < 0.05$; *** $p<0.001$.

clinical variables. The results showed that both evaluations with the MSQI and EpSS were significantly associated with SNOT-25 scores and ENS6Q scores in pre-op evaluations (Table 2). Further analysis using multivariate regression models revealed that SNOT-25 was a significant predictor of EpSS and MSQI in pre-op evaluations (Table 3).

To determine which ENS symptoms were associated with extensive daytime sleepiness (EpSS > 10) in ENS patients, we further compared symptom scores of each ENS6Q item between ENS patients with and without daytime sleepiness (Figure 2). ENS patients experiencing sleepiness suffered from more "dryness of nose" and "suffocation" symptoms than those not experiencing daytime sleepiness (Figure 2a and 2b).

Using SNOT-25 and ENS6Q metrics to detect excessive sleepiness

ROC curves were generated, and the AUC was calculated to

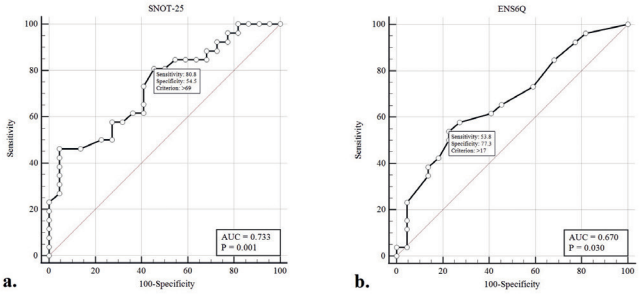

Figure 3. Receiver operating characteristic curves to detect excessive sleepiness (Epworth sleepiness scale > 10) using the variables of the Sinonasal Outcome Test-25 (SNOT-25) score (a) and Empty Nose Syndrome 6-item Questionnaire (ENS6Q) score (b). The optimal cutoffs for these metrics (maximizing the sum of sensitivity and specificity) are indicated.

evaluate the sensitivity and specificity of the SNOT-25 and ENS6Q scores in detecting excessive sleepiness (EpSS > 10) in our participants. The ROC curves of SNOT-25 (AUC = 0.733, p = 0.001) and ENS6Q (AUC = 0.670, p = 0.030) had AUCs that were significantly greater than 0.5 (Figure 3). The optimal cut-off values for these variables (maximizing the sum of sensitivity and specificity) were SNOT-25 > 69 (Youden index J: 0.416; sensitivity: 80.8%, specificity: 54.5%) and ENS6Q > 17 (Youden index J: 0.311; sensitivity: 53.8%, specificity: 77.3%).

Discussion

This is the first study to evaluate sleep quality and sleepiness in patients with ENS. In the present study, we investigated sleep impairment in patients with ENS using the EpSS and MSQI. The results demonstrated a high prevalence of excessive sleepiness (EpSS > 10, 54.2%) and significant sleep dysfunction (MSQI = 28.1 ± 7.8) in ENS patients. Evaluation of the severity of ENS by SNOT-25 and ENS6Q correlated well with sleep evaluation by EpSS and MSQI. SNOT-25 scores were predictors of EpSS and MSQI scores in pre-op evaluations. These results indicated that severe ENS symptoms may lead to significant sleep dysfunction and sleepiness. Our previous study revealed that sleep dysfunction and empty nose symptoms contribute to the psychological burden experienced by patients with ENS [12,15]. The psychological burden of anxiety and depression in ENS patients was the most important factor of surgical outcomes and a predictor of post-operative residual disease [12]. Thus, it is important to routinely evaluate the sleep quality in patients with ENS and offer appropriate management and treatment in severe cases. These findings also emphasize screening for these conditions and structuring care around both surgical reconstruction and cognitive-behavioural therapy, according to the patients' situation, through collaboration with specialists in sleep, psychiatry, and psychology, for optimal outcomes.

Table 2. Simple regression analysis for sleep evaluations in patients with empty nose syndrome.

	EpSS score			MSQI score		
Variables	**coefficient**	**SE**	**P**	**coefficient**	**SE**	**P**
Age	0.05	0.07	0.451	-0.13	0.09	0.151
Sex	-1.32	2.20	0.552	-0.40	2.92	0.891
BMI	0.10	0.24	0.497	0.56	0.3	0.071
Pre-op SNOT-25	0.12	0.03	<0.001***	0.23	0.04	<0.001***
Pre-op ENS6Q	0.48	0.15	0.003**	0.73	0.19	<0.001***

EpSS, Epworth Sleepiness Scale; MSQI, modified sleep quality index; SNOT-25, 25-Item Sino-Nasal Outcome Test; ENS6Q, Empty Nose Syndrome 6-item. Questionnaire; SE, standard error; BMI, body mass index. ** p < 0.01; *** p<0.001.

Table 3. Multiple regression analysis for the sleep evaluations in patients with empty nose syndrome.

	EpSS score			MSQI score		
Variables	**coefficient**	**SE**	**P**	**coefficient**	**SE**	**P**
Age	0.09	0.06	0.164	-0.06	0.07	0.380
Sex	-0.49	2.08	0.814	2.02	2.33	0.392
BMI	-0.16	0.23	0.497	0.24	0.26	0.344
Pre-op SNOT-25	0.18	0.05	0.024*	0.20	0.05	<0.001***
Pre-op ENS6Q	0.11	0.20	0.384	0.16	0.23	0.487

EpSS, Epworth Sleepiness Scale; MSQI, modified sleep quality index; SNOT-25, 25-Item Sino-Nasal Outcome Test; ENS6Q, Empty Nose Syndrome 6-item Questionnaire; SE, standard error; * p < 0.05; *** p<0.001

Previous studies have demonstrated that rhinologic disorders such as nasal septal deviation, allergic rhinitis, and chronic rhinosinusitis have been shown to cause extensive sleep impairment [20]. Treatment of these rhinologic disorders may lead to clinically meaningful reductions in disease burden and improvements in both overall sleep quality and patient-reported fatigue [21]. The pathophysiology of sleep impairment in rhinologic disorders has not been comprehensively described; however, previous studies have demonstrated that sleep impairment may result from obstructive structural pathologies, such as nasal septal deviation and inflammatory sinonasal conditions, including allergic rhinitis and chronic rhinosinusitis [22-24]. Our previous study [15] revealed a robust association between sleep dysfunction and empty-nose symptom domains in patients with ENS. It is possible that empty nose symptoms, such as dryness, difficulty with nasal breathing, and suffocation, may negatively affect sleep quality in ENS patients [25]. Poor sleep quality can further aggravate the psychological burden on these patients. Thus, awareness and appropriate management of sleep problems is one of the most critical issues in patients with ENS. In the current study, surgical reconstruction with Medpor reduced ENS symptoms, improved sleep quality, and diminished sleepiness. The inferior turbinate is crucial in providing resistance to nasal airflow and redirecting airflow to the upper part of nasal cavity. Extensive removal of turbinate tissue leads to a larger airspace and turbulent airflow and may cause an air hunger sensation and a need to breathe deeply [4]. In a study of nasal computational fluid dynamics simulations, airflow velocity and lateral wall shearing stress decreased after resection of the inferior turbinates. However, surgical reconstruction contributed to increased nasal airflow velocity, lateral wall shearing stress, and better mucosal cooling during inspiration [5,6]. Thus, the purpose of surgery is to reconstruct the geographic contour of the nasal cavity, increase resistance, and deflect airflow from insensitive tissue to unoperatic areas. Studies have demonstrated that turbinate reconstruction surgery by augmentation of the inferior meatus with various materials resulted in long-term clinical improvements in ENS patients, indicating that these procedures are safe and effective [11,12,25]. The current study further confirmed that nasal reconstruction with submucosal Medpor implantation significantly improved rhinologic and sleep dysfunction in ENS patients.

To determine which ENS symptoms were associated with extensive daytime sleepiness (EpSS > 10) in ENS patients, we further compared symptom scores of each ENS6Q item between ENS patients with and without daytime sleepiness. The results

showed that ENS patients experiencing sleepiness suffered from significantly more "dryness of nose" and "suffocation" symptoms. These symptoms may have the most substantial impact on sleep impairment and sleepiness in patients with ENS. The identification of these associations allows for targeted symptom improvement to reduce sleep dysfunction in patients with ENS.

Sleep dysfunction was associated with higher SNOT-25 and ENS6Q scores preoperatively. Thus, we next aimed to identify ENS patients with excessive sleepiness (EpSS >10) using ROC curve analysis with preoperative SNOT-25 and ENS6Q scores. ROC curve analysis revealed that a SNOT-25 score of > 69 and an ENS6Q score of > 17 were predictors of preoperative excessive sleepiness. Recognizing individuals with significant sleep impairment using appropriate instruments and providing appropriate psychological interventions are critical for optimizing therapeutic outcomes.

This study has several limitations that warrant consideration. First, this study evaluated ENS patients using four questionnaires without an objective evaluation of sleep quality. Future studies using polysomnography are necessary to clarify our results on patient-reported outcomes. Second, patient-reported measures are vulnerable to self-reported biases such as variations in internal standards, priorities, or the interpretation of a given instrument. The placebo effect cannot be totally excluded without the inclusion of a sham surgery group. However, similar results observed in repeated measurements at 3, 6, and 12 months postoperatively diminished this concern. Third, subjects in the control group were not "normal/ healthy" people. These participants visited otolaryngology outpatient clinic for problems other than nasal diseases. They may experience sleep problems because of their disease. However, the symptom scores in the four questionnaires were low for the participants in the control group, comparing to those in the ENS patients. This further emphasized the significant disease burden in patients with ENS.

Conclusions

Patients with ENS experienced significantly impaired sleep quality and sleepiness. Nasal reconstruction surgery improved the sleep quality in ENS patients. The severity of sleep dysfunction correlated well with the severity of ENS symptoms. Recognizing individuals with significant sleep impairment and sleepiness and providing appropriate management of sleep problems are critical issues for ENS patients.

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Authorship contribution

TJL and PWW designed the study. CCH, CCL, and PWW performed data collection and analysis and drafted the manuscript. CHF, CCH, CCL, CCC, and PHC helped with the enrolment of participants and collection of clinical data. YSL, PWW, and CCH contributed to data interpretation. All authors participated in the scientific discussions and approved the final manuscript.

Conflicts of interest

The authors declare no conflict of interest.

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Ta-Jen Lee and Pei-Wen Wu
Division of Rhinology
Department of Otolaryngology
Chang Gung Memorial Hospital and
Chang Gung University
Taoyuan
Taiwan
No. 5, Fu-Shin Street
Kweishan
Taoyuan 333
Taiwan

Tel: +886-3-3281200 ext. 8466
Fax: +886-3-3979361
E-mail:
Ta-Jen Lee: entlee@cgmh.org.tw
Pei-Wen Wu: a9665@cgmh.org.tw

This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

Table S1. The SNOT-25 scores reported by patients with empty nose syndrome.

Items	Pre-op	Post-op	P value †
1. Need to blow nose	2.3 ± 1.7	1.7 ± 1.4	0.029*
2. Sneezing	1.8 ± 1.4	1.3 ± 1.2	0.011*
3. Runny nose	2.0 ± 1.5	1.6 ± 1.4	0.027*
4. Cough	2.1 ± 1.7	1.3 ± 1.3	<0.001***
5. Postnasal discharge	3.3 ± 1.7	2.0 ± 1.6	<0.001***
6. Thick nasal discharge	2.6 ± 1.9	1.9 ± 1.5	0.031*
7. Ear fullness	2.2 ± 1.8	1.3 ± 1.4	0.002**
8. Dizziness	2.7 ± 1.5	1.3 ± 1.3	<0.001***
9. Ear pain	1.4 ± 1.6	0.7 ± 0.9	0.010*
10. Facial pain/pressure	1.6 ± 1.7	0.9 ± 1.2	0.011*
11. Difficulty falling asleep	3.4 ± 1.6	1.7 ± 1.4	<0.001***
12. Waking up at night	3.7 ± 1.3	1.8 ± 1.5	<0.001***
13. Lack of good night's sleep	3.8 ± 1.4	2.0 ± 1.5	<0.001***
14. Waking up tired	4.0 ± 1.3	1.8 ± 1.5	<0.001***
15. Fatigue	4.0 ± 1.3	2.0 ± 1.6	<0.001***
16. Reduced productivity	3.6 ± 1.5	1.8 ± 1.5	<0.001***
17. Reduced concentration	3.7 ± 1.5	1.7 ± 1.4	<0.001***
18. Frustration/restlessness/irritability	3.5 ± 1.5	1.6 ± 1.5	<0.001***
19. Sadness	3.3 ± 1.6	1.5 ± 1.4	<0.001***
20. Embarrassment	3.1 ± 1.7	1.3 ± 1.4	<0.001***
21. Dryness	3.7 ± 1.4	1.7 ± 1.5	<0.001***
22. Difficulty with nasal breathing	4.1 ± 1.2	1.7 ± 1.4	<0.001***
23. Suffocation	3.6 ± 1.6	1.5 ± 1.4	<0.001***
24. Nose is too open	1.9 ± 2.0	1.0 ± 1.3	0.001**
25. Nasal crusting	1.9 ± 1.7	1.0 ± 1.0	0.001**
Total score	73.3 ± 22.7	37.9 ± 25.3	<0.001***

Data are represented as mean ± SD. SNOT-25, 25-Item Sino-Nasal Outcome Test; pre-op, pre-operative; post-op, 6 months post-operative. † Wilcoxon signed-ranks test analyzed between pre-op and 6 months post-op. * $p < 0.05$; ** $p < 0.01$; *** $p<0.001$.

Table S2. The ENS6Q scores reported by patients with empty nose syndrome.

Items	Pre-op	Post-op	P value †
1. Dryness	3.7 ± 1.4	1.7 ± 1.5	<0.001***
2. Sense of diminished nasal airflow	3.7 ± 1.4	1.3 ± 1.3	<0.001***
3. Suffocation	3.6 ± 1.6	1.5 ± 1.4	<0.001***
4. Nose feels too open	1.9 ± 2.0	1.0 ± 1.3	0.001**
5. Nasal crusting	1.9 ± 1.7	1.0 ± 1.0	0.001**
6. Nasal burning	1.6 ± 1.8	0.8 ± 1.5	0.002**
Total score	16.8 ± 5.2	7.4 ± 5.5	<0.001***

Data are represented as mean ± SD. ENS6Q, Empty Nose Syndrome 6- item Questionnaire; pre-op, pre-operative; post-op, 6 months post- operative. † Wilcoxon signed-ranks test analyzed between pre-op and 6 months post-op symptom scores. ** $p < 0.01$; *** $p<0.001$.

Table S3. Measurement of sleepiness by the Epworth Sleepiness Scale in patients with empty nose syndrome.

Items	Pre-op	3 months post-op	6 months post-op	1 year post-op	P value †
1. Doze as sitting and reading	1.7 ± 0.9	1.2 ± 0.9	1.2 ± 0.9	1.2 ± 0.9	0.003**
2. Doze as watching TV	1.7 ± 1.0	1.1 ± 0.8	1.0 ± 0.8	1.2 ± 0.8	< 0.001***
3. Doze as sitting, inactive in a public place	1.5 ± 1.0	0.7 ± 0.8	0.8 ± 0.8	1.0 ± 1.0	< 0.001***
4. Doze as a passenger in a car for an hour without a break	1.9 ± 0.9	1.1 ± 0.8	1.3 ± 0.9	1.4 ± 1.0	< 0.001***
5. Doze as lying down to rest in the afternoon when circumstances permit	1.7 ± 1.0	1.1 ± 0.9	1.4 ± 0.9	1.5 ± 1.0	0.055
6. Doze as sitting and talking to someone	0.7 ± 0.9	0.5 ± 0.7	0.5 ± 0.7	0.5 ± 0.8	0.110
7. Doze as sitting quietly after a lunch without alcohol	1.5 ± 1.0	0.9 ± 0.9	1.0 ± 0.9	1.3 ± 1.0	0.007**
8. Doze in a car, while stopped for a few minutes in the traffic	0.7 ± 0.9	0.5 ± 0.7	0.4 ± 0.6	0.3 ± 0.5	0.024*
Total score	11.3 ± 5.9	7.1 ± 5.3	7.5 ± 4.9	8.3 ± 5.2	<0.001***

Data are represented as mean ± SD. Pre-op, preoperative; post-op, postoperative. † Wilcoxon signed-ranks test analyzed between pre-op and 6 months post-op symptom scores. * p < 0.05; ** p < 0.01; *** p<0.001.

Table S4. Measurement of sleep quality by the modified sleep quality index in patients with empty nose syndrome.

Items	Pre-op	3 months post-op	6 months post-op	1 year post-op	P value †
1. Cannot get to sleep within 30 minutes	2.4 ± 0.8	1.5 ± 1.0	1.6 ± 1.0	1.5 ± 1.0	< 0.001***
2. Wake up in the middle of the night or early morning	2.4 ± 0.8	1.7 ± 1.0	1.7 ± 1.0	1.7 ± 1.1	< 0.001***
3. Have to get up to use the bathroom	2.2 ± 0.9	1.9 ± 1.0	1.7 ± 1.1	1.8 ± 1.1	0.006**
4. Cannot breathe comfortably	2.7 ± 0.8	1.4 ± 1.1	1.3 ± 1.0	1.6 ± 1.2	< 0.001***
5. Cough or snore loudly	2.5 ± 0.8	1.6 ± 1.0	1.5 ± 1.0	1.6 ± 1.0	< 0.001***
6. Feel too cold	1.3 ± 1.1	0.6 ± 0.9	0.7 ± 0.9	0.8 ± 1.1	0.003**
7. Feel too hot	1.5 ± 1.2	0.8 ± 1.0	0.9 ± 1.0	1.0 ± 0.8	0.005**
8. Had bad dreams	1.5 ± 1.1	0.9 ± 0.9	0.8 ± 0.8	1.0 ± 1.0	< 0.001***
9. Have pain	1.4 ± 1.1	0.8 ± 1.0	0.9 ± 1.0	1.0 ± 1.1	0.013*
10. Loud snore	2.0 ± 1.1	1.5 ± 1.1	1.3 ± 1.0	1.6 ± 1.1	0.001**
11. Long pauses between breaths while asleep	1.3 ± 1.3	0.8 ± 1.0	0.6 ± 0.8	1.0 ± 1.1	0.002**
12. How would you rate your sleep quality overall?	2.6 ± 0.6	1.4 ± 0.9	1.2 ± 0.9	1.5 ± 0.9	< 0.001***
13. How often have you taken medicine to help you sleep?	1.1 ± 1.3	0.7 ± 1.1	0.7 ± 1.0	0.5 ± 0.9	0.058
14. How often have you had trouble staying awake while driving, eating meals, or engaging in social activity?	1.2 ± 1.2	0.6 ± 1.0	0.5 ± 0.8	0.8 ± 1.0	< 0.001***
15. How much of a problem has it been for you to keep up enough enthusiasm to get things done?	2.0 ± 0.9	1.0 ± 0.8	1.0 ± 0.9	1.2 ± 1.0	< 0.001***
Total score	28.1 ± 7.8	17.1 ± 8.5	16.5 ± 8.8	18.5 ± 10.2	<0.001***

Data are represented as mean ± SD. Pre-op, preoperative; post-op, postoperative. † Wilcoxon signed-ranks test analyzed between pre-op and 6 months post-op symptom scores. * p < 0.05; ** p < 0.01; *** p<0.001