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ORIGINAL RESEARCH

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Comparison of SNOT-25 and ENS6Q in evaluating patients with empty nose syndrome

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Abstract

Objectives: Patients with empty nose syndrome (ENS) experience paradoxical nasal obstruction and various psychological burdens. This study aimed to compare ENS-specific questionnaires of sino-nasal outcome test-25 (SNOT-25) and empty nose syndrome 6-item questionnaire (ENS6Q) in the peri-operative evaluation of ENS.

Methods: This was a prospective case series study. Patients with ENS were recruited and evaluated with the SNOT-25, ENS6Q, beck depression inventory-II (BDI-II), and beck anxiety inventory (BAI) before and 6 months after nasal reconstruction surgery.

Results: Seventy-four ENS patients were enrolled during the study period. All four evaluations revealed significant improvements after surgery. Pre-operative SNOT-25 scores exhibited a significant correlation with pre-operative ENS6Q ($r = 0.682$), BDI-II ($r = 0.485$), and BAI scores ($r = 0.608$) ($p < 0.001$), as well as a weak correlation with post-operative SNOT-25 ($r = 0.336$), BDI-II ($r = 0.266$), and BAI scores ($r = 0.235$) ($p < 0.05$). Additionally, pre-operative ENS6Q scores were significantly correlated with pre-operative BDI-II ($r = 0.434$), BAI ($r = 0.521$) ($p < 0.001$), and post-operative ENS6Q scores ($r = 0.262$, $p < 0.05$). However, there was no correlation between pre-operative ENS6Q scores and post-operative BDI-II and BAI scores.

Conclusions: Both SNOT-25 and ENS6Q were helpful in evaluating peri-operative symptoms for patients with ENS. Although the ENS6Q score had a good correlation with the BDI-II and BAI scores preoperatively, it was not associated with post-operative BDI-II and BAI scores. Hence, a simultaneous psychological assessment is necessary when evaluating patients using the ENS6Q.

Level of Evidence: 2c

KEYWORDS
Beck anxiety inventory, Beck depression inventory II, empty nose syndrome, empty nose syndrome 6-item questionnaire, Sino-nasal outcome test-25

Po-Hung Chang and Ta-Jen Lee have contributed equally to this study.

1 | INTRODUCTION

Empty nose syndrome (ENS) is a complicated condition with a spectrum of symptoms including paradoxical nasal obstruction, impaired sense of air passing in the nose, and nasal suffocation.[1–3] ENS patients may also experience significant psychiatric burdens and sleep dysfunction. Thus, affected patients usually report there is a considerable negative impact on the quality of life.[4–8] Although the pathophysiology of ENS is not fully understood, changes in the nasal airflow and impaired recovery of mucosal neurosensory systems after excessive surgical resection of turbinate tissue are considered the main factors causing ENS.[9–13]

The Sino-nasal Outcome Test-25 (SNOT-25), developed by Houser in 2001, is a modification of the SNOT-20 with five additional ENS-specific symptoms: dryness, difficulty with nasal breathing, suffocation, excessively open nose, and nasal crusting.[14] In addition to the original 20 items, SNOT-25 comprises rhinogenic symptom domain, extra-nasal rhinological symptom domain, ear/facial symptom domain, sleep dysfunction domain, psychological dysfunction domain, and empty nose symptom domain.[1,7] The participants score 0 to 5 (indicating none to severe symptoms) for each item, with a maximum score of 125 points. Assessments using validated instruments including the SNOT-25, Beck Anxiety Inventory (BAI),[15] and the Beck Depression Inventory-II (BDI-II),[16] and our previous studies confirmed ENS patients experienced a significant burden of anxiety and depression, and benefited from surgical treatment with submucosal porous high-density polyethylene (Medpor; Porex Surgical, Inc.) reconstruction.[13,14,17–19] There was a good correlation between the perioperative changes in the BAI and BDI-II scores as well as in the sleep dysfunction and empty nose symptom domains of the SNOT-25.[7] Additionally, psychological evaluation could predict outcomes and detect patients with residual disease after surgical reconstruction.

The Empty Nose Syndrome 6-item Questionnaire (ENS6Q), developed by Nayak in 2016, is a validated, ENS-specific detection instrument.[20,21] The ENS6Q contains six items: dryness, lack of air sensation going through the nasal cavities, suffocation, nose feeling too open, nasal crusting, and nasal burning. Participants rate their symptoms in each item from 0 (no symptoms) to 5 (severe symptoms), with a maximum score of 30 points. A measured ENS6Q score ≥ 10.5 suggests the possible presence of ENS, according to a previous report.[20] Furthermore, the severity of ENS6Q symptoms was positively correlated with that of depression and anxiety.[4]

Since SNOT-25 and ENS6Q are both validated questionnaire instruments for evaluating ENS patients and have been reported to have a good correlation with psychological burdens and surgical outcomes, in the present study, we further investigated the association of the perioperative results of these two measurements with other psychological evaluations, such as anxiety and depression. These results may help in choosing tools for the evaluation and management of patients with ENS.

2 | MATERIALS AND METHODS

Patients

Patients with ENS were prospectively recruited in the Department of Otolaryngology of our institution between October 2016 and January 2021. Demographic data and clinical characteristics of the patients were collected. History of previous nasal surgery was determined by patient's statement, medical chart review (our hospital only), and findings on nasal endoscopy and/or computed tomography scan exams. We excluded those with a congenital craniofacial anomaly, other sino-nasal diseases such as nasal polyps or rhinosinusitis, and those previously diagnosed with psychiatric disorders, such as major depression, schizophrenia, or bipolar disorder by psychiatrists. All patients provided informed consent upon enrollment for participating in the study. The Institutional Review Board of Chang Gung Memorial Hospital approved this study (IRB numbers: 201601703A3, 201802147A3, and 201902001A3).

The ENS diagnosis was based on a patent nasal airway assessed by nasal endoscopy and accompanying subjective nasal obstruction. A patent nasal airway means the air space between the inferior turbinate, the nasal septum, and the nasal floor was clearly confirmed without contact of the mucosa of two parts during a nasal endoscopy examination. A cotton test was performed at enrollment as previously described.[14] Improvement in breathing after placing a humidified cotton ball in the widest nasal cavity and breathing through the nose indicated a positive cotton test.[14] Patients received conservative treatment including intranasal topical corticosteroids and nasal warm saline irrigation for at least 3 months. Patients without improvement after conservative treatment

TABLE 1 Clinical characteristics of the study participants

Case number, *n*	74
Age (year)	50.0 ± 12.3
Female: male, *n*	20: 54
Smoker, *n* (%)	10 (13.5)
Serum IgE (IU/ml)	172.9 ± 289.8
Previous nasal surgery:	
Inferior turbinate surgery, *n* (%)	74 (100)
Nasal septal surgery, *n* (%)	51 (68.9)
Endoscopic sinus surgery, *n* (%)	22 (29.7)
Caldwell-Luc operation, *n* (%)	7 (9.5)
Pre-op SNOT-25	71.0 ± 21.0
Post-op SNOT-25	37.9 ± 24.1
Pre-op ENS6Q	15.9 ± 5.3
Post-op ENS6Q	7.5 ± 5.2
Pre-op BDI-II	20.6 ± 14.4
Post-op BDI-II	8.6 ± 9.4
Pre-op BAI	20.1 ± 12.8
Post-op BAI	10.6 ± 10.1

Note: Data are represented as mean ± SD.
Abbreviations: BAI, beck anxiety inventory; BDI-II, beck depression inventory II; ENS6Q, empty nose syndrome 6-item questionnaire; post-op, 6 months post-operative; pre-op, pre-operative; SNOT-25, sino-nasal outcome test-25.

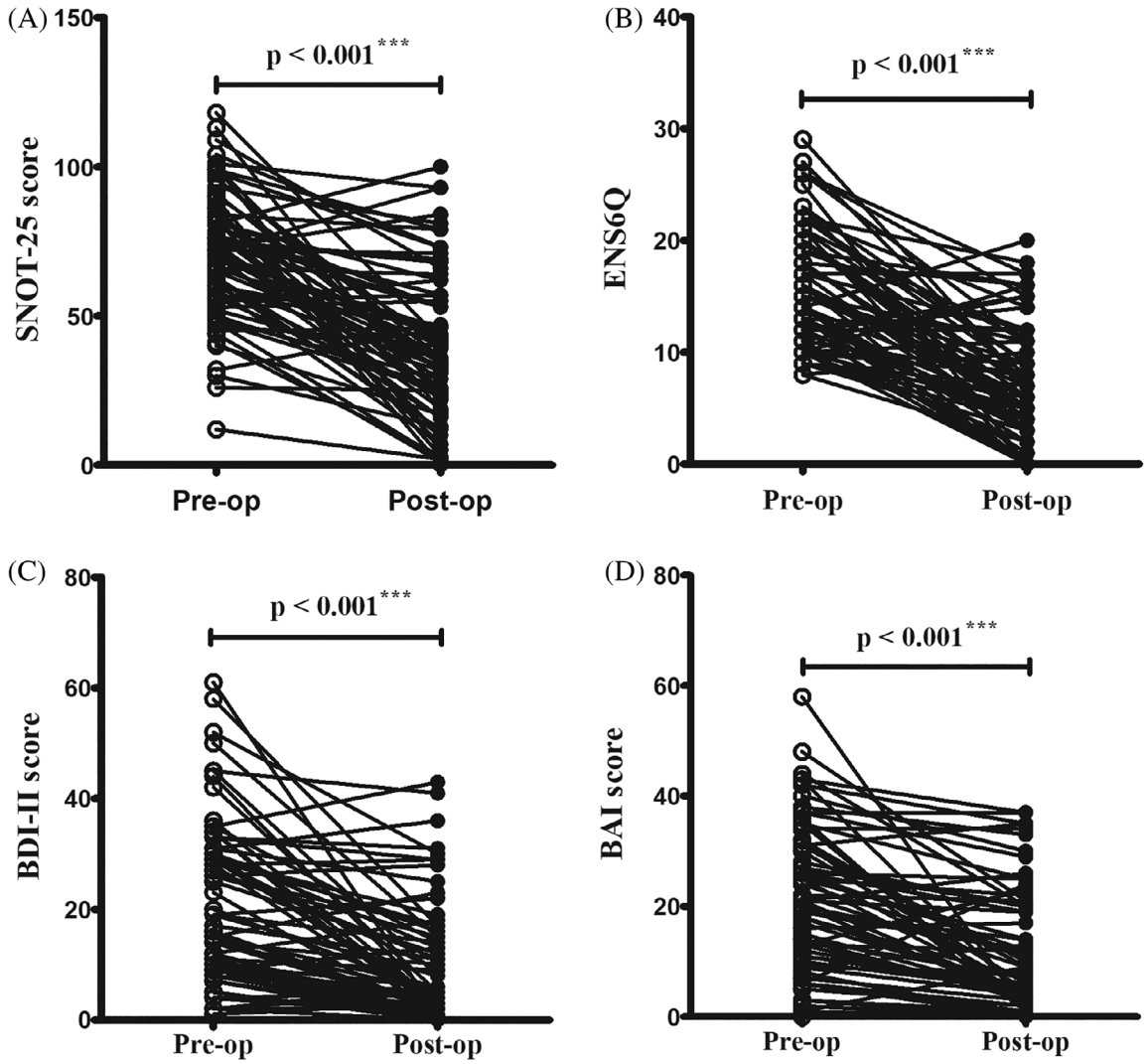

FIGURE 1 Perioperative questionnaires evaluation of empty nose syndrome (ENS) patients. Surgical reconstruction of nasal cavity by submucosal Medpor implantation significantly improved symptoms of ENS patients evaluated by (A) sinonasal outcome test-25 (SNOT-25), (B) empty nose syndrome 6-item questionnaire (ENS6Q), (C) beck depression inventory-II (BDI-II), and (D) beck anxiety inventory (BAI). Pre-op, pre-operative; post-op, 6 months post-operative. ***$p < 0.001$

TABLE 2 Correlation analysis between results of peri-operative questionnares evaluation

		Pre-op SNOT-25		Pre-op ENS6Q	
		Pearson's *r* (95% CI)	*p*	Pearson's *r* (95% CI)	*p*
Pre-op	SNOT-25			0.682 (0.537–0.788)	<0.001**
	ENS6Q	0.682 (0.537–0.788)	<0.001**		
	BDI-II	0.485 (0.288–0.642)	<0.001**	0.434 (0.228–0.603)	<0.001**
	BAI	0.608 (0.441–0.735)	<0.001**	0.521 (0.332–0.670)	<0.001**
Post-op	SNOT-25	0.336 (0.116–0.524)	0.004*	0.200 (−0.030–0.410)	0.088
	ENS6Q	0.190 (−0.040–0.401)	0.105	0.262 (0.035–0.462)	0.024*
	BDI-II	0.266 (0.039–0.466)	0.022*	0.064 (−0.167–0.289)	0.586
	BAI	0.235 (0.007–0.440)	0.044*	0.164 (−0.067–0.378)	0.162

Note: Data are represented as mean ± SD.

Abbreviations: BDI-II, Beck Depression Inventory II; BAI, Beck Anxiety Inventory; CI, confidence interval; ENS6Q, Empty Nose Syndrome 6-item Questionnaire; post-op, 6 months post-operative; pre-op, pre-operative; SNOT-25, sino-nasal outcome test-25.

* $p < 0.05$.

** $p < 0.01$.

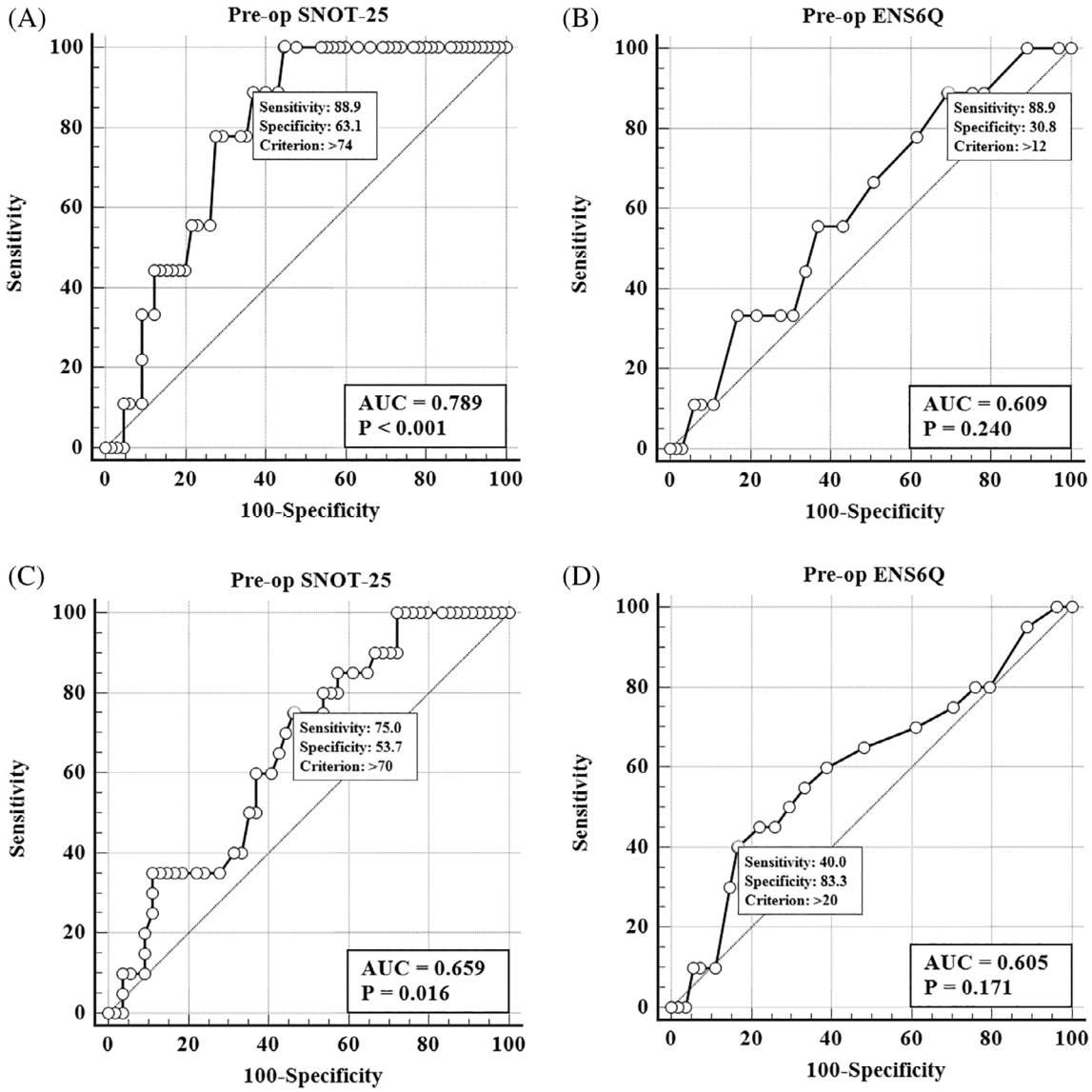

FIGURE 2 Receiver operating characteristic curves to detect post-operative (post-op) moderate-to-severe depression (BDI-II ≥20) using the variables of pre-operative (pre-op) (A) SNOT-25 and (B) ENS6Q; and to detect post-op moderate-to-severe anxiety (BAI ≥16) using the variables of pre-op (C) SNOT-25 and (D) ENS6Q. The optimal cut-offs for these metrics (maximizing the sum of sensitivity and specificity) are indicated

then received submucosal Medpor implantation under nasal endoscopic assistance as described previously.[17,18] In brief, Medpor implantation was performed via the creation of a submucosal pocket on the lateral nasal wall under local anesthesia. Five patients who did not undergo reconstruction surgery were excluded from the analysis.

Patients were followed up at the outpatient clinic every week in the first month, and then every 1 or 3 months after surgery, depending on the recovery of nasal condition. Patients also received intranasal topical corticosteroids and nasal warm saline irrigation 2 weeks after surgery.

Patient-reported outcome measures

The SNOT-25, ENS6Q, BAI, and BDI-II were used to assess patients with ENS before (pre-op) and at 6 months after surgery (post-op). Symptoms were assessed using the SNOT-25 and ENS6Q scores from 0 (no symptom) to 5 (severe symptom) for each item. The BAI and BDI-II both consist of 21 items. Patients rated each symptom from 0 (no symptoms) to 3 (severe symptoms), with a total score of 0–63. Total BAI/BDI-II scores of 0–13/0–7, 14–19/8–15, 20–28/16–25, and 29–63/26–63 indicate normal, mild, moderate, and severe anxiety/depression, respectively.[15,16,22]

Statistical analyses

Data were statistically analyzed using GraphPad Prism 5 (GraphPad Prism Software, Inc., San Diego, CA, USA) and are shown as the mean ± SD. Continuous variables were analyzed using paired t-tests between pre- and post-op measurements. Correlations were investigated using Pearson's correlation coefficient (r, 0–0.2: very weak, 0.2–0.4: weak, 0.4–0.6: moderate, 0.6–0.0.8: strong, 0.8–1.0: very

strong correlation). To identify and characterize the specificity and sensitivity of the pre-op SNOT-25 and ENS6Q in the prediction of post-op moderate-to-severe depression (BDI-II ≥20) and anxiety (BAI ≥16), receiver operating characteristic (ROC) curves were generated, and the area under the ROC curve (AUC) was calculated. A $p < 0.05$ indicated statistical significance.

3 | RESULTS

Characteristics of the patients

Seventy-four ENS patients were enrolled and completed at least 6 months post-op follow-up during the study period. The clinical characteristics of the study population are demonstrated in Table 1. All patients had a history of turbinate surgery, while 68.9% had a history of septal surgery, and 39.2% had undergone prior sinus surgery.

Patient-reported outcome measures

Total scores, as well as pre-op and post-op SNOT-25 (Table S1) and ENS6Q (Table S2) of each item, are presented. The mean pre-op and 6 months post-op SNOT-25 scores were 71.0 ± 21.0 and 37.9 ± 24.1, respectively. The mean pre-op and 6 months post-op ENS6Q scores were 15.9 ± 5.3 and 7.5 ± 5.2, respectively. The mean pre-op and 6 months post-op BDI-II scores were 20.6 ± 14.4 and 8.6 ± 9.4, respectively. The mean pre-op and 6 months post-op BAI scores were 20.1 ± 12.8 and 10.6 ± 10.1, respectively (Table 1). All four evaluations showed a significant improvement ($P < 0.001$) after surgery (Figure 1).

Association analysis

Pearson's correlation analysis of the results of the perioperative questionnaire evaluation is shown in Table 2. Pre-op SNOT-25 scores exhibited a good correlation with pre-op ENS6Q ($r = 0.682$, $p < 0.001$), BDI-II ($r = 0.485$, $p < 0.001$), and BAI scores ($r = 0.608$, $p < 0.001$), while were weakly correlated with the post-op SNOT-25 ($r = 0.336$, $p = 0.004$), BDI-II ($r = 0.266$, $p = 0.022$), and BAI scores ($r = 0.235$, $p = 0.044$). However, there was no correlation between pre-op SNOT-25 and post-op ENS6Q scores. Additionally, pre-op ENS6Q scores were strongly correlated with pre-op BDI-II ($r = 0.434$, $p < 0.001$), BAI ($r = 0.521$, $p < 0.001$), and post-op ENS6Q scores ($r = 0.262$, $p = 0.024$). There was no correlation between pre-op ENS6Q scores and post-op BDI-II and BAI scores.

Using pre-op SNOT-25 and ENS6Q metrics to predict post-op moderate-to-severe anxiety and depression

Given the concern that patients with moderate-to-severe anxiety (BAI ≥16) and depression (BDI-II ≥20) warrant aggressive intervention and therapy, ROC curves were generated, and the AUC was calculated to evaluate whether the pre-op SNOT-25 and ENS6Q scores would predict post-op moderate-to-severe anxiety and depression in our patients (Figure 2). Among the 74 patients with ENS, 20 experienced moderate-to-severe anxiety and nine experienced moderate-to-severe depression after surgery. The pre-op SNOT-25 score had ROC curves with AUCs >0.5 in predicting post-op anxiety (AUC = 0.695, $p = 0.016$) and moderate-to-severe depression (AUC = 0.789, $p < 0.001$). The optimal cutoffs for these evaluations (maximizing the sum of sensitivity and specificity) were a SNOT-25 score of >71 in predicting post-op moderate-to-severe anxiety (sensitivity: 75.0%, specificity: 53.7%) and a SNOT-25 score of >74 in predicting post-op moderate-to-severe depression (sensitivity: 88.9%, specificity: 63.1%).

4 | DISCUSSION

Since SNOT-25 and ENS6Q are both validated questionnaire instruments for evaluating ENS patients and have been reported to have a good correlation with psychological burdens and surgical outcomes, this study first compared the results of the SNOT-25 and ENS6Q evaluations in the same ENS cohort and investigated their relationship with psychological evaluations such as depression and anxiety. Our results reveal that the SNOT-25, ENS6Q, BAI, and BDI-II scores significantly improved ($p < 0.001$) after surgery. Pre-op SNOT-25 scores were significantly related to pre-op ENS6Q, BAI, BDI-II, post-op SNOT-25, BAI, and BDI-II scores, but not to post-op ENS6Q scores. However, pre-op ENS6Q scores exhibited a significant association with pre-op SNOT-25, BAI, BDI-II, and post-op ENS6Q, but not with post-op SNOT-25, BAI, and BDI-II scores. Pre-op SNOT-25 was better correlated with post-op psychological evaluation than pre-op ENS6Q.

Previous studies have reported a significant psychological burden in ENS patients, such as depression and anxiety.[4,6,7] The psychological burden is the most important predictor for surgical outcomes and post-op residual disease in ENS patients.[19] Hence, we sought to identify patients with post-op moderate-to-severe anxiety and depression using ROC curve analysis of pre-op SNOT-25 and ENS6Q scores. ROC curve study indicated that a SNOT-25 score of >70 and a SNOT-25 score of >74 were predictors of post-op moderate-to-severe anxiety and depression, respectively. Recognizing individuals who may experience post-op moderate-to-severe anxiety and depression, as well as providing appropriate pre-op psychological adjuvant therapy, are critical to achieving optimal outcomes of surgery. However, pre-op ENS6Q scores did not generate a ROC curve with AUCs significantly >0.5 in predicting both moderate-to-severe anxiety and depression.

The ENS6Q was first developed to allow for significant discrimination between patients with ENS and other sino-nasal diseases, with high specificity and sensitivity in detecting ENS patients being shown in a previous study.[20] The cut-off score of ENS6Q for reliably predicting ENS was determined to be 10.5 and an ENS6Q ≥ 12 was considered reliable in differentiating patients with ENS from those with primary nasal obstruction in previous studies.[20,23] Nevertheless, no psychological domain was included in the ENS6Q, despite the fact

that ENS patients usually experience significant psychological symptoms.[4] Thus, our results suggest a concurrent psychiatric evaluation, such as BAI and BDI-II, in addition to the ENS6Q during the assessment of ENS patients. Alternatively, the SNOT-25 is another choice because it is a comprehensive evaluation containing rhinogenic symptom domain, extra-nasal rhinological symptom domain, ear/facial symptom domain, sleep dysfunction domain, psychological dysfunction domain, and empty nose symptom domain. Jiang et al. and our cohorts confirmed the SNOT-25 as a useful tool for evaluating ENS patients.[1,7,19] Nevertheless, it may require subjective nasal obstruction, objective paradoxical findings of the patent nasal airway, and an evaluation of the response to intervention, such as a cotton test, to confirm the diagnosis of ENS.[21]

Our previous studies emphasized the importance of psychological evaluation, especially in cases of anxiety and depression, in managing ENS patients.[19] Pre-op psychological measurement could be beneficial for patient selection and surgical outcome prediction. A post-op evaluation may also be helpful in identifying residual diseases in ENS patients. These findings highlight the need for screening these conditions and providing care in both surgery and cognitive-behavioral therapy through the teamwork of specialists in otolaryngology, psychiatry, and psychology. Although the ENS6Q score had a good correlation with the BAI and BDI-II scores preoperatively, it was not associated with post-op BAI and BDI-II scores. Care should be taken that the psychological burden may not be relieved after surgery in some patients with ENS. Hence, simultaneous psychological assessment is necessary when evaluating patients with the ENS6Q alone.

There are several limitations to this study that warrant consideration. First, the placebo effect may have influenced the results because a control group of ENS patients who did not undergo surgery or received sham surgery was not included in this study. Second, studies on patient-reported measures are vulnerable to self-reported biases. However, this study aimed to compare the results of the SNOT-25 and ENS6Q perioperatively. All patients completed four questionnaires perioperatively at the same time to reduce self-reported bias and the placebo effect. Third, excluding patients with previously diagnosed psychiatric disorders may eliminate ENS patients comorbid psychiatric disorders. However, it is difficult to evaluate the symptoms of ENS in patients with major depression or bipolar and differentiate the psychiatric symptoms from psychiatric disorders in these patients. Additionally, patients with major depression or bipolar usually receive psychiatric therapy, which may interfere with surgical outcome measurements in ENS. Thus, the instability of these symptoms and functional impairments by other factors, especially the fluctuating psychological symptoms, were not comprehensively reviewed. Future studies collaborating with other specialists in psychiatry and psychology are necessary to clarify these findings.

5 | CONCLUSION

Both SNOT-25 and ENS6Q are helpful in perioperative symptom evaluation in patients with ENS. Although the ENS6Q score had a good correlation with the BAI and BDI-II scores preoperatively, it was not associated with the post-op BAI and BDI-II scores. Hence, a simultaneous psychological assessment is necessary when evaluating patients using the ENS6Q.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Ta-Jen Lee and Po-Hung Chang participated in the study design. Chien-Chia Huang, Cheng-Chi Lee, and Pei-Wen Wu performed the data collection and analysis and drafted the manuscript. Chia-Hsiang Fu, Chi-Che Huang, Cheng-Chi Lee, and Po-Hung Chang helped with the enrollment of participants and the collection of clinical data. Ta-Jen Lee, Po-Hung Chang, and Chien-Chia Huang contributed to data interpretation. All authors participated in scientific discussions and approved the final manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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