

Evaluation of Empty Nose Syndrome Scores in Patients Undergoing Extended Endoscopic Transnasal Sellar Surgery

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Abstract

Background: Several large series have established endoscopic transnasal sellar surgery as the procedure of choice for removal of tumors in the sellar area. Although this procedure provides a less invasive approach to the sella, it entails complications such as nasal bleeding, impaired olfactory function, atrophic rhinitis, synechia, etc. No studies have yet reported potential morbidities such as empty nose syndrome (ENS), although patients have a relatively empty nasal cavity after surgery. Therefore, we sought to verify the percentage of patients who truly met the diagnostic criteria for ENS after endoscopic transnasal sellar surgery, determine the variation between pre- and postoperative scores in each Empty Nose Syndrome 6-Item Questionnaire (ENS6Q) item, and further evaluate the symptoms that may affect the patients the most after surgery. **Methods:** Between March 2015 and January 2019, eventually 11 patients who underwent extended endoscopic transnasal sellar surgery in Shin Kong Wu Ho-Su Memorial Hospital, a tertiary referral medical center in Taipei, Taiwan, were enrolled. The patients completed the recently validated ENS6Q after surgery. **Results:** One patient met the objective diagnostic criteria for ENS (score ≥ 11 in ENS6Q). Significant differences were observed in the pre- and postoperative total ENS6Q scores. The pre- and postoperative scores of “nose feeling too open” and nasal crusting showed statistically significant differences. Further, compared with the other items, the postoperative score of nasal crusting increased most obviously, and it may be the most apparent operation-related symptom. **Conclusion:** This study is the first to report the possibility of developing ENS after endoscopic transnasal sellar surgery. Although the transnasal endoscopic approach is a safe

and minimally invasive procedure for the treatment of sellar lesions, possible complications such as ENS should be considered.

Keywords

Endoscopic Transnasal Sellar Surgery, Empty Nose Syndrome, ENS6Q, Nasal Crusting, Aerodynamics of Nasal Airflow

1. Introduction

Empty nose syndrome (ENS) is an infrequent, late complication of sinonasal procedures, especially turbinate surgery. Paradoxical nasal obstruction, nasal crusting, nasal dryness, and a persistent feeling of dyspnea are the most common symptoms [1]. Although the etiology of ENS remains uncertain, anatomical changes leading to alterations in local environment and excessive nasal permeability affecting neurosensitive receptors and humidification and conditioning of inhaled air are strongly implicated [1]. The diagnosis of ENS is frequently associated with the presence of paradoxical nasal obstruction despite an objectively patent nasal airway. Patients with ENS exhibit varied prominent symptoms, including dyspnea, nasal and pharyngeal dryness, facial or nasal pain, crusting, hyposmia, and depression. ENS significantly influences the quality of life of the patients, and the associated psychological factors are responsible for patient discomfort [2].

Endoscopic transnasal sellar surgery has been validated as a safe and effective method for removing tumors in the sellar region [3]. Although it is a popular approach to treat sellar lesions, the procedure still entails some complications such as nasal bleeding, impaired olfactory function, atrophic rhinitis, synechiae, etc. [3] [4]. To the best of our knowledge, no study has yet demonstrated potential morbidities such as empty nose syndrome, despite the fact that these patients are under an empty status in their nasal cavity after the extended endoscopic transnasal surgery. Thus, through this study, we aimed to evaluate the correlation of ENS with extended endoscopic transnasal surgery.

2. Materials and Methods

2.1. Patient Selection

Between March 2015 and January 2019, 32 patients with sellar tumors who underwent transnasal sellar surgery in Shin Kong Wu Ho-Su Memorial Hospital were recruited.

2.2. Exclusion Criteria

The records of the 32 patients were retrospectively analyzed. Patients who were undergoing microscopic transnasal sellar surgery ($n = 6$), those who had tumors without cavernous sinus extension ($n = 13$), those unavailable for regular fol-

low-ups (n = 7), and those unable to finish the questionnaire (n = 3) were excluded.

2.3. Preoperative Survey and Postoperative Follow-Up

Ultimately, 11 patients (6 men and 5 women, age range: 18 - 81 years, median age: 59 years) who underwent extended endoscopic transnasal surgery owing to bulky tumor size and cavernous sinus or optic chiasm extension were enrolled. None of them had undergone nasal surgery earlier. For each patient, the symptom score was assessed using the Empty Nose Syndrome 6-Item Questionnaire (ENS6Q); the ENS6Q is a recently validated questionnaire consisting of six items that quantify the symptoms associated with ENS, and each item is rated on a score from 0 (*no symptoms*) to 5 (*severe symptoms*) [5]. The patients completed the ENS6Q, for which a Chinese translation has also been validated, 6 months after the surgery (Table 1).

2.4. Operative Setting

Patients were placed supine on the operating table, under general anesthesia and orotracheal intubation. The procedure consisted of sinus and sellar stages performed using rigid endoscopes (Karl Storz, GmbH and Co, Tuttlingen, Germany) with a diameter of 4 mm and length of 18 cm, at angles of 0°, 30°, 45°, and 70°. Topical 4% xylocaine or Bosmin-soaked cotton pledgets were placed into each naris, and 1% lidocaine with 1:100,000 epinephrine was injected into the nasal mucosa, with particular consideration to the septum on the side of planned nasoseptal flap harvest. The natural ostium of the sphenoid sinus was identified bilaterally. A pedicled nasoseptal flap was then harvested. Bilateral sphenoidotomies were performed, with particular attention to preserving the vascular pedicle to the contralateral nasoseptal flap. A posterior septectomy (15 - 20 mm) was performed for binarial access to the sphenoid sinus. Left ethmoidectomy was performed and a part of the middle turbinate was removed to create the corridor. The mucosa of the sphenoid sinus was totally removed to avoid postoperative mucocele formation. Moreover, the sphenoid sinus septations and rostrum of the sphenoid sinus were drilled down to create the surgical space. Key anatomical landmarks including the dorsum sella, tuberculum sella, sella, bilateral optico-carotid recesses, and clinoidal carotid protuberances were thereafter identified. The bone over the sella was removed using a diamond burr and Kerrison rongeurs. Tumor debulking was performed using ring curettes, suction, and an aspirator. As soon as the tumor resection was completed, the area was irrigated and hemostasis was achieved. Finally, the sellar floor was reconstructed in a graded manner, depending on the extent of the skull base defects. The exposed area in the nasal cavity after the procedure is shown in Figure 1.

2.5. Statistical Analyses

Initially, the total score of the ENS6Q with a score cutoff of 11 was analyzed as

Table 1. The Empty Nose Syndrome 6-item Questionnaire (ENS6Q).

Symptom	No problem	Very mild	Mild	Moderate	Severe	Extremely severe
Dryness	0	1	2	3	4	5
Sense of diminished airway	0	1	2	3	4	5
Suffocation	0	1	2	3	4	5
Nose feels too open	0	1	2	3	4	5
Nasal crusting	0	1	2	3	4	5
Nasal burning	0	1	2	3	4	5

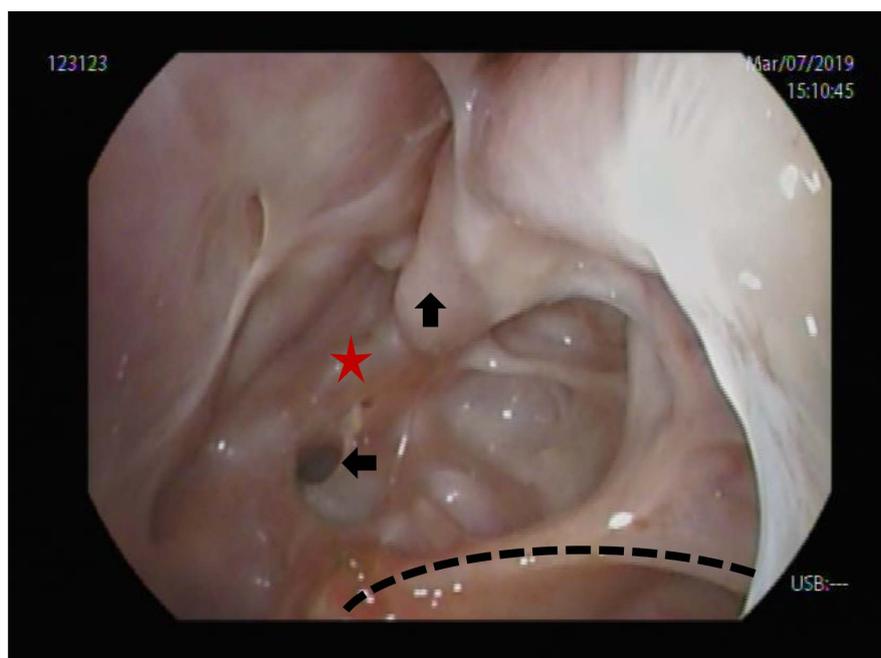


Figure 1. Endoscopic view after extended endoscopic transnasal sellar surgery. ---: Posterior border of the left maxillary sinus opening. ★: Nasoseptal flap. ↑: Remnant of the left middle turbinate. ◄: Opening of the sphenoid sinus.

an objective diagnostic criterion for ENS [5]. Subsequently, the variation between the scores of each ENS6Q item before and after surgery was analyzed. A Wilcoxon test was applied to calculate the *p*-values; *p* < 0.05 was defined as statistically significant. All statistical analyses were performed on a personal computer by using the statistical package MedCalc for Windows (Version 19.0.7, MedCalc manual).

3. Results

Table 2 shows the demographic results of the 11 patients who underwent extended endoscopic transnasal surgery from March 2015 to January 2019. Macroadenoma was the major component of the total pathologies (6/11). All patients exhibited invasion of cavernous sinus part of the internal carotid artery, and 10 of them showed compression at the optic chiasm.

Table 2. Patient pathologies and demographic characteristics.

Patient (No.)	Gender	Age	Pathology
1	Male	76	Metastatic adenocarcinoma
2	Male	53	Adenoma
3	Female	81	Adenoma
4	Male	66	Adenoma
5	Male	68	Adenoma
6	Female	18	Rathke cleft cyst
7	Female	29	Rathke cleft cyst
8	Male	52	Craniopharyngioma
9	Male	76	Adenoma
10	Female	59	Adenoma
11	Female	76	Rathke cleft cyst
Median		59	

The ENS6Q questionnaire was applied to evaluate the diagnosis of ENS. **Table 3** shows that one of the total 11 patients met the diagnostic criteria for ENS (total score ≥ 11) after surgery. Although the postoperative ENS6Q scores of other patients did not satisfy the diagnostic criteria, the patients still showed increased severity of symptoms after surgery, compared with their preoperative scores. **Figure 2** shows significant differences in the total ENS6Q scores of the patients before and after surgery ($p < 0.05$). **Table 4** reveals that two items (nose feeling too open and nasal crusting) showed statistically significant difference between the preoperative and postoperative scores when the Wilcoxon test was applied. To determine the item that may have been the most bothering symptom after undergoing the surgery, the postoperative score of each item in the ENS6Q questionnaire was further analyzed by applying the Kruskal-Wallis test. The result showed that compared with the other items, the score of nasal crusting increased most obviously after surgery, suggesting that it may be the most apparent operation-related symptom.

4. Discussion

In the past decades, several large series have established the endoscopic transphenoidal approach as the procedure of choice for treating pituitary tumors, demonstrating better outcomes and fewer major complications than those associated with a transcranial approach [6] [7]. Although the endoscopic approach is safe and efficient, several studies in the literature have discussed complications arising from the surgery, including nasal bleeding resulting from the approach itself, impaired olfactory function, atrophic rhinitis, synechia, mucoperiosteal flap necrosis, and external nasal deformities [4]. However, little has been explicitly stated about the potential morbidity of ENS, despite the presence of more than adequate intranasal airspace after transnasal endoscopic sellar surgery.

Table 3. Pre- and postoperative ENS6Q scores.

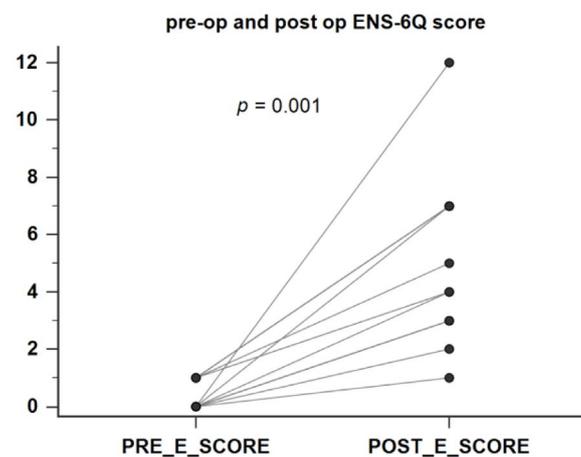
Patient (No.)	Pre-op (score)	Post-op (score)
1	1	7
2	1	5
3	1	4
4	0	2
5	0	12*
6	0	3
7	0	1
8	0	4
9	0	3
10	1	7
11	0	7

*A score cutoff of 11 as an objective diagnostic criterion for empty nose syndrome.

Table 4. Analysis of the differences in pre- and postoperative scores of individual items in the ENS6Q.

Pre-op and post-op differences	Median difference	95% Confidence interval	p-value
ENS-6Q score	4.25	2.5000 to 7.0000	0.0010*
Dryness	0.75	0.0000 to 2.5000	0.0625
Sense of diminished nasal airflow	0.5	0.0000 to 1.0000	0.125
Suffocation	0	0.0000 to 0.0000	0
Nose feels too open	1	0.0000 to 2.0000	0.0313*
Crusting	1	0.5000 to 2.0000	0.0039*
Burning	0	0.0000 to 0.5000	NA

* $p < 0.05$ was considered statistically significant.

**Figure 2.** Pre- and postoperative ENS6Q scores. A tendency of increased total ENS6Q score was observed after the operation. The differences in the pre- and postoperative ENS6Q scores were statistically significant.

ENS, a term originally coined by Eugene Kern and Moore in 1994, described the empty space in the region of the inferior and middle turbinates on coronal computed tomography images of patients who had undergone partial or total inferior and middle turbinectomy [8]. ENS is a diagnosis of exclusion, as it must be differentiated from chronic rhinosinusitis, autoimmune diseases of the nose, and primary atrophic rhinitis. ENS is empirically diagnosed according to the presence of a history of turbinate surgery, clinical examination, and relevant symptoms including varying degrees of nasal crusting, dryness, paradoxical nasal obstruction, thick nasal discharge, postnasal drip, or facial pain [1] [2].

In this study, the ENS6Q was applied as a subjective measure of symptoms that were highly correlated with ENS. The ENS6Q is a recently validated and widely used disease-specific questionnaire to discriminate patients suspected of having ENS [5]. The questionnaire can be completed in approximately 2 min and constitutes a good marker for ENS.

According to our past experience with endoscopic transnasal sellar surgery, even several patients who did not meet the diagnostic criteria of the ENS6Q developed nasal symptoms similar to those listed in the diagnostic items of ENS. This provoked our interests in evaluating the potential links between ENS and extended endoscopic transnasal surgery. In this study, we found that one of the included patients met the diagnostic criteria of ENS6Q (Table 3). In addition, the total score (Figure 2) and two (nose feeling too open and nasal crusting) of the six items in the ENS6Q showed significant differences before and after surgery (Table 4). The *p*-values for two (suffocation and burning sensation) of the remaining four items that showed no statistical significance in the Wilcoxon test were unavailable owing to the characteristics of the data. As no patient experienced suffocation before or after the surgery, the *p*-value remained 0 after applying Wilcoxon test. Meanwhile, owing to the high homogeneity of the preoperative and postoperative scores with regard to a burning sensation, *p* values for the included patients were unavailable.

In our surgical practice, in order to create the surgical corridor and expose the whole sellar anatomy, we partially resected the left middle turbinate and created a posterior septal window. This distorts the anatomy of the nasal cavity. Dayal *et al.* applied virtual surgery and computational fluid dynamics to simulate the aerodynamics of nasal airflow before and after turbinectomy. They found that the efficiency of humidification significantly decreased after both inferior turbinectomy and middle turbinectomy [9]. Decreased humidification function may predispose nasal dryness, facilitating crust formation in the nose and a sense of airflow change. Houser describes four subtypes of ENS: 1) ENS secondary to inferior turbinate resection (ENS-IT); 2) ENS secondary to middle turbinate resection (ENS-MT); 3) ENS secondary to both inferior and middle turbinate (ENS-both); and 4) ENS after turbinate-sparing procedures [10] [11]. Therefore, we speculate that the partial middle turbinectomy and posterior septectomy may play certain roles in influencing the items in the ENS6Q, especially in patients undergoing extended endoscopic transnasal sellar surgery.

Despite the anatomical factor, the neurosensory mechanism has a role in the sensation of the nasal cavity. TRPM8 is a well-known specific trigeminal cool thermoreceptor involved in the sensation of nasal patency [11]. This thermoreceptor is activated when high-speed air passes through the nostril and induces the evaporation of water from the mucosa. Adequate mucosal cooling achieved by effective turbulent airflow activates the thermoreceptors. In patients who undergo endoscopic transnasal sellar surgery, the alterations of the aerodynamics from turbulent airflow to laminar airflow due to turbinate resection may fail to activate the thermoreceptors. Loss of neural sensitivity further aggravates compromised mucosal cooling; consequently, the sensation of nasal patency is not elicited.

Besides the nasal symptoms, patients with ENS suffer from extra-sinonasal symptoms, including reduced concentration; chronic fatigue; and mood problems such as frustration, irritability, anger, and depression owing to the constant abnormal breathing sensations [1] [2]. However, these psychologic burdens may be balanced off by other more distracting factors. We believe that concerns over the skull base tumor and recovery may have distracted the focus of the patients from the symptoms of empty nose. This may also explain the limited links between ENS and extended endoscopic transnasal sellar surgery in this study.

The study limitations relate to the fact that it was performed retrospectively. In addition, this is a relatively small sample size study due to the limited number of patients who were indicated for endoscopic transnasal sellar surgery generally. Though a small number of subjects may limit statistical power, our study elucidates the potential link between ENS and extended endoscopic transnasal sellar surgery.

5. Conclusion

This study is the first to report the relationship of ENS with extended endoscopic transnasal sellar surgery in a tertiary referral medical center. Although this is a safe and effective procedure, possible complications such as ENS should be considered.

Author Contribution

Yu-Hsuan Kuo: study design, composed main manuscript, data analysis; Chia-Jung Lee: collected the data, performed the analysis; Hsing-Mei Wu: contributed data collection and analysis tool; Chung-Yu Hao: contributed substantially to the conception, surgical technique verified; Yung-Hui Liu: surgical technique verified; Yih-Jeng Tsai: study design, revised and verified the manuscript, provided final approval of the version to publish, general coordinator.

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Research Involving Human Participants and/or Animals

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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