Original Research Article

Olfactory-Specific Quality of Life Outcomes after Endoscopic Endonasal Surgery of the Sella

Allergy & Rhinology
Volume 12: 1–7

DOI: 10.1177/21526567211045041
journals.sagepub.com/home/aar
SAGE

Milap D. Raikundalia, MD[1], Ryan J. Huang, MHS[2], Lyndon Chan, MBBS[1], Tracy Truong, MB[3], Maragatha Kuchibhatla, PhD[3], James Merchant, MB[3], Ralph Abi Hachem, MD[1,4], Patrick J. Codd, MD[4], Ali R. Zomorodi, MD[4], Jordan I. Teitelbaum, DO[1], Bradley J. Goldstein, MD, PhD[1], and David W. Jang, MD[1,4]

Abstract

Objective: To assess olfactory outcomes as measured by an olfactory-specific quality of life (QOL) questionnaire in patients undergoing EESBS for sellar lesions.
Design: Retrospective case series.
Setting: Tertiary academic medical center.
Participants: In total, 36 patients undergoing EESBS for lesions limited to the sella were evaluated.
Main Outcome Measures: The following were performed before and three months after surgery: 22-Item Sinonasal Outcomes Test (SNOT-22), University of Pennsylvania Smell Identification Test (UPSIT), and the Assessment of Self-reported Olfactory Functioning (ASOF), which has three domains: subjective olfactory capability scale (SOC), smell-related problems (SRP), and olfactory-related quality of life (ORQ).
Results: Median age at surgery was 52.5 years, with a median tumor size of 1.8 cm (range: 0.2 to 3.9 cm). Pre- and postoperative median scores were 35 [34, 36.2] and 34.5 [32, 36] for UPSIT, 21 [7.5, 33.5] and 21.5 [6.8, 35.7] for SNOT-22, 10 [9, 10] and 9 [8, 10] for ASOF-SOC, 5 [4.8, 5] and 4.5 [4, 5] for ASOF-SRP, and 5 [5, 5] and 5 [4.5, 5] for ASOF-ORQ. There was no significant change in the two of the three domains of the ASOF. Correlation between ASOF and UPSIT scores were weak. Older age and larger tumor size were associated with worsened olfaction after surgery.
Conclusions: Patients did not experience significant changes in olfactory-specific QOL three months after EESBS, as measured by two domains of the ASOF. The ASOF may serve as a useful adjunctive tool for assessing olfaction after surgery. The lack of correlation between UPSIT and ASOF suggests the need for more research in subjective olfactory-related quality of life after surgery.

Keywords

endoscopic minimally invasive surgery of the skull base, olfaction, quality of life

Introduction

The advent of endonasal endoscopic skull base surgery (EESBS) has revolutionized the management of difficult to reach lesions of the cranial base. Recent literature has demonstrated higher rates of complete tumor resection and improved visualization, in addition to lower rates of diabetes insipidus, olfactory dysfunction, and septal perforation with EESBS.[1,2] However, EESBS of the sella typically involves disruption of the sphenoid sinus and posterior septal mucosa, which contains olfactory fibers. Therefore, olfactory dysfunction after EESBS,

[1]Department of Head and Neck Surgery & Communication Sciences, Duke University, Durham, USA
[2]Duke University School of Medicine, Durham, USA
[3]Department of Biostatistics and Bioinformatics, Duke University, Durham, USA
[4]Department of Neurosurgery, Duke University, Durham, USA

Corresponding Author:
David W. Jang, Department of Head and Neck Surgery & Communication Sciences, Duke University, 200 Trent Drive, DUMC 3805, Durham, NC 27710, USA.
Email: david.jang@duke.edu

has been recognized as a major complication. Patients with olfactory impairment are susceptible to deleterious or decreased food consumption, neglect of personal hygiene, imperception to environmental hazards, and depression.[3]

The degree to which patients experience olfactory dysfunction and the time course for recovery after EESBS is unclear. Several studies have demonstrated no significant changes at various timepoints after surgery,[4–10] with a recent meta-analysis showing no significant worsening of olfaction.[11] However, other studies have reported significant worsening.[12–16] These studies analyzed olfactory outcomes anywhere between one and twelve months after surgery, with three months being the most common postoperative timepoint. A number of surgical factors have been associated with olfactory preservation or dysfunction after EESBS. Preservation of the "olfactory strip," or the superoposterior nasal mucosa containing olfactory free nerve endings, has been shown to preserve olfaction.[7,9,10] At the same time, harvesting of the nasoseptal flap (NSF) as well as use of electrocautery have been associated with worsened olfaction.[12,13,17]

Studies investigating olfaction after EESBS have used a variety of subjective and objective instruments. The UPSIT[5,6,9,10,12] and the Sniffin Sticks test[14,17] have been the most commonly used objective olfactory tests. As for subjective quality of life testing, only general sinonasal outcomes instruments such as the 20- or 22-Item Sinonasal Outcomes Test (SNOT),[7–9,18,19] the Nasal Symptom Score,[7] the Nasal Obstruction Symptom Evaluation[18,19] and the Anterior Skull Base Inventory[8] have been used. However, none of these are olfactory-specific. Therefore, olfactory-specific questionnaires, as utilized for chronic rhinosinusitis, are needed to provide additional insight into olfactory outcomes after EESBS. The purpose of this study was to assess olfactory outcomes as measured by the Assessment of Self-Reported Olfactory Functioning (ASOF) questionnaire, an olfactory-specific quality of life (QOL) questionnaire in patients undergoing EESBS for sellar lesions.[20]

Methods

This study was approved by the Institutional Review Board at Duke University Hospital. A retrospective medical record review was conducted on adult patients who underwent EESBS with the Duke Skull Base Center for sellar lesions between January 2017 and December 2019. Patients who underwent an approach beyond the sella, such as transplanar, transpterygoid, or transclival, were excluded. Information related to patient demographics, smoking status, tumor type, tumor size, use of NSF, middle turbinate resection, and postoperative radiation were recorded.

The ASOF, UPSIT, and SNOT-22 instruments were administered at the preoperative visit, which was typically one or two weeks prior to surgery, and at three months postoperatively. For patients who missed their three-month postoperative visit, assessments were performed at the next visit up to but no later than six months postoperatively. Only patients with pre- and postoperative UPSIT and ASOF data were included in the analysis. The ASOF is a validated quality of life psychometric questionnaire specifically for olfaction disorders.[20] It consists of three subdomains which include the Subjective Olfactory Capability Scale (SOC), which rates overall olfactory ability from a scale of 0 to 10, the Smell-Related Problems Scale (SRP), and the Olfactory-related Quality of Life Scale (ORQ). (Figure 1)

Operative Technique

All cases included in this analysis were collaborative procedures performed by rhinology and neurosurgery. In general, bilateral sphenoidotomy, rescue flap harvest, and removal of the rostrum and intersinus septum were performed. Ethmoidectomy with middle or superior turbinate resection was left to the discretion of the rhinologist. Middle turbinate resection was partial and unilateral, with the exception of one case in which it was partial and bilateral. Electrocautery was used judiciously for rescue flap harvest and for NSF harvest when required. The superior incision of the NSF and the rescue flap was made at the level of the sphenoid natural os, at least 1 cm below the cribriform plate, below the olfactory fibers. The size of the posterior septectomy was also at the discretion of the surgeons, but was approximately 1 to 1.5 cm in length.

The reconstructive method was based on presence and flow rate of cerebrospinal fluid (CSF) leak, size of defect, and surgeon preference. When no leak was present, the sphenoid sinus was simply lined with Gelfoam (Pfizer, New York, NY) with or without a free mucosal graft from the middle turbinate. Absorbable packing material (Nasopore [Polyganics, Groningen, the Netherlands] or PosiSep [Hemostasis, St. Paul, MN]) was placed in the nasal cavity. For low-flow CSF leaks, an abdominal fat graft supported by non-absorbable packing was used. Packing was removed after five to seven days. For high-flow CSF leaks with a visible dural defect, a NSF with or without abdominal fat was used for reconstruction. Packing was removed after five to seven days, but bilateral Doyle splints (Medtronic, Jacksonville, FL) were left in place for three to six weeks to promote re-epithelialization of the septum donor site. Endoscopic debridement was performed at minimum one month and three months after surgery.

Statistical Analysis

Study data were collected and managed using Research Electronic Data Capture (REDCap).[21] Medians [Q1 = 25th percentile, Q3 = 75th percentile] were presented for continuous variables while frequencies (%) were presented for categorical variables. The baseline and follow-up olfactory scores were compared using Wilcoxon signed rank tests with Bonferroni correction when appropriate. Spearman's

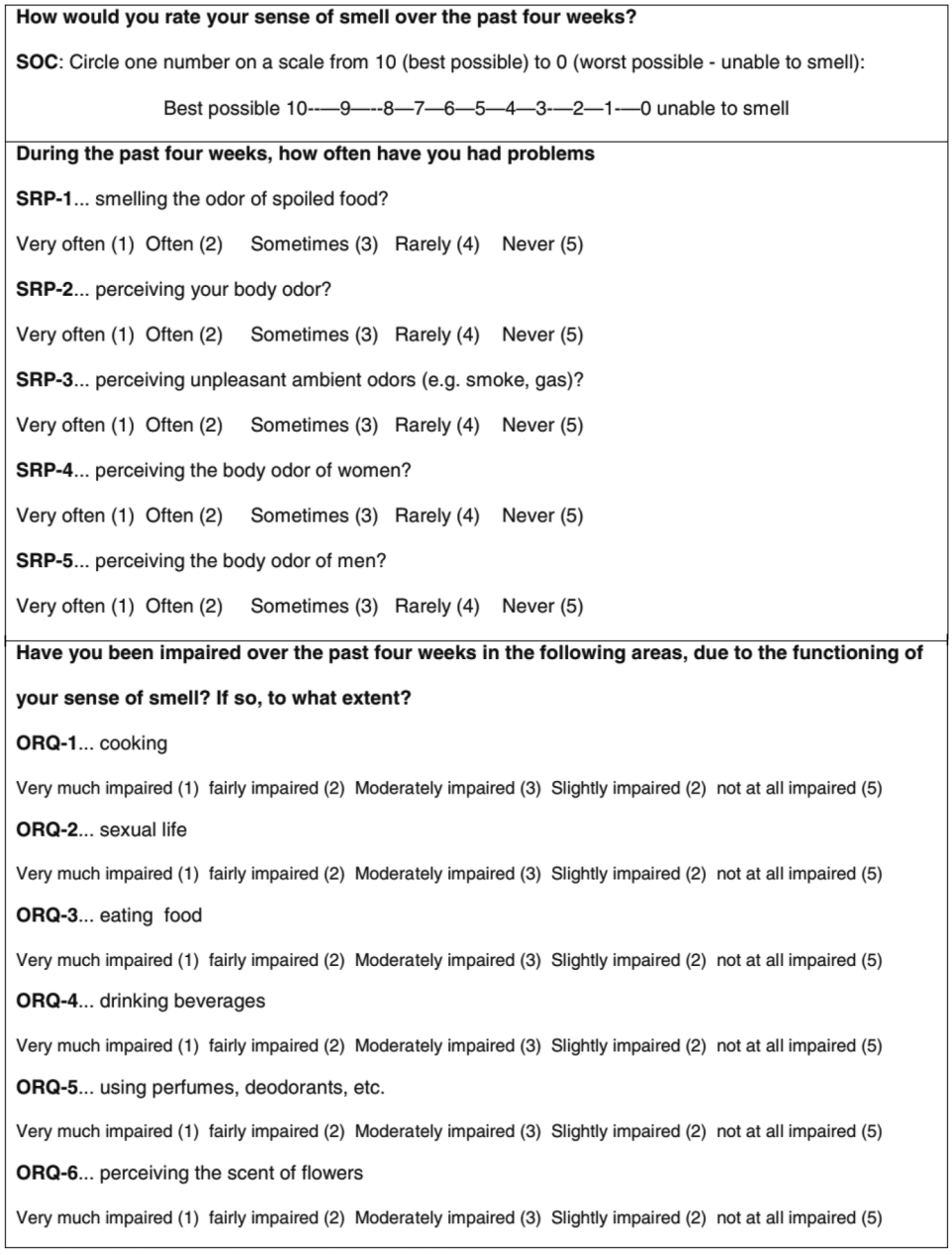

Figure 1. Assessment of self-reported olfactory functioning and olfaction related quality of life (ASOF). Adapted from Pusswald G, Auff E, Lehrner J. Development of a Brief Self-Report Inventory to Measure Olfactory Dysfunction and Quality of Life in Patients with Problems with the Sense of Smell. Chemosensory Perception. 2012;5(3-4):292 to 299. The ASOF can be obtained from http://www.psimistri.com.

correlation was calculated for the changes in UPSIT score compared to the changes in the ASOF scores to assess the monotonic relationship between these scores. Furthermore, we defined worsening UPSIT or ASOF as a binary outcome indicating a negative change score. In order to identify factors associated with these outcomes, univariate analyses were performed for each patient's characteristic. Tumor pathology was dichotomized into whether the patient had pituitary adenoma or not. Continuous variables were compared between worsening and not worsening groups using Wilcoxon rank sum tests while categorical variables were compared using Fisher's exact tests. If an incomplete SNOT-22 questionnaire had at least 50% of items completed, item-level missingness was imputed using mean of the completed items. The imputation method was utilized by Hopkins et al. when missing data was encountered in their study to validate the SNOT-22 questionnaire, and is consistent with studies utilizing other patient-based outcomes measures.[22] All analyses were performed in R 3.5.3 (R Core Team, 2019).[23]

Results

A total of 36 patients met inclusion criteria, completing both the ASOF and the UPSIT before and after surgery. Complete SNOT-22 data were available for 31 patients. 11 patients (30.6%) were male. Median age was 52.5 [35, 60.8] years (range: 20 to 73 years). 4 (11.1%) of patients were active smokers. 5 patients (13.9%) underwent NSF reconstruction. 16 patients (44.4%) underwent middle turbinate resection. 2 patients (5.6%) underwent postoperative stereotactic radiation. Median tumor size was 1.8 [1.2, 2.2] cm (range: 0.2 to 3.9 cm). Information related to tumor size and pathology are found in Table 1.

For scores on outcomes measures, there was no significant worsening of the SNOT-22 or two domains of the ASOF (SOC, SRP). In contrast, there was statistically significant worsening of the UPSIT and ASOF-ORQ. (Table 2). Spearman's correlation was estimated to assess for monotonic relationship. No strong correlation between the change in UPSIT and ASOF measures was found ($|r_s| \leq 0.15$). (Table 3)

On univariate analysis, male sex, smoking status, tumor size, nasoseptal flap, middle turbinate resection, radiation, and adenoma on histology were not associated with worsening UPSIT. Age, however, was associated with worsening UPSIT. Specifically, the median age in the worsening UPSIT group was 58 [35, 66.2] compared to 40 [34.8, 54] ($p = 0.034$). (Table 4) A larger tumor size was associated with worsening ASOF-SOC on univariate analysis (2 [1.6, 2.8] vs. 1.5 [0.9, 2]; $p = 0.017$). (Table 5)

Table 1. Characteristics of Patients Undergoing Transsellar EESBS.

Characteristics	Total (n = 36)
Male	11 (30.6%)
Age at surgery (years), median [Q1, Q3]	52.5 [35, 60.8]
Smoker	4 (11.1%)
Tumor size (cm), median [Q1, Q3]	1.8 [1.2, 2.2]
Pathology	
Pituitary Adenoma Non-secreting	16 (44.4%)
Pituitary Adenoma ACTH	5 (13.9%)
Pituitary Adenoma GH	2 (5.6%)
Pituitary Adenoma Prolactin	8 (22.2%)
Craniopharyngioma	1 (2.8%)
Chordoma	1 (2.8%)
Meningioma	1 (2.8%)
Fibro-osseous	1 (2.8%)
Rathke Cleft Cyst	1 (2.8%)
Nasoseptal flap	5 (13.9%)
Middle turbinate resection	
None	20 (55.6%)
Unilateral	15 (41.7%)
Bilateral	1 (2.8%)
Radiation	2 (5.6%)

Q1 – 25th percentile; Q3 – 75th percentile.

Table 2. Olfactory Assessments at Baseline and Postoperative Status.

Outcomes	Baseline	Postoperative	Change	P-value
UPSIT (n = 36)	35 [34, 36.2]	34.5 [32, 36]	−1 [−3, 0.2]	**0.008***
SNOT-22 (n = 31)	21 [7.5, 33.5]	21.5 [6.8, 35.7]	−3 [−6.6, 6]	0.537
ASOF SOC (n = 34)	10 [9, 10]	9 [8, 10]	0 [−2, 0]	0.033
ASOF SRP (n = 36)	5 [4.8, 5]	4.5 [4, 5]	0 [−0.8, 0.1]	0.030
ASOF ORQ (n = 34)	5 [5, 5]	5 [4.5, 5]	0 [−0.5, 0]	**0.013***

Abbreviations: ASOF: Assessment of Self-reported Olfactory Functioning; ORQ: olfactory-related quality of life; SNOT-22: 22-Item Sinonasal Outcomes Test (SNOT-22); SOC: subjective olfactory capability scale; SRP: smell-related problems; UPSIT: University of Pennsylvania Smell Identification Test.
Median [Q1: 25th percentile; Q3: 75th percentile] presented.
*Denotes statistical significance. Bonferroni correction was applied to the ASOF with statistical significance set at $p < 0.0166$.

Table 3. Correlation Between ASOF Domains and UPSIT.

Outcomes.	n.	Spearman's correlation with UPSIT.
ASOF-SOC.	34.	−0.10.
ASOF-SRP.	36.	−0.11.
ASOF-ORQ.	34.	0.14.

Abbreviations: ASOF: Assessment of Self-reported Olfactory Functioning; ORQ: olfactory-related quality of life; SOC: subjective olfactory capability scale; SRP: smell-related problems; UPSIT: University of Pennsylvania Smell Identification Test.

Table 4. Univariate Analysis for Worsening UPSIT Score.

Characteristics	No (n = 16)	Yes (n = 20)	P-value
Age at surgery	40 [34.8, 54]	58 [35, 66.2]	**0.034***
Male	7 (43.8%)	4 (20.0%)	0.159
Smoker	2 (12.5%)	2 (10%)	1.000
Tumor size	1.7 [1, 2.2]	1.8 [1.4, 2.4]	0.599
Nasoseptal flap	3 (18.8%)	2 (10.0%)	0.637
Middle turbinate resection	7 (43.8%)	9 (45%)	1.000
Radiation	0 (0.0%)	2 (10.0%)	0.489
Adenoma on histology	14 (87.5%)	17 (85.0%)	1.000

Abbreviation: UPSIT: University of Pennsylvania Smell Identification Test.
Median [Q1: 25th percentile; Q3: 75th percentile] or number (%) presented.

Discussion

Disruption of the olfactory epithelium during EESBS raises the concern for postoperative olfactory dysfunction. Therefore, investigating the factors influencing olfactory dysfunction after EESBS is critical. Numerous studies have

Table 5. Univariate Analysis for Worsening ASOF SOC, SRP and ORQ Scores.

	Worsening ASOF SOC			Worsening ASOF SRP			Worsening ASOF ORQ		
Characteristics	No (n = 19)	Yes (n = 15)	P-value	No (n = 20)	Yes (n = 16)	P-value	No (n = 20)	Yes (n = 14)	P-value
Age at surgery	37 [35, 63]	54 [37.5, 57]	0.835	50 [35, 63]	54.5 [34.8, 58.5]	0.861	43 [35, 63]	55.5 [44.2, 59.5]	0.587
Male	9 (47.4%)	2 (13.3%)	0.064	7 (35.0%)	4 (25.0%)	0.718	8 (40.0%)	3 (21.4%)	0.295
Smoker	3 (15.8%)	1 (6.7%)	0.613	4 (20.0%)	0 (0.0%)	0.113	3 (15.0%)	1 (7.1%)	0.627
Tumor size	1.5 [0.9, 2]	2 [1.6, 2.8]	**0.017***	1.6 [1, 2]	2 [1.5, 2.8]	0.104	1.6 [1, 2]	2 [1.6, 2.7]	0.079
Nasoseptal flap	2 (10.5%)	3 (20.0%)	0.634	4 (20.0%)	1 (6.2%)	0.355	4 (20.0%)	1 (7.1%)	0.379
Middle turbinate resection	10 (52.7%)	5 (33.3%)	0.588	8 (40.0%)	8 (40.0%)	0.611	8 (40.0%)	6 (42.9%)	1.000
Radiation	1 (5.3%)	1 (7.1%)	1.000	2 (10.0%)	0 (0.0%)	0.496	1 (5.0%)	1 (7.7%)	1.000
Adenoma on histology	17 (89.5%)	12 (80.0%)	.634	17 (85.0%)	14 (87.5%)	1.000	17 (85.0%)	12 (85.7%)	1.000

Abbreviations: ASOF: Assessment of Self-reported Olfactory Functioning; ORQ: olfactory-related quality of life; SOC: subjective olfactory capability scale; SRP: smell-related problems.
Median [Q1: 25th percentile; Q3: 75th percentile] or number (%) presented.

investigated olfactory outcomes after EESBS. Several studies have demonstrated no significant changes anywhere from one to twelve months after EESBS, with three-month outcomes being the most commonly reported.[4–10] In contrast, Tam et al. demonstrated worsened UPSIT scores six months after EESBS.[12] Similarly, Hong et al. found that use of electrocautery was associated with subjective olfactory loss at three months,[13] and Cingoz et al. demonstrated worsening olfactory recognition on the Sniffin Sticks test at eight weeks.[14] Consistent with these studies, we also found a statistically significant decrease in postoperative UPSIT scores at three to six months following EESBS of the sella. However, it should be noted that the median difference in UPSIT scores in our cohort (−1) is likely not clinically significant. This is supported by the fact that there was no significant difference in olfactory-specific QOL scores as measured by the ASOF. Based on these findings, we conclude that EESBS of the sella does not seem to result in olfactory changes that significantly impact a patient's QOL. At the same time, we should point out that 10 out of 36 patients (27.8%) in our cohort experienced a clinically significant drop in UPSIT (defined as 3 points or more) at three months. This is important for pre-operative counseling.

Our results also point to the utility of an olfactory-specific quality of life instrument to assess olfaction after EESBS. Olfactory-specific quality of life questionnaires have not been widely used in otolaryngology and skull base surgery. Soler et al. reported use of a modified version of the Questionnaire of Olfactory Disorders to assess olfactory outcomes after surgery for chronic rhinosinusitis.[24] This study is the first to utilize a validated olfactory-specific quality of life questionnaire after endoscopic skull base surgery.

This study also investigated whether certain clinical factors were associated with worsening olfactory outcomes after EESBS. We found that while tumor size, turbinate resection, radiation, smoking status, or NSF use were not associated with worsening on the UPSIT, older patients had worsening after surgery. Similarly, Kim et al. demonstrated worse outcomes with older age.[18] This suggests that older patients may have less olfactory "reserve". We also found that larger tumor size was associated with worsening of the ASOF-SOC. This is consistent with a study by Kim et al.,[19] who demonstrated worsening smell identification scores with large tumors, presumably due to greater disruption of sinonasal anatomy. Although our sample size was too small to perform a multivariate analysis, it is worthwhile as a future endeavor to examine whether age and tumor size are risk factors for worsened olfactory outcomes. With the change in UPSIT ranging from −7 to +5 in our patient cohort, there are clearly certain patients who have much poorer olfactory outcomes.

Our study raises the question of the best tools for assessing olfaction after EESBS. For objective testing, most studies have utilized self-administered smell identification tests such as the UPSIT or the Brief Smell Identification Test. Although such smell identification testing is convenient, it is unclear if this type of suprathreshold testing is appropriate in this setting. Kim et al. utilized the Connecticut Chemosensory Clinical Research Center Test, which has an olfactory threshold testing component, to show worsened outcomes after EESBS.[19] Similarly, the Sniffin Sticks test, which has a threshold component, has been used to show worsened scores after EESBS.[14] For subjective testing, studies have mainly focused general sinonasal outcomes instruments, such as the SNOT-22, which have an olfactory-related item. However, an olfactory-specific QOL questionnaire such as the ASOF can provide additional insight into the patient's everyday experience as it relates to olfaction.

Limitations of this study pertain to attrition bias and recall bias associated with patient questionnaires due to the retrospective nature of the study. The majority of patients who underwent EESBS during the study period were not included due to lack of follow-up and incomplete data, leading to a small sample size. We also did not utilize olfactory threshold testing, which may shed useful insight into optimal testing. Finally, we did not follow patients beyond three months, even though further changes in olfaction can occur beyond that.

Conclusion

Patients did not experience significant changes in olfactory-specific QOL three months after EESBS, as measured by two domains of the ASOF. The ASOF may serve as a useful adjunctive tool for assessing olfaction after surgery. The lack of correlation between UPSIT and ASOF suggests the need for more research in subjective olfactory-related quality of life after surgery.

Acknowledgments

The Duke Biostatistics, Epidemiology, and Research Design Methods Core's support of this project was made possible in part by CTSA Grant (UL1TR002553) from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH), and the NIH Roadmap for Medical Research. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of NCATS or NIH.

Author Contributions

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

Not applicable, because this article does not contain any studies with human or animal subjects.

Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

Informed Consent

Not applicable, because this article does not contain any studies with human or animal subjects.

ORCID iDs

Ryan J. Huang https://orcid.org/0000-0002-2155-6273
Jordan I. Teitelbaum https://orcid.org/0000-0001-5042-0669

Trial Registration

Not applicable, because this article does not contain any clinical trials.

References

1. Kahilogullari G, Beton S, Al-Beyati ES, et al. Olfactory functions after transsphenoidal pituitary surgery: endoscopic versus microscopic approach. *Laryngoscope*. 2013;123(9):2112–2119.
2. Li A, Liu W, Cao P, Zheng Y, Bu Z, Zhou T. Endoscopic versus microscopic transsphenoidal surgery in the treatment of pituitary adenoma: a systematic review and meta-analysis. *World Neurosurg*. 2017;101:236–246.
3. Croy I, Nordin S, Hummel T. Olfactory disorders and quality of life--an updated review. *Chem Senses*. 2014;39(3):185–194.
4. Griffiths CF, Barkhoudarian G, Cutler A, et al. Analysis of olfaction after bilateral nasoseptal rescue flap transsphenoidal approach with olfactory mucosal preservation. *Otolaryngol Head Neck Surg*. 2019;161(5):881–889.
5. Chaaban MR, Chaudhry AL, Riley KO, Woodworth BA. Objective assessment of olfaction after transsphenoidal pituitary surgery. *Am J Rhinol Allergy*. 2015;29(5):365–368.
6. Hart CK, Theodosopoulos PV, Zimmer LA. Olfactory changes after endoscopic pituitary tumor resection. *Otolaryngol Head Neck Surg*. 2010;142(1):95–97.
7. Harvey RJ, Winder M, Davidson A, et al. The olfactory strip and its preservation in endoscopic pituitary surgery maintains smell and sinonasal function. *J Neurol Surg Part B, Skull Base*. 2015;76(6):464–470.
8. Hong SD, Nam DH, Kong DS, Kim HY, Chung SK, Dhong HJ. Endoscopic modified transseptal transsphenoidal approach for maximal preservation of sinonasal quality of life and olfaction. *World Neurosurg*. 2016;87:162–169.
9. Puccinelli CL, Yin LX, O'Brien EK, et al. Long-term olfaction outcomes in transnasal endoscopic skull-base surgery: a prospective cohort study comparing electrocautery and cold knife upper septal limb incision techniques. *Int Forum Allergy Rhinol*. 2019;9(5):493–500.
10. Upadhyay S, Buohliqah L, Dolci RLL, Otto BA, Prevedello DM, Carrau RL. Periodic olfactory assessment in patients undergoing skull base surgery with preservation of the olfactory strip. *Laryngoscope*. 2017;127(9):1970–1975.
11. Yin LX, Low CM, Puccinelli CL, et al. Olfactory outcomes after endoscopic skull base surgery: a systematic review and meta-analysis. *Laryngoscope*. 2019;129(9):1998–2007.
12. Tam S, Duggal N, Rotenberg BW. Olfactory outcomes following endoscopic pituitary surgery with or without septal flap reconstruction: a randomized controlled trial. *Int Forum Allergy Rhinol*. 2013;3(1):62–65.
13. Hong SD, Nam DH, Park J, Kim HY, Chung SK, Dhong HJ. Olfactory outcomes after endoscopic pituitary surgery with nasoseptal "rescue" flaps: electrocautery versus cold knife. *Am J Rhinol Allergy*. 2014;28(6):517–519.
14. Cingoz ID, Kizmazoglu C, Guvenc G, Sayin M, Imre A, Yuceer N. Evaluation of the olfactory function with the "Sniffin' sticks" test after endoscopic transsphenoidal pituitary surgery. *J Craniofac Surg*. 2018;29(4):1002–1005.
15. Greig SR, Cooper TJ, Sommer DD, Nair S, Wright ED. Objective sinonasal functional outcomes in endoscopic anterior skull-base surgery: an evidence-based review with recommendations. *Int Forum Allergy Rhinol*. 2016;6(10):1040–1046.
16. Alobid I, Ensenat J, Marino-Sanchez F, et al. Impairment of olfaction and mucociliary clearance after expanded endonasal approach using vascularized septal flap reconstruction for skull base tumors. *Neurosurgery*. 2013;72(4):540–546.
17. Soyka MB, Serra C, Regli L, Meier E, Holzmann D. Long-term olfactory outcome after nasoseptal flap reconstructions in midline skull base surgery. *Am J Rhinol Allergy*. 2017;31(5):334–337.
18. Kim BY, Son HL, Kang SG, et al. Postoperative nasal symptoms associated with an endoscopic endonasal transsphenoidal approach.

European Archives of Oto-rhino-Laryngology: Official Journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS): Affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery. 2013;270(4): 1355–1359.

19. Kim DH, Hong YK, Jeun SS, et al. Can tumor size be a predictive factor of olfactory dysfunction after endoscopic endonasal transsphenoidal approach? *J Craniofac Surg*. 2018;29(3):543–546.
20. Pusswald G, Auff E, Lehrner J. Development of a brief self-report inventory to measure olfactory dysfunction and quality of life in patients with problems with the sense of smell. *Chemosens Percept*. 2012;5(3–4):292–299.
21. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377–381.
22. Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item sinonasal outcome test. *Clin Otolaryngol*. 2009;34(5):447–454.
23. R Core Team R: A language and environment for statistical computing. R Foundation for Statistical Computing. Web site. https://www.R-project.org/. Published 2020. Accessed September 16, 2021.
24. Soler ZM, Smith TL, Alt JA, Ramakrishnan VR, Mace JC, Schlosser RJ. Olfactory-specific quality of life outcomes after endoscopic sinus surgery. *Int Forum Allergy Rhinol*. 2016;6(4):407–413.