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Effect of Omega-3 Supplementation in Patients With Smell Dysfunction Following Endoscopic Sellar and Parasellar Tumor Resection: A Multicenter Prospective Randomized Controlled Trial

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BACKGROUND: Endoscopic endonasal approaches pose the potential risk of olfactory loss. Loss of olfaction and potentially taste can be permanent and greatly affect patients' quality of life. Treatments for olfactory loss have had limited success. Omega-3 supplementation may be a therapeutic option with its effect on wound healing and nerve regeneration.

OBJECTIVE: To evaluate the impact on olfaction in patients treated with omega-3 supplementation following endoscopic skull base tumor resection.

METHODS: In this multi-institutional, prospective, randomized controlled trial, 110 patients with sellar or parasellar tumors undergoing endoscopic resection were randomized to nasal saline irrigations or nasal saline irrigations plus omega-3 supplementation. The University of Pennsylvania Smell Identification Test (UPSIT) was administered preoperatively and at 6 wk, 3 mo, and 6 mo postoperatively.

RESULTS: Eighty-seven patients completed all 6 mo of follow-up (41 control arm, 46 omega-3 arm). At 6 wk postoperatively, 25% of patients in both groups experienced a clinically significant loss in olfaction. At 3 and 6 mo, patients receiving omega-3 demonstrated significantly less persistent olfactory loss compared to patients without supplementation ($P = .02$ and $P = .01$, respectively). After controlling for multiple confounding variables, omega-3 supplementation was found to be protective against olfactory loss (odds ratio [OR] 0.05, 95% CI 0.003-0.81, $P = .03$). Tumor functionality was a significant independent predictor for olfactory loss (OR 32.7, 95% CI 1.15-929.5, $P = .04$).

CONCLUSION: Omega-3 supplementation appears to be protective for the olfactory system during the healing period in patients who undergo endoscopic resection of sellar and parasellar masses.

KEY WORDS: Olfactory loss, Skull base, Pituitary, Endoscopic, Smell, Therapeutics, Sella

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Olfactory dysfunction has a significant impact on quality of life and is associated with loss of taste, depression, social isolation, and increased morbidity and mortality.[1,2] Endoscopic endonasal skull base surgeries can cause both transient and permanent olfactory loss.[3-10] Olfactory nerve fibers traverse the cribriform plate, superior turbinate, superior nasal septum, and middle turbinates, placing them at risk during endonasal surgery.[11] However, the rate of reported postoperative olfactory loss widely varies from 9% to 88%, using both patient self-reported changes and validated olfactory tests. Prior studies also evaluated the elevation of a pedicled nasoseptal mucosal flap for skull base reconstruction as a potential risk factor of postsurgical olfactory loss with conflicting results.[6-8,10]

Therapeutic options for olfactory loss at this time are limited, and furthermore, duration of loss negatively correlates with recovery of

ABBREVIATIONS: **ACTH,** adrenocorticotropic hormone; **CI,** confidence interval; **DHA,** docosahexaenoic acid; **GH,** growth hormone; **OR,** odds ratio; **UPSIT,** University of Pennsylvania Smell Identification Test

olfaction.[12] Currently, olfactory training has the strongest evidence as appropriate therapy for olfactory dysfunction, whereas topical nasal steroid irrigations have also shown promise in treating smell loss due to nonsinonasal disease.[13-16] Numerous investigational drugs and vitamins have been proposed such as zinc, theophylline, and vitamin A, but none have proven their efficacy in randomized controlled trials.[17-19] However, given the olfactory neuroepithelium and both central and peripheral olfactory nerves' inherent ability to regenerate, researchers continue to investigate potential novel treatment options.[20]

Omega-3 polyunsaturated fatty acids are essential components of membrane phospholipids with significant influences on gene expression. Animal models deficient in docosahexaenoic acid (DHA), an essential omega-3 fatty acid and a component of fish oil, show evidence of olfactory dysfunction.[21] In a large cross-sectional study with 5-yr follow-up, older adults with diets rich in fatty acids had reduced odds of having olfactory impairment.[22] In addition to its potential olfactory protective effects, omega-3 supplementation has shown the potential to promote neuroprotection and improve outcomes following peripheral nerve injury.[23] Following traumatic neurological injury, supplementation of omega-3 fatty acids exhibits a therapeutic potential via direct neuroprotective effects as well as increased antioxidant and anti-inflammatory amino acids production.[24] These protective, neuroregenerative, and anti-inflammatory properties of omega-3 may be beneficial in olfactory loss due to peripheral olfactory nerve damage, scar formation, and inflammation following endoscopic skull base surgery.

In this study, we aimed to evaluate the baseline olfactory function in patients with sellar or parasellar masses and conducted a prospective, randomized controlled clinical trial evaluating the effect of omega-3 supplementation on olfactory function in these patients undergoing endoscopic transsphenoidal approaches.

METHODS

This was a multi-institutional, prospective, randomized controlled trial conducted with informed patient consent and approval from all programs' institutional review boards. This trial was registered on clinicaltrials.gov under clinical trial number NCT02529332.

Participants

Patients undergoing endoscopic transsphenoidal resection of either sellar or parasellar masses were eligible for the study. Exclusion criteria were the following: patients less than 18 yr of age, those with a history of liver disease or abnormal liver function tests, specific diabetic patients with contraindication to omega-3 supplementation, history of sinonasal disease, and those on blood thinners aside from nonsteroidal anti-inflammatory drugs and cardioprotective aspirin (81 mg).

Intervention

Baseline olfaction was evaluated during a preoperative visit using the University of Pennsylvania Smell Identification Test (UPSIT), a 40-point "scratch and sniff" forced-choice questionnaire and validated tool for olfaction assessment.[25] Patients were randomized in a 1:1 ratio to either the treatment or control arm, regardless of underlying tumor pathology. All patients underwent endoscopic transsphenoidal surgery for sellar or parasellar masses by experienced rhinology and neurosurgery teams.

All patients were instructed to perform nasal rinses with saline irrigation twice daily postoperatively with instruction handouts provided. Patients in the treatment arm also received omega-3 supplementation (1 capsule of Nature Made Ultra Omega-3 Fish Oil 1400 mg twice daily, which contain 2000 mg of omega-3 total), whereas the control arm was asked to perform nasal saline irrigations postoperatively twice daily but did not take any other supplementation. Subsequent UPSIT olfactory tests were administered at 6 wk, 3 mo, and 6 mo postoperatively.

Outcomes

The primary outcome of this study was to evaluate the impact of olfaction in patients treated with omega-3 supplementation compared to control, as determined by postoperative UPSIT scores at 6 wk, 3 mo, and 6 mo postendoscopic resection of a sella or parasellar mass. A 10% reduction in UPSIT score from baseline has been shown to indicate a clinically significant olfactory loss.[8] Other independent variables including patient demographics (age, gender, smoking status, race, and Charlson index), tumor pathology, tumor size, and treatment strategy (ie, use of a nasoseptal flap and postoperative radiation) were also evaluated.

Randomization and Statistical Analysis

Patients were recruited for the study preoperatively from the outpatient clinic of a rhinologist or neurosurgeon. Simple randomization was performed through a computerized random number generator operated by a nonmedical member of the study team. Participants were assigned a study group with 1:1 allocation (odd number: control arm, even number: treatment arm).

Statistical analyses were performed using Stata statistical software, 13.0 (StataCorp, College Station, Texas). For continuous variables, the Wilcoxon rank-sum test was used. For categorical variables, Fisher's exact test was used. Adjusted odds ratios (OR) with 95% CI were calculated using multivariate logistic regression analysis, adjusted for patient demographics, preoperative UPSIT score, tumor characteristics, and treatment strategies. Using an alpha level of 0.05 and a power of 0.80, our study was powered to detect a clinically significant loss (10% reduction in UPSIT score) across intervention groups with a minimum of 41 patients per group. Anticipating up to a 25% attrition rate, the study aimed to enroll 110 participants (approximately 55 patients per group).

RESULTS

A total of 110 patients were enrolled in this study between September 2014 and April 2018 and were randomized to either control group or the omega-3 treatment group as shown in Figure 1. Twenty-three patients (14 from the control group and 9 from the treatment group) were lost to follow-up during the 6-mo period and, thus, excluded from the analyses. The remaining 87 patients completed all UPSIT evaluations up to 6 mo postoperatively and were included in this study. Demographic data are outlined in Table 1. A total of 46 patients were randomized to receive omega-3 supplementation and saline irrigations

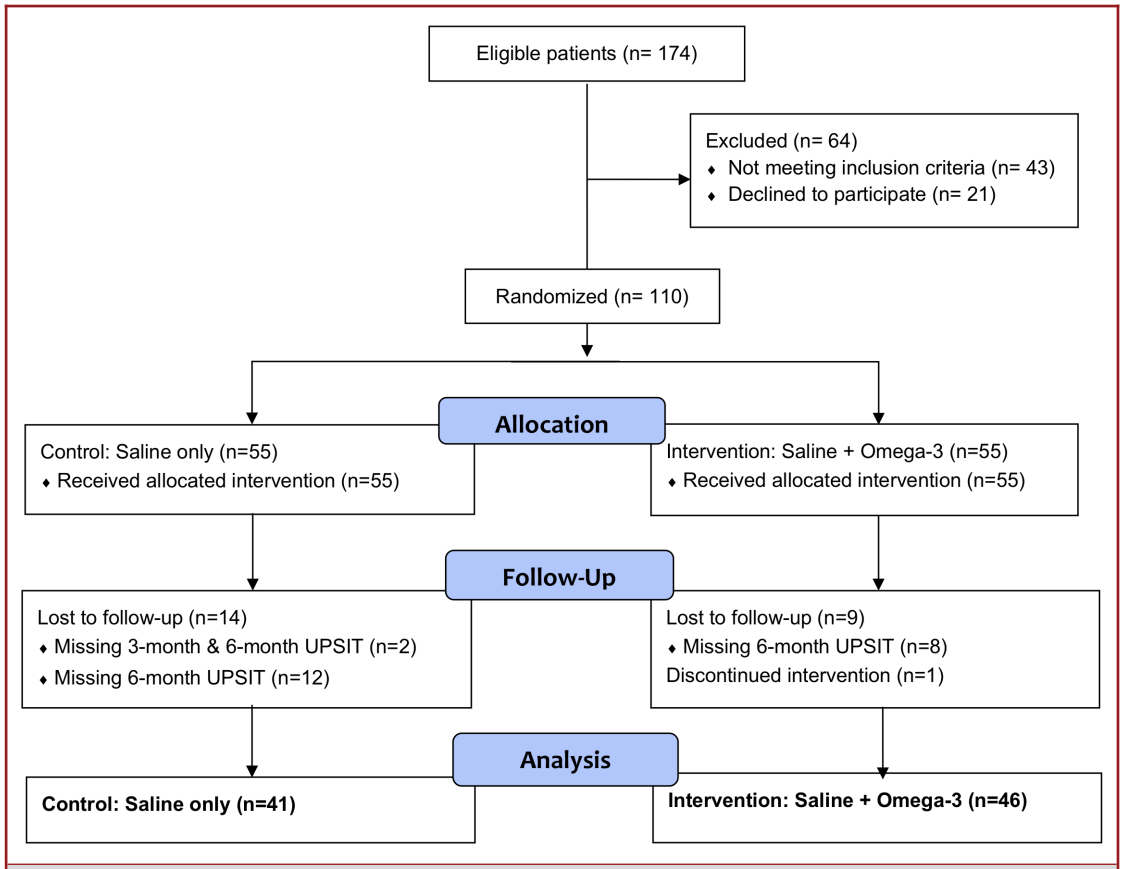

FIGURE 1. *CONSORT flow diagram.*

postoperatively, whereas 41 patients received saline irrigations alone. The mean patient age was 55.9 and 53.6 yr for the treatment and control groups, respectively ($P = .28$). There were no differences in patient characteristics between the 2 groups in terms of age, gender, race, smoking history, and comorbidities as measured by the Charlson index score.

Tumor characteristics were similar between the 2 patient groups. The majority of patients had macroadenomas with suprasellar extension and nonfunctioning pituitary tumors. Figure 2 demonstrates the breakdown of the different tumor types included in this study: nonfunctioning pituitary adenoma (77%), functioning pituitary adenoma (17%), craniopharyngioma (3.4%), and meningioma (2.3%). The meningiomas enrolled were all suprasellar tumors arising from the tuberculum sellae; none were olfactory groove meningiomas.

The average baseline UPSIT score for all patients was 35.0 (out of 40), with no difference between the omega-3 and control groups. Of the 87 patients, 24 (27.6%) had an abnormal baseline UPSIT score (<34 points) preoperatively, all categorized as subclinical losses with mild olfactory dysfunction. No patients had baseline sinonasal disorders including chronic rhinosinusitis or rhinitis, as these diagnoses were exclusion criteria for enrollment. Tumor type and the presence of a functioning adenoma did not contribute to a baseline olfactory dysfunction ($P = .76$).

Clinically significant postoperative olfactory loss was determined to be at least a 10% reduction of UPSIT scores compared to the patient's own preoperative baseline. Patients taking omega-3 supplementation were less likely to have an olfactory loss postendoscopic transsphenoidal surgery compared to patients who were untreated. These results were significant at the 3-mo ($P = .02$) and 6-mo follow-up ($P = .01$, Table 2). At 6 wk postoperatively, all patients had a decrease in olfaction scores; approximately one quarter of patients in both groups experienced a clinically significant olfactory loss. The average UPSIT score was 32.1 points for the omega-3 treatment group compared to 33.4 points for the control group, representing an absolute decrease of 2.72 and 1.85 points, respectively (Figure 3). However, for those treated with omega-3, olfactory function returned to baseline in a significant majority of the patients (93.5%) by 3 mo postoperatively, with no statistical difference in UPSIT scores at either 3 or 6 mo follow-up compared to baseline. In the untreated group, 26.8% of patients continued to demonstrate clinically significant smell

TABLE 1. Descriptive Characteristics

Characteristics	Omega treatment		*P* value
	No (N = 41)	Yes (N = 46)	
Age (yr), mean (SD)	53.6 (10.3)	55.9 (10.0)	.28
Gender			.41
Male (%)	16 (39.0)	22 (47.8)	
Female (%)	25 (61.0)	24 (52.2)	
Race			.77
Caucasian (%)	26 (63.4)	26 (56.5)	
Black (%)	6 (14.6)	5 (10.9)	
Asian (%)	5 (12.2)	8 (17.4)	
Hispanic (%)	4 (9.8)	7 (15.2)	
Smoking			.66
No (%)	38 (92.7)	44 (95.7)	
Yes (%)	3 (7.3)	2 (4.3)	
Charlson Index, mean (SD)	1.2 (1.2)	1.2 (1.4)	.87
Preoperative UPSIT, mean (SD)	35.3 (2.5)	34.8 (2.6)	.44
Suprasellar extension			.40
No (%)	9 (22.0)	6 (13.0)	
Yes (%)	32 (78.0)	40 (87.0)	
Macroadenoma			1.00
No (%)	4 (10.5)	4 (10.0)	
Yes (%)	34 (89.5)	40 (90.0)	
Functioning tumor			1.00
No (%)	31 (81.6)	36 (81.8)	
Yes (%)	7 (18.4)	8 (18.2)	
Tumor volume, mean (SD)	5.2 (3.2)	5.4 (3.5)	.75
Nasoseptal flap			.32
No (%)	24 (58.5)	22 (47.8)	
Yes (%)	17 (41.5)	24 (52.2)	
Postoperative XRT			.60
No (%)	35 (85.4)	41 (89.1)	
Yes (%)	6 (14.6)	5 (10.9)	

SD, standard deviation; UPSIT, University of Pennsylvania Smell Identification Test; XRT, radiation therapy.

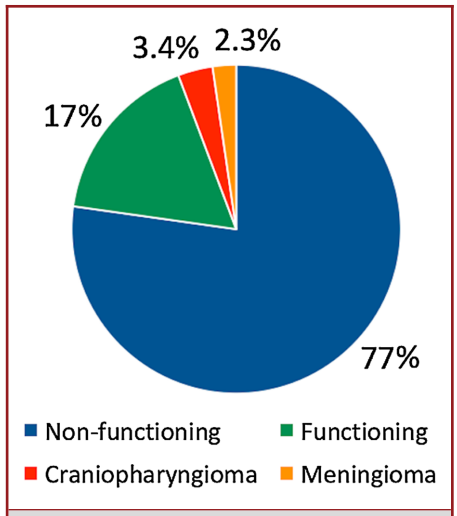

FIGURE 2. *Breakdown of tumor pathology of patients included in this study: nonfunctioning pituitary adenoma, functioning pituitary adenoma, meningioma, and craniopharyngioma.*

loss compared to their baseline at 3 mo postoperatively, which persisted through the 6-mo follow-up.

Prognostic factors contributing to postoperative olfactory loss at 6 mo were evaluated using a multivariate logistic regression model (Table 3). At the 6-mo postoperative time point, there was no difference in inherent patient characteristics between those who had a clinically significant olfactory loss and those who did not. After adjusting for other independent variables, omega-3 supplementation was found to be a protective agent against olfactory loss (OR 0.05, 95% CI 0.003-0.81, $P = .03$).

The presence of a functioning pituitary adenoma was also a significant independent risk factor for postoperative olfactory dysfunction with an OR of 32.7 (95% CI 1.15-929.5). Larger tumor size and suprasellar extension were not risk factors for postoperative olfactory dysfunction. Similarly, the placement of a nasoseptal flap for tumor reconstruction and postoperative radiation did not independently contribute to smell loss.

DISCUSSION

This randomized controlled study prospectively evaluated the effect of endoscopic endonasal surgery on olfaction. Olfactory loss is an important risk of endoscopic skull base surgery, with 26.4% of all patients experiencing postoperative olfactory loss at 6 wk and 13.8% at 6 mo. These rates of olfactory loss are in keeping with previously reported data.[26]

In this study, patients who were randomized to 2000 mg omega-3 supplementation daily were less likely to develop permanent postoperative olfactory loss. Although patients from both groups had similar rates of olfactory dysfunction postoperatively at 6 wk, the return of olfaction in the omega-3 group was noticeable by 3 and 6 mo postoperatively and independent of other tumor variables and patient characteristics.

Olfactory dysfunction postendoscopic skull base tumor resection has been commonly reported, and the rate of smell loss in the literature widely ranges from 9% to 88%. Initial postoperative smell loss is related to both the actual physical obstruction of airflow to the olfactory cleft from crusting and edema, but also to inflammatory injury to the olfactory fibers. Although gross, macroscopic inflammation of the nasal tissues resolves quickly during the healing period, and follow-up clinic endoscopic exams do not demonstrate significant crusting or tissue swelling, we know, from both preclinical and clinical studies investigating other forms of inflammatory olfactory loss, that not only can microscopic inflammation persist, but that olfactory nerves can suffer irreversible damage if the initial inflammatory insult is simply great enough.[27-30] This inflammation-triggered loss is similar in mechanism to the permanent smell loss rhinologists

TABLE 2. A Comparison of Postoperative Changes in Olfaction With or Without Omega-3 Treatment at 1.5, 3, and 6 Months

	Omega-3 treatment								
	No (N = 41)				Yes (N = 46)				
	Postoperative olfactory loss				Postoperative olfactory loss				
	No		Yes		No		Yes		
Month	N	%	N	%	N	%	N	%	*P* value
1.5	31	75.6	10	24.4	33	71.7	13	28.3	.81
3	30	73.2	11	26.8	43	93.5	3	6.5	.02
6	31	75.6	10	24.4	44	95.7	2	4.3	.01

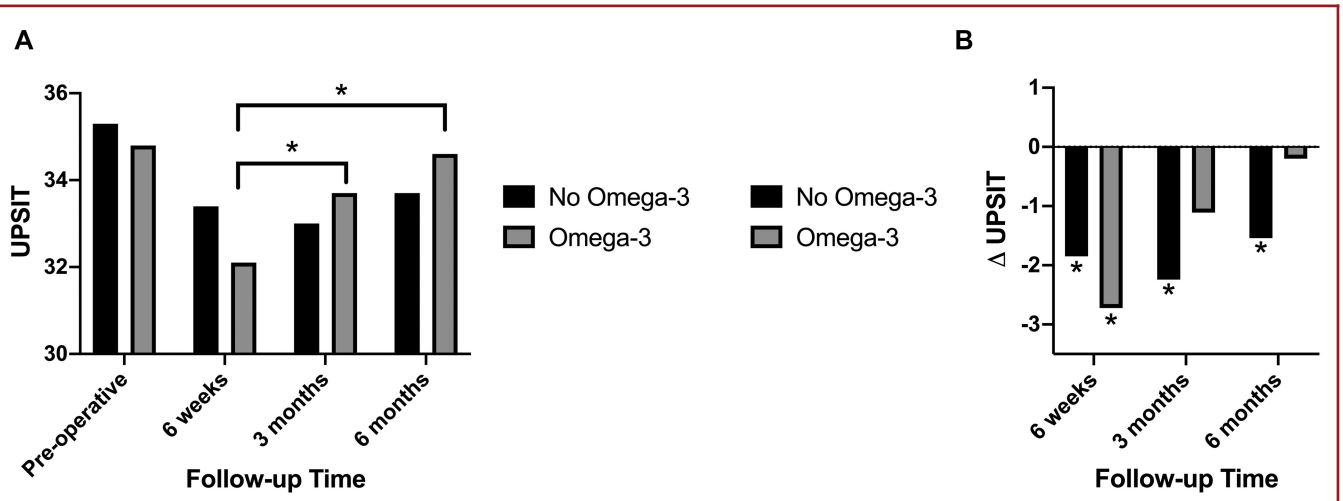

FIGURE 3. *Patients treated with omega-3 regained olfactory function by 6 mo postendoscopic tumor resection.* **A**, *The average UPSIT score of the control and treatment groups at baseline, 6 wk, 3 mo, and 6 mo postoperatively. All patients had a decrease in UPSIT scores at 6 wk of follow-up. Patients treated with omega-3 showed a significant improvement in olfaction at 3 and 6 mo (34.6 points) compared to 6 wk postoperatively (32.1 points, P = .001), whereas the mean UPSIT score for the control group remained unchanged.* **B**, *The average decrease in UPSIT score at each follow-up period compared to baseline. Patients treated with omega-3 only had a statistically significant olfactory loss at the 6-wk postoperative visit, which returned to baseline at the 3 and 6-mo time points.* $^{*}P < .05$.

often see in patients following a simple viral upper respiratory infection.[27]

The exact mechanism of effect of omega-3 supplementation on olfaction has yet to be elucidated, but we hypothesize it may have potential benefits through neural regeneration vs direct anti-inflammatory protective effects on the olfactory mucosa. Omega-3 polyunsaturated fatty acids have been shown to improve synaptic plasticity and neurotransmitter function and display neuroprotective effects.[31] Their anti-inflammatory properties include inhibition of the NF-κB pathway and the production of proresolving mediators that actively reduce inflammation.[32] In animal models, rats deficient in DHA, a type of omega-3, had difficulty in odor-discrimination tasks, highlighting the importance of omega-3 in olfactory function.[21,33] Promisingly, the potential of omega-3 for olfactory improvement has been explored in other clinical pathologies with randomized controlled trials.[34,35] In adults with mild cognitive impairment, a diet of DHA phospholipids resulted in improvements in validated olfactory tests after 12 wk.[34]

There were no patient-reported adverse events associated with taking omega-3 supplementation in our study. Although not regulated, omega-3 is considered a supplement and has the FDA label of "GRAS" or "generally recognized as safe." Patients with diabetes were initially excluded from this study given a possible suggested adverse relationship between the effect of omega-3 fatty acids on the risk of type 2 diabetes unless already placed on the supplement by their primary care providers.[36] However, more recent studies have suggested that omega-3 has both cardiovascular and renal protective effects for patients with diabetes, allowing us to include these patients.[37,38]

TABLE 3. Prognostic Factors Affecting Postoperative Olfactory Loss (With a Clinically Significant Change) at 6 Months

	Univariate analysis			Multivariate analysis[a]	
Characteristics	**No loss (N = 75)**	**Loss (N = 12)**	***P* value**	**Odds ratio (95% CI)**	***P* value**
Age, mean (SD)	55.0 (9.47)	53.7 (14.3)	.79	1.10 (0.96-1.25)	.16
Gender (%)			.22		
Male	35 (46.7)	3 (25.0)		Reference	
Female	40 (53.3)	9 (75.0)		3.71 (0.54-25.4)	.18
Race (%)			.35		
Caucasian	43 (57.3)	9 (75.0)		Reference	
Non-Caucasian	32 (42.7)	3 (25.0)		0.47 (0.06-3.91)	.48
Smoking (%)			.53		
No	71 (94.7)	11 (91.7)		Reference	
Yes	4 (5.3)	1 (8.3)		2.53 (0.06-105)	.63
Charlson index, mean (SD)	1.19 (1.26)	1.42 (1.68)	.89	0.77 (0.34-1.76)	.54
Preoperative UPSIT			.73		
Abnormal (<34)	20 (26.7)	4 (33.3)		Reference	
Normal (>34)	55 (73.3)	8 (66.7)		0.30 (0.04-2.52)	.27
Suprasella (%)			.21		
No	11 (14.7)	4 (33.3)		Reference	
Yes	64 (85.3)	8 (66.7)		0.20 (0.01-3.77)	.28
Macroadenoma (%)			.07		
No	5 (7.04)	3 (27.3)		Reference	
Yes	66 (93.0)	8 (72.7)		1.61 (0.03-77.4)	.81
Functioning tumor (%)			.02		
No	61 (85.9)	6 (54.6)		Reference	
Yes	10 (14.1)	5 (45.5)		32.7 (1.15-929.5)	.04
Tumor volume, mean (SD)	5.24 (2.90)	5.51 (5.53)	.45	1.35 (0.85-2.17)	.20
Nasoseptal flap (%)			.76		
No	39 (52.0)	7 (58.3)		Reference	
Yes	36 (48.0)	5 (41.7)		0.67 (0.11-4.17)	.68
Postoperative XRT (%)			.17		
No	67 (89.3)	9 (75)		Reference	
Yes	8 (10.7)	3 (25)		0.30 (0.03-26.3)	.60
Omega-3 (%)			.01		
No	31 (41.3)	44 (58.7)		Reference	
Yes	10 (83.3)	2 (16.7)		0.05 (0.003-0.81)	.03

SD, standard deviation; UPSIT, University of Pennsylvania Smell Identification Test; XRT, radiation therapy.
[a]All variables in the table were used as covariates for the analysis. For continuous variables (age, Charlson comorbidity index, and tumor volume): odds ratio per 1 unit increment.

Interestingly, 28% of the patients in this study presented with subclinical olfactory dysfunction preoperatively based on their baseline abnormal UPSIT scores. Previous studies have shown similar decreased UPSIT scores at baseline in patients undergoing endoscopic endonasal skull base approaches.[7] These patients were not at greater risk to develop worsening olfaction postoperatively, nor were they associated with larger or functioning tumors at presentation. Noting a patient's smell loss that may be subclinical can be important for counseling as well as clinical documentation preoperatively.

Surprisingly, larger tumors and those with suprasellar extension were not risk factors for postoperative smell loss, despite these tumors requiring extended endoscopic approaches. Previous studies suggested that harvesting of a nasoseptal flap during endoscopic transsphenoidal surgery may contribute to olfactory dysfunction,[5,8] but more recent studies have shown no changes in olfactory function following nasoseptal flap elevation.[3,7,10] In our study, the utilization of a nasoseptal flap was not an independent risk factor for olfactory dysfunction postoperatively. In our study, pedicled nasoseptal flaps were raised starting at the inferior aspect of the natural sphenoid os, extending anteriorly along the nasal septum, and gradually curving superiorly towards skull base after reaching the axilla of the middle turbinate while preserving 1 to 2 cm of mucosa superiorly. This incision pattern allows us to avoid most of the olfactory nerve fibers at risk during flap harvest and thus may explain why nasoseptal flap elevation does not contribute to postsurgical olfactory dysfunction in this study. Furthermore, the authors of this study do not typically resect the middle or superior turbinates, which may also have influenced olfactory outcomes in prior studies.

In our study, we did find that the presence of functioning or secreting pituitary tumors was an independent risk factor for postoperative olfactory loss at 6 mo. These patients did not present with lower baseline UPSIT scores. Previous studies have also shown that patients with functional tumors such as adrenocorticotropic hormone (ACTH) and growth hormone (GH)-secreting adenomas had greater loss of smell postoperatively.[8] In a prospective study, Rotenberg et al[8] also found that patients with ACTH and GH-secreting tumors had a 26% and 32% decline in olfactory scores postoperatively compared to those with nonsecretory tumors (13%). Functional tumors tend to be smaller in size on presentation, but there is a higher degree of inflammation, friability, and hypertrophy of the nasal bones and mucosa that make surgical dissection more complex and impactful to the tissue at that time of surgery. Examples of this can be found in acromegalic patients often needing complex septoplasty as part of the approach, or patients with Cushing's disease presenting with friable, edematous mucosal surfaces at baseline, often leading to susceptibility to bleeding at the slightest touch.

This study sheds light on omega-3 as a promising therapeutic for postoperative induced olfactory dysfunction. It is uncertain whether omega-3 supplementation may be a useful therapeutic in other etiologies of smell loss such as postviral, post-trauma, loss related to sinonasal inflammation, or idiopathic causes, but this would be worth investigating in the future.

Limitations

As a prospective randomized controlled trial evaluating the impact of omega-3 on postoperative olfactory loss, this study was adequately powered to detect a clinically significant difference between groups using objective olfactory outcomes (UPSIT) and represents one of the largest studies of its nature. One limitation of this study was that the control group was not given a placebo pill in addition to the saline irrigations. However, saline nasal irrigations were a novel and complex regimen for most patients undergoing endoscopic skull base surgery, and they were counseled about the mechanism by which this intervention could speed healing and ameliorate symptoms postoperatively, which served as our placebo in itself. It is important to note that, in this study, patients were not specifically advised to undergo olfactory training or perform nasal irrigations with steroids, both of which have recently been shown to improve olfactory dysfunction.[13,14] This is because, at the time of the study protocol development and initial implementation, the positive clinical effect of olfactory training and topical steroid irrigations had not yet been established.

CONCLUSION

In this study, we demonstrate that olfactory dysfunction is an important risk of endoscopic endonasal surgery and almost one third of patients may have olfactory dysfunction at baseline preoperatively. Postendoscopic resection of sellar and suprasellar tumors and supplementation with omega-3 have potential olfactory benefits and may prevent an initial postoperative olfactory loss from becoming permanent.

Disclosures

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article. Dr Patel is a consultant for Medtronic Inc and Stryker; is on the advisory board for Optinose; and has received honorarium from Intersect ENT. Dr Hwang is a consultant for Medtronic Inc, Arrinex, 480 Biomedical, Bioinspire, and Canon. Dr Nayak is a consultant for Medtronic Inc, Olympus America, Cook Medical, and Lannett and is on the advisory board for Sinopsys and Hydravascular. Dr S. K. Wise is a consultant for NeurENT, SinopSys Surgical, and Stryker and is on the advisory board for ALK-Abello and OptiNose. Dr DelGaudio is a consultant for Medtronic and has received grant support from Spirox. Dr Levy has received grant support from Triological Society and National Center for Advancing Translational Sciences of the National Institutes of Health under Award Numbers UL1TR002378 and KL2TR002381; the content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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COMMENT

This article represents the results of the Stanford led multicenter RCT which has studied the effect of Omega-3 supplementation after transnasal endoscopic surgery for seller & parasellar tumors. Analysis of the relatively evenly divided omega-3 and control arms demonstrated better olfactory function at 3 & 6 months post procedure in the omega-3 group.

This is another novel application of the use of Omega-3 supplementation which demonstrates benefit in neurological disorders. As yet the precise mechanism for this remains elusive. A number of noteworthy findings were reported by the authors.

"The presence of a functioning pituitary adenoma was also a significant independent risk factor 128 for postoperative olfactory dysfunction with an odds ratio of 32.7 (95% CI: 1.15-929.5); The study comprised 17% functioning adenomas (n = 15)."

This is interesting as previously functioning adenomas whether micro or macro especially in acromegaly have been reported as being associated with olfactory improvement, though this was with Transnasal microsurgery.[1] The authors nasoseptal flap technique was not independently associated with smell loss though other studies have found it to be a risk factor.

Over all this study represents a novel application of omega-3 supplementation to olfactory function after pituitary surgery. Olfactory dysfunction or loss is a serious risk after endoscopic trans nasal surgery and that appropriate preoperative patient counselling is warranted.

Future studies to assess the performance of omega-3 versus olfactory training with nasal steroids should be encouraged.

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