ORIGINAL CONTRIBUTION

Rhinology, 47, 172-180, 2009

Evaluation of prognostic factors for olfaction in nasal polyposis treated by Endoscopic Sinus Surgery*

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SUMMARY

Aim: *This prospective study aimed to assess treatment outcome on olfaction in patients undergoing Endoscopic Sinus Surgery (ESS) for nasal polyposis, and to evaluate the role of previous sinus surgery and the duration of olfactory deficit as prognostic factors for olfaction improvement.*

Methods: *In total, 116 patients with nasal polyposis who underwent ESS were studied. Olfactory testing was performed using the Sniffin' Sticks test, preoperatively and 1-, 3- and 6-month postoperatively.*

Results: *The values of the composite threshold discrimination identification score were significantly lower in patients with long duration of olfactory deficit and history of previous sinus surgery in all testing sessions. Adjustment for preoperative olfactory measures and all potential confounders revealed that both parameters remained strong independent predictors of normal olfactory function; a successful outcome was more frequent in patients with short duration of olfactory deficit and in patients who had not undergone previous sinus surgeries. However all patients achieved a significant stepwise increment of all indices of olfactory function over time, after ESS.*

Conclusions: *Duration of olfactory deficit and previous sinus surgery presented highly significant predictive value for the short-term outcome of the olfactory function after ESS. However all patients suffering from nasal polyposis will probably improve olfaction significantly in a period up to six months after surgery.*

Key words: olfaction, nasal polyposis, Sniffin' Sticks, olfactory disorders, endoscopic sinus surgery

INTRODUCTION

Nasal polyps are known to be strongly associated with olfactory disorders resistant to treatment [(1)]. Endoscopic Sinus Surgery (ESS) is considered the gold standard for the therapy of nasal polyps persistent to medical treatment, and its successful results have already been described extensively [(2-4)]. Until recently, the evaluation of olfaction was mainly based on each patient's self-reported symptoms and rarely quantitative olfactory tests were performed and used as criterion for improvement, leading thus to criticism of the outcomes claimed. This has probably happened because of lack of simple, fast and reliable methods of olfactory testing in the past. Although several olfactory tests were introduced during the past two decades, only a few of them proved successful, including the University of Pennsylvania Smell Identification Test (UPSIT) [(5)] and a new objective olfactory test developed by Kobal and Hummel [(6)], which became recently commercially available under the name "Sniffin' Sticks". Previous work has already established its test-retest reliability and its validity in comparison with established measures of olfactory sensitivity obtained by the UPSIT [(7)]. Little is known, also, about the factors that predict improvement of olfaction after ESS, despite the increasing importance of outcome evaluation in the determination of specific treatment protocols. The overall success rates of ESS in restoring olfaction in patients with are poorly documented [(8)], too. It has been reported that factors like duration of olfactory dysfunction and previous sinus surgeries for nasal polyps are important predictive factors for the surgical outcome on olfaction [(8-11)].

The aim of the present study was to evaluate the prognostic value of specific parameters, such as duration of the disease

*Received for publication: May 26, 2008; accepted: October 20, 2008

and previous sinus surgery, as independent predictors of the outcome of ESS on the recovery of the olfactory function, in patients suffering from nasal polyposis, using the "Sniffin' Sticks" test. Another goal of our study was to find out the expected values of olfactory function after surgery. The results of this study might prove useful in better counselling of our patients who suffer from nasal polyposis, regarding the likelihood of recovering olfaction after ESS.

MATERIALS AND METHODS

Patients

We studied 116 patients who underwent ESS for nasal polyposis from April 2004 to March 2007 at the Department of Otolaryngology, University Hospital of Alex/polis (Alex/polis, Greece). Diagnosis was made on the basis of history, clinical examination, nasal endoscopy, sinus computerized tomography (CT) scan and olfactory testing. CT scans were graded according to the Lund-Mackay CT scoring system [(12)]. Pre- and post-operative endoscopy was performed using the Malm's grading system [(13)]. According to this, all patients suffered from severe sinonasal polyposis and were classified as stage 3. Additionally, all presented a total score over 16 (average 18, range 17-24) according the Lund-Mackay CT scoring system, as there was bilateral ethmoid disease with involvement of 3 or more dependent sinuses and ostio-meatal complex on each side in all patients.

Data from the history of the subjects were recorded, including age, gender, presence of allergic rhinitis, Samter's triad, prior sinus surgeries, current and past smoking habits, duration of olfactory dysfunction, and presence of other symptoms, such as taste dysfunction. All patients were unsuccessfully treated with maximal medical therapy (antibiotics, oral and nasal steroids) for at least 1 month before surgery. In particular, we provided antibiotics (clarithromycin or amoxicillin/clavulanic acid) for 20 days, oral corticosteroids (50 mg of prednisolone daily for 14 days and then tapered over 10 days) and, finally, topical steroids (nasal spray of budesonide 100 mg) administered intranasally twice daily for 3 weeks. Patients with persistent nasal polyposis underwent ESS, according to the Messerklinger technique [(14,15)] (antrostomy, ethmoidectomy, sphenoidotomy, opening of the frontal sinus) with the use of a microdebrider device.

Post-operatively, treatment included nasal endoscopy and cleaning of crusts and debris, lysis of adhesions and removal of any single polypoid mass at the Department of Otorhinolaryngology at 1-, 3- and 6-month periods. All patients were asked to stop smoking and to rinse their nose with sodium chloride and apply topical steroids (budesonide 100 mg - twice daily) for a 6-month period. Antibiotics were given after surgery if purulent secretion was present (usually clarithromycin 500 mg twice daily for 10 days).

The care of the human subjects for this study was approved by the local Institutional Review Board. All subjects were volunteers and were fully explained the aim, the design and the clinical implications of the study. The investigations were performed in accordance with the principles of the Declaration of Helsinki/HongKong.

Olfactory testing

Identical olfactory tests were performed pre- and post operatively at 1, 3 and 6 months in a bilateral mode, using the "Sniffin' Sticks" test package (Burghardt, Wedel, Germany). The "Sniffin' sticks" test battery included specific tests for odour threshold (OT), odour discrimination (OD) and odour identification (OI).

The OT test was performed with n-butanol, using a 1:2 dilution series with 16 stages and beginning with 4% [(16)]. The test was evaluated using a single-staircase, triple-forced choice procedure. In the suprathreshold OD test, triplets of pens were presented in a randomized order, with two containing the same odorant and the third a different odorant. The patients had to detect which of the three pens smelled differently from the other two. For the OI test 16 odorants were presented in suprathreshold intensity. The examined was asked to identify individual odorants from a list of four descriptors, using a multiple-choice procedure. In all three tests, subjects were blindfolded to avoid visual identification of the odorant-containing pens and the obtained score was an integral, ranging from 0 to 16.

Finally, the results of the three tests were combined to form an overall score called "composite threshold-discrimination-identification score" (TDI) [(7,17)]. TDI represented the sum of the results obtained for OT, OD and OI tests and might prove useful in daily clinical practice as a single indicator of olfactory performance. The TDI score ranged from 0 to 48, with values ≤ 15 considered consistent with anosmia, and values between 16 and 34.5 considered as hyposmia [(18)]. All subjects completed the test. The time needed for the complete examination ranged from 20 to 30 min. Their scores for OT, OD and OI tasks were related to the duration of olfactory symptoms and prior sinus surgeries.

Statistics

Statistical analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS), version 11.0 (SPSS, Inc., Chicago, IL, USA). The normality of continuous variables was tested with the Kolmogorov-Smirnov test. Continuous variables were expressed as mean ± standard deviation and categorical variables were expressed as frequencies and percentages. The chi-square test was used to evaluate any potential association between categorical variables. Student's t-test was used to compare the indices of olfactory function between groups of patients according to the duration of olfactory dysfunction and the history of previous sinus surgery at each time frame. Repeated measures analysis of variance (ANOVA) was used to examine the changes of the indices of olfactory function throughout the follow up time; post hoc analysis was performed using Bonferroni's correction. The

Table 1. Demographic and clinical characteristics of the patients.

	No of patients	Percentage (%)
Gender		
Male	45	38.8
Female	71	61.2
Age		
≤ 35 years	23	19.8
36 – 55 years	59	50.9
> 55 years	34	29.3
Duration of olfactory dysfunction		
≤ 10 years	60	51.7
> 10 years	56	48.3
Samter's disease		
No	98	84.5
Yes	18	15.5
Allergic rhinitis		
No	54	46.6
Yes	62	53.4
Smoking		
No	72	62.1
Yes	44	37.9
Previous surgeries		
No	78	67.2
Yes	38	32.8
Taste disorders		
No	96	82.8
Yes	20	17.2

interaction between duration of olfactory loss or the history of previous sinus surgery and the change of all indices over time was established by two-way analysis of variance. One-way analysis of covariance (ANCOVA) was performed to investigate the effect of the duration of olfactory deficit and the history of previous sinus surgery on the olfactory function 6 months after surgery, adjusting for baseline scores and other potential confounders (gender, age, Samter's triad, smoking, allergic rhinitis and taste disorder). A natural log transformation of the indices of olfactory function was performed, when necessary, to satisfy the assumptions of ANOVA. Marginal homogeneity test was used to determine changes of olfactory function from one measurement to another. Odds ratio (OR) with 95% confidence interval (CI) was estimated as the measure of association of the duration of olfactory deficit and the history of previous sinus surgery with normal olfactory function. All tests were two tailed and statistical significance was considered for p values less than 0.05.

RESULTS

The study group included 116 patients who underwent ESS with a mean age of 47.5 ± 13.1 years (range, 25-78; median age 44 years). Seventy-one (61.2%) of them were females, with a mean age of 45.3 ± 12.8 years and 45 (38.8%) were males, with mean age 49 ± 13.2 years. Ninety-nine (85%) patients were anosmics and 17 (15%) were hyposmics, according to the preoperative quantitative assessment of the olfactory function with the use of Sniffin' Sticks test. Among the anosmic patients 58 (59%) were males and 41 (41%) females, whereas among the hyposmics 13 (76%) were males and 4 (24%) females. Clinical and preoperative data of the patients are presented in Table 1.

The duration of olfactory deficit ranged from 1 to 25 years, with a median duration of 8 years (interquartile range, 3-10 years). Subsequently, patients were classified either as having short or long duration of olfactory deficit, if the duration of the symptoms was ≤ 10 years or > 10 years, respectively. Longer duration of olfactory dysfunction was more frequent in patients aged from 35-55 and > 55 years old compared to patients younger than 35 years old (59.3% and 52.9% vs 13.0%, respectively, p = 0.001). The trend of higher incidence of long duration of olfactory dysfunction in patients having the Samter's triad compared to those without the triad (66.7% vs 44.9%) and in patients with allergic rhinitis compared to those without it (54.8% vs 40.7%) did not reach statistical significance (p = 0.089 and p = 0.130, respectively).

Table 2. Olfactory function (mean values ± SD) of the patients who underwent Endoscopic Sinus Surgery in relation to the duration of olfactory dysfunction.

		Postoperatively			
	Preoperatively	1st month	3rd month	6th month	P value
OT score					0.001*
Olfactory dysfunction ≤10 years	0,58 ± 0,98	4,72 ± 1,76	5,52 ± 1,76	6,33 ± 1,73	<0.001#
Olfactory dysfunction >10 years	0,22 ± 0,60	2,05 ± 2,09	3,30 ± 2,25	3,84 ± 2,45	<0.001#
OD score					0,011*
Olfactory dysfunction ≤10 years	6,86 ± 3,24	11,93 ± 3,22	13,10 ± 2,90	14,38 ± 1,93	<0.001#
Olfactory dysfunction >10 years	3,99 ± 3,28	7,36 ± 4,85	9,82 ± 4,68	11,01 ± 4,96	<0.001#
OI score					0,030*
Olfactory dysfunction ≤10 years	6,02 ± 2,99	11,42 ± 3,10	12,48 ± 2,87	13,68 ± 2,02	<0.001#
Olfactory dysfunction >10 years	3,05 ± 2,90	6,98 ± 4,67	8,83 ± 4,64	9,80 ± 4,81	<0.001#
TDI score					<0,001*
Olfactory dysfunction ≤10 years	13,45 ± 6,86	28,06 ± 7,67	31,10 ± 6,90	34,40 ± 5,34	<0.001#
Olfactory dysfunction >10 years	7,27 ± 6,53	16,39 ± 11,31	21,96 ± 11,34	24,66 ± 11,91	<0.001#

* statistical significance for the interaction between the duration of olfactory dysfunction and the change over time (two-way mixed ANOVA)

\# statistical significance between the different time frames within each group (one-way repeated measures ANOVA).

Table 3. Olfactory function (mean values ± SD) of the patients who underwent Endoscopic Sinus Surgery in relation to the history of prior sinus surgery.

		Postoperatively			
	Preoperatively	1st month	3rd month	6th month	P value
OT score					<0.001*
No prior sinus surgery	0,53 ± 0,87	4,24 ± 2,02	5,16 ± 1,82	5,95 ± 1,84	<0.001#
prior sinus surgery	0,16 ± 0,68	1,78 ± 2,08	2,99 ± 2,47	3,43 ± 2,66	<0.001#
OD score					0,002*
No prior sinus surgery	6,47 ± 3,18	11,46 ± 3,31	12,80 ± 3,06	14,10 ± 2,74	<0.001#
prior sinus surgery	3,42 ± 3,40	6,16 ± 5,07	8,89 ± 4,94	10,00 ± 4,91	<0.001#
OI score					<0.001*
No prior sinus surgery	5,51 ± 2,94	10,98 ± 3,19	12,20 ± 3,00	13,33 ± 2,70	<0.001#
prior sinus surgery	2,68 ± 3,17	5,79 ± 4,85	7,68 ± 4,74	8,68 ± 4,75	<0.001#
TDI score					<0.001*
No prior sinus surgery	12,51 ± 6,66	26,67 ± 8,08	30,16 ± 7,34	33,39 ± 6,91	<0.001#
prior sinus surgery	6,26 ± 7,01	13,72 ± 11,79	19,57 ± 11,96	22,12 ± 11,98	<0.001#

* statistical significance for the interaction between the history of prior sinus surgery and the change over time (two-way mixed ANOVA)
\# statistical significance between the different time frames within each group (one-way repeated measures ANOVA).

Thirty-eight (32.8%) of patients had a history of previous sinus surgery. All patients had been operated according to the Messerklinger technique. The incidence of previous sinus surgery was significantly higher in females than in males (44.4% vs 25.4%, $p = 0.033$), in patients having the Samter's triad than in those without the triad (66.7% vs 26.5%, $p = 0.001$), in patients with allergic rhinitis than in those without it (46.8% vs 16.7%, $p = 0.001$) and in patients with long duration of olfactory deficit than in patients with shorter duration (53.6% vs 13.3%, $p < 0.001$).

Duration of Olfactory Deficit

The pre- and post- operative values of all indices of olfactory function in relation to duration of olfactory dysfunction (≤ 10 years vs > 10 years) are shown in Table 2. One-way repeated measures ANOVA showed a statistically significant increment of TDI score over time in both patients with short duration of olfactory dysfunction ($p < 0.001$) and patients with long duration of olfactory dysfunction ($p < 0.001$). Post hoc analysis, using Bonferonni's adjustment for the number of comparisons, was performed next; TDI score exhibited highly significant elevation of 108.6% in patients with short duration of olfactory loss and of 125.4% in patients with longer duration (both $p < 0.001$) on the 1st post-operative month. Smaller but statistically significant improvements of TDI score were observed on the 3rd (10.8% in patients with short duration of olfactory deficit and 34.0% in patients with a long duration of olfactory deficit; both $p < 0.001$) and 6th postoperative month (10.6% in patients with short duration of olfactory deficit and 12.3% in patients with long duration of olfactory deficit; both $p < 0.001$, Figure 1). Similar changes over time of OT, OD and OI scores were observed in both patients with short (all three $p < 0.001$) and long duration of olfactory dysfunction (all three $p < 0.001$).

The improvement over time of all indices of olfactory function was not similar between patients with short or long duration of olfactory loss, since the two-way mixed ANOVA showed that the interaction between the duration of olfactory loss and the change over time was statistically significant for odour threshold ($p < 0.001$), odour discrimination ($p = 0.011$), odour identification ($p = 0.030$) tests and for the overall TDI score ($p < 0.001$; Table 2). Regarding to TDI score, it was increased more dramatically, especially during the 1st month after the surgery, in patients with short duration of olfactory loss, with a mean increase of 2.9/month versus 2.6/month in patients with long duration of olfactory loss; overall, patients with long duration of olfactory deficit demonstrated a significantly smaller increase of the TDI score during the post-operative follow-up when compared to patients with short duration of olfactory deficit (17.39 ± 8.80 vs 20.94 ± 6.30, $p = 0.015$).

When the TDI score was compared between patients with short (≤ 10 years) and long (> 10 years) duration of olfactory deficit, it was found that patients with longer duration exhibited highly significant lower scores compared to patients with

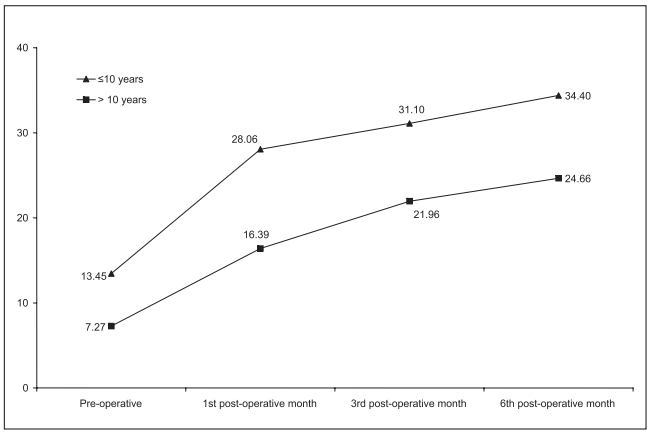

Figure 1. Olfactory function expressed as the mean TDI score of the 116 patients who underwent Endoscopic Sinus Surgery in relation to the duration of olfactory dysfunction. TDI score significantly stepwise improved in both groups (both $p < 0.001$), with a similar pattern between patients (p value for interaction < 0.001).

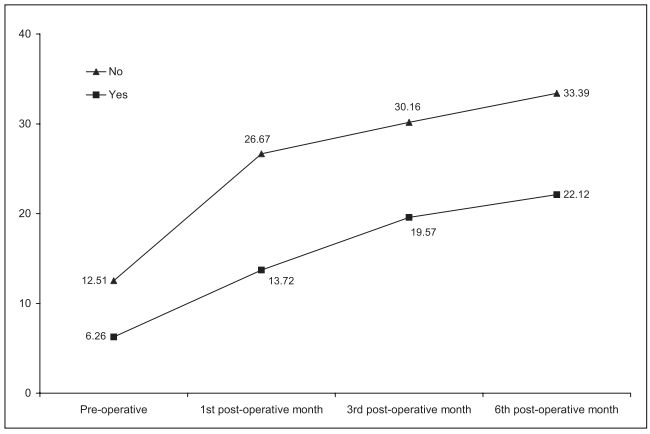

Figure 2. Olfactory function expressed as the mean TDI score of the 116 patients who underwent Endoscopic Sinus Surgery in relation to previous sinus surgeries. TDI score significantly stepwise improved in both groups (both $p < 0.001$), with a similar pattern between patients (p value for interaction < 0.001).

shorter duration of the olfactory symptoms in all time frames (all $p < 0.001$); odour threshold ($p = 0.020$ for pre-operative scores and $p < 0.001$ for the three post-operative time frames), discrimination (all $p < 0.001$) and identification (all $p < 0.001$) scores showed a similar trend between these two groups of patients in all time frames.

Previous Sinus Surgeries

The pre- and post-operative values of all indices of olfactory function in relation to previous sinus surgery are shown in Table 3. One-way repeated measures ANOVA showed a statistically significant stepwise increment of TDI score over time in both patients without previous sinus surgery ($p < 0.001$) and in patients with previous sinus surgery ($p < 0.001$). Post hoc analysis, using Bonferonni's adjustment for the number of comparisons, was performed next; TDI score exhibited highly significant elevation of 113.2% in patients without previous sinus surgery and of 119.2% in patients with previous sinus surgery (both $p < 0.001$) on the 1st postoperative month. Smaller but statistically significant improvements of TDI score were observed on the 3rd month after the surgery (13.1% in patients without previous sinus surgery and 42.6% in patients with previous sinus surgery; both $p < 0.001$). On the 6th postoperative month, whereas TDI score continued to increase in patients without previous sinus surgery (10.7%, $p < 0.001$), it remained approximately at the same level in patients with previous sinus surgery ($p = 0.118$, Figure 2). Similar changes over time of OT, OD and OI scores were observed in patients without previous sinus surgery (all three $p < 0.001$) and in patients with previous sinus surgery (all three $p < 0.001$). In particular, patients without previous sinus surgeries showed a statistically significant stepwise increment at all three post-operative examinations over time (all $p < 0.001$); on the other hand, in patients with previous sinus surgery these indices continued to increase until the 3rd month after the surgery, but they didn't change after that ($p = 0.192$ for OT; $p = 0.194$ for OD and $p = 0.141$ for OI).

Consequently, the improvement over time of olfactory function was not similar between patients with or without previous sinus surgeries, as it was disclosed by two-way mixed ANOVA, which showed a statistically significant interaction between the presence of previous sinus surgery and the change of TDI score over time ($p < 0.001$) (Table 3). In this regard, TDI score was increased more dramatically in patients without previous sinus surgery, with a mean increase of 2.9/month versus 2.4/month in patients with previous sinus surgery; overall, patients with previous sinus surgery demonstrated a significantly smaller increase of the TDI score during the post-operative follow-up when compared to patients without previous sinus surgery (15.86 ± 8.69 vs 20.87 ± 6.77, $p = 0.003$). The negative effect of previous sinus surgery on the course of the post-operative recovery was reflected on all olfactory examinations in a statistically significant extent (OT: $p < 0.001$, OD: $p = 0.002$, OI: $p < 0.001$).

When the TDI score was compared between patients with or without previous sinus surgery, it was found that patients with previous sinus surgery performed significantly worse than patients without previous sinus surgery in all time frames (all $p < 0.001$); OT ($p = 0.015$ for pre-operative scores and $p < 0.001$ for the three post-operative time frames), OD (all $p < 0.001$) and OI (all $p < 0.001$) scores showed a similar trend between these two groups of patients in all time frames.

Consequently, we considered as an outcome of interest the olfactory function of patients 6 months after the surgery. After adjustment for baseline (preoperatively) TDI score and all other potential confounders as well, analysis of covariance showed that the final TDI score on the 6th postoperative month was significantly lower in the group of patients with long (> 10 years) duration of olfactory loss (adjusted mean value ± standard error; 27.16 ± 1.06 vs 32.06 ± 1.02, $p = 0.017$) and in the group of patients with previous sinus surgery (25.29 ± 1.26 vs 31.84 ± 0.85, $p = 0.017$). The independent negative effect of longer duration of olfactory deficit and the presence of previous sinus surgery on the course of the final recovery was reflected on all olfactory examinations in a statistically significant extent (OT: $p < 0.001$ and $p = 0.044$, OD: $p = 0.097$ and $p = 0.036$, OI: $p = 0.027$ and $p = 0.007$, respectively).

In the sequence, we considered the duration of olfactory loss as a continuous variable (in years) and we examined the relationship between the duration of olfactory deficit and the final TDI score on the 6th postoperative month, controlling for baseline TDI score and all other potential confounders. There was a statistically significant negative correlation between the duration of olfactory deficit and the final TDI score, only when the duration of olfactory deficit was ≤ 10 years ($r = -0.416$, $p = 0.001$) and not greater than 10 years ($r = -0.138$, $p = 0.314$). In particular, for every one-year

Table 4. Olfactory function (anosmia=A, hyposmia=H, or normosmia=N) of our population preoperatively and 1, 3 and 6 months after FESS.

		Short duration of olfactory dysfunction (n=60)	Long duration of olfactory dysfunction (n=56)	Without history of PSS (n=78)	With history of PSS (n=38)
Pre-operatively	A	48 (80)	51 (91)	62 (80)	37 (98)
	H	12 (20)	5 (9)	16 (20)	1 (2)
	N	0	0	0	0
1 month post-operatively	A	5 (8)	26 (46)	8 (10)	23 (61)
	H	53 (88)	28 (50)	66 (85)	15 (39)
	N	2 (4)	2 (4)	4 (5)	0
3 months post-operatively	A	2 (4)	19 (34)	4 (5)	17 (45)
	H	40 (66)	35 (62)	56 (72)	19 (50)
	N	18 (30)	2 (4)	18 (23)	2 (5)
6 months post-operatively	A	0	15 (27)	2 (3)	13 (34)
	H	26 (43)	30 (53)	36 (46)	20 (53)
	N	34 (57)	11 (20)	40 (51)	5 (13)

Note: Data are number of subjects and percentage (%); PSS, previous sinus surgery.

increase of the duration of olfactory loss the TDI score on the 6th postoperative month reduces by 1.65 (95% CI = −2.73 to −0.57; p = 0.003) until the first 10 years of the olfactory deficit, and it reduces only by 0.22 (95% CI = −0.33 to 0.50; p = 0.542) for duration of olfactory deficit more than 10 years.

Based on the overall TDI score, patients' olfactory function was categorized as anosmia (TDI score < 15), hyposmia (TDI score from 16 to 34.5) and normal olfactory function (TDI score > 34.5) [18]. The distribution of patients in these three categories of olfactory function in relation to the duration of olfactory dysfunction and previous sinus surgery are shown in Table 4. Marginal homogeneity test showed a statistically significant improvement of olfactory function from one measurement to another in patients with short duration of olfactory dysfunction (all p < 0.001), patients with long duration of olfactory dysfunction (all p < 0.010) and in patients without previous sinus surgery (all p < 0.001). On the contrary, the olfactory function of patients with history of previous sinus surgery significantly improved at the 1st and 3rd post-operative month (p < 0.001 and p = 0.005, respectively), but no significant change was observed at the 6th month (p = 0.071 compared to 3rd month). The percentage of normal olfactory performance at the 6-month follow-up was higher for patients with short duration of olfactory deficit compared to longer duration (56.7% vs 19.6%, p < 0.001; OR = 5.35, 95% CI = 2.32 to 12.31) and for new patients compared to patients with previous sinus surgery (51.3% vs 13.2%, p < 0.001; OR = 6.94, 95% CI = 2.45 to 19.63). Multivariate logistic regression analysis adjusting for all major confounders revealed that both duration of olfactory deficit (p = 0.050) and previous sinus surgery (p = 0.045) remained strong independent predictors of normal olfactory function; a successful outcome was 2.6 times more common in patients with short duration of olfactory deficit than in patients with longer duration (aOR = 2.60, 95% CI = 1.00 to 6.77) and 3 times more common in new patients than in patients with previous sinus surgery (aOR = 3.06, 95% CI = 1.11 to 9.67).

DISCUSSION

The present study described the post-operative course of olfactory function in patients with severe nasal polyposis after ESS and explored the correlation and predictive ability of the above factors, on the rehabilitation of the olfactory function. We focused on specific prognostic factors, including the duration of olfactory deficit and previous sinus surgery, which have not been quantitatively discussed. We used an objective quantitative method of assessment of the olfactory function, the Sniffin' sticks test, because the evaluation of the olfactory function based only on each patient's self-reported symptoms may lead to unreliable results, since it has been reported that many patients with nasal polyps are not aware of their exact smell deficits [19]. We performed olfactory testing at 1, 3 and 6 months after ESS, and explored the predictive value of these factors on the final outcome on olfaction, as well as their correlation. The end-point testing session of 6 months was selected because it corresponds to the end of the major tissue remodeling changes inside the lamina propria [20]. We also examined various other parameters, such as demographic data of the patients, the presence of allergic rhinitis, Samter's triad, smoking habits and taste disorders.

We found that in general, all patients independently of their pre-operative clinical characteristics achieved a similar statistically significant stepwise increment of TDI score over time, especially at the 1-month postoperative measurement. Preoperative evaluation of the olfaction showed that patients with a long duration of olfactory deficit and history of previous sinus surgery presented with worse olfactory measures, owed probably to the negative effect of polyps preventing neural signal generation and probably in olfactory mucosa degeneration. However, all groups of patients on average improved significantly the olfactory function after ESS. This was evident in all the olfactory tests of the Sniffin' Sticks (OT, OI, OD and TDI). Improvement rates were higher during the first month after ESS, but this tendency continued up to 6 months after surgery in both groups.

More specifically, according to the duration of olfactory loss, patients with duration of symptoms less than 10 years, presented higher improvement rates on their olfactory rehabilitation over time than patients with a longer duration of olfactory deficit. Thus, a total of 56.7% of the patients with a short course of olfactory symptoms achieved normal olfactory function, in comparison with a total of 19.6% of the patients with duration of olfactory deficit exceeding 10 years. Analyzing the TDI score of the olfactory function 6 months after surgery, after adjustment for baseline (preoperative) TDI score and all other potential confounders as well, we found that the effect of duration of olfactory loss was statistically significant. Similarly, duration of symptom-related differences in the adjusted odour threshold, discrimination and identification scores of the 6th postoperative month were found. Consequently, better results regarding the olfactory function in patients with short duration of olfactory deficit after ESS should be expected. It appears thus, that duration of olfactory loss is a strong predictive factor for the objective outcome of ESS on olfaction, especially in the short-term period after ESS. It appears that the limit of 10 years of symptoms is critical, because patients operated before this time period, may present improvement of the olfactory function, albeit negatively correlated with the duration of symptoms. Patients with duration of symptoms exceeding 10 years are not expected to improve.

Additionally, we found that although the majority of patients were anosmic preoperatively, there was no anosmic patient among those with duration of olfactory loss less than 10 years. On the other hand, a total of 27% of patients with a long duration of olfactory symptoms remained anosmic 6 months after surgery. Improvement of olfactory function from one testing session the next was statistically significant in both patient groups. Patients with duration of olfactory loss less than 10 years yielded an odds ratio of normal olfactory function of only 5.4 (95% CI = 2.3-12.3) compared to those with a duration of olfactory loss exceeding 10 years. This finding supports the great importance of early diagnosis and treatment of sinonasal disorders, to obtain the best therapeutic result. According to various studies, the duration of the olfactory deficit was also found to exert a strong negative impact on olfactory rehabilitation after ESS [2,3,8,19,21-23]. However, Sobol et al. [24] found that the severity of disease as expressed by the extent of disease and severity and duration of symptoms did not significantly affect outcome at 6-month follow-up but only at 12-month follow-up.

According to history of previous sinus surgery, patients with positive history presented lower improvement rates on their olfactory function post-operatively than patients who underwent ESS for the first time. It was found that on the 6th post-operative month, a total of 51.3% of the patients operated for the first time presented with normal olfactory function, in comparison with 13.2% of the patients who had a history of previous sinus surgery. Furthermore, in order to find out the prognostic value of previous sinus surgery as an independent factor, we correlated this parameter with the final postoperative outcome on the olfactory function, 6 months after surgery. Analyzing the TDI score of the olfactory function 6 months after surgery, after adjustment for baseline (preoperative) TDI score and all other potential confounders as well, we found that the effect of previous sinus surgery was statistically significant, too. Also, differences related to previous sinus surgery in all types of olfactory testing on the 6th post-operative month were found. Consequently, better results regarding the olfactory function in patients with no history of previous sinus surgery after ESS should be expected. It appears thus, that history of previous sinus surgery has a strong negative predictive value as well on the objective outcome of ESS on olfaction.
Additionally, we found that although the majority of patients were anosmic preoperatively, only 3% of the patients who were operated for the first time, in contrast to the 34% of patients with previous sinus surgeries remained anosmic 6 months after surgery. This emphasizes the need for a successful ESS technique and adequate post-operative care. Improvement of olfactory function from one measurement to another in both groups of patients was statistically significant. Patients without previous sinus surgery yielded an odds ratio of normal olfactory function of 6.9 (95% CI = 2.5-19.6) compared to those with a history of previous sinus surgery. Other studies also proved that history of previous sinus surgery is strongly associated with poorer results after ESS [2,19,21,24-26]. Sobol et al. [24] found that previous sinus surgery was a negative significant indicator of poorer outcome at 12-month follow-up, although there was not any significant importance of this parameter 6 months after surgery. Similarly, Senior et al. [3] found that, on late follow-up (7.8 years), symptomatic improvement in non revision patients was better than in patients submitted to revision surgery, and this finding was particularly prominent with respect to change in the sense of smell. The authors, however, did not notice any significant difference in overall symptom improvement on initial follow-up (1.5 years) between the two groups of patients. Also, according to various studies there was a significant trend toward long duration of olfactory disturbances resulting in increased need for revision surgeries [2,3,23-24].

Improvement of the olfactory function is probably owed to a combination of appropriate surgical technique and adequate and consistent treatment postoperatively. The surgeon should apply the least invasive surgical procedure that does not cause significant damage to the olfactory neuroepithelium, with minimal intraoperative bleeding. We have adopted the Messerklinger technique, because the disease may be followed, preserving the integrity of the middle nasal turbinate, with the exception of cases with concha bullosa, and protecting thus, the olfactory neuroepithelium.

According to this study, patients with a short duration of olfactory deficit who were operated for the first time are nearly 2.6

and 3 times more likely to reverse olfaction after ESS in comparison with persons who presented a duration of olfactory loss over 10 years and had a positive history of previous sinus surgery, as we can see from the TDI score. However all are candidates for ESS as concerns the olfactory function. The improvement in olfactory function after ESS may be attributed to the re-opening of nasal passages after the surgical removal of nasal polyps [26], the removal of the pathological mucosa in the ethmoid cells [27] and appropriate postoperative care [28]. The accessibility to the olfactory cleft as well as the absence of postoperative edema, granulation and scar tissues in the olfactory region may be important factors for recovery [25]. It should be mentioned, however, that the duration of olfactory deficit is a strong negative predictive factor because olfactory deficit may reflect the severity of the disease. On this ground, olfaction impairment could be a useful diagnostic tool for estimating nasal polyposis. Early diagnosis and appropriate treatment should prevent nasal polyposis to involve the olfactory mucosa, resulting in olfactory deficit. Also patients with a history of previous sinus surgery are poorer candidates than patients not submitted to previous nasal surgery, probably owed to injury of the olfactory epithelium during the surgical procedure, because revision ESS for nasal polyps carries technical risks due to the loss of surgical landmarks. This explains the higher rate of complications in revision surgery [13,14,24]. Another possible reason is the presence of adhesions around the cribriform plate in patients with previous sinus surgery, hindering the local tissues from adequate recovery [19]. This could, also, explain why many patients, without any opacification in computerized tomography post-operatively, remain anosmic or hyposmic, without any improvement in olfaction, although improvement in other symptoms, such as nasal obstruction, headaches, or nasal drainage is evident. The strong correlation between the duration of olfactory loss, as it reflects the severity of the disease, and the need for revision surgeries is explained by the fact that polyps have been shown to be refractory with a tendency to recur despite successful surgical intervention [22,29]. Our results indicate that appropriate surgical treatment in an early stage of the disease lessens the possibility the pathology to recur and a new sinus surgery to be needed.

It appears, thus, that although only short-term results were available from the present study and longer follow-up is needed, our findings may be useful for allowing us to counsel our patients more accurately on the likelihood of objective improvement of their olfactory function after ESS.

In conclusion we found that following ESS and careful postoperative follow-up, patients present a continuous olfactory improvement over time. Duration of olfactory loss and history of previous sinus surgery were found to be independently and significantly predictive of the objective outcome on olfactory rehabilitation at six months after ESS, irrespective to their preoperative clinical characteristics. Finally, we provided expected values of olfactory function in 3 time periods after surgery, useful for better counseling our patients for the possibility of improving or fully restoring olfactory function after ESS, with the use of an objective method of testing olfaction.

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