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Usefulness of our proposed olfactory scoring system during endoscopic sinus surgery in patients with chronic rhinosinusitis

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Abstract

Introduction The primary aim of the current study was to examine the usefulness of our proposed olfactory scoring system in chronic rhinosinusitis (CRS) patients with olfactory disorders ($n=213$) receiving endoscopic sinus surgery (ESS).

Materials and methods Analyzed patients were divided into two groups: an eosinophilic CRS (ECRS) group ($n=153$); and a non-ECRS group ($n=60$). The T&T recognition threshold test was used to evaluate olfaction at baseline and at 3 and 12 months after ESS. Patients with mean recognition threshold <2.0 at 3 or 12 months or with a decrease of ≥ 1.0 as compared with baseline were defined as showing clinical improvement. We scored mucosal conditions as normal (0 points), edema (1 point), and polyp (2 points) at the canopy of olfactory cleft (OC), middle and superior turbinates, superior nasal meatus, and sphenoethmoidal recess during ESS. The total score of OCs (SOCs) was calculated (range 0–20 points). We compared SOCs between ECRS and non-ECRS groups. Factors related to olfactory improvement were also investigated using uni- and multivariate analyses.

Results SOCs in the ECRS and non-ECRS groups showed significant correlations with mean recognition thresholds at baseline and at 3 and 12 months. In the multivariate analysis for predicting improvement of mean recognition threshold, lower SOCs were significantly associated with olfactory improvement factors at 3 and 12 months postoperatively in the ECRS group.

Conclusion SOCs appears promising for estimating olfactory prognosis after ESS in CRS patients.

Keywords Olfactory cleft · Scoring system · Endoscopic sinus surgery · Chronic rhinosinusitis · Olfactory disorder

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Abbreviations

CRS	Chronic rhinosinusitis
ESS	Endoscopic sinus surgery
CT	Computed tomography
SD	Standard deviation
ECRS	Eosinophilic chronic rhinosinusitis
OC	Olfactory cleft
SOC	Score of olfactory clefts
OR	Odds ratio

Introduction

Olfactory impairment is a common complaint and is recognized in 60–80% of patients with chronic rhinosinusitis (CRS) [1–3]. Olfactory dysfunction is likely due to a combination of mechanical obstruction from edematous mucosa or polyposis (preventing smell molecules from reaching the olfactory nerve) and injury to the olfactory neuroepithelium

caused by chronic inflammation, which can result in sensorineural disorders and inhibition of neo-genesis of the olfactory nerve over prolonged periods [1, 2, 4]. Clinically, focusing on olfactory dysfunction is important for the treatment of CRS. In particular, olfactory function at the region where the olfactory nerve is mainly distributed should be evaluated.

The treatment method for patients with CRS includes initial medical management prior to the consideration of surgery [5–7]. In Japan, the number of cases of eosinophilic CRS (ECRS) has been increasing [6]. ECRS patients suffer from olfactory impairment in the early phase. Medical management includes macrolide antibiotics and corticosteroid therapy [5–7]. Among CRS patients refractory to medical management, endoscopic sinus surgery (ESS) can achieve olfactory improvement [8–11]. However, it is not possible to achieve olfactory improvement some cases receiving ESS. Age, disease duration, presence of asthma, presence of polyp at the olfactory cleft (OC), ethmoid sinus lesions and higher levels of non-specific immunoglobulin (Ig)E have been reported as predictors linked to outcomes for olfactory function [3, 12–15].

Olfactory epithelium in humans is mainly located in the OC, and is widely distributed around the superior turbinate, middle turbinate, and nasal septum [16–19]. In Japan, the average areas of OC in adult individuals have reported as: 3.20 cm^2 (right side) and 2.84 cm^2 (left side) laterally, and 1.10 cm^2 (right side) and 1.15 cm^2 (left side) medially, respectively [20–22]. Thus, to evaluate olfactory function, precise assessment according to sites in the OC will be required [23]. Attempts to quantify the severity of inflammatory lesions in CRS patients and to evaluate the relationship with olfactory impairment have revolved around computed tomography (CT) staging. However, the most commonly used CT scoring system focuses on the paranasal sinuses alone and does not assess disease severity at the OC [24–26].

Since 1996, we have routinely assessed olfactory function in CRS patients receiving ESS using an olfactory scoring system we developed focusing on macroscopic findings at the OC during surgery. The primary aim of the current study was to examine the utility of our proposed scoring system for olfactory function in CRS patients receiving ESS.

Patients and methods

Patients

Between June 2008 and September 2016, a total of 990 CRS patients received ESS in our department. Of these, 213 patients with preoperative mean recognition threshold > 2.2 as assessed by T&T olfactometer (Takasago Industry, Tokyo, Japan) were analyzed (mean ± standard deviation (SD) age = 53.4 ± 14.2 years; 132 males, 81 females). Categorization of CRS into subgroups may harbor essential implications for the treatment and expected long-term clinical outcomes [27]. Thus, based on the diagnostic criteria from the Japanese Epidemiological Survey of Refractory Eosinophilic Chronic Rhinosinusitis Study [28], analyzed subjects were divided into two groups: an ECRS group ($n = 163$; mean ± SD age = 53.4 ± 16.4 years; 91 males, 62 females), and a non-ECRS group ($n = 50$, mean ± SD age = 55.3 ± 13.1 years; 41 males, 19 females).

The ethics committee meeting in our institution approved all study protocols (approval number, 1512) and this study strictly followed all regulations of the Declaration of Helsinki.

Our proposed scoring system for olfactory function and study endpoints

In our department, we have routinely focused on five relevant olfactory nerve distribution areas at OCs for patients receiving ESS: (1) canopy of the OC; (2) middle turbinate; (3) superior turbinate; (4) superior meatus; and (5) sphenoethmoidal recess. We scored each area by following macroscopic mucosal findings: normal, 0 points; edema, 1 point; and polyp, 2 points. The sum of points in the five areas on both sides (score of OCs, SOCs) was calculated, ranging from 0 to 20 points (Fig. 1). SOCs in this study were determined through discussion with three experienced, expert rhinologists during ESS.

We retrospectively examined the relationship between SOCs and olfactory disorder. We also compared baseline characteristics (laboratory data, SOCs, olfactory tests, respiratory function and presence of underlying diseases such as asthma, etc.). Furthermore, variables related to the

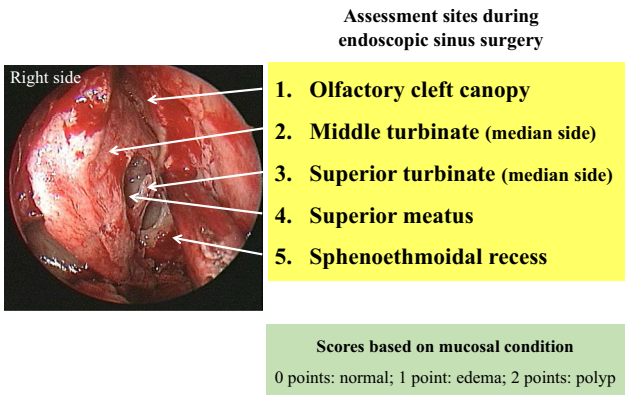

Fig. 1 Our proposed olfactory scoring system, focusing on macroscopic findings during ESS. Score of olfactory clefts (SOCs) indicates the sum of scores based on mucosal condition at the above five assessment sites on both sides (range 0–20 points)

improvement of mean recognition thresholds after ESS were investigated using uni- and multivariate analyses.

Olfactory tests

Olfactory tests were performed using the T&T olfactometer and intravenous olfaction test, both of which are covered by health insurance and are commonly used for olfactory examination in Japan.

The T&T olfactory test consists of five odorants: (A) b-phenyl ethyl alcohol, which smells like a rose; (B) methyl cyclopentenolone, which smells like burning; (C) iso-valeric acid, which smells like sweat; (D) g-undecalactone, which smells like fruit; and (E) skatole, which smells like garbage. Recognition thresholds were determined for each odorant. The mean value for these five recognition thresholds was defined as olfactometry function [29].

Postoperative olfactory function was evaluated at 3 and 12 months using the T&T olfactometer. Postoperative olfactory changes were determined by subtraction (ΔT&T = preoperative mean recognition threshold—postoperative mean recognition threshold) as reported in a previous study [3]. Patients were defined as two groups: "improvement group", when postoperative mean recognition threshold was ≤ 2.0, and/or when ΔT&T was ≥ 1.0; and "unchanged group", when the finding was other than those described above.

The intravenous olfactory test has also seen wide use for assessing olfactory function [30]. The intravenous olfactory test was performed using prosultiamine, providing a garlic or onion smell (alinamin; Takeda Pharmaceutical Company, Osaka, Japan). A dose of 10 mg (2 ml) of alinamin was injected into an antecubital vein at a constant rate over 20 s. Patients who did and did not recognize the alinamin odor were categorized to the response and non-response groups.

Respiratory function test

Patients with respiratory disorder were defined as those with following conditions as assessed by spirometry: (1) percentage predicted vital capacity < 80%; and/or (2) percentage predicted forced expiratory volume in 1.0 s < 70%.

Statistical analysis

Categorical parameters were compared using Fisher's exact test. Continuous parameters were compared by Welch's t test, the Mann–Whitney *U* test or Spearman's rank correlation coefficient r_s, as applicable. For predicting treatment outcomes (i.e., improvement or unchanged), candidate variables were selected from univariate analysis; parameters showing values $p < 0.10$ were entered into multivariate logistic regression analysis. The following parameters potentially related to outcomes from ESS in mean recognition thresholds were examined in univariate analyses: age, sex, preoperative mean recognition threshold, intravenous olfactory test, presence of asthma, respiratory dysfunction, blood eosinophil count (%), total IgE level, presence of perennial or seasonal allergic rhinitis, presence of mucosal lesions at ethmoid sinus or sphenoethmoidal sinus, and SOCs. Clinical data are shown as mean (± SD) unless otherwise mentioned. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using StatFlex® version 6 (Atec, Osaka, Japan).

Results

Data from ECRS and non-ECRS groups

In baseline characteristics, in terms of age and sex, no significant difference was found between the ECRS ($n = 153$) and non-ECRS groups ($n = 60$). Mean SOCs and recognition thresholds in the two groups were 12.97 ± 5.36 and 5.16 ± 1.05, respectively, in the ECRS group, and 6.57 ± 6.12 and 4.30 ± 1.43, respectively, in the non-ECRS group. Significant differences between groups were seen for both SOCs and mean recognition thresholds ($p < 0.001$ each). According to analysis of each assessment site in SOCs, the superior meatus showed the highest score in both groups (Fig. 2). In all assessment sites, SOCs was significantly higher in the ECRS group than in the non-ECRS group. SOCs correlated significantly with preoperative mean recognition thresholds in both ECRS ($r_s = 0.515$, $p < 0.001$) and non-ECRS groups ($r_s = 0.398$, $p < 0.001$) (Fig. 3). Similarly, as for the relationship between SOCs and postoperative mean recognition thresholds, SOCs correlated significantly with ECRS at 3 months ($r_s = 0.347$, $p < 0.001$), ECRS at 12 months ($r_s = 0.342$, $p = 0.002$), non-ECRS at 3 months ($r_s = 0.408$, $p = 0.007$) and non-ECRS at 12 months ($r_s = 0.617$, $p = 0.001$) (Fig. 4). We also examined the relationship between preoperative mean recognition thresholds and SOCs according to assessment site (Table 1). In the ECRS group, significant correlations were found for the sphenoethmoidal recess ($r_s = 0.262$, $p = 0.016$) and OC canopy ($r_s = 0.418$, $p = 0.001$), while in the non-ECRS group, significant correlations were found for the superior turbinate ($r_s = 0.440$, $p = 0.007$), superior meatus ($r_s = 0.511$, $p = 0.001$) and OC canopy ($r_s = 0.554$, $p = 0.001$).

Comparison of SOCs between improvement and unchanged groups

SOCs were analyzed in relation to postoperative olfactory changes. In comparing SOCs between the improvement and unchanged groups, significantly higher scores were observed

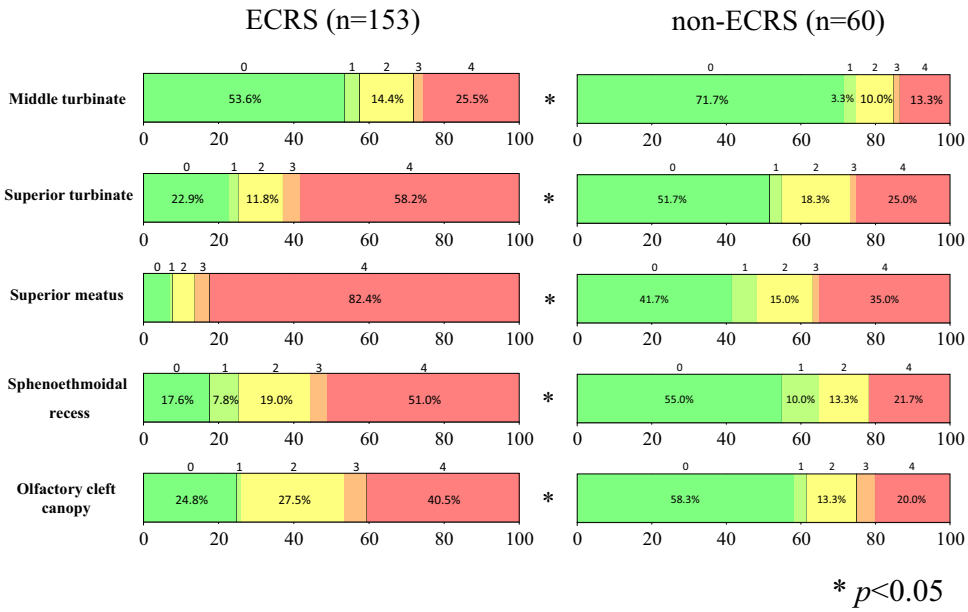

Fig. 2 SOCs in five assessment sites in the ERCS and non-ECRS groups. At all assessment points, SOCs was significantly higher in the ECRS group than in the non-ECRS group. Numbers above each bar graph indicate SOCs and those below each bar graph indicate percentage. Asterisks indicate significant differences in each site between ECRS and non-ECRS ($p < 0.05$)

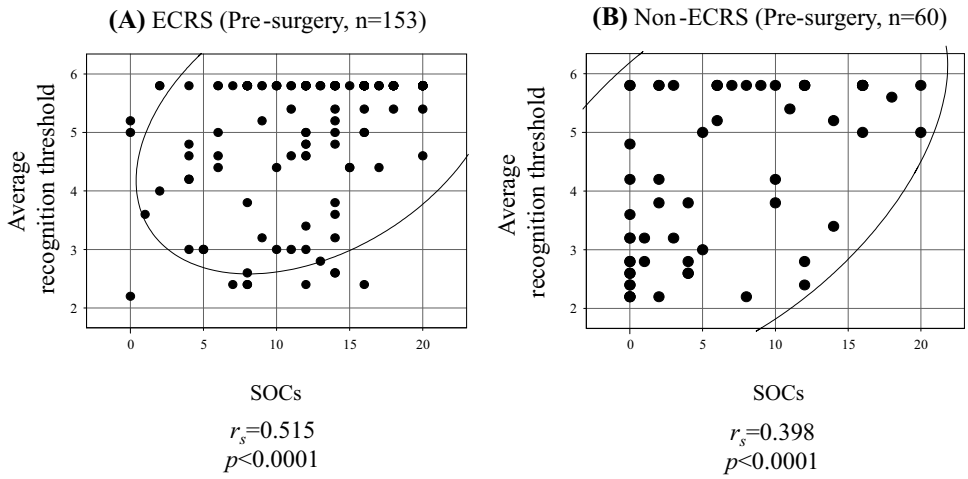

Fig. 3 Correlation between SOCs and baseline mean recognition thresholds in the ECRS group (**a**) and non-ECRS group (**b**)

in the unchanged group in the ECRS at 3 and 12 months and in the non-ECRS at 12 months (Fig. 5). According to analysis of SOCs at each assessment site, sphenoethmoidal recess and OC canopy in ECRS at 3 months were significantly higher in the unchanged group, and those in the middle turbinate, sphenoethmoidal recess and OC canopy at ECRS 12 months were significantly higher in the unchanged group (Supplementary Fig. 1), while those in the superior meatus in the non-ERCS group at 3 months and those in the superior meatus and OC canopy in the non-ERCS at 12 months were significantly higher in the unchanged group (Supplementary Figs. 1, 2).

Uni- and multivariate analyses

Results for univariate analyses in terms of treatment outcomes (improvement or unchanged) are shown in Table 2. Variables showing values of $p < 0.10$ in univariate analyses were entered into logistic regression analyses. In ECRS at 3 months, presence of respiratory dysfunction (odds ratio (OR) 3.084, $p = 0.025$) and SOCs (OR 1.094, $p = 0.029$), and in ECRS at 12 months, mean recognition threshold (OR 2.266, $p = 0.006$) and SOCs (OR 1.134, $p = 0.017$) were identified as significant predictors (Table 3). On the other hand, in the non-ECRS group, no significant variables were found although near-significance of SOCs was observed in non-ECRS at 3 months ($p = 0.058$) (Table 3).

Discussion

The current study primarily sought to examine the usefulness of our scoring system (SOCs) in CRS patients undergoing ESS, focusing on macroscopic findings at the OC during

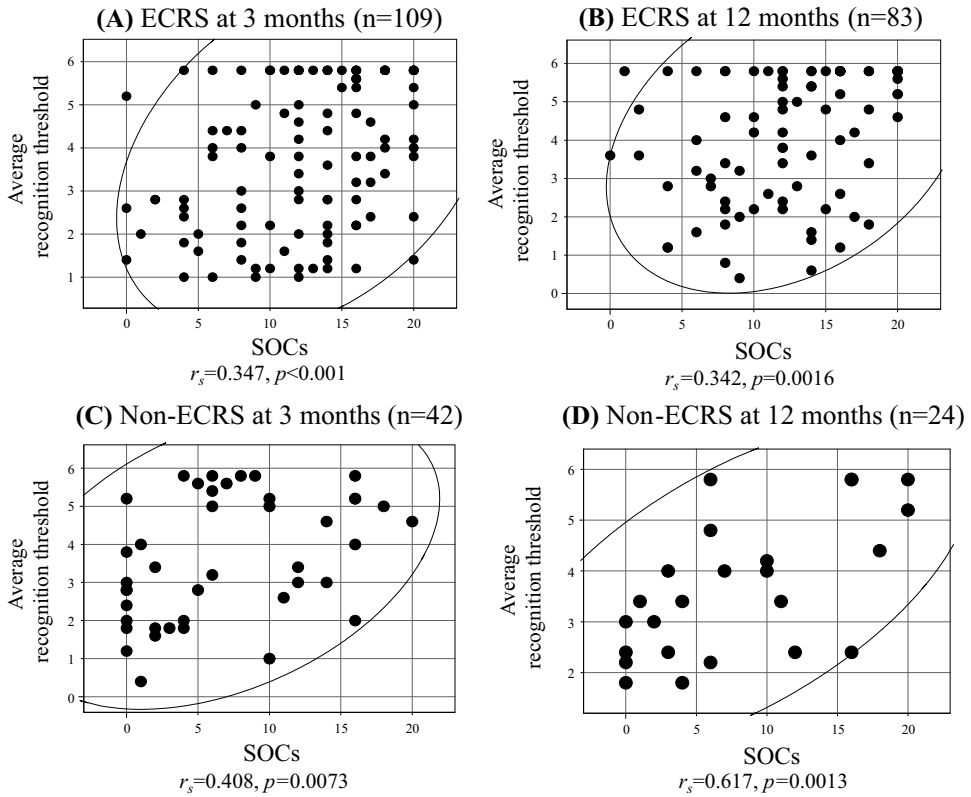

Fig. 4 Correlation between SOCs and mean recognition thresholds at 3 and 12 months in the ECRS group (**a, b**) and non-ECRS group (**c, d**)

Table 1 Correlation between pre-ESS average recognition threshold and SOCs according to assessment site

	Middle turbinate		Superior turbinate		Superior meatus		Sphenoethmoidal recess		Olfactory cleft canopy	
	r_s	p value	r_s	p value	r_s	p value	r_s	p value	r_s	p value
ECRS	0.166	0.458	0.225	0.074	0.156	0.572	0.262	0.016	0.418	0.001
non-ECRS	0.084	> 0.999	0.440	0.007	0.511	0.001	0.272	0.419	0.554	0.001

ESS endoscopic sinus surgery, *SOCs* score of olfactory clefts, *ECRS* eosinophilic chronic rhinosinusitis

surgery. In our results, SOCs correlated with both pre- and postoperative mean recognition thresholds, and in multivariate analyses, SOCs was significant in the ECRS group. These results denoted that our proposed olfactory scoring system may be helpful for predicting treatment outcomes in CRS patients undergoing ESS.

The SOCs focused on the mucosal condition of olfactory neuroepithelium area that consisted of the nasal septum up to the canopy, middle turbinate, superior turbinate, superior nasal meatus, and sphenoethmoidal recess [16–19]. These relevant sites at the OC require intensive operation in CRS patients with olfactory disorder. The SOCs has three grading scales (0, 1, and 2 points), allowing unification with previous reports about endoscopic scores [31–33]. Furthermore, the significant correlation of SOCs with both pre- and postoperative severity of olfactory disorder can provide useful information for the management in CRS patients undergoing ESS. We therefore believe that the SOCs offers a valid and useful scoring system.

One of the major findings in our study was that in the examination of SOCs according to assessment sites, results differed between the ECRS and non-ECRS groups. In other words, higher SOCs in the ECRS group were prominent at all assessment points, indicating differences in pathophysiology between the two groups. Previous cross-sectional studies have demonstrated that mucosal eosinophilia infiltration correlated significantly with worse disease severity in CRS patients and that eosinophilic cationic protein and eosinophilic-derived neurotoxin can directly affect the neurological function [34–36]. Such findings may be associated with our current results.

In our results, in the ECRS group, SOCs of the sphenoethmoidal recess and OC canopy correlated significantly

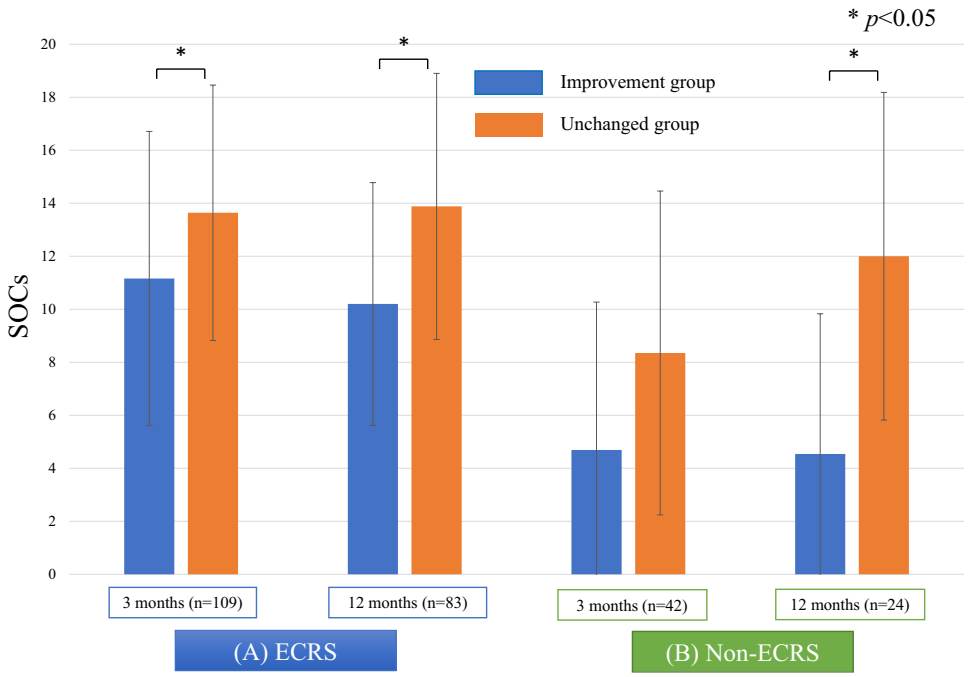

Fig. 5 Comparison of SOCs between improvement group and unchanged group in the ECRS group (**a**) and non-ECRS group (**b**)

with baseline mean recognition thresholds and significantly higher SOCs of sphenoethmoidal recess and OC canopy were found at 3 and 12 months after ESS in the unchanged group. Presence of nasal polyps located vertically from the OC canopy to the sphenoethmoidal recess may account for these results. Ventilatory disturbance to the olfactory mucosa caused by nasal polyps and eosinophilic infiltration related to direct olfactory mucosal injury can lead to olfactory impairment [37].

In surgical treatment for OC lesions, complete eradication of these inflamed mucosal lesions is an important treatment strategy [11]. However, the presence of olfactory neuroepithelium can make this surgical procedure difficult. From the perspective of maintaining olfactory function, preservation of olfactory mucosa may be desirable [11]. Recently, the usefulness of an absorbable gelatin dressing impregnated with triamcinolone within the OC on polypoid rhinosinusitis smell disorders in patients with CRS undergoing ESS has been reported [38]. This technique has also been used in our department.

Significantly higher SOCs of the middle turbinate in ECRS were also found at 12 months after ESS in the unchanged group. A recent CT analysis of the OC in CRS patients demonstrated that the percent opacification as determined by two- and three-dimensional, computerized volumetric analysis of the anterior plane displayed the strongest correlations with objective olfaction [23]. These reports may be linked to our current results.

In the non-ECRS group, SOCs of the superior turbinate and superior meatus (located horizontally in the olfactory nerve distribution area) correlated significantly with baseline mean recognition thresholds and significantly higher SOCs for the superior meatus was found at 3 and 12 months after ESS in the unchanged group. The near-significance of posterior ethmoid sinus lesions and sphenoidal sinus lesions in univariate analyses may account for our results at 12 months. In several non-ECRS patients, due to olfactory nerve injury caused by inflammatory infiltration in the paranasal sinus such as posterior ethmoid sinus and the related olfactory impairment, olfactory function may not improve even after ESS.

We acknowledge several limitations to this study. First, this was a single-center, retrospective study. Second, in both ECRS and non-ECRS groups, missing data after ESS may have potentially led to bias. Third, the current study was based on CRS patients from a certain ethnic background, and additional investigations on different ethnic populations are required to further verify the usefulness of SOCs. However, our results indicated that SOCs correlated with olfactory function pre- and post-ESS and were significant in the ECRS group in multivariate analysis.

In conclusion, clinicians need to be aware of the importance of macroscopic findings at OC in ESS from the viewpoint of patient olfactory prognosis. Our proposed olfactory scoring system during ESS appears promising for estimating olfactory prognosis after ESS for patients with CRS.

Table 2 Univariate analysis of factors in the ECRS and non-ECRS groups

	ECRS group						Non-ECRS group					
	At 3 months ($n=109$)			At 12 months ($n=83$)			At 3 months ($n=42$)			At 12 months ($n=24$)		
	Improvement ($n=56$)	Unchanged ($n=53$)	p value	Improvement ($n=35$)	Unchanged ($n=48$)	p value	Improvement ($n=16$)	Unchanged ($n=26$)	p value	Improvement ($n=13$)	Unchanged ($n=11$)	p value
Age (years)	52.2 ± 13.0	55.0 ± 11.8	0.252	52.2 ± 13.0	55.0 ± 11.8	0.323	53.2 ± 15.4	56.8 ± 16.5	0.371	51.9 ± 10.4	60.5 ± 15.1	0.025
Sex, men/women	4/28	18/35	0.09	17/18	26/22	0.614	8/8	7/19	0.13	8/5	8/3	0.562
Asthma, yes/no	50.0% (28/56)	54.7% (29/53)	0.622	42.9% (15/35)	60.4% (29/48)	0.113	12.5% (2/16)	3.8% (1/26)	0.29	7.7% (1/13)	9.1% (1/11)	0.902
Respiratory disorder, yes/no	18.50% (10/54)	40.00% (18/45)	0.018	25.7% (9/35)	37.0% (17/46)	0.283	6.3% (1/16)	25.0% (6/24)	0.126	0% (0/13)	33.3% (3/9)	0.055
Peripheral eosinophils (%)	8.69 ± 4.36	8.09 ± 4.10	0.459	8.67 ± 4.68	8.18 ± 4.59	0.534	2.68 ± 2.29	2.45 ± 1.57	0.856	2.38 ± 1.30	3.13 ± 2.14	0.505
Total IgE (IU/ml)	379.4 ± 776.4	360.6 ± 526.3	0.886	312.7 ± 550.2	285.0 ± 353.9	0.378	141.7 ± 121.4	447.0 ± 1350.0	0.32	122.3 ± 111.1	207.2 ± 386.1	0.794
Seasonal allergic rhinitis, yes/no	60.70% (34/56)	64.20% (34/53)	0.711	71.4% (25/35)	54.2% (26/48)	0.111	37.5% (6/16)	50.0% (13/26)	0.234	61.5% (8/13)	36.4% (4/11)	0.219
Perennial allergic rhinitis, yes/no	53.60% (30:26)	54.7% (29/53)	0.905	51.5% (18/35)	43.8% (21/48)	0.489	31.3% (5/16)	38.5% (10/26)	0.636	38.5% (5/13)	18.2% (2/11)	0.276
T&T olfactometry	5.17 ± 1.06	5.08 ± 1.07	0.649	4.63 ± 1.30	5.52 ± 0.56	< 0.001	3.94 ± 1.39	4.57 ± 1.36	0.101	3.80 ± 1.32	5.29 ± 0.93	0.006
Intravenous olfactory test-positive, yes/no	92.9% (52/56)	78.8% (41/52)	0. 035	94.3% (33/35)	81.3% (39/48)	0.084	93.8% (15/16)	73.1% (19/26)	0. 098	92.3% (12/13)	81.8% (9/11)	0.439
SOCs	11.16 ± 5.55	13.64 ± 4.82	0.014	10.20 ± 4.58	13.88 ± 5.02	0.001	4.69 ± 5.58	8.35 ± 6.11	0.051	4.54 ± 5.29	12.00 ± 6.18	0.005
Posterior ethmoid sinus lesion	2.93 ± 1.58	3.02 ± 1.26	0.742	2.86 ± 1.59	3.25 ± 1.11	0.441	1.19 ± 1.17	1.65 ± 1.57	0.434	0.92 ± 1.26	2.18 ± 1.66	0.058
Sphenoidal sinus lesion	0.96 ± 1.29	1.36 ± 1.63	0.167	0.74 ± 0.92	1.36 ± 1.61	0.161	0.44 ± 1.09	0.73 ± 1.34	0.402	0.15 ± 0.56	1.00 ± 1.61	0.086

Data are presented as percentage, number or average ± standard deviation

ECRS eosinophilic chronic rhinosinusitis, *SOCs* score of olfactory clefts

Table 3 Multivariate analyses of factors linked to improvement of average recognition threshold after endoscopic sinus surgery

	Odds ratio	*p* value	95% CI
ECRS at 3 months			
SOCs	1.094	0.029	1.001–1.186
Sex	0.559	0.195	0.232–1.348
Intravenous olfactory test	0.334	0.1	0.090–1.236
Respiratory dysfunction	3.084	0.025	1.152–8.258
ECRS at 12 months			
SOCs	1.134	0.017	1.023–1.257
Average recognition threshold	2.266	0.006	1.267–4.051
Intravenous olfactory test	0.294	0.172	0.051–1.703
Non-ECRS at 3 months			
Intravenous olfactory test	0.167	0.116	0.018–1.557
SOCs	1.119	0.058	0.996–1.258
Non-ECRS at 12 months			
SOCs	1.004	0.978	0.734–1.374
Average recognition threshold	2.791	0.112	0.787–9.902
Age	1.012	0.839	0.905–1.131
Posterior ethmoid sinus mucosal lesion	2.005	0.261	0.596–6.748
Sphenoethmoidal mucosal lesion	1.496	0.557	0.390–5.738

ECRS eosinophilic chronic rhinosinusitis, *SOCs* score of olfactory clefts, *CI* confidence interval

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Author contributions Conception and design of the study: KT, KO, YM, and MS; acquisition of data: KO, KT, KH, HT, HO, YK, and YY; analysis and interpretation of data: KO, KT, KH, MS, and HN; drafting of the article: KO, KT, and HN.

Compliance with ethical standards

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Conflict of interest All authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The ethics committee meeting in our institution approved all study protocols (approval number 1512). Written informed consent from the participants was waived due to the retrospective nature of this study.

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