ORIGINAL RESEARCH

# Predictors and prognosis of respiratory epithelial adenomatoid hamartoma in sinonasal cavities

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## Abstract

**Objective:** Respiratory epithelial adenomatoid hamartoma (REAH) is classified as a histopathologic diagnosis and often identified in sinus surgery for chronic rhinosinusitis (CRS). The purpose of this study was to clarify the frequency and predictors of REAH and prognosis of CRS with REAH in CRS cases.

**Methods:** In the first study, we histologically reviewed sinonasal polyps and mucosal tissue specimens obtained from patients who underwent endoscopic sinus surgery (ESS) for CRS to reveal how many REAH were involved in ESS cases. We compared REAH and non-REAH groups in terms of preoperative symptoms and endoscopic, imaging and blood examination findings to elucidate predictors of REAH genesis. In the second study, we compared the data 3 months after surgery such as endoscopic and imaging findings and olfactory test to evaluate prognosis of CRS with REAH.

**Results:** The prevalence of REAH was 15.5% of all 304 cases in the first and second studies combined. Higher polyp score in the middle meatus was an independent predictor of the presence of REAH ($p = .02$). Presence of REAH was significantly associated with the enlargement of olfactory cleft polyps ($p < .01$), increasing postoperative scores of standard olfactory tests ($p = .03$), and decline of ratio of improvement ($p < .01$) measured using T&T olfactometry.

**Conclusions:** Higher polyp score in the middle meatus is an independent predictor of REAH. Olfactory function is difficult to recover after surgery in REAH patients because it is associated with recurrent polyps in the olfactory cleft.

**KEYWORDS**
chronic rhinosinusitis, nasal polyps, nose neoplasms, olfactory disorders

## 1 | INTRODUCTION

Respiratory epithelial adenomatoid hamartoma (REAH) is a classified pathologic diagnosis and was first reported by Wenig and Heffner[1] in a review of 31 cases in 1995. Although REAH has been previously considered very rare,[2] there has been a recent increase in the number of reports about it.[3–7] In particular, REAH is often diagnosed accidentally by postoperative pathological examination after endoscopic sinus surgery (ESS), which is presumed to be chronic sinusitis (CRS) with nasal polyps.[3–7]

The etiology of REAH is unknown yet. Some authors hypothesize that it is hyperplasia of the respiratory epithelium because REAH histopathologically presents multilayered and ciliated respiratory epithelium, often with a mix of mucocytes with pseudogland formation.[7] Others hypothesize that it may be a neoplastic entity because of rarely reported concomitant presentation with sinonasal adenocarcinoma.[8] Although there are several reports regarding predictors of REAH,[6,7] the name of this disease is not fully recognized yet. There have been a few reports comparing the prognosis of REAH and effective treatments for REAH. Nguyen et al.[9] reported that excision of polyps after nasalization of the ethmoidal labyrinths may improve olfaction. In addition, they published a prognostic study of REAH, which found that the presence or absence of REAH was not relevant.[10]

Therefore, we conducted two studies to reveal the followings: (1) the actual existence of REAH and its frequency; (2) factors for preoperatively predicting the presence of REAH; and (3) postoperative prognosis for CRS with REAH.

## 2 | MATERIALS AND METHODS

In the first study, we examined the presence of REAH in the pathological specimens of ESS cases. After dividing the patients into the REAH group and the non-REAH group, the preoperative data were compared to discover predictors. In the second study, we compared data 3 months after surgery to evaluate prognosis of CRS with REAH.

### 2.1 | Materials and methods of the first study

Subjects included patients who were diagnosed with CRS and underwent ESS in our hospital from August 2010 to November 2014 (for 4 years and 4 months). Their nasal polyps or sinus mucosa were collected as pathological specimens during surgery and reviewed by two otolaryngologists (H.M. and M.K.) and one pathologist (K.U.). A pathological feature of REAH is a polypoid mass in which ciliated respiratory epithelia invaginate into its subepithelial layer and which forms large and small gland ducts or cysts with no atypia[3,11,12] (Figure 1). Its lumen is lined with pseudostratified ciliated epithelium, in which goblet cells are prominent and mucus retention fills in gland ducts and cysts. These findings were used as pathological diagnostic criteria. The subjects were divided into REAH and non-REAH groups.

The survey items were age, gender, history of surgery, duration of illness, unilateral or bilateral, symptoms, imaging findings, nasal polyp size, peripheral blood leukocytes count including peripheral blood eosinophil–leukocyte ratio, and presence or absence of eosinophilic CRS. Symptoms were evaluated based on the presence or absence of rhinorrhea, nasal obstruction, postnasal drip, facial pain, headache, and olfactory dysfunction. Imaging findings are based on sinus CT and evaluated at six anatomical regions: the frontal sinus, anterior and posterior ethmoid sinuses, maxillary sinus, sphenoid sinus, and ostiomeatal complex (OMC). Degrees of opacification of these sinuses/complex were measured using a three-grade scale (0: no abnormality,
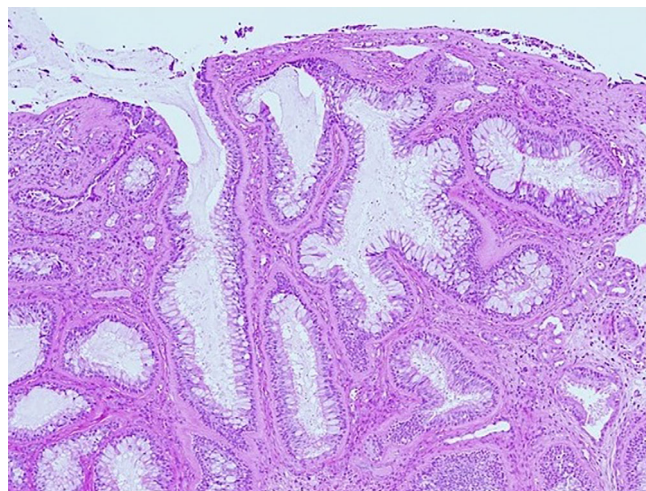


**FIGURE 1** Histological features of REAH. Multilayered ciliated respiratory epithelium proliferates, invaginates downward into the submucosal layer, and forms large and small gland ducts or cysts with no atypia. The gland ducts and cysts are lined by respiratory epithelium admixed with numerous mucin-secreting goblet cells.

1: partial opacification, 2: total opacification) by the Lund–Mackey system.[13] The size of nasal polyps was evaluated separately for the middle meatus and the olfactory cleft. Middle meatus polyps were scored on a five-point scale (0–4 points),[14] and olfactory cleft polyps were scored on a four-point scale (0: none, 1: edema of olfactory cleft, 2: presence of polyps 3: full of polyps). Eosinophilic CRS was diagnosed based on the Japanese epidemiological survey of refractory eosinophilic chronic rhinosinusitis scoring system[15] and the number of eosinophils in the nasal polyp or mucosa.

In the univariate analysis, the chi-square ($\chi^2$) test for independence was used to test for differences in ratio. The Mann–Whitney $U$ test was used to determine differences in average values between the two groups. Differences were regarded as significant when $p < .05$. In the multivariate analysis, binomial logistic regression analysis was performed using items having a significance probability when $p < .25$ as explanatory variables. Statistical analyses were performed using IBM SPSS Statistics software version 22 (IBM).

### 2.2 | Materials and methods of the second study

The second study was done to determine the postoperative prognosis for CRS with REAH. In the second study, subjects were patients who were diagnosed with CRS and who underwent ESS in our hospital from June 2015 to December 2018 (3 years and 7 months). We surveyed their age, gender, unilateral or bilateral, peripheral blood leukocyte count including eosinophils, presence or absence of bronchial asthma, and presence or absence of eosinophilic CRS. In addition, subjective self-report of olfactory dysfunction using visual analog scale, T&T olfactometry (the Japanese standard olfactory test),[16] Open Essence (odor identification test for Japanese),[17] the intravenous olfactory test, rhinomanometry, imaging findings, endoscopic score of

Lund–Kennedy system,[18] and nasal polyp size were examined before and 3 months after surgery. The intravenous olfactory test is an injection of thiamine propyl disulfide that induces the sensation of a garlic-like odor and is widely used as one of the subjective olfactory tests in Japan.[16] Preoperative data were used as explanatory variables in this study described below, and postoperative data were used as objective variables. Improvement was defined as cases in which the recognition threshold scores of a standard olfactory test became 2.0 or less, or got better by 1.0 or more points than before surgery, according to the criteria established by the Japanese Rhinologic Society.[16]

In the second study, univariate analysis (the $\chi^2$ test and Mann–Whitney $U$ test) was performed with the presence or absence of REAH as the explanatory variable and the postoperative data as the objective variable. By this method, we first investigated which of the postoperative data, and which of the prognosis data of CRS, correlates with the presence or absence of REAH. Next, the univariate analysis was performed individually using the postoperative data that showed a significant difference in these univariate analyzes as the objective variable

and all the preoperative data as explanatory variables. In this way, we investigated which preoperative data other than REAH correlates with the postoperative data. Then, a multiple regression analysis or a binomial logistic regression analysis was performed using the preoperative data with a $p$ value of less than .25 and the presence or absence of REAH as explanatory variables and the postoperative data as the objective variable. We will illustrate this with an example in which the first univariate analysis correlates the presence or absence of REAH with the postoperative standard olfaction test result. In that case, a univariate analysis would be performed with all preoperative data (CT score, polyp score, olfactory test, etc.) as explanatory variables and the standard olfactory test result as the objective variable. We then performed a multivariate analysis with all data with $p$ values below .25 and REAH as explanatory variables and the standard olfactory test result as the objective variable. The procedure is used to examine factors that are truly correlated with the preoperative standard olfactory test result. IBM SPSS Statistics version 25 (IBM) was used for these statistical analyses.

**TABLE 1** Univariate analysis about predictors of REAH in the first study

| | REAH (34 cases) | non-REAH (148 cases) | *p* |
| --- | --- | --- | --- |
| Sex (male:female) | 22:12 | 85:63 | .438 |
| Age (mean ± SD) | 54 ± 15 (years) | 54 ± 16 (years) | .791 |
| Duration of illness (mean ± SD) | 182 ± 188 (month) | 129 ± 176 (month) | .126 |
| Symptoms | | | |
| Bilateral (%) | 79.4 | 67.6 | .180 |
| Rhinorrhea (%) | 35.3 | 44.6 | .325 |
| Nasal obstruction (%) | 73.5 | 57.4 | .088 |
| Post nasal drip (%) | 8.8 | 21.6 | .100 |
| Facial pain or headache (%) | 11.8 | 16.2 | .518 |
| Olfactory dysfunction (%) | 55.9 | 37.2 | .048* |
| CT scores | | | |
| Frontal sinus score (mean ± SD) | 2.2 ± 1.4 | 1.9 ± 1.3 | .180 |
| Anterior ethmoid sinus score (mean ± SD) | 2.4 ± 1.1 | 2.0 ± 1.2 | .062 |
| Posterior ethmoid sinus score (mean ± SD) | 2.1 ± 1.0 | 1.8 ± 1.1 | .210 |
| Maxillary sinus score (mean ± SD) | 2.3 ± 0.9 | 2.9 ± 1.4 | .297 |
| Sphenoid sinus score (mean ± SD) | 1.9 ± 1.4 | 1.6 ± 1.2 | .324 |
| Ostiomeatal complex score (mean ± SD) | 2.4 ± 1.1 | 1.8 ± 1.1 | .015* |
| Total sinus score (mean ± SD) | 13.2 ± 5.6 | 11.1 ± 5.5 | .102 |
| Nasal polyps | | | |
| Middle meatus polyp score (mean ± SD) | 2.6 ± 1.3 | 1.7 ± 1.4 | .002** |
| Olfactory cleft polyp score (mean ± SD) | 1.6 ± 1.4 | 0.9 ± 1.2 | .005** |
| CRS with nasal polyps (%) | 91.2 | 70.3 | .014* |
| Peripheral blood call | | | |
| Peripheral blood leukocyte count (mean ± SD) | 6798 ± 1776 | 6408 ± 1686 | .233 |
| Peripheral blood eosinophil count (mean ± SD) | 320 ± 275 | 389 ± 390 | .452 |
| Peripheral blood eosinophil ratio (mean ± SD) | 5.2 ± 4.7(%) | 6.6 ± 10.4 (%) | .333 |
| Eosinophilic CRS (%) | 52.9 | 54.1 | .907 |

*Note*: *$p$ < 0.05; **$p$ < 0.01.

In this study, information on the research was consented in advance by the subjects or disclosed to them. We ensured that research subjects had the opportunity to refuse the implementation or continuation of the research. This study was approved by the Clinical Research Ethics Review Committee of Mie University Hospital (approved number: H2021-025).

## 3 | RESULTS

The prevalence of REAH was 15.5% of the 304 cases in the first and second studies combined. Higher scores for middle nasal polyps were an independent predictor of the presence of REAH (2.6 for the REAH group and 1.7 for the non-REAH group). The presence of REAH was significantly associated with the postoperative prognosis such as the enlargement of olfactory cleft polyps, increasing scores on standard olfactory tests, and a decline in improvement measured by T&T olfactometry.

### 3.1 | Results of the first study

A total of 182 cases were examined in the first study, 34 of which (18.7%) involved REAH. Univariate analyses found significant differences in degrees of olfactory dysfunction, opacification of OMC, scores of nasal polyps in the middle meatus and olfactory cleft, percentage of CRS with nasal polyps (Table 1). These scores were higher in the REAH group than the non-REAH group. Because the respective powers ($1 - \beta$ err prob) were .999, .874, .894, .838, and 1.000, the sample size was considered sufficient. Three cases (8.8%) of REAH

were chronic rhinosinusitis without nasal polyps, which were diagnosed by the tissues of the thickened mucosae and polyps of the sinuses. Multivariate analysis showed that only middle meatus polyps were an independent predictor of REAH with an odds ratio of 1.55 for the presence of REAH (Table 2). On the other hand, period of illness, peripheral blood eosinophil count, peripheral blood eosinophil ratio, and presence or absence of eosinophilic CRS were not significantly different between the REAH and non-REAH groups.

### 3.2 | Results of the second study

The second study included 122 cases, 13 of which (10.7%) had REAH in tissues. Combined with the first study, 47 of 304 cases (15.5%) had REAH. In the second study, olfactory cleft polyps were observed in 49 of 122 cases, collected in 29 cases, and in the remaining 20 cases, the polyps were small and removed with a microdebrider. Of the 13 cases of REAH, eight were present in olfactory cleft polyps. Two cases were in common nasal meatus polyps, one case was in a middle turbinate polyp, a middle meatus polyp, and an ethmoidal cell polyp. By univariate analysis, postoperative subjective symptom scores of olfactory dysfunctions, standard olfactory test results, endoscopic score, and middle meatus and olfactory cleft polyps in REAH group were significantly higher than those in the non-REAH group, and odor identification test results were lower in REAH group (Table 3). Because the respective powers ($1 - \beta$ err prob) were .907, .775, .995, .830, .999, and .924, the sample size was considered almost sufficient. According to the ratio of olfactory improvement measured by a standard olfactory test, the improvement rate in the non-REAH group was 91%, whereas that in the REAH group was 67%, which represents a

**TABLE 2** Multivariate analysis about predictors of REAH in the first study

|  | Partial regression coefficient | p | 95% confidence coefficient | | Odds ratio |
| --- | --- | --- | --- | --- | --- |
| (constant) | −2.42 | .00 | | | 0.09 |
| Middle meatus polyp score | 0.44 | .02 | 1.17 | 2.06 | 1.55 |

**TABLE 3** Univariate analysis about prognosis of chronic rhinosinusitis with REAH in the second study

|  | REAH (13 cases) | non-REAH (109 cases) | p |
| --- | --- | --- | --- |
| Total sinus score (mean ± SD) | 4.7 ± 1.1 | 3.9 ± 1.8 | .154 |
| Endoscopic score (mean ± SD) | 3.3 ± 1.2 | 1.7 ± 1.6 | .001* |
| Middle meatus polyp score (mean ± SD) | 0.7 ± 0.6 | 0.3 ± 0.4 | .011* |
| Olfactory cleft polyp score (mean ± SD) | 1.1 ± 0.7 | 0.2 ± 0.4 | .000** |
| VAS of olfactory dysfunction (mean ± SD) | 41 ± 29 | 67 ± 29 | .010* |
| Odor identification test (mean ± SD) | 31 ± 21 | 51 ± 22 | .011* |
| Standard olfactory test (mean ± SD) | 3.3 ± 2.1 | 1.8 ± 1.5 | .031* |
| Intravenous olfactory test (%) | 92 | 97 | .417 |
| Ratio of olfactory improvement (%) | 67 | 91 | .046* |
| Rhinomanometry (mean ± SD, Pa/cm³/S) | 0.31 ± 0.15 | 0.24 ± 0.08 | .213 |

Note: *$p < 0.05$; **$p < 0.01$.

**TABLE 4**  Multivariate analysis about prognosis of chronic rhinosinusitis with REAH in the second study

| | Partial regression coefficient | p | 95% confidence coefficient Lower limits | Upper limits | |
|---|---|---|---|---|---|
| Postoperative standard olfactory test | | | | | Odds ratio |
| (constant) | −0.93 | .11 | −2.07 | 0.21 | |
| Standard olfactory test | 0.35 | <.01 | 0.15 | 0.56 | |
| Middle meatus polyp score | 0.38 | .02 | 0.05 | 0.7 | |
| Intravenous olfactory test | 0.9 | <.01 | 0.33 | 1.47 | |
| REAH | 1.08 | .03 | 0.13 | 2.03 | |
| Postoperative olfactory cleft polyp score | | | | | |
| (constant) | −0.02 | .86 | −0.21 | 0.18 | |
| Olfactory cleft polyp score | 0.19 | <.01 | 0.1 | 0.28 | |
| REAH | 0.61 | <.01 | 0.3 | 0.92 | |
| Ratio of olfactory improvement | | | | | Odds ratio |
| (constant) | 5.59 | <.02 | | | 0.1 |
| Peripheral blood eosinophil ratio | −0.16 | .01 | 0.75 | 0.97 | 0.85 |
| Intravenous olfactory test | −4.33 | <.01 | <0.01 | 0.20 | 0.01 |
| REAH | −3.61 | <.01 | <0.01 | 0.38 | 0.03 |

significantly decrease in improvement ($p = .046$, power $= .999$). Therefore, multivariate analysis was performed using these six items as explanatory variables. As the result, the presence of REAH was significantly associated with the postoperative standard olfactory test scores ($p = .03$), scores of olfactory cleft polyps ($p < .01$), and the ratio of olfactory improvement judged by standard olfactory test ($p < .01$) (Table 4). The postoperative standard olfactory test results were affected by the preoperative test results, middle meatus polyp scores, and intravenous olfactory test in addition to the presence of REAH. The postoperative olfactory cleft polyp scores showed significant correlations with the presence of REAH and preoperative olfactory cleft polyp scores, respectively. In addition, the intravenous olfactory test results and the peripheral blood eosinophil ratio significantly correlated with the ratio of olfactory improvement.

# 4 | DISCUSSION

Although previous studies reported that the prevalence of REAH was as high as 40%–48% in studies of olfactory cleft polyps,[5,7] our results show that the prevalence of REAH is relatively low at 15.5% (47 of 304 cases). This difference can be explained as follows. First, no study revealed the prevalence rate in cases of ESS. Second, our study included CRS without polyps, in which case pathological examination was performed on the thickened sinus mucosa. Hence, unlike past reports, the subjects are not limited to the olfactory cleft polyps alone. When limited to olfactory cleft polyps, our study revealed REAH prevalence of 27.6% (8 of 29 cases). Other reasons cited for increasing the rate of REAH diagnoses are (i) a systematic checkup of the olfactory clefts on any sinonasal CT scan and during endoscopic surgery; (ii) a systematic individualization of the surgical specimens removed from

the olfactory clefts and from the ethmoidal labyrinths for pathological processing; and (iii) highly experienced pathologists with great knowledge of REAH's histological features since 2003.[19] On the other hand, in the same Japanese report, REAH was pathologically confirmed in 10 of 36 olfactory cleft polyps patients (27.8%) and in 10 of 109 ECRS patients (9.2%),[20] which is comparable to this report. However, REAH also exists in mucous membranes and polyps other than the olfactory cleft as reported in this study. Therefore, we consider that the presence of REAH cases should be examined in all ESS even if they had no olfactory cleft polyps.

Our study showed the predictors of REAH were olfactory dysfunction, CT opacification of OMC, and nasal polyp scores of the middle meatus and olfactory cleft in univariate analysis. In multivariate analysis, the size of nasal polyps in the middle meatus was the only independent predictor. Therefore, it is likely that REAH contributes to an increase in polyps and thickening of mucous membranes centering on the middle meatus (OMC) and olfactory cleft, leading to induce olfactory dysfunction. First, we checked whether the data from this survey could be compared to other reports. Most reports used the Lund-Mackay CT score[13] to evaluate CT, with a preoperative mean of 9.9–17.1 of 24 points.[21–24] The scores in this study are 13.2 and 11.1, so they are considered to be equivalent to the previous reports. The evaluation of polyps varies further from report to report and is difficult to compare. However, when the maximum score in each report is 100%, the preoperative score of the ESS cases is 25 to 85%.[21,22] Some of these studies targeted only CRS with nasal polyps. In this study, the preoperative score is 21%–33%, with the highest polyp score of 4 in the middle meatus being 100%. This includes CRS without nasal polyps and is therefore considered a good assessment.

One meta-analysis study reported the epidemiology of REAH showing a mean age of 54 years (range, 9–86 years) and a male to

female ratio of 3:2.[24] This is in perfect agreement with our REAH group data. However, it is also in close agreement with the data for the non-REAH group, with no significant differences between them. Therefore, unfortunately, it is difficult to differentiate between them.

A previous study reported that predictors of REAH were duration of nasal polyposis (>10 years) and history of asthma.[7] In our first study, however, the period of illness and eosinophilic inflammation (peripheral blood eosinophil count, peripheral blood eosinophil ratio, and type of CRS) did not show a significant difference between the both groups in univariate analysis. This difference may be due to individual backgrounds of chronic inflammation such as history of asthma and period of nasal polyps, which can be associated with onset of REAH. However, our results suggest that the predictors of the onset of REAH are polyp scores and mucosal thickening. Therefore, it is impossible to conclude whether REAH is induced by inflammation with the increase in polyps, or REAH occurs primarily and polyps increase subsequently, leading to close natural ostium. Another possibility is that REAH is found as an isolated lesion in some cases and as a part of inflammatory polyps in others. A full understanding of the etiology of REAH will likely require additional clinical studies.

Regarding features about image findings of REAH, a previous study reported that the sensitivity and specificity for the presence of REAH are 88% and 74%, respectively, if the width of olfactory cleft is 10 mm or more.[25] Images of REAH, T2-weighted MRI showed a hyperintense mass with heterogeneous features, whereas T1-weighted MRI contrast-enhanced images showed a homogeneous enhancement following gadolinium injection.[26] In our study, however, the feature of the image findings was the only OMC opacification of CT in univariate analysis. Our study did not examine MRI because we do not usually require routine MRI for ESS of CRS, so we cannot compare results from MRI in the previous study and those from CT in our study. These are limitations of the first study. Future studies may evaluate olfactory cleft and radiologic interpretations in MRI and more detailed diagnostic imaging may improve the accuracy of preoperative diagnosis of REAH. Another limitation is that only surgical cases for sinusitis were included in this study, thus excluding cases without sinusitis or without surgery.

The second study was conducted with the aim of clarifying the prognosis of CRS with REAH. In univariate analysis, the postoperative subjective symptom of olfactory dysfunction, odor identification test and standard olfactory test results, size of middle meatus polyps and olfactory cleft polyps, and the olfactory improvement ratio measured by standard olfactory test were significantly worse in the REAH group. In multivariate analysis, additionally, the postoperative standard olfactory test results and the size of olfactory cleft polyps were significantly higher, and olfactory improvement ratio was lower in REAH group. As with the first survey, we checked whether the data from this survey could be compared to the previous reports. Postoperative polyp scores vary in the same way as preoperative polyp scores, but are reported to be 2%–20% with a maximum score of 100%.[21,22] The polyp score of the middle meatus is 8%–18% in our report. The polyp score of the olfactory cleft score is 7–37, but it is difficult to compare to other reports because there is no report that

evaluates only the olfactory cleft. Regarding the reports of the olfactory function, the same standard olfactory test as in this study improved from 5.3 to 3.5–4.2 by ESS.[20,27] In this study as well, the score improved from 4.7–2.5 on average, so it is considered that the surgery was equivalent. From these results, it appears that in patients with CRS with REAH, olfactory dysfunction is unlikely to improve and nasal polyps in the olfactory cleft are likely to recur after ESS. That is, recurrence of polyps in the olfactory cleft after surgery exacerbates the olfactory function. Regarding olfactory prognosis of CRS with REAH, a previous study reported that 13 of 27 (48%) patients with REAH still complained of olfactory disorders postoperatively.[28] Another study reported that 13% (3/23) of anosmic patients with REAH did not change their anosmia after surgery.[29] In our study, four of 12 (33%) patients did not improve their olfactory dysfunction and three patients (25%) remained anosmic. Although the sample size was small, the number of cases with residual olfactory dysfunction and the number of cases with anosmia after surgery were statistically equivalent. On the other hand, in the same Japanese report, the VAS of olfactory dysfunction improved from 15 to 57 by ESS,[20] which we consider equivalent to the improvement of 8–41 in this study. As for recurrence of REAH, it was reported that 15 of 363 (4%) patients had recurrence of REAH, and all of them required reoperation.[6] Another study demonstrated REAH in 8.9% of nasal cavities at primary surgery versus REAH in 54.8% at revision surgery, meaning that REAH is found more frequently at revision surgery.[30] In our study, postoperative mucosal thickening and polyp recurrence were more likely to occur in the REAH group. However, no reoperation cases have been diagnosed with REAH, and no REAH cases have yet required reoperation. Therefore, if recurrence of REAH is defined as proven by pathological examination, there are no confirmed cases of recurrence at this time. One reason for this is that the second study only evaluated patients at 3 months postoperatively, which is a limitation. That is not sufficient because it generally takes several years for REAH to recur.[6] It is necessary to continue long-term follow-up and investigate the presence of REAH when reoperation is required. The same is true for the olfactory. Longer evaluation is desirable, considering that olfaction may worsen over time postoperatively.

## 5 | CONCLUSION

REAH exists in CRS cases with a certain proportion, especially in those with larger polyps in the middle meatus. For these patients, it is difficult to improve their olfactory dysfunction after surgery because polyps in the olfactory clefts are likely to recur. Therefore, CRS patients with REAH should be followed carefully after surgery.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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