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Outcomes of endoscopic sinus surgery in patients with central compartment atopic disease

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ABSTRACT

Background: Central compartment atopic disease (CCAD) is a subtype of chronic rhinosinusitis (CRS). Research focusing on the endoscopic sinus surgery (ESS) outcomes of CCAD is limited. This study aimed to evaluate the outcomes of ESS in CCAD and compared to 2 following subtypes: chronic rhinosinusitis with nasal polyps (CRSwNP) and concomitant polypoid disease in the central compartment (CRSwNP/CC) and CRSwNP not otherwise specified (CRSwNP NOS).

Methods: This case-control study enrolled patients with bilateral CRSwNP who underwent ESS and had at least 1 year of follow-up. Patients were classified into CCAD, CRSwNP/CC, and CRSwNP NOS. The demographic data, preoperative disease severity, and surgery outcomes, including CRS control status, endoscopic score, and symptom scores at 1 year postoperatively, were collected. We defined well controlled and partly controlled as appropriate disease control.

Results: This study screened 259 patients and enrolled 138 patients with complete medical records and 1-year follow-up (CCAD N = 51, CRSwNP/CC N = 55, CRSwNP NOS N = 32). Among them, appropriate disease control was achieved in 84.3% of patients (43/51) in the CCAD group, 69.1% (38/55) in the CRSwNP/CC group, and 93.7% (30/32) in the CRSwNP NOS group ($P = 0.029$). Then we performed post-hoc analysis using appropriate disease control and uncontrolled. There was a significant difference between CRSwNP/CC and CRSwNP NOS ($P = 0.007$), but no significant difference compared CCAD group to CRSwNP/CC group ($P = 0.065$) and CRSwNP NOS group ($P = 0.199$). There were significant differences in endoscopic E-score among groups ($P < 0.001$). In post-hoc analysis, we found that CRSwNP/CC (Median [IQR], 33.32 [42.14]) had a significantly worse E-score than CCAD (8.33 [16.67]) and CRSwNP NOS (4.17 [8.30]). Also, postoperative olfactory visual analog scale (VAS) scores significantly differed among groups ($P = 0.043$). However, post-hoc analysis showed no difference between any 2 groups. There were

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The data from the chronic rhinosinusitis research database from January 2018 to December 2021 in the First Affiliated Hospital of Sun Yat-sen University. This study was approved by the Ethics Committee of the First Affiliated Hospital of Sun Yat-sen University (Registration number: ChiCTR1900023434).

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no differences in postoperative VAS scores of obstruction ($P = 0.159$), rhinorrhea ($P = 0.398$), and headache/facial pain ($P = 0.092$).

Conclusion: Most CCAD patients had good surgical outcomes 1 year after surgery. Meanwhile, the CRSwNP/CC group had the fewest patients under appropriate disease control.

Keywords: Chronic rhinosinusitis, Central compartment atopic disease, Outcomes, Endoscopic sinus surgery, Control status

INTRODUCTION

Chronic rhinosinusitis (CRS) is a common disease characterized by inflammation of the nose and the paranasal sinuses that lasts more than 12 weeks. CRS affects 5%–12% of individuals worldwide[1–4] and about 8% in China.[2] CRS was traditionally classified into 2 phenotypes: chronic rhinosinusitis with nasal polyps (CRSwNP) and without nasal polyps (CRSsNP) according to the absence or presence of nasal polyps. Recently, CRS has been classified into 2 inflammatory endotypes: eosinophilic CRS (eCRS) and non-eosinophilic CRS (non-eCRS) based on the eosinophilia in nasal polyp tissue. eCRS was related to severe disease, worse CRS control after surgery, and higher revision surgery rate.[5–7]

Central compartment atopic disease (CCAD) is a novel phenotype of CRSwNP, first described by DelGaudio et al[8] in 2017. CCAD is characterized by polypoid changes in the central compartment of the nasal cavity, including the superior turbinate (ST), the middle turbinate (MT), and the posterosuperior nasal septum (PSNS). The diagnosis is based on endoscopy findings of polyps or polypoid change of origin in the central compartment, while radiologic findings may provide clues to the presence of CCAD.[9] Most studies were conducted in the West, suggesting that CCAD is strongly associated with inhalant allergy.[10–12] However, our recent study revealed that only 37% of Chinese CCAD patients had systemic allergy based on skin and serum testing, and 23% had allergic rhinitis (AR).[13] Interestingly, we found that CCAD had highly systemic and local eosinophilic infiltration. 97.4% of CCAD was eCRS, based on the criteria of the ratio of eosinophils more than 10% of total inflammatory cells.[13] This raises the question of whether the outcomes of CCAD are as poor as those of eCRS.

The surgical outcomes of CCAD have only been reported in 2 studies so far.[14,15] Steehler et al[15] reported that the polyp recurrence rate and revision surgery rate in CCAD was lower than CRSwNP NOS (polyps originating from middle meatus but not middle turbinate). However, they did not focus on the other outcomes, such as disease control, symptom score, endoscopic score, and quality of life. Shih et al[14] reported that CCAD had a more significant improvement in 22-Item Sino-Nasal Outcome Test (SNOT-22) after ESS, but the follow-up time was only 3 months. Herein, we conducted this case-control study to assess the comprehensive ESS outcomes of CCAD from Southern China, including CRS control status, endoscopic score, symptom scores, and quality of life (QOL) SNOT-22, and compared them with the other 2 CRSwNP subtypes.

MATERIALS AND METHODS

Subjects

This is a retrospective analysis of the prospectively collected data from the CRS research database from January 2018 to December 2021 in our hospital. Adult patients with CRS (≥18 years) who underwent primary ESS were screened. Patients with incomplete imaging and medical records were excluded from the study. Medical charts, preoperative nasal endoscopy images and computed tomography (CT) images, surgical records, and postoperative nasal endoscopy images were reviewed. The flow chart of this study is presented in Fig. 1. The Ethics Committee for Clinical Research and Animal Trials of the First Affiliated Hospital of Sun Yat-sen University approved the

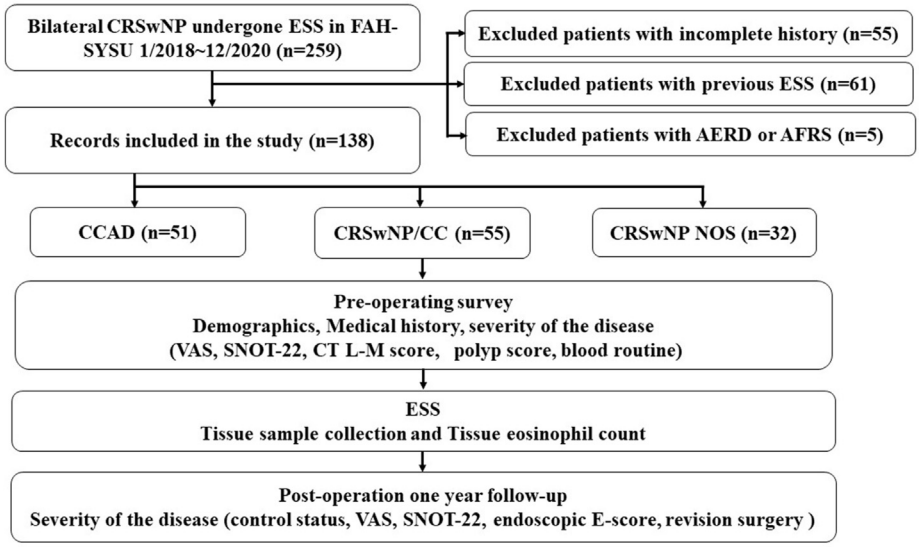

Fig. 1 The flow-chart of this study. CRSwNP = chronic rhinosinusitis with nasal polyps; ESS = endoscopic sinus surgery; AERD = aspirin-exacerbated respiratory disease; AFRS = allergic fungal rhinosinusitis; CCAD = central compartment atopic disease; CRSwNP/CC = sinonasal polyps and central compartment involvement; CRSwNP NOS = chronic rhinosinusitis with nasal polyposis not otherwise specified; VAS=Visual Analogue Scale; SNOT-22 = 22-Item Sino-Nasal Outcome Test; CT L-M score = Lund-Mackay score of sinus computed tomography; E score = postoperative endoscopic score

study. All participants provided written informed consent.

Diagnosis criteria

We followed the European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS 2020) to diagnose CRSwNP.[16] Pulmonologists diagnosed asthma according to the Global Initiative of Asthma (GINA) Guidelines.[17] It is based on the history of characteristic symptom patterns and evidence of variable expiratory airflow limitation. This was documented by bronchodilator reversibility testing or other tests. A positive bronchodilator responsiveness (reversibility) test was defined as an increase in forced expiratory volume (FEV1) of forced vital capacity (FVC) of more than 12% and 200 ml. A positive bronchial challenge test was defined as a decrease in FEV1 or FVC greater than 20% and >200 ml from baseline. Allergic rhinitis (AR) diagnosis was based on rhinitis symptoms and positive allergy testing results.[18]

Serum total IgE (tIgE) and specific IgE (sIgE) tests were measured. Serum tIgE was measured using enzyme-linked immunosorbent assay. The composition of serum sIgE was determined with a wide range of locally prevalent allergens and detected by the UniCAP automatic allergen detector (Famasia, Sweden). For any airborne, sIgE over 0.35 kU/L is a positive result for atopy.

Exclusion criteria

Patients who underwent previous sinus surgery or middle turbinate surgery were excluded. Patients who had antrochoanal polyps, ciliary dysfunction, or oral or nasal glucocorticoids in the last month were also excluded. Furthermore, patients with aspirin-exacerbated respiratory disease (AERD) and allergic fungal rhinosinusitis (AFRS) were excluded because these diseases were uncommon in China.

Classification of CRSwNP: CCAD, CRSwNP/CC and CRSwNP NOS

CRSwNP was classified according to previous works done by DelGaudio et al[10,19] and our group.[13] Endoscopic images acquired during the first visit and surgical notes were reviewed to confirm the polyp origin site before the final diagnosis. Patients whose polyp origin was unable to be identified were excluded. Patients with polyps emanating from the lateral surface of the middle turbinate (MT) were also categorized as having CCAD, despite nasal polyps (NP) located in the middle meatus. Computed tomography (CT) features of centrally limited disease in paranasal

sinuses without involvement in the roof or the lateral wall of the ethmoid sinus could aid in diagnosing CCAD. Patients with both sinonasal polyps and concomitant polypoid disease in the central compartment (CRSwNP/CC) were grouped. In this group, CT mainly showed diffuse pansinusitis with central compartment opacification. CRSwNP NOS included patients with bilateral polyps or polypoid changes originating from the middle meatus, ostiomeatal complex, and maxillary sinus but without a polypoid change in the central compartment. The central compartment spared was the typical CT feature in the CRSwNP NOS group.[13] The main points regarding the differential diagnosis of CCAD, CRSwNP/CC, and CRSwNP NOS are listed in Supplement Table 1. The typical endoscopic and CT images of the 3 groups are presented in Fig. 2.

Baseline assessment and outcome measures

The baseline data were collected at the first visit (−14 to −7 day before surgery). Baseline data included demographics, comorbidity (AR and asthma), Lund-Mackay score of sinus computed tomography (CT),[20] polyp origin, and polyp score of endoscopic examinations,[21] peripheral blood eosinophil count and ratio, visual analog scale (VAS) of 4 main symptoms of CRS (nasal obstruction, discharge, olfactory loss, and headache/facial pain, scale 0–10 for each),[16] total nasal symptoms score (TNSS) (sum of the 4 above symptoms, scale 0–40), SNOT-22 (scale 0–110),[22] and its 5 domains.[23] No systemic steroids were administered to our patients in the month prior to the baseline assessment.

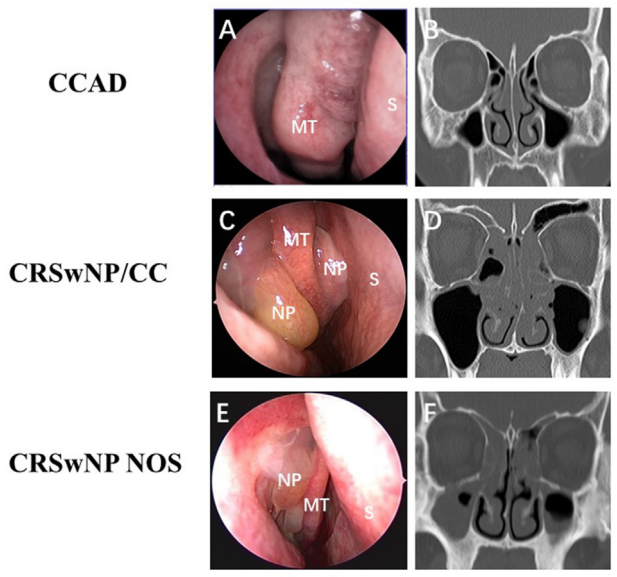

Fig. 2 Representative CT and endoscopic images for CCAD (A, B), CRSwNP/CC (C, D), and CRSwNP NOS (E, F) before surgery. MT = middle turbinate, S = septum, NP = nasal polyps

Surgery and postoperative treatment

All the patients underwent ESS performed by the same senior rhinology specialist, thereby reducing the risk of inconsistency or bias for a particular procedure. The extent of surgery was determined by sinus involvement based on CT examination. FESS was performed using the Messerklinger technique,[24] and involved full maxillary antrostomy, ethmoidectomy, sphenoidotomy, and frontal sinusotomy, but with MT preservation. Extensive endoscopic sinus surgery (EESS)[25] was performed using the "full house FESS" technique, with full maxillary antrostomy, total ethmoidectomy, wide sphenoidotomy, and frontal pathway clearance according to our previous study. The inferior two-thirds of MT was resected.

At the end of the surgery, patients were packed with NasoPore (Stryker, Australia) or Merocel (Medtronic, USA), depending on the bleeding in the surgical field. Merocel was removed 48 hours after surgery. As per our routine postoperative protocol, 48 hours after the surgery or 1 day after Merocel was removed, patients started nasal saline irrigations twice daily for 1 month, and then once daily on a long-term basis; budesonide nasal spray twice daily (128 μg/per nostril, bid) for 1 month, and then 64 μg/per nostril twice daily on a long-term basis. Endoscopic debridement of sinonasal cavities was at week 1, week 2, month 1, month 2, and month 3 after surgery.

If the patient achieved well controlled, all medications were stopped. If patients did not achieve well controlled, budesonide nasal spray would keep being used. Antihistamine was not routinely used for each patient unless with AR, and the symptoms of AR were not controlled by steroid nasal spray alone.

Tissue sample collection and evaluation of inflammatory endotypes

Nasal polyp tissues were harvested during surgery. Blocks of formalin-fixed paraffin-

embedded nasal polyp tissue were assessed on H&E. Slides were observed at 40 × magnification. Two independent observers counted tissue eosinophils and other inflammatory cells, and their numbers were reported as the mean of counts in 5 randomized, non-overlapping fields. Eosinophilic CRS (eCRS) was defined as the count of tissue eosinophils greater than 10/HPF (high-power field).[26,27]

Outcomes assessment

The primary endpoint was CRS control status (Supplement Table 2)[16] at 1 year postoperatively, which was categorized as well controlled, partly controlled, and uncontrolled. We defined well controlled and partly controlled as appropriate disease control. The secondary endpoints were postoperative endoscopic score (E-score),[28] TNSS, VAS of the 4 main symptoms, SNOT-22, and its 5 domains.

Statistical analysis

The sample size was estimated based on the findings of our pilot study by using CRS uncontrolled rate at 1 year after surgery as the primary outcome. We used a parallel design and set CRSwNP/CC as the control group. The uncontrolled rate was 30% in CRSwNP/CC and 7% in CCAD. We estimated the sample size was 45 per group with a power equal to 80% and a two-tailed α value of 0.05. The sample size calculation was performed using PASS (version 15). Because in the studies,[14,15] CCAD is often compared to CRSwNP NOS, we also enrolled CRSwNP NOS with the same sample size.

Normally distributed data is presented as mean ± SD and abnormal data as median (Interquartile Range). Continuous variables with a normal distribution were analyzed using Student's t-test for two-group comparison and One-way ANOVA for three-group comparison. Post-hoc multiple comparisons used LSD when equal variances were assumed, otherwise used Tamhane's. The variables with an abnormal distribution were analyzed using the Mann-Whitney *U* test for two-group comparisons and Kruskal-Wallis test for three-group comparison. The comparison of categorical variables was analyzed using the chi-square test. Statistical significance was set at $P < 0.05$. Statistical analyses were performed using SPSS (version 25.0, IBM Crop, Armonk, NY) and presented using GraphPad Prism software (version 9.0).

RESULTS

Demographics and comorbidities

Two hundred fifty-nine patients were screened; of these, 138 patients were recruited, with 51 in the CCAD group, 55 in the CRSwNP/CC group, and 32 in the CRSwNP NOS group. There was no significant difference across groups for gender and CRS disease course. Ages were significantly different among groups ($P = 0.004$). The CRSwNP/CC (Median [IQR], 48.00 [17.00] years) was older than the CRSwNP NOS (33.00 [19.00] years). For comorbid diseases, the proportion of asthma had a significant difference among groups ($P = 0.017$). Approximately 37% of the CCAD and 32% of the CRSwNP/CC had asthma, both of which were significantly higher than the CRSwNP NOS (3.7%). On the contrary, the proportion of atopy or AR did not differ among groups ($P > 0.05$). (Table 1).

Baseline disease characteristics

Symptoms, polyp score, and CT score

The symptom TNSS ($P = 0.007$), VAS of obstruction ($P < 0.001$), olfactory ($P = 0.027$), and headache/facial pain ($P = 0.019$) were significantly different among the 3 groups, but not rhinorrhea ($P = 0.347$). In the post-hoc analysis, TNSS and obstruction VAS in the CRSwNP/CC (24.43 ± 1.21, 9.00 [2.75]) was significantly higher than the CCAD (17.75 ± 1.61, 5.50 [6.75]) and the CRSwNP NOS (19.71 ± 1.86, 6.00 [3.50]). Meanwhile, olfactory VAS in the CRSwNP/CC (9.00 [3.50]) was significantly worse than the CRSwNP NOS (5.00 [9.00]), but did not differ from the CCAD (8.50 [4.00]). Moreover, the CCAD (0.00 [1.50]) had the mildest headache/facial pain VAS compared to the CRSwNP/CC (1.75 [4.38]) and the CRSwNP NOS (2.00 [5.50]) (Table 1).

In addition, the polyp score ($P < 0.001$) and CT Lund-Mackay score ($P < 0.001$) had significant differences in groups. Consistent with symptoms, the polyp score and CT score in the CRSwNP/CC (6.00 [1.00], 19.50 [4.00]) were significantly worse than the CCAD (5.00 [2.25], 12.00 [5.00]) and the CRSwNP NOS (4.00 [3.00], 10.00 [6.00]) (Table 1).

Guo et al. World Allergy Organization Journal (2024) 17:100859
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	Total (N = 138)	CCAD (N = 51)	CRSwNP/CC (N = 55)	CRSwNP NOS (N = 32)	*P*
Gender (male/female)	88/50	34/17	34/21	20/12	0.866
Age (Y)*	45.00 (22.00)	44.00 (23.00)	48.00 (17.00)[c]	33.00 (19.00)	0.004
Disease duration (Y)	5.00 (8.00)	4.00 (7.00)	5.00 (8.00)	5.00 (9.00)	0.362
Atopy	43 (38.7%)	15 (40.5%)	21 (42.9%)	7 (28.0%)	0.446
Allergic rhinitis	41 (29.1%)	15 (28.8%)	18 (32.1%)	8 (24.2%)	0.730
Asthma*	37 (26.2%)	19 (37.0%)[b]	18 (32.3%)[c]	3 (7.7%)	0.017
tIgE (IU/ml)*	85.31 (105.05)	82.28 (94.25)	107.25 (150.73)[c]	40.30 (83.65)	0.005
TNSS*	20.71 ± 0.94	17.75 ± 1.61[a]	24.43 ± 1.21[c]	19.71 ± 1.86	0.007
VAS of obstruction*	7.00 (5.00)	5.50 (6.75)[a]	9.00 (2.75)[c]	6.00 (3.50)	<0.001
VAS of rhinorrhea	6.00 (5.25)	5.50 (7.00)	6.25 (4.50)	6.00 (4.50)	0.347
VAS of olfactory*	8.00 (5.50)	8.50 (4.00)	9.00 (3.50)[c]	5.00 (9.00)	0.027
VAS of headache/facial pain*	1.00 (4.00)	0.00 (1.50)[a,b]	1.75 (4.38)	2.00 (5.50)	0.019
Polyp score*	6.00 (2.00)	5.00 (2.25)[a]	6.00 (1.00)[c]	4.00 (3.00)	<0.001
Lund-Mackay score*	14.00 (9.00)	12.00 (5.00)[a]	19.50 (4.00)[c]	10.00 (6.00)	<0.001
Blood Eos count (× 10^9/L)*	0.23 (0.27)	0.30 (0.22)[b]	0.23 (0.33)	0.16 (0.15)	0.029
Blood Eos%*	3.60 (3.90)	4.40 (4.10)[b]	3.30 (4.20)	2.40 (3.43)	0.039
Tissue Eos count (/HPF)*	11.20 (34.75)	30.40 (48.37)[b]	13.00 (27.95)	2.40 (10.80)	0.001
Tissue Eos%*	29.66 (45.92)	37.70 (35.25)[b]	26.64 (48.33)	6.12 (30.87)	0.002
eCRS (>10/HPF) (%)*	52.9	67.6[b]	57.5[c]	25.9	0.003
eCRS (>10%) (%)*	65.4	83.8[b]	65.0[c]	40.7	0.002

SNOT-22*	28.50 (35.50)	29.50 (35.75)[a]	46.00 (29.00)[c]	18.00 (19.00)	<0.001
Rhinologic symptoms*	14.60 ± 0.83	14.29 ± 1.36[a]	19.00 ± 1.03[c]	11.29 ± 1.27	<0.001
Extra-nasal rhinologic symptoms*	4.58 ± 0.42	3.82 ± 0.83[a]	6.53 ± 0.66[c]	3.62 ± 0.52	0.005
Ear/facial symptoms*	3.00 (5.00)	3.00 (5.00)[b]	6.00 (5.50)[c]	2.00 (3.00)	<0.001
Psychological dysfunction*	5.00 (12.00)	5.00 (11.00)	11.00 (17.00)[c]	2.00 (9.00)	0.006
Sleep dysfunction*	4.00 (11.00)	6.00 (11.00)[b]	10.00 (11.00)[c]	0.00 (2.00)	<0.001

Table 1. Demographics and characteristics of patients in subgroups of CRSwNP. *Categorical variable data were presented by N (%); numerical variable data were presented by mean ± SD (normal distribution) or median (Interquartile Range) (abnormal distribution). CCAD = central compartment atopic disease; CRSwNP/CC = sinonasal polyps and central compartment involvement; CRSwNP NOS = chronic rhinosinusitis with nasal polyposis not otherwise specified; SNOT-22 = 22-Item Sino-Nasal Outcome Test; TNSS = total nasal symptoms score; VAS = Visual Analogue Scale; eCRS = eosinophilic chronic rhinosinusitis. *Presented statistical difference within groups. [a]Presented statistical difference between the CCAD group and the CRSwNP/CC group. [b]Presented statistical difference between the CCAD group and the CRSwNP NOS group. [c]Presented statistical difference between the CRSwNP/CC group and the CRSwNP NOS group*

Inflammatory endotypes

The 3 groups had significant differences in both blood ($P < 0.05$) and tissue ($P < 0.005$) eosinophilia. In the post-hoc analysis, the CCAD group had higher blood eosinophil ratio (Median [IQR], 4.40 [4.10] %) than the CRSwNP NOS (2.40 [3.43] %), but did not differ from the CRSwNP/CC (3.30 [4.20] %). Likewise, the CCAD group had higher polyp tissue eosinophilic count and ratio (30.40 [48.37]/HPF, 37.70%), compared with the CRSwNP NOS (2.40 [10.80]/HPF, 26.64%), but did not differ from the CRSwNP/CC (13.00 [27.95]/HPF, 6.12%) (Table 1).

In terms of the inflammatory endotype, the CCAD (83.8%) and the CRSwNP/CC (65.0%) groups had higher proportion of eCRS than the CRSwNP NOS (40.7%) but did not differ significantly from each other based on the criterion of tissue eosinophil count greater than 10% in polyp tissue (Table 1).

Quality of life

The total SNOT-22 score and all 5 domains significantly differed among groups (all $P < 0.01$). Again, the CRSwNP/CC (46.00 [29.00], 19.00 ± 1.03, 6.53 ± 0.66) had higher SNOT-22, rhinologic, and extra-nasal rhinologic symptom scores than the CCAD (29.50 [35.75], 14.29 ± 1.36, 3.82 ± 0.83) and the CRwNP NOS (18.00 [19.00], 11.29 ± 1.27, 3.62 ± 0.52). The CRSwNP/CC (6.00 [5.50], 10.00 [11.00]) and the CCAD (3.00 [5.00], 6.00 [11.00]) had higher ear/facial and sleep dysfunction than the CRSwNP NOS (2.00 [3.00], 0.00 [2.00]). The CRSwNP/CC (11.00 [17.00]) had higher psychological dysfunction score than the CRSwNP NOS (2.00 [9.00]) (Table 1).

Surgery extent and surgical outcomes

The proportion of patients who underwent full-house FESS significantly differed among groups (CCAD 58.0%, CRSwNP/CC 87.5%, and CRSwNP NOS 27.3%, $P < 0.001$). In the post-hoc analysis, there are significant differences among any 2 groups. There is no significant difference among groups in the proportion of inferior turbinectomy ($P = 0.485$) and septoplasty ($P = 0.097$). The surgery extent in subgroups is presented in Supplement Table 3.

	Total N = 138	CCAD N = 51	CRSwNP/CC N = 55	CRSwNP NOS N = 32
Well controlled	67	26 (51.0%)	20 (36.4%)	21 (65.6%)
Partly controlled	44	17 (33.3%)	18 (32.7%)	9 (28.1%)
Uncontrolled	27	8 (15.7%)	17 (30.9%)	2 (6.3%)

Table 2. Control status of patients in subgroups of CRSwNP 1 year after surgery. *Data were presented as N (%). CCAD = central compartment atopic disease; CRSwNP/CC = sinonasal polyps and central compartment involvement; CRSwNP NOS = chronic rhinosinusitis with nasal polyposis not otherwise specified*

During the follow-up period, 3 patients (3/138, 2.2%) underwent revision surgery (1 per group), and 2 patients with asthma in the CRSwNP/CC group used omalizumab because of their CRS uncontrol status postoperatively.

Control status

Totally, well controlled status was achieved in 67 of 138 patients (48.5%), with 44 (31.9%) in partly controlled and 27 (19.6%) in uncontrolled status (Table 2, Fig. 3A). In the post-hoc analysis, the CRSwNP/CC group had the highest uncontrolled rate (30.9%), compared with 15.7% in the CCAD and 6.3% in the CRSwNP NOS. There is no significant difference between the CCAD group and the CRSwNP NOS group (see Fig. 3).

Symptom, endoscopic score and quality of life

The postoperative SNOT-22 and its five domains showed no significant difference across groups (Table 3). However, there were statistically significant differences in the change value (Fig. 4). The E-score was significantly different among groups ($P < 0.001$) (Table 3, Fig. 3B). The CRSwNP/CC (33.32 [42.14]) had the worst E-score compared to the CCAD (8.33 [16.67]) and the CRSwNP NOS (4.17 [8.30]), without significant difference in the latter 2. The typical endoscopic images of the 3 groups are presented in Supplement Fig. 1 (A-F).

The postoperative SNOT-22 and its 5 domains showed no significant difference across groups

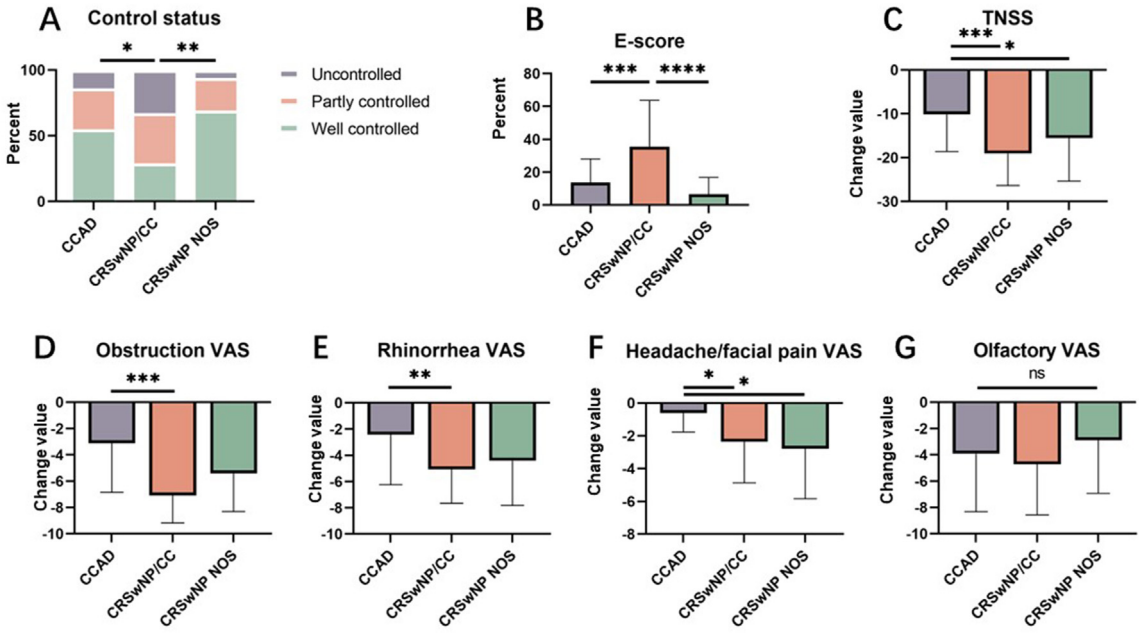

Fig. 3 Control status, change of TNSS and VAS between baseline and 1 year after surgery of 3 groups, and statistical analysis of postoperative endoscopic score (E-score) of 3 groups at 1 year after surgery. * presented $p < 0.05$, ** presented $p < 0.01$, ***presented $p < 0.001$, ****presented $p < 0.0001$. TNSS = total nasal symptoms score; VAS=Visual Analogue Scale

	Total	CCAD	CRSwNP/CC	CRSwNP NOS	*P*
E-score (%)*	10.00 (29.17)	8.33 (16.67)[a]	33.32 (42.14)[b]	4.17 (8.30)	<0.001
TNSS	5.00 (8.00)	5.00 (7.00)	5.00 (9.00)	3.00 (9.00)	0.124
MCID in TNSS (%)	81.4	69.2	92	84.2	0.105
VAS of obstruction	1.00 (2.50)	1.00 (3.00)	1.50 (2.50)	0.00 (2.00)	0.159
VAS of rhinorrhea	1.00 (2.00)	1.00 (2.25)	1.00 (2.00)	0.00 (3.00)	0.398
VAS of olfactory*	1.00 (4.00)	1.00 (4.00)	2.00 (4.75)	0.00 (2.00)	0.043
VAS of headache/facial pain	0.00 (0.00)	0.00 (0.00)	0.00 (0.75)	0.00 (0.00)	0.092
SNOT-22	6.00 (13.75)	6.00 (12.00)	8.50 (15.75)	4.00 (16.25)	0.208
Rhinologic symptoms	3.00 (6.00)	4.00 (4.50)	4.00 (7.00)	1.00 (6.00)	0.244
Extra-nasal rhinologic symptoms	1.00 (2.00)	0.00 (1.50)	1.00 (2.00)	1.00 (2.00)	0.459
Ear/facial symptoms	0.00 (1.00)	0.00 (1.00)	0.00 (2.00)	0.00 (2.00)	0.608
Psychological dysfunction	0.00 (3.00)	0.00 (2.50)	0.00 (2.00)	0.00 (3.00)	0.872
Sleep dysfunction	0.00 (2.00)	0.00 (3.00)	0.00 (2.00)	0.00 (1.00)	0.806
MCID in SNOT-22 (%)*	68.6	62.5[a]	93.8[b]	52.6	0.027

Table 3. Postoperative endoscopic score, symptoms and SNOT-22 in subgroups of CRSwNP at 1 year after surgery. *Categorical variable data were presented by N (%); numerical variable data were presented by mean ± SD (normal distribution) or median (Interquartile Range) (abnormal distribution). CCAD = central compartment atopic disease; CRSwNP/CC = sinonasal polyps and central compartment involvement; CRSwNP NOS = chronic rhinosinusitis with nasal polyposis not otherwise specified; TNSS = total nasal symptoms score; VAS = Visual Analogue Scale; SNOT-22 = 22-Item Sino-Nasal Outcome Test; MCID = minimal clinically important difference. *presented statistical difference within groups. [a]presented statistical difference between the CCAD group and the CRSwNP/CC group; [b]presented statistical difference between the CRSwNP/CC group and the CRSwNP NOS group.*

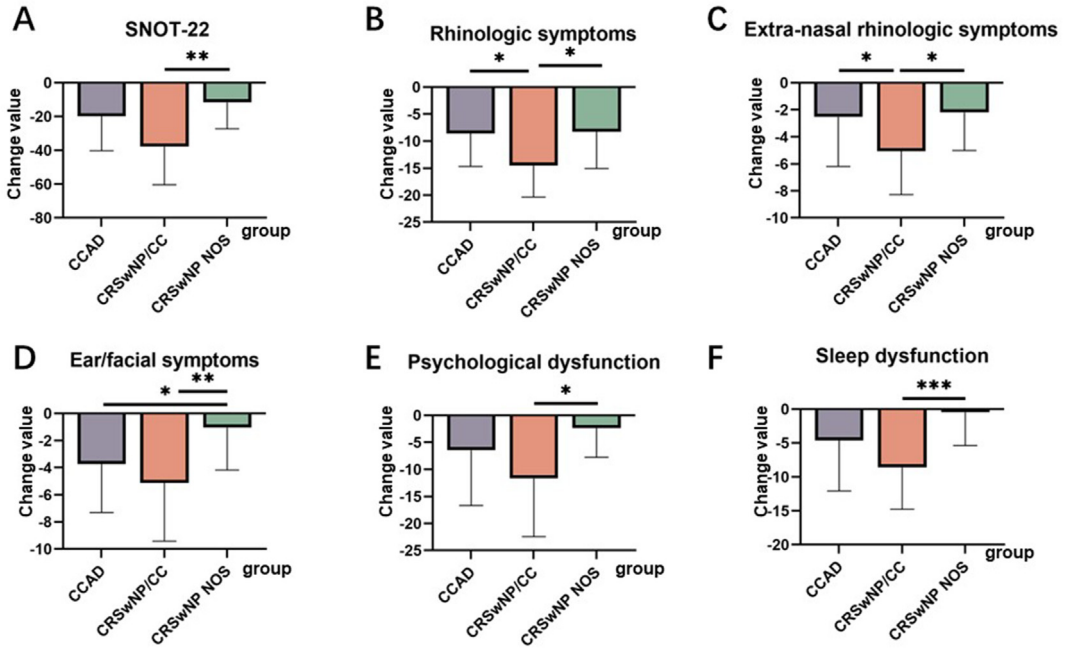

Fig. 4 Change of SNOT-22 and its 5 domains between baseline and 1 year after surgery; *presented $p < 0.05$, ** presented $p < 0.01$, ***presented $p < 0.001$. SNOT-22 = 22-Item Sino-Nasal Outcome Test

(Table 3). MCID was defined as the change of SNOT-22 greater than or equal to 8.9.[29] In total, 68.6% of patients achieved MCID in SNOT-22. There is significant difference among groups ($P = 0.027$). The CRSwNP/CC had the highest proportion of patients who achieved MCID (93.8%), compared to the CCAD (62.5%) and the CRSwNP NOS (52.6%).

When comparing the change before and after surgery, we found TNSS, 4 individual symptoms, SNOT-22, and its 5 domains improved significantly in all the groups, except the domains of ear/facial symptoms and sleep dysfunction in the CRSwNP NOS group (Table 4).

When we compared the changes across groups, we found statistical significance in the change of TNSS, VAS of obstruction, rhinorrhea, and headache/facial pain among the 3 groups ($P < 0.05$) (Fig. 3C–F), except VAS of olfactory (Fig. 3 G). In post-hoc analysis, the CRSwNP/CC and the CRSwNP NOS had higher change in TNSS and headache/facial pain VAS compared to the CCAD. And CRSwNP/CC had higher change in obstruction and rhinorrhea VAS compared to the CCAD.

DISCUSSION

CCAD is a newly identified subtype of CRSwNP that involves the central sinonasal compartment based on endoscopic and CT findings. In our previous study,[13] we found distinct geographic differences between CCAD in the West and CCAD in Asia. We had a detailed discussion in our previous study[13] to compare and analyze these differences, regarding the low prevalence of allergy, the high prevalence of asthma, and the eosinophilic inflammatory profile. Then we enlarged the sample size and followed up with our patients for over a year. And now we report the surgical outcomes of CCAD in the current study. The characteristics of CCAD in the current study were consistent with those of the previous study.[13] To avoid duplicates, we did not discuss the differences in characteristics in the present study.

The current study comprehensively assessed the outcomes by CRS control levels, QOL SNOT-22, symptoms VAS score, endoscopic score, and revision surgery. One year after the surgery, we found that the CCAD group had generally good surgery outcomes. Forty-three patients in the

	CCAD			CRSwNP/CC			CRSwNP NOS		
	Pre-	Post-	*P*	Pre-	Post-	*P*	Pre-	Post-	*P*
TNSS	18.50 (15.00)	5.00 (7.00)	<0.001	25.00 (8.50)	5.00 (9.00)	<0.001	18.00 (13.00)	3.00 (9.00)	<0.001
Obstruction	5.50 (6.75)	1.00 (3.00)	<0.001	9.00 (2.75)	1.50 (2.50)	<0.001	6.00 (3.50)	0.00 (2.00)	<0.001
Rhinorrhea	5.50 (7.00)	1.00 (2.25)	0.002	6.25 (4.50)	1.00 (2.00)	<0.001	6.00 (4.50)	0.00 (3.00)	<0.001
Olfactory	8.50 (4.00)	1.00 (4.00)	<0.001	9.00 (3.50)	2.00 (4.75)	<0.001	5.00 (9.00)	0.00 (2.00)	0.01
headache/facial pain	0.00 (1.50)	0.00 (0.00)	0.004	1.75 (4.38)	0.00 (0.75)	<0.001	2.00 (5.50)	0.00 (0.00)	0.001
SNOT-22	29.50 (35.75)	6.00 (12.00)	<0.001	46.21 ± 3.92	10.53 ± 1.47	<0.001	18.00 (19.00)	4.00 (16.25)	0.002
Rhinologic symptoms	15.00 (10.50)	4.00 (4.50)	<0.001	8.50 (15.75)	4.00 (7.00)	<0.001	10.00 (11.50)	1.00 (6.00)	<0.001
Extra-nasal rhinologic symptoms	3.00 (6.00)	0.00 (1.50)	0.019	19.00 (5.50)	1.00 (2.00)	<0.001	3.00 (3.00)	1.00 (2.00)	0.004
Ear/facial symptoms	3.00 (5.00)	0.00 (1.00)	<0.001	6.00 (5.00)	0.00 (2.00)	<0.001	2.00 (3.00)	0.00 (2.00)	0.066
Psychological dysfunction	5.00 (11.00)	0.00 (2.50)	0.023	6.00 (5.50)	0.00 (2.00)	0.013	2.00 (9.00)	0.00 (3.00)	0.013
Sleep dysfunction	6.00 (11.00)	0.00 (3.00)	0.016	11.00 (17.00)	0.00 (2.00)	0.001	0.00 (2.00)	0.00 (1.00)	0.516

Table 4. Symptoms score and SNOT-22 at baseline and 1 year after surgery. *CCAD = central compartment atopic disease; CRSwNP/CC = sinonasal polyps and central compartment involvement; CRSwNP NOS = chronic rhinosinusitis with nasal polyposis, not otherwise specified; pre- = pre-operation; post- = post-operation, TNSS = total nasal symptoms score; SNOT-22 = 22-Item Sino-Nasal Outcome Test*

CCAD group (84.3%) achieved appropriate disease control of CRS. The revision surgery rate was 2.0%, and no patient underwent biologics treatment. Furthermore, the CCAD group significantly improved in symptom TNSS and each individual score compared to baseline. Also, the CCAD group had a significant change in SNOT-22 and all 5 domains after treatment, in which 62.5% of patients achieved MCID in SNOT-22. Although our results revealed that CCAD was a T2-high disease with high local eosinophil infiltration (count 30.40 eos/HPF and ratio 37.7%) and high blood eosinophilia (count 0.30 $\times$ 10^9/L and ratio 4.4%), it generally achieved good outcomes 1 year postoperatively. These may be due to the disease not involving all the sinus mucosa. When surgery removes the inflammatory tissue and opens the sinuses with long-term postoperative nasal corticosteroid spray, sinus inflammation is under control.

Until now, 2 studies have focused on the ESS outcomes of CCAD. Steehler et al[15] reported the polyp recurrence rate was 7.9% and the revision surgery rate was 5.3% in CCAD 1 year after surgery, both of which were lower than CRSwNP NOS (27% and 29.7%, respectively). In the current study, the revision surgery rate was 2% in CCAD and 3% in CRSwNP NOS, which were comparable. The CRSwNP NOS group also had the most patients who achieved control status postoperatively (93.7%). Our pathology results found that CRSwNP NOS had the lowest eosinophil infiltration (2.40/HPF and 6.1%). However, Steehler et al[15] reported that the CRSwNP NOS group had a higher polyp recurrence and revision surgery rate than the CCAD group. This may be due to differences in eosinophilia in the West and in Asia. In a global multicenter study, Wang XD et al[30] found that CRSwNP in China has lower eosinophilic endotype than CRSwNP in the West. They reported that more than 50% of patients with CRSwNP in Benelux, Berlin, Adelaide, and Tonchigi showed a predominantly eosinophilic endotype compared with less than 30% of patients in Beijing and Chendu in China.[30] The CRSwNP NOS patients in the Steehler et al study[15] may have a higher degree of eosinophilia than our patients. Many studies have reported that tissue eosinophilic infiltration is associated with surgical outcomes.[5,7,31] And non-eCRS had better surgical outcomes than eCRS.[32,33] Shih LC et al[14] reported that CCAD had a greater improvement in SNOT-22 after 3 months after ESS. We had a longer follow-up time of 1 year. We also found that CCAD had significant improvements in SNOT-22 and its 5 domains.

We also compared the baseline disease burden, the postoperative VAS scores and SNOT-22, and the change of these measures among groups. At baseline, there were significant differences across groups in SNOT-22 and its 5 domains, as well as the symptom scores of obstruction, olfactory, and headache/facial pain, except for rhinorrhea. Surprisingly, in the postoperative follow-up, we found no significant difference among groups in the outcomes above. However, when we compared the change in outcomes between baseline and 1 year postoperatively, we found significant differences among the 3 groups. CCAD had less change in the VAS scores of obstruction, rhinorrhea, and headache/facial pain, but not olfactory, compared to CRSwNP/CC. In addition, CRSwNP/CC had the least proportion (69.1%) of patients achieving CRS control postoperatively. However, it had the largest proportion (93.8%) of patients achieving an MCID in SNOT-22 after ESS. This is consistent with previous studies.[34,35] Hopkins et al[35] found that the preoperative SNOT-22 score was a strong predictor of postoperative SNOT-22, with those having higher preoperative scores achieving greater reductions but having persistently higher scores postoperatively.

In other studies, CRSwNP group had worse outcomes compared to CCAD group. However, CRSwNP NOS group had better efficacy than CCAD group in our study, although CRSwNP NOS group is a subtype of CRSwNP. There are 2 possible reasons for this. Firstly, most polyp tissues are characterized by the dominance of eosinophils, especially in White patients, but there is a high proportion of neutrophilic polyps in Asian patients.[4]

This study has some limitations. First, this is a retrospective analysis of the prospectively collected data from the CRS research database. A prospective design study is needed to assess the outcomes. Second, longer follow-up is needed to

understand the long-term outcomes of ESS for CCAD.

CONCLUSION

This is the first article to report the comprehensive outcomes of CCAD 1 year after surgery. The results suggest that most patients with CCAD may achieve controlled status postoperatively, even though this group had high local and blood eosinophilia.

Abbreviations

CCAD, Central compartment atopic disease; CRS, chronic rhinosinusitis; ESS, endoscopic sinus surgery; CRSwNP, chronic rhinosinusitis with nasal polyps; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP/CC, chronic rhinosinusitis with nasal polyps and concomitant polypoid disease in the central compartment; CRSwNP NOS, chronic rhinosinusitis with nasal polyps not otherwise specified; eCRS, eosinophilic CRS; non-eCRS, non-eosinophilic CRS; ST, superior turbinate; MT, middle turbinate; PNSS, posterosuperior nasal septum; AR, allergic rhinitis; CT, computed tomography; FEV1, Forced Expiratory Volume; FVC, forced vital capacity; tIgE, serum total IgE; sIgE, serum specific IgE; ZERD, aspirin-exacerbated respiratory disease; AFRS, allergic fungal rhinosinusitis; NP, nasal polyps; VAS, visual analog scale; TNSS, total nasal symptoms score; SNOT-22, 22-Item Sino-Nasal Outcome Test; E-score, postoperative endoscopic score; MCID, minimal clinically important difference.

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Ethics Statement

The Ethics Committee for Clinical Research and Animal Trials approved the study. All participants provided written informed consent.

Availability of data and materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Author contribution

Yuanyuan Guo: Data curation, Writing- Original draft preparation.
Zhiying Nie: Methodology, Software.
Chuxin Chen: Data curation, Software.
Zhaofeng Xu: software.
Wendong Liu: Validation.
Yinyan Lai: Methodology.
Yunping Fan: Visualization.
Jianbo Shi: Supervision and surgeon.
Fenghong Chen: Study design, writing-reviewing and editing.

Declaration of competing interest

The authors declare that they have no conflicts of interest and have consented to publication.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.waojou.2023.100859.

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