

Computed Tomography Findings Can Help Identify Different Chronic Rhinosinusitis With Nasal Polyp Phenotypes

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Abstract

Background: Chronic rhinosinusitis with nasal polyps (CRSwNPs) has several phenotypes.

Objectives: The goal of this study was to evaluate computed tomography (CT) findings associated with each CRSwNP phenotype.

Methods: Patient charts between January 2015 and March 2019 were retrospectively reviewed. Patient groups, including allergic fungal rhinosinusitis (AFRS), aspirin-exacerbated respiratory disease (AERD), central compartment atopic disease (CCAD) and CRSwNP not otherwise specified (CRSwNP NOS), were determined by standard criteria. The oldest CT scan available was reviewed for Lund–Mackay (LM) score, septal involvement of inflammatory disease, opacification of olfactory clefts, nasal cavity opacification, and oblique positioning of the middle turbinates. Nonparametric analyses of variance were performed with correction for multiple comparisons.

Results: A total of 356 patients had scans available for review; 80 (23%) patients were categorized into the AFRS group, 101 (28%) in the AERD group, 43 (12%) in the CCAD group, and 132 (37%) in the CRSwNP NOS group. Septal inflammatory involvement and oblique middle turbinate orientation on CT scans was higher in both AERD patients and CCAD patients as compared to AFRS and CRSwNP NOS patients ($P < .05$). Olfactory cleft opacification was increased in the AERD group compared to all other diagnoses ($P < .05$). The CCAD group showed lower LM scores compared to all other groups ($P < .05$), and the AFRS group revealed the greatest differences between left and right LM grades, representing unilaterality of disease ($P < .05$).

Conclusion: CRSwNP encompasses many subsets of disease, which have varying treatments and intraoperative findings. Preoperative CT findings can be used to differentiate between these groups to improve prediction of diagnoses and patient counseling.

Keywords

aspirin-exacerbated respiratory disease, allergic fungal rhinosinusitis, central compartment atopic disease, chronic rhinosinusitis with nasal polyp, computed tomography, phenotype

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNPs) is a common diagnosis, thought to affect 25% of patients with chronic sinusitis.¹ There are several phenotypes of CRSwNP, including allergic fungal rhinosinusitis (AFRS) and aspirin-exacerbated respiratory disease (AERD).² Recently, central compartment atopic disease (CCAD) has been described as a subset of patients with centrally located nasal inflammation and polyp disease related to inhalant allergy.³ Oftentimes, patient

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symptoms and exam findings are similar for these subgroups of inflammatory disease, making them difficult to differentiate from each other.

As treatment options and counseling vary between these subsets of patients, it is useful to evaluate tools for early identification of CRSwNP phenotype. Preoperative computed tomography (CT) findings may aid in this evaluation, with previous work focusing on common diagnoses for unilateral compared to bilateral disease processes.^{4,5} For example, AFRS patients often demonstrate unilateral disease, heterogeneous opacification, and expansion of the sinuses.⁶ Recently, our group and others have identified that patients with CCAD demonstrate septal and centrally located mucosal thickening on CT scan.³ From our clinical experience, centrally located disease can lead to olfactory cleft opacification, a CT finding which has been shown to be associated with hyposmia.⁷ In addition, centrally located disease in our patients has anecdotally been found to lead to oblique positioning of the middle turbinates, potentially from long-standing lateral displacement by polyps and inflammation. The objective of this study was to evaluate potential differences in preoperative CT imaging findings among patients with various CRSwNP phenotypes.

Materials and Methods

Patients with CRSwNP were identified from attending surgeon operative logs. Charts from patients seen at the Emory University Sinus, Nasal and Allergy Center between January 2015 and March 2019 were retrospectively reviewed (IRB Approval #IRB00107743). Patients were classified into 1 of the 4 inflammatory polyp groups, including 3 previously described CRSwNP phenotypes: AFRS, AERD, and CCAD. CCAD included patients with endoscopic findings of polypoid involvement of the middle turbinate, with or without the superior turbinate and superior nasal septum. AERD was diagnosed based on 3 criteria: nasal polyps, asthma, and documented aspirin sensitivity, with either respiratory reactions to nonsteroidal anti-inflammatory medications or positive aspirin challenge. Patients meeting criteria for AFRS had documented eosinophilic mucin, noninvasive fungal elements, nasal polyps, clinical allergy symptoms, and radiographic findings consistent with the disease.⁸ Patients not meeting criteria for any of these phenotypic groups were classified as CRSwNP not otherwise specified (CRSwNP NOS). This classification was determined by the treating rhinologist.

Images were reviewed by L. T. R. and J. M. D. The oldest CT scan available was evaluated for several imaging findings: Lund-Mackay (LM) score, septal involvement of inflammatory disease, opacification of olfactory clefts, nasal cavity opacification, and oblique positioning

of the middle turbinates (Table 1). LM score was determined by standard criteria.⁹ Septal involvement was graded on a 0 to 2 categorical scale, with 0 representing no septal involvement, 1 representing unilateral disease, and 2 representing bilateral involvement of the septum. Opacification of the olfactory cleft and middle turbinate oblique positioning were similarly graded based on no (0), unilateral (1), or bilateral (2) disease. Of note, middle turbinate positioning was determined in relation to septal position, to control for septal deflection or deviation. Oblique positioning was caused by soft tissue inflammation and an approximate 30° angle was considered oblique positioning. Nasal cavity opacification was graded on each side from 0 to 4 based on the percentage of the nasal airway obstructed by inflammation on the CT imaging (Table 1). These scores were calculated on both the left and right sides for a total score of 0 to 8. Nonparametric 1-way analyses of variance (ANOVAs) were performed with correction for multiple comparisons between patient groups.

Results

A total of 356 patients had scans available for review. Eighty (23%) patients were classified into the AFRS group, 101 (28%) in the AERD group, 43 (12%) in the CCAD group, and 132 (37%) in the CRSwNP NOS group. Due to nonparametric distribution of the data, mean rank scores and post hoc analyses for each CT grading system of the 4 inflammatory groups were compared and are reported below (Table 2; Figure 1).

LM Score

One-way ANOVA revealed differences in LM scoring between the 4 groups ($\chi^2(3) = 52.19$, $P < .001$, with mean rank scores of AFRS = 181.68, CRSwNP NOS = 179.67, AERD = 214.56 and CCAD = 80.24). Absolute values of differences between left and right LM scores were also found to be different between groups ($\chi^2(3) = 47.63$, $P < .001$, with mean rank scores of AFRS = 242.85, CRSwNP NOS = 167.02, AERD = 145.78 and CCAD = 161.99). Post hoc analyses are shown in Figure 1 with the CCAD group showing lower overall LM scores than all other patient groups and the AFRS group revealing the greatest differences between left and right LM grades (Table 2; Figures 1 to 3).

Septal Inflammatory Disease

Differences in septal inflammation were seen between the 4 groups ($\chi^2(3) = 52.89$, $P < .001$, with mean rank scores of AFRS = 87.14, CRSwNP NOS = 121.74, AERD = 177.63 and CCAD = 156.60). Septal inflammatory involvement was seen at a higher rate in both AERD patients (unilateral—5%, bilateral—67%) and

Table 1. Scoring Systems for CT Scans.

Grading System	Scoring Criteria
Lund–Mackay score	0 = none 1 = partial opacification 2 = complete opacification Total score = 0–24 (0–2 for each maxillary, anterior ethmoid, posterior ethmoid, sphenoid, and frontal sinus, 0 or 2 for OMC obstruction)
Septal inflammation	0 = none 1 = unilateral 2 = bilateral
Olfactory cleft opacification	0 = none 1 = unilateral 2 = bilateral
Middle turbinate oblique positioning	0 = none 1 = unilateral 2 = bilateral
Nasal cavity opacification	0 = none 1 = <25% unilateral opacification 2 = 25%–50% unilateral opacification 3 = 50%–75% unilateral opacification 4 = >75% unilateral opacification Total = 0–8 (graded bilaterally)

Abbreviation: OMC, Ostiomeatal Complex.

Table 2. Comparison of CT Findings Among Patient Groups.

Diagnosis	n (%)	LM Score	Difference in LM Score Laterality	Nasal Cavity Opacification	Oblique Middle Turbinate	Olfactory Cleft Opacification	Septal Inflammation
AFRS	80 (23)	High	+	High	–	–	–
AERD	101 (28)	High	–	High	+	+	+
CCAD	43 (12)	Low	–	Low	+	–	+
CRSwNP NOS	132 (37)	High	–	Moderate	–	–	–

Abbreviations: AERD, aspirin-exacerbated respiratory disease; AFRS, allergic fungal rhinosinusitis; CCAD, central compartment atopic disease; CRSwNP, chronic rhinosinusitis with polyps; LM, Lund–Mackay; NOS, not otherwise specified.

CT finding differences between subgroups identified. Statistical significance exists between results labeled +/– or low/moderate/high on post hoc analysis.

CCAD patients (unilateral—none, bilateral—56%) as compared to AFRS (unilateral—6%, bilateral—6%) and CRSwNP NOS (unilateral—10%, bilateral—27%) patients (Table 2; Figures 1 and 2).

Opacification of Olfactory Clefts

Differences were identified in olfactory cleft opacification ($\chi^2(3)=32.91$, $P<.001$, with mean rank scores of AFRS=165.30, CRSwNP NOS=153.05, AERD=224.49 and CCAD=173.17) with increased olfactory cleft opacification in the AERD group (unilateral—4%, bilateral—69%) as compared to all other

diagnoses, AFRS (unilateral—35%, bilateral—25%), CCAD (unilateral—9%, bilateral—42%), and CRSwNP NOS (unilateral—17%, bilateral—28%) (Tables 2; Figures 1 and 4).

Nasal Cavity Opacification

One-way ANOVA revealed differences between group ranks in nasal opacification ($\chi^2(3)=48.22$, $P<.001$, with mean rank scores of AFRS=200.26, CRSwNP NOS=163.37, AERD=218.63 and CCAD=104.31). Nasal cavity opacification scores were highest in AERD and AFRS patients, lower in the CRSwNP

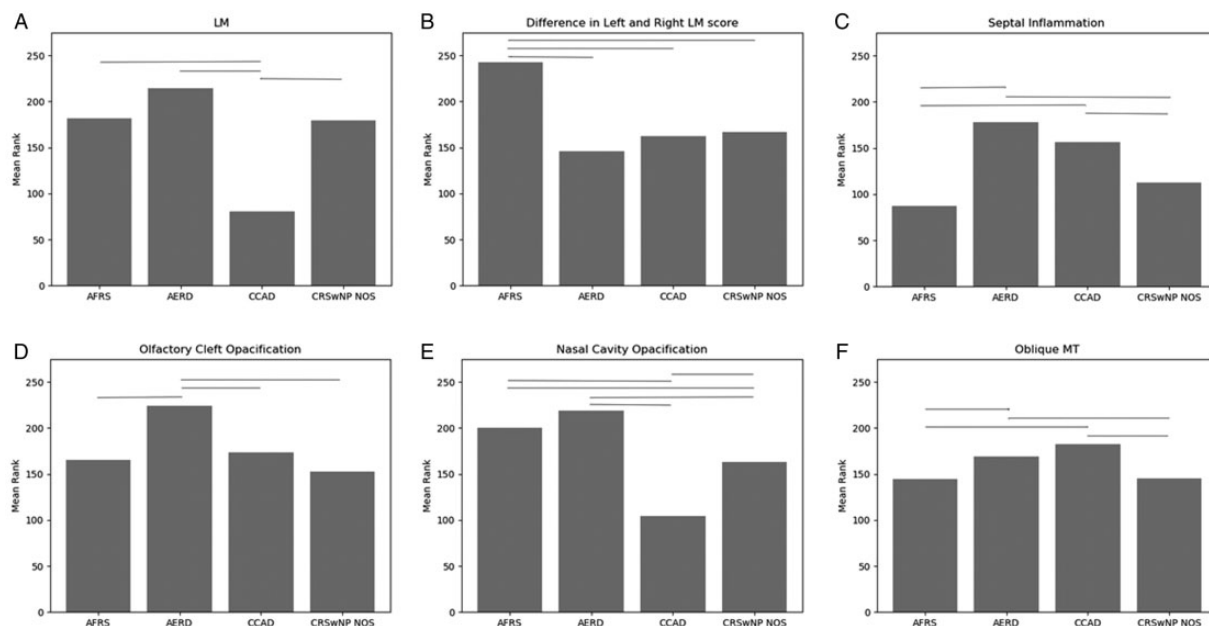


Figure 1. Post hoc analyses of CT findings among patient groups. Bar graphs depict mean rank scores. Horizontal lines indicate group comparisons with statistical significance ($P < .05$) on post hoc analysis. A, LM scores. B, Differences between left and right LM scores. C, Septal inflammation. D, Olfactory cleft opacification. E, Nasal cavity opacification. F, Oblique middle turbinate positioning. AERD, aspirin-exacerbated respiratory disease; AFRS, allergic fungal rhinosinusitis; CCAD, central compartment atopic disease; CRSwNP, chronic rhinosinusitis with polyps; LM, Lund-Mackay; MT, Middle Turbinate; NOS, not otherwise specified.

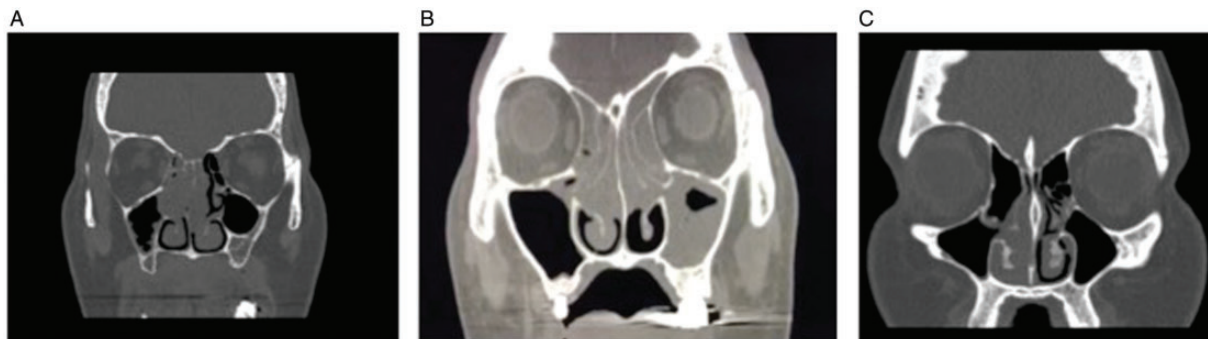


Figure 2. Typical Findings of a CCAD patient. A, Septal inflammation. B, Oblique middle turbinate positioning. C, Low overall LM score.

NOS group, and lowest in CCAD. Nasal opacification scores were found to be different between all permutations of groups with the exception of AFRS patients when compared to AERD patients, which showed nonsignificant differences between nasal cavity opacification mean rank scores (Table 2; Figures 1, 2, and 4).

Oblique Middle Turbinates

Differences were identified in middle turbinate orientation ($\chi^2(3) = 29.31$, $P < .001$, with mean rank scores of AFRS = 144.82, CRSwNP NOS = 145.52, AERD = 169.29 and CCAD = 182.20). Both AERD patients (unilateral—4%, bilateral—14%) and CCAD

patients (unilateral—7%, bilateral—20%) more commonly showed oblique middle turbinate orientation on CT scans as compared to AFRS (unilateral—1%, bilateral—none) and CRSwNP NOS (unilateral—2%, bilateral—2%) patients (Table 2; Figures 1, 2, and 4).

Discussion

In this retrospective study, we have identified several imaging differences between CRSwNP subgroups. These radiologic differences are important as they correspond to clinical findings. CCAD is defined as superior septal, middle, and/or superior turbinate polyps and inflammation, with sinus involvement occurring only in advanced disease or when a secondary diagnosis of

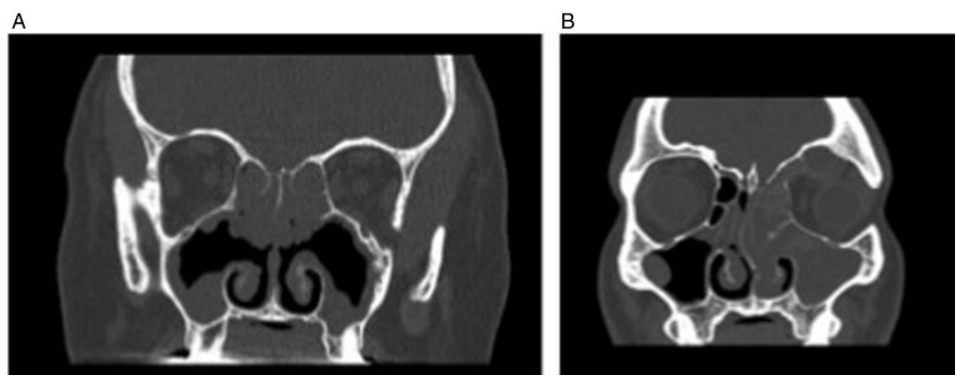


Figure 3. Comparison of typical CT findings in (A) AERD: central nasal cavity opacification and (B) AFRS: unilateral opacification (differences in LM scores between left and right sides).

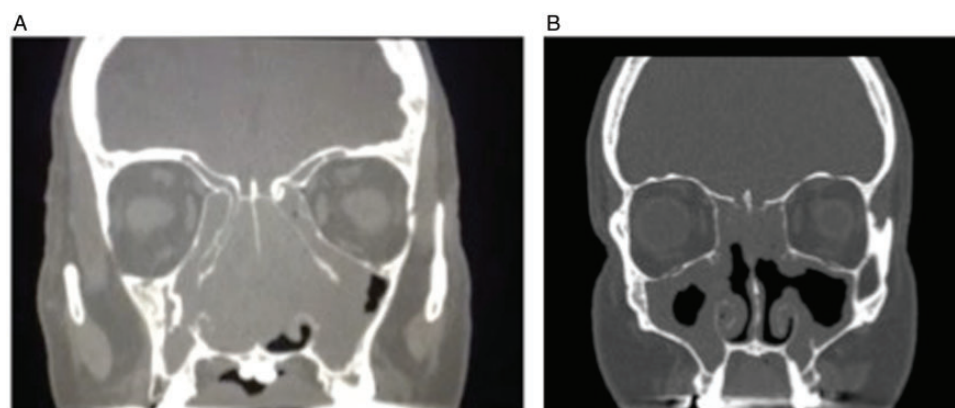


Figure 4. Typical Findings of an AERD patient. A, Oblique middle turbinate positioning and nasal cavity opacification. B, Olfactory opacification.

another CRSwNP phenotype also exists.³ In line with prior work on CCAD,³ our patients revealed radiologic centrally located disease, which is evidenced in this study by septal inflammation, oblique middle turbinate positioning, but low overall LM scores. AERD is defined by nasal polyps, asthma, and aspirin-exacerbated respiratory symptoms. These patients often have long-standing disease with multiple surgeries before proper diagnosis is made. In line with this long-standing disease, on imaging, we found that these patients are differentiated from CCAD by more advanced sinus involvement, olfactory opacification, and higher LM scores. The high incidence of septal inflammation in AERD patients is consistent with a recent report by DelGaudio et al., showing over 80% of AERD patients exhibiting endoscopic evidence of central compartment polypoid involvement.¹⁰ Our imaging findings are also consistent with prior retrospective analyses of patients with AFRS,¹¹ which have identified a high incidence of unilateral disease in this subgroup as compared to other CRSwNP patients.

To our knowledge, this is the first study to investigate oblique middle turbinate positioning on CT scan, which

is indicative of the centrally located disease seen in both AERD and CCAD. This is likely the result of persistent centrally located disease which has caused lateralization of the turbinates over time, related to the contribution of inhalant allergies seen in both CCAD and AERD.¹⁰ Prior work by Hamizan et al. identified a high incidence of inhalant allergic status in patients with centrally located inflammation on CT.¹² Similarly, isolated middle turbinate polyps or edema, which may be an early manifestation of CCAD, have been highly associated with inhalant allergies in prior studies.^{13,14}

Our results find that olfactory cleft opacification is seen at an increased rate in AERD but not in CCAD, perhaps explained by the higher overall disease burden of AERD as compared to CCAD. Olfactory cleft opacification is a late finding in very advanced CCAD but is more common in AERD. Nasal cavity opacification scores were found to be the highest in AERD and AFRS patients, lower in the CRSwNP NOS group, and lowest in CCAD patients. Nasal cavity opacification is common in AERD and AFRS patients due to high polyp burden, while CCAD patients have been found to

have centrally located polyps that only cause complete nasal cavity opacification in very advanced cases.

While history and operative findings are most critical for determination of CRSwNP phenotype, identifying any of the individual radiologic findings evaluated in this study can help narrow down the diagnosis preoperatively. But as can be seen in Table 2, using the sum of all of these findings can identify a unique fingerprint for the CT scan, which can be helpful in making the diagnosis of a specific CRSwNP phenotype. Preoperative decisions, such as when to consider aspirin challenge or allergy testing for AFRS or CCAD, or when to discuss with pathology for consideration of eosinophilic mucin evaluation, may all be aided by CT findings.

There are several limitations of this study as it is retrospective in nature. Patients were identified based on surgical logs, which introduces potential selection bias. Images were also reviewed by one of the treating rhinologists of the group, familiar with a subset of patients, which introduces bias as well. After reviewing multiple scans together to verify consistency, images were reviewed by only 1 reviewer, another weakness of our study. While the LM scoring system is widely used in the literature, evaluations of other imaging findings were graded using simple scoring systems which were developed by the study team (Table 1). In addition, while the oldest CT scan was used for evaluation, some patients had undergone previous surgery before presenting to Emory Clinic with prior resection of the middle turbinates and thus were not included in all analyses of the study. Patients may have had varying levels of medical treatment prior to their scan as well.

Future work in this area includes validation of these imaging predictions in a prospective study by evaluating CT scans in a blinded fashion to predict diagnosis prior to surgery. The long-term goal of this work is to improve preoperative diagnosis and counseling, specifically in regards to allergy testing and treatment and aspirin sensitivity evaluation. As CCAD is hypothesized to progress after middle turbinate resection,¹⁰ diagnostic predictions from CT evaluation may improve preoperative planning. As we continue to further delineate and classify CRSwNP groups by phenotype and endotype, we can improve identification of appropriate treatments for all subgroups of CRSwNP patients.

Conclusion

CRSwNP includes a wide spectrum of subgroups. Preoperative CT findings are distinctly different and may be useful to differentiate between these groups. These differences may also improve our understanding of variances in pathophysiology and progression of disease in different inflammatory and CRSwNP groups.

Authors' Note

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Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: S. K. W.—consultant (Stryker, NeurENT), Scientific Advisory Board (OptiNose, SinopSys Surgical, ALK-Abello); J. M. D.—consultant (Medtronic), research support (Spirox); L. T. R.—consultant (Tissium); and the other authors (S. M. and J. S. S.) have nothing to disclose.

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