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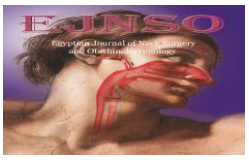

Central Compartment Atopic Disease: Clinical Characteristics and Cellular Endotypes in the Egyptian Population

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Abstract:

Background: In the current study, we aim to investigate the clinical presentations and cellular endotypes of Central Compartment Atopic Disease (CCAD) in the Egyptian population and its percentage relative to the total number of patients with chronic rhinosinusitis with nasal polyps (CRSwNP).

Patients and Methods: A total of 101 patients diagnosed with CRSwNP at Ain Shams University Hospital were included in our study after approval of the Research Ethics committee of Ainshams University with a registration number: FMASU R126/2024. Patients were categorized into two groups only: those with CCAD (N=14) and those with other types of CRSwNP (N=87). Age, sex, smoking status, family history of allergies, presence of allergic rhinitis, bronchial asthma, urticaria, and angioedema were among the clinical data gathered. The intensity of the symptoms was evaluated using the Sinonasal Outcome Test (SNOT-22) score. The eosinophilic count in peripheral blood, total IgE levels, radiological scores, skin prick test (SPT) results, and endoscopic scores were all part of the diagnostic work-up. Specifically, pathologies were fixed in 10% buffered formaline to assess cellular infiltration. Hematoxylin and eosin was used to stain sections of the paraffin-embedded tissue that were 3–4 micrometer thick. Cellular infiltration grading was done according to Shioda and Mishima system, (1+ occasional cells, 2+ few cells,3+moderate number of cells,4+clumps).

Results: Comparing the 2 groups showed no significant differences in age, sex, smoking status, family history of allergy, presence of allergic rhinitis, bronchial asthma, urticaria, or angioedema between the two groups. However, the SNOT score was significantly lower in the CCAD group (median 21) compared to the other CRSwNP group (median 48), $p < .001$. This suggests that patients with CCAD experience less severe symptoms. The CCAD group had significantly higher total IgE levels (median 160 IU/ml) compared to the other CRSwNP group (median 120 IU/ml), $p = .002$ (Figure 2). Additionally, the radiological and endoscopic scores were significantly lower in the CCAD group indicating less severe disease involvement. The radiological score had the highest diagnostic accuracy for distinguishing CCAD from other CRSwNP types, with an area under the curve (AUC) of .98.

Conclusion: This study provides a comprehensive analysis of clinical characteristics and the **cellular** endotypes of CCAD in an Egyptian population. The significant differences in total IgE levels and radiological scores between CCAD and other CRSwNP types emphasize the need for targeted diagnostic tools and personalized treatment strategies. Future research should focus on elucidating the underlying mechanisms driving these differences to enhance the management of CCAD.

Keywords: Chronic rhinosinusitis with nasal polyps, central compartment atopic disease, chronic rhinosinusitis.

Introduction

Chronic rhinosinusitis (CRS) is an inflammatory disease. Based on the existence or lack of nasal polyposis, it is generally separated into two main entities: chronic rhinosinusitis with nasal polyposis (CRSwNP) and chronic rhinosinusitis without nasal polyposis (CRSsNP). Because there are numerous

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variations within this broad category, CRSwNP is especially interesting. Eosinophilic CRSwNP (ENP) and non-eosinophilic CRSwNP (NENP) are the two categories of CRSwNP based on the local infiltration by eosinophils. [1]

DelGaudio et al. have identified a novel CRS phenotype called central compartment atopic disease (CCAD). [2] CCAD is a unique nasal inflammatory CRSwNP subtype that is linked to a low frequency of asthma and a high incidence of allergies. [3]

Described in 2017, CCAD is a nasal inflammatory polypoid condition that affects the upper nasal septum with or without affection of the superior turbinate and/or middle turbinate. It is strongly linked to inhalant allergy. These central compartment structures' inhalant allergen deposition is correlated with the direction of typical nasal airflow. [4]

Usually, the only symptoms of early CCAD are polypoid changes or edema; as the disease advances, discrete polyps appear. The medial ethmoidal region and the ostium of the maxillary sinus are two central sinus cavities that may become involved if CCAD polypoid changes continue to progress. At this point, the orbit and base of the skull typically maintain a rim of peripheral clearing. This involvement of sinuses happens when the polypoid changes in the central compartment reach the sinus outflow tracts. This can happen through direct polyp extension from lateral surface of middle turbinate or through middle turbinate lateralization from the central polypoidal changes. [5]

This research aims to address this gap by investigating the clinical characteristics and cellular endotypes of CCAD in an Egyptian population. By comparing these findings with other types of CRSwNP, we hope to delineate the unique features of CCAD and provide insights into its pathophysiology. This research will contribute to a better understanding of CCAD and support the development of personalized therapeutic approaches for affected patients.

Patients and methods:

Study Population A total of 101 patients diagnosed with CRSwNP at Ain Shams University Hospital were included in our study after approval of the Research Ethics committee of Ainshams University with a registration number: FMASU R126/2024. Patients were categorized into two groups only: those with CCAD (N=14) and those with other types of CRSwNP (N=87).

Data Collection Age, sex, smoking status, family history of allergies, presence of allergic rhinitis, bronchial asthma, urticaria, and angioedema were among the clinical data gathered. The intensity of the symptoms was evaluated using the Sinonasal Outcome Test (SNOT-22) score. The eosinophilic count in peripheral blood, total IgE levels, radiological scores, skin prick test (SPT) results, and endoscopic scores were all part of the diagnostic work-up. Specifically, pathologies were fixed in 10% buffered formaline to assess cellular infiltration. Hematoxylin and eosin was used to stain sections of the paraffin-embedded tissue that were 3–4 micrometer thick. Cellular infiltration grading was done according to Shioda and Mishima system, (1+ occasional cells, 2+ few cells,3+moderate number of cells,4+clumps). [6]

Statistical analysis:

•The tools used for the statistical analysis were MedCalc® Statistical Software version 22.009 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2021) and IBM© SPSS© Statistics version 27 (IBM© Corp. Armonk, NY).

Skewed numerical variables were presented as median and interquartile range and inter-group variances were

compared using the Mann-Whitney test. Categorical variables are presented as counts and percentage and between-group differences are compared using Fisher's exact test. Ordinal data are compared using linear by linear association.

The diagnostic value of continuous predictors is examined using receiver-operating characteristic (ROC) curve analysis. The area under the ROC curve (AUC) is interpreted as follows: AUC ≥ .90 = excellent, AUC .80 - .89 = good, AUC .70 - .79 = fair, AUC < .70 = poor.

p-Values < 0.05 are considered statistically significant.

Results

Clinical Characteristics Table 1 summarizes the clinical characteristics of patients with CCAD and other types of CRSwNP. There were no significant differences in age, sex, smoking status, family history of allergy, presence of allergic rhinitis, bronchial asthma, urticaria, or angioedema between the two groups. However, the SNOT score was significantly lower in the CCAD group (median 21) compared to the other CRSwNP group (median 48), p < .001. This suggests that patients with CCAD experience less severe symptoms.

Diagnostic Work-Up Table 2 details the results of the diagnostic work-up. The CCAD group had significantly higher total IgE levels (median 160 IU/ml) compared to the other CRSwNP group (median 120 IU/ml), p = .002 (Figure 2). Additionally, the radiological and endoscopic scores were significantly lower in the CCAD group (Figures 3 and 4), indicating less severe disease involvement. ROC curve analysis (Table 3) demonstrated that the radiological score had the highest diagnostic accuracy for distinguishing CCAD from other CRSwNP types, with an area under the curve (AUC) of .98 (Figure 5).

Table 1. The Clinical characteristics of patients with CCAD and other types of CRSwNP

Variable	CCAD (N=14)	Other types of CRSwNP (N=87)	p-Value
Age (years)	30 (28 to 39)	30 (28 to 39)	.719 †
Male sex	8 (57.1%)	45 (51.7%)	.779 ‡
Smoker	4 (28.6%)	20 (23.0%)	.736 ‡
Family history of allergy	8 (57.1%)	44 (50.6%)	.776 ‡
Seasonal allergic rhinitis	7 (50.0%)	39 (44.8%)	.778 ‡
Perennial allergic rhinitis	4 (28.6%)	23 (26.4%)	>.999 ‡
Bronchial asthma	3 (21.4%)	33 (37.9%)	.368 ‡
Urticaria	1 (7.1%)	14 (16.1%)	.687 ‡
Angioedema	1 (7.1%)	7 (8.0%)	>.999 ‡
SNOT score	21 (15 to 33)	48 (38 to 70)	**<.001** †

Data are median (interquartile range) or counts (percentage).
†. Mann-Whitney U-test. ‡. Fisher's exact test.

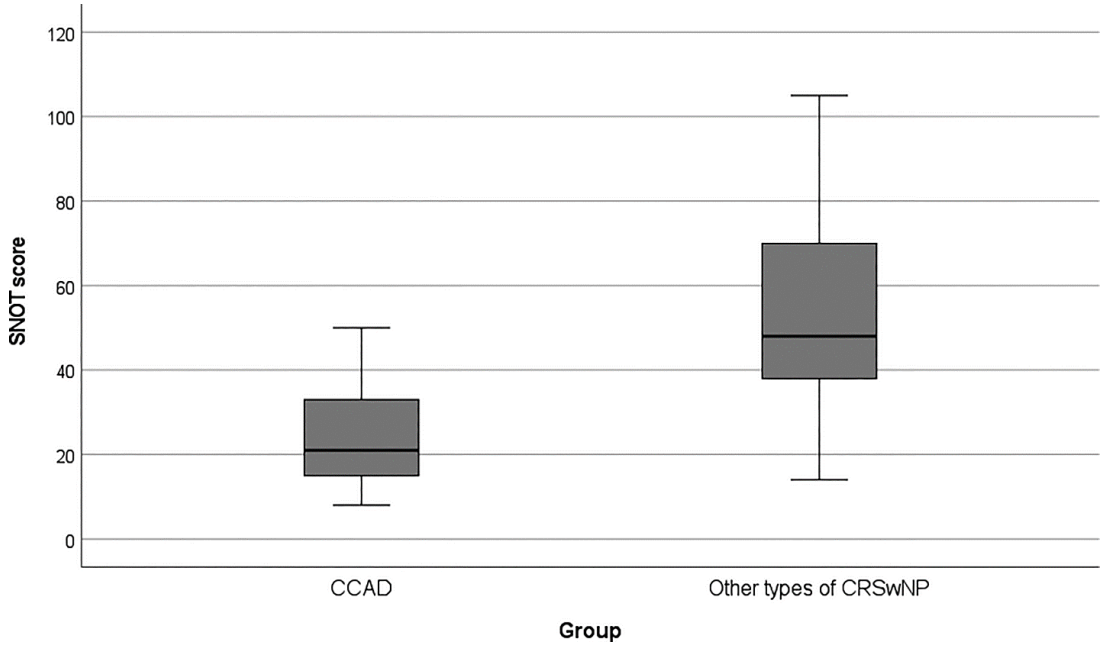

Figure (1) Box plot illustrating the SNOT score in patients with CCAD and other types of CRSwNP

Table 2. Results of diagnostic work-up in patients with CCAD or other types of CRSwNP

Variable	CCAD (N=14)	Other types of CRSwNP (N=87)	p-Value
Eosinophilic count in peripheral blood (%)	2.6 (2.0 to 3.7)	2.5 (2.0 to 3.2)	.638 †
Total IgE (IU/ml)	160 (146 to 170)	120 (107 to 150)	**.002** †
Radiological score	5 (4 to 6)	13 (12 to 18)	**<.001** †
Monosensitive SPT	3 (21.4%)	14 (16.1%)	.700 ‡
Polyensitive SPT	6 (42.9%)	24 (27.6%)	.344 ‡
Endoscopic score	5 (4 to 6)	8 (6 to 11)	**<.001** †
Eosinophilic endotype			.640 §
1+	5 (35.7%)	37 (42.5%)	
2+	4 (28.6%)	23 (26.4%)	
3+	4 (28.6%)	22 (25.3%)	
4+	1 (7.1%)	5 (5.7%)	
Lymphocytic endotype			.501 §
1+	1 (7.1%)	11 (12.6%)	
2+	3 (21.4%)	19 (21.8%)	
3+	6 (42.9%)	38 (43.7%)	
4+	4 (28.6%)	19 (21.8%)	
Neutrophilic endotype			.622 §
1+	11 (78.6%)	73 (83.9%)	
2+	3 (21.4%)	14 (16.1%)	
3+	0 (0.0%)	0 (0.0%)	
4+	0 (0.0%)	0 (0.0%)	
Plasma cell endotype			.677 §
1+	4 (28.6%)	31 (35.6%)	
2+	7 (50.0%)	40 (46.0%)	
3+	2 (14.3%)	10 (11.5%)	
4+	1 (7.1%)	6 (6.9%)	
Two-year recurrence	2 (14.3%)	28 (32.2%)	.221 ‡

Data are median (interquartile range) or counts (percentage).
†. Mann-Whitney U-test. ‡. Fisher's exact test. §. Linear by linear association

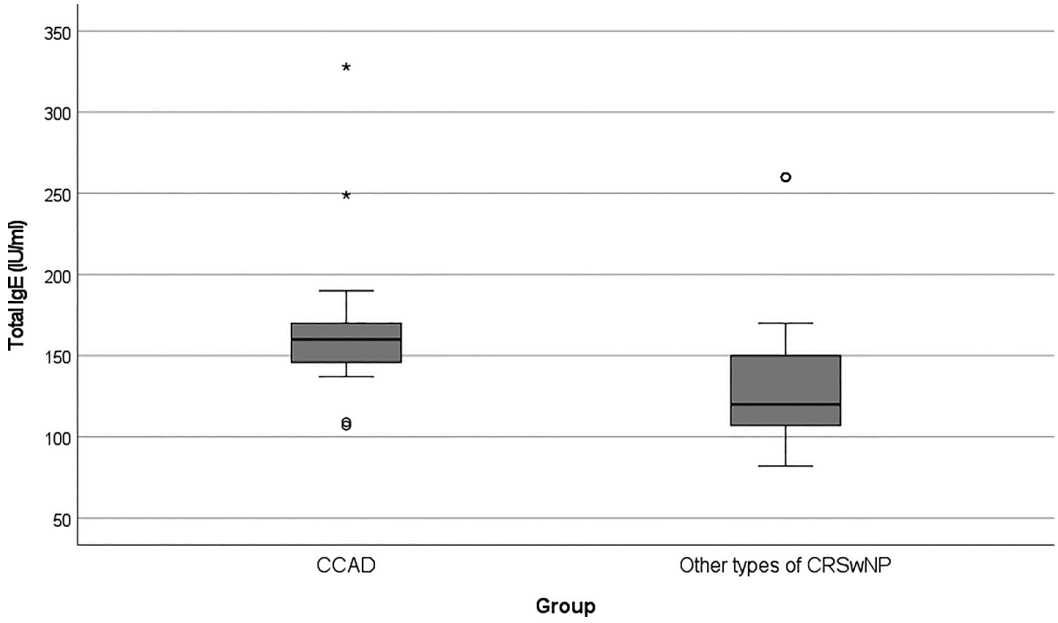

Figure (2) Box plot illustrating total IgE level in patients with CCAD and other types of CRSwNP

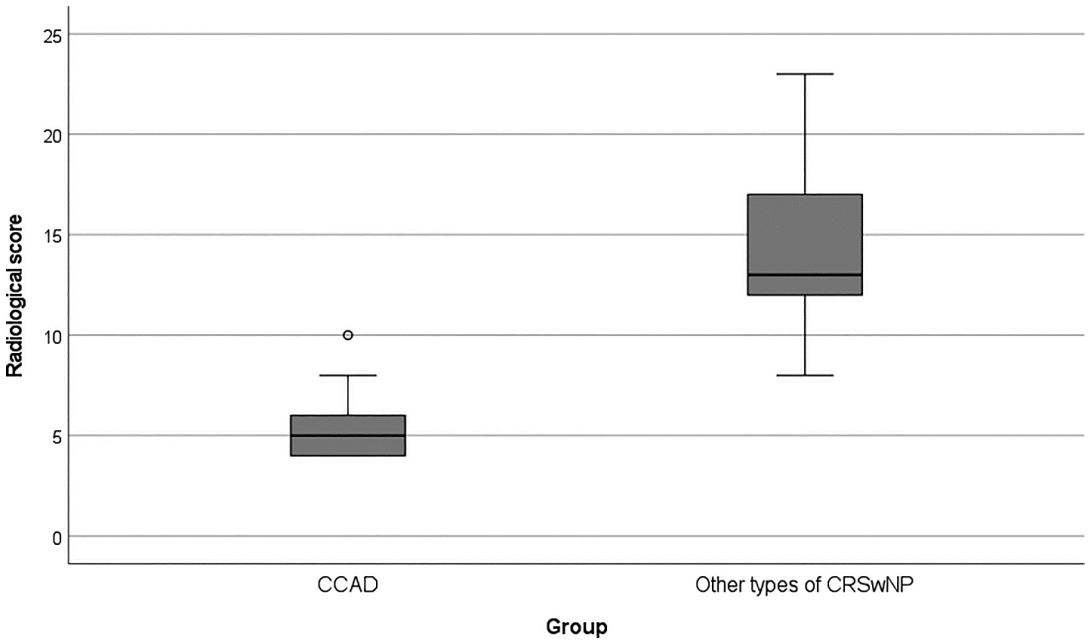

Figure (3) . Box plot illustrating the radiological score in patients with CCAD and other types of CRSwNP

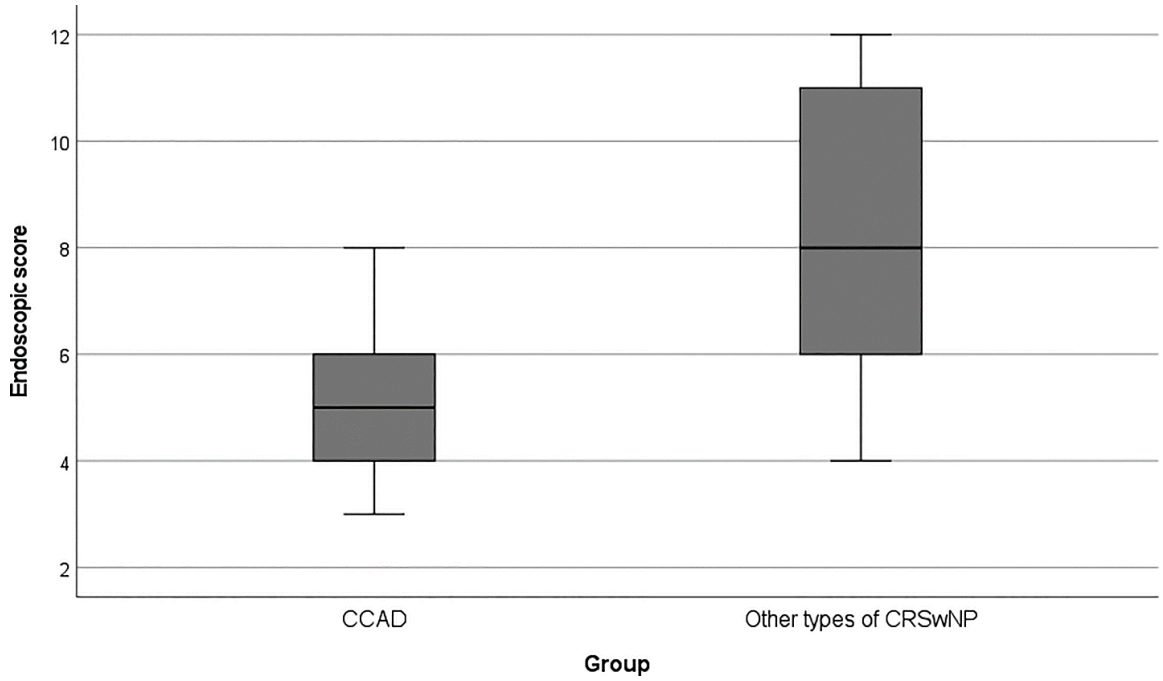

Figure (4) Box plot illustrating the endoscopic score in patients with CCAD and other types of CRSwNP

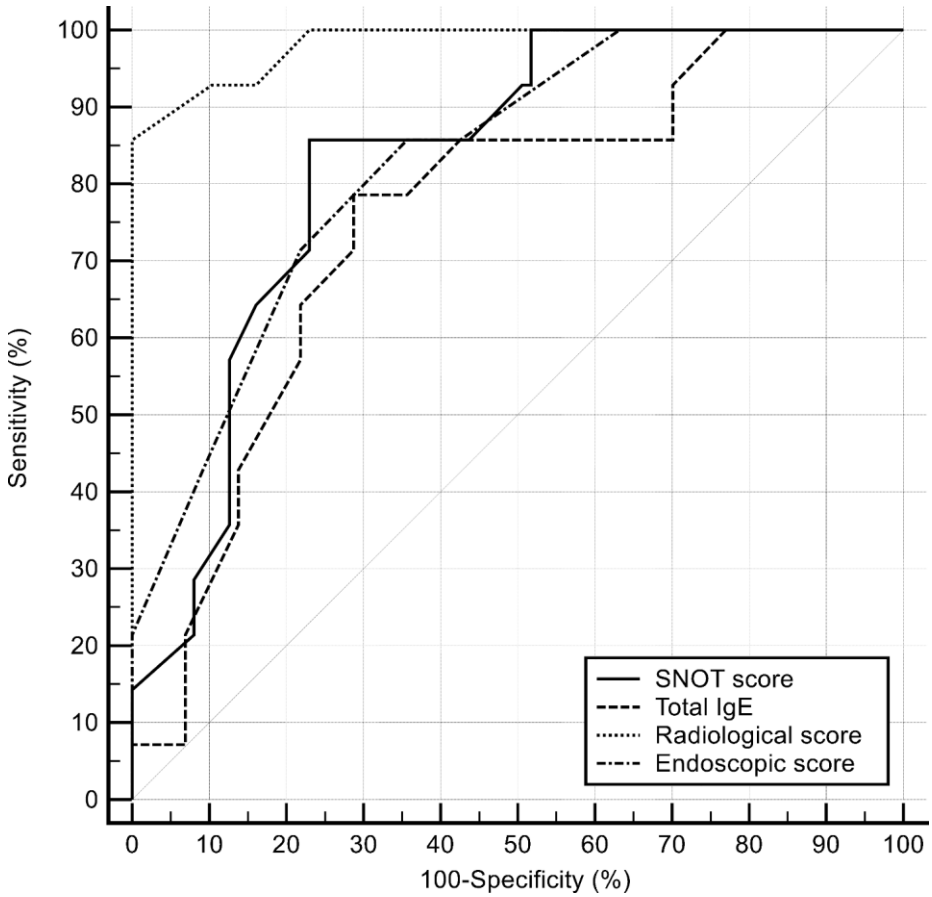

Figure (5) Receiver-operating characteristic (ROC) curves for discrimination between CCAD and other types of CRSwNP.

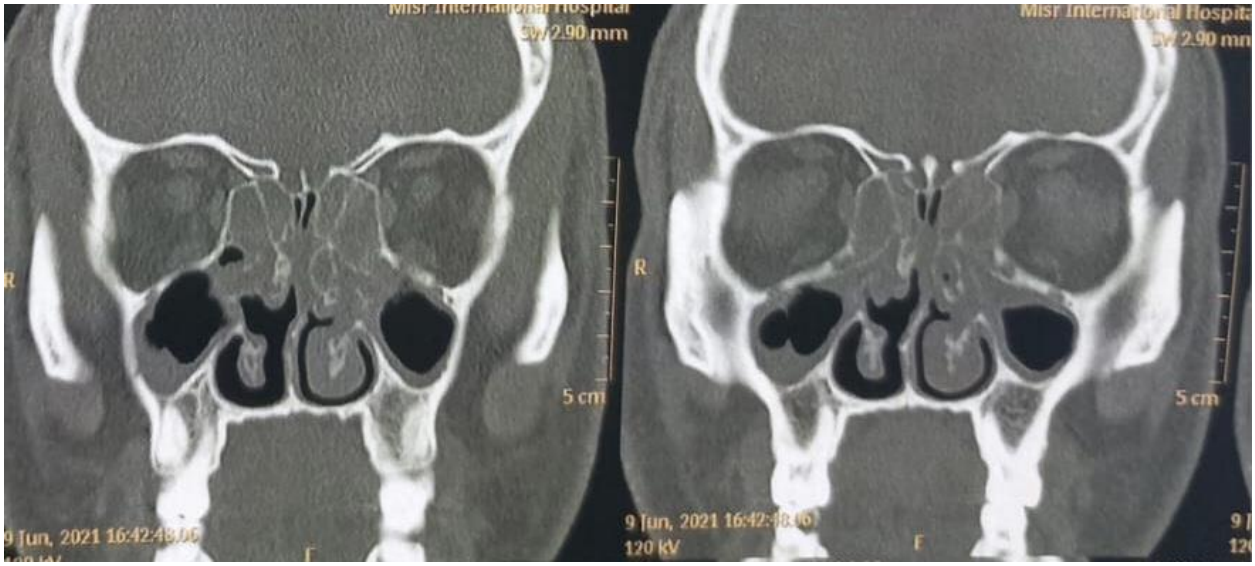

Figure (6) : CT showed only affection of central sinuses in CCAD

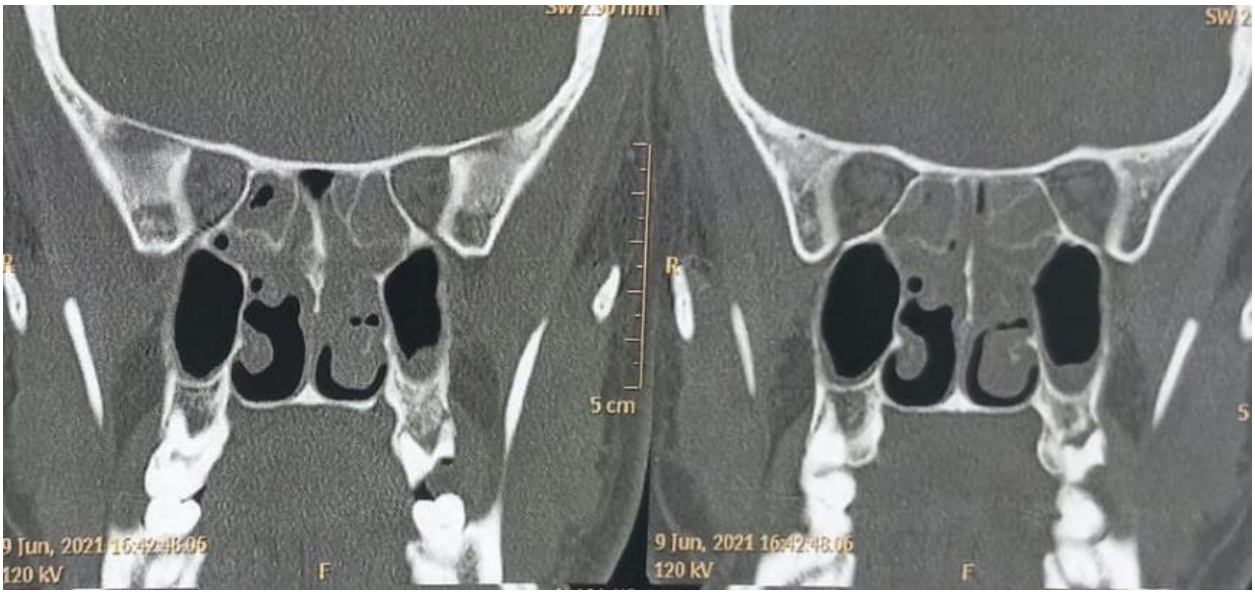

Figure (7) : CT showed only affection of central sinuses in CCAD

Table 3. ROC curve analysis for discrimination between CCAD and other types of CRSwNP

Variable	SNOT score	Total IgE	Radiological score	Endoscopic score
AUC	.83	.76	.98	.83
SE	.05	.07	.01	.05
95% CI	.74 to .90	.66 to .84	.93 to .998	.74 to .90
p-Value †	<.0001	.0001	<.0001	<.0001
Youden index J	.63	.50	.86	.50
Associated criterion	≤36	>139	≤7	≤6
Sensitivity (%)	86	79	86	86
95% CI	57 – 98	49 - 95	57 - 98	57 - 98
Specificity (%)	77	71	100	64
95% CI	67- 85	60 - 81	96 - 100	53 - 74

95% CI = 95% confidence interval, AUC = area under the ROC curve, SE = standard error.
†. DeLong method.

Discussion:

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a significant health issue worldwide, affecting approximately 2-4% of the general population. This condition is characterized by persistent inflammation of the nasal and paranasal sinus mucosa, leading to the formation of polyps. Among the various subtypes of CRSwNP, Central Compartment Atopic Disease (CCAD) has been increasingly recognized. CCAD primarily involves the central compartment of the nasal cavity, including the middle turbinate, septum, and superior turbinate, and is frequently associated with atopic conditions such as asthma and allergic rhinitis.

The pathogenesis of CCAD remains poorly understood, with hypotheses suggesting a predominant role of systemic atopy and localized immune responses. The identification of distinct clinical and immunological profiles in CCAD patients is essential for improving diagnostic accuracy and developing targeted treatments. Previous studies have highlighted the significance of inflammatory cell profiles, including eosinophils, lymphocytes, neutrophils,

and plasma cells, in differentiating CRSwNP subtypes. However, limited data are available on the specific characteristics and the cellular endotypes of CCAD, particularly in non-Western populations.

Clinical Characteristics

Our study indicated that CCAD group have lower incidence of asthma than other types of CRSwNP although not significant yet was noticeable. Also, SNOT-22 score was significantly less suggesting less symptoms. These results explained by limited extension of the pathology in CCAD patients, similar results were noticed by **Kong et al.** [7]

This study indicates that CCAD in the Egyptian population is characterized by higher total IgE levels and lower radiological and endoscopic scores compared to other types of CRSwNP. These findings are consistent with previous studies that have suggested a strong association between atopy and CCAD. For instance, a study by Kong et al. (2021) reported elevated IgE levels in CCAD patients, supporting our results. Similarly, they have emphasized the less severe radiological involvement in CCAD, as observed in the current study. [7-8]

However, our analysis of cellular infiltration of the four inflammatory cells (lymphocytes, eosinophils, plasma cells and neutrophils) not found significant differences in cellular endotypes between CCAD and other CRSwNP groups. This contrasts with findings from Western populations where distinct eosinophilic and neutrophilic endotypes have been noted. In our research the frequency of eosinophils and lymphocytes were slightly higher in CCAD group but to a nonsignificant level. This discrepancy could be attributed to genetic, environmental, or methodological differences across studies.

In Chinese eosinophilic and lymphocytic infiltration were the higher populations in the CCAD and percentage of eosinophils in pathological infiltrations was higher than NENP, Percentage of peripheral blood eosinophils was higher in CCAD group comparing with NENP group (7) but in our research peripheral blood eosinophils showed no significant value between CCAD group and CRSwNP group.

Regarding the outcomes of endoscopic sinus surgery (ESS), our study found that patients with CCAD had a lower recurrence rate compared to those with other types of CRSwNP. This aligns with the findings of Guo et al (2024), who reported favorable surgical outcomes and lower revision rates in CCAD patients. Additionally, they reported that the improvement in SNOT-22 scores post-ESS was more significant in CCAD patients, indicating better symptomatic relief. These results highlight the efficacy of ESS in managing CCAD, particularly when combined with targeted allergy treatment. [9]

Conclusion

This study provides a comprehensive analysis of clinical characteristics and the cellular endotypes of CCAD in an Egyptian population. The significant differences in total IgE levels and radiological scores between CCAD and other CRSwNP types emphasize the need for targeted diagnostic tools and personalized treatment strategies. Future research should focus on elucidating the underlying mechanisms driving these differences to enhance the management of CCAD.

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Conflicts of interest: No

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