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REVIEW ARTIKEL

A Literature Review on Central Compartment Atopic Disease as a Phenotype of Chronic Rhinosinusitis Type 2

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ABSTRACT

Background: Central compartment atopic disease (CCAD) is a chronic rhinosinusitis phenotype characterized by polypoid inflammatory remodeling of the middle turbinates, superior turbinates, and posterosuperior nasal septum. Recent diagnostic proposals define CCAD by central sinonasal tissue remodeling in patients displaying features of an IgE-mediated allergic response, while classifying the condition as type 2 dominant and eosinophilic. Objective: This review synthesizes current evidence regarding CCAD as a distinct phenotype in type chronic rhinosinusitis, emphasizing anatomy, allergies, inflammatory endotypes, radiography, differential diagnosis, and therapeutic implications. Methods: A narrative literature review was conducted using articles from 2016 to 2026 published in Scopus-indexed peer-reviewed journals. Results: Current studies demonstrate a significant association between CCAD and inhalant allergy or aeroallergen sensitization, although the strength of the relationship between systemic allergy and asthma varies among populations. Eosinophilia and a cytokine profile marked by IL-5 and IL-13 in central compartment chronic rhinosinusitis confirm type 2 characteristics. Conclusion: CCAD should be considered an anatomically oriented, allergy-related manifestation of chronic rhinosinusitis type 2, rather than simply a diffuse nasal polyp.

Keywords: *endoscopic sinus surgery, type 2 inflammation, nasal polyps, chronic rhinosinusitis, and allergic rhinitis.*

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INTRODUCTION

Chronic rhinosinusitis (CRS) is described by persistent sinonasal symptoms and objective signs of mucosal inflammation detected via nasal endoscopy or computed tomography (Fokkens et al., 2023). Contemporary classifications of chronic rhinosinusitis (CRS) distinguish between phenotypes, such as CRSwNP, and inflammatory endotypes, which include type 2, type 1, and type 3 immunological profiles (Bachert et al., 2020).

Type 2 CRS is marked by eosinophilic inflammation, epithelial cytokine activation, and a clinical manifestation frequently associated with nasal polyps, olfactory impairment, and concurrent asthma (Stevens et al., 2019; Tomassen et al., 2016). Consensus recommendations emphasize that the management of CRS should consider the severity of symptoms, endoscopic findings, CT scan severity, asthma comorbidities, prior surgeries, the necessity for systemic corticosteroids, and the inflammatory phenotype (Orlandi et al., 2021).

CCAD was delineated as a variant of CRS marked by polypoid pathology primarily affecting the central nasal structures, rather than simply presenting as diffuse lateral sinus polyposis (DelGaudio et al., 2017). The center compartment is made up of the middle turbinate, the superior turbinate, and the posterosuperior nasal septum. This is an important part of the diagnostic framework (Barrow et al., 2025). The CCAD is therapeutically important because it provides a systematic structure for the overlap of allergic rhinitis, central nasal edema, olfactory dysfunction, and CRSwNP-like illness (Kong et al., 2022). This entity is significant because radiological or endoscopic central compartment illness can predict inhalant allergen sensitivity in individuals with CRS (Lau et al., 2024).

This review assembles evidence for CCAD as an anatomically focused, predominantly type 2 CRS phenotype, while adhering to rigorous citation standards for publication preparation. Recent reviews and diagnostic recommendations support this comprehension of CCAD (Barrow et al., 2025; Kong et al., 2022).

METHODS

The conceptual search utilized the terms “central compartment atopic disease,” “central compartment disease,” “central-compartment-type chronic rhinosinusitis,” “type 2 chronic rhinosinusitis,” “chronic rhinosinusitis with nasal polyps,” “allergic rhinitis,” “eosinophilic inflammation,” “biologics,” and “endoscopic sinus surgery.”

The inclusion methodology favors English-language studies published in peer-reviewed journals indexed by Scopus from 2016 to 2026. Previous articles were not included because they did not meet the 10-year historical criteria for journal preparation.

This review includes the first CCAD cohort, studies on radiology, cytokines, and biomarkers, studies on surgical outcomes, studies on sensitivity to aeroallergens, recent consensus documents, and important biologic trials related to CRSwNP type 2.

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DEFINITION AND HISTORICAL DEVELOPMENT OF CCAD

DelGaudio et al. (2017) characterized CCAD in a patient presenting with described CCAD in a patient exhibiting sinonasal symptoms and central polypoid mucosal alterations affecting the superior turbinate, the middle turbinate, and posterosuperior septum. The same study indicated that this pattern represents a constrained allergic inhalation process affecting central structures of ethmoidal origin (DelGaudio et al., 2017). This diagnostic hypothesis is supported by studies demonstrating that middle turbinate edema functions as an endoscopic indicator for inhalant allergies Subsequent radiological studies have shown that mucosal disease confined to the middle turbinate on CT is associated with the allergic phenotype of chronic rhinosinusitis (CRS) (Hamizan et al., 2018).

CCAD demonstrated a higher prevalence of allergies in comparison to CRSwNP or unspecified conditions within a tertiary rhinology cohort (Marcus et al., 2020). Study found a link between CCAD in Southern Chinese people and asthma and eosinophilia. However, they showed a lower prevalence of systemic allergens, as determined by skin and serum tests (Nie et al., 2023). These geographic differences show that CCAD should not be reduced to a single systemic allergy phenotype. Current evidence supports CCAD as a primary compartmental inflammatory phenotype, distinguished by variability in systemic allergy, localized aeroallergen sensitivity, asthma, and eosinophilia across diverse populations (Aaron et al., 2025; Edwards et al., 2022). Barrow et al. (2025) addressed definitional inconsistencies by proposing diagnostic criteria centered on the remodeling of nasal cavity and central sinus tissue in individuals displaying traits of an IgE-mediated allergic response. This approach is significant as previous research utilized various combinations of endoscopy, CT, allergy testing, and histology to delineate CCAD (Barrow et al., 2025).

ANATOMICAL AND RADIOLOGICAL PHENOTYPE

Anatomically, CCAD is primarily characterized by polypoid enlargement or inflammatory remodeling of the middle turbinate, superior turbinate, and posterosuperior septum (DelGaudio et al., 2017). This pattern is different from typical diffuse CRSwNP because the initial burden may be localized medially instead of being spread out across the lateral sinonasal cavity (Roland et al., 2020). Radiological examination remains an adjunctive test rather than the sole assessment, as emerging diagnostic concepts emphasize endoscopic central tissue remodeling (Barrow et al., 2025).

In a Southeast Asian cohort, endoscopic central compartment disease served as a superior predictor of annual inhalant allergen sensitization relative to radiological central compartment disease.This finding highlights the imperative of thorough nasal endoscopy in settings marked by widespread annual allergic rhinitis and house dust mite sensitization (Lau et al., 2024). Clinically and radiologically, the allergic phenotype of CRSwNP has been recognized as a central or allergy-related disease pattern (Abdullah et al., 2020). Thus, radiological centrality must be evaluated using symptoms, endoscopy,

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aeroallergen testing, tissue inflammation, and differential diagnosis (Grayson et al., 2019).

IMMUNOPATHOLOGY: CCAD AS A TYPE 2 CRS PHENOTYPE

CRS exhibits immunological heterogeneity, and biomarker clustering has identified multiple inflammatory endotypes rather than a singular, uniform disease etiology (Tomassen et al., 2016). Type 2 inflammation in CRS is clinically linked to nasal polyps, concurrent asthma, anosmia, and allergic mucin (Stevens et al., 2019). Central compartment CRS is linked to hyposmia or anosmia, identified as an eosinophilic subtype, and is marked by elevated IL-13 and IL-5 expression in middle turbinate tissue. This supports the notion that CCAD exists within the continuum of type 2 CRS, where central tissue inflammation is marked by eosinophilia and elevated cytokine levels (Lin et al., 2021).

Whole-slide imaging of Chinese CCAD displayed histological features and cellular endotypes suggestive of eosinophilic inflammation (Kong et al., 2022). An autonomous inflammatory profiling study revealed that CCAD exhibits a distinct inflammatory pattern, differentiating it from other CRSwNP symptoms (Rubel et al., 2023). In CCAD, systemic and local aeroallergen sensitivity may not be fully aligned. Some patients may have local sinonasal allergen-specific IgE patterns that are different from those found in systemic allergy testing (Edwards et al., 2022). There were similarities in allergen-sensitivity patterns between CCAD and allergic rhinitis. The intersection of CCAD and allergic rhinitis validates the formal evaluation and treatment of allergic rhinitis in patients with central compartment disease (Tripathi et al., 2022; Wise et al., 2023).

CLINICAL PRESENTATION AND DIFFERENTIAL DIAGNOSIS

Individuals with CCAD frequently exhibit symptoms such as nasal obstruction, nasal congestion, rhinorrhea, sneezing, postnasal drip, and anosmia (Kong et al., 2023). Olfactory dysfunction is clinically significant because CCAD may impact the olfactory clefts and the mid-nasal mucosa (S. S. Huang et al., 2023). Asthma was less prevalent in CCAD compared to other forms of CRSwNP (Marcus et al., 2020). Study by Shih et al. found a link between CCAD and asthma and allergic rhinitis symptoms in Taiwanese patients (Shih et al., 2022). The Southern Chinese cohort published demonstrated that CCAD may be associated with asthma and significant eosinophilia, even when systemic allergy testing produces rare positive outcomes. These data suggest that ethnicity, geography, allergen exposure, and diagnostic criteria may influence the observed comorbidity patterns of CCAD (Nie et al., 2023).

The differential diagnosis must include aspirin-exacerbated respiratory disease, laterally dominant nasal polyps, diffuse chronic rhinosinusitis with nasal polyps (CRSwNP), adenomatoid hamartoma of the respiratory epithelium, allergic fungal rhinosinusitis, and olfactory cleft disease. The distinction between lateral-dominant nasal polyps is clinically relevant due to the distinct patterns of comorbidities and outcomes linked to central- and lateral-dominant polyps (Shih et al., 2022). Diagnostic challenges persist owing to the

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utilization of inconsistent definitions in research and the simultaneous presence of central compartment disease alongside diffuse CRSwNP (Moreno-Luna et al., 2025). A recent extensive study found that CCAD has distinct clinical and immunological traits compared to other CRS subtypes, underscoring the need for standardized diagnostic criteria (Vizcarra-Melgar et al., 2025).

THERAPEUTIC IMPLICATIONS

The primary therapy for CCAD must address the inflammation in CRS and allergic rhinitis, considering the phenotype's significant association with aeroallergen sensitization and central tissue remodeling (DelGaudio et al., 2017). The consensus guidelines for CRS and allergic rhinitis recommend intranasal corticosteroids, saline irrigation, allergen avoidance when feasible, and the treatment of allergic rhinitis (Fokkens et al., 2023; Wise et al., 2023).

Endoscopic sinus surgery is warranted when central polypoid disease, obstruction, olfactory dysfunction, or persistent symptoms which are unresponsive to treatment. The rates of polyp recurrence and revision surgery in CCAD were lower in than in other CRSwNP subtypes, which suggests that CCAD may have better postoperative survival (Steehler et al., 2021). Majority of CCAD patients managed their disease well one year after endoscopic sinus surgery (Guo et al., 2024). Enhanced olfactory outcomes following functional endoscopic sinus surgery in CCAD (S. K. Huang et al., 2023). Allergen immunotherapy is a medically viable adjunct when aeroallergen sensitivity is apparent. Meerwein et al. specifically investigated allergen immunotherapy following surgery in individuals with CCAD exposed to house dust mites, highlighting the imperative for research into allergy-oriented postoperative interventions (Meerwein et al., 2025).

Biologic therapy ought to be assessed according to established criteria for severe, uncontrolled CRSwNP, rather than merely the presence of CCAD. In a phase 3 trial, dupilumab reduced the size and pain of nasal polyps in individuals with severe CRSwNP (Bachert et al., 2020). Omalizumab enhanced endoscopic findings and outcomes in individuals with severe CRSwNP exhibiting lacking response to intranasal corticosteroids (Gevaert et al., 2020). Mepolizumab diminished nasal polyps and improved nasal airflow in patients with recurrent severe CRSwNP, as evidenced by the SYNAPSE study (H(Han et al., 2021). Modern biological decision-making in CRSwNP must consider type 2 inflammation, the necessity for systemic corticosteroids, anosmia, coexisting asthma, the impact on quality of life, and previous surgical interventions (Fokkens et al., 2023). A thorough biological investigation elucidated that CRSwNP biologics specifically target type 2 pathways, encompassing IL-4, IL-5, IL-13, and IgE (Bachert et al., 2020).

RESEARCH GAPS AND FUTURE DIRECTIONS

A major gap in research is diagnostic heterogeneity. Barrow et al. underscored that inconsistent criteria have led to conflicting results in published CCAD research (Barrow et al., 2025). Subsequent cohorts should record endoscopic central remodeling, CT distribution,

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systemic allergy testing, Local Allergen-specific IgE, tissue eosinophils, blood eosinophils, total IgE, asthma status, SNOT-22, olfactory testing, Lund-Mackay score, recurrence, and revision surgery. This reporting framework is supported by variables employed in various recent clinical, biomarker, and outcome studies (Edwards et al., 2022; Guo et al., 2024; Rubel et al., 2023).

Population-level studies are essential because of the distinctive patterns of allergy and asthma identified in CCAD cohorts from North America, Southern China, Taiwan, Singapore, and the Bronx (Aaron et al., 2025; Marcus et al., 2020; Nie et al., 2023). Consequently, multicenter studies must classify CCAD according to geography, year-round allergen exposure, ethnic background, and asthma phenotype (Lau et al., 2024).

Treatment studies should clarify whether allergy-targeted medications, surgical procedures, or biologic agents are more appropriate for specific CCAD subgroups. Recent studies suggest that postoperative allergen immunotherapy may require an integrated care pathway encompassing both rhinology and allergy specialties (Meerwein et al., 2025).

CONCLUSION

CCAD is more accurately described as an allergy-associated central compartment phenotype in type 2 chronic rhinosinusitis, rather than simply a synonym for diffuse CRSwNP (DelGaudio et al., 2017). Its architectural feature is polypoid remodeling of central nasal tissues, while its immunological profile is chiefly eosinophilic and type 2 dominant (Barrow et al., 2025). Current evidence supports endoscopy as the primary diagnostic tool, CT as an adjunctive mapping technique, and allergy assessment as a therapeutically relevant component of the evaluation (Hamizan et al., 2018; Lau et al., 2024). Therapy must encompass standard CRS pharmacotherapy, allergic rhinitis intervention, individualized surgical procedures, and biologic selection exclusively upon the fulfillment of criteria for severe and uncontrolled CRSwNP (Fokkens et al., 2023). Future publication-quality studies should utilize standardized CCAD criteria, prospectively collect local and systemic biomarkers, and categorize outcomes based on location and comorbidities. This study is essential to determine whether CCAD requires a different treatment protocol in comparison to the general management of CRSwNP (Vizcarra-Melgar et al., 2025).

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Table 1. A summary of the studies that compare CCAD and CRS type 2

Study	Design / population	Definition or diagnostic focus	Main finding	Type 2 / allergy relevance	Implication for CCAD review
Shih et al. (2022)	Taiwanese case-control study.	CCAD versus lateral-dominant nasal polyps.	CCAD was associated with asthma and allergic rhinitis symptoms.	Showed regional comorbidity pattern.	Emphasized population-specific phenotype differences.
Kong et al. (2022)	Chinese cohort with whole-slide imaging.	CCAD defined by serologic IgE plus endoscopic/radiologic findings.	Identified cellular endotype features in Chinese CCAD.	Supported eosinophilic tissue inflammation.	Added histopathologic evidence.
Nie et al. (2023)	Southern China clinical cohort.	CCAD in Southern Chinese CRSwNP.	CCAD was associated with asthma and eosinophilia but lower systemic allergy incidence.	Challenged a purely systemic allergy definition.	Highlighted geographic heterogeneity.
Rubel et al. (2023)	Inflammatory profiling study.	CCAD compared with other CRSwNP phenotypes.	CCAD showed a distinct inflammatory profile.	Placed CCAD within the CRSwNP inflammatory spectrum.	Supported biomarker-based differentiation.
Huang et al. (2023)	Retrospective surgical outcome study.	CCAD with olfactory dysfunction undergoing FESS.	FESS improved olfactory function in CCAD.	Central disease affects smell-related mucosa.	Supported surgery as a functional treatment option.
Lau et al. (2024)	Primary CRS cohort in Southeast Asia.	Endoscopic and radiologic CCD as predictors of perennial allergen sensitization.	Endoscopic CCD predicted inhalant allergy better than radiologic CCD.	Important for perennial allergic rhinitis settings.	Reinforced endoscopy as a diagnostic priority.
Guo et al. (2024)	Outcome study after ESS.	CCAD and CRSwNP/central compartment groups.	Most CCAD patients achieved good one-year surgical control.	Suggested favorable postoperative course in true CCAD.	Supported postoperative prognosis counseling.

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Study	Design / population	Definition or diagnostic focus	Main finding	Type 2 / allergy relevance	Implication for CCAD review
Aaron et al. (2025)	Bronx population study.	CCAD characterization in a high asthma and aeroallergen-burden region.	Described CCAD in a population with high background airway disease.	Added evidence of demographic and geographic variability.	Supported population-specific analysis.
Meerwein et al. (2025)	Postoperative HDM-sensitized CCAD cohort.	AIT after surgery in HDM-sensitized CCAD.	Assessed whether AIT influenced postoperative disease progression.	Focused on allergen-directed therapy.	Supported study of combined surgery and allergy treatment.
Barrow et al. (2025)	Literature analysis and diagnostic criteria proposal.	Standardized diagnostic criteria for CCAD.	Proposed central tissue remodeling plus IgE-mediated allergic features as diagnostic cornerstone.	Defined CCAD as type 2 dominant and eosinophilic.	Provided current diagnostic framework.
Moreno-Luna et al. (2025)	Diagnostic challenge review/article.	CCAD in type 2 CRS.	Emphasized diagnostic difficulty and overlap with other CRS patterns.	Focused on CCAD within type 2 CRS.	Supported careful differential diagnosis.
Vizcarra-Melgar et al. (2025)	Systematic review of phenotypic features.	CCAD compared with other CRS types.	CCAD showed distinct clinical and immunologic features and favorable ESS outcomes.	Confirmed heterogeneity of allergy and eosinophilia.	Supported need for standardized criteria.