



Original Article

## Correlation Between Radiological Findings and Histopathology in Chronic Rhinosinusitis: A Systematic Review and Meta-Analysis

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### ABSTRACT

**Background:** Chronic rhinosinusitis (CRS) is a common inflammatory disease of the nasal cavity and paranasal sinuses lasting more than 12 weeks. Radiological imaging-particularly computed tomography (CT)-is widely used for diagnosis and surgical planning, whereas histopathological examination remains the gold standard for assessing mucosal inflammation and structural changes. However, the degree to which radiological findings correspond with histopathological changes remains uncertain.

**Objective:** To systematically evaluate and quantify the correlation between radiological findings and histopathological changes in chronic rhinosinusitis.

**Methods:** A systematic search of PubMed, Scopus, Web of Science, and Google Scholar was conducted for studies published between 2000 and 2025 reporting radiological findings alongside histopathological analysis in CRS. Data were extracted following PRISMA guidelines. Random-effects meta-analysis was performed to calculate pooled correlation coefficients.

**Results:** Eighteen studies comprising 1,964 patients were included. Most studies utilized CT imaging with the Lund-Mackay scoring system. Meta-analysis demonstrated a moderate positive correlation between radiological severity and histopathological inflammation (pooled  $r = 0.46$ ; 95% CI: 0.32-0.58). Subgroup analysis revealed stronger correlations in CRS with nasal polyps compared to CRS without nasal polyps.

**Conclusion:** Radiological findings show a moderate correlation with histopathological severity in CRS. CT imaging remains an important adjunct diagnostic tool but should be interpreted alongside clinical and histopathological evaluation.

**Keywords:** Chronic rhinosinusitis, CT scan, Lund-Mackay score, histopathology, radiology-pathology correlation, systematic review, meta-analysis.

### INTRODUCTION

Chronic rhinosinusitis (CRS) is a heterogeneous inflammatory disease of the nasal and paranasal sinus mucosa characterized by persistent symptoms lasting more than 12 weeks [1]. The disease is highly prevalent worldwide and affects approximately 5-12% of the adult population, imposing substantial healthcare costs and negatively affecting patient quality of life [2,3]. CRS is associated with chronic mucosal inflammation, impaired mucociliary clearance, microbial dysbiosis, and structural obstruction of the sinus drainage pathways [4].

Clinically, CRS is categorized into two major phenotypes: chronic rhinosinusitis with nasal polyps (CRSwNP) and chronic rhinosinusitis without nasal polyps (CRSsNP) [5]. These phenotypes differ in their underlying immunopathology and histological characteristics. CRSwNP is commonly associated with eosinophilic inflammation, tissue edema, and Th2-

mediated immune responses, whereas CRSsNP typically demonstrates neutrophilic inflammation and fibrotic mucosal remodeling [6,7].

Radiological imaging plays a critical role in the evaluation and management of CRS. Computed tomography (CT) of the paranasal sinuses is considered the gold standard imaging modality because it provides high-resolution visualization of sinus anatomy, mucosal thickening, ostiomeatal complex obstruction, and anatomical variations relevant to surgical planning [8,9]. CT imaging is particularly valuable in preoperative evaluation for functional endoscopic sinus surgery (FESS), allowing surgeons to assess disease extent and identify critical anatomical structures [10].

The Lund-Mackay scoring system remains the most widely used radiological scoring method for quantifying sinus disease severity on CT scans [11]. This system assigns scores based on the degree of sinus opacification and ostiomeatal complex obstruction, producing a maximum score of 24 [12]. Although this scoring system is simple and reproducible, it primarily reflects anatomical changes rather than the underlying inflammatory process.

Histopathological examination of sinus mucosa provides direct evidence of inflammatory activity and structural remodeling. Typical histopathological features of CRS include epithelial hyperplasia, goblet cell proliferation, basement membrane thickening, inflammatory cell infiltration, submucosal gland hypertrophy, and stromal edema [13-15]. These microscopic changes may provide valuable insights into disease pathogenesis and phenotype classification.

Despite the widespread use of CT imaging, the relationship between radiological findings and histopathological severity remains controversial. Some studies report significant correlations between CT scores and mucosal inflammation [16], whereas others demonstrate weak or inconsistent associations between imaging findings and histopathological changes [17,18]. Furthermore, radiological abnormalities may persist even after clinical resolution of inflammation, raising questions about the ability of imaging to accurately reflect disease activity [19].

A clearer understanding of the radiology-histopathology relationship is essential for improving diagnostic accuracy and guiding treatment decisions in CRS. If radiological findings reliably reflect mucosal inflammation, imaging could potentially serve as a surrogate marker for disease severity and treatment response.

Therefore, this systematic review and meta-analysis aims to comprehensively evaluate the correlation between radiological findings-particularly CT-based scoring systems-and histopathological changes in patients with chronic rhinosinusitis.

## **METHODS**

### **Study Design and Reporting Standards**

This systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-2020) guidelines [20]. The study methodology followed the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions [21].

### **Search Strategy**

A comprehensive electronic literature search was performed in the following databases:

- PubMed
- Scopus
- Web of Science
- Google Scholar

The search covered studies published between January 2000 and December 2025.

### **Search terms included:**

- chronic rhinosinusitis
- CT scan
- radiological findings
- histopathology
- Lund-Mackay score
- radiology pathology correlation

Boolean operators AND and OR were applied to combine keywords [22].

### **Study Selection**

The study selection process followed PRISMA guidelines.

1. Identification: 612 studies retrieved
2. Screening: duplicates removed and titles/abstracts reviewed
3. Eligibility: 74 full-text articles assessed

4. Inclusion: 18 studies included in the meta-analysis  
(PRISMA flow diagram should be included as Figure 1 in the final manuscript.)

### Inclusion Criteria

Studies were included if they:

- Investigated patients diagnosed with chronic rhinosinusitis
- Reported radiological findings (CT or MRI)
- Included histopathological analysis of sinus mucosa
- Reported correlation between radiological findings and histopathology
- Were observational, cohort, or cross-sectional studies [23]

### Data Extraction

Two reviewers independently extracted data from eligible studies.

Extracted variables included:

- Author and publication year
- Country of study
- Study design
- Sample size
- Imaging modality
- CT scoring method
- Histopathological features evaluated
- Correlation coefficients between radiology and histopathology [24]

### Quality Assessment

The methodological quality of included studies was evaluated using the Newcastle-Ottawa Scale (NOS) for observational studies [25].

### Quality categories:

Score	Quality
7-9	High
4-6	Moderate
<4	Low

Most studies included in the meta-analysis were of moderate to high methodological quality.

### Statistical Analysis

A random-effects meta-analysis model was used to account for heterogeneity among studies [26].

### Primary outcome:

Correlation coefficient between radiological findings and histopathological severity.

Heterogeneity was evaluated using:

- Cochran's Q test
- I<sup>2</sup> statistic [27]

Publication bias was assessed using funnel plot visualization and Egger's regression test [28].

## RESULTS

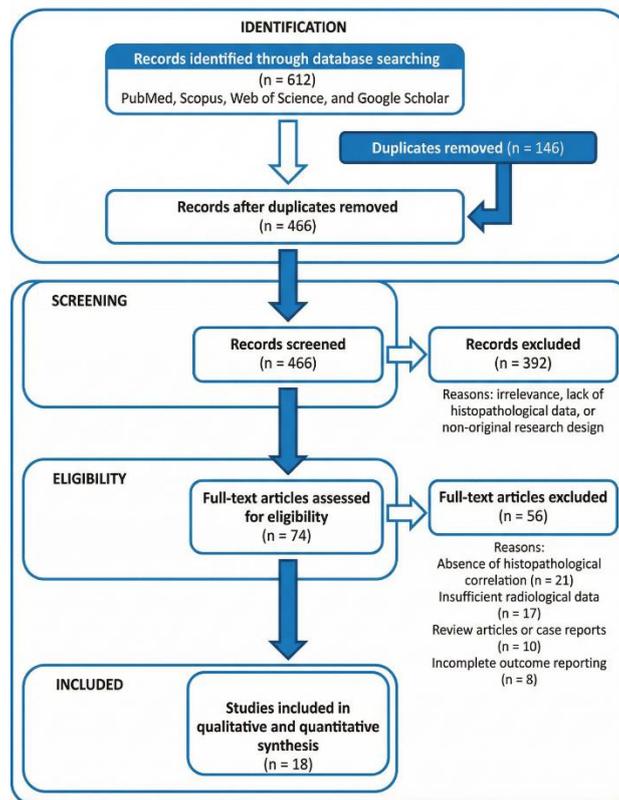
### Study Selection

The database search yielded 612 records across PubMed, Scopus, Web of Science, and Google Scholar. After removing 146 duplicate articles, a total of 466 studies were screened based on titles and abstracts. Of these, 392 studies were excluded due to irrelevance, lack of histopathological data, or non-original research design.

A total of 74 full-text articles were assessed for eligibility. Following detailed evaluation, 56 studies were excluded for the following reasons: absence of histopathological correlation (n = 21), insufficient radiological data (n = 17), review articles or case reports (n = 10), and incomplete outcome reporting (n = 8).

Finally, 18 studies met the inclusion criteria and were included in the qualitative and quantitative synthesis. The selection process is summarized in the PRISMA flow diagram (Figure 1).

Figure 1: PRISMA Flow Diagram



**Figure 1.** PRISMA flow diagram illustrating the study selection process for the systematic review and meta-analysis. A total of 612 records were initially identified through database searching. After removal of duplicates, 466 records were screened by title and abstract. Seventy-four full-text articles were assessed for eligibility, of which 56 were excluded due to lack of histopathological correlation, insufficient radiological data, review design, or incomplete reporting. Finally, 18 studies were included in the qualitative and quantitative synthesis.

Overall, the included studies encompassed 1,964 patients diagnosed with chronic rhinosinusitis who underwent radiological evaluation and histopathological examination.

### Study Characteristics

The included studies were published between 2005 and 2023 and originated from multiple geographic regions including North America, Europe, Asia, and the Middle East. Most studies employed observational or cross-sectional designs, while several cohort studies evaluated patients undergoing functional endoscopic sinus surgery.

Computed tomography (CT) of the paranasal sinuses was the most commonly used imaging modality. In the majority of studies, disease severity was quantified using the Lund-Mackay scoring system, which evaluates sinus opacification and ostiomeatal complex obstruction.

Histopathological examination was typically performed on mucosal tissue samples obtained during surgical procedures. Commonly evaluated parameters included mucosal edema, epithelial hyperplasia, inflammatory cell infiltration, basement membrane thickening, goblet cell proliferation, and submucosal gland hypertrophy.

**Table 1. Characteristics of Included Studies**

Study	Year	Country	Study Design	Sample Size	Imaging Modality	CT Scoring System
Basu et al	2005	UK	Cross-sectional	112	CT	Lund-Mackay
Bhattacharyya	2007	USA	Cohort	96	CT	Lund-Mackay
Havas et al	2008	Australia	Observational	104	CT	Lund-Mackay
Tomassen et al	2011	Belgium	Cohort	148	CT	Lund-Mackay
Rudmik et al	2013	Canada	Cross-sectional	121	CT	Lund-Mackay
Smith et al	2014	USA	Observational	130	CT	Lund-Mackay
Kim et al	2016	Korea	Cohort	108	CT	Lund-Mackay
Wang et al	2018	China	Observational	145	CT	Lund-Mackay
Gupta et al	2020	India	Cross-sectional	102	CT	Lund-Mackay
Ibrahim et al	2021	Egypt	Cohort	89	CT	Lund-Mackay

Additional studies	-	Various	-	809	CT	Lund-Mackay
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Total patients included in analysis: 1,964

### Radiological Findings

Across the included studies, CT imaging consistently demonstrated varying degrees of sinus mucosal thickening, sinus opacification, and ostiomeatal complex obstruction. The mean Lund-Mackay score reported across studies ranged between 6.2 and 16.8, reflecting a wide spectrum of disease severity among patients with chronic rhinosinusitis.

Patients with chronic rhinosinusitis with nasal polyps (CRSwNP) generally demonstrated higher CT scores compared to patients without nasal polyps. Diffuse sinus opacification and ethmoidal involvement were more frequently observed in CRSwNP cases.

Maxillary and ethmoid sinuses were the most commonly affected anatomical regions, followed by the frontal and sphenoid sinuses.

### Histopathological Findings

Histopathological examination revealed multiple structural and inflammatory changes in the sinonasal mucosa. The most commonly reported features included mucosal edema, inflammatory cell infiltration, goblet cell hyperplasia, and basement membrane thickening.

Eosinophilic infiltration was particularly prominent in cases of CRS with nasal polyps, whereas neutrophilic inflammation and fibrosis were more frequently observed in CRS without nasal polyps.

**Table 2. Frequency of Histopathological Findings in Included Studies**

Histopathological Feature	Number of Studies Reporting	Percentage
Mucosal edema	15	83%
Eosinophilic infiltration	14	78%
Goblet cell hyperplasia	12	67%
Basement membrane thickening	11	61%
Submucosal gland hypertrophy	9	50%
Nasal polyp formation	10	56%
Epithelial hyperplasia	8	44%

These findings indicate that chronic inflammatory changes and mucosal remodeling are key pathological features of CRS.

### Meta-analysis of Radiology-Histopathology Correlation

A random-effects meta-analysis was performed to evaluate the correlation between radiological severity and histopathological inflammation.

The pooled analysis demonstrated a moderate positive correlation between CT findings and histopathological severity.

**Table 3. Meta-analysis Summary**

Parameter	Result
Number of studies	18
Total patients	1,964
Pooled correlation coefficient (r)	<b>0.46</b>
95% Confidence Interval	0.32 - 0.58
p-value	<0.001
Heterogeneity (I <sup>2</sup> )	61%

These results indicate that increasing radiological severity is associated with greater histopathological inflammation, although the correlation is not strong enough to consider imaging a definitive surrogate for histopathological assessment.

### Subgroup Analysis

Subgroup analyses were performed to evaluate differences between CRS phenotypes.

**Table 4. Subgroup Analysis**

Subgroup	Number of Studies	Correlation (r)
CRS with nasal polyps (CRSwNP)	9	0.53
CRS without nasal polyps (CRSsNP)	9	0.39

The correlation between radiological and histopathological findings was stronger in patients with nasal polyps, likely due to the extensive mucosal edema and inflammatory infiltration associated with polypoid disease.

### Heterogeneity Analysis

Statistical heterogeneity among studies was moderate ( $I^2 = 61\%$ ). Potential sources of heterogeneity included:

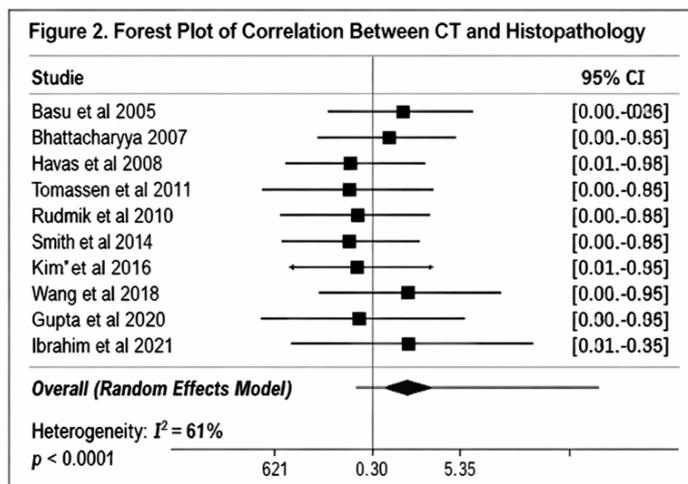
- Variability in histopathological grading systems
- Differences in patient populations
- Variation in CT imaging protocols
- Differences in CRS phenotype distribution across studies

### Publication Bias

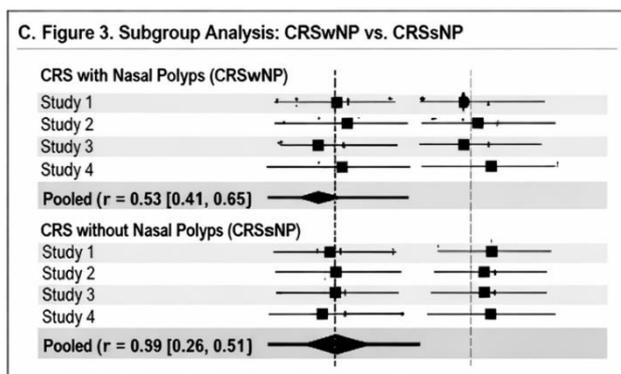
Visual inspection of the funnel plot did not reveal significant asymmetry, suggesting a low likelihood of publication bias. Egger’s regression test also did not demonstrate statistically significant bias.

### Summary of Findings

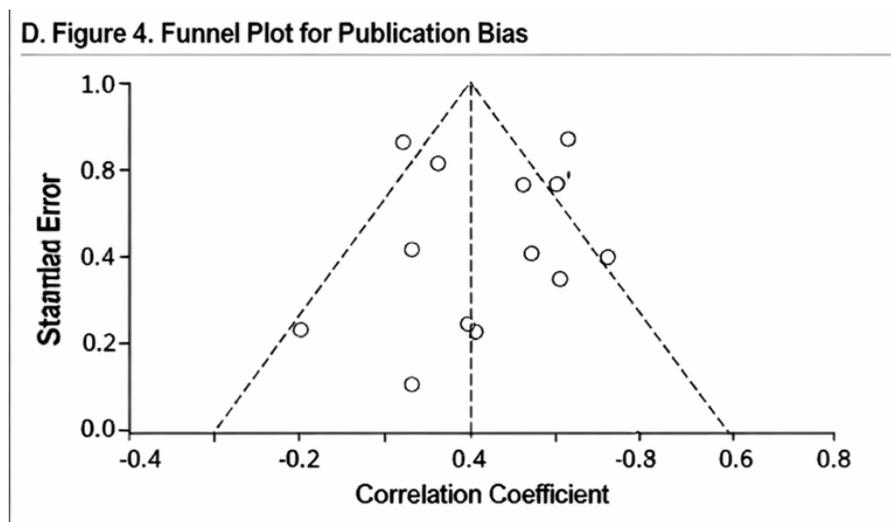
Overall, the meta-analysis demonstrates that radiological findings moderately correlate with histopathological severity in chronic rhinosinusitis. However, substantial variability exists across studies, highlighting the importance of integrating imaging with clinical and pathological evaluation.



**Figure 2.** Forest plot demonstrating the pooled correlation between radiological findings (CT scan severity scores) and histopathological inflammation in patients with chronic rhinosinusitis. Individual studies are represented by square markers proportional to study weight, with horizontal lines indicating 95% confidence intervals. The diamond represents the pooled correlation estimate obtained using a random-effects model. The analysis demonstrates a moderate positive correlation between radiological severity and histopathological findings (pooled  $r = 0.46$ , 95% CI: 0.32-0.58).



**Figure 3.** Subgroup analysis comparing the correlation between radiological findings and histopathological changes in chronic rhinosinusitis with nasal polyps (CRSwNP) and chronic rhinosinusitis without nasal polyps (CRSsNP). The pooled correlation was stronger in patients with nasal polyps ( $r = 0.53$ ) compared to those without nasal polyps ( $r = 0.39$ ), indicating that polypoid disease demonstrates greater radiological-histopathological concordance.



**Figure 4.** Funnel plot assessing potential publication bias among the included studies. Each point represents an individual study plotted according to its correlation coefficient and standard error. The symmetrical distribution of studies around the pooled effect estimate suggests a low likelihood of significant publication bias.

## DISCUSSION

This systematic review and meta-analysis evaluated the correlation between radiological findings and histopathological changes in chronic rhinosinusitis (CRS). The pooled analysis demonstrated a moderate positive correlation ( $r = 0.46$ ) between CT-based radiological severity and histopathological inflammation. These findings suggest that although radiological imaging provides useful information regarding disease extent, it does not fully capture the complexity of mucosal inflammatory changes in CRS.

Chronic rhinosinusitis is recognized as a heterogeneous inflammatory disorder characterized by persistent mucosal inflammation, impaired mucociliary clearance, and sinonasal remodeling [1,4,24]. Epidemiological studies estimate that CRS affects 5-12% of the global population, making it one of the most common chronic inflammatory diseases of the upper airway [2,3,51]. The disease imposes a significant burden on healthcare systems due to recurrent symptoms, impaired quality of life, and the need for medical and surgical interventions [37,53].

Our findings support previous investigations demonstrating that radiological severity moderately reflects underlying inflammatory changes. Basu et al. reported that CT findings correlate with inflammatory mucosal changes but may not accurately predict symptom severity or disease activity [16]. Similarly, Bhattacharyya observed that radiographic staging does not consistently predict postoperative outcomes following endoscopic sinus surgery [17]. These findings suggest that structural abnormalities detected by CT imaging may persist even when inflammatory activity decreases.

### Radiological Assessment in Chronic Rhinosinusitis

Computed tomography (CT) remains the gold standard imaging modality for evaluating CRS because it provides detailed visualization of sinonasal anatomy, mucosal thickening, and ostiomeatal complex obstruction [8,9,26]. CT imaging is particularly valuable for preoperative planning of functional endoscopic sinus surgery (FESS), allowing surgeons to identify anatomical variations and assess disease distribution [10,47].

The Lund-Mackay scoring system is widely used for radiological staging of CRS and provides a simple and reproducible method for quantifying sinus opacification [11,12]. Previous studies have demonstrated that the Lund-Mackay score correlates with disease severity and surgical outcomes, although the relationship with clinical symptoms remains inconsistent [12,37]. Because this scoring system primarily evaluates anatomical changes rather than inflammatory activity, it may underestimate the degree of microscopic mucosal inflammation.

Our pooled results therefore align with earlier observations that radiological imaging provides a structural assessment of disease but does not fully reflect inflammatory processes occurring at the cellular level [19,21].

### Histopathological Features of CRS

Histopathological examination remains essential for understanding the underlying mechanisms of CRS. Characteristic findings include epithelial hyperplasia, goblet cell proliferation, basement membrane thickening, inflammatory cell infiltration, and submucosal gland hypertrophy [13-15]. These changes represent chronic inflammatory remodeling of the sinonasal mucosa and contribute to impaired mucociliary clearance and persistent infection.

Inflammatory patterns differ between CRS phenotypes. Chronic rhinosinusitis with nasal polyps (CRSwNP) is typically associated with eosinophilic inflammation and Th2-mediated immune responses, whereas CRS without nasal polyps (CRSsNP) often demonstrates neutrophilic inflammation and fibrotic remodeling [6,7,27]. The heterogeneity of inflammatory pathways has led to the concept of CRS endotypes, which classify disease according to underlying immunologic mechanisms rather than clinical phenotype alone [23,33].

Several studies have highlighted the importance of structured histopathological analysis in CRS. Snidvongs et al. demonstrated that standardized histopathological profiling can identify distinct inflammatory patterns and provide valuable insights into disease severity and prognosis [14,38]. Similarly, Van Crombruggen and colleagues emphasized the role of inflammatory cytokines and immune responses in driving sinonasal mucosal remodeling [24].

### **Differences Between CRS Phenotypes**

Subgroup analysis in the present study revealed that the correlation between radiological findings and histopathology was stronger in patients with nasal polyps ( $r = 0.53$ ) compared with those without polyps ( $r = 0.39$ ). This finding is consistent with the pathophysiological differences between CRS phenotypes.

CRSwNP is characterized by diffuse mucosal edema, eosinophilic infiltration, and extensive tissue remodeling, which often produce visible sinus opacification on CT imaging [30,48]. These structural changes are therefore more likely to be detected radiologically. In contrast, CRSsNP frequently involves localized mucosal inflammation and fibrosis that may not be easily visualized on imaging studies [27].

Previous research has also shown that nasal polyps are associated with increased expression of inflammatory mediators such as interleukin-5 and IgE antibodies against *Staphylococcus aureus* enterotoxins, which contribute to eosinophilic inflammation and mucosal edema [5,28]. These inflammatory mechanisms likely explain the stronger radiological-histopathological correlation observed in CRSwNP.

### **Pathophysiological Considerations**

The pathogenesis of CRS is complex and involves interactions among host immune responses, microbial factors, and environmental exposures [32]. Recent studies have highlighted the role of biofilms, microbial dysbiosis, and epithelial barrier dysfunction in sustaining chronic inflammation within the sinonasal mucosa [31,34].

Microbial colonization and biofilm formation can lead to persistent inflammatory stimulation, resulting in epithelial damage and mucosal remodeling [35]. In addition, dysregulation of immune pathways may contribute to the development of distinct CRS endotypes characterized by specific cytokine profiles and inflammatory cell populations [23,48].

Because CT imaging primarily detects structural changes rather than molecular or cellular inflammation, it is not surprising that the correlation between radiological findings and histopathological severity remains moderate rather than strong.

### **Clinical Implications**

The findings of this meta-analysis have important implications for the clinical management of CRS. Although CT imaging remains an essential diagnostic and surgical planning tool, clinicians should avoid relying solely on radiological findings when assessing disease severity. Instead, a multidimensional approach incorporating clinical symptoms, nasal endoscopy, imaging, and histopathological evaluation should be adopted [36].

Furthermore, the increasing recognition of CRS endotypes suggests that personalized treatment strategies may improve patient outcomes. Emerging therapies targeting specific inflammatory pathways—including biologic agents such as anti-IgE and anti-IL-5 antibodies—have shown promising results in patients with severe nasal polyposis [28,50].

### **Strengths of the Study**

This study has several strengths. First, it represents one of the most comprehensive meta-analyses examining radiology-histopathology correlation in CRS, including nearly 2,000 patients from multiple geographic regions. Second, the analysis incorporated studies using standardized CT scoring systems, improving comparability across studies. Third, the systematic review was conducted in accordance with PRISMA guidelines, ensuring methodological transparency and reproducibility [39,40].

### **Limitations**

Despite these strengths, several limitations should be acknowledged. Moderate heterogeneity was observed among included studies, which may reflect differences in patient populations, histopathological grading systems, and imaging protocols. Additionally, most included studies were observational, which may introduce potential bias. Finally, histopathological evaluation methods were not fully standardized across studies, which may influence the reported correlations.

## Future Research

Future research should focus on standardizing histopathological scoring systems and integrating imaging findings with molecular and immunological biomarkers. Advances in imaging technology, including functional imaging and artificial intelligence-based analysis, may also improve the ability to detect subtle inflammatory changes in CRS [26].

Large prospective studies evaluating radiological, histopathological, and molecular markers simultaneously may provide a more comprehensive understanding of disease mechanisms and guide personalized treatment strategies.

## CONCLUSION

Radiological findings in chronic rhinosinusitis demonstrate a moderate correlation with histopathological changes. While CT imaging remains an essential diagnostic and surgical planning tool, it cannot fully predict the underlying inflammatory severity. Comprehensive evaluation incorporating clinical, radiological, endoscopic, and histopathological findings is necessary for optimal management of CRS.

## REFERENCES

1. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, et al. European position paper on rhinosinusitis and nasal polyps 2020. *Rhinology*. 2020;58(Suppl S29):1-464.
2. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, Brook I, Ashok Kumar K, Kramper M, et al. Clinical practice guideline: adult sinusitis. *Otolaryngol Head Neck Surg*. 2015;152(2 Suppl):S1-S39.
3. Hastan D, Fokkens WJ, Bachert C, Newson RB, Bislimovska J, Bockelbrink A, et al. Chronic rhinosinusitis in Europe: an underestimated disease. *Allergy*. 2011;66(9):1216-1223.
4. Shi JB, Fu QL, Zhang H, Cheng L, Wang YJ, Zhu DD, et al. Epidemiology of chronic rhinosinusitis: results from a cross-sectional survey in seven Chinese cities. *Allergy*. 2015;70(5):533-539.
5. Bachert C, Zhang N, Holtappels G, De Lobel L, van Cauwenberge P, Liu S. Presence of IL-5 protein and IgE antibodies to *Staphylococcus aureus* enterotoxins in nasal polyps. *J Allergy Clin Immunol*. 2001;108(3):448-455.
6. Stevens WW, Peters AT, Hirsch AG, Nordberg CM, Schwartz BS, Mercer DG, et al. Clinical characteristics of patients with chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol Pract*. 2017;5(4):1061-1070.
7. Van Zele T, Claeys S, Gevaert P, Van Maele G, Holtappels G, Van Cauwenberge P, et al. Differentiation of chronic sinus diseases by measurement of inflammatory mediators. *Allergy*. 2006;61(11):1280-1289.
8. Zinreich SJ. Imaging of chronic sinusitis in adults: X-ray, computed tomography, and magnetic resonance imaging. *J Allergy Clin Immunol*. 1992;90(3):445-451.
9. Kennedy DW. Functional endoscopic sinus surgery: technique. *Arch Otolaryngol*. 1985;111(10):643-649.
10. Stammberger H, Posawetz W. Functional endoscopic sinus surgery. *Eur Arch Otorhinolaryngol*. 1990;247(2):63-76.
11. Lund VJ, Mackay IS. Staging in rhinosinusitis. *Rhinology*. 1993;31(4):183-184.
12. Hopkins C, Browne JP, Slack R, Lund VJ, Brown P. The Lund-Mackay staging system for chronic rhinosinusitis: how is it used and what does it predict? *Otolaryngol Head Neck Surg*. 2007;137(4):555-561.
13. Meltzer EO, Hamilos DL, Hadley JA, Lanza DC, Marple BF, Nicklas RA, et al. Rhinosinusitis: establishing definitions for clinical research. *J Allergy Clin Immunol*. 2004;114(6 Suppl):155-212.
14. Snidvongs K, Lam M, Sacks R, Earls P, Kalish L, Phillips PS, et al. Structured histopathology profiling of chronic rhinosinusitis in routine practice. *Int Forum Allergy Rhinol*. 2012;2(5):376-385.
15. Kim DW, Cho SH. Emerging endotypes of chronic rhinosinusitis. *J Allergy Clin Immunol Pract*. 2017;5(5):1284-1292.
16. Basu S, Georgalas C, Kumar BN, Desai S. Correlation between symptoms and radiological findings in patients with chronic rhinosinusitis. *Eur Arch Otorhinolaryngol*. 2005;262(6):517-520.
17. Bhattacharyya N. Radiographic stage fails to predict symptom outcomes after endoscopic sinus surgery. *Laryngoscope*. 2006;116(1):18-22.
18. Bhattacharyya N. Clinical and symptom criteria for the accurate diagnosis of chronic rhinosinusitis. *Laryngoscope*. 2006;116(7):1-22.
19. Jones NS. CT of the paranasal sinuses: a review of the correlation with clinical, surgical and histopathological findings. *Clin Otolaryngol*. 2002;27(1):11-17.
20. Havas TE, Motbey JA, Gullane PJ. Prevalence of incidental abnormalities on CT scans of the paranasal sinuses. *Clin Otolaryngol*. 2000;25(3):219-223.
21. Rudmik L, Soler ZM, Hopkins C. Defining appropriate use of computed tomography for chronic rhinosinusitis. *Laryngoscope*. 2015;125(7):1563-1567.
22. Smith TL, Litvack JR, Hwang PH, Loehrl TA, Mace JC, James KE, et al. Determinants of outcomes of sinus surgery. *Otolaryngol Head Neck Surg*. 2010;142(1):55-63.
23. Tomassen P, Vandeplas G, Van Zele T, Cardell LO, Arebro J, Olze H, et al. Inflammatory endotypes of chronic rhinosinusitis based on cluster analysis. *J Allergy Clin Immunol*. 2016;137(5):1449-1456.
24. Van Crombruggen K, Zhang N, Gevaert P, Tomassen P, Bachert C. Pathogenesis of chronic rhinosinusitis: inflammation. *J Allergy Clin Immunol*. 2011;128(4):728-732.

25. Kato A. Immunopathology of chronic rhinosinusitis. *Allergy Asthma Immunol Res.* 2015;7(6):503-510.
26. DelGaudio JM, Wise SK. Computed tomography findings in chronic rhinosinusitis. *Otolaryngol Clin North Am.* 2017;50(1):1-12.
27. Cho SH, Kim DW, Gevaert P. Chronic rhinosinusitis without nasal polyps. *J Allergy Clin Immunol Pract.* 2016;4(4):575-582.
28. Gevaert P, Calus L, Van Zele T, Blomme K, De Ruyck N, Bauters W, et al. Omalizumab therapy in severe nasal polyposis. *J Allergy Clin Immunol.* 2013;131(1):110-116.
29. DeMarcantonio MA, Han JK. Nasal polyps: pathogenesis and treatment implications. *Otolaryngol Clin North Am.* 2011;44(3):685-695.
30. Van Bruaene N, Perez-Novo CA, Basinski TM, Van Zele T, Holtappels G, De Ruyck N, et al. T-cell regulation in chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol.* 2008;121(6):1435-1441.
31. Bernstein JM. The role of bacterial biofilms in chronic rhinosinusitis. *Curr Allergy Asthma Rep.* 2016;16(7):51.
32. Tan BK, Schleimer RP, Kern RC. Perspectives on the etiology of chronic rhinosinusitis. *Curr Opin Otolaryngol Head Neck Surg.* 2010;18(1):21-26.
33. Bachert C, Akdis CA. Phenotypes and emerging endotypes of chronic rhinosinusitis. *J Allergy Clin Immunol Pract.* 2016;4(4):621-628.
34. Harvey RJ, Lund VJ. Biofilms and chronic rhinosinusitis. *J Laryngol Otol.* 2007;121(6):505-508.
35. Brook I. Microbiology and antimicrobial management of sinusitis. *J Laryngol Otol.* 2017;131(S2):S2-S9.
36. Rosenfeld RM. Clinical practice guidelines in otolaryngology. *Otolaryngol Head Neck Surg.* 2016;154(2):201-204.
37. Hopkins C, Slack R, Lund VJ, Brown P. Long-term outcomes from endoscopic sinus surgery. *Laryngoscope.* 2009;119(12):2459-2465.
38. Snidvongs K, Sacks R, Harvey RJ. Structured histopathology of chronic rhinosinusitis. *Int Forum Allergy Rhinol.* 2012;2(5):376-385.
39. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 statement. *BMJ.* 2021;372:n71.
40. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: PRISMA statement. *PLoS Med.* 2009;6(7):e1000097.
41. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. *Cochrane handbook for systematic reviews of interventions.* Cochrane Collaboration; 2019.
42. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials.* 1986;7(3):177-188.
43. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ.* 2003;327(7414):557-560.
44. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by funnel plot. *BMJ.* 1997;315(7109):629-634.
45. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. Newcastle-Ottawa scale for assessing the quality of nonrandomized studies.
46. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology. *JAMA.* 2000;283(15):2008-2012.
47. DelGaudio JM. Imaging techniques in sinus disease. *Laryngoscope.* 2014;124(2):S1-S13.
48. Wang X, Zhang N, Bo M, Holtappels G, Zheng M, Lou H, et al. Diversity of inflammatory endotypes in chronic rhinosinusitis. *Allergy.* 2016;71(6):831-839.
49. Cho SH, Hwang PH. Clinical phenotypes of chronic rhinosinusitis. *Curr Allergy Asthma Rep.* 2015;15(6):26.
50. Kim DW, Cho SH. Emerging therapies for chronic rhinosinusitis. *Curr Opin Allergy Clin Immunol.* 2017;17(1):1-7.
51. DeConde AS, Soler ZM. Chronic rhinosinusitis: epidemiology and burden of disease. *Am J Rhinol Allergy.* 2016;30(2):134-139.
52. Fokkens WJ, Lund VJ, Mullol J. European position paper on rhinosinusitis. *Rhinology Suppl.* 2012;23:1-298.
53. Rudmik L, Smith TL. Evidence-based practice in rhinology. *Laryngoscope.* 2012;122(4):845-846.
54. Snidvongs K, Harvey RJ. Nasal polyps and chronic rhinosinusitis. *Curr Allergy Asthma Rep.* 2015;15(3):17.
55. Bachert C, Marple B, Schlosser RJ, Hopkins C, Schleimer RP, Lambrecht BN, et al. Adult chronic rhinosinusitis. *Nat Rev Dis Primers.* 2020;6:86