JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Assessment of chronic rhinosinusitis severity indicators: radiological and clinical perspective

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Abstract

Introduction: Chronic rhinosinusitis (CRS) is inflammation of the nasal cavity and paranasal sinus mucosa. The aim of this study was to examine which of the available radiological and clinical parameters is the best indicator of the CRS severity.

Methodology: In order to classify CRS, we used both a subjective assessment tool such as SNOT-22 questionnaire, as well as an objective tool such as clinical examination. We introduced three forms of CRS (mild, moderate and severe). Within these groups, we evaluated the computerized tomography (CT) parameters used as an indicator of bone remodeling, the Lund-Mackay score (LMS), CT properties of the soft tissue content in the maxillary sinuses, presence of nasal polypus (NP), presence of fungal infection and parameters indicating allergic status.

Results: Frequencies of NP, positive eosinophil count, presence of fungi, areas of high attenuation, and duration of CRS and LMS significantly increased with the increased severity of CRS. Anterior wall thickness and density increased in the severe forms of CRS in the group assessed by SNOT-22. Positive correlation was detected between LMS and maximal density of sinus content and between duration of CRS and anterior wall thickness.

Conclusions: Morphological changes of sinus wall detected in CT could be a useful indicator of CRS severity. Changes in bone morphology are more likely to occur in patients with longer-lasting CRS. The presence of fungi, allergic inflammation of any origin and nasal polypus potentiates more severe forms of CRS both clinically and subjectively.

Key words: infection; chronic rhinosinusitis; CT; osteitis; maxillary sinus.

J Infect Dev Ctries 2023; 17(6):854-859. doi:10.3855/jidc.17959

(Received 19 January 2023 – Accepted 06 February 2023)

Introduction

Chronic rhinosinusitis (CRS) is defined as inflammation of the nasal cavity and paranasal sinus mucosa lasting for 12 weeks or longer [1]. Commonly present signs and symptoms are nasal drainage, nasal obstruction, fever, headache, cough and anosmia [2]. CRS are common in patients with reported allergies, since IgE hypersensitivity could be the origin of this condition [3,4]. Among the numerous causes of CRS, there is increasing evidence highlighting a very important role of fungi.

Computerized tomography (CT) is the primary medical imaging technique used once CRS is suspected [5]. So far, researchers have used CT scans in order to investigate different radiological parameters which are not strictly specific to CRS, but have been reported and analyzed in previous studies [6]. Additionally, previous research showed radiologic evidence of bone involvement in CRS [7-10].

We wanted to examine which of the available radiological and clinical parameters is the best indicator of the severity of CRS. In order to classify the severity of CRS, we used both a subjective assessment tool such as the SNOT-22 questionnaire, as well as an objective tool such as clinical examination and introduced three forms of CRS (mild, moderate and severe). Within these groups, we evaluated the CT parameters used as an indicator of bone remodeling, the extent of paranasal sinus involvement by Lund-Mackay score (LMS), CT properties of the soft tissue content in the maxillary sinuses, presence of nasal polyposis, presence of fungal infection and parameters indicating allergic status of these patients.

Methodology

Study population

This research was conducted as a cross-sectional clinical study carried out in the Center for Radiological Diagnostics of the School of Dental Medicine, University of Belgrade as well as in the Clinical Center of Serbia, Medical School, University of Belgrade. Approval for this study was obtained from the Ethical Committee of the Clinical Centre of Serbia (5030/5) and the Ethical Committee of the Faculty of Medicine University of Belgrade (29/VI-3). Informed consent was obtained from all of the patients.

Inclusion criteria

The inclusion criteria for this study were a clinical diagnosis of CRS made by an ear, nose, and throat (ENT) specialist according to the (2020) adult CRS guidelines [11], as well as the clinically relevant indication for CT of the paranasal sinuses. Exclusion criteria were cases of previously diagnosed CRS resolved by medical treatment and/or sinonasal surgery, history of traumatic lesions of the facial skeleton and endodontic treatment of teeth in both maxilla within one year.

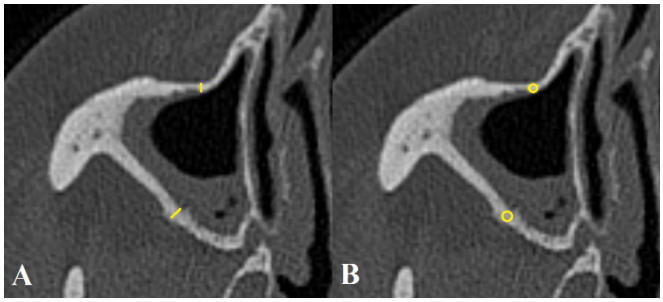
Data collection

The collected data included: (i) patient's demographics and historical data including duration of CRS (ii) anterior rhinoscopy results; (iii) total serum IgE Ab, absolute eosinophil count in blood and skin prick test (SPT) on different allergen); (iv) detection of fungal infection, (v) CT imaging of paranasal sinuses.

Clinical examination

All patients were examined by an ENT specialist who estimated the presence of nasal symptoms (nasal obstruction, nasal secretion, postnasal discharge, impaired or lost sense of smell, facial sense of pressure) for more than 12 weeks and nasal rhinoscopic/endoscopic findings including the presence oedema, discharge, and presence of nasal polypus (NP).

Figure 1. Sinus wall thickness (A) and density (B) measurement.



Each parameter was scored separately for left/right side, and all were summed up from 0 to 14 [12]. Rhinological scoring index for all observed parameters was suggested as follows: 0-4: '0 index' as mild CRS, 5-9: '1 index' as moderate CRS and 10-14: '2 index' as severe CRS.

Total serum IgE, eosinophil count and SPT

A concentration of total IgE Ab in serum was measured by enzyme-linked immunosorbent assay (Euroimmun AG, Lübeck, Germany). Results were interpreted as negative (< 100 kU/L), and positive (≥ 100 kU/L). The blood sample was taken before SPT and put into the tube containing ethylene-diamine-tetra acetic acid (EDTA). Eosinophil counting was performed with Fuchs-Rosenthal counting chamber. Results < 350 per mm^3 were considered as negative. SPT was done for allergens such as epithelia, pollens, dust mite and fungi.

Fungal detection

The presence of fungi was investigated using the previously described methodology of sinonasal secretion flow and aspiration from maxillary sinuses [6]. Patients with at least one fungus-positive maxillary sinus were regarded as positive.

Radiological examination

CT scanning of paranasal sinuses was performed without contrast enhancement in the supine position and analyzed using multi-planar reconstruction. For LMS, each sinus (maxillary, anterior ethmoidal, posterior ethmoidal, sphenoidal, and frontal) was scored on the following scale: 0 = no opacification; 1 = partial opacification; and 2 = complete opacification. The ostiomeatal complex was also scored as 0 = no obstruction or 2 = fully obstructed. The possible score for each side ranged from 0 to 12, and the total score from 0 to 24 [13].

In order to detect possible changes in maxillary sinus walls morphology, each sinus was assessed separately. Measurements were performed in the same axial plane at the level where the inferior turbinate attaches to the maxillary sinus wall. Both density and thickness were measured at the middle portion of anterior and posterior sinus wall (Figure 1). Thickness was measured by a direct line perpendicular to the wall, calculated in millimeters, while density was measured with region of interest (ROI) expressed in Hounsfield units. The measurements were performed 3 times randomly and the average value was recorded.

Afterwards, the paranasal sinus CT scans were analyzed for the presence of content in maxillary sinuses. Sinus content was assessed in terms of homogeneity as homogenous and non-homogenous, presence of high attenuation areas and density of sinus content (maximal and mean). These parameters were evaluated in the soft tissue window.

LMS was assessed by two experienced radiologists, with a strong inter-rater reliability (Kappa value of 0.813), while for the sinus content quality assessment of homogeneity and presence of high attenuation areas the inter-rater reliability was moderate (Kappa values 0.745 and 0.791, respectively).

SNOT -22 questionnaire

SNOT-22 is a validated standard test that consists of 22 questions covering 5 main domains: (1) nasal, (2) extra nasal, (3) ear/facial symptoms, (4) psychological, and (5) sleep dysfunction [27]. All the patients completed the SNOT-22. This patient-reported survey was used to assess 12 nasal symptoms and 10 psychological and behavioral symptoms, each rated on scale of 0 (absent) to 5 (severe) within a total score range of 0 to 110. We subdivided our study group based on the results of this questionnaire into the ones with mild form of CRS (score range 0-40), moderate (score range 40-80) and severe CRS (score > 80).

Statistical analysis

The Kolmogorov-Smirnov test was used to test data distribution normality. One-way analysis of variance (ANOVA) was used to assess the differences in density and thickness of sinus walls, density of sinus soft tissue content, LMS and duration of CRS (in years) between the investigated groups. The Pearson correlation was used to assess the correlation between density and thickness of sinus walls, density of sinus soft tissue content, LMS and duration of CRS. The association between the form of CRS and prevalence of different radiological and clinical findings was examined using the Chi-square test. Statistical analysis was performed in SPSS 17.0 statistical software and the results were considered statistically significant at the 0.05 level.

Results

Clinical characteristics and sociodemographic data of cohort

This study included 52 eligible patients, 18 female and 34 males, with an age range of 21 to 71 (45.6 ± 14.1) years. Based on the results of the clinical assessment of CRS all patients were subdivided into 3 groups: mild CRS (16 patients), moderate CRS (16 patients) and severe CRS (20 patients). The same categories were formed according to the results of SNOT-22 questionnaire with the following patient distribution: mild CRS (16 patients), moderate CRS (14 patients) and severe CRS (22 patients).

Clinical findings in mild, moderate and severe forms of CRS

As shown in Table 1, we detected increase in frequency of NP with the increased severity of CRS and with significant differences between mild, moderate and severe in SNOT-22 group ($p = 0.010$), while in the

Table 1. Clinical and radiological findings in mild, moderate and severe form of chronic rhinosinusitis (CRS).

	CRS assessed by clinical examination			χ^2			CRS assessed by SNOT-22 questionnaire			χ^2		
	Mild	**Moderate**	**Severe**	**Value**	**Df**	***p***	**Mild**	**Moderate**	**Severe**	**Value**	**Df**	***p***
Nasal polypus												
Yes	12.5%	50%	45%	5.85	2	0.054	6.2%	50%	50%	9.14	2	0.010*
No	87.5%	50%	55%				93.8%	75%	50%			
Positive IgE												
Yes	50%	37.5%	80%	7.136	2	0.028*	37.5%	50%	77.3%	6.648	2	0.039*
No	50%	62.5%	20%				62.5%	50%	22.7%			
Serum eosinophils												
Yes	37.5%	31.2%	70%	6.38	2	0.041*	25%	57.1%	59.1%	4.943	2	0.084
No	62.5%	68.8%	30%				75%	42.9%	40.9%			
Presence of fungi												
Yes	6.2%	18.7%	45%	7.60	2	0.022*	0%	28.6	40.9%	8.398	2	0.015*
No	93.8%	81.3%	55%				100%	71.4%	59.1%			
Homogeneity of sinus content												
Yes	56.2%	62.5%	35%	3.050	2	0.218	68.7%	57.1%	31.8%	5.445	2	0.066
No	43.8%	37.5%	65%				31.3%	42.9%	68.2%			
High attenuation areas in sinus content												
Yes	18.7%	12.5%	40%	4.067	2	0.131	12.5%	7.1%	45.4%	8.623	2	0.013*
No	81.3%	87.5%	60%				87.5%	92.9%	54.6%			

*$p \leq 0.05$.

clinically assessed CRS was close to significance (p = 0.054). Similar trend is observed for the presence of IgE positivity, with statistical significance in both scaling groups (p = 0.028, p = 0.039). While the positive eosinophil count increases with the severity of CRS in both groups, the statistical difference was present only in the clinically assessed one (p = 0.041). Fungi were significantly more frequent in the severe forms of CRS, in both scaling groups (p = 0.022, p = 0.015).

Radiological findings in mild, moderate and severe forms of CRS

The frequency of non-homogenous sinus content was the highest in the severe CRS groups (Table 1), but without significance (p = 0.218, p = 0.066). In accordance with these data, areas of high attenuation within sinus content were most frequently detected in severe forms of CRS with the significant difference only in SNOT-22 assessed group (p = 0.013).

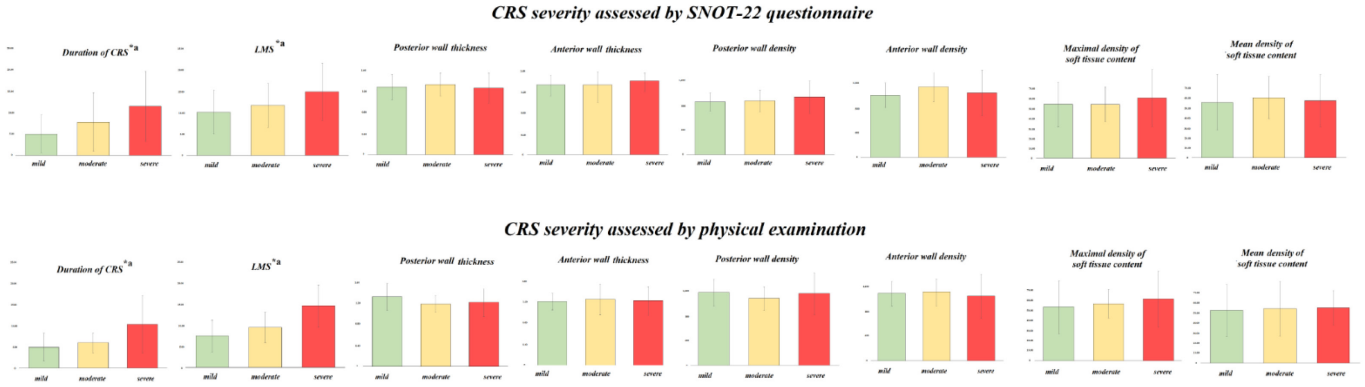
As shown in Figure 2, duration of CRS significantly increased with the increase of severity, assessed by both classification tools (p < 0.05). This finding occurred primarily due to significant difference between mild and severe form of CRS assessed both clinically (5.81 ± 3.80 vs. 12.00 ± 7.70) and by SNOT-22 (5.06 ± 4.51 vs. 11.55 ± 8.11), while differences in other comparisons were insignificant. LMS also showed significant increase between mild, moderate and severe CRS (p = 0.000 for SNOT-22 and p = 0.044 for clinically assessed CRS). Significant differences between the groups were detected in clinically assessed CRS between moderate and severe (10.81 ± 4.05 vs. 16.60 ± 5.78, p = 0.003) and mild and severe (8.50 ± 4.24 vs. 16.60 ± 5.78, p = 0.000). In SNOT-22 assessed CRS significant difference in LMS was detected only between mild and severe CRS (9.94 ± 4.93 vs. 14.59 ± 6.50, p = 0.048). Between the forms of CRS based on SNOT-22 results, a slight increasing trend of anterior wall thickness and density was observed, but without significance. Thickness and density of posterior wall and mean density of sinus content showed no increasing or decreasing trend, in both scaling methods. Maximal density of sinus content was increasing with the increased severity of CRS but no statistical significance was recorded.

Additionally, when analyzing possible correlations between variables given in Figure 2, positive correlation was detected between LMS and maximal density of sinus content (p = 0.006, r^2 = 0.967) and between duration of CRS and anterior wall thickness (p = 0.05, r^2 = 0.385).

Discussion

The bone of the sinus wall is not a static structure since it responds to various external and internal factors by a process of remodeling [14]. Previous studies have shown that bony thickening of sinus walls could be detected in patients with CRS [14,15]. In order to detect possible radiological signs of sinus bone involvement in patients with CRS, we evaluated sinus wall thickness and density. Our research demonstrated increase in bone thickness and density in the anterior maxillary sinus wall with increased severity of CRS in the group of patients categorized according to the results of SNOT-22. These results are in accordance with previous studies which also showed higher scores of SNOT-22 in CRS patients with neoosteogenesis and osteitis (bone thickness ≥ 3 mm) [16,17]. Osteitis is the generally accepted term for inflammation in bone that lacks marrow space. As a result, the bone appears thickened, irregular and heterogeneous on CT [18]. We have also found significant positive correlation between

Figure 2. Differences in investigated parameters between mild, moderate and severe form of CRS. Bar charts present the parametric data as mean ± standard deviation.



*p ≤ 0.05 (significant differences between the forms of CRS); ap ≤ 0.05 (significant differences between mild and severe form of CRS).

the duration of CRS and anterior wall thickness, indicating that the bone changes are more likely to occur in patients with longer-lasting CRS. Practically, clinical significance of bone remodeling in CRS lies mainly in the fact that it could be observed as an indicator of the subjectively assessed disease severity and duration of the inflammatory process. The positive correlation between morphological changes of the sinus walls and extent of sinus involvement in patients with CRS has already been demonstrated [19]. Even so, our data showed a slight positive trend in an anterior wall thickness and density between mild, moderate and severe CRS assessed by SNOT-22, despite significant increase in LMS. Additionally, we didn't find correlation between LMS and sinus wall properties. It is important to state that the absence of detectable changes in the posterior sinus wall morphology between mild, moderate and severe CRS in both groups, implies that this issue needs thorough analysis in future studies.

As previously mentioned, some researchers suggested that bone thickening occurs as the result of long-lasting inflammation [20]. Correlation analysis of our data partially supported this statement since we detected a significant positive correlation between the duration of CRS and the extent of anterior sinus wall thickening.

Our study showed significantly higher frequencies of fungal infection with the increase of CRS severity, in both scaling groups. These data indicate that the presence of fungi potentiates more severe forms of CRS. The data we reported showed significant increasing trend in IgE and eosinophil positivity, within mild, moderate and severe forms of CRS. Thus, we can conclude that allergic inflammation of any origin, fungal, or other etiology, exacerbates the disease both clinically and subjectively. Additionally, the results of qualitative analysis of soft tissue content within maxillary sinus showed that both non-homogenous content and high attenuation areas were predominantly present in severe forms of CRS. Maximal density of the sinus soft tissue content showed increasing trend within the groups, formed by both scaling methods. These findings could also be explained by the quality of mucinous collections. Allergic mucin is thick, tenacious, and highly viscous, and usually presented as high attenuation material on CT. Its presence contributes to the increased density as well as the non-homogenous appearance of the content within the sinus.

NP are inflammatory lesions that project into the nasal airway. CRS with NP is an important clinical entity diagnosed by the presence of both subjective and objective evidence of chronic sinonasal inflammation [21]. As shown by the present study, presence of NP significantly differed between the three investigated forms formed by the results of SNOT-22 questionnaire, suggesting that their presence has a great impact on patients' symptoms and quality of life. For example, a study that compared sleep disturbances in a group of patients with CRSwNP and controls, showed that difficulties in falling asleep, difficulties in falling asleep after nocturnal awakening, involuntarily inadequate sleep time and inefficient sleep occur in a significantly higher proportion in patients with CRSwNP [22].

Thus, it is not surprising that we detected significant increase in the LMS values and duration of CRS within mild, moderate and severe forms of CRS. LMS represents an extent of involvement of all paranasal sinuses, and it is expected to be higher in more severe forms of the disease. Likewise, increased duration of CRS increases the possibility of complications as well as superinfections and subsequent changes of the sinus walls. Moreover, the interactions between all above mentioned conditions should not be neglected.

Conclusions

The results of our research imply that increased bone thickness and density of sinus wall could be a useful indicator of CRS severity and that these changes in bone morphology are more likely to occur in patients with longer-lasting CRS. The presence of fungi potentiates more severe forms of CRS while allergic inflammation of any origin, fungal or other etiology, exacerbates the disease both clinically and subjectively. The presence of nasal polypus is an important predictor of both subjectively and clinically assessed CRS due to evident impact on patients' symptoms and quality of life.

Acknowledgements

This research was a part of Dr Aleksandra Barac's PhD thesis.

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Conflict of interests: No conflict of interests is declared.