



Application of questionnaires in the assessment of clinical severity of chronic rhinosinuitis

Primena upitnika u proceni kliničke ispoljenosti hroničnog rinosinuzitisa

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Abstract

Background/Aim. Diagnosis of chronic rhinosinuitis (CRS) is based on clinical symptoms, and confirmed with endoscopic findings and computed tomography (CT) scans of paranasal sinuses. However, the results of numerous studies have shown that the symptoms that patients report are not in correlation with the degree of the disease spread obtained by radiological findings. The aim of our study was to examine if there is a correlation between the degree of symptoms intensity of the non-polypous and polypous form of CRS and the degree of the disease spread, obtained on the basis of radiological diagnostics. **Methods.** A total of 60 patients, of which 30 patients with CRS without nasal polyps (CRSsNP) and 30 with CRS with nasal polyps (CRSwNP), were included in this cross-sectional study. Symptoms were evaluated using two questionnaires: Sino-Nasal Outcome Test 22 (SNOT-22) and Visual Analogue Score (VAS). The Lund Mackay CT score was used as a radiological parameter of the disease expansion. In addition, each of the subjects

was examined for sensitivity to standard inhalation allergens. **Results.** In patients with CRSsNP, there were statistically significant positive correlations between the Lund Mackay CT score and the SNOT-22 score ($r = 0.578$, $p = 0.001$) and between the Lund Mackay CT score and the VAS ($r = 0.408$, $p = 0.025$). We found no correlation between the both questionnaire scores and the Lund Mackay score in CRSwNP patients. In patients with CRSwNP, a statistically significant difference was found in the values of SNOT-22 between patients with and without sensitivity to inhalation allergens, with higher values of the score in patients with allergy ($p = 0.039$). **Conclusion.** There is a positive correlation between the severity of the symptoms and the radiological findings only in patients with CRSsNP, which suggests that application of these questionnaires would be possible only in the case of this clinical entity.

Key words: rhinitis; sinusitis; chronic disease; surveys and questionnaires; signs and symptoms; diagnosis.

Apstrakt

Uvod/Cilj. Dijagnoza hroničnog rinosinuzitisa (HRS) se postavlja na osnovu kliničkih simptoma, a potvrđuje na osnovu endoskopskog nalaza i snimaka kompjuterizovane tomografije (KT) paranazalnih sinusa. Međutim, rezultati brojnih studija su pokazali da simptomi koje bolesnici navode nisu u korelaciji sa stepenom proširenosti bolesti koji se dobija radiološkim pretragama. Cilj naše studije je bio da se ispita da li postoji korelacija između stepena izraženosti simptoma nepolipozne i polipozne forme HRS i stepena proširenosti bolesti, dobijenim na osnovu radiološke dijagnostike. **Metode.** U ovu studiju preseka bilo je uključeno ukupno 60 bolesnika, od toga 30 bolesnika sa nepolipoznom i 30 sa polipoznom formom HRS. Simptomi su procenjeni primenom dva upitnika: *Sino-nasal Outcome Test*

om – 22 (SNOT-22) i *Visual Analogue Score*-om (VAS). Kao radiološki parameter proširenosti bolesti korišćen je *Lund Mackay* KT skor. Pored toga, svakom od ispitanika je ispitivana senzitivnost na standardne inhalacione alergene. **Rezultati.** Kod nepolipozne forme HRS postoje statistički značajne pozitivne korelacije između Lund Mackay KT skora i vrednosti SNOT-22 skora ($r = 0,578$; $p = 0,001$), kao i između Lund Mackay KT skora i VAS ($r = 0,408$, $p = 0.025$). Kod polipozne forme HRS nije pokazana statistički značajna korelacija između Lund Mackay KT skora i vrednosti oba upitnika. Kod bolesnika sa polipoznom formom bolesti je uočena statistički značajna razlika u vrednostima SNOT-22 upitnika između bolesnika sa i bez preosetljivosti na inhalacione alergene, pri čemu su veće vrednosti skora bile kod bolesnika sa alergijom ($p = 0,039$). **Zaključak.** Dobijeni rezultati su pokazali da postoji pozitivna statistička

povezanost između težine simptoma i radioloških nalaza samo u slučaju nepolipozne forme HRS, što govori u prilog tome da bi opravdanost za eventualnu primenu ovi upitnici imali samo u slučaju ovog kliničnog entiteta.

Introduction

According to the criteria published in the European Position Paper on Rhinosinusitis and Nasal Polyps, EPOS 2012, chronic rhinosinusitis (CRS) is defined as a disease characterized by the presence of at least two symptoms which persist for at least 12 weeks, and one of the symptoms should be either nasal blockage or nasal discharge: anterior/ posterior nasal drip, while the facial pain/pressure and reduction or loss of smell may or may not be present^{1,2}. There are two forms of this disease: chronic rhinosinusitis without nasal polyps (CRSsNP) and chronic rhinosinusitis with nasal polyps (CRSwNP)^{1,2}. These two forms have different histological finding, based on the dominant cellular infiltrate, as well as immunological one on the basis of the dominant profile of cytokines and chemokines^{3,4}. According to the presence of nasal symptoms, there is no clear difference between these two forms of the disease⁵. The prevalence of CRS is increasing, and the cost of its treating represents a major economic burden^{6,7}. Also, the poor quality of life of CRS patients should not be ignored. The diagnosis of the disease, as well as the decision on its further treatment, is based on the already mentioned clinical symptoms. However, additional diagnostic procedures, such as endoscopic examination and/or computed tomography (CT) of paranasal sinuses are required for the final diagnosis. The presence of CRS symptoms and the degree of the disease spread, estimated on the basis of endoscopy and CT scan, often do not correlate, so Stankiewicz and Chow^{8,9} have shown in their studies that 53% of patients with a clinical diagnosis of CRS, based on the present symptoms, have had no disease presentation on CT or the finding has been minimal. CT is certainly a diagnostic gold standard, but it is not routinely used because of the high dose of radiation and the cost of the procedure. It is only used in cases of unsuccessful medical treatment, preparation for surgical treatment and in the case of threatening complications of CRS². Nowadays, questionnaires are used to obtain information on the quality of life and the severity of the disease based on clinical symptoms^{10,11}. However, the diagnosis of CRS, estimating the extent of the disease spread and the decision about the necessary therapy based on clinical symptoms only are not reliable.

The aim of this study was to examine whether symptoms of CRS, assessed by questionnaires, correlate with the degree of CRS spread, estimated on CT scans of paranasal sinuses, and to demonstrate whether it is possible to apply these questionnaires as a part of standard diagnostic procedures.

Methods

This study was conducted in the Department of Otolaryngology of the tertiary care hospital Military Medical Academy (MMA) in Belgrade, Serbia. The protocol of inves-

Ključne reči:

rinitis; sinusitis; hronična bolest; ankete i upitnici; znaci i simptomi; dijagnoza.

tigation was approved by the Ethics Committee of MMA and written informed consent was obtained from all participants. Sixty (n = 60) patients who met the criteria for the diagnosis of CRS and were candidates for functional endoscopic sinus surgery (FESS), after an unsuccessful medical treatment, were included in the study. Thirty patients had CRS without nasal polyps (CRSsNP) and the other thirty had CRS with nasal polyps (CRSwNP). Patients were diagnosed with CRS according to the EPOS 2012 criteria². Anterior and posterior rhinoscopy was performed in all patients, followed by an endoscopic examination after which the patients were divided into two groups: CRSsNP and CRSwNP. Exclusion criteria included: presence of systemic diseases involving the nasal cavity (Vegener's granulomatosis, Churg – Strauss syndrome, sarcoidosis, etc.), the presence of fungal rhinosinusitis, the use of antihistamines, corticosteroids and antibiotics at least three weeks before the surgery, previous endoscopic sinus surgery (ESS) or other surgery in the nasal area and paranasal cavities, patients under the age of 18, and pregnancy.

Before their surgical treatment, patients were asked to fill out two questionnaires about the severity of their symptoms. The first questionnaire was the Sino-Nasal Outcome Test 22 (SNOT-22), which offers the answers for 22 symptoms: the need to blow nose, sneezing, runny nose, nasal obstruction, loss of smell or taste, cough, post-nasal discharge, thick nasal discharge, ear fullness, dizziness, ear pain, facial pain/pressure, difficulty falling asleep, waking up at night, lack of a good night's sleep, waking up tired, fatigue, reduced productivity, reduced concentration, frustration/restlessness/irritation, sadness, embarrassed. Patients circled the numbers depending on the severity of the symptoms: 0 – “no problem,” 1 – “very mild problem,” 2 – “mild or slight problem,” 3 – “moderate problem,” 4 – “severe problem,” and 5 – “extremely severe problem.” The maximum score of this questionnaire is 110.

The Visual Analogue Score (VAS) questionnaire contains answers offered for 18 symptoms: headache, nasal obstruction, nasal discharge, postnasal discharge, impaired sense of smell, facial fullness, dental pain, facial pain/pressure, epiphora, cough, epistaxis, deposition of dried secretion in the nose, general health condition, fatigue, fever, nausea, vomiting, diarrhea. Patients evaluated the symptoms by placing a vertical hatch mark on a scale of 0 to 10 cm depending on the severity of their symptoms. Depending on where on the scale the hatch mark was placed the values of these symptoms ranged between 0 (without symptoms) and 10 (the worst symptom). Ten out of these 18 symptoms were included in the final evaluation score: headache, nasal obstruction, nasal discharge, postnasal discharge, impaired sense of smell, facial fullness, facial pain/pressure, cough, fatigue, nausea. The maximum score of the questionnaire was

100. Both questionnaires also had questions about the patient's age and gender.

As a gold standard for estimating the degree of the CRS spread, we used CT scans of paranasal cavities in coronal, axial and sagittal planes. The CT findings were estimated by the Lund-Mackay score¹². Each of the paranasal sinuses on both sides of the face were estimated as follows: 0 – a complete lucency in the sinus, 1 – a partial opacity and 2 – a complete opacity. The score was determined bilaterally for the anterior ethmoidal cells, posterior ethmoidal cells, maxillary, sphenoidal and frontal sinus. An additional bilateral score was included for the ostiomeatal complex: 0 – not occluded, 2 – occluded. The maximum value of the Lund Mackay CT score was 24.

Each of the patients was tested on hypersensitivity to standard inhalation allergens, based on which it was assessed whether the presence/absence of sensitivity to allergens had an effect on the severity of symptoms and/or the degree of CRS spread. We used the standard battery with fifteen respiratory allergens for skin prick tests (Soluprick® SQ, Hørsholm, Denmark).

Using statistical analysis, it was examined whether there was a difference between the scores of the symptoms (SNOT-22 and VAS) and Lund Mackay CT scores between CRSsNP and CRSwNP. Comparison of Lund Mackay ques-

tionnaire scores and individual symptom severity between CRSwNP and CRSsNP patients was performed using the Mann-Whitney test. Pearson's correlation test was used to estimate the correlation between the questionnaire score values and the values of individual symptoms derived from tests and the Lund Mackay CT scores. The p values < 0.05 were considered statistically significant. All data was processed in the SPSS 20.0 software package.

Results

In the group of patients with CRSsNP, there were 12 (40%) men and 18 women (60%), while in the CRSwNP group there were 18 (60%) men and 12 (40%) women. The average age of respondents with CRSsNP was 36.77 ± 10.41 , and of those with CRSwNP was 49.90 ± 13.28 (Table 1).

In patients with CRSsNP, the average Lund Mackay CT score was 6.57 ± 1.04 . The average intensity of symptoms obtained using SNOT-22 was 52.60 ± 19.36 , while this value in the case of VAS questionnaire was 45.53 ± 17.04 . The average Lund Mackay CT score in CRSwNP patients was 18.10 ± 4.26 , while the average value of SNOT-22 questionnaire was 47.77 ± 19.56 and that of VAS was 48.27 ± 16.08 . We found no significant differences between CRSsNP and CRSwNP regarding the total SNOT-22 and VAS score (Table 2).

Table 1

Demographic data of patients included in the study

Type of sinusitis	Age (years)			Gender, n (%)	
	min	max	mean \pm SD	male	female
CRSsNP (n = 30)	19	63	36.77 ± 10.41	12 (40)	18 (60)
CRSwNP (n = 30)	23	77	49.90 ± 13.28	18 (60)	12 (40)

CRSsNP – chronic sinusitis without nasal polyps; CRSwNP – chronic sinusitis with nasal polyps; SD – standard deviation.

Table 2

Average values of Lund Mackay CT score, SNOT-22 and VAS questionnaires in patients with CRSsNP and CRSwNP (n= 30)

Questionnaire/Test	CRSsNP (n = 30)			CRSwNP (n = 30)		
	min	max	mean \pm SD	min	max	mean \pm SD
Lund Mackay CT score	5	9	6.57 ± 1.040	12	24	18.10 ± 4.26
SNOT-22	11	86	52.60 ± 19.36	18	96	47.77 ± 19.56
VAS	15	82	45.53 ± 17.04	16	86	48.27 ± 16.08

CT – computed tomography; SNOT-22 – Sino-Nasal-Outcome Test 22; VAS – Visual Analogue Score; CRSsNP – chronic rhinosinusitis without nasal polyps; CRSwNP – chronic rhinosinusitis with nasal polyps; SD – standard deviation.

Table 3

Correlation between questionnaires and individual symptoms and Lund Mackay CT score in patients with CRSsNP

Questionnaire/Symptom	Pearson's correlation coefficient	Sig. (2-tailed)
SNOT- 22	0.578	0.001
VAS	0.408	0.025
Nasal obstruction	0.437	0.016
Facial fullness	0.421	0.021

CT – computed tomography; CRSsNP – chronic rhinosinusitis without nasal polyps; SNOT-22 – Sino-Nasal Outcome Test 22; VAS – Visual Analogue Score.

Pearson's correlation analysis confirmed that there was a statistically significant positive correlation between Lund Mackay CT score and the scores of SNOT-22 ($r = 0.578$, $p = 0.001$) and VAS ($r = 0.408$, $p = 0.025$) questionnaires in patients with CRSsNP (Figures 1 and 2). Also, in these patients, there was a statistically confirmed correlation between Lund Mackay CT score and individual symptoms: nasal obstruction ($r = 0.437$, $p = 0.016$) and facial fullness ($r = 0.421$, $p = 0.021$) (Table 3).

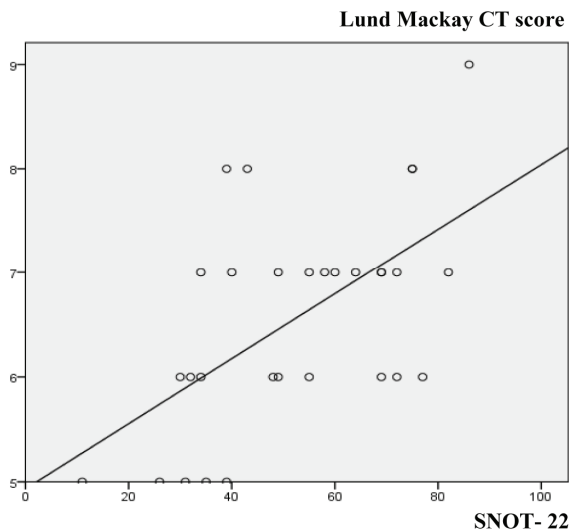


Fig. 1 – Correlation between Sino-Nasal Outcome Test 22 (SNOT- 22) questionnaire and Lund Mackay computed tomography (CT) score in patients with CRSsNP.

In patients with CRSwNP, there was a poor correlation between Lund Mackay CT score and the total questionnaire scores (SNOT-22, VAS), but Lund Mackay CT score correlated with individual symptoms that entered in VAS questionnaire: nasal obstruction ($r = 0.391$, $p = 0.033$) and smell impairment ($r = 0.466$, $p = 0.009$) (Table 4).

Table 4
Correlation between individual symptoms and Lund Mackay CT score in patients with CRSwNP

Symptom	Pearson's correlation coefficient	Sig. (2-tailed)
Nasal obstruction	0.391	0.033
Impaired sense of smell	0.466	0.009

CT – computed tomography; CRSwNP – chronic rhinosinusitis with nasal polyps.

Table 5
Differences in SNOT-22 and VAS questionnaire values and Lund Mackay CT scores between CRSsNP and CRSwNP

Statistical parameters	Lund Mackay CT score	SNOT- 22	VAS
Mann-Whitney <i>U</i>	0.000	376.500	423.500
Wilcoxon <i>W</i>	465.000	841.500	888.500
<i>Z</i>	-6.692	-1.087	-0.392
Asymp. Sig. (2-tailed)	0.000	0.277	0.695

SNOT-22 – Sino-Nasal Outcome Test 22; VAS – Visual Analogue Score; CRSsNP – chronic rhinosinusitis without nasal polyps; CRSwNP – chronic rhinosinusitis with nasal polyps. CT – computed tomography.

Lund Mackay CT score

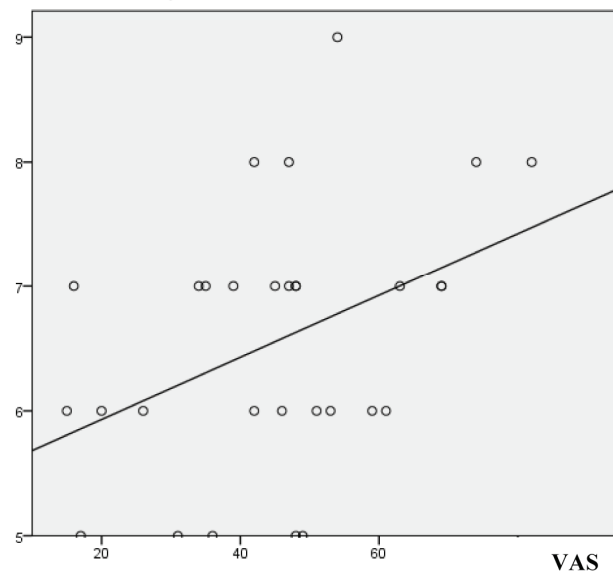


Fig. 2 – Correlation between Visual Analogue Score (VAS) questionnaire and Lund Mackay computed tomography (CT) score in patients with chronic rhinosinusitis without nasal polyps (CRSsNP).

In patients with CRSwNP, the average Lund Mackay CT score was significantly higher in comparison to patients with CRSsNP ($p = 0.000$) (Table 5).

Using the Mann-Whitney test, the average values of the individual symptoms that entered the final VAS score were compared between CRSwNP and CRSsNP. It was shown that there was a statistically significant difference in the values of individual symptoms between these two forms of CRS. Headache ($p = 0.037$), fatigue ($p = 0.033$) and nausea ($p = 0.001$) were significantly higher in CRSsNP, whereas nasal obstruction ($p = 0.000$), nasal discharge ($p = 0.003$) and impaired sense of smell ($p = 0.000$) were higher in patients with CRSwNP (Table 6).

In patients with CRSsNP, there was no statistically significant difference in the values of SNOT-22, VAS and Lund Mackay CT scores between non-allergic and allergic patients (Table 7). However, the average value of the SNOT-22 score was significantly higher in allergic CRSwNP patients comparing to non-allergic ones ($p = 0.039$). In the values of VAS and Lund Mackay, no difference was found between the groups of subjects with and without hypersensitivity to inhalation allergens (Table 7).

Table 6
Differences of individual symptom scores between CRSsNP and CRSwNP

Symptoms	CRSsNP (sum of ranks)	CRSwNP (sum of ranks)	<i>p</i>
Headache	1053.00	777.00	0.037
Nasal obstruction	674.00	1156.00	0.000
Nasal discharge	713.50	1116.50	0.003
Postnasal discharge	856.50	973.50	0.381
Facial fullness	862.50	967.50	0.431
Impaired sense of smell	665.50	1164.50	0.000
Facial pain/pressure	1023.50	806.50	0.101
Cough	938.00	892.00	0.730
Fatigue	1057.50	772.50	0.033
Nausea	1115.00	715.00	0.001

CRSsNP – chronic rhinosinusitis without nasal polyps; CRSwNP – chronic rhinoisusitis with nasal polyps.

Table 7
Differences of SNOT-22, VAS and Lund Mackay CT score between patients with and without allergen sensitivity in patients with CRSsNP and CRSwNP

Statistical parameter	CRSsNP			CRSwNP		
	Lund Mackay CT score	SNOT- 22	VAS	Lund Mackay CT score	SNOT- 22	VAS
Mann-Whitney <i>U</i>	93.500	106.000	109.500	79.000	38.500	57.000
Wilcoxon <i>W</i>	246.500	259.000	200.500	107.000	314.500	333.000
<i>Z</i>	-0.743	-0.189	-0.042	-0.074	-2.060	-1.153
Asymp. Sig. (2-tailed)	0.458	0.850	0.967	0.941	0.039	0.249
Exact Sig. [2*(1-tailed Sig.)]	0.483	0.869	0.967	0.962	0.037	0.266

SNOT-22 – Sino-Nasal Outcome Test 22; VAS – Visual Analogue Score; CT – computed tomography; CRSsNP – chronic rhinosinusitis without nasal polyps; CRSwNP – chronic rhinosinusitis with nasal polyps.

Discussion

CRS is a heterogeneous disease, based on both etiopathogenesis and its clinical characteristics. The diagnostic procedures used are not consistent all around the world, which additionally complicates the recognition and treatment of the disease.

The aim of this study was to examine which symptoms of CRS correlate with Lund Mackay CT score depending on the disease form: polypous or non-polypous one. It was noticed that there were no differences in the total SNOT-22 and VAS symptom scores between these two forms of the disease. However, there was a statistically significant difference in the values of the Lund Mackay CT score between the CRSsNP and CRSwNP patients. Our results are in accordance with previous ones that patients with CRSwNP have higher endoscopic and CT scores than the patients with CRSsNP¹³.

In patients with CRSsNP, both questionnaires (SNOT 22 and VAS) were in correlation with the values of the Lund Mackay CT score, indicating that these questionnaires can be used for assessment the severity of this form of the disease. In subjects suffering from CRSwNP, we found no similar results and our findings could confirm results of previously

published studies in which subjective symptoms do not often correlate with the severity of CRS¹⁴⁻¹⁸.

In our study, headache, fatigue and nausea were shown to be significantly more noticeable in patients with CRSsNP, while nasal obstruction, nasal discharge and impaired sense of smell were of higher intensity in CRSwNP patients. Bannerji et al.¹⁹ had previously demonstrated that patients with CRSwNP have higher values of nasal obstruction and hyposmia, while CRSsNP patients often suffer from pressure in the face and headache. It is important to understand that the way in which patients experience their symptoms depends on their mental status. One of the key symptoms in CRS patients is headache. Therefore, it can be assumed that presence of headache was the main reason why the value of SNOT 22 was lower in CRSwNP than in CRSsNP, although the degree of the disease spread was greater in patients with CRSwNP. The results of numerous studies show a statistically significantly lower presence of headache as a symptom of CRSwNP when compared to CRSsNP^{5, 18-20}. In a study conducted by Drake-Lee et al.²¹ it has been shown that only 35% of patients with nasal polyposis complained of headache. In a Stammberger and Wolf²² study, it has been explained that the presence of pain in CRS is the result of local release of substance P in the nasal mucosa as well as its cen-

tral release into *dura mater*. Substance P is the main neurotransmitter for pain, and it is released in the nasal mucosa after stimulation of the so-called polymodal receptors. They are positioned along the entire nasal mucosa and can react to mechanical, thermal and chemical stimuli. Stammberger and Wolf²² state that in cases of the edematous mucous membrane, there is contact of adjacent mucosal surfaces, primarily on the level of the ostiomeatal complex, which leads to the local release of substance P. In the nasal mucosa, substance P has a role of strong inflammatory mediator, leading to increased blood vessel permeability, plasma extravasation, relaxation of smooth muscle fibers, and glandular hypersecretion. All these effects lead to an increase of mucous membrane edema and an increase in the sensation of pain. On the other hand, there is a belief that due to the lack of local innervation, nasal polyps are painless inflammatory structures that can be greatly increased before they cause any discomfort in patients²³. Lately, more and more studies have shown that headache in CRSwNP is caused by other diseases such as migraine and tension headache^{24, 25}. The International Headache Association, in its etiological classification, does not even include CRS but only the acute rhinosinusitis²⁶, although according to EPOS guidelines, headache is one of the diagnostic criteria. The results of our study indicate a lower intensity of headache in patients with CRSwNP corroborating with previous points. The explanation for this may be the fact that polyps as painless structures, gradually occupy space in the nasal cavities and thus do not allow edematous mucous membranes to contact, causing the effect of an "airbag" that does not allow the local release of substance P. However, further experimental studies are necessary to confirm our findings.

In patients with CRSwNP, there was a statistically significant difference in the values of the SNOT-22 questionnaire between patients with and without hypersensitivity to inhalation allergens in favor of patients with allergy. The connection between allergic rhinitis and nasal polyposis has long been known and according to the results in the EPOS 2012 guidelines it ranges between 10% and 64%². Allergic rhinitis is considered as a factor that is more often associated

with CRSwNP, which is explained with the existence of Th2 immune response in both diseases, or with similar profile of inflammatory mediators in allergic rhinitis and nasal polyposis. Pathohistologically, CRSwNP is characterized by an edematous stroma with albumin precipitation, forming of pseudocysts, and subepithelial and perivascular infiltration of inflammatory cells, primarily eosinophils²⁷. The presence of edema in patients with allergic rhinitis leads to additional disturbance in ventilation and drainage of paranasal sinuses and creates a precondition for enhanced local inflammatory response, and thus increases the intensity of nasal symptoms.

Conclusion

The results of our investigation showed that the values of the intensity of symptoms obtained by using the SNOT-22 and VAS questionnaires correlate with the radiological indicators of severity of disease such as Lund Mackay CT score only in patients with CRSsNP, whereas no correlation was observed in subjects with CRSwNP. In patients with CRSsNP, symptoms that correlated with Lund Mackay CT score were nasal obstruction and facial fullness, while in the CRSwNP patients these symptoms were nasal obstruction and impaired sense of smell. The results presented here could have practical significance in diagnosis, evaluation of the quality of life, and in assessment of medical and surgical treatment efficacy in patients with CRS, although the possible application of these questionnaires would be only in patients with CRSsNP.

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R E F E R E N C E S

1. Fokkens W, Lund V, Mullol J. European Position Paper on Rhinosinusitis and Nasal Polyps group. European position paper on rhinosinusitis and nasal polyps 2007. *Rhinol Suppl* 2007; 20: 1–136.
2. Fokkens WJ, Lund VJ, Mullol J, Bachert C, Alobid I, Baroody F, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2012. *Rhinol Suppl* 2012; 23: 3 p preceding table of contents, 1–298.
3. Zhang N, Holtappels G, Claeys C, Huang G, van Cauwenberge P, Bachert C. Pattern of inflammation and impact of *Staphylococcus aureus* enterotoxins in nasal polyps from southern China. *Am J Rhinol* 2006; 20(4): 445–50.
4. Johansson L, Akerlund A, Holmberg K, Melen I, Bende M. Prevalence of nasal polyps in adults: the Skovde population-based study. *Ann Otol Rhinol Laryngol* 2003; 112(7): 625–9.
5. Dietz de Loos DA, Hopkins C, Fokkens WJ. Symptoms in chronic rhinosinusitis with and without nasal polyps. *Laryngoscope* 2013; 123(1): 57–63.
6. Durr DG, Desrosiers MY, Dassa C. Impact of rhinosinusitis in health care delivery: the Quebec experience. *J Otolaryngol* 2001; 30(2): 93–7.
7. Goetzel RZ, Hawkins K, Ozminkowski RJ, Wang S. The health and productivity cost burden of the "top 10" physical and mental health conditions affecting six large U.S. employers in 1999. *J Occup Environ Med* 2003; 45(1): 5–14.
8. Stankiewicz JA, Chow JM. Nasal endoscopy and the definition and diagnosis of chronic rhinosinusitis. *Otolaryngol Head Neck Surg* 2002; 126(6): 623–7.
9. Stankiewicz JA, Chow JM. A diagnostic dilemma for chronic rhinosinusitis: definition accuracy and validity. *Am J Rhinol* 2002; 16(4): 199–202.

10. *van Oene CM, van Reij EJJ, Sprangers MAG, Fokkens WJ*. Quality assessment of disease-specific quality of life questionnaires for rhinitis and rhinosinusitis: a systematic review. *Allergy* 2007; 62(12): 1359–70.
11. *Morley AD, Sharp HR*. A review of sinonasal outcome scoring systems: which is best? *Clin Otolaryngol Allied Sci* 2006; 31(2): 103–9.
12. *Lund VJ, Mackay IS*. Staging in rhinosinusitis. *Rhinology* 1993; 31(4): 183–4.
13. *Toros SZ, Böllükbaşı S, Naiboğlu B, Er B, Akkaynak C, Nosbari H*, et al. Comparative outcomes of endoscopic sinus surgery in patients with chronic sinusitis and nasal polyps. *Eur Arch Otorhinolaryngol* 2007; 264(9):1003-8.
14. *Ryan WR, Ramachandra T, Hvang PH*. Correlations between symptoms, nasal endoscopy, and in-office computed tomography in post-surgical chronic rhinosinusitis patients. *Laryngoscope* 2011; 121(3): 674–8.
15. *Razmpa E, Saedi B, Dostee A, Ordobadee M*. Correlation of pre-operative sinusitis patients' characteristics with final diagnostic findings. *Acta Med Iran* 2013; 51(8): 525–9.
16. *Basu S, Georgalas C, Kumar BN, Desai S*. Correlation between symptoms and radiological findings in patients with chronic rhinosinusitis: an evaluation study using the Sinonasal Assessment Questionnaire and Lund-Mackay grading system. *Eur Arch Otorhinolaryngol* 2005; 262(9): 751–4.
17. *Hopkins C, Browne JP, Slack R, Lund V, 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): 555–61.
18. *Eweiss AZ, Lund VJ, Barlow J, Rose G*. Do patients with chronic rhinosinusitis with nasal polyps suffer with facial pain? *Rhinology* 2013; 51(3): 231–5.
19. *Banerji A, Piccirillo JF, Thawley SE, Levitt RG, Sechtman KB, Krampfer MA* et al. Chronic rhinosinusitis patients with polyps or polypoid mucosa have a greater burden of illness. *Am J Rhinol* 2007; 21(1): 19–26.
20. *Bhattacharyya N*. Assessing the additional disease burden of polyps in chronic rhinosinusitis. *Ann Otol Rhinol Laryngol* 2009; 118(3): 185–9.
21. *Drake-Lee AB, Lowe D, Swanston A, Grace A*. Clinical profile and recurrence of nasal polyps. *J Laryngol Otol* 1984; 98(8): 783–93.
22. *Stammlerberger H, Wolf G*. Headaches and sinus disease: the endoscopic approach. *Ann Otol Rhinol Laryngol Suppl* 1988; 134: 3–23.
23. *Schor DI*. Headache and facial pain- the role of the paranasal sinuses: a literature review. *J Craniomandibular Pract* 1993; 11(1): 36–47.
24. *Ling FT, Kountakis SE*. Important clinical symptoms in patients undergoing functional endoscopic sinus surgery for chronic rhinosinusitis. *Laryngoscope* 2007; 117(6): 1090–3.
25. *West B, Jones NS*. Endoscopy-negative, computed tomography-negative facial pain in a nasal clinic. *Laryngoscope* 2001; 111(4 Pt 1): 581–6.
26. *Headache Classification Subcommittee of the International Headache Society*. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia* 2004; 24 Suppl 1: 9–160.
27. *Van Crombruggen Koen, Zhang N, Gevaert P, Tomassen P, Bachert C*. Pathogenesis of chronic rhinosinusitis: Inflammation. *J Allergy Clin Immunol* 2011; 128(4): 728–32.

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