Imane Ammouze [1], Jure Urbančič [2]

Characteristics of Patients with Nasal Complaints who do not Fulfil the Criteria for Primary Chronic Rhinosinusitis

Značilnosti bolnikov z nosnimi težavami, ki ne dosegajo meril za primarni kronični rinosinuzitis

ABSTRACT

KEY WORDS: primary chronic rhinosinusitis, quality of life, EPOS, diagnosis

BACKGROUNDS. Chronic rhinosinusitis (CRS) is a common chronic disease of the sinuses and the nasal mucosa. The diagnosis is confirmed when all the clinical and endoscopic criteria are fulfilled. In real-life situations, patients presenting similar symptoms sometimes do not fulfil the proposed criteria for chronic rhinosinusitis. METHODS. In our study, we compared patients who failed to fulfil all of the criteria for primary CRS during the diagnostics and were enrolled from the clinical database updated from 2015 to the present time into the control group, which had no nasal issues. We analyzed their clinical characteristics, number of previous nasal surgeries, the results from Sino-nasal Outcome Test-22 (SNOT-22) Questionnaire, Visual Analogue Scale for total nasal problems, objective and subjective smell report and respective computer tomography (CT), and endoscopic scores. RESULTS. 97 patients and 21 controls with no nasal pathology met all inclusion and exclusion criteria of the study. We found no difference in age distribution, number of outpatient visits and number of previous surgeries. However, we found a statistically significant difference in objective smell score, visual analog and SNOT-22 score, Lund-Mackay and Kennedy-Lund score. DISCUSSION. The measured olfactory function combined with the quality of life assessment and reasonable clinical assessment might help to identify the subgroup of patients with mild nasal problems. Nevertheless, we cannot be sure whether this is the final presentation of their disease or whether some will develop primary chronic rhinosinusitis in the future as there is no current test to predict the progress of such symptoms.

[1] Imane Ammouze, štud. med., Faculty of Medicine and Pharmacy of Rabat, Imp. Souissi, 10100 Rabat, Morocco
[2] Asist. Jure Urbančič, dr. med., Klinika za otorinolaringologijo in cervikofacialno kirurgijo, Univerzitetni klinični center Ljubljana, Zaloška cesta 2, 1000 Ljubljana; Katedra za otorinolaringologijo, Medicinska fakulteta, Univerza v Ljubljani, Zaloška cesta 2, 1000 Ljubljana

IZVLEČEK

KLJUČNE BESEDE: primarni kronični rinosinuzitis, kakovost življenja, EPOS, diagnostika

IZHODIŠČA. Kronični rinosinuzitis je pogosta bolezen sluznice nosu in obnosnih votlin. Diagnozo potrdimo z znanimi kliničnimi in endoskopskimi merili. V klinični praksi pa večkrat najdemo bolnike, ki imajo simptome, podobne kroničnemu rinosinuzitisu, a ne izpolnjujejo meril za diagnozo. METODE. V raziskavi smo primerjali bolnike brez izpolnjenih meril za diagnozo kroničnega rinosinuzitisa s kontrolno skupino, ki nima nosnih težav. Podatke smo pridobili iz baze podatkov, ki sega v leto 2015. Primerjali smo njihove klinične značilnosti, število prejšnjih operacij v nosnem predelu, dosežen rezultat pri sinonazalnem testu izida 22 (Sino-Nasal Outcome Test, SNOT-22), vizualni analogni lestvici (Visual Analog Scale, VAS), objektivnih in subjektivnih ocenah voha in rezultate računalniške tomografije in endoskopije. REZULTATI. 97 bolnikov in 21 kontrolnih preiskovancev je ustrezalo merilom za vključitev. Razlik nismo našli pri starosti, številu obiskov v ambulanti in številu predhodnih posegov. Statistično značilne razlike pa smo našli v objektivni oceni voha, oceni VAS in SNOT-22 ter v Lund-Mackayjevi in Kennedy-Lundovi oceni. RAZPRAVA. Izmerjena vohalna funkcija, oceno kakovosti življenja in ustrezna klinična preiskava bi lahko pomagale poiskati bolnike z milimi nosnimi težavami. Vseeno pa ne vemo, ali je trenutno stanje teh bolnikov dokončno, Morda se bo sčasoma izkazalo, da njihova bolezen vseeno ustreza merilom za primarni kronični rinosinuzitis, saj trenutno ne obstajajo preiskave, ki bi lahko napovedale razvoj simptomov.

BACKGROUNDS

Chronic rhinosinusitis (CRS) is a common chronic disease of the sinuses and the nasal mucosa *(1)*. It's prevalence is estimated at 10.9% for the general European population *(2)*. The diagnosis is confirmed when all the European Position Paper on the Primary Care Diagnosis and Management of Rhinosinusitis and Nasal Polyps 2020 (EPOS 2020) criteria are fulfilled – primary criteria are related to the history of the disease, and secondary criteria can be assessed only after an endoscopy of the nose, which is almost inclusively available at the otolaryngologists' (ear, nose and throat, ENT) outpatient offices *(1, 3)*. EPOS 2020 recognizes the main differentiation between primary CRS and secondary CRS as adapted from the work of Grayson and colleagues *(4)*. In real-life situations, patients presenting similar symptoms sometimes do not fulfil the proposed criteria for CRS and fail to get a CRS diagnosis. This study compares the clinical characteristics of patients not fulfilling the EPOS 2020 criteria for primary CRS and of those not having any nasal issues. The authors believe that patients in our group may be clinically closer to patients without nasal problems *(5)*. Therefore, we hypothesize that the difference in clinical attributes should not be significant.

METHODS

The study was performed at the University Medical Centre Ljubljana, Department for Otorhinolaryngology and Cervicofacial Surgery, from August 1, 2021, to August 27, 2021. Patients were enrolled from the clinical database, which had been continuously updated since 2015 to the present time. At the start of our study, the database comprised of more than 1,300 patients, all of whom had signed an institutional approval for collecting the data. We were searching for cases initially entered as probable CRS but which failed to fulfil all of the criteria for pri-

mary CRS during the diagnostics *(1)*. Mean age, sex distribution, asthma, allergy, and gastroesophageal reflux disease prevalence were calculated. All patients filled out the Slovenian Sino-nasal Outcome Test-22 (SNOT-22) Questionnaire with Visual Analogue Scale (VAS) for total nasal problems and a subjective smell report *(5)*. Patients had also done the Sniffin' Sticks Screening 12 Test (SST-12) *(6)*. With SST-12, a score of 6 and less is defined as anosmia, and normosmia is defined by a score of at least 11 *(7)*. We reviewed the number of previous nasal surgeries, their respective computer tomography (CT) scores and endoscopic scores *(8, 9)*. We used the x^2-test and multiple T-tests to compare the groups. Statistical software Statistical Product and Service Solutions 20 (SPSS-20, IBM, Armonk, USA) and Prism 6 (GraphPad Software, San Diego, USA) were used. Before the study, we received approval from the Slovenian national ethical committee (decision number 0120-297/2017/3).

RESULTS

We identified 97 patients with nasal complaints not diagnosed as primary CRS and 21 controls with no nasal pathology who met all inclusion and exclusion criteria of the study. The mean age in the first group was 50.9 ± 16.3 years, 53 patients were females (54.6%) and 44 males (45.4%). Patients came to the outpatient clinic 1–3 times, with the average of 1.2 visits. 17.5% of the patients had an allergy, 5.2% had asthma, and 23.3% had gastroesophageal reflux disease (GERD). The mean number of previous surgeries was 0.2 ± 0.5. All patients reported having an ordinary sense of smell. In the second group, the mean age was 48.2 ± 11.8, 10 patients were females (47.6%) and 11 males (52.4%), all patients came to the outpatient clinic only once and had no previous surgeries. All patient characteristics of both groups are shown in table 1.

Table 1. Patient characteristics. GERD – gastroesophageal reflux disease, SNOT-22 – Sino-nasal Outcome Test-22, SD – standard deviation.

n=118	Non-primary CRS	No nasal pathology	p-value
Female/male	53/44 (54.6/45.4%)	10/11 (47.6/52.4%)	0.64‡
Allergy	17 (17.5%)	–	–
Asthma	5 (5.2%)	–	–
GERD[a]	20 (23.3%)	–	–
Normal smell	97 (100.0%)	–	–
Age (mean, min.–max., SD)	50.9 (18–81, 16.3)	48.2 (11.8)	0.61
Outpatient visits (mean, min.–max., SD)	1.2 (1–3, 0.5)	1.0 (0.0)	0.21
Sniffin' Sticks 12[b] (mean, min.–max., SD)	9.3 (6–12, 1.7)	11.0 (0.4)	0.0027
Number of previous surgeries[c] (mean, min.–max., SD)	0.2 (0–3, 0.5)	0.0 (0.0)	0.21
Lund-Mackay score[d] (mean, min.–max., SD)	2.33 (0–9, 2.8)	0.0 (0.0)	0.0115
VAS (mean, min.–max., SD)	3.8 (0–10, 2.8)	0.2 (0.4)	0.0001
Kennedy-Lund (mean, min.–max., SD)	1.5 (0–6, 1.7)	0.0 (0.0)	0.006
Hadley score (mean, min.–max., SD)	0.3 (0–4, 0.8)	0.0 (0.0)	0.24
Total SNOT-22 score[e] (mean, min.–max., SD)	19.9 (0–81, 17.15)	3.8 (3.1)	0.0039

[a] n= 86, [b] n= 50, [c] n= 82, [d] n= 48, [e] n= 95, ‡ χ^2 test,

In the first group, olfactory function was assessed in 50 patients using the SST-12, the mean result was 9.3 ± 1.7. The Lund-Mackay score calculated in 48 patients was 2.33 ± 2.8. The Kennedy-Lund score was 1.5 ± 1.7, and the Hadley score was 0.3 ± 0.8. The VAS score was 3.8 ± 2.8. The total SNOT-22 score was 19.9 ± 17.15.

In the control group, the SST-12 test score was 11.0 ± 0.4. All of the Lund-Mackay scores, the Kennedy-Lund score and Hadley scores were null. The VAS score was 0.2 ± 0.4. The total SNOT-22 score was 3.8 ± 3.1.

Both groups consisted of patients with similar sex ($p = 0.64$) and age distribution ($p = 0.61$). The number of outpatient visits was also similar ($p = 0.21$). The groups didn't differ in the number of previous surgeries ($p = 0.21$). The Hadley score showed no difference either ($p = 0.24$). However, the SST-12 test score was significantly lower in the group without any nasal complaints (9.3 versus 11.0, $p = 0.0027$). Also, the Lund-Mackay, Kennedy-Lund, and SNOT-22 scores showed a statistically significant difference between the two groups ($p < 0.05$).

DISCUSSION

CRS is a complex and clinically widely diverse disease *(1)*. Even when comparing a group of patients not fulfilling the criteria for primary CRS to the patients of the control group not having any nasal symptoms, the clear-cut difference in clinical and quality of life (QOL) parameters is hard to anticipate.

We have compared a group of patients with non-primary CRS and a control group of patients with no nasal pathology. The patients in both groups had similar age, sex ratio, outpatient visits, the same number of previous nasal surgeries and equal Hadley scores. We have disregarded the information about allergy due to a similar percentage of affected individuals in our non-primary CRS group as in the general public and the lack of exact data in our control group *(2)*. The distribution of patients with asthma and patients with GERD in our non-primary CRS group was similar as reported in epidemiologic studies *(10, 11)*.

An altered sense of smell might be a significant sign of nasal disease. It is well known that self-rated olfaction does not correlate significantly to the measured olfactory performance, consequently, self-reported ordinary sense of smell might not be appropriate for evaluation *(12)*. Therefore, we used the SST-12 for a more objective olfactory assessment, which showed significant differences between both groups as shown in table 1. The non-CRS group had a mean score within the hyposmia interval. In contrast, the no nose pathology group had a mean score compatible with normosmia, well above the anosmia limit *(12)*. Our data suggests that there might be some olfactory impairment associated with the non-primary CRS group.

The Lund-Mackay CT score and Kennedy--Lund endoscopic score were significantly higher in our non-primary CRS group. We could attribute this finding to the possibility of some patients having a secondary CRS, prolonged or post-viral acute rhinosinusitis (ARS) or just repetitive episodes of ARS *(1)*. According to the published population estimates from Fokkens and colleagues, this might not be a hallmark of the whole cohort since the controls had no CT or endoscopic signs as shown in table 1 *(1)*. The VAS score was also significantly higher in our non-primary CRS group, which may reflect the same fact. According to EPOS 2020, the mean VAS value of the non-primary CRS group translates to »not bothersome symptoms« *(1)*.

The comparison of the mean score of the SNOT-22 questionnaire, which is used to assess the QOL of patients with CRS, shows a significant difference between the group of non-primary CRS and the controls (table 1). The values for non-primary CRS

are considered mild according to the validated Slovenian version of the SNOT-22 test *(5)*. This means the patients from our non-primary CRS group fall just under the cut-off values of the CRS cohort *(1, 5)*. The results obtained from the data analysis partially supported the hypothesis of the non-primary CRS group being similar to the controls without CRS. Both groups are not entirely different and at the same time not entirely the same. Other studies of CRS signs and symptoms also do not always find a consistency of clinical signs in a wide range of real-life presentations. This results in poor patient stratification, when some symptoms and some signs are present, but do not entirely fulfill the EPOS 2020 criteria *(1)*. We believe the symptoms themselves may prompt further diagnostics with endoscopy and CT, but the observed changes still do not fulfil the beforementioned criteria for primary CRS. The objective data rejects the hypothesis, on the other hand, the Lund-Mackay, Kennedy-Lund or Hadley scores are not nearly close to the values seen in patients with primary CRS *(5)*.

QOL results are even more interesting. The proven difference is somewhat expected. The patients who were referred to the tertiary outpatient institution with some nose complaints or diagnostic signs that would eventually impact their QOL all had a mild severity of symptoms. They also present values regarded as too low to offer any treatment *(1)*.

The main bias of our study is the fact that we cannot be sure whether present signs and symptoms represent the final presentation of the patients' disease or whether some of them will develop primary CRS in the future as there is no current test to predict the progress of such symptoms *(1)*.

This is the first study that has explored the characteristics of patients with nose problems not fulfilling the criteria for primary CRS diagnosis. Further studies on similar samples of patients might give more insight on how to better diagnose, treat and predict the outcomes of such patients.

The measured olfactory function combined with the QOL assessment and reasonable clinical investigation might help to identify the subgroup of patients with mild nasal problems.

REFERENCES

1. Fokkens WJ, Lund VJ, Hopkins C, et al. European position paper on rhinosinusitis and nasal polyps 2020. Rhinology. 2020; 58 (S29): 1–464.
2. Hastan D, Fokkens WJ, Bachert C, et al. Chronic rhinosinusitis in Europe – An underestimated disease. A GA^{2}LEN study. Allergy. 2011; 66 (9): 1216–23.
3. Bachert C, Pawankar R, Zhang L, et al. ICON: Chronic rhinosinusitis. World Allergy Organ J. 2014; 7 (1): 25.
4. Grayson JW, Hopkins C, Mori E, et al. Contemporary classification of chronic rhinosinusitis beyond polyps vs no polyps: A review. JAMA Otolaryngol Head Neck Surg. 2020; 146 (9): 831–8.
5. Urbančič J, Soklič Košak T, Jenko K, et al. SNOT-22: ovrednotenje vprašalnika in ocena zdravljenja kroničnega rinosinuzitisa. Med Razgl, 2016; 55 (2): 39–45.
6. Soler ZM, Hyer JM, Karnezis TT, et al. The Olfactory Cleft Endoscopy Scale correlates with olfactory metrics in patients with chronic rhinosinusitis. Int Forum Allergy Rhinol. 2016; 6 (3): 293–8.
7. Hummel T, Konnerth CG, Rosenheim K, et al. Screening of olfactory function with a four-minute odor identification test: Reliability, normative data, and investigations in patients with olfactory loss. Ann Otol Rhinol Laryngol. 2001; 110 (10): 976–81.
8. Lund VJ, Kennedy DW. Staging for rhinosinusitis. Otolaryngol Head Neck Surg. 1997; 117 (3 Pt 2): S35–40.
9. Meltzer EO, Hamilos DL, Hadley JA, et al. Rhinosinusitis: Developing guidance for clinical trials. J Allergy Clin Immunol. 2006; 118 (5): S17–61.
10. To T, Stanojevic S, Moores, et al. Global asthma prevalence in adults: Findings from the cross-sectional world health survey. BMC Public Health. 2012; 12 (1).
11. Richter JE, Rubenstein JH. Presentation and epidemiology of gastroesophageal reflux disease. Gastroenterology. 2018; 154 (2): 267–76.
12. Shu CH, Hummel T, Lee PL, et al. The proportion of self-rated olfactory dysfunction does not change across the life span. Am J Rhinol Allergy. 23 (4): 413–6.