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Identifying clinical symptoms for improving the symptomatic diagnosis of chronic rhinosinusitis

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Abstract

BACKGROUND—Current symptom criteria for identifying patients with chronic rhinosinusitis (CRS) has poor specificity.

OBJECTIVE—To test the hypothesis that symptoms drawn from the task force on rhinosinusitis (RSTF) criteria and the International Headache Society (IHS) criteria for primary headaches can differentiate CRS patients from those with CRS-symptoms but no evidence for inflammation (non-CRS).

METHODS—A retrospective cohort study from a total of 140 charts of patients who received a diagnostic CT scan for CRS symptoms in a tertiary care clinic. The study was conducted in two phases: 1) using a retrospective review of otolaryngologist-documented symptoms (ODS) in the medical record and 2) using patient-reported symptoms (PRS) on a prospectively collected customized review of systems form from a separate cohort. A radiographic gold standard differentiated CRS from non-CRS patients.

RESULTS—Subjects in the CRS and non-CRS group were matched for age and race and almost universally met symptomatic criteria as defined by the RSTF in both study phases. In both study phases, facial pain, but not facial pressure, was negatively predictive for CRS ($p<0.05$). Similarly, hyposmia was positively predictive, while facial pain of a pulsating quality and photophobia were negatively predictive ($p<0.05$) although analysis of PRS was significant only when symptom frequency was considered. Nonetheless, significant overlap exists between the prevalence and frequency of symptoms in both groups.

CONCLUSION—The symptom-based diagnosis of CRS is challenging but symptoms of hyposmia are positively predictive while facial pain, a throbbing quality, headaches and photophobia are negatively predictive and show promise for improving the specificity of CRS diagnosis. Further validation studies are needed.

Keywords

Chronic rhinosinusitis; sinusitis; diagnosis; symptoms; headache disorders

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BACKGROUND

Chronic rhinosinusitis (CRS) is one of the most common chronic diagnoses made in offices. Recent studies estimate approximately 20 million Americans visit physicians' offices for CRS with a net yearly cost in the United States of over $1.8 billion.[1, 2] CRS is seen by a variety of healthcare professionals, including primary care physicians, allergists, and otolaryngologists. With this high prevalence and large cost, diagnostic accuracy and therapeutic efficiency are critical, however the clinical diagnosis of CRS remains a challenge- especially to the nonspecialist without ready access to nasal endoscopy and point-of-care computed tomography (CT).

The original 1997 Task Force on Rhinosinusitis (RSTF) defined CRS symptomatically by the presence of 2 or more major factors or 1 major and 2 minor factors for >12 weeks[3]. Major factors included facial pain/pressure, nasal obstruction/blockage, nasal purulent discharge, hyposmia/anosmia, or purulence in the nasal cavity on examination. Minor factors included headache, fever, halitosis, fatigue, dental pain, cough, or ear pain/pressure. Hwang et al. found that the sensitivity of these 1997 criteria was 89%, but the specificity was only 2%[4]. They concluded that the poor specificity and predictive value of these symptomatic criteria might make them inadequate to serve as the diagnostic standard for CRS- a finding which has been further supported in more recent studies[5]. The definition was thus updated by the rhinosinusitis guidelines issued by the American Academy of Otolaryngology (AAO) in 2007 to require the presence of two or more RSTF major criteria symptoms and either radiographic or endoscopic evidence of inflammation for the diagnosis of CRS[6] (Table 1). Bhattacharyya and Lee found that adding nasal endoscopy findings to the 2007 CRS symptoms improved the specificity to 84.1% when CT was the gold standard for CRS[7].

Currently, the decision to further work up or refer a patient for CRS management remains largely clinical, but the poor specificity of symptom criteria potentially limits many non-specialist physicians' ability to correctly recognize patients with CRS. Our current study attempts to identify items drawn from the RSTF criteria and the International Headache Society (IHS) criteria for primary headaches to differentiate CRS patients from those with CRS-symptoms but no objective evidence of inflammation (non-CRS). We hypothesized that by identifying specific symptoms, patients without CRS could be spared the risks and costs of unnecessary antibiotics and radiation exposure. Toward these ends, we conducted this study to identify potential symptoms that may improve the specificity of a symptom-based diagnosis of CRS for validation in a larger prospective study.

METHODS

Selection criteria

Using billing records, we identified 140 charts of patients who presented to the Northwestern Medical Faculty Foundation Otolaryngology clinic who were evaluated for symptoms of chronic rhinosinusitis. Charts were included in the study if: 1) sinusitis complaints lasted for a duration of 12 weeks or more, and 2) if a point of care sinus CT was used to assess for radiographic evidence of sinusitis. Charts were excluded if: 1) The patient had an acute upper respiratory infection within 2 weeks of evaluation, 2) They had prior endoscopic sinus surgery for CRS, and 3) If the physician had not recorded a standardized history (ODS-phase) or patients did not complete a standardized review of systems (PRS-phase). We acknowledge that this study design selected a cohort of patients who had a high index of suspicion for CRS and may not be externally valid for all patients with CRS symptoms. However, since these patients were receiving a point of care CT scan to aid in

the diagnosis of CRS, we still feel that this patient population is a relevant population for study.

Study design

An *a priori* power calculation was performed for a sample size of 60 (assuming an equal distribution of CRS and non-CRS patients) showing an 80% power to detect a difference in symptom prevalence of 40%. This study was conducted in two phases- in the otolaryngologist documented symtom (ODS)-phase of the study, we performed a retrospective analysis of 60 charts of a single otolaryngologist who prospectively completed a standardized history at the time of encounter that included the cardinal symptoms of CRS and primary headaches as defined by the 1997/2007 Task Force on Rhinosinusitis and the International Headache Society (IHS) respectively (See Table 1)[3, 6, 8].

After analysis of the data obtained from the first phase of the study, there was concern for possible selection bias involved in which patients were chosen for further CT evaluation-specifically because patients with facial pain were found more frequently in the non-CRS group. Since the ODS-phase represented the patients selected by a single otolaryngologist for CT evaluation, we designed a patient-reported symptom (PRS) phase of the study. In this phase, a separate group of 80 charts meeting the inclusion and exclusion criteria were identified from CT scan orders by any otolaryngologist at our institution. All patients in the second phase of the study had completed a prospectively collected standardized review of systems sheet. Using a patient reported Likert-scale, we assessed the frequency of multiple symptoms drawn from the RSTF and IHS criteria, with minor modifications. The symptom inventory included 1) disambiguated items from the RSTF criteria that specifically separated parallel items (e.g “facial pain and/or pressure” into “facial pain” and “facial pressure”); 2) additional non-overlapping nasal symptoms drawn from the SNOT-22 questionnaire[9]; and 3) IHS criteria symptoms drawn from the American Migraine Prevalence and Prevention (AMPP) survey[10]. For CRS and nasal symptoms, patients reported their symptoms on a 5-point Likert-scale with the following frequency descriptors: 1) Never, 2) Rarely, 3) Sometimes, 4) Usually, 5) Always. For the IHS criteria derived symptoms, the following Likert-scale was used: 1) Never, 2) Rarely, 3) Less than half the time, 4) More than half the time, as was used in the AMPP survey. In the ODS phase, IHS criteria symptoms were only recorded when the patient admitted to facial pain but not pressure. Patients without facial pain were assumed to have none of the IHS criteria symptoms since the IHS lists these symptoms only in association with pain. In the PRS phase, these symptoms were recorded when the patient complained of either facial pain or pressure. We made this modification because we were unsure if we could be potentially missing IHS criteria symptoms being experienced in association with isolated facial pressure. Again in the PRS phase, patients without facial pain or pressure were assumed to have none of the IHS symptoms.

Charts were also analyzed for objective findings of CRS as seen on endoscopy or CT scan on the day of examination. A positive endoscopy was defined as any nasal endoscopy in which purulence, middle meatal edema or nasal polyps was described by the examining otolaryngologist. A CT scan with a Lund-Mackay score ≥4 was used as the diagnostic gold standard for CRS [11, 12]. The primary encounter diagnosis recorded in the chart was also collected. Using the CT, endoscopy and symptoms, charts were classified into those with objective evidence and clinical impression for CRS (referred to as CRS patients in this paper) and those with symptoms but no evidence of CRS (referred to as non-CRS patients in this paper). In the first phase of the study, the encounter diagnosis always corresponded with the CT findings. In the second phase of the study, there were a total of 4/80 charts in which the encounter diagnosis did not correspond to the CT findings. In these cases we reexamined the medical record, as well as the CT and endoscopy findings, and reconciled the results based on the facts and findings available. In these charts, the disconcordance arose from

either documentation of Lund-Mckay score of >4 but a non-CRS primary encounter diagnosis or a Lund-Mckay score between 0–3 which was associated with an encounter diagnosis of CRS. Since we chose a gold standard diagnosis of Lund-Mackay score ≥4, these charts were classified as CRS or non-CRS based on the radiographic findings. The protocol for this study was reviewed and approved by the Institutional Review Board (IRB) at Northwestern University.

Statistical Analysis

The symptom frequencies in the two groups (CRS and non-CRS) were compared. Results were analyzed with univariate statistics with contingency tables (chi-square test or the Fisher's exact test) used for dichotomous variables and the Mann-Whitney-U test for ordinal variables. A Student's t-test was performed for continuous variables. For analysis of PRS, the analysis was performed using a dichotomous "never" and "present" analysis as well as a frequency based ordinal analysis. In the never/present dichotomous analysis, any patient-reported symptom frequency greater than "never" was considered "present". This was done as the never/present analysis may more closely reflect medical history gathering in the clinical setting, while the frequency-based analysis may provide further resolution on the nature of the CRS symptom. All statistical analysis was carried out on SPSS (IBM Corporation, Armonk, New York). A $p<0.05$ was used to define statistical significance. Since this study served as an exploratory study in preparation for a larger validation study, correction for multiple testing was not performed.

RESULTS

Study group characteristics

In the analysis of ODS, we identified charts from a cohort of 60 patients whose histories were documented by a single practitioner (See Table 2). In this phase, there were no significant differences between CRS and non-CRS patients in terms of age, sex and race. Non-CRS patients were significantly more likely to have a recorded history of nasal allergies. In the analysis of these results, there were no patients who met symptomatic criteria for primary cluster headaches. In the PRS phase, we identified a total of 80 charts of patients seen by any otolaryngologist who received a CT scan and completed the prospectively collected standardized review of systems form (Table 2). Patients from the non-CRS group were more likely to be women but were similar in age, self-reported nasal allergies and asthma status. As expected, the presence of polyps, purulence or middle meatal edema on endoscopic exam was significantly associated with CRS status.

Prevalence of RSTF symptom components and guideline-based symptomatic diagnosis of CRS and migraine

In the ODS phase, all patients met symptomatic criteria for CRS using the definitions established by the 2007 RSTF criteria. Of the individual component symptoms, facial pain/pressure was significantly more common in the non-CRS group, while hyposmia/anosmia was more common in the CRS group (Table 2). Among CRS patients, the most prevalent symptoms in descending order were facial pain/pressure, nasal obstruction, purulent nasal discharge and hyposmia/anosmia. If facial pain was considered a form of headache, 55.6% of non-CRS patients and 24.2% of CRS patients met IHS criteria for a diagnosis of migraine headache ($p<0.013$). In the PRS phase, 95.2% of non-CRS patients and 94.8% of CRS patients self-reported RSTF symptom criteria for CRS. In this phase there were no statistically significant differences in the prevalence of individual patient-reported RSTF symptom components. Additionally, 41.5% and 28.2% of non-CRS and CRS patients respectively had symptoms consistent with migraine as defined by the IHS criteria ($p=0.214$).

Comparison of the prevalence of symptoms from an expanded CRS/rhinitis symptom inventory

The prevalence of an expanded list of nasal-specific symptoms was then compared between CRS and non-CRS patients in both phases (Table 3). This showed that the prevalence of facial pain, but not facial pressure, was significantly higher in the non-CRS group in both phases of the study (ODS-phase OR 0.29 95% CI 0.10–0.88, PRS-phase 0.33 95% CI 0.12–0.92; $p<0.05$). In the ODS-phase, the presence of a decreased sense of smell predicted CRS status while the presence of headaches was associated with a non-CRS diagnosis. Otherwise, the other 1997 RSTF criteria and items drawn from the SNOT-22, including nasal or eye itching and sneezing were not significantly different between CRS and non-CRS groups in both study phases.

Comparison of the prevalence of items in the IHS criteria and other headache associated symptoms

We then analyzed the presence of symptoms associated with facial pain (Table 4). Only the presence of a pulsating or throbbing quality to the facial pain was negatively associated with CRS status in both study phases (ODS-phase OR 0.30 95% CI 0.09–1.04, PRS-phase OR 0.36 95% CI 0.14–0.96; $p<0.05$). Only in the ODS phase were exacerbations of facial pain with physical activity, photophobia, phonophobia and dizziness negatively associated with CRS status.

Comparison of the median patient-reported symptom frequencies

The median frequency of symptoms was then analyzed in the PRS phase (Table 5). The frequency of facial pain was significantly higher in non-CRS patients (median= 3- “Sometimes”) when compared with CRS patients (median= 2.5- between “Rarely” and “Sometimes”). Unlike the dichotomous never/present analysis, smell loss was significantly more frequent in CRS patients (median= 2- “Rarely”) compared with non-CRS patients (median= 1- “Never”). Headaches, a pulsating quality and photophobia were also significantly less frequent in CRS patients.

DISCUSSION

After examining an extensive list of items drawn from the RSTF (1997 and 2007) criteria, IHS criteria, SNOT-22 and other symptom exacerbating triggers, we find very few symptoms that positively or negatively predict for objective signs of inflammation among patients with CRS symptoms who received a CT scan for further evaluation. In both phases of the study, only a loss of sense of smell was positively predictive of CRS, although it was statistically significant in the PRS phase only when the frequency of the symptom was analyzed. Using two separate sets of patients and methods of assessing symptoms, we find that facial pain, and not pressure, was a negative predictor for CRS. To our knowledge, our study is the first study to specifically examine separate elements of the RSTF criteria into individual, unambiguous symptoms and also to apply the IHS primary headache symptoms to examine patients with radiographically documented CRS. A previous study by Mehle had applied the IHS criteria to examine patients with self-described “sinus headaches” and concluded that most sinus headaches were migraine or migraine variants. Even among patients they diagnosed as migraine, they found a “surprisingly” high rate (~20%) of radiographic sinus disease (Lund-Mckay score >5). We believe there are seemingly subtle, but significant differences between a cohort of patients with self-described “sinus headache” and a cohort of patients who meet the symptomatic definition of CRS[13].

These findings support the findings of other studies that evaluated clinical symptoms for predicting CRS defined by a radiographic gold standard. In a previous prospective study of

78 patients meeting subjective criteria for CRS, Stankiewicz and Chow showed that only 47% had a positive CT scan. They reported no significant differences in symptoms although direct statistical comparison of symptom prevalence does not appear to have been performed. Furthermore, in their study, facial pain/pressure/headache were combined into a single item [14]. Similarly, other previous studies that used the RSTF criteria verbatim have failed to demonstrate the symptomatic differences between CRS and non-CRS groups[4]. Conversely, several other groups have demonstrated that hyposmia was positively associated with CRS diagnosis while facial pain and headache were negatively associated[5, 15, 16]. One possible explanation for these conflicting findings is that these studies are confounded by the investigator's selection bias for symptoms requiring further imaging work up. Furthermore, the set-up, layout and wording of questionnaires used to assess respiratory symptoms has been shown to significantly impact the prevalence estimates of each individual symptom[17].

Despite several studies showing that facial pain is far from universal (29–61% of cases) among CRS sufferers[5, 18], facial pain seems to be established in the minds of patients and physicians as one of the most common presenting symptoms of CRS patients[19]. On the other end of the spectrum, the IHS recognizes sinus headache only in relation to acute rhinosinusitis and describes these as a frontal headache associated with face, ear, or tooth pain that also demonstrates clinical evidence of purulent nasal drainage, nasal obstruction, hyposmia/anosmia and/or fever. The IHS specifically states that CRS is not a validated cause of headache or facial pain unless it relapses into an acute stage of rhinosinusitis[8]. The Sinus, Allergy and Migraine Study (SAMS) found that of 2991 patients with a self diagnosis or physician diagnosis of sinus headache, 80% had migraine with or without aura, 8% had migrainous headache, 8% had episodic tension headache, and 4% had "other" headaches according to IHS criteria[20]. Furthermore other studies have demonstrated that headache, a highly ranked disabling symptom, is rarely improved with endoscopic sinus surgery[21]. In our study, we show that facial pain or headache is negatively associated with CRS status, and also find that separating facial pressure from facial pain changes the diagnostic utility of the symptom descriptor. Nonetheless, facial pain is still a common symptom with between 41–61% of CRS patients in our study endorsing the presence of facial pain even though it was usually rare in frequency. We also show that in the setting of classic CRS symptoms, the presence of specific facial pain characteristics may also lead away from a CRS diagnosis, namely a pulsatile quality and associated photophobia. Other possible negatively correlated findings include phonophobia, or dizziness although this was only seen in the otolaryngologist-documented part of the study. It is possible that a larger study may validate these additional symptoms of likely lesser effect size.

Many studies have been conducted to find a set of disease-specific tools to accurately predict CRS [22]. Popular examples of these include the Rhinosinusitis Disability Index (RSDI), the Sinonasal Outcomes Test (SNOT-22), and the Chronic Sinusitis Survey (CSS). However when compared with CT results, many of these questionnaire scores do not correlate with the Lund-MacKay CT scan score [23]. The paucity of positive and negative symptoms that predict CRS status present a dilemma to physicians trying to accurately diagnose and treat the disease, especially given the significant symptomatic overlap between rhinitis, migraine variants and sinusitis[24, 25]. Furthermore, differing forms of medical therapy are advocated for each entity[26], thus the importance of endoscopy cannot be overstressed. Our study also demonstrated that a positive nasal endoscopy finding was strongly predictive of a subsequent positive CT. Indeed, the sensitivity of endoscopy in the entire cohort was 61% but specificity was 94%. Furthermore, the non-specific nature of CRS symptoms also requires a thorough evaluation to exclude other pathology in the differential diagnosis (e.g laryngopharyngeal reflux, nasal lesions, adenoid hypertrophy etc.) prior to recommending CT for further evaluation.

Our study, and the work of others, demonstrates that CRS is difficult to accurately diagnose solely based on clinical symptoms. However, contrary to popular belief, facial pain is an inaccurate predictor of CRS and may actually negatively predict for the disease among patients with classic CRS symptoms. Likewise, migraine symptoms, as defined by the IHS, are present in approximately 25% of CRS patients if facial pain is considered a form of headache. Thus, a careful screening for nasal symptoms and the evaluation for a pulsatile quality and associated photophobia may help distinguish CRS from a migraine but its presence does not rule out CRS. A limitation of this study was its retrospective design, relatively small size, and that the patients in this study were likely selected for further CT evaluation due to high clinical suspicion for CRS. Thus, a prospective study examining the relationship between symptoms identified in this study and radiographic correlates, regardless of clinical impression of the need for CT imaging, may provide a more accurate estimate of the sensitivity and specificity of specific symptoms, or symptoms used in series.

CONCLUSION

Among patients with symptoms of CRS who received a CT scan for further diagnosis, the presence of headaches and facial pain with a pulsatile quality and associated photophobia were negatively associated with objective evidence for inflammation in the paranasal sinuses. The presence of hyposmia or anosmia positively predicts for CRS. However, the discriminatory power of these individual symptoms remains modest and reinforces the importance of endoscopy and/or radiographic imaging for accurately identifying CRS patients.

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Table 1

Symptomatic criteria for definition of chronic rhinosinusitis, migraine headaches and tension type headaches.

2007 RSTF diagnostic criteria for chronic rhinosinusitis[25]
12 or more weeks of 2 or more of the following symptoms
1 Mucopurulent drainage (anterior, posterior) or both
2 Nasal obstruction (blockage)
3 Facial pain-pressure-fullness
4 Decreased sense of smell
AND
1 Purulent mucus or edema in the middle meatus
2 Polyps in the nasal cavity, and/or
3 Inflammation of the paranasal sinuses on imaging

Symptoms that define migraine headaches[8]
At least 5 attacks of headaches fulfilling the following criteria
Headache attacks lasting 4–72 hours
Headache has at least two of the following characteristics
1 Unilateral location
2 Pulsating Quality
3 Moderate or severe pain intensity
4 Aggravation by routine physical activity
Headache has at least one of the following:
1 no nausea and/or vomiting
2 photophobia and phonophobia

Symptoms that define tension-type headaches[8]
Headache attacks lasting 30 minutes to 7 days
Headache has at least two of the following characteristics
1 bilateral location
2 non-pulsating quality
3 mild to moderate pain intensity
4 no aggravation with routine physical activity
Headache has at least one of the following:
1 no nausea and/or vomiting
2 no photophobia and phonophobia

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Table 2

Patient characteristics for ODS- otolaryngologist-recorded and PRS- patient-reported symptoms

	ODS-otolaryngologist recorded			PRS- patient-reported		
	non-CRS (N=27)	**CRS (N=33)**	**P-value**	**non-CRS (N=41)**	**CRS (N=39)**	**P-value**
Mean age (SD)	40.4 (10.9)	43.2 (13.2)	0.395	36.1 (10.9)	39.3 (11.1)	0.845
Sex						
Male, N (%)	7 (26%)	15 (46%)	0.118	10 (24%)	18 (46%)	0.041
Female, N (%)	20 (74%)	18 (55%)	0.118	31 (76%)	21 (54%)	0.041
Race						
Caucasian, N (%)	12 (44%)	20 (61%)	0.212	29 (71%)	27 (69%)	0.8836
African American, N (%)	3 (11%)	3 (9%)		5 (12%)	2 (5%)	
Asian, N (%)	1 (4%)	0 (0%)		5 (12%)	8 (21%)	
Hispanic, N (%)	3 (11%)	4 (12%)		2 (5%)	2 (5.1%)	
Medical history/exam						
History of Asthma, N (%)	5 (19%)	7 (21%)	0.863	6 (15%)	7 (17%)	0.65
History of Nasal Allergies, N (%)	18 (67%)	12 (36%)	0.04	17 (41.5%)	20 (51.3%)	0.604
Polyps, purulence or middle meatal edema on endoscopy, N (%)	3 (11.1%)	22 (67%)	**0.001**	1 (2.4%)	22 (56.4%)	<**0.001**
Task Force Major Criteria:						
Facial pain/pressure, N (%)	26 (96%)	26 (79%)	**0.047**	37 (90%)	30 (77%)	0.1065
Nasal obstruction, N (%)	23 (85%)	25 (76%)	0.364	36 (88%)	35 (90%)	0.7839
Nasal purulent discharge, N (%)	13 (48%)	22 (67%)	0.148	37 (90%)	36 (92%)	0.744
Hyposmia/anosmia, N (%)	5 (19%)	21 (64%)	<**0.001**	17 (42%)	22 (56%)	0.1813
Taskforce CRS symptoms, N (%)	27 (100%)	33 (100%)	1.00	39 (95.2%)	37 (94.8%)	0.971
IHS Migraine Criteria:						
IHS migraine criteria, N (%)	15 (55.6%)	8 (24.2%)	**0.013**	17 (41.5%)	11 (28.2%)	0.214

Table 3

Prevalence of individual CRS/Rhinitis symptoms in CRS and non-CRS groups

	ODS-otolaryngologist-recorded			PRS – patient-reported[2]		
	non-CRS (N=27)	CRS (N=33)	P-value	non-CRS (N=41)	CRS (N=39)	P-value
Facial pain, N (%)	20 (74.1%)	15 (45.5%)	**0.025**	33 (82.5%)	23 (60.5%)	**0.031**
Facial pressure, N (%)	22 (81.5%)	24 (72.7%)	0.425	36 (90.0%)	30 (78.9%)	0.176
Nasal congestion, N (%)	23 (85.2%)	25 (75.8%)	0.364	36 (87.8%)	35 (92.1%)	0.527
Clear nasal discharge, N (%)	NA	NA	NA	30 (93.8%)	30 (93.8%)	1.000
Discolored nasal discharge, N (%)	13 (48.1%)	22 (66.7%)	0.148	29 (72.5%)	32 (82.1%)	0.312
Post-nasal drip, N (%)	22 (81.5%)	27 (81.8%)	0.973	37 (90.2%)	34 (87.2%)	0.665
Decreased smell, N (%)	5 (18.5%)	21 (63.6%)	**<0.001**	17 (41.5%)	22 (56.4%)	0.181
Headaches, N (%)	20 (74.1%)	15 (45.5%)	**0.025**	38 (92.7%)	31 (79.5%)	0.087
Fevers, N (%)	7 (25.9%)	6 (18.2%)	0.469	14 (34.1%)	10 (25.6%)	0.407
Cough, N (%)	17 (63.0%)	19 (57.6%)	0.672	32 (78.0%)	26 (66.7%)	0.254
Bad breath, N (%)	9 (33.3%)	10 (30.3%)	0.802	29 (70.7%)	23 (59.0%)	0.339
Fatigue, N (%)	24 (88.9%)	21 (63.6%)	0.025	33 (80.5%)	31 (81.6%)	0.916
Dental pain, N (%)	11 (40.7%)	9 (27.3%)	0.271	20 (48.8%)	22 (56.4%)	0.495
Nasal itching, N (%)	NA	NA	NA	28 (68.3%)	24 (63.2%)	0.631
Sneezing, N (%)	NA	NA	NA	33 (80.5%)	35 (89.7%)	0.247
Eye itching, N (%)	NA	NA	NA	32 (78.0%)	28 (71.8%)	0.519

[2] In phase 2 of the study, subjects were asked about associated symptoms only if they reported facial pain or pressure. The never/present analysis was done by converting results of a Likert scale into a dichotomous variable of “never” and any symptom patient-reported more frequently than “never” was considered “present”

NA- Not consistently recorded during this phase of the study

Table 4

Prevalence, characteristics and associated symptoms with the facial pain.

	ODS- otolaryngologist recorded*			PRS-patient-reported*		
	non-CRS (N=27)	**CRS (N=33)**	**P-value**	**non-CRS (N=41)**	**CRS (N=39)**	**P-value**
Reporting pain/pressure^	26 (96.3%)	26 (78.8%)	**0.047**	37 (90.2%)	30 (76.9%)	0.1065
Median duration of pain/pressure, hours (SD)	<3#	>72, <168#		2 (140)	5 (166)	0.820
Unilateral symptoms, N (%)	6 (30.0%)	1 (6.7%)	0.124+	28 (68.3%)	21 (53.8%)	0.185
Pulsating/throbbing quality, N (%)	11 (40.7%)	5 (15.2%)	**0.026**	32 (78.0%)	22 (56.4%)	**0.039**
Moderate/severe intensity, N (%)	11 (40.7%)	8 (27.2%)	0.271	30 (73.2%)	25 (64.1%)	0.382
Exacerbated by physical activity, N (%)	11 (40.7%)	4 (15.2%)	**0.026**	24 (58.5%)	17 (43.6%)	0.181
Associated nausea, N (%)	8 (29.6%)	5 (15.2%)	0.176	21 (51.2%)	18 (46.2%)	0.651
Associated light sensitivity, N (%)	14 (51.9%)	6 (18.2%)	**0.006**	25 (61.0%)	18 (46.2%)	0.184
Associated noise sensitivity, N (%)	10 (37.0%)	3 (9.1%)	**0.012**+	23 (56.1%)	16 (41.0%)	0.178
Associated smell sensitivity, N (%)	NA	NA	NA	16 (39.0%)	13 (33.3%)	0.597
Associated dizziness, N (%)	6 (22.2%)	1 (3.0%)	**0.039**+	13 (31.7%)	14 (35.9%)	0.692
Associated visual aura, N (%)	8 (40.0%)	3 (9.1%)	0.026+	14 (34.1%)	14 (35.9%)	0.870
Associated numbness/tingling, N (%)	2 (7.4%)	0 (0.0%)	0.198+	5 (12.2%)	8 (20.5%)	0.314

*In the phase 1, the physician only recorded associated symptoms only if patients reported facial pain.

^In phase 2 of the study, subjects were asked about associated symptoms only if they reported facial pain or pressure. This analysis was done by converting results of a Likert scale into a dichotomous variable of “never” and “present”

#In phase 1 of the study, duration of facial pain was recorded in four categories “never”, “<3 hours”, “>3 days(72 hours),<7 days(168 hrs), and constant

+Fisher’s exact test was utilized for infrequent symptoms

Table 5

Median symptom frequencies of patient-reported symptoms

PRS-patient-reported symptom Symptom	Non-CRS			CRS			
	N (Valid)	Median	SD	N (Valid)	Median	SD	P-value
CRS/Rhinitis symptoms*							
Facial pain	40	3.00	1.30	38	2.50	1.28	**0.014**
Facial pressure	40	3.00	1.13	38	3.00	1.29	0.099
Nasal obstruction	41	4.00	1.30	38	4.00	1.16	0.325
Clear nasal discharge	32	4.00	1.12	32	3.00	1.05	0.127
Discolored nasal discharge	40	2.00	1.15	39	3.00	1.20	0.087
Post-nasal drip	41	3.00	1.22	39	3.00	1.33	0.937
Loss of sense of smell	41	1.00	1.03	39	2.00	1.40	**0.040**
Headaches	41	3.00	1.05	39	3.00	1.14	**0.032**
Fevers	41	1.00	0.71	39	1.00	0.62	0.447
Coughing	41	2.00	1.09	39	2.00	1.33	0.781
Bad breath	41	2.00	1.13	38	2.00	0.94	0.160
Fatigue	40	3.00	1.22	38	3.00	1.33	0.375
Tooth pain	41	1.00	1.17	39	2.00	1.02	0.703
Nasal itching	41	2.00	1.24	38	2.00	1.11	0.65
Sneezing	41	2.00	1.24	39	3.00	0.89	0.319
Eye itching	41	3.00	1.22	39	2.00	1.08	0.353
Factors associated with facial pain/pressure#							
Unilateral facial pain	41	2.00	1.16	39	2.00	1.27	0.621
Pulsating/throbbing quality	41	3.00	1.21	39	2.00	1.20	**0.015**
Moderate or severe intensity	41	3.00	1.23	39	2.00	1.25	0.231
Exacerbated by physical activity	41	2.00	1.02	39	1.00	1.06	0.282
Associated nausea	41	2.00	1.12	39	1.00	0.97	0.309
Light sensitivity	41	2.00	1.26	39	1.00	1.02	**0.050**
Noise sensitivity	41	2.00	1.22	39	1.00	1.00	0.106
Smell sensitivity	41	1.00	1.03	39	1.00	0.79	0.386
Associated dizziness	41	2.00	0.94	39	1.00	0.85	0.079

PRS-patient-reported symptom Symptom	Non-CRS			CRS			
	N (Valid)	Median	SD	N (Valid)	Median	SD	P-value
Associated visual aura	41	1.00	0.87	39	1.00	0.72	0.959
Associated sensory disturbance	41	1.00	0.69	39	1.00	0.55	0.356

*For CRS/Rhinitis symptoms, patients reported their symptoms on a 5-point Likert-scale with the following frequency descriptors: 1. Never 2. Rarely 3. Sometimes 4. Usually 5. Always;

#For the factors associated with facial pain/pressure, the following Likert-scale was used 1. Never 2. Rarely 3. Less than half the time 4. More than half the time