Published in final edited form as:

Int Forum Allergy Rhinol. 2015 August ; 5(8): 682–690. doi:10.1002/alr.21539.

Characterization of facial pain associated with chronic rhinosinusitis using validated pain evaluation instruments

Adam S. DeConde, MD¹, Jess C. Mace, MPH², Shaelene Ashby, PhD³, Timothy L. Smith, MD, MPH², Richard R. Orlandi, MD³, and Jeremiah A. Alt, MD, PhD³

¹Department of Surgery, Division of Otolaryngology-Head & Neck Surgery, University of California San Diego, San Diego, CA., USA

²Department of Otolaryngology – Head and Neck Surgery, Division of Rhinology, Oregon Health & Science University, Portland, OR., USA

³Sinus and Skull Base Surgery Program, Division of Otolaryngology - Head and Neck Surgery, Department of Surgery; University of Utah, Salt Lake City, Utah, USA

Abstract

Background—Prior investigations into facial pain associated with chronic rhinosinusitis (CRS) have yielded important results, but have yet to utilize pain-specific outcome measures. This study seeks to characterize facial pain associated with CRS using validated pain-specific instruments.

Methods—Adults with CRS were enrolled into a prospective, cross-sectional study along with control participants presenting with non-CRS diagnoses. Facial pain was characterized in both groups using the Brief Pain Inventory Short Form (BPI-SF) and the Short-Form McGill Pain Questionnaire (SF-MPQ). CRS-specific measures of disease were measured including the Sinonasal Outcome Test-22 (SNOT-22), nasal endoscopy, and computed tomography scoring.

Results—Patients were comprised of CRS with nasal polypsis (CRSwNP; n=25), CRS without nasal polypsis (CRSSNP; n=30), and control participants (n=8). Subjects with CRSwNP and CRSSNP were less likely to be pain free than controls (16.0%, 6.7% and 62.5% respectively, p=0.001) and carried greater burden of pain as measured by the BPI-SF and SF-MPQ than controls (p=0.002 and p=0.017, respectively). Pain in CRS was most commonly located around the eyes and characterized as ‘throbbing’ and ‘aching’. Nasal polyp status was not associated with differences in character, severity, or location of pain.

Conclusions—Subjects with CRS have a greater burden of facial pain relative to control subjects across several standardized pain measures. Further, facial pain in CRS significantly correlated to QOL and CRS-specific disease severity measures. Study across larger cohorts using

Corresponding Author: Jeremiah Alt, MD, PhD, University of Utah, Department of Surgery; Division of Otolaryngology – Head & Neck Surgery, Sinus and Skull Base Surgery Program, 50 North Medical Drive, SOM 3C120, Salt Lake City, Utah 84132, PH: 801-587-8368, FAX: 801-585-5744, jeremiah.alt@hsc.utah.edu.

Conflict of interest: Timothy L. Smith, Jess C. Mace, and Jeremiah A. Alt are supported by a grant from the National Institute on Deafness and Other Communication Disorders (NIDCD), one of the National Institutes of Health, Bethesda, MD (R01 DC005805; PI/PD: TL Smith). Public clinical trial registration (www.clinicaltrials.gov) ID# NCT01332136. Timothy L. Smith and Adam S. DeConde are consultants for IntersectENT, Inc (Menlo Park, CA) which is not affiliated with this investigation. Richard R. Orlandi is a consultant for Medtronic ENT (Jacksonville, FL) which is not affiliated with this research.

standardized pain measures is warranted to clarify the association of facial pain with chronic rhinosinusitis.

MeSH Key Words

sinusitis; facial pain; outcome assessment; data collection; endoscopy

INTRODUCTION

Two major chronic rhinosinusitis (CRS) guidelines include presence of facial pain as part of the clinical diagnostic criteria for CRS.^{1,2} However, the association of facial pain with CRS continues to be controversial, such that the EPOS guidelines highlight literature demonstrating that only a minority of subjects with CRS experience facial pain.² The recommendation of including facial pain/pressure in the AAO-HNSF adult rhinosinusitis guidelines is based on a study reporting only on 'facial pressure' which highlights the wide range of terminology used to describe and connote pain by both patients and physicians.^{3,4} The caution of the EPOS guidelines and the ambiguity of the adult rhinosinusitis guidelines with the cited literature reflect the need for a systematic characterization of facial pain in subjects with CRS.

Prior investigations into facial pain and CRS have been limited by a lack of validated outcomes measures. Investigation of pain in the context of CRS has generally been undertaken by either reporting of 'facial pain' by patients,^{5,6} by extracting an item from a CRS-specific measure^{7,8} or using a visual analog scale.⁹ There is ambiguity in the reporting merely of the binary presence or absence of 'facial pain' inasmuch as patients may minimize or exaggerate symptoms when forced into one of these two options.^{5,6} Extraction of facial pain data from visual analog scales and CRS-specific measures are difficult to interpret because facial pain and facial pressure are often grouped together.^{7,9} Furthermore, this data is often reported in subjects that have elected surgical treatment,^{8,9} which may be a biased interpretation as prior study has shown that differential symptom burden is associated with therapeutic decisions.^{10,11}

The goal of the present study is to provide an accurate characterization and frequency of facial pain in patients presenting to a rhinologic practice with CRS with and without nasal polyposis.

MATERIALS and METHODS

Patient Populations & Inclusion Criteria

Adult patients (≥ 18 years of age) presenting to the University of Utah, Sinus & Skull Base clinic with a current diagnosis of CRS, as defined by the 2007 Adult Sinusitis Guideline and endorsed by the American Academy of Otolaryngology-Head and Neck Surgery, were approached about study participation by the enrolling physician after completion of standard clinical appointments. Each patient had undergone previous treatment with oral, broad spectrum or culture directed antibiotics (2 weeks duration) and either topical nasal corticosteroid sprays (3 week duration) or a 5-day trial of systemic steroid therapy. The

Institutional Review Board at the University of Utah provided annual review and approval for all study protocols (IRB #61810).

Study case participants provided informed consent and were required to complete all necessary enrollment procedures and pain scale questionnaires in English during the initial enrollment meeting. Each participant was also asked to report demographic, social/medical history data including: age, gender, household income, current tobacco use, alcohol consumption, nasal polyposis, depression by physician diagnosis, asthma, allergies (both by reported patient history or confirmed skin prick or modified radioallergosorbent testing), acetylsalicylic acid (ASA) intolerance, cystic fibrosis, obstructive sleep apnea (OSA), and a history of both prior sinus surgery and headache and/or facial pain. Subjects were stratified into CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP) as these phenotypes may represent heterogeneous inflammatory processes² and prior study has suggested that subjects with CRSwNP do not have facial pain unless there is an acute bacterial infection.⁶

Study control participants with other head or neck disorders not associated with secondary head or facial pain (see exclusion criteria below) who presented to the Sinus & Skull Base clinic without evidence of CRS, on either computed tomography (CT) or visual endoscopy exam if indicated or had a clinical history inconsistent with CRS and did not require endoscopy or imaging, were approached about study enrollment. All consenting control participants were asked to provide the same demographic and social/medical history.

Exclusion criteria

Participants diagnosed with a concurrent exacerbation of recurrent acute sinusitis were excluded from final analyses due to the heterogeneity of the disease etiology. Study participants with a history of OSA or secondary headache and/or facial pain attributable to a medical condition other than CRS were excluded due to potential influences on pain scale questionnaires. All patients with comorbid disorders of the cranium, neck, eyes, ears, teeth, mouth, or cervical structures were excluded due to the potential influence of pain symptoms unrelated to CRS. In addition, all study participants who failed to complete all QOL and pain scale questionnaires during the initial enrollment meeting were excluded from final analyses.

Quality of Life and Pain Severity Questionnaires

Disease-Specific Quality of Life Measures—Participants completed the Sinonasal Outcome Test-22 (SNOT-22). The SNOT-22 is a 22-item test used to assess symptom severity of CRS.¹² Lower total scores (range: 0–110) on the SNOT-22 indicate better overall QOL and symptom severity. Five distinct symptom domains of the SNOT-22 have been previously described and include rhinologic symptoms (range: 0–30), extra-nasal rhinologic symptoms (range: 0–15), ear/facial symptoms (range: 0–25), psychological dysfunction (range: 0–35), and sleep dysfunction (range: 0–25).¹³

Patient-Reported Sinonasal Pain Severity Measures

Participants were asked to complete two validated pain scales to evaluate sinus-specific pain severity. The Brief Pain Inventory Short Form (BPI-SF) is a validated and widely used tool to measure both clinical pain severity and interference across a variety of disease processes (e.g., low back pain,¹⁴ painful diabetic neuropathy,¹⁵ and temporomandibular joint dysfunction).¹⁶ Pain severity was evaluated by instructing patients to indicate, on a scale from 0 – 10, how severe current sinus pain is at its “worst (in past 24 hours)”, “least (in past 24 hours)”, “average”, and “right now”. The arithmetic mean of those four scores is calculated and reported (range: 0–10). Pain interference was evaluated by asking participants how much sinus pain interferes with daily activities including: general activity, walking ability, normal work, mood, enjoyment of life, relations with other people, and sleep on a 0 (“Does not interfere”) to 10 (“Completely interferes”) scale. Pain interference is reported as the mean of the seven interference items (range: 0–10). Higher scores represent more pain severity and interference. Additionally, participants were asked to designate the precise location of their sinus-related facial and/or head pain on a diagram that was modified to include only an enlarged diagram of the head instead of the entire body (Figure 1).

Study participants were asked to complete the Short-Form McGill Pain Questionnaire (SF-MPQ) which consists of 15 pain descriptors ranked on a Likert scale from 0 (“None”) to 3 (“Severe”).¹⁷ The first 11 pain descriptor item scores are summarized (range: 0–33) to represent the sensory dimension of sinus-related pain (eg. throbbing, aching) while the remaining 4 descriptor item scores are summarized (range: 0–12) to represent the affective dimension of sinus-related pain (eg. fearful, sickening). The initial total score of the SF-MPQ can be calculated by adding the domain scores of the sensory dimension and affective dimension (range: 0–45). Additionally, the Present Pain Intensity (PPI) scale is used to indicate overall pain intensity by ranking current pain from 0 (“No pain”) to 5 (“Excruciating”). A final total score on the SF-MPQ can be calculated by adding the PPI to the initial total score (range: 0–50). In addition to the pain descriptors, the SF-MPQ includes a visual analogue scale (VAS) to provide an overall pain intensity measure that was modified to a Likert scale from 0–10 and again directed the subjects to refer to sinus pain.

Clinical Measures of Disease Severity

Study participants were evaluated for CRS disease severity using high-resolution computed tomography (CT) with bone and soft tissue windows and 1.0mm contiguous images in the coronal plane. Images were evaluated and staged by the enrolling physician in accordance with the Lund-Mackay bilateral scoring system (range: 0–24), with higher scores indicating worse severity of disease.¹⁸ This scoring system quantifies the degree of image opacification in the maxillary, ethmoidal, sphenoidal, ostiomeatal complex, and frontal sinus regions using a scale (0–1–2).

Study participants were also evaluated via endoscopic examinations using rigid, 30° endoscopes (SCB Xenon 175, Karl Storz, Tuttlingen, Germany). Endoscopic exams were scored by the enrolling physician using the bilateral Lund-Kennedy endoscopy scoring system (range: 0–20), which quantifies bilateral, pathologic states within the paranasal sinuses including the presence of: polypoid, discharge, edema, scarring, and crusting using

the same standard scale (0–1–2). Higher total scores indicate worse visualized disease severity.¹⁹ The enrolling physician was blinded to all other study data when both clinical measures were scored.

Data Management, Sampling Size Estimations, and Statistical Analysis

Study data were collected using standardized clinical research forms, stripped of all protected health information, and manually entered into a relational database (Microsoft Access; Microsoft Corp., Redmond, WA) by a trained research coordinator. Statistical analysis was accomplished using a commercially available statistical software application (SPSS v.22, IBM Corp., Armonk, NY). Two-tailed sample size estimations (Table 1) were determined for correlation coefficients (R) between pain scale scores and other measures of disease severity, assuming 80% power (1- β error probability) and a 0.050 alpha (α) level. The current sample size is adequately powered to detect weak correlation coefficients ($r > 0.300$) for most reported bivariate linear associations.

Descriptive and graphical analytics were used to assess all study variables and confirm assumptions of normality and distribution of continuous data. Chi-square (χ^2) testing with both 2×2 and 2×3 contingency tables, Mann-Whitney U tests, and Kruskal-Wallis tests were used to evaluate differences in patient characteristics, reported QOL, and pain scale questionnaire scores between CRSsNP, CRSwNP, and control participants. Significant differences were determined using the 0.050 α level. Pearson's correlation coefficients (R_p) or Spearman's rank correlation coefficients (R_s) were used to evaluate potential linear associations between pain severity measures and all other continuous study covariates where appropriate.

RESULTS

Study Population Characteristics

A total of 63 study participants met all inclusion criteria and were enrolled in this prospective cross-sectional investigation between August, 2013 and August, 2014. This group was comprised of CRS with nasal polyposis (CRSwNP; n=25), CRS without nasal polyposis (CRSsNP; n=30) and control participants (n=8). The control patients consisted of patients with septal deviation in isolation (n=1), septal deviation in conjunction with bilateral inferior turbinate hypertrophy (n=5), asymptomatic sphenoid mucocoele (n=1), and encephalocoele (n=1). Six of 8 controls (75%) underwent CT, and 5 of 8 underwent sinonasal endoscopy (62.5%) as part of clinical evaluation. All patients with CRS underwent both radiography and endoscopy examinations. Overall patient characteristics across patient subgroups are described in Table 2. Control participants were significantly less likely to have comorbid allergies or a history of prior sinus surgery compared to both CRSwNP and CRSsNP, however the prevalence of allergy and prior sinus surgery between CRSwNP and CRSsNP groups was not significantly different from each other ($p = 0.808$).

Control participants reported significantly better disease-specific QOL scores compared to both CRSwNP and CRSsNP on the SNOT-22 total mean scores, rhinologic symptom scores, and ear/facial symptom scores, as well as significantly less disease severity as measured by

CT and endoscopy scores (Table 3). When comparing bivariate differences in baseline QOL between CRSwNP and CRSsNP only the mean SNOT-22 rhinologic domain scores were significantly better in the CRSsNP subgroup ($p=0.024$). Likewise, CRSsNP were found to have significantly better mean CT scores ($p<0.001$) and endoscopy scores ($p=0.004$) compared to their CRSwNP counterparts.

Pain severity scores were evaluated across all three study subgroups for both the BPI-SF (Table 4) and SF-MPQ (Table 5). Mean BPI-SF pain severity scores of the BPI-SF were significantly better in control subjects compared to CRSwNP ($p=0.002$) and CRSsNP ($p<0.001$) separately, however CRSwNP and CRSsNP were not significantly different from each other ($p=0.549$). Similarly BPI-SF pain interference scores were significantly better in control subjects compared to CRSwNP ($p=0.002$) and CRSsNP ($p<0.001$) separately, however CRSwNP and CRSsNP were not significantly different from each other ($p=0.173$). The prevalence of pain reported using the BPI-SF was found to be mostly located above and below the eyes in both the CRSwNP and CRSsNP groups (Table 4, Figure 2). No significant differences between CRSwNP and CRSsNP were found in the reported prevalence of any facial pain location as measured by the BPI-SF survey (all $p \geq 0.092$).

The impact of facial pain related to CRS was characterized further using the SF-MPQ scores between CRS subgroups and control participants (Table 5). Control participants reported significantly lower mean pain severity measures compared to CRSwNP and CRSsNP, while those two CRS subgroups did not report significantly different average scores for total SF-MPQ ($p=0.991$), sensory dimension ($p=0.792$), affective dimension ($p=0.931$), present pain inventory ($p=0.934$), or VAS scores ($p=0.895$). The frequency of participants reporting each type of pain descriptor was evaluated across CRSwNP, CRSsNP, and controls. The percentage of CRSwNP patients reported pain characterized largely as aching (80.0%), throbbing (75.0%), tiring-exhausting (73.9%), and heavy (60.0%). The percentage of CRSsNP patients reported pain characterized as tender (82.1%), throbbing (76.7%), aching (72.4%), and tiring-exhausting (69.0%). The only significant difference in the prevalence of pain descriptors on the SF-MPQ, between CRSwNP and CRSsNP, was a higher reported frequency of tender pain in the CRSsNP subgroup ($p=0.038$). All other pain descriptors were found to have similar prevalence between CRSwNP and CRSsNP ($p \geq 0.083$).

Bivariate correlation coefficients between clinical measures of disease severity and pain severity measures were compared for CRSwNP, CRSsNP, and control participants. No significant correlations were found between CT scores and any of the patient-reported pain severity scores for any subgroup ($p \geq 0.206$). Likewise, no significant correlations were found between endoscopy scores and any pain severity scores for either CRSwNP ($p = 0.557$) or CRSsNP ($p = 0.171$).

Bivariate correlation of total SNOT-22 scores revealed positive strong to very strong correlations ($r = 0.482 - 0.735$, $p<0.050$; Table 6) with all pain measures. Analysis of the SNOT-22 domains revealed that both subtypes of CRS demonstrate strong correlations between pain measures and the ear/facial, psychological, sleep domains (Table 6). In subjects with CRSsNP sinus-specific domains did not correlate ($p>0.050$) with pain measures with the exception of the ear/facial symptoms, which contains the item

investigating ‘facial pain/pressure.’ In contrast, in subjects with CRSwNP there was strong correlation between the SNOT-22 rhinologic domain scores and BPI-SF Pain interference scores, total SF-MPQ scores, and both the sensory and affective dimensions of the SF-MPQ ($r=0.483-0.557$, $p<0.050$).

DISCUSSION

The present study advances our understanding and characterization of facial pain in CRS. The majority of subjects with CRS in this cohort were burdened by facial pain relative to controls across several standardized pain measures. The pain associated with CRS manifests predominantly as a throbbing and aching pain around and between the eyes. Polyp status was not associated with differences in character, severity, or location of pain, although aching was most commonly reported in CRSwNP compared to tenderness in CRSsNP. Cumulative endoscopy scores and cumulative radiographic CT scores did not significantly correlate with the burden of pain severity.

The literature describing pain associated with CRS reports a wide range of prevalence. The discrepancy may be in part due to the treatment selection bias inherent in surgical cohorts. Such studies likely include subjects with higher burden or wide-ranging impact of disease compared to subjects that elect continued medical management as has been demonstrated in another North American cohort.^{10,11} Regardless, literature reporting pain in surgical cohorts tend to report pain^{8,9} or headache^{8,9,20} in the majority of subjects at baseline with significant improvements postoperatively. In contrast, cross-sectional studies evaluating subjects with CRS upon presentation report pain in only a minority of patients with CRS.⁵⁻⁷ These cross-sectional studies have been influential, and have shifted the perception that patients with chronic rhinosinusitis rarely have pain^{2,5,21} unless experiencing an acute exacerbation.

The present study is the only cross-sectional study with a control group and yielded data that contradicts the prior cross-sectional studies. Subjects with CRS, regardless of polyp status, were burdened by pain at significantly higher levels than controls, and significantly higher than other published data on facial pain and CRS. In fact, rates of facial pain in prior studies are comparable to the controls in the present study.⁵⁻⁷ Although these prior studies are reporting rare pain in a minority of subjects with CRS, they are limited by a lack of validated instruments to accurately measure the pain and none compare to a control group. Use of validated pain instruments may increase sensitivity, providing subjects with a wider array of terms to discern and report pain related to CRS, and help explain the discrepancy between the present and prior studies. This discrepancy, though, highlights the fact that prior studies are either opaque in how pain information was extracted or are incomprehensive.⁵⁻⁷

Prior investigations have suggested that subjects with CRSwNP and CRSsNP tend to portray different symptom profiles. With regards to facial pain, Poetker et al²² reported that subjects with nasal polyposis experienced less pain than patients with CRSsNP on a VAS. There are also data suggesting that subjects with CRSwNP feel pain only in the context of viscid secretions and that absent viscid secretions facial pain is rare,⁵ again suggesting that different underlying pathophysiology manifest unique symptoms. The present study failed to find a significant association between subjects with and without polyposis, but a larger

sample size might lead to the detection of a difference, as well as examination of the frequency of viscid secretion, which was not captured by the current study design (Table 1).

Unfortunately, little is known of the underlying mechanisms that produce pain associated with CRS, but several mechanisms that may all contribute to some degree to the manifestation of facial pain in CRS have been postulated. It has been hypothesized that occlusion of the osteomeatal complex may lead to gas resorption of the sinuses with painful negative pressures,²³ yet most subjects with CRS have an open osteomeatal complex.²⁴ Patients' observations that pain and pressure is postural may reflect painful dilatation of vessels;²⁵ however, postural pain is also observed in subjects with simply tension type headache.²⁵ Local inflammatory mediators can excite nerves locally within the sinonasal mucosa directly eliciting pain. For example, maxillary rhinosinusitis can cause dental pain through the stimulation of the trigeminal nerve.²¹ In addition, local tissue destruction and inflammatory mediators may influence the central mechanism of pain via immune-to-brain communication through afferent autonomic neuronal transmission, transport across the blood brain barrier through the circumventricular organs and/or direct passage across the blood brain barrier.²⁷

The impact of inflammatory cytokines on the central nervous system have been associated with both pain as well as other health-related factors associated with chronic inflammation and sickness behavior such as disruption of sleep²⁷ and mood.²¹ Interleukin-1[Beta] (IL-1[Beta]) and tumor necrosis factor-[alpha] (TNF-[alpha]) are two key pro-inflammatory cytokines with a pivotal role in the immune-to-brain pathway of communication. They are both upregulated in subjects with CRS^{28,29} and are two potential pro-inflammatory cytokines that have been implicated in fatigue,³⁰ sleep dysfunction,²⁷ depression,³¹ and pain.³² Characterizing the differential cytokine profiles of CRS subtypes and identifying associated symptom profiles may be an important step in understanding why some subjects experience greater health-related burden of disease,²⁷ which is an important predictor of electing surgical intervention over continued medical therapy.¹⁰

The present study found significant correlations between measures of pain with CRS-specific QOL measures (Table 6), specifically in the psychologic and sleep domains. There was also a strong correlation between pain measures and the ear/facial symptoms domain, which was expected given that the item of 'facial pain/pressure' falls into this domain. The correlation of pain with the sleep and psychologic burden is not unexpected either. The recognition that pain and depression correlate has been recognized in the dental, orthopedic and gynecologic literature.³⁴ The association is known as the depression-pain dyad given that they often are comorbid, exacerbate each other, and share common biological pathways.³⁴ Understanding how CRS symptoms fuel depression and pain will help improve treatment algorithms and outcomes. Future study will also need to factor in the impact of other health-related issues that both impact and are influenced by pain, such as sleep quality and mood, and the underlying mechanisms that contribute this set of symptoms.

The current study has begun to improve our understanding of facial pain and CRS, and found that when using pain-specific instruments indeed the majority of subjects with CRS experience pain greater than controls. These findings raise a number of important questions

for further study including the correlation of various inflammatory cytokines with symptoms of pain as well as the interplay of mood and sleep dysfunction on pain in CRS. Furthermore, the introduction of validated pain instruments into the rhinology literature may help to better clarify the symptom profile nuances that could potentially distinguish patients with migraine from patients with pain secondary to CRS. An improved understanding of these issues will help refine medical and surgical therapies for patients that suffer from these most debilitating symptoms of CRS as well as assist in our understanding of how those therapies improve facial pain associated with CRS.

CONCLUSIONS

Subjects with CRS commonly experienced pain in this cohort in contrast to prior cross-sectional studies. This pain was most commonly described as a throbbing and aching sensation around the eyes. No difference was identified between subjects with and without nasal polyposis. Pain burdens correlated with total SNOT-22 scores, and specifically the domains investigating sleep and psychological impairments associated with the disease. Future study investigating the impact of comorbid sleep, depression, and pain as well as the underlying cytokine profiles associated with these most debilitating symptoms may help refine patient therapies and expectations.

References

1. Benninger MS, Ferguson BJ, Hadley JA, Hamilos DL, Jacobs M, Kennedy DW, et al. Adult chronic rhinosinusitis: definitions, diagnosis, epidemiology, and pathophysiology. *Otolaryngol Head Neck Surg.* 2003; 129(3 Suppl):S1–32. [PubMed: 12958561]
2. Fokkens WJ, Lund VJ, Mullol J, et al. EPOS 2012: European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. *Rhinology.* 2012; 50(1):1–12. [PubMed: 22469599]
3. Bhattacharyya N. The Economic Burden and Symptom Manifestations of Chronic Rhinosinusitis. *Am J Rhinol.* 2003; 17(1):27–32. [PubMed: 12693653]
4. Jensen MP, Johnson LE, Gertz KJ, Galer BS, Gammaitoni AR. The words patients use to describe chronic pain: implications for measuring pain quality. *Pain.* 2013; 154(12):2722–2728. [PubMed: 23933183]
5. Clifton NJ, Jones NS. Prevalence of facial pain in 108 consecutive patients with paranasal mucopurulent discharge at endoscopy. *J Laryngol Otol.* 2007; 121(4):345–348. [PubMed: 17156506]
6. Fahy C, Jones NS. Nasal polyposis and facial pain. *Clin Otolaryngol Allied Sci.* 2001; 26(6):510–513. [PubMed: 11843934]
7. Eweiss AZ, Lund VJ, Barlow J, Rose G. Do patients with chronic rhinosinusitis with nasal polyps suffer with facial pain? *Rhinology.* 2013; 51(3):231–235. [PubMed: 23943729]
8. Chester AC, Antisdel JL, Sindwani R. Symptom-specific outcomes of endoscopic sinus surgery: A systematic review. *Otolaryngol Head Neck Surg.* 2009; 140(5):633–639. [PubMed: 19393402]
9. Ling FTK, Kountakis SE. Important Clinical Symptoms in Patients Undergoing Functional Endoscopic Sinus Surgery for Chronic Rhinosinusitis. *Laryngoscope.* 2007; 117(6):1090–1093. [PubMed: 17440425]
10. DeConde AS, Mace JC, Bodner T, et al. SNOT-22 quality of life domains differentially predict treatment modality selection in chronic rhinosinusitis. *Int Forum Allergy Rhinol.* 2014; 4(12):972–979. [PubMed: 25323055]
11. Soler ZM, Rudmik L, Hwang PH, Mace JC, Schlosser RJ, Smith TL. Patient-centered decision making in the treatment of chronic rhinosinusitis. *Laryngoscope.* 2013; 123(10):2341–2346. [PubMed: 23856802]

12. Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item Sinonasal Outcome Test. *Clin Otolaryngol*. 2009; 34(5):447–454. [PubMed: 19793277]
13. DeConde AS, Bodner TE, Mace JC, Smith TL. Response shift in quality of life after endoscopic sinus surgery for chronic rhinosinusitis. *JAMA Otolaryngol Head Neck Surg*. 2014; 140(8):712–719. [PubMed: 25074504]
14. Gammaitoni AR, Galer BS, Lacouture P, Domingos J, Schlagheck T. Effectiveness and safety of new oxycodone/acetaminophen formulations with reduced acetaminophen for the treatment of low back pain. *Pain Med*. 2003; 4(1):21–30. [PubMed: 12873275]
15. Galer BS, Ganas A, Jensen MP. Painful diabetic polyneuropathy: epidemiology, pain description, and quality of life. *Diabetes Res Clin Pract*. 2000; 47(2):123–128. [PubMed: 10670912]
16. Thie NM, Prasad NG, Major PW. Evaluation of glucosamine sulfate compared to ibuprofen for the treatment of temporomandibular joint osteoarthritis: a randomized double blind controlled 3 month clinical trial. *J Rheumatol*. 2001; 28(6):1347–1355. [PubMed: 11409130]
17. Melzack R. The short-form McGill Pain Questionnaire. *Pain*. 1987; 30(2):191–197. [PubMed: 3670870]
18. Lund VJ, Mackay IS. Staging in rhinosinusitis. *Rhinology*. 1993; 31(4):183–184. [PubMed: 8140385]
19. Lund VJ, Kennedy DW. Staging for rhinosinusitis. *Otolaryngol Head Neck Surg*. 1997; 117(3 Pt 2):S35–40. [PubMed: 9334786]
20. Moretz WH, Kountakis SE. Subjective headache before and after endoscopic sinus surgery. *Am J Rhinol*. 2006; 20(3):305–307. [PubMed: 16871934]
21. Eccles R. Mechanisms of the symptoms of rhinosinusitis. *Rhinology*. 2011; 49(2):131–138. [PubMed: 21751530]
22. Poetker DM, Mendolia-Loffredo S, Smith TL. Outcomes of endoscopic sinus surgery for chronic rhinosinusitis associated with sinonasal polyposis. *Am J Rhinol*. 2007; 21(1):84–88. [PubMed: 17283567]
23. Whittet HB. Infraorbital nerve dehiscence: the anatomic cause of maxillary sinus “vacuum headache”? *Otolaryngol Head Neck Surg*. 1992; 107(1):21–28. [PubMed: 1528598]
24. Snidvongs K, Chin D, Sacks R, Earls P, Harvey RJ. Eosinophilic rhinosinusitis is not a disease of ostiomeatal occlusion. *Laryngoscope*. 2013; 123(5):1070–1074. [PubMed: 23553255]
25. Falck B, Svanholm H, Aust R, Bäcklund L. The relationship between body posture and pressure in occluded maxillary sinus of man. *Rhinology*. 1989; 27(3):161–167. [PubMed: 2637473]
26. Jones NS. Midfacial segment pain: implications for rhinitis and rhinosinusitis. *Clin Allergy Immunol*. 2007; 19:323–333. [PubMed: 17153023]
27. Alt JA, Smith TL. Chronic rhinosinusitis and sleep: a contemporary review. *Int Forum Allergy Rhinol*. 2013; 3(11):941–949. [PubMed: 24039230]
28. Erbek SS, Yurtcu E, Erbek S, Atac FB, Sahin FI, Cakmak O. Proinflammatory cytokine single nucleotide polymorphisms in nasal polyposis. *Arch Otolaryngol Head Neck Surg*. 2007; 133(7):705–709. [PubMed: 17638785]
29. Mfuna Endam L, Cormier C, Bossé Y, Filali-Mouhim A, Desrosiers M. Association of IL1A, IL1B, and TNF gene polymorphisms with chronic rhinosinusitis with and without nasal polyposis: A replication study. *Arch Otolaryngol Head Neck Surg*. 2010; 136(2):187–192. [PubMed: 20157068]
30. Omdal R, Gunnarsson R. The effect of interleukin-1 blockade on fatigue in rheumatoid arthritis--a pilot study. *Rheumatol Int*. 2005; 25(6):481–484. [PubMed: 15071755]
31. Illi J, Miaskowski C, Cooper B, et al. Association between pro- and anti-inflammatory cytokine genes and a symptom cluster of pain, fatigue, sleep disturbance, and depression. *Cytokine*. 2012; 58(3):437–447. [PubMed: 22450224]
32. Leung L, Cahill CM. TNF-alpha and neuropathic pain--a review. *J Neuroinflammation*. 2010; 7:27. [PubMed: 20398373]
33. Harris M, Feinmann C, Wise M, Treasure F. Temporomandibular joint and orofacial pain: clinical and medicolegal management problems. *Br Dent J*. 1993; 174(4):129–136. [PubMed: 8443008]

34. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: A literature review. *Arch Intern Med.* 2003; 163(20):2433–2445. [PubMed: 14609780]

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Figure 1. Modified diagram for sinus-related facial and/or head pain. Yellow area, above right eye; Blue area, above left eye; Gray area, below right eye; Green area, below left eye; Red area, between eyes; Black area, top of head; Orange area, back of head; Brown area, right temple; Purple area, left temple.

Figure 2.
Frequency and location of reported facial pain in study participants with chronic rhinosinusitis (n=55).

Table 1

Sample size estimations for correlation coefficients (R) between pain-scale scores and outcome measures of disease severity

R²	Effect Size (R)	Sample Size
0.200	0.447	34
0.250	0.500	26
0.300	0.547	21
0.350	0.591	17
0.400	0.632	14
0.450	0.671	12
0.500	0.707	11
0.550	0.742	9

R²; coefficient of determination

Table 2

Comparison of baseline characteristics of chronic rhinosinusitis study groups and controls

Characteristics:	CRS _w NP (n=25)		CRS _s NP (n=30)		Controls (n=8)		p-value
	Mean [SD]	N(%)	Mean [SD]	N(%)	Mean [SD]	N(%)	
Age (years)	43.6 [16.7]		51.1 [16.7]		43.8 [19.1]		0.212
Males		16 (64.0)		13 (43.3)		4 (50.0)	
Females		9 (36.0)		17 (56.7)		4 (50.0)	0.308
Depression		3 (12.0)		3 (10.0)		1 (12.5)	0.964
Asthma		12 (48.0)		12 (40.0)		1 (12.5)	0.203
Allergy		14 (56.0)		16 (53.3)		0 (0.0)	0.015
ASA sensitivity		6 (24.0)		3 (10.0)		0 (0.0)	0.156
Tobacco smoking		0 (0.0)		1 (3.3)		1 (12.5)	0.214
Alcohol consumption		9 (36.0)		7 (23.3)		3 (37.5)	0.529
Prior sinus surgery		18 (72.0)		20 (69.0)*		0 (0.0)	<0.001
Cystic fibrosis		2 (8.0)		0 (0.0)		0 (0.0)	0.217

* Valid percentages are reported to account for any missing data.

CRS_wNP, chronic rhinosinusitis with nasal polyposis; CRS_sNP, chronic rhinosinusitis without nasal polyposis; SD, standard deviation; ASA, acetylsalicylic acid

Table 3

Comparison of quality of life and disease severity measures of chronic rhinosinusitis study groups and controls

QOL Scores:	CRSwNP (n=25)	CRSsNP (n=30)	Controls (n=8)	p-value
	Mean [SD]	Mean [SD]	Mean [SD]	
SNOT-22 Total Score	56.2 [21.3]	57.4 [17.3]	31.9 [23.6]	0.033
Rhinologic symptom	19.3 [4.6]	16.6 [4.4]	10.3 [6.6]	0.001
Extra-nasal rhinologic symptoms	7.8 [3.5]	8.3 [3.1]	4.0 [5.3]	0.057
Ear/facial symptoms	9.6 [6.0]	11.1 [4.7]	3.9 [3.7]	0.005
Psychological dysfunction	16.4 [9.3]	17.9 [7.7]	10.9 [9.1]	0.139
Sleep dysfunction	14.7 [6.5]	14.9 [6.0]	9.8 [8.6]	0.277
Clinical Measures of Disease Severity:				
Lund-Mackay CT Scores	17.5 [4.8]	9.5 [5.3]	1.2 [1.6]*	<0.001
Lund-Kennedy Endoscopy Scores	7.4 [3.6]	4.9 [2.4]	2.0 [0.0]**	<0.001

CRSwNP, chronic rhinosinusitis with nasal polyposis; CRSsNP, chronic rhinosinusitis without nasal polyposis; SD, standard deviation; SNOT-22, 22-item Sinonasal Outcome Test; CT, computed tomography.

* Data available for 6/8 control subjects.

** Data available for 5/8 control subjects.

Table 4

Comparison of Brief Pain Inventory Short Form (BPI-SF) Scores Between Chronic Rhinosinusitis Study Groups and Controls

Pain Severity Measures:	CRSwNP (n=25)		CRSSNP (n=30)		Controls (n=8)		p-value
	Mean [SD]	N (%)	Mean [SD]	N (%)	Mean [SD]	N (%)	
BPI-SF Pain severity	3.2 [2.0]		3.6 [1.9]		0.7 [1.1]		0.002
BPI-SF Pain interference	2.7 [2.5]		3.8 [2.8]		0.4 [0.8]		0.002
Pain Location:							
No pain	----	4 (16.0)	----	2 (6.7)	----	5 (62.5)	0.001
Above right eye	----	15 (60.0)	----	16 (53.3)	----	1 (12.5)	0.060
Above left eye	----	15 (60.0)	----	17 (56.7)	----	1 (12.5)	0.052
Below right eye	----	14 (56.0)	----	16 (53.3)	----	1 (12.5)	0.083
Below left eye	----	15 (60.0)	----	16 (53.3)	----	1 (12.5)	0.060
Between eyes	----	11 (44.0)	----	17 (56.7)	----	0 (0.0)	0.016
Top of head	----	3 (12.0)	----	5 (16.7)	----	0 (0.0)	0.449
Back of head	----	2 (8.0)	----	8 (26.7)	----	1 (12.5)	0.178
Right temple	----	4 (16.0)	----	10 (33.3)	----	2 (25.0)	0.339
Left temple	----	5 (20.0)	----	12 (40.0)	----	2 (25.0)	0.259

* Valid percentages are reported to account for any missing data.

CRSwNP, chronic rhinosinusitis with nasal polypsis; CRSSNP, chronic rhinosinusitis without nasal polypsis; SD, standard deviation; BPI-SF, Brief Pain Inventory Short Form

Table 5

Comparison of the Short Form McGill Pain Questionnaire (SF-MPQ) Scores Between Chronic Rhinosinusitis Study Groups and Controls

Pain Severity Measures:	CRSwNP (n=25)		CRSSNP (n=30)		Controls (n=8)		p-value
	Mean [SD]	N(%)	Mean [SD]	N(%)	Mean [SD]	N(%)	
Total SF-MPQ	12.5 [11.0]	----	11.7 [8.7]	----	2.6 [4.6]	----	0.017
Sensory dimension	9.5 [8.1]	----	9.9 [7.3]	----	2.3 [4.2]	----	0.014
Affective dimension	3.0 [3.2]	----	2.6 [2.1]	----	0.4 [0.7]	----	0.023
PPI Score	2.0 [1.2]	----	2.1 [1.3]	----	0.9 [1.2]	----	0.071
VAS Score	3.5 [2.7]	----	3.6 [2.5]	----	0.5 [1.1]	----	0.004
Pain Descriptors:							
Throbbing	1.4 [1.0]	18 (75.0)	1.4 [1.0]	23 (76.7)	0.4 [0.5]	3 (37.5)	0.082
Shooting	0.7 [1.0]	10 (43.5)	0.7 [1.1]	10 (35.7)	0.3 [0.7]	1 (12.5)	0.289
Stabbing	0.9 [1.1]	11 (47.8)	0.9 [1.1]	14 (48.3)	0.1 [0.4]	1 (12.5)	0.167
Sharp	1.0 [1.0]	14 (58.3)	0.7 [1.0]	10 (34.5)	0.1 [0.4]	1 (12.5)	0.046
Cramping	0.5 [0.9]	8 (33.3)	0.2 [0.6]	5 (17.2)	0.0 [0.0]	0 (0.0)	0.104
Knawing	0.8 [1.1]	9 (36.0)	0.7 [1.0]	12 (41.4)	0.4 [1.1]	1 (12.5)	0.316
Hot-burning	0.4 [0.9]	5 (20.8)	0.7 [0.9]	12 (42.9)	0.3 [0.7]	1 (12.5)	0.115
Aching	1.6 [1.0]	20 (80.0)	1.3 [1.0]	21 (72.4)	0.4 [0.7]	2 (25.0)	0.012
Heavy	1.1 [1.1]	15 (60.0)	0.8 [0.9]	16 (55.2)	0.0 [0.0]	0 (0.0)	0.010
Tender	0.9 [0.9]	13 (54.2)	1.3 [0.9]	23 (82.1)	0.3 [0.7]	1 (12.5)	0.001
Splitting	0.9 [1.0]	12 (50.0)	1.1 [1.1]	16 (57.1)	0.1 [0.4]	1 (12.5)	0.082
Tiring-exhausting	1.4 [1.1]	17 (73.9)	1.4 [1.2]	20 (69.0)	0.3 [0.7]	1 (12.5)	0.005
Sickening	0.7 [1.0]	10 (43.5)	0.7 [0.8]	14 (48.3)	0.1 [0.4]	1 (12.5)	0.187
Fearful	0.4 [0.6]	6 (26.1)	0.2 [0.6]	4 (14.8)	0.0 [0.0]	0 (0.0)	0.219
Punishing-cruel	0.4 [0.9]	5 (21.7)	0.3 [0.6]	7 (28.0)	0.0 [0.0]	0 (0.0)	0.244

*Valid percentages are reported to account for any missing data.

P-values for the pain descriptors compares the frequency of patients reporting each particular pain type across CRSwNP, CRSSNP, and control participants. CRSwNP, chronic rhinosinusitis with nasal polypoid; CRSSNP, chronic rhinosinusitis without nasal polypoid; SD, standard deviation; SF-MPQ, Short Form McGill Pain Questionnaire; PPI, Present Pain Intensity; VAS, visual analog scale

Table 6
Bivariate correlation coefficients between SNOT-22 domain survey scores and pain severity measures within CRSwNP, CRSsNP, and controls

	SNOT-22 Scores					
	Rhinologic symptoms R	Extra-nasal symptoms R	Ear/facial symptoms R	Psychological dysfunction R	Sleep dysfunction R	Total R
CRSwNP - Pain Severity Measures:						
BPL-SF Pain severity	0.186	0.161	0.637*	0.691**	0.475*	0.600*
BPL-SF Pain interference	0.505*	0.389	0.680**	0.659**	0.471*	0.677**
Total SF-MPQ	0.552*	0.442*	0.748**	0.791**	0.643*	0.735**
Sensory dimension	0.557*	0.463*	0.737**	0.771**	0.632*	0.730**
Affective dimension	0.483*	0.392	0.732**	0.796**	0.574*	0.716**
PPI Score	0.315	0.204	0.587*	0.569*	0.359*	0.491*
VAS Score	0.355	0.321	0.659**	0.752**	0.518*	0.669**
CRSsNP - Pain Severity Measures:						
BPL-SF Pain severity	−0.001	0.007	0.412*	0.613**	0.564*	0.482*
BPL-SF Pain interference	0.231	0.075	0.355	0.760**	0.720*	0.711**
Total SF-MPQ	0.360	0.207	0.588*	0.726**	0.598*	0.639*
Sensory dimension	0.238	0.231	0.575*	0.684**	0.463*	0.604*
Affective dimension	0.333	0.100	0.484*	0.739**	0.625*	0.588*
PPI Score	0.057	0.076	0.508*	0.670**	0.456*	0.541*
VAS Score	0.064	0.226	0.719**	0.745**	0.493*	0.668**
Controls - Pain Severity Measures:						
BPL-SF Pain severity	0.456	0.553	0.588	0.125	0.452	0.495
BPL-SF Pain interference	0.408	0.309	0.257	0.158	0.592	0.514
Total SF-MPQ	0.498	0.553	0.695	0.167	0.369	0.454
Sensory dimension	0.466	0.571	0.689	0.138	0.345	0.436
Affective dimension	0.517	0.309	0.538	0.268	0.371	0.405
PPI Score	0.498	0.553	0.695	0.167	0.369	0.454
VAS Score	0.345	0.359	0.257	0.095	0.544	0.483

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p-value <0.050;
**
p-value<0.001.

BPI-SF, Brief Pain Inventory Short Form; SNOT-22, 22-item Sinonasal Outcome Test; SF-MPQ, Short Form McGill Pain Questionnaire; PPI, Present Pain Intensity; VAS, visual analog scale; CRSwNP, chronic rhinosinusitis with nasal polyposis; CRSsNP, chronic rhinosinusitis without nasal polyposis;