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Elimination of Pain Improves Specificity of Clinical Diagnostic Criteria for Adult Chronic Rhinosinusitis

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Objective: Determine whether the elimination of pain improves accuracy of clinical diagnostic criteria for adult chronic rhinosinusitis.

Study Design: Retrospective cohort study.

Methods: History, symptoms, nasal endoscopy, and computed tomography (CT) results were analyzed for 1,186 adults referred to an academic otolaryngology clinic with presumptive diagnosis of chronic rhinosinusitis. Clinical diagnosis was rendered using the 1997 Rhinosinusitis Taskforce (RSTF) Guidelines and a modified version eliminating facial pain, ear pain, dental pain, and headache.

Results: Four hundred seventy-nine subjects (40%) met inclusion criteria. Among subjects positive by RSTF guidelines, 45% lacked objective evidence of sinonasal inflammation by CT, 48% by endoscopy, and 34% by either modality. Applying modified RSTF diagnostic criteria, 39% lacked sinonasal inflammation by CT, 38% by endoscopy, and 24% by either modality. Using either abnormal CT or endoscopy as the reference standard, modified diagnostic criteria yielded a statistically significant increase in specificity from 37.1% to 65.1%, with a nonsignificant decrease in sensitivity from 79.2% to 70.3%. Analysis of comorbidities revealed temporomandibular joint disorder, chronic cervical pain, depression/anxiety, and psychiatric medication use to be negatively associated with objective inflammation on CT or endoscopy.

Conclusion: Clinical diagnostic criteria overestimate the prevalence of chronic rhinosinusitis. Removing facial pain, ear pain, dental pain, and headache increased specificity without a concordant loss in sensitivity. Given the high prevalence of sinusitis, improved clinical diagnostic criteria may assist primary care providers in more accurately predicting the presence of inflammation, thereby reducing inappropriate antibiotic use or delayed referral for evaluation of primary headache syndromes.

Key Words: Chronic sinusitis, facial pain, diagnosis, clinical symptoms, computed tomography.

Level of Evidence: 4.

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INTRODUCTION

Rhinosinusitis is a highly prevalent disease resulting in a considerable burden on the healthcare system. In a 2012 survey, 12% of U.S. adults reported being diagnosed with rhinosinusitis in the last year,[1] resulting in more than 20 million annual diagnoses.[2] A review of ambulatory care data from 2006 to 2010 demonstrated that rhinosinusitis accounted for more antibiotic prescriptions than any other condition,[3] with $11 billion in direct healthcare costs.[1,2] Further studies have demonstrated a substantial relationship between acute and chronic rhinosinusitis (CRS) and decreased work productivity,[4] absenteeism,[5] and reduced quality of life, suggesting substantial additional indirect costs.[6]

Despite the sizeable impact of rhinosinusitis, considerable variation in diagnosis and management exists across medical specialties.[7,8] The observed variation in treatment of rhinosinusitis may be due to the fact that gold-standard diagnostic criteria remain elusive, and evaluation in the primary care setting does not have the benefit of nasal endoscopy to gain objective evidence of sinus disease. Furthermore, the correlation between symptoms and objective findings is imperfect.[9,10] The prevalence of abnormal sinus computed tomography (CT) in patients reporting symptoms of rhinosinusitis has been reported to be only 65% to 80%.[9,11–14] Numerous conditions may mimic the presentation of rhinosinusitis, including allergic and nonallergic rhinitis, as well as neurologic disorders such as vascular, migraine, or cluster headaches; trigeminal neuralgia; and atypical facial pain.

The 1997 Task Force on Rhinosinusitis (RSTF) defined CRS as the presence of two or more major factors or one major and two minor factors (see Table I) persisting for at least 12 weeks.[15] The 2016 International Consensus Statement on Rhinosinusitis (ICOR) updated

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TABLE I.
Original and Modified 1997 Rhinosinusitis Task Force Diagnostic Criteria for CRS.

	RSTF	mRSTF
Major Factors	Facial pain/pressure	Facial pressure
	Facial congestion/fullness	Facial congestion/fullness
	Nasal obstruction/blockage	Nasal obstruction/blockage
	Anosmia/hyposmia	Anosmia/hyposmia
	Nasal discharge/purulence/discolored postnasal drainage	Nasal discharge/purulence/discolored postnasal drainage
	Purulence in nasal cavity on examination	Purulence in nasal cavity on examination
	Fever (acute rhinosinusitis only)	Fever (acute rhinosinusitis only)
Minor Factors	Headache	Fatigue
	Fatigue	Halitosis
	Halitosis	Cough
	Cough	Fever (all nonacute)
	Dental pain	
	Ear pain/pressure/fullness	
	Fever (all nonacute)	

CRS = chronic rhinosinusitis; mRSTF = Modified Rhinosinusitis Task Force Criteria; RSTF = Rhinosinusitis Task Force Criteria.

diagnostic criteria for CRS to consist of 12 weeks of at least two of the following symptoms: nasal obstruction/congestion, anterior/posterior nasal discharge, facial pain/pressure/fullness, and decreased sense of smell. The 2016 guidelines also added the requirement for objective verification of mucosal inflammation, polyps, and/or purulent sinus drainage via CT or nasal endoscopy for definitive diagnosis of CRS.[16]

Updated diagnostic criteria for CRS continue to include pain as an indicator for sinusitis, although studies have demonstrated poor correlation between facial pain or headache and objective evidence of paranasal sinus inflammation. In rhinologic patients with radiographically or endoscopically confirmed CRS, only 16% to 20% complained of facial pain.[17–19] Similarly, 75% to 97% of patients with facial pain attributed to sinus disease lacked radiographic evidence of inflammation on CT.[20–22] Many patients with facial pain may actually have primary headache, with 88% of sinus headache sufferers meeting diagnostic criteria for migraine.[23] Nevertheless, neurologic sources of these symptoms may be mistaken for CRS in the primary care setting.[24,25]

The 2016 ICOR guidelines require the confirmation of symptomatic CRS with objective findings on endoscopy or CT; however, nasal endoscopy is generally unavailable and CT may be underutilized in the primary care setting. In a study by Tan et al., only 50% of CRS with nasal polyposis (CRSwNP) and 25% of CRS without nasal polyposis (CRSsNP) subjects underwent CT ordered by the primary care physician (PCP); furthermore, patients were more likely to undergo CT evaluation after initial diagnosis and treatment.[26] These data suggest that despite updated diagnostic guidelines for CRS requiring CT or nasal endoscopy, many PCPs rely on symptom-based diagnostic criteria that may have high sensitivity but inappropriately low specificity in predicting sinus disease.[27,28]

Given the frequent misattribution of facial pain and headache to sinusitis rather than other potential underlying etiologies, the accuracy of symptom-based clinical criteria for CRS may improve with the elimination of pain, although this does not appear to have been evaluated to date. In this study, we assess the impact on diagnostic accuracy of removal of facial pain and headache from clinical diagnostic criteria for CRS.

MATERIALS AND METHODS

Billing records were used to identify adult patients referred to the Department of Otolaryngology at Virginia Commonwealth University from November 2008 until June 2015 with a diagnosis of sinusitis. Exclusion criteria included a history of sinonasal surgery, facial trauma, or prior sinus CT, as well as those without subsequent CT or endoscopic evaluation.

Initial otolaryngology encounter notes were reviewed for gender, age, previous rhinosinusitis diagnosis, prior imaging, presenting symptoms, exam findings, medical comorbidities, and current and past medications. Results of nasal endoscopy and sinus CT performed within 3 months of the initial encounter were included. A subsequent diagnosis of a neurologic disorder such as migraine or atypical facial pain was noted.

For each patient, CRS was retrospectively diagnosed by applying the 1997 RSTF diagnostic criteria (see Table I).[15] A modified clinical diagnostic algorithm (mRSTF) was created by removing facial, dental, ear pain, and headache from the symptoms (see Table I). These four symptoms were chosen for elimination because each negatively predicted inflammation on CT or endoscopy in our population. Radiologic presence of mucosal disease was evaluated using the Lund-Mackay scoring system[29]; scores $\geq$3 were considered indicative of sinusitis.[11,30] Endoscopic disease burden was rated using the Modified Lund-Kennedy (MLK) scoring system,[31] with scores $\geq$2 considered positive for sinusitis.

Clinical and demographic characteristics were summarized by descriptive statistics. Sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were calculated for RSTF and mRSTF criteria using either CT or endoscopy as the objective standard for sinusitis, as per the 2016 ICOR guidelines. A binomial z-test was used to compare RSTF and mRSTF in sensitivity, specificity, accuracy,

TABLE II.
Relationship Between Presenting Symptoms and Objective Evidence of Inflammation Using Either CT or Nasal Endoscopy as the Reference Standard.

Symptom	N	Regression Coefficient	Standard Error	Odds Ratio	95% CI	*P* Value
Facial pain	84	−.652	0.196	0.52	(0.35 to 0.77)	0.001*
Facial pressure	120	0.352	0.196	1.42	(0.97 to 2.09)	0.073
Nasal obstruction	217	1.157	0.198	3.18	(2.16 to 4.69)	0.000*
Purulent rhinorrhea	153	1.173	0.205	3.23	(2.16 to 4.83)	0.000*
Anosmia/hyposmia	74	1.278	0.294	3.59	(2.02 to 6.39)	0.000*
Headache	130	−.574	0.190	0.56	(0.39 to 0.82)	0.002*
Fatigue	32	−.282	0.282	0.75	(0.43 to 1.31)	0.319
Dental pain	14	−.759	0.369	0.47	(0.23 to 0.97)	0.040*
Ear pressure/pain	52	−.533	0.225	0.59	(0.38 to 0.91)	0.018*
Cough	66	0.374	0.241	1.45	(0.91 to 2.33)	0.121
Halitosis	15	−.153	0.409	0.86	(0.39 to 1.91)	0.709
Fever	12	0.663	0.585	1.94	(0.62 to 6.11)	0.257

*Signifies statistical significance.
CI = confidence interval; CT = computed tomography; N = number of subjects.

PPV, and NPV. Somers' D was used to measure the concordant rate between clinical diagnostic criteria and CT. Logistic regression was used to test association of symptoms with CT and endoscopy scores. Forest plots via a logistic regression were used to illustrate the associations of comorbid conditions with diagnostic results. Significance was determined using the type I error of 5%. Statistical analysis was performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC). This study was reviewed and approved by the Institutional Review Board of Virginia Commonwealth University.

RESULTS

The query of billing records identified 1,186 potential subjects; of those, 479 (40.4%) met inclusion criteria. There were 317 (66.2%) females and 162 (33.8%) males; with mean age 50.3 years (standard deviation (SD) ± 15.1, range 19–89). Utilizing RSTF criteria, 349 (72.9%) met criteria for diagnosis of CRS, versus 271 (56.6%) using mRSTF criteria.

Among subjects, 396 (82.7%) underwent CT after initial otolaryngology evaluation, with average Lund-Mackay score 5.1 (SD ± 5.6, range 0–24, median 3), and 203 (51.3%) with Lund-Mackay > 3, meeting criteria for sinusitis. There were 388 (81.0%) subjects with nasal endoscopy performed at the initial encounter, with mean MLK score 1.6 (SD ± 2.0, range 0–10, median 1) and 179 (46.1%) with MLK > 2, meeting criteria for sinusitis. There were 293 (61.2%) subjects who fulfilled either CT or endoscopic criteria for sinusitis, and 101 (21.1%) who fulfilled both CT and endoscopic criteria. Concordance between CT and endoscopy for diagnosing sinusitis was fair, with a Kappa coefficient of 0.302 (95% confidence interval [CI] 0.196–0.407, $P < 0.0001$). The frequency of symptoms and their associations with objective evidence of sinusitis is presented in Table II.

Of those subjects with RSTF diagnosis of CRS, 54.8% had CT evidence, 52.0% had endoscopic evidence, and 66.5% had either CT or endoscopic evidence of sinusitis. Of those who met mRSTF criteria, 60.6% had CT evidence, 61.6% had endoscopic evidence, and 76.0% had either CT or endoscopic evidence of sinusitis. The concordance between either positive CT or endoscopy and RSTF diagnosis was 29.4%, with Somers' D of 0.163 ($P < 0.0001$), whereas the concordance between either CT or endoscopy and mRSTF was 45.7%, with Somers' D of 0.354 ($P < 0.0001$). Sensitivity, specificity, and accuracy of both diagnostic criteria were evaluated using abnormal CT, abnormal endoscopy, or either abnormal CT or endoscopy as the reference standard for diagnosis of sinusitis (see Table III). Use of mRSTF criteria resulted in a large increase in specificity ($P < 0.05$) but correspondingly small, nonsignificant trend toward decrease in sensitivity.

Comorbidities were analyzed for association with CT or endoscopic findings. Among our subjects, 4.4% had fibromyalgia; 6.1% had neuropathy; 11.1% had chronic cervical pain; 14.4% had a history of migraine; 7.3% had temporomandibular joint disorder (TMD); 18.8% had a history of depression or anxiety; and 33.9% reported a history of psychiatric medication use. Subjects with any one of these comorbidities were less likely to have sinusitis on either CT or endoscopy (relative risk [RR] = 0.69, 95% CI 0.578–0.828, $P < 0.0001$). Individually, a history of chronic cervical pain (RR = 0.62, 95% CI 0.442–0.872, $P = 0.0006$), TMD (RR = 0.54, 95% CI 0.341–0.862, $P = 0.0007$), depression/anxiety (RR = 0.81, 95% CI 0.650–1.00, $P = 0.031$), and prior use of psychiatric medications (RR = 0.85, 95% CI 0.724–1.00, $P = 0.047$) were inversely associated with the presence of sinusitis on either CT or endoscopy (see Fig. 1).

DISCUSSION

Prior studies have shown poor correlation between symptoms and endoscopic or radiographic evidence of CRS.[14,32] Updated 2016 ICOR diagnostic criteria emphasized the need for objective evidence of sinonasal inflammation to confirm the diagnosis of CRS. Whereas this requirement is readily applicable to practicing otolaryngologists, endoscopy is not available and CT may be underused

TABLE III.
Sensitivity, Specificity, Accuracy, PPV, and NPV of Clinical and Modified Clinical Diagnostic Criteria for CRS Using CT, Nasal Endoscopy, and CT or Nasal Endoscopy as the Reference Standard.

Epidemiology Data		N	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
CT	RSTF	161	79.3	31.1	55.8	54.8	58.8
	mRSTF	143	70.4	51.8	61.4	60.6	62.5
	Difference	18	−8.9	+20.7	+5.6	+5.8	+3.7
	P value	–	0.181	0.030*	0.301	0.292	0.418
Endoscopy	RSTF	146	81.6	35.4	56.7	52.0	69.2
	mRSTF	135	75.4	59.8	67.0	61.6	74.0
	Difference	11	−6.2	+24.4	+10.3	+9.6	+4.8
	P value	–	0.410	0.063	0.265	0.285	0.484
CT or Endoscopy	RSTF	245	79.2	37.1	62.8	66.5	53.1
	mRSTF	215	70.3	65.1	68.3	76.0	58.2
	Difference	30	−8.9	+28	+5.5	+9.5	+5.1
	P value	–	0.082	0.0003*	0.179	0.072	0.196

P values calculated using one-sided binomial test.
*Denotes statistical significance.
CT = computed tomography; mRSTF = Modified Rhinosinusitis Task Force Criteria; N = number of subjects; NPV = negative predictive value; PPV = positive predictive value; RSTF = Rhinosinusitis Task Force Criteria.

by PCPs.[26] Clinical diagnostic criteria established by the 1997 RSTF and updated in the 2016 ICOR statement both include pain as a symptom contributing to the diagnosis of CRS. Although facial pain or headache can indeed be due to CRS, several studies have established that facial pain and sinus headache are frequently migrainous or otherwise neurologic in etiology.[33–36] A reliance on symptom-based diagnosis, as is likely the norm in the primary care setting, may lead to frequent misattribution of neurologic facial pain to CRS, leading to the inappropriate prescription of antibiotics and delay in management of underlying pathology.

The current study seeks to determine whether elimination of pain-related symptoms could improve clinical accuracy for diagnosis of CRS via symptom-based criteria. The 1997 RSTF criteria were chosen for analysis

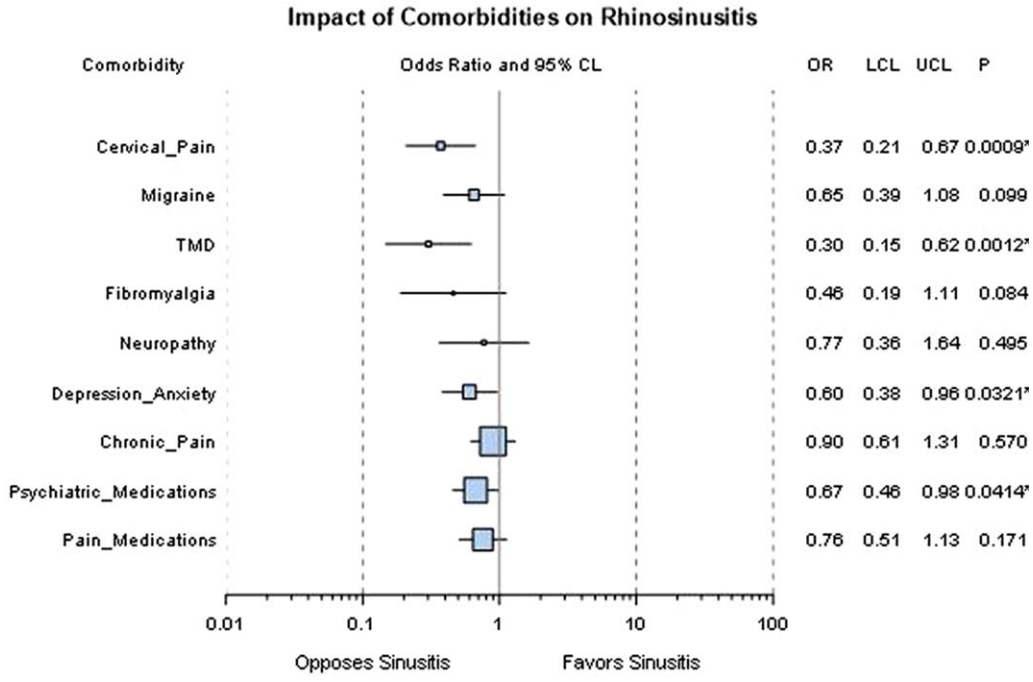

Fig. 1. Forest plot demonstrating impact of individual comorbid conditions on the diagnosis of rhinosinusitis using either computed tomography or nasal endoscopy as the reference standard.
Box sizes represent the prevalence of symptoms.
*Denotes statistical significance.
LCL = lower confidence limit; OR = odds ratio; TMD = temporomandibular joint disease; UCL = upper confidence limit. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

because these guidelines do not require objective confirmation of sinonasal inflammation, and thus may better represent the diagnostic process employed by PCPs. When applied retroactively to our cohort, mRSTF criteria resulted in a significant increase in specificity without a concordant loss of sensitivity in the diagnosis of CRS. There was an upward trend in overall diagnostic accuracy for mRSTF criteria, regardless of whether CT, endoscopy, or either CT or endoscopy were used as the reference standard for sinonasal inflammation.

Applying traditional RSTF criteria to our data demonstrated a PPV of 54.8% for abnormal CT, similar to published data.[10] This low PPV portends frequent false-positive clinical diagnoses of sinusitis, supporting the notion that symptom-based diagnostic criteria are poorly suited to differentiating CRS from other diseases that may manifest similar symptoms.[37–39] Use of mRSTF criteria led to no statistical change in PPV or NPV, although both trended higher. Despite more stringent criteria, the reduction of false positive diagnoses seen with the elimination of headache and pain from the mRSTF criteria did not result in a significant loss of sensitivity or NPV within our study population.

Prior studies have demonstrated that nasal obstruction,[40–43] postnasal drip,[42] purulent rhinorrhea,[41,43] and smell disturbances[42–45] are associated with the presence of sinonasal inflammation. Likewise, the current study demonstrated that subjects with purulent rhinorrhea, nasal obstruction, and anosmia were more likely to have abnormal CT or endoscopy, and that patients with headache, facial, dental, and ear pain were more likely to have normal radiographic or endoscopy.

Comorbidities characterized by chronic head and neck pain, particularly cervical pain and TMD, negatively predicted the presence of sinusitis on CT or endoscopy within this study population. Migraines and fibromyalgia both narrowly missed statistical significance as negative predictors of sinus disease. Additionally, patients with a history of depression/anxiety and psychiatric medication use were less likely to have objection inflammation. These findings suggest that subjects with comorbidities characterized by chronic head and neck pain or depression/anxiety may have lower pretest probabilities of CRS, and thus benefit from earlier CT and neurologic evaluation, rather than trials of extended antimicrobial therapy. Prior work by Tan et al. supports the notion that upfront CT may be advantageous over empiric antibiotic therapy in the primary care setting.[46–48]

Rhinosinusitis is a highly prevalent disease resulting in considerable personal and societal costs.[1,3–6] Although 20 million diagnoses of sinusitis are made in the United States annually, a growing body of research indicates that accurate diagnosis of sinusitis, especially using symptom-based criteria, is problematic. Use of objective modalities such as CT or nasal endoscopy may improve diagnostic accuracy, but are underused or unavailable in the primary care setting where many initial diagnoses of CRS are made. Moreover, upfront CT has been suggested to be more cost-efficient in most circumstances when compared to empiric antibiosis,[46,47] but if overused may produce an unacceptable increase in the incidental finding of mucosal thickening and unnecessary treatment of presumed sinusitis.[49] An improved ability to parse out symptomatic sinonasal inflammation is critical in optimizing diagnosis of CRS. In this study, the elimination of headache, ear, dental, and facial pain from clinical criteria significantly improved specificity without sacrificing sensitivity, and may be applicable to a broader population undergoing evaluation by PCPs for possible CRS.

This study is limited by selection bias, in that our population consisted of patients with suspected CRS referred to an academic otolaryngology practice. The presence of a comparison group without symptoms of CRS would help control for confounding variables and demonstrate baseline characteristics in a healthy population. Additionally, the retrospective design and lack of standardized questionnaires or endoscopic rating systems may have reduced the reliability of data extracted from the study population. Broad, poorly defined symptoms such as pain may be particularly difficult to operationalize when performing a retrospective review.[50] In the absence of a structured method for querying symptoms, patients might focus on more tangible symptoms of CRS, such as obstruction or drainage, leading to an underrepresentation of facial pain/pressure in participants with legitimate inflammatory disease.

Gender is another potential source of bias because women constituted 66.2% of the study population and are more likely to report facial pain and headache.[51] Lal et al demonstrated that women presented with higher Sino-Nasal Outcome Test 22 and lower Lund-Mackay scores than men,[52] indicating a tendency to report more severe sinonasal symptoms despite lesser objective evidence of inflammation. An over-representation of women within this cohort could result in a misleadingly low specificity for diagnostic criteria. However, gender subgroup analysis showed minimal effect. For the entire cohort, using abnormal CT or endoscopy as the reference standard, the specificity and sensitivity of the mRSTF criteria were 65.1% and 70.3%, respectively, whereas these changed to 68.2% and 67.8% for male subjects, and to 64.1% and 72.0% for female subjects, respectively.

This study was designed to assess diagnostic accuracy for CRS using clinical criteria in previously undiagnosed patients, as may frequently present to PCPs. Patients with a history of sinonasal surgery were excluded because one might reasonably expect that a positive CT or endoscopy led to prior surgical intervention. Excluding patients with previous surgery could bias the population to less significant disease, impacting sensitivity or specificity calculations. Additionally, the predictive value of pain for true inflammatory disease could potentially differ in the postoperative population.

Not all study participants had both CT and nasal endoscopy performed. Given the imperfect concordance between these modalities found among subjects who underwent both procedures, it is possible that patients with only a negative CT or endoscopy were considered not to have sinusitis; although if performed, a second test may have been positive. This would result in an inappropriately low estimation of sensitivity within the

study population; however, we would expect that this effect would alter specificity and sensitivity calculations for both RSTF and mRSTF diagnostic criteria in parallel fashion, and thus not likely impact the nature of our conclusions. Future prospective studies could employ validated questionnaires and endoscopy-scoring systems to verify whether the trends identified in this retrospective cohort can be generalized to a greater population with presumed CRS.

CONCLUSION

The elimination of facial pain, dental pain, ear pain, and headache from clinical diagnostic criteria for CRS resulted in significantly improved specificity for diagnosis of sinusitis as confirmed via CT or nasal endoscopy. Ongoing research is necessary to optimize diagnostic algorithms for CRS, particularly in the primary care setting, which may in turn lead to decreased inappropriate antibiotic use and delay in management of primary headache syndromes.

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