

Symptoms and Clinical Findings in Primary Headache Syndrome Versus Chronic Rhinosinusitis

Daniel D. Sharbel, MD¹ , Harry C. Owen, BSc²,
Joshua C. Yelverton, MD¹, Mingsi Li, MD¹, Thomas Holmes, MD¹,
and Stilianos E. Kountakis, MD, PhD¹

Abstract

Background: Primary headache syndrome (PHS) patients frequently present to otolaryngologists with sinonasal complaints and diagnosis of chronic rhinosinusitis (CRS) due to symptomatic overlap. In this study, we compare demographic, subjective, and objective clinical findings of patients with PHS versus CRS.

Methods: We retrospectively reviewed a database of patients presenting to a single tertiary care Rhinology clinic from December 2011–July 2017. Sino-Nasal Outcome Test-22 (SNOT) scores and Lund-Kennedy endoscopy scores were obtained. Lund-MacKay CT scores were calculated, if available. Requirement of headache specialist management was compared between PHS and CRS groups. Patients with both CRS and PHS (CRScPHS) that required headache specialist management were compared to patients with CRS without PHS (CRSsPHS) and patients with PHS alone using Kruskal-Wallis analysis of variance. Receiver operating characteristic (ROC) analyses were carried out to determine significant diagnostic thresholds.

Results: One-hundred four PHS patients and 130 CRS patients were included. PHS patients (72.1%) were more likely than CRS patients to require headache specialist management (6.9%, $p < 0.0001$). CRSsPHS patients had significantly higher Nasal domain scores compared to PHS patients ($p = 0.042$) but not compared to CRScPHS patients ($p > 0.99$). CRScPHS ($p = 0.0003$) and PHS ($p < 0.0001$) subgroups of patients had significantly higher Aural/Facial domain scores compared to CRSsPHS patients. PHS patients also had significantly higher Sleep domains scores compared to CRSsPHS patients ($p < 0.0001$). Both CRScPHS and CRSsPHS subgroups had significantly higher nasal endoscopy scores ($p < 0.0001$) and CT scores ($p = 0.04$ & $p < 0.0001$, respectively) compared to the PHS group. Aural/Facial domain score of 4, nasal endoscopy score of 4, and CT score of 2 were found to be reliable diagnostic thresholds for absence of CRS.

Conclusions: The SNOT-22 may be used to distinguish PHS from CRS based upon the Aural/Facial and Sleep domains. Patients with CRS have more severe Nasal domain scores and worse objective endoscopy and CT findings.

Keywords

headache, chronic rhinosinusitis, Sino-Nasal Outcome Test, primary headache syndrome, facial pain, migraine

Introduction

The diagnosis of “sinus headache,” whether self-diagnosed, or physician-diagnosed, is a common reason for visits to practicing otolaryngologists’ offices, despite its rarity.¹ Primary headache syndromes (PHS), such as migraines, cluster headache, sluder neuralgia, and hemicrania continua, are often associated with physiologic phenomena mimicking signs and symptoms of rhinosinusitis, such as nasal congestion, rhinorrhea, conjunctival injection, lacrimation, eyelid edema, and pain

¹Department of Otolaryngology-Head and Neck Surgery, Medical College of Georgia, Augusta University, Augusta, Georgia

²Medical College of Georgia, Augusta University, Augusta, Georgia

Corresponding Author:

Daniel D. Sharbel, Department of Otolaryngology-Head and Neck Surgery, Medical College of Georgia, Augusta University, 1120 15th Street, BP-4109, Augusta, GA 30912, USA.

Email: dsharbel@augusta.edu

in the temporal or periorbital areas.² As a result, physicians with little experience treating sinusitis patients are often faced with a diagnostic challenge, and as Novis et al. have suggested, PHS is often misdiagnosed as sinusitis by primary care or emergency medicine physicians.^{3,4} Foroughipour et al. described a cohort of patients diagnosed with “sinus headache,” in which 96% of patients received antibiotic therapy, 56% of patients underwent nasal endoscopy, and 29% of patients underwent nasal septoplasty, despite the fact that only 5% of the patients received a final diagnosis of chronic rhinosinusitis (CRS).⁵ These reports suggest that CRS is poorly understood outside of otolaryngology, and that confusion with PHS contributes significantly to unnecessary or incorrect treatment of these patients.

In 1997, the Rhinosinusitis Task Force stated that 2 major factors or 1 major and 2 minor factors were necessary to have a strong history consistent with CRS.⁶ Notably, facial pain/pressure was identified as a major factor, while headache was noted as a minor factor. However, in a 2003 update, it was noted that significant inaccuracies existed in the symptom-based system of diagnosis of CRS set forth by the 1997 article.⁷ From that time, objective clinical data, such as rigid nasal endoscopy and computed tomography (CT) scoring have been required for determining a diagnosis of CRS. In today's practice, CRS is defined by the American Academy of Otolaryngology-Head and Neck Surgery by presence two or more of the four cardinal symptoms: 1) mucopurulent drainage, 2) nasal obstruction, 3) facial pain-pressure-fullness, or 4) decreased sense of smell. Additionally, documentation of inflammation via one of three findings is required for diagnosis: 1) purulent discharge or edema in the middle meatus or anterior ethmoid region, 2) presence of polyps in the nasal cavity or middle meatus, or 3) radiographic imaging showing inflammation of the paranasal sinuses.⁸

PHS as classified by the third edition of the International Classification of Headache Disorders (ICHD) falls under the umbrella diagnoses of migraine, tension-type headache, trigeminal autonomic cephalalgias, and other primary headache disorders.⁹ The third edition of the ICHD also sets forth criteria for “headache attributed to sinusitis (Table 1).” However, it notes that both migraine and tension-type headaches can be mistaken for headaches due to sinusitis because of similarity of distribution and, in the case of migraines, accompanying nasal autonomic symptoms. Additionally, it notes that clinical findings of acute sinusitis are not enough criteria to diagnose headaches attributed to sinusitis. Distinguishing between PHS and CRS, therefore, remains a common diagnostic challenge for clinicians. We sought to clarify presenting symptoms and clinical characteristics most commonly found in

PHS and CRS at the time of initial clinical presentation. By doing so, we hope to aid the clinician in determining if a patient's symptoms are truly of sinogenic origin or due to PHS.

Methods

This study was approved by the Institutional Review Board at Augusta University. This study is a retrospective review of a prospectively collected database from the senior author's (SEK) academic tertiary-referral practice from December 2011 to July 2017. Patients >18 years old with a diagnosis of either a primary headache syndrome or CRS were included. Patients <18 years old or who did not have a diagnosis of a primary headache syndrome or CRS were excluded. All patients were asked to rate their symptoms on a numerical scoring scale using the validated 22-item Sino-Nasal Outcome Test (SNOT-22)¹⁰ prior to being seen by the physician. During the encounter, rigid nasal endoscopy was performed and graded according to the Lund-Kennedy scoring system.¹¹ If CT was available, this was reviewed and graded according to the Lund-MacKay scoring system.¹² Patients in whom PHS was suspected by profile of SNOT-22 scores then underwent application of ICHD criteria for presumptive diagnosis.⁹ The lack of sinogenic secondary cause was also excluded by negative nasal endoscopy and/or imaging. A CT was obtained if the patient had persistent symptoms despite medical treatment, which included normal saline irrigations and an intranasal steroid spray. A control group of CRS patients was then collected from the database. This included patients with either eosinophilic or non-eosinophilic CRS with or without polyps. Demographic data, symptom scores, endoscopy scores, and CT scores were then compiled from the initial encounter for each patient. Charts were then retrospectively reviewed for requirement of headache specialist management for symptomatic PHS.

Gender, racial distribution, and need for headache specialist management were compared using a chi-square analysis, while mean age was compared using the unpaired, two-tailed student's *t*-test. Patients in the CRS group with PHS (CRScPHS) requiring headache specialist management were then compared to patients without PHS (CRSsPHS) and PHS alone groups using the Kruskal-Wallis non-parametric analysis of variance (ANOVA). Variables evaluated included overall SNOT-22 scores, Lund-MacKay CT scores, and Lund-Kennedy nasal endoscopy scores. SNOT-22 major domains were divided into Nasal, Aural/Facial, Sleep, and Emotional categories as described by Feng et al. and were also compared between groups.¹³ Post-hoc comparisons were made using Dunn's multiple comparisons test. We then compared mean individual SNOT-22 subdomains

Table 1. International Classification of Headache Disorders (ICHD) Diagnostic Criteria for Headache Attributed to Rhinosinusitis.

Criterion	Description
A)	Frontal headache accompanied by pain in one or more regions of the face, ears, or teeth and fulfilling criteria C and D
B)	Clinical, Nasal endoscopic, CT and/or MRI imaging, and/or laboratory evidence of acute or acute-on-chronic rhinosinusitis
C)	Headache and facial pain develop simultaneously with onset or acute exacerbation of rhinosinusitis
D)	Headache and/or facial pain resolve within 7 days after remission or successful treatment of acute or acute-on-chronic rhinosinusitis

Table 2. Patient Demographics.

Variable	Primary Headache	Chronic Rhinosinusitis	p-Value
Average age (years)	49.8	49.5	0.87
Gender, N (%)			
Female	83 (79.8%)	64 (49.2%)	<0.0001
Male	21 (20.2%)	66 (50.8%)	
Race, N (%)			
Caucasian	67 (64.4%)	74 (56.9%)	0.24
African American	32 (30.8%)	51 (39.2%)	0.18
Asian	3 (2.9%)	2 (1.5%)	0.48
Hispanic	2 (1.9%)	3 (2.3%)	0.84

between the CRS and PHS subgroups. A $p < 0.05$ was considered significant. Receiver operating characteristic (ROC) analyses were then performed using CT and nasal endoscopy scores as well as significant major domains and subdomains discovered on respective ANOVA and t -test analyses to identify predictive diagnostic thresholds.

Results

Demographic Data

There were 104 patients with PHS and 130 patients with CRS. Demographic data comparisons between the two groups can be found in Table 2. There was no significant difference in age or racial distribution between the two groups. However, there were significantly more female patients in the PHS group (79.8%) compared to the CRS group (49.2%, $p < 0.0001$).

Subjective & Objective Clinical Factors

Seventy-five (72.1%) PHS patients required management by a headache specialist compared to only 9 (6.9%) of CRS patients (Figure 1, $p < 0.0001$). ANOVA comparison of CRScPHS patients to CRSsPHS and PHS groups can be found in Table 3. Notably, there was significant difference among ranked median SNOT-22 scores ($p = 0.04$), but these were not statistically significant on post-hoc analysis (Table 4). Ranked

median differences were also significant for the Nasal ($p = 0.01$), Aural/Facial ($p < 0.0001$), and Sleep ($p < 0.0001$) domains. Notably, CRScPHS patients demonstrated significantly higher Aural/Facial domain scores than CRSsPHS patients ($p < 0.0001$) but not when compared to the PHS group ($p = 0.28$). CRScPHS patients demonstrated no significant difference in nasal endoscopy or CT scores compared to CRSsPHS patients. As expected, both CRScPHS and CRSsPHS patients had significantly higher nasal endoscopy and CT scores compared to the PHS group. Upon comparison of mean SNOT-22 subdomains between the CRS and PHS groups, all scores in the Nasal subdomains were also significantly higher in the CRS group except Sneezing and Cough ($p < 0.05$, Figure 2). Meanwhile, PHS patients demonstrated significantly higher total Aural/Facial and Sleep domain scores ($p < 0.0001$) and across all subdomains except Dizziness ($p < 0.05$).

Diagnostic Predictors

ROC analysis of predictive diagnostic factors for presence of PHS or CRS can be found in Table 5. Notably, an Aural/Facial domain cutoff score ≥ 4 carried significant negative predictive value (NPV) of 82.8% for presence of CRS. A nasal endoscopy cutoff score of 4 and CT cutoff score of 2 both carried more robust

Patients Requiring Headache Specialist Management

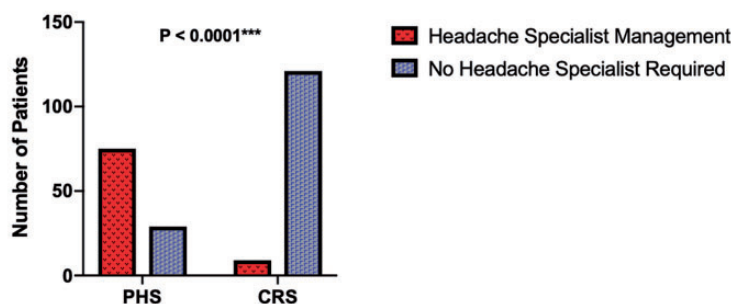


Figure 1. Comparison of primary headache syndrome (PHS) and chronic rhinosinusitis (CRS) patients requiring headache specialist management.

Table 3. Kruskal–Wallis ANOVA for Subjective and Objective Clinical Factors.

Variable, Median (IQR)	PHS (n = 104)	CRSsPHS (n = 121)	CRScPHS (n = 9)	Kruskal–Wallis H	P-value
SNOT-22	46 (34.3–61)	40 (26.5–56)	67 (37.5–77.5)	6.6	0.04
Nasal domain	14 (10–20)	18 (11–26)	14 (11.5–33)	8.5	0.01
Aural/facial domain	13 (8–16)	4 (2–7.3)	13 (8–16)	42.8	<0.0001
Sleep domain	22.5 (14–30)	22 (14.5–33)	22 (14.5–33)	25.3	<0.0001
Emotional domain	1 (0–3)	0 (0–4.5)	0 (0–3)	2.9	0.23
Nasal endoscopy scores	0 (0–2)	6 (4–9)	6 (4–10.5)	128.4	<0.0001
CT scores	0 (0–0)	10 (7–17)	11.5 (9–14)	31.7	<0.0001

ANOVA: Analysis of Variance; IQR: Interquartile Range; PHS: Primary Headache Syndrome; CRSsPHS: Chronic Rhinosinusitis without Primary Headache Syndrome; CRScPHS: Chronic Rhinosinusitis with Primary Headache Syndrome; SNOT: Sinonasal Outcomes Test; CT: Computed Tomography

Table 4. Post-Hoc Comparisons of Subgroups, p-Value.

Variable	CRScPHS vs CRSsPHS	CRScPHS vs PHS	CRSsPHS vs PHS
SNOT-22	0.11	0.52	0.19
Nasal domain	>0.99	0.49	0.02
Aural/facial domain	0.0003	0.28	<0.0001
Sleep domain	0.054	>0.99	<0.0001
Emotional domain	>0.99	>0.99	0.27
Nasal endoscopy scores	>0.99	<0.0001	<0.0001
CT scores	>0.99	0.04	<0.0001

PHS: Primary Headache Syndrome; CRSsPHS: Chronic Rhinosinusitis without Primary Headache Syndrome; CRScPHS: Chronic Rhinosinusitis with Primary Headache Syndrome; SNOT: Sinonasal Outcomes Test; CT: Computed Tomography.

positive and negative predictive value for presence or absence of CRS.

Discussion

In our analysis, we found that PHS patients had similar overall scores on SNOT-22 surveys compared to CRS patients but reported more severe symptoms in the Aural/Facial and Sleep portions of the survey. Meanwhile, CRS patients reported more severe symptoms in the Nasal portion of the SNOT-22 survey, and

had higher nasal endoscopy and CT scores, indicating objectively more severe disease. Additionally, PHS patients were significantly more likely to be female and were more likely to require symptomatic management by a headache specialist. Interestingly, CRScPHS patients demonstrated significantly greater Aural/Facial domain scores compared to CRSsPHS, but otherwise, these patients demonstrated similar overall SNOT-22 and Nasal, Sleep, and Emotional domain scores as well as CT and nasal endoscopy scores. It is also worth noting that 8/9 (89%) CRScPHS patients ultimately required surgery due to failure of medical therapy and severity of sinusitis, while the one nonsurgical patient from this subgroup was offered surgery but failed to follow up.

The overuse of the diagnosis of “sinus headache,” has been documented throughout the literature. In a multi-site study looking at 2,991 patients with either self-diagnosed or physician-diagnosed sinus headache, Schreiber et al. found that 80% of patients were actually diagnosed with migraine with or without aura. An additional 8% of patients were diagnosed with probable migraine.¹⁴ Foroughipour et al. found that of 58 patients diagnosed with “sinus headache” by their primary care physician, only 5% received the final diagnosis of sinusitis following comprehensive otolaryngology examination, while the other 95% were diagnosed with a primary headache syndrome.⁵ The Sinus Allergy and

Comparison of SNOT-22 Domains Between PHS and CRS Groups

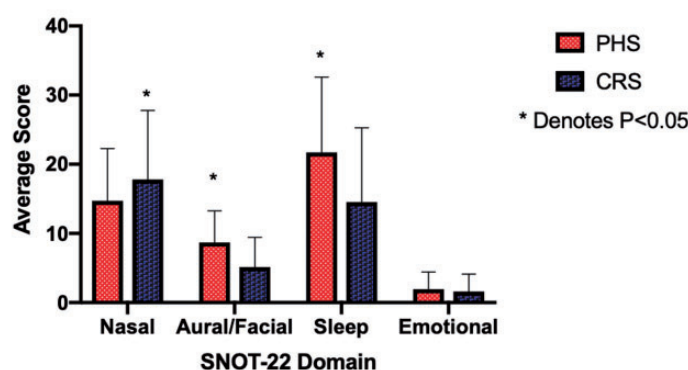


Figure 2. Comparison of SNOT-22 domains between primary headache syndrome (PHS) and chronic rhinosinusitis (CRS) groups. *P-Value < 0.05.

Table 5. Diagnostic Predictors in the CRS and PHS Populations.

Predictor	Cutoff	AUC	NPV	PPV	Sensitivity	Specificity
CRS						
Aural/facial domain	4	0.71	82.8%	58.1%	89.4%	44.2%
CRS/PHS discovery subdomain ratio	0.6	0.77	73.0%	84.7%	71.6%	85.6%
Nasal domain/aural facial + sleep domain ratio	0.7	0.79	73.9%	82.1%	74.4%	81.7%
Nasal endoscopy score	4	0.92	87.5%	86.2%	89.8%	83.2%
Computed tomography score	2	0.99	100.0%	96.4%	100.0%	41.2%
PHS						
PHS/CRS discovery subdomain ratio	1.7	0.81	85.1%	75.0%	84.9%	75.4%
Aural facial + sleep/nasal domain ratio	1.4	0.8	82.4%	75.0%	81.0%	76.7%

CRS: Chronic rhinosinusitis; PHS: Primary headache syndrome; AUC: Area under receiver operating characteristic curve; NPV: Negative Predictive Value; PPV: Positive Predictive Value.

CRS Discovery Subdomains: Loss of Smell or Taste, Thick Discharge, Runny Nose, Post-Nasal Discharge, Need to Blow Nose.

PHS Discovery Subdomains: Facial Pain/Pressure, Difficulty Falling Asleep, Ear Pain, Lack of Sleep, Fatigue, Wake up Tired, Reduced Productivity, Frustrated/Restless/Irritable, Reduced Concentration.

Migraine Study (SAMS) analyzed 100 consecutive patients who were self-diagnosed with “sinus headache.”¹⁵ Using ICHD criteria, they diagnosed 86% of patients with migraine or probable migraine, while only 3% were diagnosed with headache secondary to rhinosinusitis. More broadly, facial pain itself has been found to be a poor predictor of the extent of objective sinus disease,^{16,17} and Hirsch et al. found that eliminating facial pain, ear pain, dental pain, and headache from Rhinosinusitis Task Force Guidelines increased specificity from 37.1% to 65.1% when compared to the “gold standard” of endoscopy or CT, without a significant decrease in sensitivity.¹⁸

It should be noted that the presence of PHS does not exclude the possibility of having sinusitis as a source of symptoms. Mehle and Kremer reported that 20% of the patients in their study diagnosed with migraines had a Lund-MacKay score ≥ 5 resulting in significant sinus disease.¹⁹ Lal et al. looked at 211 patients who presented to

a rhinology clinic for sinus-related headache, pressure, pain, or fullness and found that 27.96% had combined rhinologic and neurologic disease present.²⁰ Because of the possibility of concurrent pathologies, Patel et al. recommended that patients presenting to otolaryngologists with sinogenic symptoms undergo thorough head and neck examination, including neurologic exam, nasal endoscopy, CT scan, application of ICHD criteria, and high clinical suspicion for migraine diagnosis.²¹ Our findings are in keeping with these recommendations, as 6.9% of CRS patients were also ultimately diagnosed with PHS and required headache specialist management. Importantly, this subgroup of patients was distinguished from CRSsPHS patients by their significantly higher Aural/Facial domain scores.

Part of the confounding picture between PHS and CRS is the presence of overlapping symptoms between the two diseases, such as lacrimation, nasal congestion, and rhinorrhea. Barbanti et al. looked at 177 consecutive

patients diagnosed with migraine headaches and found that 45.8% exhibited unilateral associated cranial autonomic symptoms.²² The SAMS study found that 75% of patients diagnosed with migraines reported autonomic symptoms during headaches, with half of the patients experiencing more than one symptom.¹ In Schreiber et al.'s study of 2,991 patients, the most common symptoms at presentation were moderate/severe pain (97%), pulsing/throbbing headache (89%), and discomfort worsened by activity (85%). The most common paranasal sinus symptoms were sinus pressure (84%), sinus pain (82%), and nasal congestion (63%).¹⁴ Foroughipour et al. found that the most common symptoms in patients with previously diagnosed "sinus headache" were sinus tenderness (70%), phonophobia (67%), photophobia (62%), and post-nasal discharge (39%).⁵

In a study related to ours, Lal et al. used the SNOT-22 on 46 patients diagnosed with PHS and found that 93.5% of patients reported the "need to blow nose", 86.9% reported postnasal drainage.²³ They used cluster analysis to help define symptoms and found that approximately two-thirds of patients formed a cluster of psychosocial items tightly associated with facial pain and pressure. In another study that included the senior author of this paper, Perry et al. examined 100 patients referred to a rhinologist with the complaint of headache but with normal CT and endoscopic evaluations.²⁴ They found SNOT-20 scores to be significantly higher in the group of patients diagnosed with PHS than in patients who had a minor complaint of headache or no headache (24.1 versus 14.6 and 12.4, respectively). In a recent well-designed study of 1,136 patients that is similar to ours, Wu et al. utilized ROC analysis to determine that a ratio of Aural/Facial domain to Nasal domain scores of 0.66, Facial Pressure/Pain subcategory score of 3.5, and Aural/Facial total domain score greater than 7.5 all strongly negatively predict the presence of CRS.²⁵ We similarly found an Aural/Facial cutoff ≥ 4 to negatively predict presence of CRS. Additionally, ratios comparing Nasal, Aural/Facial, and Sleep domains as well as summed discovery subdomains were found to positively and negatively predict presence of CRS and PHS, respectively. However, the clinical utility of these ratios remains relatively limited for the practicing otolaryngologist or primary care clinician. Most importantly, the positive and negative predictive values of a nasal endoscopy score of 4 and CT score of 2 were much more robust for predicting presence or absence of CRS. The value of a thorough otolaryngologic evaluation for CRS cannot, therefore, be overstated.

Our study's strength lies in its use of validated subjective patient survey (SNOT-22) scores, CT scores, and nasal endoscopy scores to delineate differing features between CRS and PHS. The major limitation of this study is that our CRS control group consists of patients

diagnosed with CRS, regardless of presenting chief complaint. Additionally, the use of survey data collected at the time of initial consultation likely results in some degree of sampling bias within our study population due to the potential heterogeneity of prior workup and treatment. Another limitation is the use of an outcome measure (SNOT-22) that was designed for use in sinonasal pathology. However, in our practice, every patient with sinonasal symptoms referred for possible CRS complete the SNOT-22 survey. Although the outcomes instrument total score was originally validated for CRS only, its completion requires the patients rate individual symptoms from 0 to 5, giving us the opportunity to evaluate individual symptom severity regardless of diagnosis. It is of significant clinical value, therefore, to note the individual scale differences in patient complaints between CRS and PHS groups.

Conclusions

Patients with PHS are more likely to present with complaint of severe symptoms in the Aural/Facial and Sleep domains of the SNOT-22 survey, while CRS patients typically present with more severe symptoms in the Nasal domain. If patient symptoms seem to be rated out of proportion to nasal endoscopy and imaging findings, the diagnosis of PHS should be suspected. Presence of PHS, however, does not exclude sinonasal pathology, and a complete otolaryngology exam should be completed on every patient who presents with the complaint of "sinus headache."

Authors' Note

Presentation: A portion of this data was presented at the Combined Sections Meeting of the Triological Society (Southern Section) in Coronado Island, California, USA on January 23, 2015.

Declaration of Conflicting Interests

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ORCID iD

Daniel D. Sharbel  <https://orcid.org/0000-0001-5466-2630>

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