# Acute radiology rarely confirms sinus disease in suspected recurrent acute rhinosinusitis

Henry P. Barham, MD<sup>1,2</sup>, Alexander S. Zhang, MBBS<sup>2</sup>, Jenna M. Christensen, PhD<sup>2</sup>, Raymond Sacks, MD<sup>2,3,4</sup> and Richard J. Harvey, MD<sup>2,3</sup>

**Background:** Episodic or recurrent sinonasal symptoms are often suspected as "sinus" in origin. With normal sinus radiology between events, the diagnosis of recurrent acute rhinosinusitis (RecARS) is made. However, other conditions can produce episodic symptoms. In this study we analyze acutely performed computed tomography (CT) in a population with suspected or self-diagnosed "sinus" disease.

**Methods:** Patients referred to a tertiary clinic for suspected RecARS were assessed. Sinus changes were defined by CT (initial assessment) and during the acute event, by a semiurgent CT performed during the symptomatic episode. Mucosal thickening, ostiomeatal compromise, and severe septal deformity were recorded. Symptom profile was assessed during both time-points with the 22-item Sino-Nasal Outcome Test (SNOT-22).

**Results:** Forty-eight patients  $(49.5 \pm 14.7 \text{ years of} age, 70.8\% \text{ female})$  were assessed. At presentation, 75% were resolute in a diagnosis of "sinus." Baseline Lund-Mackay scores were <6 (median O [interquartile range 1]). Ostiomeatal compromise was 6.8% left and 4.5% right at baseline. Of the patients who returned for acute CT (n = 27), SNOT-22 and subdomains were similar to baseline.

Septal deviation was similar (13.6% vs 15.3%). Acutely, ostiomeatal compromise was 0% left and 7.4% right (n = 2). Of these 2 patients with ostiomeatal compromise, 1 was diagnosed with RecARS (4%) and the other with triptanresponsive migraine, with incidental sinus changes. Final diagnosis was rhinitis (47%), headache/migraine (37%), and facial pain otherwise undefined (12.5%).

**Conclusion:** Patients with a history of "recurrent acute sinusitis" and normal CT scans between episodes rarely have abnormal CT findings during acute exacerbations of symptoms. Antibiotics and surgical intervention are often inappropriate in this population. © 2017 ARS-AAOA, LLC.

#### Key Words:

migraine; radiology; recurrent acute; rhinitis; rhinosinusitis; SNOT-22

#### How to Cite this Article:

Barham HP, Zhang AS, Christensen JM, Sacks R, Harvey RJ. Acute radiology rarely confirms sinus disease in suspected recurrent acute rhinosinusitis. *Int Forum Allergy Rhinol.* 2017;XX:1-8.

A cute rhinosinusitis is a well-defined entity and resolves within 12 weeks, usually in <2 weeks.<sup>1</sup> It can

Received: 28 August 2015; Revised: 1 November 2016; Accepted: 15 November 2016 DOI: 10.1002/alr.21925

View this article online at wileyonlinelibrary.com.

1

be either simple viral rhinosinusitis or have a bacterial component.<sup>2</sup> Inflammatory sinus changes completely resolve after these events. However, in a situation where recurrent sinus inflammation occurs in the absence of chronic changes, recurrent acute rhinosinusitis has been used to describe this clinical entity. Recurrent acute rhinosinusitis (RecARS) is estimated to affect 1 in 3000 Western adults.<sup>1</sup> Although debate exists regarding its true existence as a diagnosis, RecARS is characterized by self-limited, distinct episodes of rhinosinusitis, lasting <4 weeks, separated by asymptomatic and radiologically normal periods. The exact number of episodes required for a diagnosis of RecARS remains in question, but recent guidelines suggest  $\geq$ 4 attacks per year to be clinically significant.<sup>3</sup> Despite its estimated prevalence, RecARS remains poorly studied, but local ostiomeatal anatomy is often implicated in the pathogenesis. Recently, its diagnosis, having been incorporated into clinical guidelines concerning the management of

<sup>&</sup>lt;sup>1</sup> Sinus and Nasal Specialists of Louisiana, Baton Rouge, LA; <sup>2</sup>Rhinology and Skull Base Research Group, St. Vincent's Centre for Applied Medical Research, University of New South Wales, Sydney, NSW, Australia; <sup>3</sup> Australian School of Advanced Medicine, Macquarie University, Sydney, NSW, Australia; <sup>4</sup> Department of Otolaryngology, University of Sydney, Sydney, NSW, Australia

Correspondence to: Henry P. Barham, MD, Sinus and Nasal Specialists of Louisiana, 8585 Picardy Avenue, Suite 512, Baton Rouge, LA 70809; e-mail: hbarham@sinusandnasalspecialist.com

Additional Supporting Information may be found in the online version of this article.

Potential conflict of interest: None provided.

Presented at the Annual ARS meeting at the AAOHNS, on September 25–27, 2015, in Dallas, TX.

adult sinusitis,<sup>3</sup> has been revised due to the paucity of data relating to the condition. <sup>2</sup> Recent systematic reviews of medical therapy for RecARS have shown no evidence for the use of oral antibiotics and limited evidence for intranasal corticosteroids.<sup>4, 5</sup> Only a small group of studies of surgical treatment, without controls, have shown improvement in the quality of life of patients undergoing surgery for RecARS.<sup>6,7</sup> A significant gap exists in our understanding of the pathogenesis of RecARS, and this paucity of research poses unanswered clinical questions and may potentially alter the management of patients with suspected RecARS, especially with regard to involvement of the ostiomeatal complex.

In this study we sought to assess the acute radiologic changes, symptom profile, and diagnosis of patients in suspected or self-diagnosed RecARS.

## Patients and methods

#### Study design

A case-series study of consecutive patients over a 6-year period undergoing evaluation of suspected RecARS was performed.

Patients were assessed at their baseline/initial clinical presentation with computed tomography (CT) imaging and symptom profile. The patients were then asked to return during the acute symptomatic episode for a clinical and radiologic assessment. For this study we obtained ethics approval from the St. Vincent's institutional ethics review board (SVH 09/083).

#### Patient population

Adult patients ( $\geq$ 18 years) with suspected RecARS, who were seen in a tertiary referral clinic were reviewed. Patients were considered to be eligible for the diagnosis of RecARS according to clinical practice guidelines on adult sinusitis.<sup>3</sup> To have a history of recurrent episodes, patients were required to have had at least 4 acute symptomatic events per year.

Nasoendoscopic assessment of patients at baseline/initial evaluation were required to be normal for inclusion in the study. In addition, these patients had "near-normal" CT assessments. "Near normal" was defined as incidental mucosal changes that were not consistent with any diagnosis.<sup>8</sup> As the diagnosis was in doubt, no treatment was instigated during the time between the initial review and subsequent evaluations.

Patients were excluded from study participation if they were <18 years of age; had been treated for diagnosis of chronic rhinosinusitis, defined according to the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS)<sup>2,9</sup>; or had systemic illnesses affecting nasal mucosa, such as immunodeficiency, cystic fibrosis, granulomatous conditions, or vasculitis.

Demographic data were recorded for age, gender, smoking status, and clinically relevant comorbidities,

including asthma and aspirin hypersensitivity. Smoking status was defined as current regular use or within past 12 months. Asthma was defined as having clinical symptoms of a chronic inflammatory disorder of the lower airways confirmed by spirometry testing.

#### Acute episode assessment

Patients were asked to return for an "acute review" during the period of their symptomatic episode. All patients were offered assessments within 24 hours of their symptoms. Those patients returning for assessment during their symptomatic episodes underwent CT imaging and questionnaire evaluation.

#### Radiologic assessment

CT scans were assessed by 2 fellowship-trained rhinologists, 1 with radiology licensing and training. Mucosal thickening, ostiomeatal compromise, and severe septal deformity were recorded. The Lund-Mackay score was used to evaluate CT imaging at all time-points.<sup>10</sup> Endoscopy was used to assess/confirm any positive radiologic Ostiomeatal complex (OMC) changes.

#### Symptom assessment

All patients' presenting symptom was recorded. The validated 22-item Sino-Nasal Outcome Test (SNOT-22) was used for disease-specific quality-of-life assessment.<sup>11</sup> SNOT-22 subdomain scores were also evaluated including: rhinitis score (5 questions): need to blow nose, sneezing, runny nose, postnasal discharge, and thick nasal discharge; sleep score (4 questions): difficulty falling asleep, waking up at night, lack of a good night's sleep, and fatigue; ear/facial symptom (4 questions): ear fullness, dizziness, ear pain, and facial pain/pressure; psychological score (5 questions): reduced productivity, reduced concentration, frustration/restlessness/irritability, sadness, and embarrassment; and sinus score (5 questions): nasal obstruction, thick discharge, need to blow nose, smell loss, facial pain. SNOT-22 and nasal symptom score (NSS) were reported as mean results for each measure.

#### **Final diagnosis**

The final diagnosis after assessment was determined by the senior author of this study with headache diagnoses closely following the International Headache Criteria (IHC).<sup>12</sup>

Migraine was defined by:

- A. At least 5 attacks fulfilling criteria B-D.
- B. Headache attacks lasting 4 to 72 hours (untreated or unsuccessfully treated).
- C. Headache with at least 2 of the following 4 characteristics:
  - 1. Unilateral location.
  - 2. Pulsating quality.
  - 3. Moderate or severe pain intensity.

- 4. Aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)
- D. During headache at least 1 of the following:
  - 1. Nausea and/or vomiting.
  - 2. Photophobia and phonophobia.

Tension headache was defined as:

- A. Headache lasting from 30 minutes to 7 days.
- B. At least 2 of the following 4 characteristics:
  - 1. Bilateral location.
  - 2. Pressing or tightening (nonpulsating) quality.
  - 3. Mild or moderate intensity.
  - 4. Not aggravated by routine physical activity such as walking or climbing stairs.
- C. Both of the following:
  - 1. No nausea or vomiting.
  - 2. No more than one of photophobia or phonophobia.

Cluster headache was defined as:

- A. Severe unilateral orbital, supraorbital, and/or temporal pain in durations of up 7 days with episodes lasting 2 to 30 minutes.
- B. At least 1 of the following symptoms or signs, ipsilateral to the pain:
  - 1. Conjunctival injection and/or lacrimation.
  - 2. Nasal congestion and/or rhinorrhea.
  - 3. Eyelid edema.
  - 4. Forehead and facial sweating.
  - 5. Forehead and facial flushing.
  - 6. Sensation of fullness in the ear.
  - 7. Miosis and/or ptosis.
- C. Attacks have a frequency above 5 per day for more than half of the time.
- D. Attacks prevented absolutely by therapeutic doses of indomethacin.
- E. Not better accounted for by another.

The diagnosis of barosinusitis was made based on a temporal association of sinus cavity pressure differential with sinus pain during domestic or international air travel on the descent only. The diagnosis of reflux rhinitis was made in patients with symptoms of gastroesophageal reflux disease who had presenting sinonasal complaints responding to antireflux interventions.

#### Statistical analysis

Statistical analysis was performed using IBM SPSS version 22.0 (IBM, Armonk, NY). The mean values for radiographic and symptom scores were compared across time-points using the Student *t* test (2-tailed) for comparisons of parametric data. The prevalence of related comorbidities and frequency of previous surgical procedures was also compared across treatment cohorts using Pearson chi-square analysis for relationships of nominal variables. Results were considered significant at p < 0.05.

#### TABLE 1. Follow-up demographics

	Returned for acute review	Lost to follow- up	p value
Number	27	21	
Age (years)	50.4	48.3	0.769
Gender (% female)	63	81	0.214
Asthma (%)	40.7	33.3	0.765
Smokers (%)	7.4	0	0.497
Prior surgery (%)	44.4	38.1	0.771

## Results

### Demographics

Forty-eight patients,  $49.5 \pm 14.7$  years of age and 70.8% female, were assessed. Of these patients, 4.3% were smokers and 37.5% were diagnosed and treated with asthma medication. Also, 41.7% had undergone prior sinonasal surgery (Figure 1). Twenty-seven patients (n = 27) returned for evaluation during a subsequent symptomatic episode. The average age of this group was  $50.4 \pm 14.5$  years, 62.9%were female, 7.4% were smokers, 40.7% were diagnosed with asthma, and 44.4% has undergone prior sinus surgery (Table 1). There was no significant difference in any of these characteristics between the patients who returned for acute evaluation and those who did not return.

#### **Baseline presentation**

At presentation, 75% were resolute that their presenting complaint was "sinus." Radiologically, baseline Lund-Mackay scores were <6 in all but 1 patient (median 0 [interquartile range 1]) (Figure 2A and B). Ostiomeatal compromise was present 6.8% on the left and 4.5% on the right at baseline. Baseline nasoendoscopy between symptomatic episodes was normal in all patients.

#### Acute symptomatic period

Of the patients who returned for evaluation during a subsequent symptomatic episode (n = 27), radiologically, acute ostiomeatal compromise was present 0% on the left and 7.4% (n = 2) on the right.

Total SNOT-22 and subdomains were similar to baseline (Figure 3A and B) and all showed no significant difference on paired *t* test. Septal deviation was similar between baseline and acute review (13.6% vs 15.3%). Final diagnosis was rhinitis (47%), headache/migraine (37%), and facial pain otherwise undefined (12.5%) (Figure 4).

#### Patients with evidence of OMC compromise

Of the 2 patients with ostiomeatal compromise, 1 was a 60-year-old man with nasoendoscopy confirming the presence of acute inflammation. He was diagnosed with





FIGURE 1. Prior sinus surgery.

RecARS (4%) and was offered surgery, but found relief of symptoms with flixonase nasal drops during his acute symptomatic periods and declined further intervention.

The second patient was a 68-year-old woman with triptan-responsive pain and facial pressure. CT also showed right maxillary mucosal thickening, but this did not correspond with the distribution of facial pain. With endoscopy not confirming acute inflammatory changes, the CT findings were considered an incidental result and the patient was diagnosed with a migraine.

#### Discussion

The diagnosis and optimal treatment for RecARS continues to be debated. A recent systematic review of all evidencebased studies concluded that there is a lack of evidence available to support the use of short-course antibiotic therapy for acute rhinosinusitis when it occurs in isolation or as a recurrent disease complex.<sup>4</sup> Similarly, there is little evidence with regard to use of intranasal corticosteroids,<sup>5</sup> and the role of surgical therapy is even less well studied. Most importantly, the pathoetiologic factors are not well defined in this condition. In true sinonasal disease, simple obstruction of sinus ostia and impaired mucociliary function does not bring about ARS in humans or animal models. Although upper respiratory viral infection has been shown to be associated with respiratory epithelial loss, severity of symptoms appears to be independent of epithelial damage.<sup>13</sup> Chronic changes, such as remodeling of the mucosa (squamous metaplasia, basement membrane thickening, subepithelial fibrosis, and neo-osteogenesis), can occur and are often present in patients with chronic sinus dysfunction,<sup>14</sup> but these patients have CRS and *not* RecARS, where the anatomy returns to normal in between episodes.

If we are more strict on the physician diagnosis of ARS, and reinforce this to patients, then it is less likely that the erroneous diagnosis of "sinusitis" would be made. However, the diagnosis of ARS is still poorly defined. The EPOS 2012 defines it as persistent symptoms or worsening after 5 days. Although the definition of acute sinusitis requires symptoms of >10 days, the vast majority of patients in this population did not have recurrent acute sinusitis as their underlying pathology. The patient population that we aimed to characterize is those with self-diagnosed or suspected recurrent acute rhinosinusitis. Most patients



FIGURE 2. (A) Baseline Lund-Mackay CT score. (B) Acute Lund-Mackay CT score. CT = computed tomography.

anecdotally have symptoms for <7 days and usually see their primary care provider and receive interventions within that period. Recurrent symptoms were defined in the study population as  $\geq 4$  acute episodes per year. Baseline nasoendoscopy between symptomatic episodes was normal in all patients. The current guidelines from EPOS 2012 show that acute bacterial rhinosinusitis (ABRS) is suggested by the presence of at least 3 symptoms/signs of:

• Discolored discharge (with unilateral predominance) and purulent secretion in the nasal cavity.





FIGURE 3. (A) Baseline SNOT-22. (B) Acute SNOT-22. SNOT-22 = 22-item Sinonasal Outcome Test.

- Severe local pain (with unilateral predominance).
- Fever (>38°C).
- Elevated erythrocyte sedimentation rate/C-reactive protein (ESR/CRP).
- "Double sickening" (ie, a deterioration after an initial milder phase of illness).
- Symptoms worsening after 5 days or persistent after 10 days.

Steadfast patient beliefs play a large role in driving treatment. Education regarding the appropriate use of antibiotics in upper respiratory tract infections, although effective in changing the practice of healthcare providers,<sup>15</sup> has not been shown to have a significant effect on limiting antibiotic use when applied to patients.<sup>16</sup> The perceived association of discolored or "purulent" secretions with bacterialinfection places pressure on physicians to prescribe antibiotics for acute "sinus" events. Neutrophils give rise to greenishyellow-colored respiratory secretions through the green, heme-containing myeloperoxidase protein contained in cytoplasmic granules.<sup>17, 18</sup> The accumulation of neutrophils in respiratory mucosa and the presence of discolored secretions, however, have been shown to be of viral, rather than bacterial, origin in the majority of upper respiratory tract infections.<sup>19</sup> There can be more than a 1000-fold increase in the nasal concentration of neutrophils in viral



FIGURE 4. Final diagnosis.



FIGURE 5. XXXXXXXXX.

7

upper respiratory tract illness.<sup>20</sup> Antibiotics are therefore not necessarily required for treatment of acute sinonasal disease, even in the presence of purulent discharge.

Sinusitis is defined as an inflammatory event and is associated with additional mucosal-based symptoms, including mucous production, discharge, and smell loss.<sup>3</sup> Intermittent or episodic symptoms are rarely sinus in origin. There was no significant difference between baseline and acute SNOT-22 subdomains in this study and this may be reflective of the lack of specific inflammatory changes in the sinonasal mucosa in the cohort. Facial pain or pressure, rather than mucosal symptoms, was often the presenting complaint on acute review. The nonsignificant difference for SNOT-22 subdomains containing facial pain/pressure is difficult to explain but may be a result of the limited study size.

RecARS has a significant disease burden. A recent study estimated that the condition incurs an average direct healthcare cost of \$1091 per annum and results in 4.2 lost work-days per year.<sup>1</sup> The condition remains poorly studied and there is a paucity of data regarding the additional burdens associated with misdiagnosis and inappropriate antibiotic use.

A recent study looking at the use of CT scan in patients presenting with suspected chronic rhinosinusitis with negative nasoendoscopic findings showed a cost benefit for upfront CT scan prior to starting therapy.<sup>21</sup> Although specific to patients with chronic rather than recurrent sinonasal complaints, the study supports the view that there are many alternate diagnoses that could account for chronic "sinuslike" symptoms.

In this study, only 4% of patients had both acute CT imaging and nasoendoscopy confirming the diagnosis of RecARS. The single patient with a final diagnosis of RecARS was treated successfully with intermittent flixonase nasal drops with resolution of symptoms. The most common final diagnoses were rhinitis (47%) and headache (37%), of which 27% were diagnosed as migraine via resolution of symptoms with triptan therapy. Although

7

#### References

- Bhattacharyya N, Grebner J, Martinson NG. Recurrent acute rhinosinusitis: epidemiology and health care cost burden. Otolaryngol Head Neck Surg. 2012;146:307–312.
- Fokkens WJ, Lund VJ, Mullol J, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2012. *Rhinol Suppl.* 2012:3 p preceding table of contents, 1–298.
- Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (update): adult sinusitis. Otolaryngol Head Neck Surg. 2015;152(Suppl): S1–39.
- Kaper NM, Breukel L, Venekamp RP, Grolman W, van der Heijden GJ. Absence of evidence for enhanced benefit of antibiotic therapy on recurrent acute rhinosinusitis episodes: a systematic review of the evidence base. Otolaryngol Head Neck Surg. 2013;149: 664–667.
- van Loon JW, van Harn RP, Venekamp RP, Kaper NM, Sachs AP, van der Heijden GJ. Limited evidence for effects of intranasal corticosteroids on symptom relief for recurrent acute rhinosinusitis. Otolaryngol Head Neck Surg. 2013;149:668–673.
- Poetker DM, Litvack JR, Mace JC, Smith TL. Recurrent acute rhinosinusitis: presentation and outcomes of sinus surgery. Am J Rhinol. 2008;22:329–333.

CT scan performed during symptomatic episodes was extremely useful in providing a definitive diagnosis, it may not be practical or financially viable in the majority of treatment centers. Our study highlights the need for caution prior to engaging in intervention, particularly endoscopic sinus surgery, in any patient referred for suspected RecARS. The population studied was from a tertiary center and the rate of "true" RecARS may be higher in a community-based practice. However, it is likely that the rate of alternate diagnoses is still very high.

## Conclusion

Episodic or recurrent sinonasal symptoms are often suspected as "sinus" in origin. With normal sinus radiology between events, the diagnosis of RecARS is made. However, other conditions can produce episodic symptoms, such as rhinitis and migraine. Most patients with episodic "sinus" disease have rhinitis or migraine as their diagnosis. RecARS is an uncommon event even in patients steadfast in their beliefs.

- Costa ML, Psaltis AJ, Nayak JV, Hwang PH. Medical therapy vs surgery for recurrent acute rhinosinusitis. *Int Forum Allergy Rhinol.* 2015;5:667–673.
- Ashraf N, Bhattacharyya N. Determination of the "incidental" Lund score for the staging of chronic rhinosinusitis. Otolaryngol Head Neck Surg. 2001;125: 483–486.
- Fokkens WJ, Lund VJ, Mullol J, et al. European Position Paper on Rhinosinuisitis and Nasal Polyps 2007. *Rhinol Suppl*. 2007;20:1–136.
- Lund VJ MI. Staging in rhinosinusitis. *Rhinology*. 1993;31:183–184.
- Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item Sinonasal Outcome Test. *Clin Otolaryngol.* 2009;34:447–454.
- The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013; 33:629–808.
- Turner RB, Hendley JO, Gwaltney JM Jr. Shedding of infected ciliated epithelial cells in rhinovirus colds. J Infect Dis. 1982;145:849–853.
- Barham HP, Osborn JL, Snidvongs K, Mrad N, Sacks R, Harvey RJ. Remodeling changes of the upper airway with chronic rhinosinusitis. *Int Forum Allergy Rhinol.* 2015;5:65–572.

- Razon Y, Ashkenazi S, Cohen A, et al. Effect of educational intervention on antibiotic prescription practices for upper respiratory infections in children: a multicentre study. J Antimicrob Chemother. 2005;56: 937–940.
- Taylor JA, Kwan-Gett TS, McMahon EM Jr. Effectiveness of a parental educational intervention in reducing antibiotic use in children: a randomized controlled trial. *Pediatr Infect Dis J*. 2005;24:489–493.
- Fenna R, Zeng J, Davey C. Structure of the green heme in myeloperoxidase. Arch Biochem Biophys. 1995;316:653–656.
- Schultz J, Kaminker K. Myeloperoxidase of the leucocyte of normal human blood. I. Content and localization. Arch Biochem Biophys. 1962;96:465–467.
- Winther B, Brofeldt S, Gronborg H, Mygind N, Pedersen M, Vejlsgaard R. Study of bacteria in the nasal cavity and nasopharynx during naturally acquired common colds. *Acta Otolaryngol*. 1984;98:315–320.
- Naclerio RM, Proud D, Lichtenstein LM, et al. Kinins are generated during experimental rhinovirus colds. J Infect Dis. 1988;157:133–142.
- Leung R, Kern R, Jordan N, et al. Upfront computed tomography scanning is more cost-beneficial than empiric medical therapy in the initial management of chronic rhinosinusitis. *Int Forum Allergy Rhi*nol. 2011;1:471–480