Accuracy of Signs and Symptoms for the Diagnosis of Acute Rhinosinusitis and Acute Bacterial Rhinosinusitis

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ABSTRACT

PURPOSE To evaluate the accuracy of signs and symptoms for the diagnosis of acute rhinosinusitis (ARS).

METHODS We searched Medline to identify studies of outpatients with clinically suspected ARS and sufficient data reported to calculate the sensitivity and specificity. Of 1,649 studies initially identified, 17 met our inclusion criteria. Acute rhinosinusitis was diagnosed by any valid reference standard, whereas acute bacterial rhinosinusitis (ABRS) was diagnosed by purulence on antral puncture or positive bacterial culture. We used bivariate meta-analysis to calculate summary estimates of test accuracy.

RESULTS Among patients with clinically suspected ARS, the prevalence of imaging confirmed ARS is 51% and ABRS is 31%. Clinical findings that best rule in ARS are purulent secretions in the middle meatus (positive likelihood ratio [LR+] 3.2) and the overall clinical impression (LR+ 3.0). The findings that best rule out ARS are the overall clinical impression (negative likelihood ratio [LR–] 0.37), normal transillumination (LR– 0.55), the absence of preceding respiratory tract infection (LR– 0.48), any nasal discharge (LR– 0.49), and purulent nasal discharge (LR– 0.54). Based on limited data, the overall clinical impression (LR+ 3.8, LR– 0.34), cacosmia (fetid odor on the breath) (LR+ 4.3, LR– 0.86) and pain in the teeth (LR+ 2.0, LR– 0.77) are the best predictors of ABRS. While several clinical decision rules have been proposed, none have been prospectively validated.

CONCLUSIONS Among patients with clinically suspected ARS, only about one-third have ABRS. The overall clinical impression, cacosmia, and pain in the teeth are the best predictors of ABRS. Clinical decision rules, including those incorporating C-reactive protein, and use of urine dipsticks are promising, but require prospective validation.

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INTRODUCTION

Acute rhinosinusitis (ARS) is defined as inflammation of the paranasal sinuses, most often the maxillary sinuses, that is caused by viruses or bacteria and has a duration of less than 6 weeks.[1] Acute rhinosinusitis is a common outpatient infection, responsible for over 3 million outpatient visits annually in the United States; the symptoms overlap considerably with that of other upper respiratory tract infections, making accurate diagnosis challenging.[2] While 75% of patients with ARS receive an antibiotic, and it is the most common reason for outpatient prescription of antibiotics,[2,3] only about one-third with sinus symptoms have a confirmed bacterial pathogen when sinus fluid is cultured.[4,5]

Helping physicians more accurately identify which patients with clinically suspected sinusitis actually have acute bacterial rhinosinusitis (ABRS) could reduce harm from inappropriate antibiotic use. A systematic review found a 5% absolute increase in the rate of cure with antibiotics for clinically diagnosed ARS, compared with an 11% increase in rate of cure with imaging-diagnosed ARS; more accurate clinical diagnosis could identify the patients most likely to benefit from antibiotics.[6] Previ-

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ous systematic reviews of the clinical diagnosis of ARS are all more than 15 years old and did not use modern analytic techniques such as bivariate meta-analysis.[7-10] The goal of the current study is therefore to perform a comprehensive meta-analysis of the clinical diagnosis of ARS and ABRS.

METHODS

Search Strategy

PubMed and Embase were searched using terms for acute rhinosinusitis and diagnostic testing (see Supplemental Table 1, available at http://www.AnnFamMed.org/content/17/2/164/suppl/DC1/, for search strategy).[11] A separate search was performed to identify studies that assessed inter-rater agreement of signs and symptoms of sinusitis. PubMed was searched using the search terms ("inter-rater" OR "interrater" OR "kappa") AND ("sinusitis" OR "sinus"). The primary searches occurred in 2017, and were updated in April, 2018.

Inclusion Criteria And Quality Assessment

We included studies of adults and children with suspected ARS or acute respiratory tract infection that reported data for the accuracy of at least 1 sign or symptom. One study[12] included patients with a clinical diagnosis of ARS for whom their physician recommended antibiotics, but the results were similar to those of studies with broader inclusion criteria. All studies took place in the outpatient setting and used radiography, ultrasound, computed tomography (CT), or antral puncture as the reference standard. We included studies in which all patients received the same reference standard. Studies involving highly specialized patient populations (ie, patients with HIV or odontogenic sinusitis, children with brain cancer, or inpatients) were excluded. There were no limits by date of publication or language.

Where studies reported findings separately by maxillary, frontal, or ethmoid sinus, only maxillary sinus findings are shown. Where individual sinuses as well as results by person are reported, results by person are shown. When it was possible to use different cut points (definitions of abnormal) for a test or reference standard, the cut point that yielded the highest diagnostic odds ratio (DOR) was selected.[13,14] Where data were reported for 2 time periods (ie, any fever or fever in the last 24 hours) we included the most recent time period in relation to the visit. Where results for more than 1 reference standard were reported for the same set of patients, data for the highest quality reference standard are reported (in descending order: positive bacterial culture of antral puncture fluid, antral puncture revealing purulent fluid, magnetic resonance imaging [MRI], CT, ultrasound, and finally radiography).[4,15-18] Acute rhinosinusitis was diagnosed when any reference standard was abnormal, and acute bacterial rhinosinusitis when inspection of antral puncture fluid or culture of puncture fluid were consistent with bacterial infection.[4,5]

To evaluate study quality, we used the Quality Assessment of Diagnostic Accuracy Studies 2 criteria, adapted for the diagnosis of acute rhinosinusitis (Supplemental Table 2).[19] Studies were classified as low risk of bias if all 4 domains were all judged to be low risk of bias. Studies with only a single domain at high risk of bias were classified as moderate risk of bias, and all other studies were classified as high risk of bias.

Data Extraction and Analysis

Each included study was reviewed by 2 investigators, who extracted data regarding study quality and the accuracy of signs and symptoms. Any discrepancies were resolved by discussion to achieve consensus, involving a third investigator if necessary. We used the MADA package in R version 3.2.2 (R Project for Statistical Computing) to perform bivariate meta-analysis for each clinical sign or symptom, and the META package to calculate summary estimates of prevalence. We determined the prevalence of sinusitis for subgroups by age and reference standard using a random effects summary measure. Summary measures of accuracy are reported for each sign or symptom. The positive likelihood hood ratios (LR+) and negative likelihood ratios (LR–) were the primary measures of diagnostic accuracy. A likelihood ratio (LR) near 1.0 means that the test adds little diagnostic information, LRs greater than 1 increase the likelihood of disease, and LRs less than 1 decrease the likelihood of disease.[20] The DOR (LR+ divided by LR–) was chosen as an overall measure of discrimination because the small numbers of studies made receiver operating characteristic curves unstable and difficult to interpret in many cases.

RESULTS

We identified 1,638 studies after removing duplicates. We also searched the reference lists of previous meta-analyses, review articles, and practice guidelines for additional articles, finding an additional 11 studies. A total of 1,649 abstracts were screened by 2 reviewers for relevance, 182 full-text articles were accessed, and a final total of 17 studies met our inclusion criteria (Supplemental Figure 1).

Study Characteristics

The characteristics of the 17 included studies are summarized in Table 1. Six were small (fewer than 100 participants), with a range of 30 to 400 participants. The

Table 1. Characteristics of Included Studies (N = 17)

Study	Population	Age Data	Reference Standard	Country	Risk of Bias
Referral setting (ENT, respiratory, or allergy clinic)					
McNeill,[13] 1963	Adults and children (n = 150, 242 sinuses) referred to ENT clinic for clinically suspected ARS	Range ≥10 y (10-19 y, n = 22; ≥20 y, n = 128)	Radiography showing mucosal thickening or any opacity	Northern Ireland	High
Axelsson et al,[21] 1976	Consecutive adults (n = 164) at ENT clinic with clinically suspected acute maxillary sinusitis	Mean 35 y	Radiography (at least 4 views) showing any mucosal thickening, air-fluid levels, or opacification	Sweden	Moderate
Berg et al,[15] 1981	Adults (n = 50) at ENT clinic with clinically suspected ARS of ≥3 weeks duration	Mean 46 y	Antral puncture revealing purulent discharge	Sweden	High
Berg et al,[22] 1985	Adults (n = 90) at ENT clinic with clinically suspected ARS of ≥3 weeks duration	Not reported	Antral puncture revealing purulent discharge	Sweden	Moderate
van Buchem et al,[5] 1995	Adults (n = 113) referred to ENT clinic with clinically suspected acute maxillary sinusitis	42% 18-29 y; 34% 30-44 y; 16% 45-59 y; and 9% ≥60 y	(1) Antral puncture showing fluid or floccules (by patient) and (2) bacterial culture of fluid (by sinus)	Netherlands	Low
Visca et al,[23] 1995	Children (n = 30) at pediatric respiratory clinic with clinically suspected ARS	Range 5-15 y	CT scan abnormal in coronal projection	Italy	High
Huang et al,[24] 2008	Consecutive adults and children (n = 217) at allergy clinic with clinically suspected ARS of <3 weeks duration	Range 4-61 y (4-9 y, n = 89; 10-19 y, n = 101; ≥20 y, n = 27)	Sinus radiograph (n = 151) or CT scan (n = 12) with >4 mm mucosal thickening, air-fluid levels, and/or increased opacity or retention cyst	USA	High
Primary care, urgent care, or emergency department setting					
Berg et al,[25] 1988	Adults (n = 155) presenting to ED with clinically suspected maxillary sinusitis of <3 months duration	Mean 38 y	Antral puncture with return of purulent or cloudy fluid	Sweden	Moderate
Williams et al,[26] 1992	Consecutive men (n = 247) presenting to VA general medicine clinic with <3 months of self-described sinusitis or at least 1 sinus symptom–median symptom duration of 11 days	Median 50 y, IQ range 40-63 y	Radiographs (4 views): mucosal thickening ≥6 mm, complete opacity, or air-fluid level	USA	Moderate
van Duijn et al,[27] 1992	Adults (n = 400, 441 episodes) presenting to primary care clinic with clinically suspected ARS	Range ≥15 y	Ultrasonography abnormal	Netherlands	Moderate
Hansen et al,[4] 1995	Consecutive adults (n = 174) at primary care clinic suspected of having acute maxillary sinusitis by their general practitioner	Median 35 y, range 18-65 y	CT scan abnormal and culture of purulent fluid positive for pathogenic bacteria	Denmark	Low
Lindbaek et al,[12] 1996	Adults (n = 201) clinically diagnosed by primary care doctor with ARS requiring antibiotics	Mean 37.8, range 15-83 y	CT scan showing air-fluid level or complete opacification	Norway	High
Laine et al,[28] 1998	Consecutive adults (n = 39) presenting to primary care clinic with clinically suspected acute maxillary sinusitis of <30 days duration	Median 37 y, range 16-68 y	Nasal aspirate with purulent or mucopurulent material	Finland	Low
Varonen et al,[29] 2003	Consecutive adults (n = 148) presenting to a primary care clinic with clinically suspected ARS of <30 days duration, 72% >5 days	Mean 39.7 y, range 18-75 y	Sinus radiographs (AP and Waters' views) showing total opacification, air-fluid level, or mucosal thickening ≥6 mm	Finland	High
Thomas et al,[30] 2006	Adults (n = 60) presenting to a VA urgent care center with clinically suspected ARS of <4 weeks duration	Mean 51 y, range 25-83 y	CT scan showing air-fluid level or complete opacification (mucosal thickening alone was not considered diagnostic)	USA	Moderate
Shaikh et al,[31] 2013	Children (n = 258) at a general pediatric clinic with clinically suspected ARS of <30 days durations (mean symptom duration 14 days)	Mean 6.4 y, range 2.0-12.9 y	Radiographs (AP and Water's views): complete opacification or any mucosal thickening	USA	Moderate
Autio et al,[32] 2015	Adults (n = 50) presenting to a military clinic with clinically suspected ARS of <4 days duration (symptoms recorded at 9-10 days after onset)	Mean 20 y, range 18-23 y	CT followed by antral puncture and bacterial culture if positive	Finland	Low

AP = anteroposterior; ARS = acute rhinosinusitis; CT = computed tomography; ED = emergency department; ENT = ear, nose, and throat; IQ = interquartile; USA = United States of America; VA = Veterans Administration.

Quality Assessment of Diagnostic Accuracy Studies 2 framework is summarized in Supplemental Table 2. Overall, 4 studies were at low risk of bias, 7 at moderate risk of bias, and 6 at high risk of bias. Common threats to validity included failure to use a high-quality reference standard, nonconsecutive sample of patients, and mask the person performing the reference standard to results of the index test. All of the studies at low risk of bias used purulent fluid or bacterial culture as the reference standard, so those results are reported separately.[33]

Prevalence of ARS and ABRS

The prevalence of acute sinusitis for patients presenting with sinus symptoms is summarized in Table 2, stratified by age group and reference standard. Prevalence ranged from 19% to 63% for adults, and from 57% to 79% for children.

Imaging studies had the highest prevalence and was similar for studies using plain film radiography or CT as the reference standard (59% vs 56%, $P = .70$). For the diagnosis of ABRS, studies using the presence of purulence from antral puncture had a higher prevalence than those using positive culture of antral puncture fluid (49% vs 31%, $P < .01$). Comparing the studies of adults only (Table 2), the prevalence of ARS was similar for studies using any imaging vs purulence on antral puncture as the reference standard (51% vs 49%), but was lower for those using bacterial culture (31%).

In the subset of all primary care, urgent care, or emergency department studies (n = 10; 1,632 patients) the prevalence of ARS was 49% (95% CI, 39-59). In the subset of studies using antral puncture or culture as the reference standard (n = 4; 411 patients), the prevalence of ABRS was 42% (95% CI, 31-55).

All studies enrolled patients with symptoms compatible with sinusitis. In a systematic review of blood tests and imaging for ARS,[11] 2 studies that recruited patients with broader inclusion criteria of cold [18] or runny nose[34] found lower ARS prevalence at 16%and 28%, respectively.

Table 2. Prevalence of ARS and ABRS in the Included Study Populations

Study	Reference Standard	No.	Prevalence, %
Studies of adults			
Berg et al,[15] 1981	Antral puncture[a]	50	50
Berg et al,[22] 1985	Antral puncture[a]	90	48
Berg et al,[25] 1988	Antral puncture[a]	155	44
Hansen et al,[4] 1995	Antral puncture[a]	174	53
Van Buchem et al,[5] 1995	Antral puncture[a]	108	49
Laine et al,[28] 1998	Antral puncture[a]	39	51
Summary for antral puncture, % (95% CI)			49 (45-53)
Hansen et al,[4] 1995	Bacterial culture[b]	174	35
Van Buchem et al,[5] 1995	Bacterial culture[b]	113	34
Autio et al,[32] 2015	Bacterial culture[b]	43	19
Summary for bacterial culture, % (95% CI)			31 (24-40)
Lindbaek et al,[12] 1996	CT	201	63
Thomas et al,[30] 2006	CT	60	45
Van Duijn et al,[27] 1992	Ultrasound	423	49
Varonen et al,[29] 2003	Radiograph	32	41
Williams et al,[26] 1992	Radiograph	247	39
Axelsson et al,[21] 1976	Radiograph	164	63
Summary for imaging, % (95% CI)			51 (48-54)
Summary for studies with adults only, % (95% CI)			48 (42-54)
Studies of adults and children			
McNeill,[13] 1963	Radiograph	242	56
Huang et al,[24] 2008	Radiograph	217	70
Summary for studies with adults and children, % (95% CI)			63 (49-75)
Studies of children			
Visca et al,[23] 1995	CT	30	57
Shaikh et al,[31] 2013	Radiograph	258	79
Summary for studies with children only, % (95% CI)			70 (45-87)

ABRS = acute bacterial rhinosinusitis; ARS = acute rhinosinusitis; CT = computed tomography.

[a] A positive antral puncture required return of purulent fluid.

[b] Bacterial culture of fluid obtained during antral puncture.

The Interrater Reliability of Signs and Symptoms

Three studies reported the interrater agreement of signs and symptoms for ARS among adult patients.[26,30,35] A value of κ from 0.0-0.2 represents slight agreement, 0.2-0.4 is fair agreement, 0.4-0.6 is good agreement, 0.6-0.8 substantial agreement, and 0.8-1.0 shows near perfect agreement. There was substantial agreement for history of cough ($\kappa = 0.70$),[35] red streak in lateral recess of oropharynx ($\kappa = 0.70$),[30] colored nasal discharge ($\kappa = 0.68$),[26] and maxillary toothache ($\kappa = 0.60$).[26] There was good agreement for sinus tenderness ($\kappa = 0.59$)[26] and history of fever ($\kappa = 0.53$).[35] There was only slight agreement for purulence on nasal inspection ($\kappa = 0.14$),[26] and considerable heterogeneity from 2 studies regarding sinus transillumination (κ values of 0.22 and 0.80).[26,30]

Accuracy of Individual Signs and Symptoms

Acute Rhinosinuitis

The individual signs and symptoms that best ruled in ARS when present were purulent secretions observed in the middle meatus, nasal speech, patient report of pain in the teeth, and purulent secretions observed in the posterior pharynx or postnasal region. The individual findings that best ruled out ARS were absence of a preceding respiratory tract infection, absence of any nasal discharge, absence of purulent nasal discharge as a symptom, and normal transillumination. The accuracy of individual signs and symptoms for the diagnosis of ARS is summarized in Table 3 (see Supplemental Table 3, for complete individual study data). Few positive findings had a LR ≥2.0 and few findings when absent had a LR ≤0.5.

Four studies reported data for the overall clinical impression as a diagnostic test for ARS, including 3 that used antral puncture as the reference standard.[15,22,25,26] The accuracy of the overall clinical impression in this study was good (LR+ 3.0, LR– 0.37), with the highest diagnostic odds ratio of any finding (DOR 8.3).

Three studies reported data for prolonged duration of symptoms and the likelihood of ARS, using cutoffs of 5, 10, and 21 days.[25,29,30] In our study, there was no clear pattern, with sensitivity ranging from 25% to 70% and specificity from 15% to 75%.

Acute Bacterial Rhinosinusitis

Six studies used purulent antral puncture fluid or positive bacterial culture as the reference standard and are summarized in Table 4.[4,5,15,25,28,32] The 3 findings that significantly increased or decreased the likelihood of ABRS were the overall clinical impression, cacosmia (fetid odor of the breath), and pain in the teeth. Individual study data using these reference standards is shown in Supplemental Table 4. No conclusions can be drawn due to the limited number of studies reporting data for each sign or symptoms.

Only 2 studies reported the accuracy of signs and symptoms for ABRS using bacterial culture of antral fluid as the reference standard.[4,32] Pain in teeth as a symptom (LR+ 2.8, LR– 0.76) and maxillary tenderness on exam (LR+ 1.8, LR– 0.71) significantly changed the likelihood of ABRS.

Accuracy of Combinations of Signs and Symptoms

Acute Rhinosinusitis

Four studies reported combinations of findings for the diagnosis of ARS (Table 5).[12,24,26,27] Lindbaek and colleagues proposed a 4-item score; patients with all 4 findings present had a LR of 25 for ARS, those with 2 or 3 findings a LR of 1.2, and those with 0 or 1 finding had a LR of 0.16.[12] Williams and colleagues developed a 5-point clinical score using maxillary toothache, abnormal transillumination, poor response to nasal decongestants or antihistamines, colored nasal discharge, or mucopurulence on examination for the diagnosis of ARS using radiography as the reference standard; likelihood ratios ranged from 6.4 for 4 or 5 points to 0.16 for 0 points.[26]

Huang and colleagues used a 4-item score for results of a urine test strip measuring the protein, pH, leukocyte esterase, and nitrite as measures of an inflammatory response in nasal discharge.[24] The samples were collected by having patients blow their nose into a piece of plastic wrap, and the scorer assigned either 0 to 2 or 0 to 3 points per item for a total range of 0 to 11 points. Using a reference standard of radiography, the highest strata of scores (≥4) had a LR of 127.[24] Van Diujn and colleagues applied a 5-item score based on a logistic regression equation to estimate the probability of sinusitis compared to ultrasonography of the sinuses as the reference standard.[27] This study is limited, like all of the others, by lack of prospective validation and the use of an imaging reference standard that is not specific for ABS.

Acute Bacterial Rhinosinusitis

Two studies reported the accuracy of combinations of signs and symptoms for the diagnosis of ABRS (Table 5).[25,36] Berg proposed a 4-item score using a reference standard of purulent antral puncture fluid. The score discriminated well: those with a score or 3 or 4 findings present had a LR of 7 for ABRS, while those with ≤1 findings present had a LR of 0.06.[25]

The most recently reported clinical decision rule used 5 signs or symptoms plus C-reactive protein (see Table 5 for scoring details) to identify patients at low risk (n = 77, 16%), moderate risk (n = 75, 49%), or high risk (n = 23, 73%) for ABRS using positive bacterial culture of antral puncture fluid as the reference standard.[36] Unfortunately, none of the above scores have been prospectively validated.

DISCUSSION

Most individual signs and symptoms have limited accuracy for the diagnosis of ARS and ABRS. Purulent secretions seen in the middle meatus and the overall clinical impression are most useful for ruling in ARS when present, while overall clinical impression, absence of a recent or preceding RTI, absence of any nasal discharge, and absence of purulent nasal discharge reduced the likelihood of ARS (Table 3). Since ARS may have a viral etiology, the more important clinical question is how to best diagnose ABRS. We

found that the overall clinical impression, cacosmia (an uncommon but highly specific finding), and pain in the teeth were the best predictors of ABRS (Table 4). Other individual signs and symptoms had positive and negative likelihood ratios between 0.5 and 2.0, indicating little diagnostic value.

Clinical decision rules have been developed for a range of other respiratory conditions, including pneumonia,[37] streptococcal pharyngitis,[38] and influenza.[39] We identified 6 clinical rules for the diagnosis of ARS or ABRS, and they have promising accuracy, but none has been prospectively validated. In some cases, including 1 of the clinical decision rules for ABRS, they incorporate point-of-care tests such as C-reactive

Table 3. Accuracy of Signs and Symptoms of ARS Diagnosed by Any Reference Standard

Sign or Symptom	# of Studies	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)[a]	LR– (95% CI)[a]	DOR (95% CI)[b]
Overall clinical impression	4	0.73 (0.66-0.79)	0.75 (0.64-0.84)	3.0 (2.1-4.4)[c]	0.37 (0.29-0.46)[c]	8.3 (4.9-13.1)[c]
Symptoms						
Nasal speech	3	0.51 (0.15-0.85)	0.73 (0.35-0.93)	1.9 (1.3-2.7)[c]	0.67 (0.37-0.91)[c]	2.9 (1.8-4.3)[c]
Pain in teeth	8	0.34 (0.21-0.50)	0.80 (0.63-0.90)	1.8 (1.2-2.5)[c]	0.83 (0.74-0.90)[c]	2.1 (1.4-3.0)[c]
Nasal discharge						
Purulent	10	0.71 (0.63-0.78)	0.54 (0.48-0.61)	1.6 (1.4-1.7)[c]	0.54 (0.44-0.56)[c]	2.9 (2.2-3.7)[c]
Any	4	0.75 (0.57-0.91)	0.49 (0.35-0.68)	1.5 (1.3-1.8)[c]	0.49 (0.24-0.82)[c]	3.5 (1.7-6.2)[c]
Maxillary or frontal pain	3	0.49 (0.15-0.83)	0.63 (0.14-0.95)	1.50 (0.86-3.50)	0.89 (0.61-1.40)	1.90 (0.61-4.50)
Maxillary pain						
Unilateral	5	0.30 (0.14-0.52)	0.80 (0.51-0.94)	1.50 (0.96-2.60)	0.90 (0.79-1.00)[c]	1.70 (0.92-3.00)
Location not specified	5	0.70 (0.42-0.88)	0.20 (0.05-0.51)	0.88 (0.73-1.00)[c]	1.60 (0.95-2.80)	0.60 (0.30-1.10)
Cacosmia[d]	5	0.23 (0.15-0.33)	0.84 (0.58-0.95)	1.50 (0.63-3.70)	0.96 (0.83-1.20)	1.70 (0.53-4.30)
Double sickening	3	0.74 (0.32-0.95)	0.41 (0.13-0.77)	1.30 (0.77-2.40)	0.69 (0.20-1.50)	2.70 (0.49-8.50)
Hyposmia or anosmia	8	0.61 (0.52-0.70)	0.54 (0.46-0.61)	1.3 (1.1-1.5)[c]	0.72 (0.59-0.87)[c]	1.9 (1.3-2.5)[c]
Cough						
Nocturnal	3	0.89 (0.80-0.94)	0.11 (0.06-0.19)	0.99 (0.87-1.10)	1.20 (0.43-2.60)	1.10 (0.35-2.60)
Any	7	0.69 (0.57-0.80)	0.40 (0.27-0.55)	1.3 (1.0-1.7)[c]	0.78 (0.60-0.98)[c]	1.5 (1.0-2.2)[c]
Preceding respiratory tract infection	5	0.87 (0.66-0.96)	0.27 (0.13-0.48)	1.2 (1.1 - 1.3)[c]	0.48 (0.30-0.72)[c]	2.6 (1.6-4.0)[c]
Pain bending forward	5	0.72 (0.56-0.84)	0.39 (0.24-0.57)	1.2 (1.0-1.5)[c]	0.71 (0.50-0.97)[c]	1.70 (0.97-2.70)
Nasal congestion or obstruction	9	0.83 (0.74-0.89)	0.24 (0.14-0.36)	1.1 (1.0-1.2)[c]	0.73 (0.56-0.93)[c]	1.5 (1.1-2.1)[c]
Fatigue or malaise	6	0.62 (0.51-0.71)	0.45 (0.32-0.59)	1.10 (0.99-1.30)	0.86 (0.72-1.00)[c]	1.30 (0.98-1.80)
Sneezing	3	0.63 (0.49-0.74)	0.39 (0.31-0.48)	1.00 (0.86-1.20)	0.96 (0.71-1.20)	1.10 (0.70-1.20)
Headache	6	0.50 (0.32-0.67)	0.50 (0.27-0.73)	1.00 (0.71-1.30)	1.00 (0.79-1.40)	1.00 (0.57-1.70)
Allergies by history	3	0.19 (0.16-0.24)	0.79 (0.72-0.85)	0.96 (0.64-1.40)	1.00 (0.93-1.10)	0.96 (0.57-1.50)
Postnasal drip	3	0.74 (0.55-0.87)	0.19 (0.07-0.45)	0.94 (0.73-1.30)	1.50 (0.64-3.40)	0.80 (0.23-2.00)
Previous sinusitis	4	0.59 (0.52-0.65)	0.27 (0.18-0.39)	0.81 (0.71-0.93)[c]	1.6 (1.1-2.2)[c]	0.55 (0.33-0.83)[c]
Signs						
Purulent secretions						
Middle meatus	5	0.15 (0.07-0.28)	0.95 (0.87-0.98)	3.2 (1.4-6.6)[c]	0.90 (0.78-0.97)[c]	3.7 (1.5-7.6)[c]
Pharyngeal or postnasal	7	0.14 (0.06-0.30)	0.92 (0.77-0.97)	1.8 (1.1-2.8)[c]	0.93 (0.87-0.98)[c]	2.0 (1.2-3.1)[c]
Any nasal	12	0.39 (0.28-0.51)	0.74 (0.63-0.82)	1.50 (0.99-2.30)	0.84 (0.67-1.00)[c]	1.90 (0.98-3.30)
Transillumination abnormal	3	0.69 (0.63-0.75)	0.56 (0.50-0.62)	1.6 (1.4-1.9)[c]	0.55 (0.44-0.67)[c]	3.0 (2.0-4.2)[c]
Sinus tenderness						
Frontal	3	0.25 (0.09-0.54)	0.75 (0.47-0.91)	1.10 (0.76-1.40)	0.99 (0.86-1.10)	1.10 (0.70-1.60)
Maxillary	12	0.44 (0.28-0.61)	0.49 (0.34-0.64)	0.88 (0.57-1.30)	1.20 (0.80-1.60)	0.81 (0.37-1.30)
Nasal mucosal thickening	3	0.82 (0.27-0.98)	0.30 (0.15-0.51)	1.10 (0.49-1.40)	0.68 (0.09-1.60)	3.00 (0.32-13.00)
Temperature >38° C	7	0.11 (0.07-0.19)	0.87 (0.79-0.92)	0.94 (0.42-1.90)	1.00 (0.91-1.10)	0.94 (0.37-2.10)

ARS = acute rhinosinusitis; DOR = diagnostic odds ratio; LR+ = positive likelihood ratio; LR– = negative likelihood ratio.

Note: Each sign or symptom was reported in 3 or more studies to be included here.

[a] A likelihood ratio near 1.0 means that the test adds little diagnostic information, a likelihood ratio >1 increases the likelihood of disease, and a likelihood ratio <1 decreases the likelihood of disease.

[b] The diagnostic odds ratio is LR+ divided by LR– and is an overall measure of diagnostic discrimination.

[c] Value is significantly < or > 1.0.

[d] Cacosmia is fetid odor on patient's breath.

protein as well as signs or symptoms to increase the accuracy of prediction.[37] Another potentially useful point-of-care test is use of a urine dipstick to detect leukocyte esterase or nitrites in nasal discharge (Table 5).[24] While it could be incorporated into a clinical decision rule or even used alone, its accuracy requires further validation. While C-reactive protein is accurate and widely used in some countries at the point of care to identify patients more or less likely to have a bacterial respiratory infection,[40,41] it is not currently available in most US outpatient settings.[11] Finally, a recent systematic review by the author found that older studies of ultrasound found that it to be approximately 80% sensitive for ARS.[11] Patients who do not have any sinus fluid detected are therefore at low risk for ARS. Thus, studies that evaluate the ability of modern handheld ultrasound devices to detect sinus fluid are needed.

An important limitation of our findings is the variety of reference standards used to define both ARS and ABRS. Because imaging may detect fluid associated with a viral upper respiratory infection, and cannot distinguish purulent from non-purulent fluid, it is likely to lead to over diagnosis of ABRS. Similarly, some patients with fluid that appears purulent may have a viral infection. Relying on these tests could lead to overtreatment with antibiotics. On the other hand, bacterial culture of antral puncture fluid is likely to be more specific but may lack sensitivity if organisms do not grow in culture. In addition, puncturing the antrum is painful and invasive, making it impractical for use in clinical practice. Ultimately, the true prevalence of ABRS among patients with clinically suspected ARS is likely to be between 31% (prevalence using bacterial culture) and 50% (prevalence using imaging) in adults.

An important question is whether detection of a bacterial pathogen in sinus fluid means that the patient will benefit from antibiotics. Most clinical trials have enrolled patients with clinically suspected sinusitis and found a small benefit (5 additional cures per 100 persons receiving an antibiotic). Trials using imaging (3 radiography, 1 CT) found a larger benefit, suggesting some validity for the concept of imaging as a reference standard.[6] To date no randomized trials of antibiotics or other interventions have enrolled patients with ABRS diagnosed by inspection of fluid.

While many studies have attempted to identify combinations of signs or symptoms that diagnose ARS or ABRS, it is equally important to determine which patients are at low likelihood of ABRS (would be unlikely to benefit from an antibiotic), as it is to identify which patients are likely to have an uncomplicated course. Thus, research to determine low risk criteria that help rule out ABRS is needed.

CONCLUSION

Only about one-third of patients with clinically suspected ARS have a positive bacterial culture of antral puncture fluid. Acute rhinosinusitis as diagnosed by

Table 4. Accuracy of Signs and Symptoms of ABRS Diagnosed by Purulent Antral Puncture or Positive Bacterial Culture

Sign or Symptom	# of Studies	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)[a]	LR– (95% CI)[a]	DOR (95% CI)[b]
Overall clinical impression	3	0.74 (0.61-0.84)	0.80 (0.72-0.87)	3.9 (2.4-5.9)[c]	0.33 (0.20-0.50)[c]	13.0 (5.0-27)[c]
Symptoms						
Cacosmia[d]	3	0.23 (0.11-0.42)	0.93 (0.59-0.99)	4.3 (0.94-14)	0.86 (0.76-0.99)[c]	5.0 (0.74-18)
Pain in teeth	3	0.38 (0.10-0.78)	0.80 (0.37-0.97)	2.0 (1.1-3.7)[c]	0.77 (0.50-0.96)[c]	2.7 (1.3-4.6)[c]
Purulent nasal discharge	3	0.64 (0.45-0.79)	0.50 (0.36-0.63)	1.3 (0.99-1.6)	0.74 (0.47-1.0)	1.8 (0.98-3.2)
Pain bending forward	3	0.64 (0.4-0.79)	0.38 (0.20-0.60)	1.0 (0.87-1.3)	0.95 (0.69-1.3)	1.2 (0.69-1.8)
Nasal congestion or obstruction	4	0.71 (0.57-0.82)	0.25 (0.10-0.52)	0.98 (0.83-1.3)	1.3 (0.70-2.3)	0.88 (0.38-1.8)
Cough	3	0.66 (0.34-0.86)	0.29 (0.12-0.55)	0.93 (0.70-1.1)	1.2 (0.79-1.7)	0.84 (0.45-1.4)
Physical examination						
Sinus tenderness, maxillary	5	0.33 (0.13-0.61)	0.57 (0.40-0.73)	0.86 (0.23-2.2)	1.2 (0.55-2.1)	0.97 (0.11-3.9)
Nasal discharge, purulent	5	0.27 (0.20-0.35)	0.66 (0.45-0.82)	0.88 (0.36-1.9)	1.2 (0.57-1.8)	0.83 (0.22-2.3)

ABRS = acute rhinosinusitis; DOR = diagnostic odds ratio; LR+ = positive likelihood ratio; LR– = negative likelihood ratio.

Note: Each sign or symptom was reported in 3 or more studies to be included here.

[a] A likelihood ratio near 1.0 means that the test adds little diagnostic information, a likelihood ratio >1 increases the likelihood of disease, and a likelihood ratio <1 decreases the likelihood of disease.

[b] The diagnostic odds ratio is LR+ divided by LR– and is an overall measure of diagnostic discrimination.

[c] Value is significantly < or > 1.0.

[d] Cacosmia is fetid odor on patient's breath.

any reference standard is significantly less likely in patients without any nasal discharge, without a complaint of purulent nasal discharge, and with normal transillumination. The overall clinical impression is also useful for both ruling in and ruling out ARS. Evidence regarding diagnosis of ABRS is limited, but we conclude that the overall clinical impression, pain in the teeth, and cacosmia are the most useful findings for clinicians trying to identify patients most likely to benefit from antibiotics. Clinical decision rules, including those incorporating C-reactive protein, and the use of urine dipsticks to test the nasal discharge are promising, but all require prospective validation.

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Key words: sinusitis; rhinosinusitis; acute sinusitis; acute rhinosinusitis; clinical diagnosis

Table 5. Combinations of Findings and Clinical Decision Rules for the Diagnosis of Acute Sinusitis

Study	Reference Standard	Findings	Interpretation		
			Result	Likelihood Ratio (95% CI)	Probability of Sinusitis, %[a]
Diagnosis of ARS					
Huang et al,[24] 2008[b]	Radiograph (n = 205) or CT (n = 12)	Leukocyte esterase: <1+ = 0, 1+ = 2, ≥2+ = 3 pH: <7.5 = 0, 7.5 = 1, 8.0 = 2, 8.5 = 3 Nitrite: none = 0, light pink = 1, dark pink = 2 Protein: <2+ = 0, 2+ = 1, 3+ = 2, 4+ = 3	4-11 2-3 0-1	127.0 (8.1-2016.0) 0.23 (0.10-0.52) 0.00 (0.00-0.06)	99 13 0
Lindbaek et al,[12] 1996	CT	Double sickening Purulent secretion in nasal cavity Purulent rhinorrhea (symptom) ESR >10	4 3 2 0-1	25.0 (3.5-177.0) 1.8 (1.1-3.2) 0.81 (0.51-1.30) 0.16 (0.09-0.30)	94 55 35 10
Williams et al,[26] 1992	Radiograph	Maxillary toothache Abnormal transillumination Poor response to decongestants or antihistamines Colored nasal discharge Mucopurulence on examination	4-5 3 2 1 0	6.4 (2.2-19.0) 2.6 (1.5-4.4) 1.10 (0.73-1.70) 0.43 (0.27-0.80) 0.16 (0.04-0.41	81 63 42 22 10
Van Diujn et al,[27] 1992	Ultrasound (A mode)	Beginning with common cold Purulent rhinorrhea Pain at bending Unilateral maxillary pain Pain in teeth	5 1-4 0	… … …	89[c] 18-82 11
Diagnosis of ABRS					
Berg et al,[25] 1988	Purulent antral puncture fluid	Purulent rhinorrhea with unilateral predominance Local pain with unilateral predominance Bilateral purulent rhinorrhea Pus in nasal cavity	3-4 2 0-1	7.0 (3.9-12.7) 1.30 (0.72-1.9) 0.06 (0.02-0.17)	82 46 4
Ebell et al,[36] 2017	Positive bacterial culture from antral fluid	Tender maxillary sinus (unilateral): 2 points Maxillary toothache: 2 points C-reactive protein >15 mg/L: 2 points Preceding upper respiratory tract illness: 1 point Purulent nasal discharge: 1 point Previous sinusitis episodes: –1 point	7-8 4-6 –1-3	5.0 (1.8-14) 1.8 (1.3-2.5) 0.35 (0.21-0.56)	77 55 19

ABRS = acute bacterial rhinosinusitis; ARS = acute rhinosinusitis; CT = computed tomography; ESR = erythrocyte sedimentation rate; LR = likelihood ratio.

[a] Calculated using the score-specific LR and a pretest probability of 40%, or taken directly from logistic model for each study.

[b] Results obtained from application of a urinalysis dipstick to nasal secretions.

[c] Probability of sinusitis calculated directly from logistic regression, so LR and its CI not estimable. Each variable is assigned a value of 1 for the presence of each finding and 0 for the absence. The score = –2.124 + 1.035*(beginning with common cold) + 0.996*(purulent rhinorrhea) + 0.95*(pain at bending) + 0.64*(unilateral maxillary pain) + 0.606*(pain in the teeth). A person with all findings present would have a maximum score of 2.103. The probability of sinusitis is calculated from exp(score)/[1 + exp(score)], so exp(2.103)/[1 + exp(2.103)]=89%. A person with none of the findings present would have a score of –2.124, or a probability of 11%.

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