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Inconclusive Evidence for Allergic Rhinitis to Predict a Prolonged or Chronic Course of Acute Rhinosinusitis

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Abstract

Objective. To systematically review the evidence on allergic rhinitis as a predictor for a prolonged or chronic course in adult patients with acute rhinosinusitis.

Data Sources. Pubmed, EMBASE, and the Cochrane library.

Review Methods. A systematic literature search was performed on March 15, 2013. During screening of title and abstract, 3 authors independently selected studies on allergic rhinitis as a predictor for the course of acute rhinosinusitis in adults. The reported study design was assessed for directness of evidence and risk of bias. We aimed to extract prior and posterior probabilities for a prolonged or chronic course of acute rhinosinusitis.

Results. Of 13,202 retrieved articles, 2 articles were eligible for study assessment. They provided a high directness of evidence but carried a high risk of bias. The studies showed an incidence of a prolonged and chronic course of, respectively, .19 (95% confidence interval [CI] .16-.23) and .05 (95% CI, .02-.13). In patients with allergic rhinitis, the incidence was .25 (95% CI, .18-.35) and .14 (95% CI, .04-.34), so the added value of allergic rhinitis to predict a prolonged course is 6% and to predict a chronic course 8%.

Conclusion and Recommendation. While the 2 included studies suggest that allergic rhinitis adds little to the prediction of a prolonged or chronic course in patients with acute rhinosinusitis, they carry a high risk of bias. As the available evidence does not provide grounds for different management of patients with and without allergic rhinitis, namely, according to clinical practice guidelines, both can be managed with expectant observation and symptomatic treatment.

Keywords

allergic rhinitis, acute rhinosinusitis, prolonged rhinosinusitis, chronic rhinosinusitis, prognosis, evidence based medicine

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Clinical Scenario

A 45-year-old man visits your ear nose throat clinic with complaints of facial pain, reduced smell, purulent rhinorrhea, and nasal obstruction since 5 days. Physical examination reveals tenderness on the right maxillary sinus, and anterior rhinoscopy shows purulent discharge. You diagnose this patient with acute rhinosinusitis. Your patient is known with allergic rhinitis (confirmed by positive skin prick testing for house dust mite and grass pollen), for which he uses an antihistamine. You intend to observe this patient expectantly, according to clinical practice guidelines. However, you consider that allergic rhinitis might increase his risk of a prolonged or chronic course of acute rhinosinusitis and wonder whether this could be a reason to deviate from guidelines.

Background

Each year, approximately 30 million adults in the United States are affected by acute rhinosinusitis (ARS) and 2% to 16% of the American population has complaints of chronic rhinosinusitis.^{1,2} In 2004, the medical costs of rhinosinusitis in the United States were \$5.8 billion.² Besides the economic consequences, patients with rhinosinusitis also have a significantly altered quality of life.³⁻⁵

ARS is a symptomatic inflammation of the nasal cavity or paranasal sinuses, with a sudden onset and resolution of symptoms within 4 weeks.⁶ Symptoms lasting for more than

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4 weeks are in general referred to as prolonged rhinosinusitis, while symptoms persisting for 12 weeks are alluded to as chronic rhinosinusitis (CRS).⁷ In 71% of patients suffering from ARS, symptoms resolve within 14 days, irrespective of antibiotic treatment.⁸ The disease is generally considered as recurrent or persisting after 60 days in up to 20% of patients,^{8,9} while after 1 year, complaints have become chronic in approximately 2%.¹⁰ Chronic bronchitis, occupational rhinitis, use of local decongestants or corticosteroids, and atopy have been identified to increase the risk for an acute rhinosinusitis to become chronic.¹¹ Allergic rhinitis (AR) has been considered to increase the risk for a recurrence of rhinosinusitis.

We aimed to assess the value of AR in predicting a prolonged or chronic course of ARS. This knowledge could help to identify patients with a worse prognosis, for which deviation from clinical practice guidelines may be considered.

Searching for Evidence

We systematically reviewed the evidence base to answer the following question: What is the value of allergic rhinitis in predicting a prolonged or chronic course in adult patients with acute rhinosinusitis?

Retrieving Studies

We retrieved publications from PubMed, EMBASE, and the Cochrane library up to March 15, 2013, assisted by our clinical librarian. We used search terms *rhinosinusitis* and *chronic* or *prolonged* with relevant synonyms. Appendix 1 (available at otojournal.org) includes our search strategy.

Three authors (KF, GN, and KR) independently screened title and abstract of retrieved records to select potentially eligible articles reporting studies on the probability of allergic rhinitis increasing the risk of a prolonged or chronic course of rhinosinusitis in adults with acute rhinosinusitis. For this they used predefined selection criteria (**Figure 1**). They removed duplicate publications and excluded studies concerning patients with fungal sinusitis, studies in children, studies in immunocompromised patients, animal or laboratory studies, diagnostic papers, systematic reviews, and case reports.

For final selection the same 3 authors independently screened full texts of eligible titles in depth and with more detail. They completed study retrieval by tracking citations of full-text articles and cross reference checking in Scopus and Web of Science for included studies and reviews, meta-analyses, and guidelines. Authors resolved any initial disagreement on eligibility and selection of articles by discussion, and the selection is therefore based on a full consensus.

Assessing Studies

Based on predefined criteria, 4 independent authors (KF, GN, KR, and NK) assessed the design of studies reported in the included articles on directness of evidence (DoE) and risk of bias (RoB). Disagreements were solved by

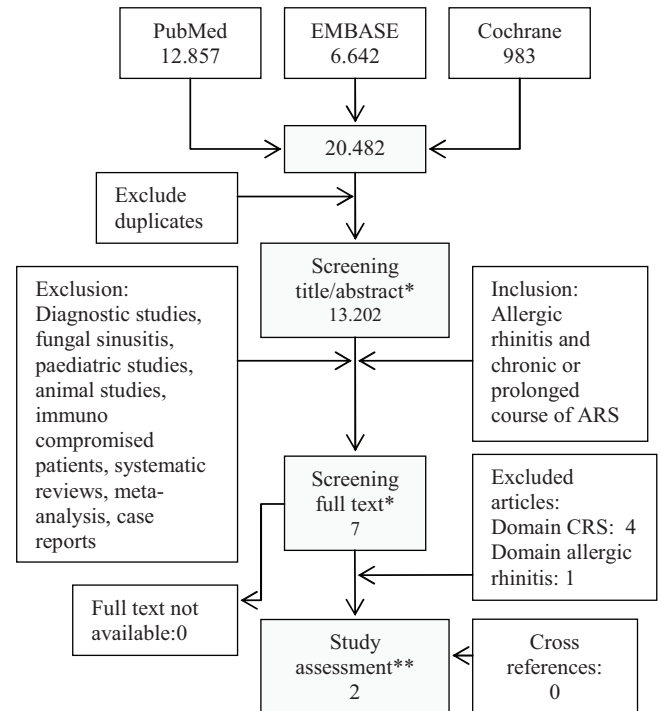


Figure 1. Flowchart (March 15, 2013).

ARS, acute rhinosinusitis; CRS, chronic rhinosinusitis; *Based on assessment by 3 independent authors. **Based on agreement by 4 independent authors.

discussion. When for the assessment of a DoE or RoB item information was not or not clearly reported, we rated it as insufficient and considered it as not satisfied. When the reporting allowed assessment, we rated it as either satisfied or not satisfied.

Assessment of the DoE involved *evaluation of patients*, notably (1) adults with ARS; *the predictor*, notably (2) allergic rhinitis; and *the outcomes*, notably (3) a prolonged (4 weeks) or chronic course (12 weeks) of acute rhinosinusitis. Studies provide less direct evidence when they include only a particular subset of patients, or assess a proxy for the predictor, or report on a surrogate for the outcome. Therefore we classified studies as providing high DoE if they satisfied all the aspects of our 3-part question, moderate DoE if they satisfied 2, and low DoE if they satisfied only 1.

Assessment of the RoB involved evaluation of the study design characteristics for *selection bias*, notably (1) inclusion of an inception cohort and (2) completeness of reported data; *information bias*, notably (3) blinding of predictor and (4) outcome, (5) standardization of predictor, and (6) outcome assessments. The fewer of these aspects are satisfied by a study, the lower the trust is we put in the viability of its findings. Hence we classified studies as carrying low RoB if they satisfied criterion 1 and 4 or 5 of the other study design features, moderate RoB if they satisfied criterion 1 and 2 or 3 of the other 5 features; the remainder was classified as high RoB. We aimed to include studies for data extraction with a high and moderate DoE and a low and moderate RoB.

Extraction and Analysis of Study Data

For the included articles, 2 authors (GN, NK) independently extracted data. We aimed to extract or recalculate the prior probability (or incidence) of a prolonged or chronic course and the predictive values for the presence (or PPV) and absence (or NPV) of AR, with accompanying 95% confidence intervals (CI). By comparing prior probabilities (or incidences) with posterior probabilities of the presence or absence of AR, we evaluated whether AR predicts a prolonged or chronic course of ARS. We excluded papers from analysis if there were no such data reported, while we present the findings as originally reported if the necessary data could not be (re)calculated.

Results

Retrieving Studies

Our initial literature search yielded 20,482 records. After removing duplicates, 13,202 unique publications remained for title and abstract screening (**Figure 1**). Of these, 7 articles were identified as potentially eligible for study assessment during screening of title and abstract, and their full texts were retrieved. Cross reference checking revealed no additional articles. After applying the selection criteria to their full text, 2 studies were included for study assessment.^{12,13} Citations of excluded articles can be found in Appendix 2 (available at otojournal.org).

Assessing Studies

While both studies provide high DoE, they carry a high RoB (**Table 1**). Thereby our aim to include moderate or low RoB studies could not be fulfilled. We decided to extract data and report the findings of these high RoB studies. Thereby one should bear in mind that this is current best available evidence. We thereby explicitly state that the accuracy of these findings should be questioned. Since we can put little trust in these studies, they cannot serve to formulate any practice recommendation.

Extraction and Analysis of Study Data

The data reported in both studies include or allow to calculate the incidence for all study patients and posterior probabilities of patients with AR for a prolonged or chronic course of ARS. These data are presented in **Table 2**.

Wide et al included 456 patients with acute frontal sinusitis (AFS) with a mean follow-up time of 4.1 months (range, 0.2-17.7 months); 12 were lost to follow-up.¹² The mean age was 38 years (range, 7-87 years). Patients were treated with antibiotics, nasal decongestants, and irrigation; 96 patients (22%) received surgical treatment (35 functional endoscopic sinus surgery [FESS], 52 trephination, 9 Caldwell-Luc, septoplasty, or other). At the 1-month control 85 out of 444 patients had a prolonged course of AFS, namely, an incidence of .19 (95% CI, .16-.23). The posterior probability for AR (or PPV) was 27 out of 106 or .25 (95% CI, .18-.35), so the added value of AR was 6%. The posterior probability for the absence of AR (or NPV) was 58 out

of 338 or .17 (95% CI, .14-.22), so the added negative value is 64%.

Ruoppi et al included 91 patients with AFS. The mean follow-up time was 3.9 years (range, 1-10 years).¹³ The mean age was 31.8 years in men and 29.2 years in women (range, 9-65 years). Patients were treated with antibiotics and nasal decongestants, allergic patients received anti-allergic medication, and 83 patients (91%) were treated surgically (54 medialization of middle turbinate, 18 polypectomy, 18 irrigation through nasofrontal duct, 11 ethmoidectomy, 8 trephining of sinus, 68 irrigation of maxillary sinus). At an undefined time of control 5 out of 91 patients had chronic rhinosinusitis, namely, an incidence of .05 (95% CI, .02-.13). The posterior probability for AR (or PPV) was 3 out of 22 or .14 (95% CI, .04-.34), so the added value for AR was 8%. The posterior probability for the absence of AR (or NPV) was 2 out of 69 or .03 (95% CI, .002-.11), so the added negative value is 92%.

Comment

With our comprehensive search in Pubmed, EMBASE, and the Cochrane Library we identified 2 studies^{12,13} reporting on AR as a predictor for a chronic or prolonged course of ARS. They report an added value of AR for predicting a prolonged and chronic course of ARS of, respectively, 6% and 8%. The added value for ruling out a prolonged and chronic course based on the absence of AR was 64% and 92%; however, it should be noted that this information will add little to decision making in patient management.

Some aspects of our findings need further consideration.

First, both studies included patients based on clinical symptoms, radiographic imaging, or both.^{12,13} This does not represent current practice, since uncomplicated ARS is a clinical diagnosis without a role for plain sinus x-rays.⁶

Second, both studies included an unidentified number of children, without describing the distribution of AR for children and adults. Children with ARS might have a different prognosis than adults.¹⁴

Third, the duration of symptoms at inclusion was not reported in 1 study and varied from 1 day to 3 weeks in the other.^{12,13} This could distort results, especially if there is a large variation between patients.

Fourth, 22% and 91% of patients underwent a form of sinus surgery.^{12,13} Wide et al reported that patients with AR underwent FESS more often.¹² This could influence results, since patients requiring operation might have a worse prognosis from nonoperated patients.¹⁵ In current clinical practice, surgical treatment is reserved for fungal rhinosinusitis and complications of ARS, recurrent rhinosinusitis, or chronic rhinosinusitis.⁶

Fifth, it is unclear how AR was diagnosed in both studies. The preferred method to diagnose AR is by skin prick testing in combination with patient history and physical examination; radioallergosorbent test (RAST) can also be applied.⁶ Further, it is unclear whether all included patients were assessed for AR. In a previous study, the prevalence of AR defined by skin prick testing in patients with acute

Table 1. Study Assessment.^a

Directness of Evidence										Risk of Bias					
Study	Characteristics	Domain	Predictor	Outcome 1	Outcome 2	Follow-up 1	Follow-up 2	DoE Score	Inception Cohort	Complete Data	Blinding of Predictor	Blinding of Outcome	Predictor Standardization	Outcome Standardization	RoB score
Wide et al. ¹²		●	●	●	○	●	○	H	○	○	☒	☒	○	●	H
Ruoppi et al. ¹³		●	●	○	●	○	●	H	○	●	☒	☒	☒	☒	H
Directness of Evidence															
Domain	Included patients with a clinical diagnosis of acute rhinosinusitis														
Predictor	Allergic rhinitis														
Outcome 1	Prolonged rhinosinusitis														
Outcome 2	Chronic rhinosinusitis														
Follow-up 1	4 weeks or longer														
Follow-up 2	12 weeks or longer														
Risk of Bias															
Inception cohort	Patients are initially free of outcome of interest														
Complete data	Adequate reporting of all patients														
Blinding of predictor	The assessor of the outcome is blinded for the predictor status														
Blinding of outcome	The assessor of predictor is blinded for the outcome														
Standardization of predictor	Protocolled, uniform assessment														
Standardization of outcome	Protocolled, uniform assessment														

Abbreviations: DoE, directness of evidence; RoB, risk of bias; H, high.

^a●, satisfied; ○, not satisfied; ☒, insufficient information/unclear.

Table 2. Results.

Study characteristics	DoE	RoB	Outcome	Prior probability (incidence) [95% CI]	Posterior probability (incidence for AR) [95% CI]	Added value (%)
Wide et al ¹²	H	H	Prolonged course (>4 weeks)	.19 [.16-.23]	.25 [.18-.35]	6
Ruoppi et al ¹³	H	H	Chronic course (undefined)	.05 [.02-.13]	.14 [.04-.34]	8

Abbreviations: DoE, directness of evidence; RoB, risk of bias; H, high; CI, confidence interval; AR, allergic rhinitis.

rhinosinusitis was 25%, corresponding to the prevalence of 27% and 24% in the studies we included.¹⁶

Sixth, we have to consider the outcomes of both studies. Wide et al defined a prolonged course as either no marked improvement after 4 weeks or persistent opacification or fluid levels on sinus radiographs.¹² So asymptomatic patients with fluid levels on X-sinus could have been regarded as suffering from prolonged rhinosinusitis. Further, the follow-up time ranged from 0.2 to 17.7 months, so an unknown number of patients missed the 1-month control. The preferred method of reporting these data would have been a hazard ratio, taking into account the amount of time that elapses before an event occurs. Although the author had access to the data necessary to calculate a hazard ratio, he did not report this. Ruoppi et al did not define the outcome chronic rhinosinusitis and neither the timing of the control or patient characteristics are described in this study.¹³

Finally, on top of the aforementioned and most importantly, as yet sound studies, namely, those with low to moderate RoB, that satisfy for deriving practice recommendations are lacking.

Conclusion and Recommendation

With a comprehensive search we identified 2 studies providing a high directness of evidence that assess the predictive value of allergic rhinitis for a prolonged and chronic course in patients with acute rhinosinusitis. However, these studies carry a high risk of bias. Given an incidence of .19 and .05, patients with AR have a 5% and 6% increased risk for, respectively, prolonged and chronic disease. Therefore, current available studies add little to the prediction for a prolonged or chronic course of acute rhinosinusitis based on presence or absence of allergic rhinitis. As yet the available evidence does not provide grounds for different management; namely, according to current clinical practice guidelines both patients with and without allergic rhinitis can be managed with expectant observation and symptomatic treatment.^{6,17}

Translating Evidence into Practice

We informed the patient presenting to our clinic with acute rhinosinusitis that to date there is no evidence that he has an increased risk of a prolonged or chronic course because of his allergic rhinitis. We explained that in most patients symptoms resolve within 14 days and that transition to chronic rhinosinusitis is rare, irrespective of antibiotic

treatment. We proposed to wait with any treatment and asked the patient to reconsult when after 2 weeks symptoms have not resolved, to which the patient agreed.

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Author Contributions

Kristine A. Frerichs, construction of the search strategy, retrieval of articles, selection of relevant articles, assessment of study quality, extraction of study data, analysis and interpretation of data, drafting figures and tables, drafting manuscript, revision of the manuscript, final approval of the version to be published; **Gea Nigten**, construction of the search strategy, retrieval of articles, selection of relevant articles, assessment of study quality, extraction of study data, analysis and interpretation of data, drafting figures and tables, drafting manuscript, revision of the manuscript, final approval of the version to be published; **Kalynda Romeijn**, construction of the search strategy, retrieval of articles, selection of relevant articles, assessment of study quality, extraction of study data, analysis and interpretation of data, drafting figures and tables, drafting manuscript, revision of the manuscript, final approval of the version to be published; **Nina M. Kaper**, formulating clinical question, selection of relevant articles, assessment of study quality, extraction of study data, analysis and interpretation of data, drafting figures and tables, drafting manuscript, revision of the manuscript, final approval of the version to be published; **Wilko Grolman**, analysis and interpretation of data, revision of the manuscript, final approval of the version to be published; **Geert J. M. G. van der Heijden**, design of study, analysis and interpretation of data, revision of the manuscript, final approval of the version to be published, supervision of study.

Disclosures

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Supplemental Material

Additional supporting information may be found at <http://oto.sagepub.com/content/by/supplemental-data>

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