ABSTRACT

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Rhinosinusitis is a significant and increasing health problem which results in a large financial burden on society. This evidence based position paper describes what is known about rhinosinusitis and nasal polyps, offers evidence based recommendations on diagnosis and treatment, and considers how we can make progress with research in this area.

Rhinitis and sinusitis usually coexist and are concurrent in most individuals; thus, the correct terminology is now rhinosinusitis. Rhinosinusitis (including nasal polyps) is defined as inflammation of the nose and the paranasal sinuses characterised by two or more symptoms, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip), ± facial pain/pressure, ± reduction or loss of smell; and either endoscopic signs of polyps and/or mucopurulent discharge primarily from middle meatus and/or; oedema/mucosal obstruction primarily in middle meatus, and/or CT changes showing mucosal changes within the ostiomeatal complex and/or sinuses.

The paper gives different definitions for epidemiology, first line and second line treatment and for research.

Furthermore the paper describes the anatomy and (patho)physiology, epidemiology and predisposing factors, inflammatory mechanisms, evidence based diagnosis, medical and surgical treatment in acute and chronic rhinosinusitis and nasal polyposis in adults and children. Evidence based schemes for diagnosis and treatment are given for the first and second line clinicians. Moreover attention is given to complications and socio-economic cost of chronic rhinosinusitis and nasal polyps. Last but not least the relation to the lower airways is discussed.

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European Position Paper on Rhinosinusitis and Nasal Polyps 2007

CONTENTS

1. Introduction

Rhinosinusitis is a significant health problem which seems to mirror the increasing frequency of allergic rhinitis and which results in a large financial burden on society [1-3]. Data on (chronic) rhinosinusitis are limited and the disease entity is badly defined. Therefore, the available data are difficult to interpret and extrapolate.

The last decade has seen the development of a number of guidelines, consensus documents and position papers on the epidemiology, diagnosis and treatment of rhinosinusitis and nasal polyposis [4-7]. In 2005 the first European Position Paper on Rhinosinusitis and Nasal Polyps (EP3OS) was published [8, 9]. This first evidence based position paper was initiated by the European Academy of Allergology and Clinical Immunology (EAACI) to consider what was known about rhinosinusitis and nasal polyps, to offer evidence-based recommendations on diagnosis and treatment, and to consider how we can make progress with research in this area. The paper has been approved by the European Rhinologic Society.

Evidence-based medicine is an important method of preparing guidelines [10, 11]. Moreover, the implementation of guidelines is equally important.

Table 1-1. Category of evidence [11]

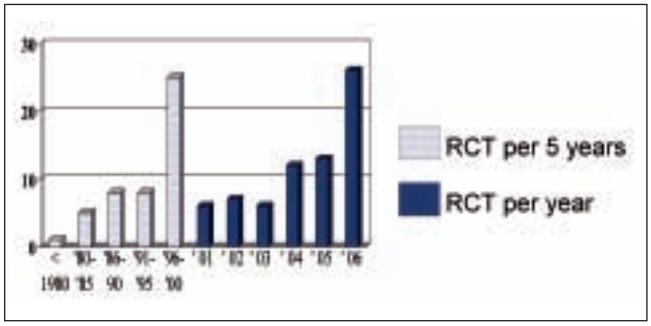
Ia	evidence from meta-analysis of randomised controlled trials
Ib	evidence from at least one randomised controlled trial
IIa	evidence from at least one controlled study without randomisation
IIb	evidence from at least one other type of quasi-experimental study
III	evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
IV	evidence from expert committee reports or opinions or clinical experience of respected authorities, or both

Table 1-2. Strength of recommendation

A	directly based on category I evidence
B	directly based on category II evidence or extrapolated recommendation from category I evidence
C	directly based on category III evidence or extrapolated recommendation from category I or II evidence
D	directly based on category IV evidence or extrapolated recommendation from category I, II or III evidence

Since the preparation of the first EP3OS document an increasing amount of evidence on the pathophysiology, diagnosis and treatment has been published (Figure 1).

Figure 1. Randomized controlled trials in chronic rhinosinusitis with or without nasal polyps. The number of trials in the last 5-6 years equals the number ever published before.



This revision is intended to be a state-of-the art review for the specialist as well as for the general practitioner:

- to update their knowledge of rhinosinusitis and nasal polyposis;
- to provide an evidence-based documented review of the diagnostic methods;
- to provide an evidence-based review of the available treatments;
- to propose a stepwise approach to the management of the disease;
- to propose guidance for definitions and outcome measurements in research in different settings.

In this revision new data have led to considerable increase in amount of available evidence and therefore to considerable changes in the schemes for diagnosis and treatment.
Moreover the whole document has been made more consistent, some chapters are significantly extended and others are added. Last but not least contributions from many other part of the world have attributed to our knowledge and understanding.

2. Definition of rhinosinusitis and nasal polyps

2-1 Introduction

Rhinitis and sinusitis usually coexist and are concurrent in most individuals; thus, the correct terminology is now rhinosinusitis. The diagnosis of rhinosinusitis is made by a wide variety of practitioners, including allergologists, otolaryngologists, pulmonologists, primary care physicians and many others. Therefore, an accurate, efficient, and accessible definition of rhinosinusitis is required. A number of groups have published reports on rhinosinusitis and its definition. In most of these reports definitions are based on symptomatology and duration of disease and a single definition is aimed at all practitioners [4, 5, 12, 13].

Due to the large differences in technical possibilities to diagnose and treat rhinosinusitis/nasal polyps by various disciplines, the need to differentiate between subgroups varies. On one hand the epidemiologist wants a workable definition that does not impose too many restrictions to study larger populations. On the other hand researchers in a clinical setting are in need of a set of clearly defined items that describes their patient population accurately and avoids the comparison of 'apples and oranges' in studies that relate to diagnosis and treatment. The taskforce tried to accommodate these different needs by offering definitions that can be applied in different circumstances. In this way the taskforce hopes to improve the comparability of studies, thereby enhancing the evidence based diagnosis and treatment of patients with rhinosinusitis and nasal polyps.

2-2 Clinical definition

2-2-1 Clinical definition of rhinosinusitis/nasal polyps

2-2-1-1 Bacteria

Rhinosinusitis (including nasal polyps) is defined as:

- inflammation of the nose and the paranasal sinuses characterised by two or more symptoms, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip):
  - ± facial pain/pressure,
  - ± reduction or loss of smell;

and either

- endoscopic signs of:
  - polyps and/or;
  - mucopurulent discharge primarily from middle meatus and/or; oedema/mucosal obstruction primarily in middle meatus,

and/or

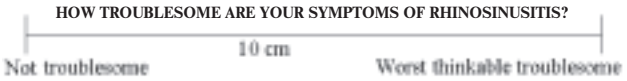
- CT changes:
  - mucosal changes within the ostiomeatal complex and/or sinuses.

2-2-2 Severity of the disease

The disease can be divided into MILD, MODERATE and SEVERE based on total severity visual analogue scale (VAS) score (0 - 10 cm):

- MILD = VAS 0-3
- MODERATE = VAS >3-7
- SEVERE = VAS >7-10

To evaluate the total severity, the patient is asked to indicate on a VAS the answer to the question:



A VAS > 5 affects patient QOL [14].

2-2-3 Duration of the disease

Acute

< 12 weeks
complete resolution of symptoms.

Chronic

> 12 weeks symptoms
without complete resolution of symptoms.

Chronic rhinosinusitis may also be subject to exacerbations

2-3 Definition for use in epidemiology studies/General Practice

For epidemiological studies the definition is based on symptomatology without ENT examination or radiology.

Acute rhinosinusitis (ARS) is defined as:

sudden onset of two or more symptoms, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip):

± facial pain/pressure,
± reduction or loss of smell;

for < 12 weeks;
with symptom free intervals if the problem is recurrent;
with validation by telephone or interview.

Questions on allergic symptoms i.e. sneezing, watery rhinorrhea, nasal itching and itchy watery eyes should be included.

Acute rhinosinusistis can occur once or more than once in a defined time period. This is usually expressed as episodes/year but there must be complete resolution of symptoms between episodes for it to constitute genuine recurrent acute rhinosinusitis.

Common cold/ acute viral rhinosinusitis is defined as:
duration of symptoms for less than 10 days.

Acute non-viral rhinosinusitis is defined as:
increase of symptoms after 5 days or persistent symptoms after 10 days with less than 12 weeks duration.

Chronic rhinosinusitis with or without nasal polyps is defined as:
presence of two or more symptoms one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip):
± facial pain/pressure;
± reduction or loss of smell;
for > 12 weeks;
with validation by telephone or interview.

Questions on allergic symptoms i.e. sneezing, watery rhinorrhea, nasal itching and itchy watery eyes should be included.

2-4 Definition for research

For research purposes acute rhinosinusitis is defined as above. Bacteriology (antral tap, middle meatal tap) and/or radiology (X-ray, CT) are advised, but not obligatory.

For research purposes chronic rhinosinusitis (CRS) is defined as above. CRS is the major finding and nasal polyposis (NP) is considered a subgroup of this entitiy. For the purpose of a study, the differentiation between CRS and NP must be based on out-patient endoscopy. The research definition is based on the presence of polyps and prior surgery.

2-4-1 Definition of chronic rhinosinusitis when no earlier sinus surgery has been performed

Chronic rhinosinusitis with nasal polyposis:
polyps bilateral, endoscopically visualised in middle meatus
Chronic rhinosinusitis without nasal polyps:
no visible polyps in middle meatus, if necessary following decongestant

This definition accepts that there is a spectrum of disease in CRS which includes polypoid change in the sinuses and/or middle meatus but excludes those with polypoid disease presenting in the nasal cavity to avoid overlap.

2-4-2 Definition of chronic rhinosinusitis when sinus surgery has been performed

Once surgery has altered the anatomy of the lateral wall, the presence of polyps is defined as bilateral pedunculated lesions as opposed to cobblestoned mucosa > 6 months after surgery on endoscopic examination. Any mucosal disease without overt polyps should be regarded as CRS.

2-4-3 Conditions for sub-analysis

The following conditions should be considered for sub-analysis:
1. aspirin sensitivity based on positive oral, bronchial or nasal provocation or an obvious history;
2. asthma/bronchial hyper-reactivity /COPD/ bronchiectasies based on symptoms, respiratory function tests;
3. allergy based on specific serum IgE or SPT's.

2-4-4 Exclusion from general studies

Patients with the following diseases should be excluded from general studies, but may be the subject of a specific study on chronic rhinosinusitis and/or nasal polyposis:
1. cystic fibrosis based on positive sweat test or DNA alleles;
2. gross immunodeficiency (congenital or acquired);
3. congenital mucociliary problems eg primary ciliary dyskinesia (PCD);
4. non-invasive fungal balls and invasive fungal disease;
5. systemic vasculitis and granulomatous diseases;
6. cocaine abuse;
7. neoplasia.

3. Chronic rhinosinusitis with or without nasal polyps

3-1 Anatomy and (patho)physiology

The nose and paranasal sinuses constitute a collection of air-filled spaces within the anterior skull. The paranasal sinuses communicate with the nasal cavity through small apertures. The nasal cavity and its adjacent paranasal sinuses are lined by pseudostratified columnar ciliated epithelium. This contains goblet cells and nasal glands, producers of nasal secretions that keep the nose moist and form a "tapis roulant" of mucus. Particles and bacteria can be caught in this mucus, rendered harmless by enzymes like lysozyme and lactoferrin, and be transported down towards the oesophagus. Cilia play an important role in mucus transport. All paranasal sinuses are normally cleared by this mucociliary transport, even though transport from large areas of sinuses passes through small openings towards the nasal cavity.

A fundamental role in the pathogenesis of rhinosinusitis is played by the ostiomeatal complex, a functional unit that comprises maxillary sinus ostia, anterior ethmoid cells and their ostia, ethmoid infundibulum, hiatus semilunaris and middle meatus. The key element is the maintenance of the ostial patency. Specifically, ostial patency significantly affects mucus composition and secretion; moreover, an open ostium allows mucociliary clearance to easily remove particulate matter and bacteria. Problems occur if the orifice is too small for the amount of mucus, if mucus production is increased, for instance during an upper respiratory tract infection (URTI), or if ciliary function is impaired. Stasis of secretions follows and bacterial export ceases, causing or exacerbating inflammation of the mucosa whilst aeration of the mucosa is decreased, causing even more ciliary dysfunction. This vicious cycle can be difficult to break, and if the condition persists, it can result as chronic rhinosinusitis. In chronic rhinosinusitis the role of ostium occlusion seems to be less pronounced than in ARS.

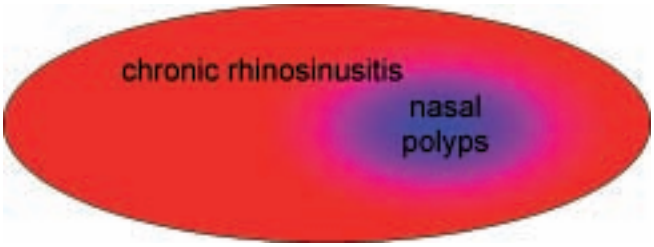
3-2 Rhinosinusitis

Rhinosinusitis is an inflammatory process involving the mucosa of the nose and one or more sinuses. The mucosa of the nose and sinuses form a continuum and thus more often than not the mucous membranes of the sinus are involved in diseases which are primarily caused by an inflammation of the nasal mucosa. Chronic rhinosinusitis is a multifactorial disease [15]. Factors contributing can be mucociliairy impairment [16, 17], (bacterial) infection [18], allergy [19], swelling of the mucosa for another reason, or rarely physical obstructions caused by morphological/anatomical variations in the nasal cavity or paranasal sinuses [20, 21]. A role in the pathogenesis of rhinosinusitis is certainly played by the ostiomeatal complex, a functional unit that comprises maxillary sinus ostia, anterior ethmoid cells and their ostia, ethmoid infundibulum, hiatus semilunaris and middle meatus. The key element is the maintenance of the ostial patency. An in depth discussion on factors contributing to chronic rhinosinusitis and nasal polyps can be found in chapter 4.

3-3 Chronic rhinosinusitis with or without nasal polyps

Chronic rhinosinusitis with or without nasal polyps is often taken together as one disease entity, because it seems impossible to clearly differentiate both entities [22-24]. Chronic rhinosinusitis with nasal polyps (CRS without NP) is considered a subgroup of chronic rhinosinusitis (CRS) (Figure 3-1).
The question remains as to why "ballooning" of mucosa develops in polyposis patients and not in all rhinosinusitis patients. Nasal polyps have a strong tendency to recur after surgery even when aeration is improved [25]. This may reflect a distinct property of the mucosa of polyp patients which has yet to be identified. Some studies have tried to divide chronic rhinosinusitis and nasal polyps based on inflammatory markers [26-30]. Although these studies point to a more pronounced eosinophilia and IL-5 expression in nasal polyps than that found in patients with chronic rhinosinusitis, these studies also point to a continuum in which differences might be found at the ends of the spectrum but at the moment no clear cut division can be made.

Figure 3-1. The spectrum of chronic rhinosinusitis and nasal polyps



Nasal polyps appear as grape-like structures in the upper nasal cavity, originating from within the ostiomeatal complex. They consist of loose connective tissue, oedema, inflammatory cells and some glands and capillaries, and are covered with varying types of epithelium, mostly respiratory pseudostratified epithelium with ciliated cells and goblet cells. Eosinophils are the most common inflammatory cells in nasal polyps, but neutrophils, mast cells, plasma cells, lymphocytes and monocytes are also present, as well as fibroblasts. IL-5 is the predominant cytokine in nasal polyposis, reflecting activation and prolonged survival of eosinophils [31].

The reason why polyps develop in some patients and not in others remains unknown. There is a definite relationship in patients with 'Samter triad': asthma, NSAID sensitivity and nasal polyps. However, not all patients with NSAID sensitivity have nasal polyps, and vice-versa. In the general population, the prevalence of nasal polyps is 4% [32]. In patients with asthma, a prevalence of 7 to 15% has been noted whereas, in NSAID sensitivity, nasal polyps are found in 36 to 60% of patients [33, 34]. It had long been assumed that allergy predisposed to nasal polyps because the symptoms of watery rhinorrhoea and mucosal swelling are present in both diseases, and eosinophils are abundant. However, epidemiological data provide no evidence for this relationship: polyps are found in 0.5 to 1.5% of patients with positive skin prick tests for common allergens [34, 35].