

# Turbinate surgery: which rhinitis are most at risk

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**Abstract.** *Background and aim:* Allergic rhinitis (AR) and non-allergic rhinitis (NAR) belong to field of vasomotor rhinitis, characterized by nasal hyper-reactivity. Since AR and NAR are two separate nosological entities, these rhinopathies can coexist in the same patient in up to 15-20% of cases. Overlapped rhinitis (ORs) are associated with intense and persistent symptoms and are often misdiagnosed. Typically, when medical treatment fails, patients undergo turbinate surgery. We evaluated which rhinopathies are most at risk of undergoing turbinate surgery and established the percentage of ORs. *Methods:* The study included 120 patients undergoing turbinate surgery for turbinate hypertrophy. Anterior rhinoscopy, nasal endoscopy, nasal cytology, skin prick tests (SPT) and/or specific IgE serum assays (CAP-RAST) were performed preoperative on all patients. *Results:* Among patients with indication for turbinate surgery, 75% suffered from AR, whereas 25% of them had NAR. On closer analysis, only 7 (8%) of allergic patients presented a “pure” allergy. NAR with eosinophils and mast cells (NARESMA) represented the most common type of superimposed rhinitis (62.5%), while NAR with mast cells (NARMA) and with eosinophils (NARES) represented 25% and 12.5% of the superimposed forms, respectively. *Conclusion:* Most of the patients undergoing turbinate surgery actually have complex forms of rhinitis. The non-allergic component of ORs often causes therapeutic failure. NARESMA overlapping ARs are at most risk of undergoing turbinate surgery. Correctly framing a rhino-allergological patient is essential in order to guarantee the most adequate treatment. Hence the importance of introducing in clinical practice investigations, including allergy tests and nasal cytology. ([www.actabiomedica.it](http://www.actabiomedica.it))

**Key words:** allergic rhinitis, non-allergic rhinitis, overlapped rhinitis, turbinate surgery, turbinate hypertrophy

## Introduction

Rhinitis is a heterogeneous group of disorders characterized by the inflammation of nasal mucosa, generally resulting in rhinorrhoea, sneezing, nasal obstruction and itching, variably associated(1). Based on the etiology, rhinitis can be mainly subdivided in infectious, inflammatory, vasomotor, medicamentous, hormonal, occupational and atrophic (2). In the context of vasomotor rhinitis, two big groups can be distinguished: allergic rhinitis (AR) and non-allergic rhinitis (NAR). These rhinopathies are characterized by nasal hyper-reactivity, the symptomatic expression of

the capacity of nasal mucosa to respond to allergenic or nonspecific stimuli, such as temperature, humidity and odours. Thanks to nasal cytology, non-allergic forms, better defined as “cellular”, have gained a nosological dignity over time. Once defined as “non-specific”, since an IgE-specific sensitization is excluded, NAR is nowadays classified according to the predominant cell types into NARES (NAR with eosinophils), NARMA (NAR with mast cells), NARNE (NAR with neutrophils) and NARESMA (NAR with eosinophils and mast cells) (3). NAR and AR, since they are two separate nosological entities, can coexist in the same patient in up to 15-20% of cases. Overlapping rhinitis

(ORs) are considered traps for allergists and otolaryngologists, due to the intense and persistent symptoms and the often misdiagnosed diagnosis, which results in failure of medical and surgical strategies (4). As a matter of fact, when medical treatments fail, patients undergo turbinate surgery with limited benefits over time, regardless of the type of surgical procedure used (5). In fact, the hypertrophy of the turbinates is one of the main causes of nasal obstruction in patients with rhinitis (6). However, turbinate hypertrophy should be considered the expression of an underlying rhinopathy and not a disease itself. Therefore, surgical treatment not associated with a tailored medical treatment, results ineffective. Hence the importance of making a precise diagnosis and of establishing, with the aid of rhinological diagnostic tools currently available to the rhinoallergologist, including nasal cytology, the possible presence of an OR.

The aim of this study was to evaluate which rhinopathies are most at risk of undergoing turbinate surgery and to establish the percentage of overlapped coexisting NRA.

## Materials and methods

120 consecutive patients, including 72 males (60%), who underwent turbinate surgery for turbinate hypertrophy at the Departments of Otolaryngology of Bologna, Foggia and Siena Hospitals were recruited. The age of the patients ranged from 18 to 71 years (mean age 46 years). Specific exclusion criteria were clinically relevant septal deviation, presence of acute or chronic upper respiratory infections, nasal polyps, previous or current specific immunotherapy, and use of nasal or oral corticosteroids, nasal or oral vasoconstrictors, antileukotrienes and antihistamines during the previous 2 weeks.

Before turbinate surgery, we carefully examined patients' clinical history and performed anterior rhinoscopy, nasal endoscopy, nasal cytology, skin prick tests (SPT) and/or specific IgE serum assays (CAP-RAST) on all patients. Preoperative nasal endoscopy was carried out by a 3.4 mm diameter flexible fiberscope (Vision-Sciences® ENT-2000). Cytological samples were collected preoperatively by Nasal

Scraping® (EP Medica, Italy), under anterior rhinoscopy, from the middle part of the inferior turbinate, according to validated criteria. Samples obtained were immediately placed on a glass slide, fixed by air drying and stained with May-Grunwald-Giemsa (MGG). Stained samples were read at optical microscopy, with a 1000x objective with oil immersion. A minimum of fifty fields is considered necessary to identify a sufficient number of cells. The predominant type of inflammatory cell, present in the sample, was considered.

Skin prick tests were performed with a commercial panel of the commonest aeroallergens and read according to the current recommendations of European Academy of Allergy and Clinical Immunology: house dust mite, grass mix, *Parietaria*, olive, cypress, mugwort, alternaria, ragweed, cat and dog dander. Moreover, allergen-specific IgE antibodies against the same allergens assayed with SPT were measured by a quantitative immunoassay (Immunocap Thermo Fisher Scientific Inc. Uppsala, Sweden), considering 0.35 kU/L the lower cut-off of the test.

Informed written consent was obtained from all participants. The study was approved by the local Ethics Committees (DDG n. 363 del 25.10.2016 e s.m.i. DDG n. 318 del 14.6.2019).

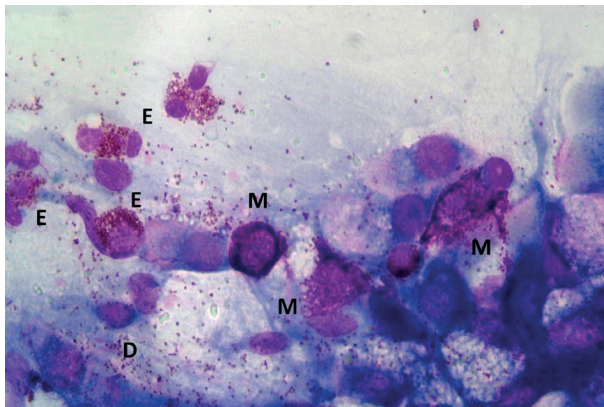
## Results

Ninety of 120 patients (75%) examined were tested positive to SPT and/or CAP-RAST. This first analysis allowed us to establish that 75% of patients undergoing turbinate surgery suffered from AR, whereas 25% of patients had NAR (Tab. 1).

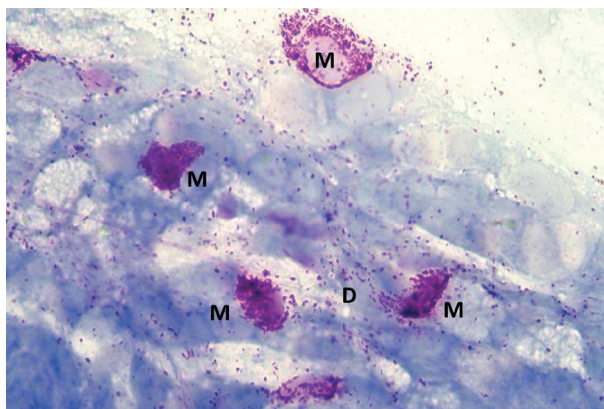
25 of the allergic patients (28%) also suffered from asthma, of which 18 (72%) had OR on nasal cytology. In the allergic group, 31 (35.5%) were mono-sensitive. Among prevalent allergens, house dust mite was the most common (42%), followed by grass mix (18%), *Parietaria* (15%), olive (9%) and other allergens (16%). However, from a cytological point of view, only 8% of patients with AR had a "pure" allergy. In fact, in 83 patients (92%) with AR coexisted a "cellular" rhinitis (OR). In particular, according to the predominant cell types, NARESMA represented the most common

**Table 1.** This table shows patients' demographic characteristics and percentages of AR and NAR.

Total sample	N (120)
<i>F</i>	48
<i>M</i>	72
<i>Mean age, years</i>	46 (10.6)
<i>Allergic rhinitis</i>	90 (75%)
<i>Non allergic rhinitis</i>	30 (25%)

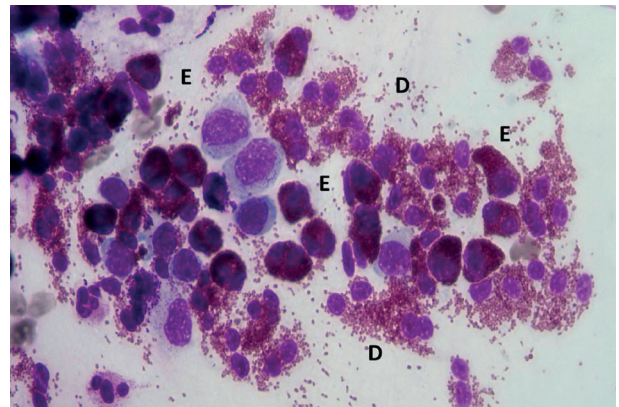


**Figure 1.** Pathological findings at nasal cytology in AR with overlapped NARESMA. E= eosinophil, M= Mast cell, D= degranulation. MGG staining. Magnification 1000x.



**Figure 2.** Nasal cytology of AR with overlapped NARMA. M= Mast cell, D= Degranulation. MGG staining. Magnification 1000x.

type of superimposed rhinitis (62.5%) (Fig. 1), while NARMA (Fig. 2) and NARES (Fig. 3) represented



**Figure 3.** Nasal cytology of AR with overlapped NARES. E= eosinophil, D= degranulation. MGG staining. Magnification 1000x.

## Discussion

The diagnosis of rhinitis is usually based on the presence of nasal signs and symptoms such as nasal congestion, nasal discharge, sneezing and nasal itching (7). In the context of vasomotor rhinitis, distinguishing between allergic and non-allergic phenotypes is extremely important for a more accurate diagnostic-therapeutic approach, which leads to better symptom control and a better quality of life for patients (8). However, understanding the subtle differences between these pathologies can be challenging since the clinical presentation of the various forms of rhinitis can be similar. The diagnosis of AR is established with the evidence of specific IgE response either by skin testing or by blood IgE assay and the presence of typical symptoms after exposure to the sensitizing aeroallergen, such as sneezing, itching, rhinorrhea and nasal obstruction. When specific IgE sensitization is clearly excluded (negative skin prick test or serum IgE assay) and there is no correlation between symptoms and their temporal onset after allergen exposure, it is assumed that the patient has a form of local allergic rhinitis or cellular rhinitis (9). Triggers for NAR patients include irritants (cigarette smoke, perfumes, cleaning products), weather changes (barometric pressure, temperature), and other strong odors (8). For a long time, NARs have been often underdiagnosed and/or labelled as “non-specific”, since they were considered rhinopathies

diagnosed purely on the basis of exclusion criteria, due to the lack of evidence concerning the incidence and, above all, the effective pathogenesis. Currently, the clinical use of nasal cytology has made it possible to formulate a more precise differential diagnosis, not only on the basis of the presence or absence of allergen sensitization, but also on the evaluation of the inflammatory cellular types infiltrating nasal mucosa. The introduction of nasal cytology in clinical practice has also allowed the identification of another subgroup of patients affected by multiple diagnostic entities (AR coexisting with NAR) complaining of symptoms that worsen in response to both allergic and non-allergic triggers. According to ARIA Guidelines, rhinocytograms of patients affected by ORs are characterized by the presence of mast cells >10% and eosinophils >20%. On the contrary, the rhinocytograms of "pure" allergic patients are negative outside the specific pollen period in the intermittent forms, and characterized by "minimal persistent inflammation" in the perennial forms (4). The non-allergic component is often misdiagnosed, thus patients with ORs are often treated with pharmacological approaches that act on the allergic component, including allergen immunotherapy (AIT), experiencing less benefit than expected. In fact, AIT has no effect on the concomitant "non-IgE mediated" component of rhinitis. Since turbinate hypertrophy is an expression of rhinitis, when medical treatment fails, patients typically undergo turbinate surgery with limited benefits over time. In light of this, we wondered if patients undergoing turbinate surgery for hypertrophy of the lower turbinates were "pure" allergic patients or if they had a "cellular" component that would reduce or nullify the benefits of the therapeutic approaches. As shown in Table 2, on closer analysis, among patients

with indication for turbinate surgery, only a very small percentage of them (8%) presented a "pure" allergy. As a matter of fact, nowadays there is a great variety of medical treatments, available to allergists and otolaryngologists, that counteract allergic symptoms with satisfactory clinical benefits (10). In addition to antihistamines and corticosteroids, which are able to suppress the immune response and/or improve symptoms, current pharmacological strategies include AIT (11). The latter is the only disease-modifying treatment for IgE-mediated allergy that alters the natural immunological course of allergic diseases and achieves long-term remission, unlike other therapies that are associated with a high risk of relapse when withdrawn (12). It is therefore not surprising that, in view of the efficacy, safety and tolerability of these treatments (13,14), patients with exclusively AR are unlikely to have little or no benefit from medical therapy, such as to need surgical treatments. On the other hand, most patients with ORs treated with AIT are unresponsive to the treatment, since AIT acts only partially on the pathophysiological mechanisms underlying rhinitis. Furthermore, as shown in Table 2, NARESMA coexisted in 62.5% of patients with ORs. In fact, it should be highlighted that, among NARs, NARESMA characteristically show more severe symptoms, resistance to antihistamines, frequent association with and rhinosinusitis, and predisposition to nasal polyposis (3, 15). In fact, in our study population, NARESMA was the most present rhinitis in the overlapping forms (62,5% versus 28% in "pure" allergic patients). For these patients, it may be necessary to combine multiple pharmacological strategies, tailored to the patient's rhinitis, and eventually surgical procedures (2). Thus, we believe that it is crucial to carefully evaluate the rhinological patient both from an anamnestic and clinical-instrumental point of view, to identify the presence of any "alarm bells" that could give rise to the suspicion of OR. In particular, Table 3 shows clinical and cytologic criteria which must lead to suspect the overlap of different rhinopathies (AR + NARESMA, NARES, NARMA) (4).

Peculiar attention should also be paid to another criticality: turbinate surgery, regardless of the type of procedure performed (laser, radiofrequencies, submucous resection of the turbinate, etc.), is fraught

**Table 2.** This table summarizes allergic patients' characteristics.

Allergic patients	N (90)
<i>Mono-sensitive allergy</i>	31 (35,5%)
<i>"Pure" AR</i>	7 (8%)
<i>Overlapped forms</i>	83 (90%)
AR + NARESMA	52 (62,5%)
AR + NARMA	21 (25%)
AR+ NARES	10 (12,5%)
<i>Asthma</i>	25 (28%)
Asthma + OR	18 (72%)

**Table 3.** When to suspect “overlapping” of different rhinopathies ( AR + NARESMA, NARMA or NARES), according to clinical and cytological criteria.

<b>Clinical criteria</b>
<ul style="list-style-type: none"> <li>• Chronic “vasomotor” rhinitis symptoms (nasal congestion, rhinorrhea, sneezing a salve), present even outside the pollen season, in a patient with positive skin prick test and/or RAST test</li> <li>• Increased “vasomotor”-type nasal reactivity to non specific stimuli (sudden changes in temperature, light stimuli, strong smells, cigarette smoke, exposure to chlorine (swimming), etc.)</li> <li>• Disturbances of taste and smell (suspect onset of nasal polyposis)</li> <li>• Positive family history of nasal polyposis, NARES, NARMA, NARESMA, asthma, sensitivity to acetylsalicylic acid, hypo-anosmia, vasomotor rhinitis labelled “non specific”, previous turbinate surgery for nasal congestion which gave poor medium- to long-term results</li> <li>• Recurrent use of nasal decongestants</li> <li>• Little or no clinical benefit following turbinate surgery for nasal congestion</li> <li>• Little or no clinical benefit following a cycle of specific immunotherapy (SIT)</li> </ul>
<b>Cytologic criteria</b>
<ul style="list-style-type: none"> <li>• In the forms with “persistent” symptoms, overlapping should be suspected in all patients with a rhinocytogram showing a cell profile different from that associated with “persistent minimal inflammation” (i.e. different form that characterised by numerous neutrophils, some lymphocytes and occasional eosinophils, with rare signs of degranulation), where there are eosinophils &gt; 20% and/or mast cells &gt;10%</li> <li>• In the forms with “intermittent” symptoms, overlapping should be suspected in all patients with a positive rhinocytogram (eosinophils &gt; 20% and/or mast cells &gt; 10%) outside the pollen season for the allergen/s identified by allergy testing (skin prick test and/or RAST test)</li> </ul>
<p>In rhinocytology, November tends to be preferred for “unraveling” overlapping rhinopathies, as this is the month in which most airborne pollens are absent.</p> <p>The presence of immune-inflammatory cells (eosinophils and/or mast cells) associated with rhinitis symptoms confirms the presence of overlapping disease.</p>

with various perioperative and postoperative complications. Bleeding, crusting and pain are the most frequently described complications, while alteration of ciliary activity and mucociliary clearance are often consequent to non-mucosal-sparing techniques. Major complications such as bone necrosis, synechiae, anosmia, and atrophic rhinitis are generally rare and associated with more aggressive techniques (16). Empty nose syndrome (ENS) represents one of the most feared sequelae of turbinate surgery, characterized by nasal dryness, crusting, and paradoxical nasal obstruction, despite an open nasal airway (17, 18). In particular, nasal mucosa of patients with ENS following excessive resection of turbinate tissue undergoes some airway remodeling and thermoreceptors down-regulation, which contribute to clinical symptoms (19). Although ENS is usually associated with aggressive procedures such as turbinectomy, even less invasive but repeated procedures could cause this syndrome over time. It has been shown that both AR and NAR patients gain benefit from turbinate

surgery to relieve nasal obstruction, however AR patients demonstrate greater improvement, probably thanks to pharmacological allergy management (20). In this perspective, patients with OR, benefiting to a lesser extent also from surgical treatment, could be repeatedly subjected to surgical procedures, with an increased risk of developing ENS. This is to further underline the importance of correctly frame the patient and to adopt the most adequate therapeutic strategy, especially since we believe that the ORs are an expression of the so-called Severe Chronic Upper Respiratory Disease (SCUAD). As a matter of fact, the definition of SCUAD includes those patients with persistent inflammation and symptoms despite guideline-guided drug treatment (21). While ARIA and EPOS guidelines provide clinicians with evidence-based treatment algorithms for allergic rhinitis (AR) and chronic rhinosinusitis (CRS) respectively, SCUAD patients still represent a therapeutic challenge (22). It has been hypothesized that defective pathways involved in the regulation of Th1

vs Th2 responses underlay this syndrome, however the pathophysiological mechanisms are not yet fully understood (23). Moreover, as shown by the results, most patients with a history of asthma had OR. Rhinitis are associated with an increased risk of early hospitalization in patients with asthma and COPD (24). Other studies suggest the importance of treating rhinitis in adults with asthma, being a significant factor associated with the risk of exacerbation (25). In this context, the only way to provide the patient with a correct diagnosis and therefore a tailor-made treatment is to make use of a clinical-instrumental approach that includes most of the diagnostic tools available today to the rhinoallergologist, such as allergy tests, rhinoendoscopy, nasal cytology and olfactometric tests.

## Conclusion

Most of the patients undergoing turbinate surgery actually have complex forms of rhinitis (e.g. cellular rhinitis and ORs). Precisely, the non-allergic component of rhinitis often causes therapeutic failure and, in particular, NARESMA overlapping ARs are at most risk of undergoing turbinate surgery. We therefore want to emphasize the importance of correctly frame the rhinoallergological patient with all the diagnostic tools available today, such as allergy tests and nasal cytology, which are too often considered second-line investigations, even though they are indispensable to reveal pathologies such as ORs, still little known and often misdiagnosed.

**Conflict of Interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

**Informed consent:** All patients included in the study signed informed consent.

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