

## Management of nasal polyposis

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**Abstract.** These guidelines are modified from the recent EAACI Position Paper. Nasal polyposis is characterized by an inflammatory process, the factors of which are summarized. Recently, *Staphylococcus aureus* enterotoxins have been identified to modify the disease. A classification system for polyps, grading systems and epidemiologic data are given, frequent comorbidities are discussed.

The diagnostic management is based on endoscopy and CT scanning. A score of severity is proposed. The therapeutic management consists of the medical treatment options, which are given with evidence-based recommendations. Surgical treatment is indicated after failure of medical treatment and commonly performed by endoscopy. Nevertheless medical

### 1. Brief definition and epidemiology of nasal polyposis

#### Clinical definition

Chronic rhinosinusitis (CRS) (including nasal polyps (NP)) is defined as:

- Inflammation of the nose and the paranasal sinuses characterised by two or more symptoms:

blockage/congestion;  
reduction or loss of smell;  
discharge: anterior/post-nasal drip;  
facial pain/pressure,

and either:

- Endoscopic signs:  
polyps;  
mucopurulent discharge from middle meatus;  
oedema/mucosal obstruction primarily in middle meatus,

and/or:

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

Nasal polyposis is defined as a subgroup of chronic rhinosinusitis, characterised by visible polyps in both middle meatus/nasal cavities as shown by nasal endoscopy. This definition accepts that there is a spectrum of diseases in CRS, including polypoid changes in the sinuses and/or middle meatus which are currently not thought of as nasal polyposis.

#### Severity of disease

The disease can be divided into MILD and MODERATE/ SEVERE on the basis of the total VAS (visual analogue scale) score (0-10 cm, no symptoms – unbearable symptoms):

MILD = VAS 0-4

MODERATE/SEVERE = VAS 5-10 (for at least one symptom)

#### Comorbidities

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 hyperreactivity/COPD based on symptoms and respiratory function tests;
3. allergy based on specific serum IgE or SPTs.

#### Differential diagnosis

The following diseases should be excluded from the diagnosis:

1. cystic fibrosis based on a positive sweat test or DNA mutation;
2. gross immunodeficiency (congenital or acquired);
3. congenital mucociliary problems such as PCD;
4. non-invasive fungal balls, allergic fungal sinusitis and invasive fungal disease;
5. systemic vasculitic and granulomatous diseases;
6. inverted papilloma and malignant tumours.

#### Epidemiology

In the light of epidemiological research, a distinction needs to be made between clinically silent NP, or preclinical cases, and symptomatic NP. Asymptomatic polyps

may be present transiently or persist, and therefore remain undiagnosed until they are discovered by routine examination. On the other hand, polyps that become symptomatic may remain undiagnosed, either because the patient is not investigated properly or because they are missed by anterior rhinoscopy. Endoscopy of the nasal cavity makes it possible to visualise NP and to give a reliable estimate of the prevalence of NP.

In a population-based study in Skövde (Sweden), Johansson *et al.*<sup>1</sup> reported a prevalence of nasal polyps of 2.7% in the total population. In this study, NP were diagnosed by nasal endoscopy and were more frequent in men (2.2 to 1), the elderly (5% at 60 years of age and older) and asthmatics. On the basis of a postal questionnaire survey in Finland, Hedman *et al.*<sup>2</sup> found that 4.3% of the adult population gave an affirmative answer to the question of whether polyps had been found in their nose. In autopsy studies, a prevalence of 2% has been found using anterior rhinoscopy.<sup>3</sup> After removing whole naso-ethmoidal blocks, nasal polyps were found in 5 out of 19 cadavers,<sup>4</sup> and in 42% of 31 autopsy samples combining endoscopy with endoscopic sinus surgery.<sup>5</sup>

It has been stated that between 0.2 and 1% of people develop nasal polyps at some stage.<sup>6</sup> In a prospective study of the incidence of symptomatic NP, Larsen and Tos<sup>7</sup> found an estimated incidence of 0.86 and 0.39 patients per thousand per year for males and females respectively. The incidence increased with age, reaching peaks of 1.68 and 0.82 patients per thousand per year for males and females respectively in the age group of 50-59 years.

When reviewing data from patient records of nearly 5000 patients from hospitals and allergy clinics in the US in 1977, the prevalence of NP was found to be 4.2%, with a higher prevalence (6.7%) in the asthmatic patients.<sup>8</sup>

In general, NP occur in all races, becoming more common with age. The average age of onset is approximately 42 years, which is 7 years older than the average age of the onset of asthma. NP are uncommon under the age of 20 and are more frequently found in men than in women.

### Factors associated with NP

#### Allergy

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<sup>8,9</sup> and this figure is comparable to that for the normal population.<sup>6</sup> On the other hand, the prevalence of allergy in patients with nasal polyps has been reported as varying from 10%<sup>10</sup> to 54%<sup>11</sup> and 64%.<sup>12</sup> Recently, Bachert *et al.*<sup>13</sup> found an association between mucosal levels of both total and specific IgE and eosinophilic infiltration in nasal polyps. These findings were unrelated to skin prick test results.

#### Asthma

Seven percent of patients with asthma have nasal polyps<sup>8</sup>; the prevalence rates are 13% in non-atopic asthma (skin prick test and total and specific IgE negative)

and 5% in atopic asthma.<sup>14</sup> Late-onset asthma is associated with the development of nasal polyps in 10-15% of patients.<sup>8</sup> One study indicates that asthma develops first in approximately 69% of patients with both asthma and NP, and NP take between 9 and 13 years to develop. In another study, ten percent developed both polyps and asthma simultaneously and the remainder developed polyps first and asthma between two and twelve years later.<sup>15</sup>

#### Aspirin sensitivity

There is a definite relationship with patients with Samter's triad: asthma, NSAID sensitivity and nasal polyps. In the general population, the prevalence of nasal polyps is 4% (2). 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.<sup>8,16</sup> In patients with aspirin sensitivity, 36-96% have nasal polyps<sup>9,14</sup> and up to 96% have radiographic changes affecting their paranasal sinuses. Patients with aspirin sensitivity, asthma and nasal polyposis are usually non-atopic, and prevalence increases above the age of 40 years. The children of patients with asthma, nasal polyps and aspirin sensitivity have nasal polyps and rhinosinusitis more often than the children of controls.<sup>17</sup>

### 2. Short review of pathophysiology

Polyposis and chronic rhinosinusitis can be viewed as the extremes of a continuum, ranging from polyposis without rhinosinusitis at one extreme to chronic rhinosinusitis without polyps at the other. Nasal polyps have a strong tendency to recur after

surgery, even when aeration is improved. This may reflect a distinct property of the mucosal inflammation of polyp patients which has yet to be identified. Some studies have tried to distinguish between chronic rhinosinusitis and nasal polyps using inflammatory markers.<sup>18-22</sup> Further data are clearly required to differentiate disease entities.

Nasal polyps appear as grape-like structures in the upper nasal cavity, mostly originating from within the ostiomeatal complex. They consist of loose connective tissue, oedema, inflammatory cells and some glands and capillaries, and are covered with various types of epithelium, but mostly respiratory pseudostratified epithelium with ciliary 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 most predominant cytokine in nasal polyposis, reflecting the activation and prolonged survival of eosinophils.<sup>23</sup> Recent findings point to metallo-proteinases as regulators of tissue destruction, and the storage of plasma proteins as the main principle of mucosal remodelling in nasal polyposis.<sup>24</sup>

**Role of staphylococcus aureus enterotoxins (SAEs)**

Early studies have shown that tissue IgE concentrations and the number of IgE-positive cells may be raised in nasal polyps, suggesting the possibility of local IgE production.<sup>25</sup> The local production of IgE is a characteristic feature of nasal polyposis, with a more than tenfold increase of IgE-producing plasma cells in NP compared to controls. Analysis of specific IgE

revealed a multiclonal IgE response in nasal polyp tissue and IgE antibodies to staphylococcus aureus enterotoxins (SAEs) in about 30-50% of patients and in about 60-80% of nasal polyp subjects with asthma.<sup>13,26,27</sup> A recent prospective study revealed that colonisation of the middle meatus with staphylococcus aureus is significantly more frequent in NP (63.6%) compared to CRS (27.3%,  $p < 0.05$ ), and is related to the prevalence of IgE antibodies to classical enterotoxins (27.8 in NP to 5.9% in CRS).<sup>28</sup> If aspirin sensitivity, including asthma, accompanied nasal polyp disease, the Staph. aureus colonisation rate was as high as 87.5%, and IgE antibodies to enterotoxins were found in 80% of cases.

Total and specific IgE in polyp homogenates is only partially reflected in the serum of these

patients. By contrast, staining of NP tissue revealed follicular structures characterised by B- and T-cells, and lymphoid agglomerates with diffuse plasma cell infiltration, demonstrating the organisation of secondary lymphoid tissue with consecutive local IgE production in NP.<sup>29</sup>

When SAE-IgE-positive nasal polyps are compared to SAE-IgE-negative, one finds a significantly higher number of IgE-positive cells and eosinophils. The more severe inflammation is also reflected by significantly increased levels of IL-5, ECP and total IgE. In conclusion, SAEs are able to induce a more severe eosinophilic inflammation as well as the synthesis of a multiclonal IgE response with high total IgE concentrations in the tissue, which would suggest that SAEs are at least modifiers of disease in nasal

Table 1  
Endoscopic appearance scores

Characteristic	Baseline	3 mo	6 mo	1 y	2 y
Polyp, left (0,1,2,3)					
Polyp, right (0,1,2,3)					
Oedema, left (0,1,2,)					
Oedema, right (0,1,2,)					
Discharge, left (0,1,2)					
Discharge, right (0,1,2)					
Postoperative scores to be used for outcome assessment only					
Scarring, left (0,1,2)					
Scarring, right (0,1,2)					
Crusting, left (0,1,2)					
Crusting, right (0,1,2)					
Total points					

0-Absence of polyps;  
 1-Polyps in middle meatus only;  
 2-Polyps beyond middle meatus but not blocking the nose completely;  
 3-Polyps completely obstructing the nose.  
 Oedema: 0-absent; 1-mild; 2-severe.  
 Discharge: 0-no discharge; 1-clear, thin discharge; 2-thick, purulent discharge.  
 Scarring: 0-absent; 1-mild; 2-severe.  
 Crusting: 0-absent; 1-mild; 2-severe.

polyposis.<sup>30</sup> Interestingly, similar findings have recently been reported in asthma, which is known to coincide with NP.<sup>31</sup>

### 3. Diagnostic management

Nasal polyps may cause nasal congestion, which can induce a feeling of pressure and fullness in the nose and paranasal cavities. This is typical for ethmoidal polyposis, which in severe cases can cause radiologically-detectable widening of the nasal and paranasal cavities, but may also cause hypertelorism. Another typical symptom is nasal discharge, which is often felt as post-nasal drip by the patient. Disorders of smell are more prevalent in patients with nasal polyps than in other chronic rhinosinusitis patients,<sup>32</sup> whereas headache and facial pain are more prevalent in CRS. During the last decade, more attention has been paid not only to symptoms but also to their effect on patient quality of life.<sup>33,34</sup>

Anterior rhinoscopy alone is inadequate to differentiate CRS from NP, but it remains the first step in the examination of patients with these diseases. Endoscopy may be performed without and with decongestion, and semi-quantitative scores for polyps, oedema, discharge, crusting and scarring (post-operatively) can be obtained (see Table 1). A number of staging systems for polyps have been proposed.<sup>35-37</sup>

CT scanning is the imaging modality of choice for confirming the extent of pathology and the anatomy. However, it should not be regarded as the primary step in the diagnosis of the condition but rather as a means of corroborating history and endoscopic examination after the failure of medical therapy.

MRI is not the primary imaging modality in nasal polyposis and is usually reserved in combination with CT for the investigation of sinister conditions such as neoplasia, or mykotic sinusitis. A range of staging systems of varying complexity based on CT scanning using stages 0-4 have been described. The Lund-Mackay system assigns scores of 0-2 depending on absence, partial or complete opacification in each sinus system and in the ostiomeatal complex, resulting in a maximum score of 12 per side (see Table 2).<sup>35</sup>

However, the correlation between CT findings and symptom scores has been shown to be consistently poor and is not a good indicator of outcome.<sup>38</sup> Since the loss of sense of smell is a typical finding in nasal polyps, the sense of smell should be documented for diagnosis as well as pre- and post-operatively.

### 4. Therapeutic management

#### Medical treatment (see Table 3)

Local corticosteroids have a documented effect on bilateral NP and also on symptoms associated with NP such as nasal blockage, secretion and sneezing, but the effect on the sense of smell is not im-

pressive. There is convincing evidence for a therapeutic effect on polyp size and nasal symptoms associated with nasal polyposis, particularly nasal blockage. Furthermore, the postoperative effect on the recurrence rate of NP with intranasal steroids is well documented. Topical steroids are therefore the first-choice treatment of NP.

There have been no studies of single treatment with systemic steroids for NP patients without concomitant treatment with topical steroids. Placebo-controlled studies and dose-effect studies are therefore lacking but there is clinical acceptance, supported by open studies,<sup>39,40</sup> that systemic steroids have a significant effect on NP. A typical scheme would involve methylprednisolone 32 mg for 5 days, 16 mg for 5 days, and 8 mg for 10 days. Long-term treatment should be limited to 8 mg per day or less.

Systemic steroids are less well-documented than intranasal steroids but open studies indicate that they are effective in polyp reduction and nasal symptoms associated with NP, and that they even have an effect on the sense of smell, by contrast with intranasal corticosteroids. The effect is reversible.

Table 2  
CT scoring system<sup>35</sup>

<i>Sinus System</i>	<i>Left</i>	<i>Right</i>
Maxillary (0,1,2)		
Anterior ethmoids (0,1,2)		
Posterior ethmoids (0,1,2)		
Sphenoid (0,1,2)		
Frontal (0,1,2)		
Ostiomeatal complex (0 or 2 only)*		
Total points		

0-no abnormalities; 1-partial opacification; 2-total opacification.

\*0-not occluded; 2-occluded

Nor is there any study available dealing with the depot injection of corticosteroids or local injection into polyps or the inferior turbinate. This sort of treatment is actually obsolete because of the risk of fat necrosis at the site of the injection or blindness following endonasal injection.

Other treatment modalities include:

- A number of clinical reports have stated that long-term, low-dose macrolide antibiotics are effective in treating chronic sinusitis incurable by surgery or glucocorticosteroid treatment. The benefit of long-term, low-dose macrolide treatment seems to be that it is, in selected cases, effective when steroids fail. Placebo-controlled studies should be performed to establish the efficacy of macrolides if this treatment is to

be accepted as evidence-based medicine.

- The effect of antileukotrienes has not been tested in controlled trials for nasal polyposis. However, a few case-controlled trials indicate that antileukotriene treatment may have a beneficial effect on nasal symptoms in patients with chronic rhinosinusitis and nasal polyposis. The findings are consistent with a subgroup of nasal polyps/asthma patients in whom leukotriene receptor antagonists may be effective, but there is no relationship with aspirin sensitivity. There is a need for controlled trials of antileukotriene treatment in nasal polyposis.

- Aspirin desensitisation consists of administering incremental oral doses to reach a maintenance dose of > 650 mg daily, inducing a refractory period of a few days.

Continuous treatment over years may lead to a significant reduction in the numbers of sinus infections per year and in the annual number of hospital admissions for the treatment of asthma, to improvements in olfaction, and to a reduction in the use of systemic corticosteroids.<sup>41</sup> Furthermore, numbers of sinus operations per year are significantly reduced. However, as a rather high dosage of aspirin has to be ingested every day, gastro-intestinal side-effects and hives are frequent, and relapses occur in cases where there is non-compliance.<sup>42</sup> In one study, however, smaller doses of aspirin were also used successfully.<sup>43</sup> Aspirin desensitisation does not seem to change the long-term course of the disease. Treatment with daily aspirin may be a therapeutic option for patients who do

Table 3

Evidence-based treatment recommendations

Therapy	Level	Grade of recommendation	Relevant
oral antibiotics short term <2 weeks	no data available		No
oral antibiotic long term ~12 weeks	III (>6)	C	Yes
topical antibiotics	no data available		No
topical steroids	I b	A	Yes
oral steroids	III	C	Yes
nasal douche	III no data in single use	C	yes for symptomatic relief
decongestant topical / oral	no data in single use		No
mucolytics	VI (1)	D	No
antimycotics - systemic	VI	D	No
antimycotics - topical	III	D	no
oral antihistamine in allergic patients	Ib (1)	B	no
allergic therapy in allergic patients	Ib (1)	B	no
allergen avoidance in allergic patients	IV	D	yes
Proton pump inhibitors	III (3)	C	no
immunotherapy	no data		no
phytotherapy	no data		no

not respond to topical and systemic corticosteroids.

**Surgical treatment**

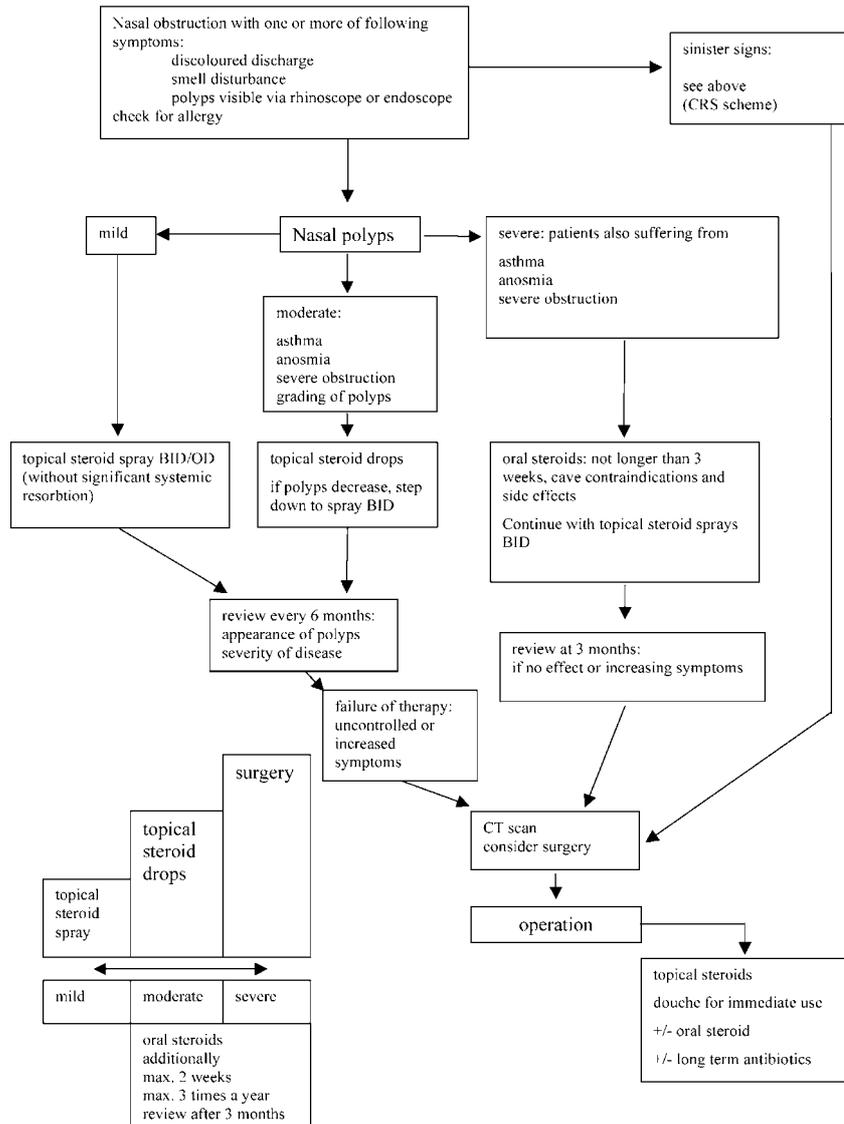
Surgical treatment, nowadays commonly performed as endoscopic sinus surgery, preferably using a microdebrider, is indicated after the failure of medical treatment. Medical therapy should be continued after surgery, and revision surgery may be necessary in patients developing recurrences, even with ongoing medical therapy. Surgical treatment with consecutive medical therapy can provide disease control in about 80% of patients when surgery aims to remove polyp tissue completely. Trials providing high-level statements of evidence for the efficacy of surgery for rhinosinusitis (with or without polyps) are lacking, as concluded by Lund.<sup>44</sup> In addition, the level of experience of endoscopic rhinosurgeons has to be established before one can compare results from different studies.<sup>45</sup> However, at least two studies have shown that aggressive medical therapy gives similar results over a one-year period,<sup>46,47</sup> underlining the need to reserve surgery for those who have failed medical therapy. ‘High-risk’ patients should be treated with aggressive long-term medication pre- and postoperatively and should be viewed as a separate group when evaluating studies.

One recent study compared surgery to long-term antibiotic treatment in patients with CRS with and without NP.<sup>46</sup> Ninety patients with CRS were equally randomised to medical or surgical therapy. Both the medical and surgical treatment of CRS resulted in significant improvements in almost all the subjective and objective parameters of CRS ( $P < .01$ ),

with no significant difference being found between the medical and surgical groups ( $P > .05$ ), except for the total nasal volume in CRS ( $P < .01$ ) and CRS without

polyposis ( $P < .01$ ) groups, in which surgical treatment resulted in greater changes.

**5. Decisional algorithms**



Algorithm

**6. Patient information**

- Nasal polyps are a chronic inflammatory disease affecting all sinuses. NP may be associated with asthma and aspirin sensitivity.
- The main symptoms are loss of smell, blocked nose, secretions

- and post-nasal drip as well as facial pain/headache.
- The primary treatment involves topical steroid sprays, which need to be applied regularly. Other treatment options may be discussed with your ENT specialist.
- Surgery may be necessary if drug treatment fails. This surgery

normally is performed from inside the nose, and is known as FESS (functional endoscopic sinus surgery). Surgery can control the symptoms of disease in up to 80% of patients, but recurrences are not infrequent.

- Topical steroids may also be necessary after surgery for long-term treatment to prevent recurrences. Please report to your doctor if you notice the onset of loss of smell or nasal obstruction.

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**CME questions**

1. What symptom is characteristic for nasal polyps rather than for chronic rhinosinusitis?
  - A – Blockage/congestion
  - B – Reduction or loss of smell
  - C – Anterior discharge
  - D – Post-nasal drip
  - E – Facial pain/pressure
  
2. Name frequent comorbidities of nasal polyps:
  - A – Aspirin sensitivity
  - B – Asthma/bronchial hyperreactivity
  - C – Allergy
  - D – Inverted papilloma
  - E – COPD
  
3. What are possible differential diagnoses of nasal polyps?
  - A – Cystic fibrosis
  - B – Congenital mucociliary problems (PCD)
  - C – Non-invasive fungal balls
  - D – Allergic fungal sinusitis
  - E – Systemic vasculitis (Churg-Strauss)
  
4. Which statement is incorrect?
  - A – NP occur in all races
  - B – NP become more common with age. The average age of onset is approximately 42 years
  - C – NP are more frequently found in women than in men
  - D – The prevalence of NP is > 5% in asthmatic patients
  - E – In cystic fibrosis, children only have polyps in the nose after initial surgery
  
5. The following cytokine is typically increased in nasal polyps and linked to eosinophilia:
  - A – Interleukin-3
  - B – Interleukin-5
  - C – Interleukin-8
  - D – Interleukin-1
  - E – ECP
  
6. Which statement is incorrect?
  - A – Staphylococcus aureus is a frequent coloniser of polyps.
  - B – Staphylococcus aureus is a frequent germ causing infections in the sinuses.
  - C – Staphylococcus aureus is able to secrete enterotoxins that can act as superantigens.
  - D – In polyps, IgE is high, and only directed to enterotoxins of Staphylococcus aureus
  - E – IgE to enterotoxins of Staphylococcus aureus cannot be found in chronic rhinosinusitis without polyps

7. Required diagnostic procedures before surgery for NPs include:

- A – Nasal endoscopy
- B – CT scan
- C – MRI
- D – Swab for bacteriology
- E – Lung function test

8. Standard treatment modalities for bilateral NPs Grade 1 include:

- A – Oral steroids
- B – Topical steroids
- C – Leukotriene receptor antagonists
- D – Antibiotics
- E – Surgery

9. Standard treatment modalities for bilateral NPs Grade 3 include:

- A – Oral steroids
- B – Topical steroids
- C – Leukotriene receptor antagonists
- D – Antibiotics
- E – Surgery

10. What is correct?

- A – The target in sinus surgery for NPs is to open the sinuses and remove all pathologic polyp tissue
- B – Because
- C – There is a chance of malignant transformation.

**Answers:** 1B; 2AC; 3ABDE; 4C; 5B; 6D; 7AB; 8B; 9ABE; 10A