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# **Original Research Article**

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# Chronic rhinosinusitis with nasal polyps: predictive factors for recurrence and revision surgery

# Pedro Salvador\*, Catarina Lombo, Francisco Moreira da Silva, Rui Fonseca

Department of Otorhinolaryngology, Hospital Senhora da Oliveira, Guimarães, Portugal

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# \*Correspondence:

Dr. Pedro Salvador,

E-mail: josepedrobsalvador@gmail.com

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## **ABSTRACT**

**Background:** Chronic rhinosinusitis with nasal polyps (CRSwNP) is an inflammatory condition which may have a significant impact on quality of life. Endoscopic sinus surgery (ESS) is indicated for patients refractory to maximal medical treatment and presents high recurrence and revision surgery rates. Aim of the study was to evaluate ESS outcome in CRSwNP management and to assess independent predictive factors for recurrence and revision surgery. **Methods:** Retrospective medical chart review of patients who underwent ESS for recalcitrant CRSwNP, from January 2013 to December 2017, with a minimum follow-up time of 12 months.

**Results:** This study enrolled 132 patients, 62.1% of whom were males, with a mean age of 43.4±11.5 years. Asthma was the most common comorbidity (39.4%, n=52) and aspirin exacerbated respiratory disease (AERD) was present in 9.8% (n=12) of the study population. We found a recurrence rate of 34.1% (n=45) and 9% (n=12) of patients required revision surgery. Multivariate analysis identified as independent variables of recurrence (95% CI): a history of asthma (OR=8.81, CI 3.87-20.03; p<0.001) and a severe Lund-Mackay score (17-24) (OR=5.85, CI 2.73-12.51; p=0.001). Revision surgery was related to a severe endoscopic Lund-Kennedy score at presentation (OR=4.05, CI 1.91-8.01, p=0.001).

**Conclusions:** CRSwNP presents a high tendency to recur after ESS. Asthma, severe sinus opacification and severe endoscopic score are poor prognostic factors that hallmark a more aggressive disease. A more extensive surgical procedure and/or middle turbinate resection with a rigorous postoperative compliance should be considered to improve long term results.

Keywords: Endoscopic sinus surgery, Nasal polyps, Predictive factors, Recurrence, Revision surgery

### **INTRODUCTION**

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a sinonasal inflammatory disease, with a prevalence in general population of 1% to 4%, responsible for a significant impact on quality of life. Several conditions are known to be associated with NP, including asthma and aspirin hypersensitivity. Endoscopic sinus surgery (ESS) is indicated in patients with CRSwNP refractory to maximal medical treatment. Despite its favorable initial

clinical and endoscopic success, recurrence rate up to 60% has been reported in literature, depending on follow up time, and 15-20% of patients require revision surgery.<sup>3</sup> Previous studies have identified higher recurrence rates in patients with history of asthma, aspirin hypersensitivity and previous sinus surgery.<sup>2</sup> Smoking history, occupational exposure and frontal sinus extension are other reported factors associated with a poorer prognosis.<sup>3-6</sup> The aim of this study were to evaluate FESS outcome in CRSwNP management and to identify

independent predictive factors of recurrence and revision surgery.

#### **METHODS**

This study was designed as a retrospective medical chart review and were included adult patients (≥18 years) diagnosed with CRSwNP who underwent ESS, from January 2013 to December 2017, in our center (Hospital Senhora de Oliveira - Guimarães, Portugal), CRSwNP was diagnosed based on clinical history, findings on nasal endoscopy and paranasal sinus CT according to definition of European Position Paper On Rhinosinusitis and Nasal Polyps.<sup>1</sup> Surgery was offered to patients who failed to improve after a trial of maximal medical treatment, including a 10-day course of oral corticosteroid therapy, topical nasal steroid for 3 months and one course of broad spectrum antibiotic. Exclusion criteria included patients with unilateral disease, fungal sinusitis, antrochoanal polyps, concomitant benign or malignant sinonasal tumors, cystic fibrosis, primary ciliary dyskinesia, and those with a follow up period inferior to 12 months. Revision surgery was offered to patients who had symptomatic nasal polyp recurrence, persistent for more than 6 months after medical treatment.

Demographic, clinical, imagiologic and surgical data were retrospectively collected. Charts were reviewed for the following variables age, sex, smoking status, occupational exposure, comorbidities (asthma, aspirinexacerbated respiratory disease and allergic rhinitis), history of sinus surgery, computed tomography (CT) scan score and hematologic parameters.

Smoking group was defined as patients with smoking habits at the time of the surgery. Patients who had stopped smoking for 6 months or longer before the surgery were defined as nonsmokers. A history of occupational inhalant dust exposure was considered positive if present on a daily basis and it was subclassified into organic (e.g. cotton, flax, pants, flour, fuel gas and wood dust) and inorganic dust (bleach, metals, cement and pesticides).

Allergic rhinitis was diagnosed based on typical symptoms following exposure to allergen complemented by results of total serum immunoglobulin E (IgE) positive concentration. fluorescence enzvme immunoassay (phadiatop, which detects specific IgE antibodies to a mixture of the most common aeroallergens) and/or positive skin prick tests. Asthma and Aspirin-exacerbated respiratory disease (AERD) were diagnosed by a pneumologist. Hypersensitivity to aspirin was diagnosed based on history of adverse respiratory reactions triggered by aspirin and/or nonsteroidal anti-inflammatory drugs (NSAID) intake. AERD was defined by presence of nasal polyps with asthma and intolerance to inhibitors of cyclooxygenase-1 (COX-1).

Nasal polyps (NP) were classified endoscopically according to Lindholdt score (LS) as grade I (polyps within the osteomeatal complex), II (polyps extending between the osteomeatal complex and the inferior border of the inferior turbinate) or III (polyps reaching the nasal floor). The score ranged from 0 to 6 and it was further subclassified in mild polyposis (score 1-2), moderate polyposis (score 3-4) and severe polyposis (score 5-6). Preoperative CT scan was classified according to the Lund-Mackay (LM) scoring system (range 0-24).8 According to this system, a higher score correlates with a more severe disease (six regions on each side, scored 0-2).<sup>7</sup> This score was also subclassified into mild (1-8), moderate (9-16) and severe (17-24). A complete blood cell count with differential cell count was performed in all patients and eosinophil parameters were collected.

All patients underwent endoscopic sinus surgery (ESS) under general anesthesia with endotracheal intubation, which included at least polypectomy complemented by infundibulotomy and a complete ethmoidectomy. Frontal and sphenoid sinus were approached according to CT and intraoperative findings. Middle turbinate was resected when it was extensively involved by NP disease and/or to obtain surgical access. After surgery patients started a 7-day course of antibiotic and a regular saline douching. The first follow up visit was scheduled one week after surgery for debridement and then patients started intranasal corticosteroid spray. Systemic corticosteroids were not prescribed perioperatively. Patients were evaluated 1, 3 and 6 months post-operatively and then every 6 months for at least one year.

Histological analysis showed tissue hypereosinophilia in every patient. None of the patients had undergone aspirin desensitization, allergen immunotherapy or monoclonal antibody therapy. Postoperative endoscopic findings in each nasal cavity were classified based on the modified Lund-Kennedy mucosal edema score (0, no visible mucosal edema; 1, mild mucosal edema without obliteration od the ethmoid cavity and confirmation of the patency of each sinus; 2, severe mucosal edema obliterating most of the ethmoid cavity and lack of confirmation of the patency of each sinus; 3, frank polyposis). Recurrence was defined as the presence of NP after surgery. Revision surgery was performed in symptomatic patients with an overall score ≥4.

# Statistical analysis

Categorical variables were described as counts or proportions and continue data were expressed as means (standard deviation). Chi-square test and the Fischer's Exact test, with a 95% confidence interval, were used to compare categorical variables. Mann-Whitney U test were used to compare non-parametric continuous variables, whereas independent and paired sample t tests were used for parametric variables, according to the normality of their distribution. One-way ANOVA testing with post hoc analysis (Bonferroni) was performed to

compare continuous variables in subgroup analysis of nasal polyps according to comorbidities (asthma and AERD). Spearman correlation was used to evaluate association between endoscopic and CT scan scores. Multivariate logistic regression analysis with forward stepwise likelihood ratio method was performed to obtain independent prognostic factor of recurrence and to assess their relative importance. Statistical analysis was performed using statistical package for the Social Sciences® (version 24.0, SPSS®). Statistical significance was accepted at p values of <0.05.

#### **RESULTS**

#### Patient characteristics

A total of 132 patients were enrolled in the study, which had a male gender predominance (male to female ratio of 1.6:1) and a mean age of  $43.4\pm11.5$  years (range 19-72 years). The mean follow up time was  $3.2\pm1.5$  years (range, 1 to 6 years). Descriptive clinical characteristics are listed in Table 1.

Table 1: Descriptive characteristics of study population (n=132).

Sociodemographic data	Value
Age (Y), mean±SD (range)	43.4±11.52
Gender	N (%)
Male,	82 (62.1)
Smoking status	
Smoker,	36 (27.3)
Inhalant dust occupational exposure,	75 (56.8)
Organic dust	63 (47.7)
Inorganic dust	12 (9.1)
Previous endoscopic sinus surgery,	9 (6.8)
Allergic rhinitis,	49 (37.1)
Asthma,	52 (39.4)
IgE mediated	30 (22.7)
Non-IgE mediated	22 (16.7)
AERD,	13 (9.8%)
Lindholdt score (0-6), mean±SD	3.8±1.4
Lund-mackay score (0-24), mean±SD	12.7±4.7
Recurrence rate,	45 (34.1)
Modified lund-kennedy score (0-6), mean±SD	2.3±1.2
Time to recurrence (Y), mean±SD	1.9±1.2
Revision surgery rate,	12 (9.0)
Follow-up time (Y), mean±SD	3.2±1.5

SD: Standard deviation; AERD: Aspirin exacerbated respiratory disease; Y: Years

Most patients were non-smokers (n=81, 61.3%). Regarding occupational exposure, 56.8% (n=75) reported a positive dust inhalant exposure history. Within this group, 85% (n=63) had exposure to organic dust and 15% (n=12) to inorganic dust. Asthma was the most common comorbidity and it was present in 52 patients (39.4%). In

this group, 58% (n=30) had non-IgE mediated asthma. AERD was present in 9.8% of patients (n=13), which represented 25% of the asthmatic group. Allergic rhinitis had a prevalence of 37.9% (n=49). Endoscopic examination revealed a mean Lindholt score of 3.8±1.4 and 30% of patients had total or near total nasal cavity obliteration (score 5-6). All patients underwent preoperative CT scan. The mean Lund-Mackay score was 12.7±4.7 and 21% of study population had a severe paranasal sinus obliteration (score 17-24). A Spearman's correlation was performed to determine the relationship between the Lindholt and Lund-Mackay score system. There was a very strong, positive correlation between the two scores: patients with higher endoscopic polyposis score presented a more extensive sinus opacification (spearman's coefficient, Rho=0.826, p=0.001) (Figure 1). Pre-operative CT LM score distribution according to comorbidity is presented in Figure 2.

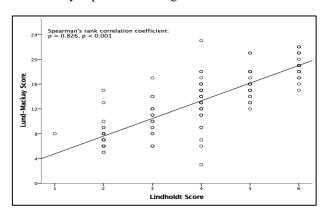


Figure 1: Relationship between endoscopic (lindholt) and computed tomography (Lund-Mackay) score systems.

Patients with AERD had the most severe Lund-Mackay score (17.9±3.6) (Table 2). One-way ANOVA analysis found a significative effect of CRSwNP subgroup on Lund-Mackay score (F (2.129)=10.864; p<0.01) and on Lund-Kennedy score (F (2.129)=8.653; p<0.01). Bonferroni pos-hoc analysis showed a significative difference on LM Score of AERD subgroup compared to patients with only nasal polyps (17.92 vs. 11.78, p=0.001) and to patients with nasal polyps and asthma (17.92 vs. 12.72, p=0.01). There was no difference in the last two groups regarding sinus opacification score (NP, 11.78 vs. NP and Asthma, 12.72, p>0.05) (Table 2).

## Assessing clinical predictors of recurrence

In the follow up time, we found recurrence in 45 patients (34.1%), with a mean endoscopic score of  $2.3\pm1.2$ , on average  $1.9\pm1.2$  years (range 0-6 years) after surgery. NP recurrence distribution in postoperative period was: 22 patients (48.9%) recurred in the first year, 12 patients (26.7%) in the second year, 8 patients (17.8%) in the third year and 3 patients (6.6%) from the fourth to the sixth year. The influence of prognostic factors on recurrence are described in Table 3.

Table 2: Analysis of disease severity scores according to presence of comorbidities.

	ANOVA				Post-hoc pairwise comparison (P value)				
Analysis	NP	NP+ASTHMA	AERD	Р ,	NP vs.	NP vs.	NP+Asthma		
				value	NP+Asthma	AERD	vs. AERD		
Lindholdt score	3.55±1.30	3.77±1.35	5.15±0.99	0.000	1	0.003	0.001		
Lund-Mackay	11.78+4.33	10.70 - 4.9	17.02 - 2.50	0.000	1	0.002	0.001		
score	11./8±4.33	12.72±4.8	17.92±3.59	0.000	1	0.002	0.001		

NP: Nasal polyposis; AERD: Aspirin exacerbated respiratory disease; Y: Years. Statistically significant parameters are highlighted on bold (p<0.05). Post-hoc analysis (Bonferroni).

Table 3: Analysis of predictor factors of recurrence.

Predictor factors	Univariate	Multivariate				
Predictor factors	No recurrence (%)	Recurrence (%)	P value	OR	CI (95%)	P value
Age (Y), mean±SD	42.1±11.3	43.8±12.1				
Gender	•				-	
Male	54 (65.9)	28 (34.1)	0.999			
Female	33 (66.0)	17 (34.0)				
Smoking status						
Smoker	20 (55.6)	16 (44.4)	0.15			
Non-smoker	67 (69.8)	29 (30.2)	'			
Inhalant dust exposure	•				-	
Organic dust	38 (60.3)	25 (39.7)	0.04			
Inorganic dust	8 (66.7)	4 (33.3)	0.94			
No exposure	41 (71.9)	16 (28.1)				
Previous surgery						
Yes	5 (35.7)	9 (6.8)	0.49			
No	82 (94.3)	123 (93.2)				
Allergic rhinitis						
Yes	38 (73.1)	14 (26.9)	0.191			
No	49 (61.3)	31 (38.8)				
Asthma						
Yes	19 (37.3)	32 (62.7)	0.001	8.81	3.87-20.03	< 0.001
No	68 (84.0)	13 (16.0)				
Asthma type						
IgE Mediated	16 (53.3)	14 (46.7)	0.004			
Non-IgE Mediated	3 (13.6)	19 (86.4)	•			
AERD						
Yes	3 (23.1)	10 (76.9)	0.001			
No	84 (70.6)	35 (29.4)				
Lindholdt score, mean±SD	3.3±1.3	4.6±1.2	0.001			
Lund-Mackay score, mean±SD	11.1±4.3	15.6±4.2	0.001	5.85	2.73-12.51	0.001
Eo (count), mean±SD	0.40±0.31	0.38±0.25	0.632			

OR: Odds ratio, CI: Confidence interval, IgE: Immunoglobulin E, AERD: Aspirin exacerbated respiratory disease; Eo: Eosinophil. Statistically significant parameters are highlighted on bold (p<0.05).

In univariate analysis, the recurrence rate was significantly related to factors such as asthma status (asthmatic, p<0.001), asthma subtype (non-IgE mediated, p=0.004), AERD (Samter's triad, p=0.001), Lindholdt score (severe, p<0.001) and Lund-Mackay score (severe, p<0.001). The other variables did not show any statistically significant relationship with surgical success. A stepwise binary logistic regression model was developed on these significant prognostic factors, to

assess independent determinants of nasal polyposis recurrence after ESS and its relative importance. According to this analysis, asthmatic patients had 8.81 times greater chance of NP recurrence compared with non-asthmatic and patients with severe Lund-Mackay score (17-24) had 5.85 times the odds of recurrence than the group with lower LM score. These two variables account for 36%-49% of variation in the model (R2 Cox and Snell =0.357, R2 Nagelkerke =0.494).

Table 4: Analysis of predictor factors for revision surgery.

Dur Bakan Carkana	Univariate		Multivariate				
Predictor factors	No recurrence (%)	Recurrence (%)	P value	OR	CI (95%)	P value	
Age (Y), mean±SD	43.6±11.5	41.0±11.8	0.452				
Gender							
Male	75 (91.5)	7 (8.5)	0.765				
Female	45 (90.0)	5 (10.0)					
Smoking status							
Smoker	33 (91.7)	3 (8.3)	0.578				
Non-smoker	87 (90.6)	9 (9.4)					
Inhalant dust exposure							
Organic dust	39 (88.6)	5 (11.4)	0.976				
Inorganic dust	8 (88.9)	1 (11.1)	0.970				
No exposure	34 (87.2)	5 (12.8)					
Previous surgery		•					
Yes	7 (77.8)	2 (22.2)	0.190				
No	113 (91.9)	10 (8.2)					
Allergic rhinitis							
Yes	48 (92.3)	4 (7.7)	0.763				
No	72 (90.0)	8 (10.0)					
Asthma		•					
Yes	42 (82.4)	9 (17.6)	0.011				
No	78 (96.3)	3 (3.7)					
Asthma type							
IgE Mediated	26 (86.7)	4 (13.3)	0.290				
Non-IgE Mediated	16 (72.7)	6 (27.3)	•				
AERD							
Yes	8 (61.5)	5 (38.5)	0.002				
No	112 (94.1)	7 (5.9)					
Lindholdt score, mean±SD	3.6±1.3	5.4±0.7	0.001				
Lund-Mackay Score, mean±SD	11.1±4.5	18.1±3.3	0.001	4.05	1.91-8.01	0.001	
Eo (count), mean±SD	$0.39\pm0.28$	$0.46\pm0.37$	0.452				

OR, Odds ratio; CI: Confidence interval; IgE: Immunoglobulin E; AERD: Aspirin exacerbated respiratory disease; Eo: Eosinophil. Statistically significant parameters are highlighted on bold (p<0.05).

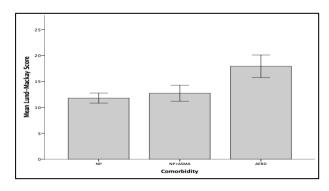


Figure 2: Distribution of Lund-Mackay score according to comorbidity.

NP, Nasal Polyposis; AERD, Aspirin Exacerbated Respiratory Disease. \* Statistically significant (p<0.05).

# Assessing clinical predictors of revision surgery

12 patients required revision surgery, which represents 9% of the study population and 26% of patients who had

recurrence of nasal polyposis. The influence of prognostic factors on revision surgery after FESS are described in Table 3. An analysis was performed to evaluate prognostic factors to undergo revision surgery. Revision surgery was related to asthma (p=0.01), AERD (p=0.002), Lund-Kennedy (p=0.001) and Lund-Mackay score (p=0.001). Multivariate analysis found a higher Lindholdt score (score 5-6) (OR=4.05, CI 95%: 1.91–8.01, p=0.001) as the only independent predictor of revision surgery.

# **DISCUSSION**

This study aimed to evaluate FESS outcome in CRWwNP management and to identify predictive factors of recurrence and of revision surgery.

#### Recurrence

During the follow up period, 34.1% of study patients had recurrence of NP, which is comparable to previous

studies that report 4-60% of recurrence rate.9-11 Although we found NP recurrence in up to 6 years after surgery, more than 90% of them were found in the first 3 years of follow up. Bassioni et al reported similar results, with 79% and 95% of recurrences in the first two and three postoperative years, respectively. Asthma and severe preoperative LM score were both independent negative predictive factors of recurrence. AERD, type of asthma and endoscopic score were significative factors annulled by the multivariate analysis model.

The association of asthma and nasal polyps has been widely described in literature. NP occurs in 7% of all asthmatic patients, while asthma is reported in 26-48% of patients with NP.1 Asthma history was present in 39% of our study population, a similar rate to previous reports.<sup>12</sup> In our study, presence of asthma was the most significative factor related to recurrence. This group of patients had 8.8 times the odds of recurrence compared to non-asthmatic patients (p<0.01). Asthma is considered a risk factor for recurrence in the literature by several authors.<sup>2,9,10</sup> The unified airway disease suggests a continuum between the upper and lower airways diseases. Some authors have suggested that the presence of asthma may influence the severity of upper respiratory tract disease.11-13 Previous studies revealed a higher nasal polyps CT score on asthmatic patients compared to nonasthmatics (18.6 vs 11.7, p<0.01).<sup>14</sup> Our results show comparable CT score between patients with and without asthma (12.72 vs 11.78, p>0.05) (Table 2).

In our study asthmatic patients were divided in subgroups of IgE mediated (atopic) and non-IgE mediated (nonatopic) asthma. Although it was not an independent predictive factor of recurrence, patients with non-IgE mediated asthma had a higher recurrence rate compared to non-atopic asthmatics (86.4% vs. 46.7%, p<0.01). NP are more common in non-atopic asthmatic patients than in atopic asthmatic patients (13% vs 5%, p<0.05).¹ Pearlman et al reported a greater LM score in non-atopic than in atopic asthmatic patients.¹⁵ Other study have reported a significative negative impact of non-IgE mediated asthma on NP recurrence (OR 8.7, p=0.012).⁵

A subset of patients with nasal polyps and asthma develop upper and/or lower reparatory tract reaction following intake of a COX-1 inhibitor. Such patients have Aspirin Exacerbated Respiratory Disease (AERD) also known as Samter's triad. 16 We found AERD in 9.8% of our study population, which is in agreement with previous studies that report an incidence of 10-16%. 16,17 This subset of patients have a more severe sinus disease, present higher recurrence rate and undergo more sinus surgeries compared to patients with NP alone. 16,17 Subgroup analysis of patients with nasal polyposis according to the presence of comorbidities, reveals a more severe sinus disease in AERD group compared to patients with asthma and with nasal polyps alone, based on endoscopic score (5.15 vs. 3.77 vs. 3.55, p=0.000) and Lund-Mackay score (17.92 vs. 12.72 vs. 11.78, p=0.001).

Stevens et al reported similar results, patients with AERD had significantly more severe sinus disease compared to NP with asthma patients and NP only patients (60% vs. 23% vs. 10%, p<0.001). Our study confirms that AERD patients had higher recurrence rate compared to patients with no aspirin hypersensitivity (76.9% vs. 29.4%, p=0.001). However, it was not an independent prognostic factor for recurrence, may be due to the reduced number of cases.

Previous authors identified severe CT score (>16/24, Lund-Mackay) as a risk factor to recurrence and revision surgery. We obtained similar results. In our study, patients with severe paranasal sinus opacification (LM score 17 - 24) had 5.85 times the odds of recurrence compared to patients with mild and moderate paranasal sinus opacification (p<0.01). On the other hand, some authors did not found any relation between CT score and surgical outcome.<sup>3</sup>

Atopy is a predisposing factor to CRS.<sup>1</sup> Although the prevalence of nasal polyposis in patients with AR is similar to that of the general population (0.5-4.5%) 1, 51-86% of CRSwNP are sensitized to at least one aeroallergen.16 Previous studies have reported nasal polyps to occur more frequently in non-atopic patients.<sup>18</sup> In our study AR had a prevalence of 37.1% and it was not a factor related to recurrence of nasal polyps. Mortuaire et al evaluated the clinical severity of disease as assessed by polyp size and LMK score and it did not differ based on allergic status.<sup>19</sup> Pearlman et al found no association between atopy and NP.<sup>15</sup>

Our results evidence a positive occupational dust exposure in 56.8%, with most patients being exposed to organic dust. Despite the higher recurrence rate in these group compared to patients with no occupational exposure (38.7% vs. 28.1%, p=0.94) it was not a predictive factor of recurrence. Hox et al studied the role of occupational exposure on success of FESS and found exposure to low molecular weight agents to be a risk factor for occurrence of CRSwNP and its recurrence after surgery.<sup>4</sup>

Tissue eosinophilia has been associated with worse outcome after ESS.<sup>20</sup> Eosinophils are the predominant cells found in 80% of CRSwNP in Western, characterized by a TH2-biased inflammation with overexpression of IL-4, IL-5 and IL-13.21 On the other hand, in Asian countries the majority of NP are TH2 negative and have a predominantly neutrophilic inflammation overexpression of INF-y and/or TH17.21 Kim et al reported a significative difference in disease control status in the subgroup of patients with eosinophilic NP, suggesting a lower disease control rate in patients with severe eosinophilic inflammation. Tissue eosinophilia was a negative prognostic factor for recurrence (17.3) vs.70.0, p=0.05).<sup>20</sup> All of our histologic data showed an eosinophilic predominance. In our study, the level of eosinophils was not related to recurrence. Peripheral blood may not reflect the inflammatory changes observed in the sinonasal mucosa.  $^{16}$ 

#### Revision surgery

In the mean follow up time  $(3.2\pm1.5 \text{ years})$  of our study, we performed revision surgery in 9% of patients. A systematic review reports similar results, with a revision surgery rate of 3% to 42%.<sup>11</sup>

A study reported that AERD patients undergo a higher number of sinus surgeries compared to asthmatic patients and to patients with NP only (2.6 vs. 1.4 vs. 1.1, p<0.001).<sup>17</sup> The authors concluded that this subgroup of patients underwent two-fold more sinus surgeries (p<0.001) and were younger at the time of the first surgery (40±13) than NP patients (43±14y, p<0.05).17 AERD patients share a TH2-inflamation with NP but present significantly increased levels of eosinophil, basophil and mast cell. Additionally it has been proven a spontaneous activation of these cells in AERD.13 A clinical advanced NP at presentation (p=0.001), presence of asthma (17.6% vs. 3.7%, p=0.01) and AERD (38.5% vs. 5.9%, p<0.01) were important factors to predict surgical revision in univariate analysis. However, the only independent factor associated with a need for revision surgery was the presence a severe endoscopic nasal polyp score at presentation. This group had 2.85 times more chance to undergo revision surgery, than patients with lower nasal polyp score (p=0.001). AERD patients had the higher endoscopic and CT scores on presentation compared to patients with asthma and nasal polyps alone. Despite not reaching statistical significance, the presence of AERD is a factor to be taken into account in order to predict recurrence and the need of surgical reintervention.

Some authors present lower polyp recurrence after more radical surgical approaches with identical peri-operative complication rate.<sup>22</sup> Jankowski et al reported lower recurrence rate with radical ethmoidectomy compared to functional ethmoidectomy (22.7% vs. 58.3%).<sup>23</sup> These authors suggest a more marked reduction in mucosal inflammatory load with a more extensive procedure and propose a meticulous resection of polyp pedicle, the site with higher inflammatory eosinophilic concentration. Wu et al performed a study on 299 patients with recurrent NP and reported a longer time to revision surgery in patients who underwent middle turbinate resection rather than preservation (4.56 vs. 3.93 years, p=0.048). This beneficial effect disappeared over 8 years.<sup>3</sup> The authors suggest that middle turbinectomy increases nasal cavity volume, which delays the onset of symptoms, and allows postoperative delivery of intranasal better corticosteroids. Furthermore, once middle turbinate mucosa is a substrate to NP growth, its removal decreases recurrence.<sup>3</sup> On the other hand some authors favor middle turbinate preservation due to its physiologic actions and because it is a surgical landmark providing less risk of complications in revision surgeries.<sup>24</sup> Hudon et al found no sustained endoscopic benefit of routine middle turbinectomy but the authors suggest to perform middle turbinectomy in revision surgeries, and in patients with floppy or polypoid middle turbinate.<sup>25</sup>

#### Limitations

This is a retrospective study based on medical charts with a potential information bias. We excluded those patients with significative missing data, such as postoperative endoscopic score evaluation. Surgeries were performed by different surgeons, with different surgical experience. Future prospective studies are needed to support our findings.

#### **CONCLUSION**

CRSwNP is a disease with a high recurrence rate following ESS. Asthma and a severe sinus opacification were independent predictive factors of recurrence. Revision surgery occurs in 10% of CRSwNP patients despite postoperative medical treatment and it was related to a severe endoscopic score. These factors signalize a more aggressive disease. In these patients, a more extended surgical procedure and middle turbinate resection should be considered in order to improve long term results.

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Institutional Ethics Committee

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