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Chronic rhinosinusitis and nasal polyposis; indicia of heterogeneity*

Vegard Bugten[1], Ståle Nordgård[1], Pål Romundstad[2], Sverre Steinsvåg[3,4]

[1] Department of Otolaryngology, Head and Neck Surgery, St Olav University Hospital of Trondheim, and Norwegian University of Science and Technology (NTNU), Trondheim, Norway
[2] Department of Public Health, Norwegian University of Science and Technology (NTNU), Trondheim, Norway
[3] Department of Otolaryngology, Head and Neck Surgery, Haukeland University Hospital, Bergen, Norway
[4] Department of Otolaryngology, Head and Neck Surgery, Sørlandet Hospital, Kristiansand, Norway

SUMMARY

Background: *Nasal polyposis (NP) is considered to be a subgroup of chronic rhinosinusitis (CRS). However differences in cellular and mediator profiles suggest that they could be distinct entities.*

Objective: *To look for group differences in characteristics and symptom severity before and after surgery in patients suffering from CRS and bilateral NP that could clinically support the hypothesis that NP and CRS are different pathological processes and to compare the effect of functional endoscopic sinus surgery (FESS) in CRS patients and NP patients.*

Materials and Methods: *Forty-five patients with CRS and 57 patients with bilateral NP were included in this prospective trial. We used t-tests for independent groups to compare preoperative symptoms as recorded on visual analogue scale (VAS). To evaluate if there were differences in symptom improvement between the groups we used analysis of covariance. Categorical variables were compared using exact tests.*

Results: *Mean age was 38 years for the CRS group and 47 years for the NP group, the difference was significant ($p = 0.0001$). NP patients underwent significantly more posterior ethmoidectomies than patients suffering from CRS ($p = 0.001$), and asthma was significantly more prevalent in NP than in CRS ($p = 0.007$). Comparing preoperative symptoms as recorded on VAS we found significant differences. While patients with NP suffered significantly more from nasal blockage and change in their sense of smell than CRS patients, patients with CRS presented with more facial pain and headache. There were no differences in symptom improvement, as both conditions responded similarly to FESS.*

Conclusion: *Differences in symptom severity, nasal endoscopy, age of patients and prevalence of asthma indicate that NP and CRS are different entities. Nevertheless, both conditions respond similarly to FESS.*

Key words: nasal polyps, sinus surgery, symptoms, visual analogue scale

INTRODUCTION

Chronic rhinosinusitis (CRS) is an inflammation in the mucosal lining of the nose and paranasal sinuses lasting for at least 12 weeks [(1)]. Nasal polyposis (NP) is considered to be a subgroup of CRS [(2)]. However, there are findings that question this assumption: in contrast to CRS without NP, an abundant eosinophilic inflammation and local immunoglobulin E production can be demonstrated in NP. It has also been suggested that *Staphylococcus*-derived superantigens may modulate disease severity and expression in NP [(3)]. Furthermore, there is conflicting evidence on whether quality of life (QOL) differs between patients with CRS and patients with nasal polyps [(4,5)]. Clinically, the two conditions may be difficult to differentiate. However, diagnostically and therapeutically such a differentiation is important. It is suggested that the use of out-patient endoscopy may be useful in that respect. [(2)]. From a diagnostic point of view it is also important to know to what extent CRS and NP can be differentiated on the basis of patient symptoms. From a therapeutic point of view it is important to know if CRS and NP respond similarly on functional endoscopic sinus surgery (FESS). Thus, the goal of this study was to compare symptoms and characteristics in patients with CRS and NP before and after surgery and to compare the effect of FESS on the two conditions. Furthermore, we wanted to look for differences that could support the assumption that CRS and NP are different entities.

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MATERIAL AND METHODS

The study was approved by the regional Committee for Medical Research Ethics of the Norwegian University of Science and Technology (NTNU). The Ombudsman for Privacy in Research, Norwegian Social Science Data Services was informed.

Material

This is a prospective study. All patients were referred to the ENT-Department St Olav's Hospital, Trondheim from general practitioners or ENT-specialists in private practice. The inclusion of patients started in February 2004 and the last patient was included in January 2006. We used the classification of rhinosinusitis from Lanza and Kennedy [6]. One hundred and two patients with the diagnosis CRS, not responding satisfactorily to medical therapy for at least 3 months, were included after informed written consent. All patients underwent surgery for the first time and had bilateral disease. Exclusion criteria were previous FESS, septoplasty performed during the same operation, systemic disease involving the nose (Wegener's granulomatosis, cystic fibrosis, Kartageners syndrome, sarcoidosis,) primary ciliary dyskinesia, pregnancy or ongoing treatment for cancer.

Methods

Preoperatively

Preoperatively we scored the endoscopic status as recommended by Lund and Kennedy [7], (0=absence of polyps, 1=polyps in middle meatus, 2=polyps beyond middle meatus, polyps left, polyps right) and the patients with CRS were divided in 2 groups depending on the presence or absence of bilateral nasal polyps.

Group 1: 45 patients with the diagnosis CRS (CRS without bilateral nasal polyps)

Group 2: 57 patients with the diagnosis NP (CRS with bilateral nasal polyps)

Before surgery CT scans were performed in all patients and the patients reported sinus related symptoms on 100 mm VAS. We recorded their age, gender, smoking habits, allergy status, asthma, and ASA intolerance. Diseases recorded in the patients were high blood pressure (CRS=2, NP=5), hypothyroidism (CRS=4, NP=2), migraine (CRS=3, NP=1), reflux oesophagitis (CRS=1, NP=1), depression (CRS=1), diabetes mellitus (NP=1), hypercholesterolemia (CRS=1, NP=2), anxiety (NP=2), arrhythmia (NP=2), angina pectoris (NP=1), Rheumatoid arthritis (NP=1), hemochromatosis (CRS=1) and hepatitis B (NP=1).

Table 1. Characteristics of the patient groups.

	CRS-group n = 45 patients	**NP-group** n = 57 patients
Female	26 (58%)	27 (47%)
Mean age (range)	38 (18-60)	47 (24-73)
Smoking (%)	12 (26%)	13 (23%)
Asthma (%)	5 (11%)	19 (33%)
Aero-allergy (%)	16 (35%)	28 (49%)
ASA-intolerance (%)	1 (2%)	7 (12%)

CRS=chronic rhinosinusitis without bilateral nasal polyps,
NP=chronic rhinosinusitis with bilateral nasal polyps,
ASA= acetylsalicyl aci

Surgical procedure

The same surgeon performed all procedures. We combined the use of mechanical instruments with a microdebrider to minimize damage to the nasal mucosa.

Postoperative care

The patients were randomized to different postoperative treatments (saline irrigation, a non-absorbable packing or postoperative debridement.), stratified by sex and the diagnosis of NP. The effects of these postoperative interventions are detailed in previous articles (8,9). All patients used saline irrigation and nasal steroid spray postoperatively. Ninety-three patients were followed up for a median of 53 weeks (range: 35-77 weeks) after surgery.

Outcome assessment and reporting

The patients recorded typical nasal symptoms such as nasal congestion/blockage, nasal discharge, headache, facial pain, sneezing, change in sense of smell and reduced general condition preoperatively and 53 weeks postoperatively. Primary outcome were differences in symptoms on VAS. Comparisons were performed between the groups preoperatively and at follow up 53 weeks postoperatively. Additionally, we compared the change in symptoms between the two groups.

As secondary outcome we evaluated patient satisfaction 53 weeks after surgery. The patients answered yes or no to the question: Are you satisfied with the result of surgery? The patients also reported if they had had episodes of acute rhinosinusitis and if they had been treated with antibiotics since the control 12 weeks after surgery.

Statistical methods

Descriptive results are presented as mean with standard deviation (SD) or range.

In the statistical analysis, we used t-tests for independent groups to compare VAS and other continuous variables and the paired sample t-test was used to evaluate symptom improvement in the patient groups. To evaluate if there were differences in symptom improvement between the patients groups we used analysis of covariance (ANCOVA) (10). Categorical variables were compared using exact tests. SPSS version 13 (SPSS Inc, Chicago, IL, USA) was used for all analysis and a two sided p-value less than 0.05 was considered significant.

RESULTS

One hundred and two patients were included in this trial (Table 1) and 93 of these were followed up for a median of 53 weeks (35-77) after surgery. Mean age was 38 years (SD = 11)

for the CRS group and 47 years (SD = 13) for the NP group; this age difference was highly statistically significant (p = 0.0001). There was a statistically significant increased prevalence of asthma in the NP group compared to the CRS group (p = 0.007). Exact test could not reveal any significant difference between the groups regarding ASA intolerance (p = 0.075) and allergy (p = 0.227).

Table 2 shows surgical procedures in the CRS group and the NP group. Using exact test we found that NP patients underwent significantly more posterior ethmoidectomies than CRS patients (p = 0.001).

Table 2. Surgical procedures in the groups.

	CRS-group n = 45 patients	**NP-group** n = 57 patients
Uncinectomy	90	110
Antrostomy	58	92
Anterior ethmoidectomy	86	110
Posterior ethmoidectomy	26	74
Sphenotomy	1	0
Frontal recess surgery	21	36
Concha bullosa media	28	13

CRS=chronic rhinosinusitis without bilateral nasal polyps
NP=Chronic rhinosinusitis with bilateral nasal polyps

Symptoms on VAS scale

Comparing symptoms in patients with NP and patients with CRS preoperatively we found significant differences on VAS for nasal congestion, headache, facial pain and change in sense of smell (Table 3). While patients with NP had more trouble with nasal blockage and change in sense of smell, patients with CRS had more facial pain and headache. Multivariable analyses adjusting for age and sex did not change these results.

At follow up we found significantly more facial pain in the CRS group and significantly more problems with sense of smell in the NP group. These differences were also evident after adjusting for age, sex, time from surgery and post operative intervention.

From preoperatively to 53 weeks postoperatively, all symptoms had improved significantly in both groups (p < 0.0001, paired sample t-test), and we found no significant difference in symptom improvement between the groups using ANCOVA.

We did additional analyses on the symptom improvement adjusting for time from surgery, postoperative intervention, gender and age in the statistical model, but there were no significant differences in symptom improvement.

Patient satisfaction

Fifty-three weeks after surgery, 96 patients reported their satisfaction, 93 at follow-up examination and 3 on the phone. In total 15 of the patients (15/96 = 15.6 %) were not satisfied. About 83% (36/43) in the CRS group were satisfied with the result of surgery and 85% (45/53) in the NP group. There was no significant difference between the groups.

Episodes of acute rhinosinusitis

Seventeen patients (17/42) in the CRS group and 18 patients (18/51) in the NP group reported at least one episode of acute rhinosinusitis during their follow up period (53 weeks after surgery). Eight patients (8/42) in the CRS group and 12 (12/51) in the NP group were treated with antibiotics during their follow up. There were no significant differences between the groups.

DISCUSSION

Messerklinger introduced nasal endoscopy to diagnose nasal diseases approximately 30 years ago [11]. Nevertheless, clear definitions of NP and CRS that enable us to differentiate between the 2 conditions have not been made until recently [2,12]. One of the purposes of this study was to identify differences in symptom severity between NP and CRS that could be used to differentiate between the conditions clinically and to add knowledge about to what extent NP and CRS should be considered as different entities. FESS is effective treatment of patients with CRS and NP [13-15]. There is however conflicting evidence as to whether NP and CRS respond similarly to surgery as only a few clinical trials assessing that have been undertaken [4,5,16,17]. Thus, another purpose of the present study was to improve our knowledge regarding the long term outcome after surgical treatment of NP and CRS. This is important both for the surgeon and the patients, so that they may have realistic expectations from surgery.

Table 3. Comparisons of mean symptom score on VAS in the groups preoperatively and 53 weeks postoperatively.

	Mean VAS (SD)						
	Nasal blockage/ congestion	Headache	Facial pain	Change in sense of smell	Nasal discharge	Sneezing	Reduced general condition
Preoperatively							
NP-group	77.4(14.7)	44.8(27.0)	34.3(30.5)	73.0(27.4)	72.1(19.1)	44.3(23.2)	62.3(22.4)
CRS-group	68.2(16.0)	61.4(23.1)	52.0(25.6)	49.2(29.3)	65.1(22.0)	40.9(24.7)	66.1(17.5)
p value (t-test)	0.004	0.001	0.002	0.0001	0.088	0.49	0.33
Postoperatively							
NP-group	26.7(24.1)	16.7(19.3)	7.5(12.2)	34.4(36.7)	31.4(26.7)	12.8(17.7)	15.9(22.9)
CRS-group	30.1(25.3)	22.5(26.3)	20.3(26.7)	16.6(23.0)	26.2(26.2)	16.1(19.2)	21.3(22.8)
p value (t-test)	0.51	0.24	0.006	0.006	0.35	0.39	0.25

CRS=chronic rhinosinusitis without bilateral nasal polyps, NP=Chronic rhinosinusitis with bilateral nasal polyps, VAS=visual analogue scale

Comparing preoperative symptoms, we found that the patients in the NP group had significantly more trouble with nasal blockage and change in their sense of smell than the patients in the CRS group. On the other hand, patients in the CRS group presented more facial pain and headache than patients in the NP group. NP is typically a bilateral disease and it has been shown that patients with more extensive polyps have more problems with nasal blockage and impaired sense of smell [18]. Therefore, the mass effect of the nasal polyps may explain the differences between the groups regarding nasal congestion and changes in sense of smell and breathe trough the nose. However, other factors, such as changes in mucus composition and the effects of inflammatory mediators on receptor cells, may also influence olfaction [19,20]. The patients with CRS have also inflammation and mucosal oedema that may interfere with the patient's ability to smell and breathe through the nose. However, as these processes are mostly localised in and around MM, it is to be expected that they do not affect ventilation and sense of smell to the same extent as NP.
A higher incidence of facial pain and headaches among CRS patients without polyps has also been shown by others [4,17]. The reason for this is unknown. Maybe different pathomechanisms are involved in the two conditions.

Our trial has demonstrated that patients with NP and CRS respond similarly to FESS. There were no significant differences in symptom improvement between the groups. Poetker et al. showed greater improvement for nasal congestion in patients with NP compared to patients without NP [4]. In contrast, Deal and Kountakis showed that patients with NP had more severe symptoms with less improvement after operative intervention and required revision surgery more frequently [5]. The fact that NP patients may need revision surgery more often is no contraindication for surgery. One measure to avoid revision surgery in NP patients could be the subsequent use of nasal steroids over an extended period of time and follow up by the doctor in order to maximise patient compliance regarding postoperative medication [21,22]. Additionally, it has been shown in previous trials that the use of a small non-absorbable packing and postoperative debridement reduce adhesions in middle meatus after FESS [8,9] and thus may reduce the need for revision surgery.

When comparing symptoms 53 weeks after surgery we found more facial pain in patients with CRS and more problems with sense of smell in the NP patients. For nasal congestion, headache, nasal discharge, sneezing and reduced general condition there were no significant differences. Recurrence of polyps frequently occurs and may explain the difference in the sense of smell between the groups. The reason for more facial pain postoperatively in CRS patients than NP patients is unclear. We found no differences in episodes of acute rhinosinusitis between the groups after surgery so infections seem unlikely as an explanation for the difference in facial pain postoperatively.

We asked our patients if they were satisfied with the result of surgery 53 weeks postoperatively. There was no significant difference between the groups. One patient with NP had revision surgery because of adhesions in MM and reccurrence of nasal polyps. On the other hand, one CRS patient had revision sinus surgery, because of frontal sinus complaints. The other unsatisfied patients were helped by medical treatment or other measures such as septum surgery, speech therapy or new mask for CPAP to treat obstructive sleep apnoea.

We found that patients treated with surgery for NP were in average 9 years older than those treated for CRS. This difference has to our knowledge not been shown previously. There may be several reasons for this: Poetker et al. have shown that NP patients report better QOL than CRS patients [4]. Then it is to be expected that patients with NP seek help at a later stage than CRS patients. Our trial has shown more facial pain and headaches in the CRS group compared to the NP group. Maybe the symptoms in the CRS group are more difficult to tolerate than the symptoms in the NP group. As a consequence of this the CRS patients undergo surgery earlier than NP patients. Another explanation for the age difference could be that NP develops later in life and from different reasons than CRS.

We found significantly more patients with asthma in the NP group than in the CRS group indicating that NP is associated with asthma to a larger extent than CRS. This is in agreement with findings from other investigations [23,24].

In our trial NP patients underwent significantly more surgery in the region of the posterior ethmoids. This probably reflects that nasal polyps develop from the mucosa of the ethmoid bone both in the region of the middle and superior meatus. For patients with CRS it generally appears that the disease mostly is caused by changes in the middle meatus and surgery in this region is often enough to cure the disease [25]. Consequently, surgical procedures are mostly uncinectomy, anterior ethmoidectomy and antrostomy to the maxillary sinus.

Based on cellular and mediator profiles it is suggested that CRS and NP are distinct disease entities within the group of chronic sinus diseases. NP has significantly higher levels of eosinophilic markers [eosinophils, eotaxin, and eosinophil cationic protein] compared with CRS. CRS is characterized by a Th1 polarization with high levels of IFN-γ and TGF-β, while NP shows a Th2 polarization with high IL-5 and immunoglobulin E concentrations [26]. Our trial supports the idea that CRS and NP are different entities by showing differences in symptom severity, nasal endoscopy, age distribution and coexisting asthma between patients with CRS and NP.

CONCLUSION

We have shown that patients with NP suffer more from nasal blockage and reduced sense of smell than patients with CRS. On the other hand, patients with CRS have more headache and facial pain than patients with NP. Both conditions respond similarly to FESS and all symptoms improve significantly after surgery. Differences in symptom severity, nasal endoscopy, age distribution and prevalence of asthma demonstrated in this study support the assumption that NP and CRS are different entities.

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Vegard Bugten, M.D.
Department of Otolaryngology, Head and Neck Surgery
St Olav University Hospital
7006 Trondheim
Norway

Tel: +47-7257 5330, +47-7257 5338
Fax: +47-7157 5766
E-mail: vegard.bugten@ntnu.no