Twelve-year long-term postoperative outcomes in patients with chronic rhinosinusitis with nasal polyps*

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Abstract

Background: Evidence regarding long-term postoperative follow-up of chronic rhinosinusitis with nasal polyps (CRSwNP) patients is scarce in the literature. The objective of the present study was to report long-term 12-year postoperative outcomes for CRSwNP patients.

Methods: CRSwNP patients were prospectively followed after endoscopic sinus surgery. Sinonasal symptoms, nasal polyp score (NPS), Barcelona Smell Test 24 (BAST-24), Lund-Mackay Score (LMS), and Medical Outcome Study Short Form-36 (SF-36) questionnaire were assessed before and 12 years after surgery.

Results: At long-term follow-up (median, 12 years), a strong improvement was noted for all patients (N=76) in nasal symptoms score, NPS, BAST-24, and LMS scores compared with baseline. No long-term improvement in SF-36 was found.

Conclusion: Patients with CRSwNP have a long-term 12-year postoperative improvement in nasal symptoms, polyp size, computed tomography, and olfaction.

Key words: chronic rhinosinusitis with nasal polyps; endoscopic sinus surgery; sinonasal symptoms; postoperative

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a frequent disease affecting 2-5% of the general population [1-4]. Appropriate medical treatment of CRSwNP includes intranasal corticosteroids (INCS), oral corticosteroids, and saline nasal irrigation. Endoscopic sinus surgery (ESS) plays an important role in patients with severe uncontrolled disease despite appropriate medical treatment [4]. The objectives of the surgical approach are removal of nasal polyps, inflamed sinus mucosa, and opening the sinus ostia. Surgery enhances mucociliary drainage, decreases the burden of inflammation, improves ventilation, and facilitates topical intranasal therapy [1].

Chronic rhinosinusitis (CRS) patients appear to have greater symptom improvement at 3, 12, and 36 months after surgery than those without nasal polyps [5]. However, recurrence following ESS is common in CRS [6] and seems to be higher in patients with nasal polyps [7] or with severe disease [8]. Recently, research on different molecular pathways of inflammation (endotypes) in patients with CRS has also shown the important role they play in the response to treatment. When the mucosal barrier is breached, a self-limited immune response is activated; type 1 immune response targets viruses, type 2 parasites, and type 3 extracellular bacteria and fungi. Patients with CRS who exhibit a type 2 endotype (characterized by cytokines IL-4, IL-5, IL-13, and activation of eosinophils and mast cells) have a tendency toward recurrence and resistance to treatment [4].

On the one hand, the average age of CRSwNP onset is 42 year [1], which means a relatively early onset. On the other hand, it is a chronic disease of the upper respiratory airway. These two facts can explain the important risk for recurrence and increasing

rates of revision surgery [9]. This emphasizes the importance of long-term postoperative follow-up. In this particular setting, evidence of outcomes for ESS in CRSwNP patients is scarce in the literature. The objective of the present study was to report long-term 12-year postoperative outcomes for patients with CRSwNP.

Materials and methods

Study population and design

Patient population

Patients with a diagnosis of moderate-to-severe CRSwNP according to EPOS guidelines and refractory to appropriate medical treatment were recruited from the outpatient clinic and scheduled for ESS.

Study design

Approval for the study was obtained by the ethical committee of our institution (HCB/2006/3345), and signed informed consent was obtained from all patients. A prospective cohort study was designed, with a follow-up protocol for all subjects meeting the inclusion criteria since 2006. The prospective protocol included three visits (preoperative, 5-year and 12-year) in which endoscopy, olfaction, sinonasal symptoms, QoL and CT were assessed. After surgery, all patients were encouraged to use nasal douching, and then to continue medical treatment for CRSwNP. Asthma treatment was not modified during the present study. Patients with sinonasal neoplasms, cystic fibrosis, ciliary dysfunction, or CRS without nasal polyposis (CRSsNP) were excluded from the study.

Surgical procedure

ESS was performed with the patient under general anesthesia by a single surgeon (I.A.). All patients required extended surgery, beginning with nasal polypectomy and followed by uncinectomy, maxillary antrostomy, complete ethmoidectomy, and sphenoidotomy. The frontal sinus was only approached in case of disease at that level.

Outcomes and assessments

Sinonasal symptoms

All patients were asked to rate five nasal symptoms (nasal obstruction, facial pain/pressure, anterior rhinorrhea, posterior discharge, and smell loss) from 0 to 4 (0, no symptom; 1, mild symptom; 2, moderate symptom; 3, severe symptom; and 4, very severe symptom) before surgery (baseline), and at the 5-year (5yr) and 12-year (12yr) follow-up visits. The total five symptom score (T5SS) was obtained with the sum of the individual symptoms (0–20). Patients with T5SS ≥ 8 had moderate-to-severe disease and were included in the study.

Nasal endoscopic findings

At baseline, 5yr and 12yr follow-up, the nasal polyps score (NPS) was assessed using a rigid 0º nasal endoscope. NPS was scored using a modified Lildholdt system (0, no nasal polyps; 1, small nasal polyps in the middle meatus not reaching the inferior border of the middle turbinate; 2, nasal polyps beyond the middle meatus but not reaching the inferior border of the lower turbinate; 3, large nasal polyps reaching the lower edge of the inferior turbinate; and 4, very large nasal polyps in contact with the floor of the nasal cavity). Total (bilateral) NPS is from 0 to 8. Patients with a total NPS ≥ 4 were classified as moderate-severe CRSwNP.

Lund-Mackay core

A CT scan of the paranasal sinuses was performed at baseline (N = 76) and at long-term 12yr follow-up (n = 32). The Lund-Mackay Score (LMS) system was used, where each sinus (maxillary, anterior ethmoidal, posterior ethmoidal, frontal, and sphenoidal) was scored for opacification (0, no opacity; 1, partial opacity; 2, complete opacity), whereas the ostiomeatal complex was scored 0 (no obstruction) or 2 (obstruction). Unilateral sinus opacity was scored from 0 to 12, and bilateral sinus opacity was scored from 0 to 24.

Barcelona Smell Test 24 (Bast-24)

Sense of smell was assessed using the BAST-24 at baseline, 5yr and 12yr follow-up [10]. BAST-24 consists of 24 odors, and after being exposed for 5 seconds to an odor, patients were asked to answer a number of questions to score smell detection, smell recognition/memory, and smell forced-choice identification.

Quality of Life (QoL)

The Medical Outcome Study Short Form (SF-36) questionnaire consists of 36 self-administered questions that cover eight health domains: physical functioning, role physical, bodily pain, general health, vitality, role emotional, social functioning, and mental health. QoL was scored from 0% to 100%, higher scores corresponding with a better QoL. Additionally, the physical component summary (PCS) and the mental component summary (MCS) scores were calculated. The Spanish version of the SF-36 has been previously used to measure QoL, with good reproducibility and validity [11].

Blood eosinophil count (BEC)

Correlations between BEC percentage and other outcomes were assessed for all patients at baseline, 5yr and 12yr follow-up.

Recurrence rates

We assessed nasal endoscopy and symptoms in order to detect long-term recurrence rates.

Statistical analysis

Data analysis was performed with the statistical package SPSS 25.0 for Windows (IBM, Armonk, NY, USA) using median ± interquartile range. Scores between baseline, 5yr and 12yr follow-up were calculated to compare the different outcomes. As the samples were related, and the data analysis with small subgroups was not normally distributed, Wilcoxon test was used. The Bonferroni correction was used to control false positives during

Table 1. Characteristics of CRSwNP patients at baseline and postoperative long-term follow-up.

	Baseline (n = 76)	Long-term (n = 39)	P Value
Age, years, mean ± SD	46.8 ± 12.7	58.8 ± 10.8	
Male, n (%)	46 (60.5)	27 (69.2)	0.361
Asthma, n (%)	41 (55.4)	19 (51.3)	0.886
N-ERD, n (%)	23 (31.1)	10 (27)	0.642
Nasal polyposis, n (%)	33 (44.6)	18 (48.6)	0.467
Blood eosinophil count, mean ± SD	6.5 ± 5.0	5.5 ± 3.8	0.379
Revision Surgery, n (%)	15 (19.7)	7 (17.9)	0.690

N-ERD = NSAID-Exacerbated Respiratory Disease; SD = Standard Deviation.

Table 2A. Comparison of the main study outcome scores for CRSwNP patients between baseline and 5-year postoperative follow-up.

	Baseline (n = 76)	5-yr follow-up (n = 39)	P Value
Total symptoms score, 0–20 (median ± IQR)	13 (10-14)	6.5 (4 - 9)	<0.001
Nasal polyp size score, 0–8 (median ± IQR)	8 (6 - 8)	1 (0 - 3.25)	<0.001
Smell detection, % median ± IQR	0 (0-5)	55 (0-100)	0.006
Smell memory, % median ± IQR	0 (0-5)	37.5 (0 - 100)	0.001
Smell identification, % median ± IQR	0 (0-0)	15 (0 - 50)	0.001
SF36 physical summary, 0-100 median ± IQR	73,13 (62,5 - 86,25)	82,5 (62,5 - 90,63)	0.127
SF36 mental summary, 0–100 median ± IQR	80,77 (62,63 - 93,25)	84,75 (63 - 92)	0.420

IQR = Interquartile Range; SF-36 = Medical Outcome Study Short Form-36 questionnaire.

Table 2B. Comparison of the main study outcome scores for CRSwNP patients between baseline and long-term postoperative follow-up.

	Baseline (n = 76)	12-yr follow-up (n = 39)	P Value
Total symptoms score, 0–20 (median ± IQR)	13 (10-14)	6 (3 - 9)	<0.001
Nasal polyp size score, 0–8 (median ± IQR)	8 (6 - 8)	2 (1 - 3)	<0.001
Smell detection, % median ± IQR	0 (0-5)	65 (0-100)	<0.001
Smell memory, % median ± IQR	0 (0-5)	15 (0 – 46.2)	0.031
Smell identification, % median ± IQR	0 (0-0)	30 (0 - 55)	<0.001
SF-36 physical summary, 0-100, median (IQR)	73.1 (62.5–86.2)	82.5 (62.5–90.6)	0.294
SF-36 mental summary, 0–100, median (IQR)	80.8 (62.6–93.2)	84.7 (63–92)	0.608
Lund Mackay Score, 0-24, median (IQR)	20 (15-22)	12 (9.2–15)	<0.001

IQR = Interquartile Range; SF-36 = Medical Outcome Study Short Form-36 questionnaire.

Table 3. Characteristics of patients at time of surgery for long-term follow-up and incomplete follow-up cohorts.

	Long-term follow-up cohort (n = 39)	Incomplete follow-up cohort (n = 37)	P Value
Age at surgery, Years (mean ± SD)	45.41 (10.8)	48.32 (14.4)	0.316
Male, N (%)	27 (69.2)	19 (51.4)	0.113
Asthma, N (%)	19 (51.3)	22 (59.4)	0.800
AERD, N (%)	10 (27)	13 (35.1)	0.423
Nasal Polyposis, N (%)	18 (48.6)	15 (40.5)	0.758
Blood Eosinophil count (mean ± SD)	5.55 ± 3.8	7.36 ± 5.9	0.808

N-ERD = NSAID-Exacerbated Respiratory Disease; SD = Standard Deviation.

multiple hypothesis testing. P values <0.05 were considered statistically significant.

Results

Of all patients at baseline (N=76, mean age 46.8 ± 13 years, 60.5% male), 16 did not respond, 14 did not wish to participate, 3 changed of city/state and 4 were reported as deceased. A total of 39 patients (51.3%) were followed with a median follow-up of 12yr [median (IQR) of 12 (11-14)]. Characteristics of the population at baseline and during follow-up are reported in Table 1. At baseline 15 patients (19.7%) had undergone prior ESS. No differences were found in the frequency of asthma, NSAIDs Exacerbated Respiratory Disease (N-ERD), gender, blood eosinophil count (BEC) percentage, and revision surgery between all patients at baseline and the patients available for long-term follow-up. Patients were recommended to use INCS (spray or drops) postoperatively to prevent nasal polyp recurrence. The compliance was assessed at long-term follow-up, and we found that 32 patients complied with INCS. Oral prednisone was administered in 2 patients, and 6 patients received Omalizumab without any differences between treated and non-treated patients (data not shown). At 5-year follow-up, there was improvement in nasal symptoms, NPS and olfaction but not in any SF-36 summary (physical or mental) or domain (Table 2A). At long-term follow-up, a strong improvement was noted in nasal symptoms score, NPS, olfaction, and LMS compared with that at baseline. No long-term improvement in QoL was found (Table 2B). No significant differences were found when we compared patients with long-term follow-up to those with incomplete follow-up (Table 3).

Sinonasal symptoms

A significant improvement occurred in the total symptom score at long-term follow-up [median (IQR) T5SS decreased from 13 (10-14) to 6 (3-9)] (Table 2B). Each of the T5SS improved significantly at long-term follow-up compared with baseline, with a median reduction of 2 points in the score for smell loss, nasal obstruction, and anterior rhinorrhea ($P < 0.001$) and 1 point for posterior rhinorrhea ($P < 0.001$) and facial pain ($P = 0.006$). In order of severity, loss of smell, nasal obstruction, anterior rhinorrhea, and posterior rhinorrhea were the four major complaints before surgery (baseline median of 4, 3, 3, and 2 score, respectively). In the subgroup analysis, both non-asthma and asthma cohorts improved for all symptoms at long-term follow-up. A significant difference was observed with better outcomes in nasal obstruction for asthmatic patients, and in loss of smell for the non-asthmatic subgroup at 12yr. No differences were observed between asthma and non-asthma patients for anterior rhinorrhea, postnasal discharge, and facial pain (Figure 1). Again, no differences were observed between non-N-ERD and N-ERD phenotypes for all nasal symptoms.

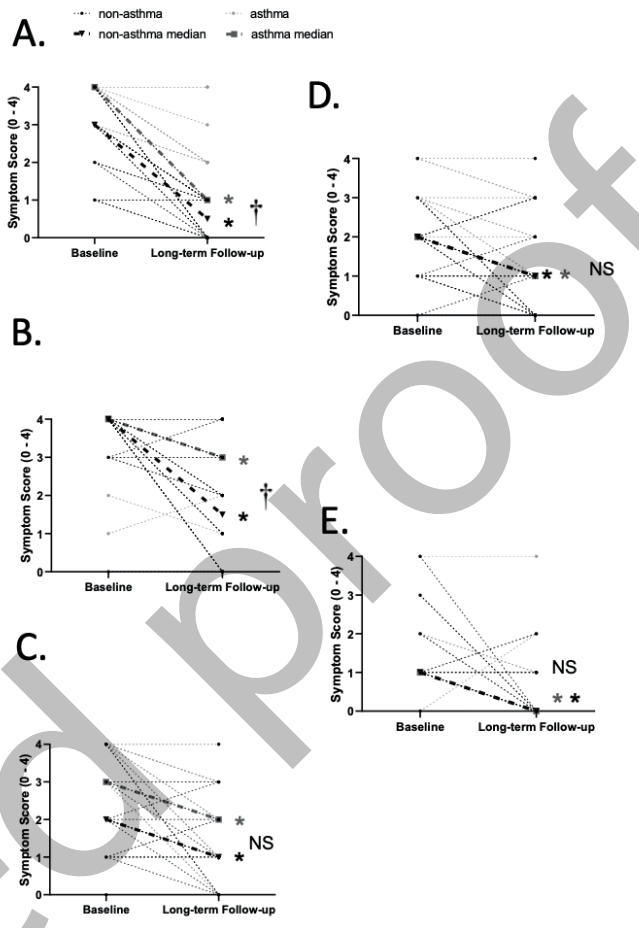

Figure 1. Time evolution of nasal symptoms in CRSwNP patients with or without asthma. A) Nasal obstruction improvement vs baseline for both non-asthma and asthma patients at long-term follow-up. B) Smell loss improvement vs baseline for both subgroups. C) Anterior rhinorrhea improvement vs baseline for non-asthmatic and asthmatic subgroups. D) Posterior rhinorrhea improvement vs baseline for non-asthmatic and asthmatic patients. E) Facial pain improvement vs baseline for non-asthma and asthma patients. *P < 0.05 difference v/s baseline; †P < 0.05 difference between non-asthma and asthma subgroups. NS, nonsignificant.

Nasal polyp score (NPS)

At baseline, all patients had severe nasal polyps [NPS median (IQR) of 8 (6 - 8)]. At 12yr, a strong decrease had occurred in the NPS for all patients [median (IQR) 2 (1 - 3)] (Table 2B). In the subgroup analysis, significant improvement compared with that at baseline was found at 12yr long-term follow-up for both non-asthma and asthma subgroups. Non-asthmatic patients had significantly better outcomes at long-term follow-up (Figure 2A). No difference in NPS was found between non-N-ERD and N-ERD phenotypes.

Lund-Mackay Score

Overall, baseline LMS showed a median of 20 (IQR: 15-22). At

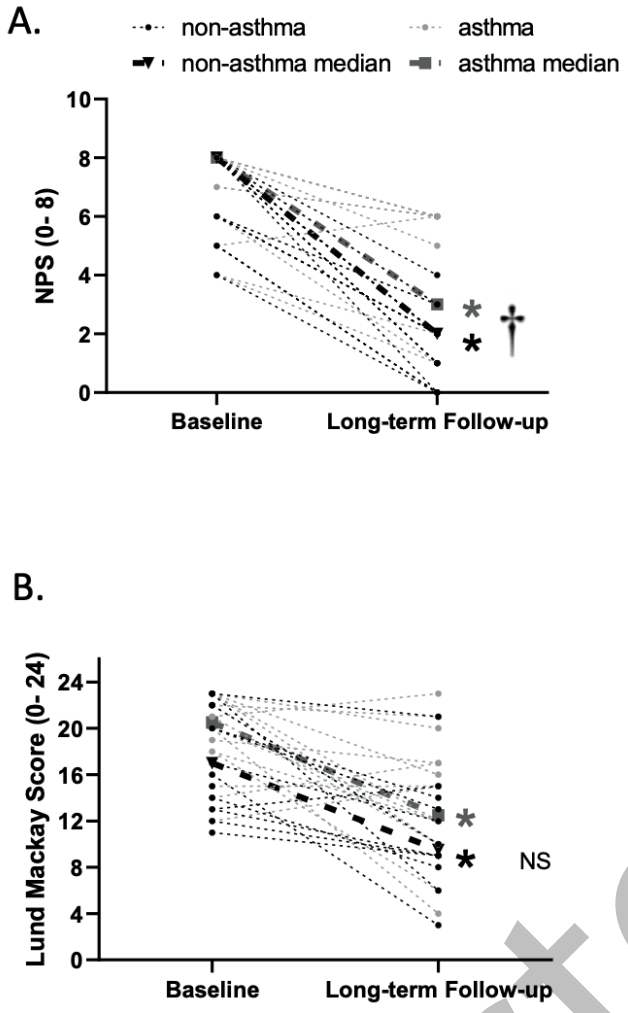

Figure 2. Time evolution of Nasal Polyp Size (NPS) and Lund & MacKay score (LMS) in CRSwNP patients with or without asthma. A) Improvement in NPS vs baseline for both non-asthma and asthma patients at long-term follow-up. B) Lund & MacKay score at baseline and long-term follow-up. *P < 0.05 difference v/s baseline; †P < 0.05 difference between non-asthma and asthma subgroups. NS, nonsignificant.

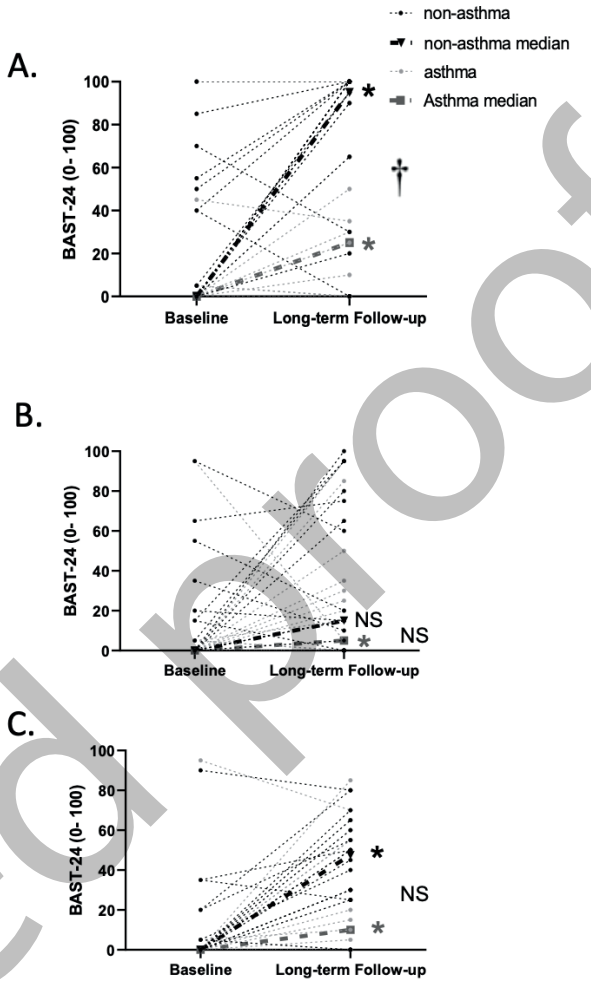

Figure 3. Time evolution of sense of smell (BAST-24) in CRSwNP patients with or without asthma. A) Smell detection compared with baseline for non-asthma and asthma cohorts. B) Smell recognition/memory vs baseline for non-asthma and asthma patients. C) Forced-choice smell identification vs baseline for non-asthma and asthma subgroups. *P < 0.05 difference vs baseline. †P < 0.05 difference between non-asthma and asthma subgroups. NS, nonsignificant.

12yr, the whole cohort had a significant decrease to 12 (9.25-15) (Table 2B). Non-asthmatic and asthmatic subgroups also improved significantly from 17 at baseline (13.75 - 22) to 9.5 (8.25 – 13.75) and from 20.5 (18 - 22.75) to 12.5 (10-16.75), respectively. No difference was found between non-asthma and asthma patients (Figure 2B). No difference in LMS was found between non-N-ERD and N-ERD patients.

BAST-24

At baseline, all patients had significant smell impairment for detection [0% (0-5)] [median % (IQR)], recognition/memory [0% (0-5)], and forced-choice identification [0% (0-0)]. At 12yr, all of them significantly improved in the three BAST-24 smell characteristics: detection 65% (0-100), memory 15% (0-46.25), and identification 30% (0-55) (P < 0.05) (Table 2B). In subgroup analysis, asthmatic patients improved in all smell characteristics. Non-asthmatic patients improved in detection and identification but did not have differences in smell recognition/memory. When comparing non-asthmatic with asthmatic patients, the non-asthma subgroup had higher detection in BAST-24, but there were no differences between them for recognition/memory and forced-choice identification (Figure 3). On the other hand, no difference was found between non-N-ERD and N-ERD phenotypes.

Quality of Life (SF-36)

Overall baseline SF-36 of CRSwNP patients showed worse scores for physical role than the general Spanish population (-0.32 De-

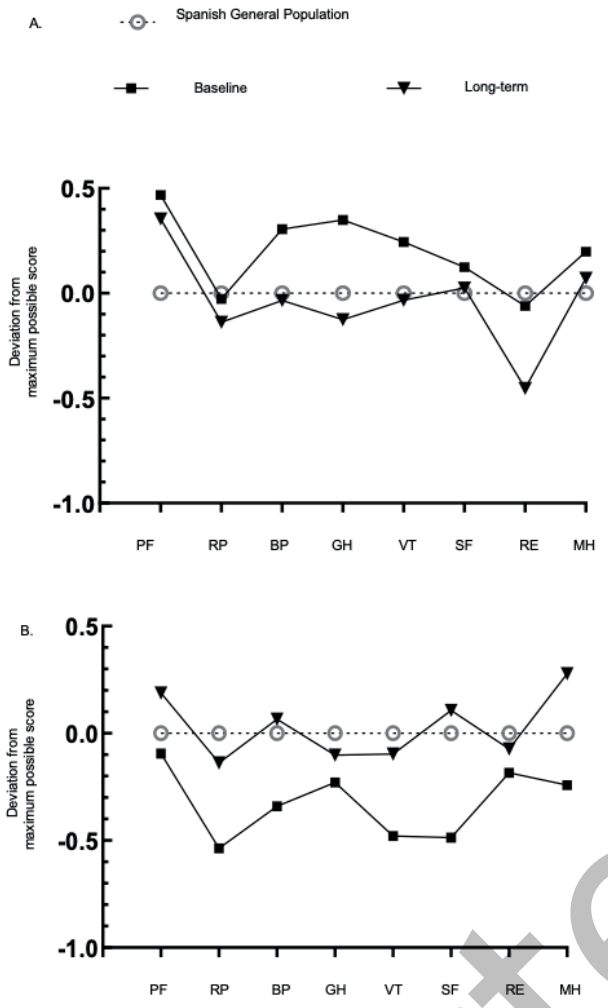

Figure 4. Quality of life in different subgroups compared at baseline and long-term with the general Spanish population. Physical functioning (PF), role physical functioning (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional functioning (RE), and mental health (MH). A) QoL at baseline and long-term for non-asthmatic patients. B) QoL at baseline and long-term for asthmatic patients. *P < 0.05 compared with the general Spanish population.

viation from maximum possible score, P = 0.016). At long-term, no significant differences were found in any SF-36 domains, nor physical or mental summaries for all patients, and for asthma and non-asthma subgroups (Figure 4). There was no significant correlation between quality of life and CRSwNP symptoms.

Blood eosinophil count

A positive moderate correlation between BEC and T5SS of the asthmatic subgroup at 12yr follow-up was found (R spearman: 0.6; P = 0.03). Also, for N-ERD patients, a correlation with total symptoms at 12yr follow-up was observed, but it did not reach significance (R: 0.55; P = 0.13). The same situation was detected in the N-ERD subgroup with LMS at 12yr follow-up (R: 0.54; P = 0.14).

Recurrence rates

Of the total cohort of patients (n = 39) at long-term follow-up, we observed that 82% (n = 32) had nasal polyp and symptom recurrence. Of them, 21.9% (n = 7) required revision ESS. For subgroup analysis, the recurrence rate for asthmatic patients was 100%. All patients with no recurrence (18%) had nasal polyps without asthma or N-ERD. 94.9% (n = 37) of the patients had frontal surgery. Of them, extended procedures were performed in 3 cases (2 patients with DRAF IIB and 1 patient with DRAF III). Of 15 patients with previous surgery at baseline, only 7 attended the long-term visit. Of those, 6 patients (85.7%) had recurrence of nasal polyps and obstruction during the 12yr follow-up period.

Discussion

The main findings of our study are 1) patients with CRSwNP maintain improvement in nasal symptoms, NPS, sense of smell (BAST-24), and sinus opacification (LMS) compared with baseline; 2) a positive moderate correlation exists between BEC percentage and symptoms at 12yr follow-up in asthmatic patients; and 3) CRSwNP has an overall recurrence rate of 82.1% and of 100% for the asthma subgroup.

Long-term studies of postoperative follow-up (more than 10 years) are scarce [12,13]. We present the long-term results of a cohort (51.3%, n = 39/76) with a 12-year follow-up period. As seen in other studies of patients of CRSwNP [14,15], we found that loss of smell and nasal obstruction were the most frequent symptoms (96.1% and 93.4% frequency, respectively). In a previous study published by our group [16], all nasal symptoms improved significantly in CRSwNP patients during a short-term postoperative follow-up period of one month. The present study shows improvement for all symptoms at 12yr follow-up after surgery. This evidence is consistent with our results. A recent study by Calus et al. [13], followed 47 patients with CRSwNP after primary or revision surgery; a long-term 12-year improvement of symptoms was observed. In the subgroup analysis, we observed that asthmatic patients had greater improvement in nasal obstruction. This outcome does not coincide with that of other long-term studies that report a higher symptom relapse in asthmatic patients [12].

Our results indicate that NPS improves during long-term follow-up after surgery, though significantly less for asthmatic patients. Morrisey et al. demonstrated that patients with CRSwNP with respiratory comorbidities like asthma [17] and N-ERD require more postoperative revision surgery in the frontal sinus [18]. Two other recent studies [12,19] associated asthma with a higher long-term recurrence rate; they defined recurrence based on nasal endoscopy and symptoms. Polyp recurrence and opacification on CT scan after surgery have also been shown to be higher in N-ERD compared with non-N-ERD patients [20,21]. Literature cor-

relating comorbidities with higher polyp recurrence and revision surgery is in line with our results and suggests that asthmatic patients have higher polyp relapse rates.

Regarding LMS, CT scans showed significant improvement at long-term follow-up. To our knowledge, this is the only study assessing CT 12yr after surgery. We did not find any differences between subgroups. However, only a total of 32 patients could be assessed with a CT at 12yr follow-up. Studies with bigger samples are needed.

In a recent study, we observed that all smell test characteristics improve after ESS [16]. For this study, better outcomes were maintained for all three BAST-24 characteristics at 12yr long-term follow-up. For subgroup results, better long-term outcomes were found on smell detection for non-asthmatic patients. This could be related to milder symptoms, lower recurrence rates, and impairment of QoL that has been observed for noncomorbid CRSwNP.

Evidence supports the fact that CRSwNP produces a significant QoL impairment [22-24]. It even generates an impairment in health utility values comparable to the one seen in asthma [25]. We found significant worse QoL in physical role functioning for CRSwNP patients at baseline. At long-term follow-up, there was a general tendency for higher scores in the majority of SF-36 domains. However, we were not able to demonstrate significant improvement in any of them. An explanation for this could be the fact that SF-36 is a general health survey. The health domains covered by SF-36 can be affected by numerous diseases and this becomes particularly true for the aging patient. It is possible that we could not find improvement in QoL, because during that 12-year period as patients became older, they can also develop other diseases or experience worsening of the preexistent that reduce their previous QoL. This could explain why the strong improvement we found in other disease-specific outcomes like sinonasal symptoms, can be absent in a more general assessment like SF-36, in which QoL can be negatively affected by multiple other factors. With regard to subgroup analysis, no difference in SF-36 for asthma and non-asthma patients was observed at 12yr follow-up.

Tissue eosinophils in CRSwNP patients has been associated with extensive disease [26] and an increased number of revision surgeries [27]. Nevertheless, there is a lack of evidence on the BEC effect on long-term postoperative outcomes. The present study correlated BEC with worse nasal symptoms at 12yr follow-up in the asthmatic subgroup. The correlation we observed between BEC and worse symptoms and LMS at 12yr follow-up in N-ERD patients could have not reached significance because of lack of power (only 9 patients could be followed for this specific subgroup analysis). Although it has been observed that higher BEC favors recurrence after ESS [28,29], Preis Sella et al. reported that blood eosinophils > 500/uL did not affect postoperative outcomes in CRSwNP [19]. More studies on how BEC can affect long-term postoperative outcomes (including symptoms) in CRSwNP patients are needed.

The high postoperative recurrence rate (82.1%) we observed at long-term follow-up in our study is similar to that reported by Calus et al. (80.9%) [13]. Recurrence after surgery seems to be higher in CRSwNP with asthma and/or N-ERD [17,18,20,21,30]. This also occurs in the long-term scenario, because we observed that asthmatic patients had a 100% recurrence at 12yr follow-up. Once more, this is consistent with other studies showing higher long-term recurrence for this particular subgroup of patients [12,19]. In addition, the high recurrence rate (85.7%) seen in patients with previous sinus surgery at baseline matches the fact that patients who have a larger number of ESS tend to experience recurrence more [31]. In a recent meta-analysis [30], patients with a primary surgery (first ESS) with a 7.4-year average follow-up had a lower recurrence rate than patients with a revision surgery (second surgery or greater) (14.3% vs 26.4%). The study concluded that N-ERD, asthma, allergic fungal rhinosinusitis (AFRS), and multiple revision surgeries, increase revision rates. Despite the fact that nasal polyps have high recurrence rates, associated symptoms are usually not severe enough to indicate revision surgery. This could explain that long-term revision surgery rates are generally much lower [30, 32, 33]. This was also the case in the present study, in which revision surgery was only performed in approximately one out of five patients, even though 82% had experienced long-term recurrence.

We also observed that 94.9% (n = 37) of the patients had frontal sinus surgery, and only 3 had an extended procedure (DRAF IIB/III). This can also affect the recurrence rates obtained, because patients that have extended procedures seem to have better outcomes. Recently, Lothrop procedure has been associated with 18% lower revision rates in AFRS patients (though it didn't reach statistical significance)[32].

Initially, research on long-term postoperative follow-up in CRS assessed only particular aspects like frontal sinus patency [34], symptom improvement [9, 35], or revision surgery rates [9, 36]. But, in general, studies did not exclude patients with CRSsNP or had shorter follow-up periods.

Evidence on long-term recurrence and revision rates of patients with CRSwNP is very limited. In a recent study by Zhang et al. [37], CRSwNP patients were randomly assigned to three different treatment groups (Functional ESS, radical ESS, and radical ESS with Draf III). The recurrence rates had the tendency to become high,

and similar between all treatment groups at 5-year follow-up. Another study on long-term revision rates after ESS in CRS patients, showed a 15.9% rate with a mean follow-up of 9.7 years. Female gender, polyposis, comorbid asthma, allergy, and family history increased the risk of revision surgery [17]. As a limitation, it was retrospective and included CRSwNP and CRSsNP patients. Vlaminck et al. [12] reported a recurrence rate of 62% during a 10-year follow-up, which was associated with local eosinophilia and eosinophilic rich mucus.

Reports of broad outcome assessments at long-term are also infrequent in the literature. Zhang et al. [37] assessed symptoms, NPS, CT scan, QoL, tissue eosinophils, BEC, and pulmonary function tests. However, this study had only a 5-year follow-up period and could only show improvement in olfaction, rhinorrhea, and QoL in the short-term (1-year) period. Calus et al. followed CRSwNP patients postoperatively and showed a long-term 12-year improvement in symptoms and NPS [13]. Nonetheless, they did not assess other outcomes like LMS, eosinophilia, QoL, and smell test.

Study limitations

1) Of the 76 patients included, only 39 could be followed for a 12-year median time. This clearly increases the risk of follow-up bias. Nevertheless, as seen in Table 1, possible variables of confusion did not show significant differences throughout the duration of the study. In the case for smoking, we did not have the percentage of smokers at baseline to compare with the 12yr follow-up visit, which is certainly a limitation. 2) We only used a generic QoL questionnaire (SF-36) because the specific questionnaire (SNOT-22) was not validated for a Spanish population. 3) The sample size was enough for statistical power; however, at long-term follow-up, with the inevitable loss of patients, there is a risk of not finding differences based on the small sample size. This risk increases even more in cases of further subdivisions like non-N-ERD and N-ERD subgroups. 4) CRSwNP is a chronic and fluctuating disease, future studies including a short-term assessment could provide stronger evidence to conclude that the long-term improvement in outcomes is owed to ESS, and not to other factors as changes in the natural course of the disease or regular medical treatment.

Conclusion

Patients with CRSwNP have a long-term (12-year average follow-up) postoperative improvement in nasal symptoms, polyp size, computed tomography, and olfaction. Future studies that include a short-term assessment could explore with higher precision that the postoperative improvement found on long-term outcomes is owed mainly to surgery.

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Authorship contribution

CA: acquisition of data, analysis of results, writing the manuscript, critical review of contents. IA: acquisition of data, study concept, analysis of results, critical review of all contents. CL, JM: analysis of results, critical review of all contents.

Conflict of interest

J. Mullol is a member of national or international advisory boards and has received speaker fees or funding for clinical trials and research projects from Allakos, AstraZeneca, Genentech, GSK, Glenmark, Menarini, Mitsubishi-Tanabe, MSD, Mylan-MEDA Pharma (Viatris), Novartis, Procter & Gamble, Regeneron Pharmaceuticals, Inc., Sanofi-Genzyme, UCB Pharma, and Uriach Group. I. Alobid has received honoraria for consultancy and conferences from Viatris, Roche, Sanofi, GSK, MSD, Salvat, Menarini and Novartis.

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