Quality-of-life outcomes after sinus surgery in allergic fungal rhinosinusitis versus nonfungal chronic rhinosinusitis

Liam Masterson, M.D., Francesco M. Egro, M.D., Jessica Bewick, M.D., Sally E. Erskine, M.D., Alan Clark, Ph.D., Amin R. Javer, M.D., and Carl M. Philpott, M.D.

ABSTRACT

Background: *Given the differences in pathophysiology between allergic fungal rhinosinusitis (AFRS) and other chronic rhinosinusitis (CRS) subgroups, it remains unclear about whether these patients respond differently to a combination of surgical and medical treatments.*

Objective: *To evaluate differences in quality-of-life (QoL) outcomes for a cohort of patients who underwent endoscopic sinus surgery (ESS) for CRS.*

Methods: *This retrospective review included patients with CRS who underwent ESS between 2010 and 2013. QoL was measured by using the 22-item Sino-Nasal Outcome Test (SNOT-22). Variables collected included baseline demographics, SNOT-22 scores before ESS and at 1, 3, 6, 9, and 12 months after ESS. Groups tested were CRS with nasal polyposis, CRS without nasal polyposis (CRSsNP), and patients with AFRS. A linear mixed- effects regression model was used to calculate the adjusted mean QoL differences.*

Results: *Among the 250 patients included, 61.6% had CRS with nasal polyposis ($n = 154$), 28.8% had CRSsNP ($n = 72$), and 9.6% had AFRS ($n = 24$). Significant differences were seen in SNOT-22 scores between pre- and postoperative visits and between the etiologic subgroups ($p < 0.001$). Multivariate analysis revealed significantly greater improvement in QoL for patients with AFRS in comparison with those with CRSsNP at the 9-month follow-up (change in SNOT-22 score, 22.6 [95% confidence interval, 1.2–44.1]; $p < 0.0$) and the 12-month follow-up (change in SNOT-22 score, 20.2 [95% confidence interval, 0.5–39.9]; $p < 0.04$).*

Conclusions: *Patients with AFRS experienced a more-prolonged QoL benefit from surgical and targeted medical intervention compared with those with CRSsNP, which may reflect the severity of inflammation that they presented with compared with other CRS subtypes.*

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Chronic rhinosinusitis (CRS) is a debilitating disease that impacts the quality of life (QoL) and productivity of patients, with significant financial implications for health care systems.[1] According to a recent analysis of U.S. National Health Interview Survey data, CRS affects ~1 in 10 adults.[2] The impact of the disease on QoL, as measured by Short Form 36 scores, is reportedly worse than other major disease states, such as congestive heart failure, chronic obstructive pulmonary disease, and back pain.[3]

Allergic fungal rhinosinusitis (AFRS) is a severe form of CRS that was first reported by Safirstein[4] and Millar *et al*.[5] in 1976 and 1981, respectively.[4,5] It is believed to be an immunologic reaction to microscopic environmental fungi.[6–8] Patients with this condition form nasal polyps and display thick fungal mucin and debris in the paranasal sinus cavities. The AFRS cycle indicates that continuous antigenic exposure, atopy, and inflammation all play key roles in the pathophysiology of the disease. Addressing each of the above factors, therefore, will provide the best chance of long-term disease control.

An integrated approach to management usually depends on complete surgical removal of all fungal disease and long-term prevention of recurrence through either immunomodulation (immunotherapy and/or corticosteroids) or fungistatic antimicrobials (*e.g.,* itraconazole). At present, recurrent disease is a frequent occurrence (especially if surgical or medical therapy are used in isolation), and, consequently, there is no consensus on the correct medical therapy.[9,10]

The Bent and Kuhn diagnostic criteria for AFRS requires the following: (a) type I (immunoglobulin E) hypersensitivity reaction to fungal subtypes (confirmed by history, skin tests, or serology), (b) the "double density sign" on computed tomography (CT), (c) nasal polyposis, (d) eosinophilic mucus, and (e) positive fungal stain of sinus contents.[11,12] A positive or negative fungal culture does not confirm or refute the diagnosis of AFRS because clinical laboratories vary in specimen handling and other capabilities that may significantly influence the rate of positive fungal cultures.[12,13] Furthermore, fungal disease may proliferate as saprophytic growth in diseased sinuses.

A variety of scoring symptoms have been developed to provide a quantitative measure of the symptomatology of CRS in studies of clinical effectiveness. The Sino-Nasal Outcome Test (SNOT-22) is an internationally validated, disease-specific QoL assessment tool developed for assessing symptom severity and the impact of rhinosinusitis.[14,15]

Investigating the relationship between patient disease characteristics and endoscopic sinus surgery (ESS) at postoperative follow-up time points is important for the physician-patient consultation. However, it remains unclear how QoL for different patient groups may change at these time intervals, especially those with AFRS versus other CRS groups (CRS with nasal polyposis [CRSwNP], CRS without nasal polyposis [CRSsNP]). This study, therefore, aimed to assess the perioperative outcomes in an unselected cohort of patients, with specific emphasis on QoL and other pertinent clinical factors.

METHODS

Study Population

This retrospective study received approval of the local clinical research and audit governance committee (James Paget University Hospital). Patients with CRS (≥16 years old) who underwent ESS between March 2010 and December 2013 at a regional tertiary referral center were included in the analysis. CRS was diagnosed based on the criteria laid down in the European Position Paper on Rhinosinusitis and Nasal Polyps in 2012.[16] In our institution, we used a modified version of the "Bent and Kuhn criteria" for AFRS, which replaces

From the Department of Ear Nose and Throat, James Paget University Hospital, Lowestoft Road, Gorleston-on-Sea, United Kingdom
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The authors have no conflicts of interest to declare pertaining to this article
Address for correspondence Carl Philpott, M.D., Norwich Medical School, University of East Anglia, Norwich, NR4 7TJ, U.K.
E-mail address: C.Philpott@uea.ac.uk

immunoglobulin E hypersensitivity with immunocompetence.[9] L. Masterson and F.M. Egro contributed equally to this work.

Only patients with preoperative and >1 postoperative available QoL scores were included in the analysis. No ethical approval was sought because this study was conducted as an audit of ESS outcomes. ESS was recommended to patients for whom maximal medical therapy failed; many patients in the AFRS group who were referred had previously undergone surgical procedures (15 of 24 patients; average, 2.13 procedures per patient).

The data recorded included self-reported patient characteristics (age, sex, race, smoking, allergic rhinitis, asthma, aspirin sensitivity, previous sinus surgery, preoperative medical therapy), diagnosis, preoperative CT findings, complications, and revision rates. Disease-specific health-related QoL was assessed by using a validated QoL instrument (SNOT-22). Patients in our unit are routinely asked to complete this questionnaire at pre- and postoperative period visits. For the purpose of this analysis, the time points considered were the last preoperative score (after maximum medical therapy) and at 3, 6, 9, and 12 months after surgery. The minimal clinically important difference for the SNOT-22 score has previously been determined as 8.9.[17]

Clinical Management

Preoperative Therapy. All the patients received a course of perioperative prednisolone (40 mg/day) and co-amoxiclav (625 mg/day), starting 7 days before surgery (unless contraindicated).

Operative Technique. Topical preparation involved buffered Moffat (cocaine) solution. The standard operative approach included debridement of nasal polyps if required and sinus dissection tailored to the preoperative CT, which would include (when appropriate) total uncinectomy and visualization of natural maxillary sinus ostia or revision of previous antrostomies (by using an angled 30° or 70° endoscope), total ethmoidectomy, sphenoidotomy, and frontal sinusotomy. Sinus cavities were lavaged with saline solution that contained baby shampoo (and with amphotericin B in cases of AFRS). A solution of Nasacort (Sanofi, Guildford, United Kingdom) and gentamicin was instilled into the maxillary and ethmoidal sinuses, and also was used to soak bilateral middle meatal spacers left *in situ* for 1 week.[18] An image guidance system (Fusion ENT Navigation System, Medtronic, MN) was used by the senior author (C. P.) for the majority of cases from 2011 onward. Any samples taken were sent for histopathology and/or microbiology, culture, and sensitivity with or without fungal stain.

Postoperative Therapy. Prednisolone 40 mg/day was continued for 1 week, with a reducing regime of 5 mg/day thereafter for 7 days. Co-amoxiclav 625 mg was continued for 1 week. Patients were advised to perform saline solution nasal douching twice daily. Topical therapy was commenced on day 7 (after removal of middle meatal spacers and debridement of debris) in cases of patients with CRSsNP, Nasonex 2 puffs twice daily (mometasone; Merck & Co, Inc, Whitehouse Station, NJ), and in patients with CRSwNP and AFRS, Pulmicort nebules (budesonide 0.5 mg per 2 mL; AstraZeneca, Luton, United Kingdom) were added to the saline solution douches. Systemic itraconazole was given selectively if fungal mucin was seen during surgery or in the postoperative period.[9] A major complication was defined as the following: (1) epistaxis > 500 mL, which required blood transfusion, placement of intranasal packs, surgical ligation, or embolization; (2) orbital trauma that required intervention; or (3) intracranial trauma that required intervention.[19]

Statistics

All data were analyzed by using IBM SPSS for Windows version 20.0 (SPSS, Inc., Chicago, IL). A p value of <0.05 was considered to be of statistical significance. First, we compared continuous variables by using one-way analysis of variance tests, and we used the χ^2 test to compare categorical variables. The mean SNOT-22 scores before ESS and at 1, 3, 6, 9, and 12 months after ESS were calculated and categorized into the three etiologic groups. The CRSsNP subgroup was chosen as the reference population to allow comparison of outcomes with other patient cohorts at the various time points.[20] Also, we carried out a multivariate linear mixed-effects regression model. If a SNOT-22 score was missing at a certain point, then the rest of the scores for that same patient were still incorporated in the final analysis. The model included fixed and random effects analysis to account for the correlation between repeated SNOT-22 score measures per patient.

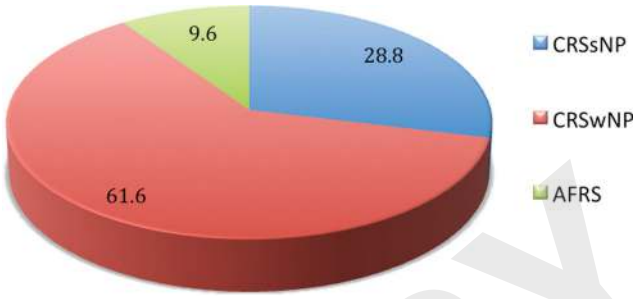

Figure 1. *Diagnostic categories (in percentages).*

RESULTS

This study included 250 patients with adequately completed SNOT-22 scores, and who met the inclusion criteria. The mean (standard deviation) age was 54.1 ± 14.6 years, with a male predominance (62%). The distribution of CRS subtypes, shown in Fig. 1, includes the following: CRSwNP, 61.6% (n = 154); CRSsNP, 28.8% (n = 72); and AFRS, 9.6% (n = 24). A total of 32% patients (n = 80) had undergone previous sinus surgery (range, 1–20; mean, 2.25 procedures). During the study period, two patients (<1%) required a further revision after initial image-guided sinus surgery; of these two patients, one had a history of ESS.

There were four patients with major complications (two specific, two nonspecific); one additional patient had a >500 mL blood loss but required no packing or transfusion (Table 1). These five patients and one additional patient required an overnight stay, although three of these six patients were private patients booked as overnight cases. Two further patients had a breach of the lamina papyracea, but there were no symptomatic issues for these patients, nor any sequelae.

The prevalence of asthma, aspirin sensitivity, and allergic rhinitis were significantly higher in the AFRS group. In addition, patients with AFRS were more likely to have undergone previous ESS surgery and to have a higher preoperative Lund-Mackay CT score. There were no significant differences for each etiologic group in terms of age, race, or smoking. Patients with CRSwNP were more likely to be men in comparison with the other groups (Table 2).

Analysis of the data for all subtypes revealed a statistically significant decrease ($p < 0.01$) in scores at the 3-month post-ESS SNOT-22 assessment (mean, 21.7) compared with preoperative assessment (mean, 54.2). Subgroup analysis showed a similar statistically significant decrease in SNOT-22 scores ($p < 0.01$): CRSwNP decreased from 53.7 to 20.3, CRSsNP decreased from 55.5 to 27.2, and AFRS decreased from 53.2 to 16.9. The results are shown in Fig. 2. This trend continued at 6, 9, and 12 months ($p < 0.01$). The mean SNOT-22 scores over time by patients with CRSwNP, CRSsNP, or AFRS are summarized in Table 3. Among the 250 patients with preoperative SNOT-22 scores, 14% (n = 36) were discharged in <3 months, 50% (n = 124) in <6 months, 58% (n = 146) in <9 months, and 69% (n = 172) in <12 months.

The linear mixed-effects regression models were performed to establish the differences of the changes in SNOT-22 scores over time among the AFRS, CRSwNP, and CRSsNP groups, and the results are shown in Table 4. After adjusting for all clinical factors, compared

Table 1 **Symptomatic patient complications**

Complication	No. of Patients (a)	No. of Revision Case(s)	Permanent Sequelae	Comment
Bleeding*	2	2	No	Discharged next day
Orbital	0	0	0	Not applicable
Intracranial	1	0	No	Post-ESS microlaryngoscopy with difficult extubation; the patient presented after 3 days with pneumocephalus but no CSF leak and was managed conservatively
General	2	1	No	TIA, resolved with no residual symptoms; PE, preceding knee surgery 3 months before ESS

ESS = endoscopic sinus surgery; CSF = cerebrospinal fluid; TIA = transient ischaemic attack; PE = pulmonary embolism.
**Of > 500 mL; required transfusion and/or packing.*

Table 2 **Patient characteristics by etiologic category**

Variable	CRSsNP	CRSwNP	AFRS	Total	*p* Value
Age, mean (SD), y	50 ± 14.5	56 ± 15	51 ± 14	54 ± 15	0.18
Sex, % men	47.2	65.6	50	58.8	**0.02**
Lund-Mackay score, mean (SD)*	11.8 ± 4.8	17.2 ± 5	20.2 ± 4.2	16 ± 5.8	**<0.001**
Asthma, %	22.2	47.4	70.8	42.4	**<0.001**
Aspirin sensitivity, %	6.3	6.8	50	11.2	**<0.001**
Allergic rhinitis, %	31.9	36.3	70.8	38.4	**0.002**
Preoperative SNOT-22 score, mean (SD)	55.0 ± 21	53 ± 22	53.2 ± 21	54 ± 22	0.79
Previous surgery, no. (%)	8 (11.1)	57 (37)	15 (62.5)	80 (32)	**<0.001**
No. operations, mean ± SE	1.2 ± 0.2	2.4 ± 0.4	2.1 ± 0.2	2.2 ± 0.3	0.53
White, no. (%)	71 (98.7)	149 (96.7)	24 (100)	244 (97.6)	0.50
Black, no. (%)	1 (1.3)	1 (0.6)	0 (0)	2 (0.8)	0.63
Asian, no. (%)	0 (0)	4 (2.6)	0 (0)	4 (1.6)	0.28
Never smoker, no. (%)	39 (54.1)	86 (55.8)	17 (70.8)	142 (56.8)	0.33
Ex-smoker, no. (%)	14 (19.4)	41 (26.6)	4 (16.7)	59 (23.6)	0.35
Current smoker, no. (%)	15 (20.8)	21 (13.6)	3 (12.5)	39 (15.6)	0.34
Total	72	154	24	250	—

CRSsNP = chronic rhinosinusitis without nasal polyposis; CRSwNP = chronic rhinosinusitis with nasal polyposis; AFRS = allergic fungal rhinosinusitis; SD = standard deviation; SNOT-22 = 22-item Sino-Nasal Outcome Test; SE = standard error. Significant p values in bold.
**Preoperative computed tomography score.*

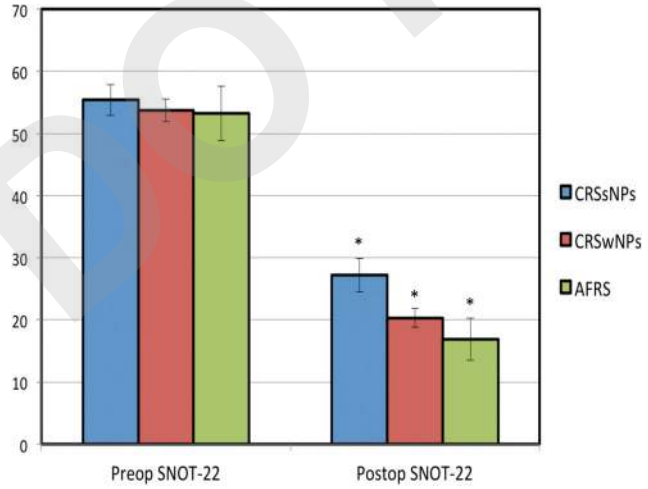

Figure 2. *Summary of pre- and postoperative Sino-Nasal Outcome Test (SNOT-22) mean score ± standard error (*p < 0.01).*

with patients with CRSsNP, there were significantly more improvements in QoL in patients with AFRS from baseline to 9 months (ΔSNOT-22, 22.6 [95% confidence interval, 1.2–44.1]; $p < 0.03$) and at the 12-month follow-up (ΔSNOT-22, 20.2 [95% confidence interval, 0.5–39.9]; $p < 0.04$). Increasing age and smoking were retained in the final model because both factors were significantly associated with adverse SNOT-22 scores (changing the point estimate of the association among AFRS, CRSwNP, or CRSsNP). Other variables not retained in the final model included asthma, race, sex, allergic rhinitis, aspirin sensitivity, and previous sinus surgery. The SNOT-22 scores before ESS and at 1, 3, 6, 9, and 12 months after surgery arranged by the three main subgroups are shown in Fig. 3.

DISCUSSION

This article provides a comprehensive assessment of QoL outcomes after surgical treatment in patients with CRS, including those with AFRS. One previous study, published in 2010, looked at surgical outcomes in patients with AFRS, but this did not provide a correlation with the other CRS subgroups.[21] Analysis of our data inferred that ~10% of all the patients with CRS who were treated had a diagnosis of AFRS. This finding would support epidemiologic data that indicates AFRS is present in 7–10% of patients with nasal polyposis and can often go undiagnosed.[22]

Clinical Outcomes

With regard to disease-specific QoL, the AFRS subgroup demonstrated significant benefit in comparison with the reference group

Table 3 **SNOT-22 scores in the postoperative period by etiologic category***

Time Point	CRSsNP	CRSwNP	AFRS	Total
Pre-ESS	55.46 ± 2.5 (72)	53.7 ± 1.8 (154)	53.2 ± 4.4 (24)	54.2 ± 2.5 (250)
Post-ESS, mo				
1	27.5 ± 2.7 (55)	21.3 ± 1.5 (127)	22.2 ± 4.4 (19)	23.1 ± 1.3 (182)
3	27.2 ± 2.7 (56)	20.3 ± 1.5 (139)	16.9 ± 3.4 (22)	21.7 ± 1.2 (214)
6	30.1 ± 3.5 (37)	20.2 ± 2.1 (86)	22.9 ± 4.8 (16)	25.7 ± 1.7 (124)
9	40.4 ± 5.3 (24)	26.1 ± 2.5 (64)	26.0 ± 5.4 (16)	29.3 ± 2.2 (104)
12	35.5 ± 4.8 (21)	25.1 ± 3.3 (41)	24.9 ± 5.6 (16)	28.6 ± 2.4 (78)

SNOT-22 = 22-item Sino-Nasal Outcome Study; CRSsNP = chronic rhinosinusitis without nasal polyposis; CRSwNP = chronic rhinosinusitis with nasal polyposis; AFRS = allergic fungal rhinosinusitis; ESS = endoscopic sinus surgery; SE = standard error.
**All values are SNOT-22 score ± SE (no. completed questionnaires).*

Table 4 **Linear mixed effects regression analysis***

Subgroup	ΔSNOT-22, average ± SE	95% CI	*p* Value
Post-ESS, 1 mo			
CRSsNP	N/A	N/A	N/A
CRSwNP	8.5 ± 5.8	−5.8 to 22.8	0.44
AFRS	6.6 ± 6.8	−10.2 to 23.4	1.0
Post-ESS, 3 mo			
CRSsNP	N/A	N/A	N/A
CRSwNP	−1.12 ± 6.6	−17.4 to 15.1	1.0
AFRS	3.5 ± 7.7	−15.5 to 22.5	1.0
Post-ESS, 6 mo			
CRSsNP	N/A	N/A	N/A
CRSwNP	4.9 ± 6.6	−11.6 to 21.3	1.0
AFRS	8.7 ± 7.8	−10.6 to 27.9	0.81
Post-ESS, 9 mo			
CRSsNP	N/A	N/A	N/A
CRSwNP	17.0 ± 7.4	−1.3 to 35.3	0.08
AFRS	22.6 ± 8.7	1.2–44.1	0.03
Post-ESS, 12 mo			
CRSsNP	N/A	N/A	N/A
CRSwNP	15.6 ± 6.8	−1.2 to 32.5	0.07
AFRS	20.2 ± 8.0	0.5–39.9	0.04

SNOT-22 = 22-item Sino-Nasal Outcome Study; SE = standard error; CI = confidence interval; ESS = endoscopic sinus surgery; CRSsNP = chronic rhinosinusitis without nasal polyposis; N/A = not applicable; CRSwNP = chronic rhinosinusitis with nasal polyposis; AFRS = allergic fungal rhinosinusitis.
**Smoking ($p < 0.03$) and age ($p < 0.05$) were retained in the final model.*
#ΔSNOT-22 is the change in quality-of-life value between the reference group (CRSsNP) and CRSwNP or AFRS.

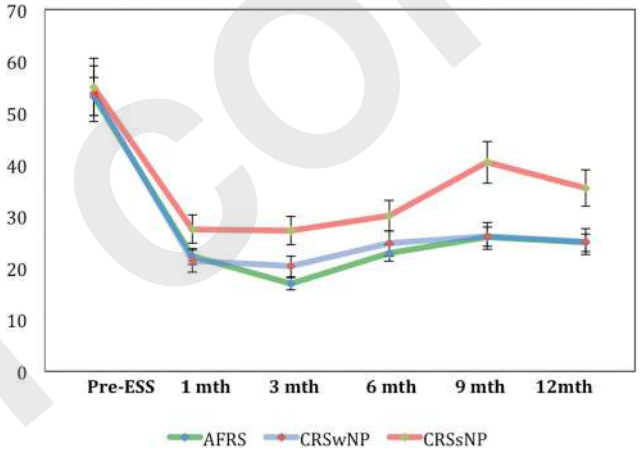

Figure 3. *Dynamic change in Sino-Nasal Outcome Test (SNOT-22) score throughout the pre- and postoperative periods. There is a significant change in SNOT-22 score for chronic rhinosinusitis without nasal polyposis (CRSsNP) versus allergic fungal rhinosinusitis (AFRS) (9-month postoperative score 22.6 [95% confidence interval, 1.2–44.1]; $p < 0.03$; and 12-month postoperative score 20.2 [95% confidence interval, 0.5–39.9]; $p < 0.04$).*

(CRSsNP). However, paradoxically, analysis of the data from this study also depicts a story of the burden of AFRS on our health care service, with more than two-thirds of all patients reporting previous surgical intervention, with an average of two procedures per patient. Analysis of our data indicates that patients with the highest preoperative SNOT-22 scores experienced the greatest reduction of symptom severity over time, which is useful clinically when counseling patients regarding the benefit that surgery may have in treating their disease. In this study, only advanced age and a positive smoking status were associated with adverse outcomes. These data agreed with previous studies,[14,23–25] which indicated very few patient factors are predictive of QoL outcomes after ESS or other targeted therapies.

Although the requirement for revision surgery did not present a major burden in this cohort, it must be stressed that our observation period was comparatively short. Recently published research[26] indicates that outcomes stabilize between 6 months and 5 years after surgery, hence, the long-term outcomes of sinus surgery can only be seen at 5 years and beyond.[27] Higher rates of previous surgery were seen in the CRSwNP and AFRS subgroups in comparison with the CRSsNP group (Table 2). The requirement for revision surgery can often be multifactorial with extent of sinus disease, anatomic abnormalities, systemic disease, inadequate surgical intervention, and variable medical management, all being contributing factors. In addition, the high level of tertiary referrals seen at this unit may confound these data by including more patients with refractory disease.

Comparison with National Epidemiologic Data

As stated, our study found the highest rate of revision surgery to be among those patients with CRSwNP and those with AFRS, with rates of previous surgery almost three-fold that of those patients without nasal polyps. This is in keeping with recent findings from the CRS Epidemiology Study, in which the combined (CRSwNP and AFRS) mean number of previous operations per patient was 3, and 57% had received previous surgical intervention.[25] However, further comparison with the CRS Epidemiology Study data would indicate an overall lower rate of revision surgery reported by our subgroups (Table 2), despite a comparatively larger disease burden (54.2 in this study group versus 43.9 in the CRS Epidemiology Study).

AFRS

The etiology and pathogenesis of AFRS is not fully understood, and appropriate treatment for this disease is also controversial. Despite the need for aggressive surgical and medical treatment, high recurrence rates have been reported.[25] AFRS has been recognized as a subcategory of CRS, in which a strong immunoglobulin E mediated hypersensitivity to the fungal element may drive the inflammatory process.[28] In recent years, results of studies have indicated that a much wider group of patients with CRS may be mediated by fungal elements and a subsequent cascade of immune effects through nonclassic pathways.[29,30]

The term AFRS itself may be inaccurate because a type I hypersensitivity reaction is not always proven, despite the evidence of the other key clinical features,[6] and perhaps the term "reactive" fungal rhinosinusitis may be more appropriate in describing this condition. The most implicated fungi in AFRS include *Aspergillus, Alternaria,* and *Curvularia,* but confirmation of this is often suboptimal in the clinical setting.[31] Laboratory studies demonstrate an interaction of the immune system with fungus in a subgroup of patients with CRS,[7,8] but this does not automatically infer that antifungals are the correct therapeutic approach.[32] Although fungi may be ubiquitous in sinuses and may initiate an inappropriate immune activation, they may not be the driving pathologic mechanism.[29,32,33] To counter this argument, recent evidence would support antifungals in the appropriate patient group (identified by the Bent and Kuhn or modified Bent and Kuhn criteria).[34,35] Similarly, some patients have also responded to alternative treatments, such as Manuka honey, which has proven antifungal properties.[9,36]

Differences between AFRS and CRSsNP

SNOT-22 scores in the AFRS group improved significantly when compared with the reference group of CRSsNP in this study, which may reflect different disease burdens and/or pathophysiology because the latter are likely to have ostiomeatal complex occlusion as a key factor. Those patients with polypoid nasal disease and AFRS in particular are known to have a higher prevalence of asthma, which reflected more widespread respiratory tract involvement and a potential different pathophysiology. Association between asthma and nasal polyposis has also been described, along with aspirin sensitivity as part of aspirin-exacerbated respiratory disease. This was first described in 1922 by Widal *et al.*[37] as a triad of symptoms, including aspirin sensitivity, asthma, and nasal polyposis, more commonly known as the Samter triad.[38] Aspirin sensitivity is also more prevalent within the polypoid phenotypes, and particularly AFRS, and again points to the significant interaction between lower and upper airway diseases.[39] It is likely that patients experience a relief in both upper and lower airways symptoms through meticulous management of their nasal disease, and, consequently, a greater increase in QoL, reflected in the lower SNOT-22 scores.[40] A qualitative study of patients with CRS found the interaction between upper and lower airways symptoms to be one of the major factors that influence QoL.[41]

Study Limitations

Limitations of this study included its no-randomized retrospective design and the relatively small sample size for patients with AFRS. However, the patients acted as their own controls, and the comparison among the subgroups allowed a within-disease analysis. Also, although most of the relevant clinical factors were represented in this analysis, it is not possible to accurately quantify patient compliance with prescribed medications in the postoperative period.

Qualitative research at our center demonstrated that compliance with treatments is a problem in patients with CRS.[41] To counteract this, patient education at the time of primary management is crucial, with a need for regular reinforcement. Differing advice from primary care practitioners may also emphasize the need for greater awareness of guidelines.[42] Analysis of recent data would indicate that clinical commissioning groups in the United Kingdom are not currently abiding by evidence-based guidelines for CRS, with 13% having restrictive referral pathways in place.[43] Also, comparison of this cohort with larger epidemiologic data sets may be inherently biased, due to the relatively large number of tertiary referrals received at this unit.

CONCLUSION

This study demonstrated that patients with AFRS (in comparison with the CRSsNP cohort) have significantly improved QoL benefit after ESS and targeted medical therapy, which is likely to reflect a more-extreme extent of mucosal inflammation, lower rates of depression, and enhanced interaction between upper and lower airway disease, which is much more prevalent in the polypoid phenotypes.[25]

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