

Original Article

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Adherence to guidelines prior to endoscopic sinus surgery in patients with chronic rhinosinusitis and asthma

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ABSTRACT

INTRODUCTION. Optimal care for patients with simultaneous chronic rhinosinusitis (CRS) and asthma is often complicated due to interaction between these conditions. This study depicts the lack of attention to asthma within the otorhinolaryngological field, and the relationship between CRS and asthma, including the risk of revision surgery in such patients.

METHODS. A retrospective cohort study was conducted on patients undergoing functional endoscopic sinus surgery (FESS) because of CRS with nasal polyps (CRSwNP) and without nasal polyps in a five-year period. Patients were examined for adherence to guidelines, asthma, revision FESS, allergies and septo-/turbino-plasty. Results were compared to international reports.

RESULTS. A total of 589 patients had FESS because of CRS of whom 203 (34.5%) had co-existing asthma. A higher risk of asthma (relative risk (RR) = 1.82 (95% confidence interval (CI): 1.29-2.56), $p < 0.001$) and revision FESS (RR = 2.20 (95% CI: 1.33-3.65), $p < 0.001$) was found in patients with CRSwNP. Attention to asthma was poor in patients with no asthma diagnosis before referral.

CONCLUSIONS. Asthma was lower in the study population than in the literature. Danish national guidelines on CRS management are insufficient regarding attention to asthma. Results call attention to the need for more multidisciplinary team management.

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Chronic rhinosinusitis (CRS) is a common condition that constitutes a significant health problem [1]. The prevalence of CRS in the Western world shows geographical variation with an overall prevalence around 10% [1]. Prevalence depends on the method by which CRS is registered. Also, it is difficult to differentiate between CRS, acute rhinosinusitis and allergic rhinitis as these conditions overlap [1]. A subgroup of patients with CRS has concurrent asthma. Thus, up to two-thirds of patients with CRS have co-existing asthma, and CRS is known to be the most prevalent comorbidity in patients with asthma [1]. This emphasises the importance of treating both conditions sufficiently to optimise the overall course [1, 2].

The international guideline European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) defines CRS as inflammation of the nose and paranasal sinuses with the presence of two or more symptoms lasting for more

than 12 weeks. Mandatory symptoms are either nasal congestion/blockage or nasal drip. Facial pain and reduction/loss of the sense of smell are other characteristic symptoms [1]. The condition is subdivided into two groups: CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP). The prevalence of CRSwNP increases with age, particularly in patients > 40 years [1]. The prevalence of CRSsNP is higher in patients < 40 years [1]. Comorbidities related to the respiratory system are frequent in CRSwNP as previous studies have suggested that up to 67% of patients with CRSwNP have co-existing asthma [1].

Clinicians use recognised guidelines to manage CRS. The EPOS has contributed to the Danish national guidelines by the Danish Rhinology Society (DRS) [1, 3]. Medical treatment with nasal corticosteroids (NC) along with saline rinse is the cornerstone in medical management of CRS. According to EPOS, care pathways for CRS recommend a duration of 6-12 weeks before moving on to further diagnostic methods and more invasive treatments [1]. Possible supplements to conservative treatment are antibiotics and systemic corticosteroids [1, 3]. Biologic treatment has also gained a footing in the field. Updates on the indication and evaluation of biologic treatment in these patients have recently been published [4].

An inadequate response to conservative treatment is an indication for surgical intervention with functional endoscopic sinus surgery (FESS) [3]. Approximately 10-15% of the half of patients with CRSwNP who need more intensive medical treatment require at least one FESS at some point [5].

Although EPOS emphasises the importance of asthma in the management of CRS, DRS guidelines do not mention asthma [1, 3]. In contrast, several guidelines on asthma management call attention to the importance of co-existing CRS, including Danish national guidelines and the Global Initiative for Asthma [6, 7].

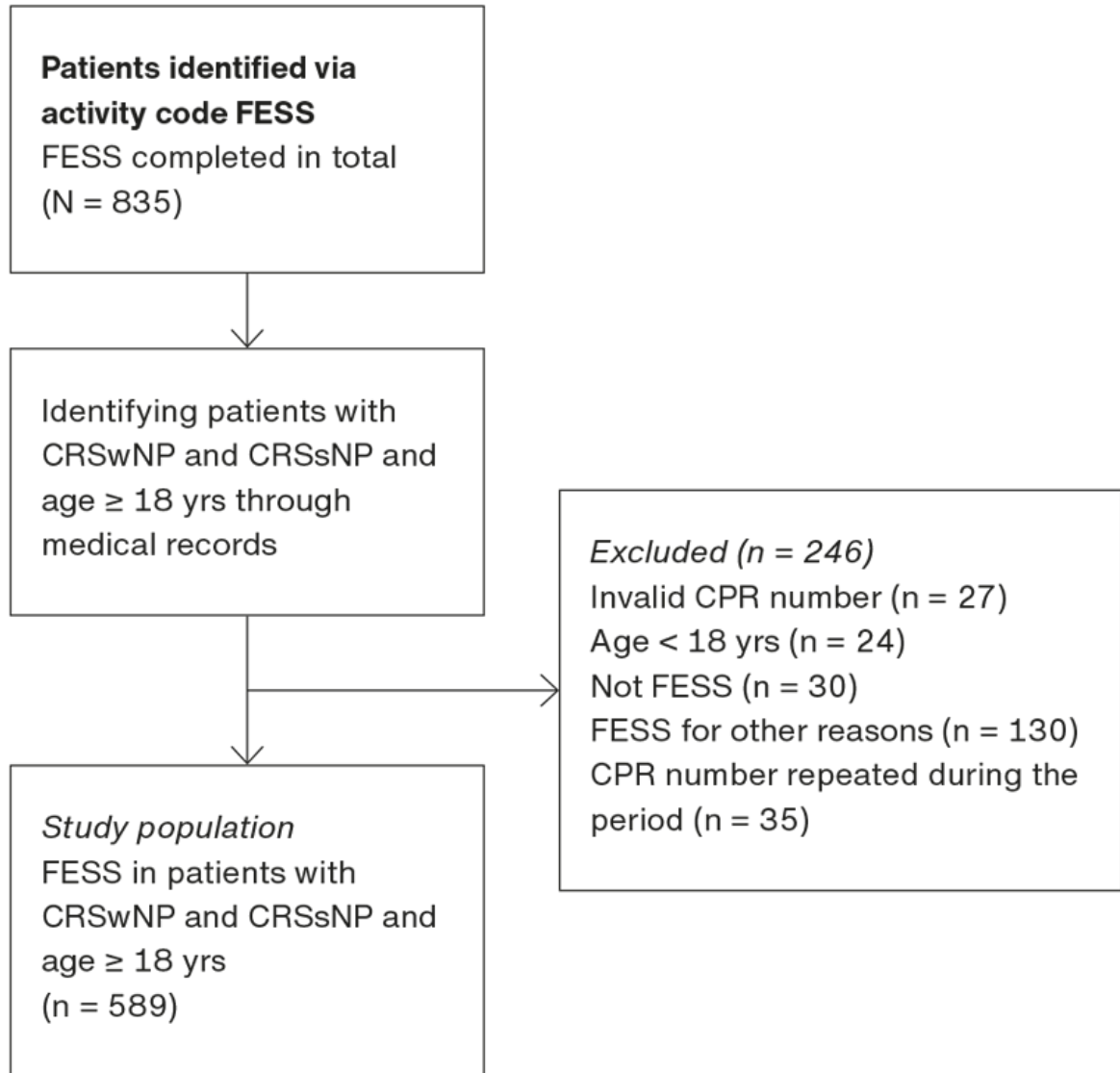
Optimal management of both CRS and asthma will likely result in a more ideal course for these patients, and patients with poor medical optimisation may recur more often, resulting in more revision surgery. This study aimed to draw attention to the importance of simultaneous treatment of these two very frequent diseases in the Danish population by investigating the co-existence of CRS and asthma in a retrospective cohort requiring FESS due to CRS.

METHODS

A retrospective cohort study was conducted at the Department of Otorhinolaryngology, Regional Hospital Gødstrup, Denmark, from 1 January 2017 to 12 December 2021. Permission to access and publish data was granted by the hospital administration. All consecutive adult patients (≥ 18 years) undergoing FESS due to CRS were included. The study population was described regarding: nasal polyposis, asthma, respiratory allergies, medical treatment of CRS, total number of FESS procedures and completion of septo-/turbino-plasty in relation to FESS/revision FESS. Finally, guideline adherence as regards to conservative treatment prior to FESS was assessed.

The selection process is presented in **Figure 1**.

FIGURE 1 Selection of the study population.



CPR number = civil registration number; CRSsNP = chronic rhinosinusitis without nasal polyps; CRSwNP = chronic rhinosinusitis with nasal polyps; FESS = functional endoscopic sinus surgery.

A total of 835 patients who had undergone FESS in the period were identified by searching the electronic patient record system (EPJ - Biportal). To identify patients with CRS, a diagnosis needed to be registered and/or EPOS criteria of CRS were to be met in the medical record. Co-existing asthma was identified by a registered diagnosis or by the presence of medication labelled with asthma as indication. For all patients, it was noted if the word “asthma” was mentioned in the medical record in relation to examination prior to FESS. Polyp status and information on allergy was also retrieved from the medical record, including the total number of FESS and FESS performed prior to the inclusion period. As for allergy, the condition was either mentioned in the medical

record, or medication labelled with allergic rhinitis as indication was found. Information on septo-/turbino­plasty in relation to FESS was found in the notes on FESS as they were both registered through an activity code. The history of medical treatment for CRS was gathered through both the medical record and the list of medications. It was noted whether the patient had tried systemic steroid at least once prior to FESS. Adherence to guidelines was defined as treatment with NC for ≥ 8 weeks prior to FESS, meaning that NC was recommended and prescribed by the clinician and/or registered as used by the patient for a period of ≥ 8 weeks prior to FESS. Thus, the focus was on the clinician's adherence to guidelines.

Data were analysed using EpiBasic in Excel and presented as percentages or means. Data for the two groups, CRSwNP and CRSsNP, were compared, and relative risks (RR) and odds ratios (OR) were calculated for relevant outcomes. A Z-test was performed to examine the significance of ORs and RRs. The χ^2 -test was used to examine the significance of the connection between CRSwNP and risk of asthma, revision FESS, asthma, systemic steroid and septo-/turbino­plasty. A p value < 0.05 was considered statistically significant.

Trial registration: not relevant.

RESULTS

In total, 246 patients were excluded from the study (Figure 1). In 27 cases, a non-existent CPR number was linked to the surgical intervention. Twenty-four FESS procedures were completed in patients younger than 18 years. In 30 cases, the surgical intervention performed was not FESS. Furthermore, 130 FESS procedures were performed for other reasons than CRS, e.g., inverted papilloma and cysts. Duplicate CPR numbers were found in 35 cases during the inclusion period. These patients were only reviewed once, but revision FESS were counted correctly.

Characteristics of the study population are listed in **Table 1**. The majority of patients were men older than 50 years with the presence of nasal polyps. Almost 80% underwent FESS for the first time. More than a third of patients (34.5%) had simultaneous CRS and asthma, which included 192 diagnosed with asthma before and 11 patients diagnosed after the current FESS procedure, and attention to asthma could be documented in only a third of medical records (36.2%).

TABLE 1 Characteristics of the study population. Patients undergoing functional endoscopic sinus surgery because of chronic rhinosinusitis from 1 January 2017 to 12 December 2021, Department of Otorhinolaryngology, Regional Hospital Gødstrup, Denmark (N = 589).

	n (%)
<i>Age, yrs</i>	
18-29	63 (10.7)
30-49	177 (30)
50-69	275 (46.7)
≥ 70	74 (12.6)
<i>Gender</i>	
Male	359 (61)
Female	230 (39)
<i>Nasal polyp?</i>	
Yes	452 (76.7)
No	137 (23.3)
<i>Revision FESS?</i>	
Yes	124 (21.1)
No	465 (78.9)
<i>Septoplasty/turbinoplasty?</i>	
Yes	124 (21.1)
No	465 (78.9)
<i>Systemic steroid?</i>	
Yes	175 (29.7)
No	414 (70.3)
<i>Allergy?</i>	
Yes	149 (25.3)
No	440 (74.7)
<i>Asthma?</i>	
Yes	203 (34.5)
No	386 (65.5)
<i>Attention to asthma prior to FESS?</i>	
Yes	213 (36.2)
No	376 (63.8)
<i>Adherence^a to guidelines prior to FESS?</i>	
Yes	584 (99.2)
No	5 (0.8)

FESS = functional endoscopic sinus surgery.

a) Correct use of treatment guidelines by the clinician prior to FESS.

Adherence to guidelines on conservative management of CRS before FESS, i.e. treatment with NC for ≥ 8 weeks, was confirmed in 584 patients (99.2%).

Table 2 illustrates a disproportion between the two groups, asthma and no asthma. Among patients diagnosed with asthma before FESS, asthma was mentioned in 95.8% of the medical records in relation to the examination. In contrast, asthma was mentioned only specifically in 7.5% of medical records of patients not diagnosed with asthma. Of the 11 asthma patients who were not diagnosed until after undergoing FESS, asthma was not mentioned specifically in any of the medical records prior to FESS.

TABLE 2 Characteristics of patients with chronic rhinosinusitis with and without asthma. Patients with asthma were divided into two groups depending on whether they were diagnosed with asthma before or after functional endoscopic sinus surgery. The values are n (%).

	Asthma (n = 203 (34.5%))		No asthma (n = 386 (65.5%))	Total (N = 589)
	diagnosed before FESS (n = 192)	diagnosed after FESS (n = 11)		
<i>Attention on asthma specifically prior to FESS?</i>				
Yes	184 (95.8)	0	29 (7.5)	213
No	8 (4.2)	11 (100)	357 (92.5)	376
<i>Nasal polyp?</i>				
Yes	166 (86.5)	8 (72.7)	278 (72)	452
No	26 (13.5)	3 (27.3)	108 (28)	137
<i>Revision FESS?</i>				
Yes	61 (31.8)	3 (27.3)	60 (15.5)	124
No	131 (68.2)	8 (72.7)	326 (84.5)	465
<i>Septoplasty/turbinoplasty?</i>				
Yes	23 (12)	4 (36.4)	97 (25.1)	124
No	169 (88)	7 (63.6)	289 (74.9)	465
<i>Allergy?</i>				
Yes	78 (40.6)	1 (9.1)	70 (18.1)	149
No	114 (59.4)	10 (90.9)	316 (81.9)	440
<i>Systemic steroid?</i>				
Yes	89 (46.4)	4 (36.4)	82 (21.2)	175
No	103 (53.6)	7 (63.6)	304 (78.8)	414

FESS = functional endoscopic sinus surgery.

Significantly more patients with CRSwNP than patients with CRSsNP had co-existing asthma (Table 3). Thus, the RR of asthma in patients with CRSwNP was 82% higher than in patients with CRSsNP (Table 3).

TABLE 3 Risk of asthma, revision functional endoscopic sinus surgery, septoplasty/turbinoplasty, allergy and use of systemic steroid in patients with chronic rhinosinusitis and nasal polyps compared with patients with chronic rhinosinusitis without nasal polyps.

	CRSwNP, n (%) (n = 452 (76.7%))	CRSsNP, n (%) (n = 137 (23.3%))	Total (N = 589)		RR		OR		
			n	p value ^a	RR (95% CI)	p value ^b	OR (95% CI)	p value ^b	
<i>Asthma?</i>									
Yes	174 (38.5)	29 (21.2)	203	< 0.001	1.82 (1.29-2.56)	< 0.001	2.33 (1.48-3.66)	< 0.001	
No	278 (61.5)	108 (78.8)	386						
<i>Revision FESS?</i>									
Yes	109 (24.1)	15 (10.9)	124	< 0.001	2.20 (1.33-3.65)	0.002	2.58 (1.45-4.61)	0.001	
No	343 (75.9)	122 (89.1)	465						
<i>Septoplasty/turbinoplasty?</i>									
Yes	81 (17.9)	43 (31.4)	124	< 0.001	0.57 (0.42-0.78)	< 0.001	0.48 (0.31-0.74)	< 0.001	
No	371 (82.1)	94 (68.6)	465						
<i>Allergy?</i>									
Yes	121 (26.8)	28 (20.4)	149	0.135	1.31 (0.91-1.88)	0.146	1.42 (0.89-2.26)	0.137	
No	331 (73.2)	109 (79.6)	440						
<i>Systemic steroid?</i>									
Yes	160 (35.4)	15 (10.9)	175	< 0.001	3.23 (1.97-5.30)	< 0.001	4.46 (2.52-7.88)	< 0.001	
No	292 (64.6)	122 (89.1)	414						

CI = confidence interval; CRSsNP = chronic rhinosinusitis without nasal polyps; CRSwNP = chronic rhinosinusitis with nasal polyps; OR = odds ratio; FESS = functional endoscopic sinus surgery; RR = relative risk.

a) χ^2 -test.
b) Z-test.

Revision FESS was significantly more prevalent among patients with CRSwNP with a RR of 120% for revision-FESS than among patients with CRSsNP (Table 3).

Allergy was related to a higher risk in patients with CRSwNP than in patients with CRSsNP, but this finding was

not statistically significant (Table 3).

The RR of treatment with systemic steroid was 223% higher in patients with CRSwNP than in patients with CRSsNP, which was statistically significant.

DISCUSSION

In this retrospective cohort study, a population of patients with CRS was examined regarding several parameters, focusing on the correlation of their condition with asthma.

This study found that only 38.5% of the patients with CRSwNP included had co-existing asthma (Table 3). This finding contrasts with both the EPOS and several previous studies, suggesting a higher prevalence [1]. This suggests that approximately 27% of patients with CRSwNP potentially have undetected and uncontrolled asthma. Considering the fact that the RR of asthma was significantly higher in CRSwNP patients than in patients with CRSsNP (Table 3), this finding is worrying. The otorhinolaryngologist's attention is not drawn to the importance of detecting undiagnosed asthma or optimising treatment of already diagnosed asthma as the Danish national guidelines on CRS management published by the DRS do not mention asthma.

The lack of attention to asthma is also reflected by the fact that asthma was mentioned in only 7.5% of the medical records of patients with no pre-existing asthma diagnosis (Table 2). As long as no examinations of the pulmonary function is implemented, many patients with CRSwNP are left with undiagnosed asthma. One way to increase the attention on asthma is to adjust Danish national guidelines to enhance clinicians' attention to this matter. Under optimal conditions, all patients with CRS, CRSwNP at least, should undergo a respiratory-related examination to detect undiagnosed asthma. This is emphasised by the fact that a statistically significant risk of asthma was seen in patients with CRSwNP compared with CRSsNP in this study, which is also consistent with knowledge from recognised literature on the subject [1]. The creation of such a standard test has been attempted, but the quality of the test awaits evaluation [8]. More multidisciplinary team management of CRS and asthma is advantageous for patients and clinicians involved alike [9].

Almost all patients received sufficient conservative treatment with NC for eight weeks or more prior to surgery (Table 1) although more precise information on patient compliance was unavailable. The outcome only reflects clinicians' adherence to guidelines and the transmission of this in practice.

This study found a statistically significantly higher risk of revision FESS in patients with CRSwNP than in patients with CRSsNP. Sella et al. [10] also reported that patients with CRSwNP were more likely to need revision FESS than patients with CRSsNP were. Additionally, they found that asthma was the only factor that was significantly related to revision FESS in both patients with CRSwNP and patients with CRSsNP. The link between asthma and revision FESS was also demonstrated in the present study, though the significance of this remains unknown. Twice as many patients with asthma as patients without asthma had revision FESS (Table 2).

Allergy was not significantly related to a higher RR in patients with CRSwNP (Table 3). This finding is in line with other studies showing that this association is controversial [1]. Allergy is a factor that comes with a risk of drawing incorrect conclusions, possibly due to insufficient diagnostics. The results concerning allergy should therefore not be ascribed much value.

A significantly higher RR of receiving treatment with systemic steroid was found in patients with CRSwNP (Table 3). Howard & Lal [11] reviewed the evidence on managing CRS with systemic steroid, and quality studies support the use in patients with CRSwNP in particular.

With respect to future management of CRS, biological medicine as a supplement to current treatment will be

seen to a higher degree. van der Lans et al. [12] examined the effect of a human monoclonal antibody (mAb), dupilumab in patients with CRSwNP. This prospective observational cohort study showed high therapeutic efficacy for severe CRSwNP [12]. Several other publications have also shown promising results for biologic treatment in patients with CRSwNP [13-15]. In a randomised, double-blinded, placebo-controlled phase-3 trial, Han et al. [15] found that mepolizumab, another mAb, improved nasal polyp size and nasal obstruction. Biological treatment will potentially play an important role in future CRS management [9, 16].

Limitations

This study had limitations due to its design. The study was retrospective, hence results depend on the content of the patient's medical records and medication lists. Danish medical records are not designed to underpin research work. Some information might be missing even though the clinician did ask relevant questions at the examination, e.g., information on respiratory symptoms and asthma. Also, lists of medications might not have been updated properly.

The data collected were recorded and analysed by the first author. Although another author was involved in data collection in unclear situations, the risk of bias remains.

CONCLUSIONS

The results of this retrospective cohort study accentuate several important findings. The relatively low prevalence of asthma found in patients with CRSwNP and the lack of attention to asthma in Danish national guidelines on CRS management show that there is room for improvement. Patients with co-existing CRS and asthma need to be detected to improve their overall course by optimising the management of both conditions. The statistically significant risk of asthma and revision FESS in patients with CRSwNP emphasises this need. It is necessary to increase attention to asthma to implement methods to identify this group of patients and initiate a higher degree of multidisciplinary management among otorhinolaryngologists and pulmonologists.

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Conflicts of interest Potential conflicts of interest have been declared. Disclosure forms provided by the authors are available with the article at ugeskriftet.dk/dmj

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