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Article

Clinical Predictors of Recurrence After Functional Endoscopic Sinus Surgery: A Prospective Study at Al-Hussein Teaching Hospital, Samawa, Iraq

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Abstract: The Background: Chronic rhinosinusitis (CRS) commonly reappears after functional endoscopic sinus surgery (FESS), and it has been found that some patients experience the need for revision surgery. It is important to define the clinical characteristics of patients that can help to determine the risk of the recurrence of the condition after surgery.
Aim: To assess the recurrence rate in patients who underwent FESS at Al-Hussein Teaching Hospital in Samawa, Iraq.
Methods: A prospective cohort study was done from December 2020. Patients over years old with CRS that was resistant to maximal medical therapy and who underwent FESS were included in the study from December 2021 and were followed for at least six months after. The demographic data and the data on the co-morbidities, CRF phenotype, Lund–Mackay computed tomography score, preoperative SNOT-22 22score, peripheral blood eosinophilia, tissue eosinophilia, surgery extent, and compliance with postoperative care were assessed in patients. For the assessment of the recurrence, both the symptoms and endoscopic examination data were used. Univariate analysis and multivariable logistic regression were done.
Results: 86 patients were included in the follow-up (mean age was 36.4 ± 11.8; 60.5% of men). 24 patients (27.9%) have shown recurrence. The univariate analysis has shown that recurrence has been associated with nasal polyposis, bronchial asthma, aspirin-exacerbated respiratory disease, previous sinus surgery, a higher Lund–Mackay score, a higher preoperative SNOT-22 score, having eosinophilia, and poor compliance with postoperative care. In the multivariable analysis, factors such as asthma (adjusted odds ratio (aOR) 3.42; 95% confidence interval (CI) 1.08-10.81), blood eosinophil count ≥300 cells/μL (aOR 3.15; 95% CI 1.02-9.74), Lund-Mackay score (aOR 1.19 per point; 95% CI 1.04-1.36), and poor postoperative adherence (aOR 3.68; 95% CI 1.17-11.55) were all independent predictors for recurrence.
In conclusion, the data showed that a significant proportion of patients experienced recurrence of sinusitis in the first year following surgery. Asthma, eosinophilia, extensive disease, and poor compliance were among the contributing factors for that recurrence. Such easily assessable preoperative and postoperative factors can facilitate the stratification of the risk of recurrence in clinical practice within Iraq.

Keywords: chronic rhinosinusitis; functional endoscopic sinus surgery; recurrence; nasal polyps; asthma; eosinophilia; Lund–Mackay score; Iraq

Introduction

Chronic rhinosinusitis (CRS) is an inflammatory condition that affects the nasal cavity, and the paranasal sinuses involving two or more symptoms that include nasal obstruction and mucus discharge maybe with or without facial pain or pressure, as well as alteration in smell for more than 12 weeks and endoscopic or radiological evidence of mucosal changes . CRS is considered an umbrella term with two traditional types, including chronic rhinosinusitis with nasal polyps (CRwNP) and chronic rhinosinusitis without nasal polyps (CRsNP). However, CRS has also recently been classified into primary and secondary CRS, alongside the type 2 inflammatory and non-type 2 inflammatory endotypes [1]. According to the data from the semi-countrywide GA²LEN study, the prevalence of CRS is over 11% of the adult population in Europe following symptom-based criteria, with variations based on the geographical location [2], [3]. Since the number of patients diagnosed with the presence of CRS using symptom-based criteria is very high; there is a necessity for endoscopy or computed tomography (CT) scan to get a proper diagnosis and this combination is accepted as the standard procedure in clinical practice [4]. It is very difficult to compare this information about such a population in Iraq, but this condition is one of the leading causes of consultation in the ENT clinics in the country, where dry climate, seasonally dust storms and the use of tobacco products are frequent and allergic conditions are quite prevalent.

The burden of CRS extends well beyond the nose. Patients report poor sleep, fatigue, impaired concentration, reduced productivity and depressed mood, and the disease-specific quality-of-life impairment is comparable to that of chronic conditions such as asthma and chronic obstructive pulmonary disease [5]. The initial management is medical and relies on saline irrigation and topical intranasal corticosteroids, supplemented in selected cases by short courses of systemic corticosteroids and, where bacterial infection is suspected, by antibiotics [6]. When symptoms persist despite appropriate medical therapy, surgery is offered. Functional endoscopic sinus surgery (FESS), developed from the work of Messerklinger and popularised by Kennedy and Stammberger, aims to restore ventilation and mucociliary clearance by removing disease from the key drainage pathways, especially the ostiomeatal complex, while preserving normal mucosa [7]. The procedure has since become the standard surgical treatment for medically refractory CRS throughout the world. Systematic reviews and large cohort studies show that FESS produces significant and durable improvement in symptoms and quality of life for most patients [8]. The English National Comparative Audit, which followed more than three thousand patients, confirmed substantial improvement in the 22-item Sinonasal Outcome Test (SNOT-22) after surgery, maintained up to five years [9]. [10].

Despite these benefits, FESS does not cure the underlying mucosal inflammation, and recurrence remains a major clinical problem. DeConde and colleagues reported that endoscopic polyp recurrence was present in approximately 35% of patients at six months and 40% at eighteen months after surgery for CRSwNP [11]. In a twelve-year follow-up study from Belgium, Calus and co-workers found that nearly four out of five patients with CRSwNP had evidence of recurrent polyps and more than one third had undergone revision surgery [12]. The English audit reported revision rates that rose steadily with time, reaching approximately one fifth of patients with polyps within five years. Database analyses from North America have described revision surgery in a significant minority of patients within a few years of the index operation, and similar figures have

been reported by single-centre studies [13]. Patients with massive polyposis appear to be at particularly high risk, with recurrence reported in more than half of such cases [14]. A meta-analysis of revision surgery in CRSwNP found considerable variation between series, which was explained partly by differences in patient selection and comorbidity [15]. Recurrence therefore represents both a direct cost to health systems and a persistent burden to patients, who may require repeated courses of systemic corticosteroids, multiple procedures and prolonged follow-up [16].

The quest for predictors of recurrence is predicated upon an increasing knowledge of the biological basis of CRS. It has been established that a significant number of patients, especially those with nasal polyps, have type 2 inflammation, characterized by the infiltration of eosinophils,

and elevated levels of interleukin-5 and interleukin-13 17along with the production of immunoglobulin E in the affected area. Tissue biomarker clustering revealed the presence of different inflammatory endotypes and different chances of asthma and recurrence [17]. The proportions of the endotypes differ geographically—European and North American populations show the presence of type 2 inflammation while the majority of East Asian patients are suffering from neutrophilic and other endotypes. However, type 2 disease has begun growing in these regions [18]. The JESREC study in Japan has developed a scoring system incorporating the presence of bilateral CRS, nasal polyps, ethmoid-dominated CT findings, and eosinophilia in blood showing the high risk of recurrence of eosinophilic CRS following surgery [19]. The relationship between tissue eosinophils count and the recurrence of polyps has been demonstrated in Chinese patients [20]. The analysis of eosinophilia in patients' blood has shown its significant correlation with surgical results in a Belgian prospective study performed over three years. Peripheral eosinophilia measurements can be employed as markers of tissue eosinophilia and, therefore, the types of eosinophilic disease [21].

Co-existing conditions significantly affect the clinical outcome. Asthma has been said to have a relationship with CRSwNP and that patients with both conditions experience more severe sinus problems and less favorable results from surgery [21]. The most severe example of this is aspirin-exacerbated respiratory disease (AERD) which involves asthma, nasal polyps and allergic reactions to aspirin and has the highest amount of recurrence and revision surgery [22]. Allergic rhinitis is a frequently found condition in CRS patients, though its significance with recurrence rate is unclear [23]. Environmental influences, especially smoking, impact mucociliary function and cause mucosal inflammation; different studies indicate that smoking contributes to lower scores of symptoms and increased revision rates following FESS, though results are not entirely conclusive [24].

Surgical aspects also have an impact on this issue. Among the points that refer to incomplete disease removal are the displacement of the middle turbinate and the presence of ethmoid cells and synechiae and scarring of Frontal recess and non-using of natural maxillary ostium [26]. The issue of surgical extent was researched as well; in some cases, more extended surgery including frontal sinuses brought out less polyp recurrence. The timing of the surgery might play a role also since those patients who get operated on the disease early have a better chance for recovery than those who wait for years. It is also undeniable that postoperative effective care is critical for the success of the surgery, and poor attitude to postoperative care has contributed to recurrence.

Evaluating patients' condition refers to a set of instruments that has been standardised. The Lund-Mackay score refers to evaluating the condition of all cavities and patency of the ostiomeatal complex in CT scans hence being the most commonly applied method. The Lund-Kennedy score is used to evaluate the presence of polyps and swelling, as well as assessing the status of the cavity

and monitor its evolution over time. The SNOT-33 34 22 35 22 36state has proven to be a valid measure and it helps collect information on the nasal function, sleep, hearing, and emotions' condition. The scores of the patients obtained after the FESS surgery serve for estimating the potential need of revising the procedure [27].

Various research studies on recurrence predictors have produced mixed outcomes. Although certain studies considered the primary variables to determine recurrence factors to be asthma, eosinophilia, and previous surgery, others found that the use of several clinical, laboratory, and histological variables proved to be more effective in solving the issue than any of the previously mentioned factors on their own. Much of the data for the analysis comes from Europe, North America, and East Asia, and whether it can be applied in the case of Middle Eastern populations is uncertain, considering the differences in climatic conditions, exposure to factors affecting the environment, genetics, health care access, and types of inflammation [28].

FESS is commonly conducted in Teaching hospitals in Iraq; however, limited local research exists that explores long-term outcomes of this technique and its failure predictors. Al-Hussein Teaching Hospital in Samawa is the main facility treating ear, nose and throat conditions in Al-Muthanna Governorate, which is mainly desert and is frequently exposed to dust storms and high temperatures in summer. Patients from this area tend to delay their presentation to hospitals and

suffer from advanced stage of disease and difficulty in adhering to regular follow-ups and purchasing medications. Knowing the predictors of surgery failure locally should help the surgeon to choose the right patients for FESS, plan the surgery extent correctly, counsel patients accordingly, and optimize the follow-up practice.

Thus, the objective of this research was to measure the recurrence rate after FESS for CRS in patients treated at Al-Hussein Teaching Hospital in Samawa in 2022 and determine the demographic, clinical, radiological, laboratory and postoperative variables related to recurrence independently [29].

Methodology

Study design and setting

The study was designed as a prospective observational cohort trial and was carried out in the Department of Otolaryngology at the Al-Hussein Teaching Hospital in Samawa in the A-Muthanna district of Iraq from December 1, 202*0*, to December 31, 202*1*. The hospital is the main tertiary referral centre for ear, nose and throat disease and the study covered both urban population of Samawa as well as the rural and desert regions around Samawa district. Patients were included in the study from January 1 to June 30, 2022, and they were followed till December 31, 2022. Hence, each of the patients received at least six months of postsurgical follow-up.

Ethical considerations

The plan of research for the study was reviewed and approved by both the Scientific and Ethical Committee of Al-Muthanna Health Directorate and the committee responsible for hospital training in the completion of this study. All potential participants were further informed of the purpose of the study as well as the methods that will be used in the study, in their language, Arabic, in order to obtain consent from them. There was no coercion imposed upon the patients to participate in this study and their medical treatment was effective regardless of whether they participated in the study or not. All identifiable information was kept separate from the data being collected, and had also been removed from the data which was stored.

Study population

Adults aged 18 years or older diagnosed with CRS according to 2020 European Position Paper on Rhinosinusitis and Nasal Polyps criteria were eligible. The diagnosis required at least two of the following symptoms for twelve weeks or more, including at least one of nasal obstruction or nasal discharge: nasal obstruction, either anterior or posterior nasal discharge, facial pain or pressure, or loss or reduction of smell in addition to endoscopic findings (polyps, mucopurulent discharge or mucosal oedema in the middle meatus) and/or CT imaging showing the same or similar findings as per ostiomeatal complex or sinus disease. All eligible subjects had permanent symptoms despite at least eight weeks of maximal medical therapy which included daily saline nasal irrigation and nasal sprays with corticosteroid, a short course of oral corticosteroids for those with polyps, and culture-directed or broad spectrum antibiotics for those with purulent discharge.

Individuals were excluded from the study if they had a case of allergic fungal rhinosinusitis or invasive fungal disease, sinonasal malignancies or inverted papillomas, antrochoanal polyp as the only pathology, cystic fibrosis, primary ciliary dyskinesia, granulomatous or vasculitic pathology, known primary or acquired immunodeficiency, or complicated acute sinusitis that needed emergency surgery, or were pregnant. Additionally, anyone that she did not attend a visit at least months or months after surgery was excluded from the analysis. There were 97 patients recruited, 11 were lost to follow-up. Thus, 86 patients were included in the analysis.

Preoperative assessment

All of the patients received a above-mentioned assessment of history and complete examination of ear, nose and throat. The following assessment variables were noted in the above standardised sheet: age, sex, place of living (urban versus rural), occupation, active smoking of cigarettes or waterpipe, duration of symptoms, diagnosis of bronchial asthma made by the doctor, presence of allergic rhinitis, history of respiratory attack after drinking aspirin or taking any NSAID and experience in surgery of sinuses. The diagnosis of allergic rhinitis has been made according to typical seasonal or perennial symptoms and increased levels of serum IGE. The patients have been

diagnosed with AERD if they happened to have asthma as well as nasal pathologies at the time of taking the medicines.

An Arabic translation of the SNOT-22 questionnaire was used to assess the severity of the disease-specific symptoms, and the patient filled out the form at the clinic with the assistance of the nurse in cases of limited literacy. After the topical decongestion and anaesthesia, rigid nasal endoscopy was done with 0°, and 30° 4-mm endoscope and the findings were evaluated according to Lund-Kennedy endoscopic score. Patients were diagnosed with either CRSwNP or CRSsNP based on the presence of bilateral polyps in the middle meatus during endoscopy. A non-contrast CT of the paranasal sinuses in axial, coronal and sagittal planes was done at the most three months before surgery and assessed by the operating surgeon and the second ENT specialist using Lund-Mackay grading system after any discrepancy was resolved by consensus. A complete blood count with differential was taken at least two weeks before surgery, with patients who had taken systemic steroids in the last four weeks repeating the test if possible. Eosinophilia was determined as eosinophil count of 300 cells or more in μL.

Surgical procedure

All surgeries were carried out under general anaesthesia with controlled hypotension by the senior ENT surgeon or senior residents supervised by a consultant. A microdebrider was used for the removal of polyps, if available. The extent of surgery performed was determined from CT

findings and endoscopic picture obtained. A total surgery ("full-house") protocol was carried out which included sphenoidotomy and dissection of the frontal recess including septoplasty and the procedures for reducing the inferior turbinates when needed for operating access or ventilation. Absorbable nasal packing or a weak non-absorbable packing was used at the end of the surgery and removed after from 24 to 48 hours.

Postoperative care and follow-up

All patients received the same postoperative treatment: a course of oral amoxicillin–clavulanate (or a macrolide if they were allergic to penicillins) for a week, high-volume daily isotonic saline irrigation twice a day, and mometasone furoate nasal spray 100 μg in each nostril twice a day for at least three months, followed by one administration per day afterwards. Patients with the nasal polyp syndrome were treated with oral prednisolone over two weeks in a tapering manner unless contraindicated. Crust and clot debridement was performed at two weeks during the clinic visit. Follow-ups were scheduled two weeks, one month, three months and six months after the surgery and end of the study period. Starting from three months and continuing until the end of the follow-up period, SNOT-22 was filled in, rigid endoscopy was performed, and Lund–Kennedy score was reported during each of patient's follow-up visits.

At each follow-up appointment, we measured the patient's compliance through structured interviews and inspection of the medicine pack. We classified a patient as noncompliant if they had used saline irrigation and intranasal corticosteroids less than 80% of the time or discontinued either medication at any time since three months before their last follow-up visit without consulting a physician.

Definition of outcome

The study's primary endpoint was recurrence of CRS in the follow-up period. Recurrence is defined as having sinonasal symptoms (defined as SNOT-22 score less than 10 of preoperative score, or greater than 30), and having an objective finding of the disease in the area of operation in the nasal cavity (recurrence of polyps of at least grade 1 in the ethmoid cavity or middle meatus, or having persistent edema with mucopurulent content that cannot be explained by a diagnosis of acute upper respiratory infection). If there was any doubt about the diagnosis of recurrence of disease then a CT scan of the sinuses was performed again. A diagnosis of recurrence of CRS can be made if the patient has any of these findings at any follow-up visit after three months.

Statistical analysis

The collected data was uploaded into Microsoft Excel and analyzed using IBM SPSS Statistics version 26. Continuous variables were checked for normality using the Shapiro–Wilk test and were stated as mean ± standard deviation; categorical variables were reported as frequencies and percentages. Comparison between groups of patients with and without recurrence was performed

using independent-samples t-test or Mann–Whitney U test for continuous variable and Pearson's chi-squared test or Fisher's exact test for categorical variable. Any variables found to have p-value

< 0.10 in univariate analysis as well as variables with clinical importance associated with recurrence were included in binary logistic regression model; in case high correlation exists between variables such as tissue eosinophilia and blood eosinophilia, AERD and asthma, variable included was the one which is applicable for all patients with a better clinical significance in order to avoid collinearity of the model. The outcomes of the analysis were presented as adjusted odds ratios (aOR) with 95% Confidence-interval (CI). Model calibration was checked using Hosmer-

Lemeshow test, and discrimination was assessed based on the area under curve (AUC). P-value < 0.05was considered to be statistically significance.

Results

Of the 97 patients enrolled, 86 completed the required follow-up and were included in the analysis. The mean duration of follow-up was 8.9 ± 1.7 months (range 6–12 months). The mean age of the cohort was 36.4 ± 11.8 years, and the largest age group was 30–44 years (43.0%). Men outnumbered women by a ratio of approximately 1.5 to 1. More than two thirds of the patients had CRSwNP, one quarter had bronchial asthma, and one third were current smokers [30]. Fifteen patients (17.4%) were undergoing revision surgery after a previous sinus operation elsewhere. The baseline characteristics are shown in Table 1.

Table 1. Baseline demographic and clinical characteristics of the study population (n = 86)

Characteristic	Value
Age, years, mean ± SD	36.4 ± 11.8
Age group 18–29 / 30–44 / ≥45 years, n (%)	28 (32.6) / 37 (43.0) / 21 (24.4)
Male sex, n (%)	52 (60.5)
Urban residence, n (%)	49 (57.0)
Current smoker, n (%)	30 (34.9)
CRS with nasal polyps, n (%)	58 (67.4)
Bronchial asthma, n (%)	22 (25.6)
Allergic rhinitis, n (%)	38 (44.2)
Aspirin-exacerbated respiratory disease, n (%)	7 (8.1)
Previous sinus surgery, n (%)	15 (17.4)
Lund–Mackay CT score, mean ± SD	13.6 ± 4.9
Preoperative SNOT-22 score, mean ± SD	52.1 ± 15.5
Blood eosinophils ≥300 cells/μL, n (%)	31 (36.0)
Comprehensive (full-house) FESS, n (%)	41 (47.7)
Poor postoperative adherence, n (%)	27 (31.4)

Recurrences were seen in 24 patients, with an overall recurrence rate of 27.9% (95% CI 18.9–38.2%). The occurrence of recurrences was significantly higher in patients with nasal polyps compared to patients without nasal polyps (36.2% vs 10.7%, p = 0.014). Recurrences also occurred significantly more frequently in asthmatic patients (54.5% vs 18.8%, p = 0.001), patients with AERD (71.4% vs 24.1%, p = 0.018), those who had undergone previous sinus surgery (53.3% vs 22.5%, p = 0.023), patients with eosinophilia (48.4% vs 16.4%, p = 0.001) and patients who were non-compliant (48.1% vs 18.6%, p = 0.005). Patients that had recurred also had greater mean Lund–Mackay score values besides higher preoperative SNOT-22 scores. Among the 58 patients with polyps, tissue eosinophilia was associated with recurrence (57.7% vs 18.8%, p = 0.002). Age, gender, allergic rhinitis, smoking and surgery extent were not statistically associated, though smoking looked to have the tendency (p = 0.067) (Table 2).

Table 2. Univariate comparison of patients with and without recurrence

Variable	Recurrence (n = 24)	No recurrence (n = 62)	p-value
Age, years, mean ± SD	37.9 ± 12.4	35.8 ± 11.6	0.46[a]
Male sex, n (%)	15 (28.8)	37 (71.2)	0.81[b]
Current smoker, n (%)	12 (40.0)	18 (60.0)	0.067[b]
CRS with nasal polyps, n (%)	21 (36.2)	37 (63.8)	0.014[b]
Bronchial asthma, n (%)	12 (54.5)	10 (45.5)	0.001[b]
Allergic rhinitis, n (%)	14 (36.8)	24 (63.2)	0.10[b]
AERD, n (%)	5 (71.4)	2 (28.6)	0.018[c]
Previous sinus surgery, n (%)	8 (53.3)	7 (46.7)	0.023[c]
Lund–Mackay score, mean ± SD	16.8 ± 4.1	12.3 ± 4.6	<0.001[a]
Preoperative SNOT-22, mean ± SD	58.2 ± 14.6	49.7 ± 15.3	0.019[a]
Blood eosinophils ≥300 cells/μL, n (%)	15 (48.4)	16 (51.6)	0.001[b]
Tissue eosinophilia >10/HPF (CRSwNP only, n = 58), n (%)	15 (57.7)	11 (42.3)	0.002[b]
Comprehensive (full-house) FESS, n (%)	13 (31.7)	28 (68.3)	0.45[b]
Poor postoperative adherence, n (%)	13 (48.1)	14 (51.9)	0.005[b]

[a] T-test for independent samples; [b] Pearson's chi-square test; [c] Fisher's exact test. The figures for categorical variables signify the percentage in each category. HPF: high power field; AERD: aspirin-exacerbated respiratory disease.

The multivariable logistic regression model contained five variables: nasal polyps, asthma, Lund–Mackay scores, eosinophilia, and adherence. AERD was not included in the multivariable analysis because every AERD subject in the study had asthma and nasal polyps. In addition, tissue eosinophilia was not included in the analytical model since it was only evaluated from biopsy material and was therefore closely correlated with blood eosinophilia. The only variables that were statistically significant in predicting outcome based on the model were Lund–Mackay scores, eosinophilia, and adherence. Nasal polyposis was not a significant predictor when adjusting for the other variables. Every additional Lund–Mackay score was associated with an increase in the odds of recurrence by 19%. In terms of its calibration, the model did well (Hosmer–Lemeshow p

= 0.61) and could explain 39% of the variation in the data set (Nagelkerke R^2 = 0.39) while accurately differentiating recurrence from non-recurrence (AUC of 0.82; 95% confidence interval [CI], 0.72–0.91) (Table 3).

Table 3. Multivariable logistic regression analysis of predictors of recurrence

Predictor	B	SE	Adjusted OR	95% CI	p-value
Bronchial asthma	1.23	0.59	3.42	1.08–10.81	0.036
Blood eosinophils ≥300 cells/μL	1.15	0.58	3.15	1.02–9.74	0.046

Lund–Mackay score (per point)	0.17	0.07	1.19	1.04–1.36	0.011
Poor postoperative adherence	1.30	0.58	3.68	1.17–11.55	0.026
CRS with nasal polyps	0.66	0.78	1.94	0.42–8.96	0.40

B: regression coefficient; SE: standard error; OR: odds ratio; CI: confidence interval.

In Table 4, the features of recurrence were noted. Most recurrences were found at three months post-intervention, with the most frequent site of recurrence being the ethmoidal cavity. Three-quarters of the recurrences comprised recurrent polyps. The SNOT-22 score of patients who experienced recurrence was significantly higher after six months as compared to the score of patients without recurrence. Seven patients (8.1% of the cohort) have undergone revision surgery, while the rest of them received medical treatment.

Table 4. Characteristics of recurrence and postoperative outcome (n = 24)

Feature	**Value**
Time to detection of recurrence, months, mean ± SD	4.6 ± 1.9
Detected at 3-month / 6-month / later visit, n (%)	13 (54.2) / 8 (33.3) / 3 (12.5)
Site: ethmoid cavity, n (%)	13 (54.2)
Site: frontal recess, n (%)	6 (25.0)
Site: maxillary antrostomy, n (%)	3 (12.5)
Site: sphenoethmoidal recess, n (%)	2 (8.3)
Type: polyp regrowth / persistent oedema with discharge, n (%)	18 (75.0) / 6 (25.0)
Associated synechiae, n (%)	5 (20.8)
6-month SNOT-22, recurrence vs no recurrence, mean ± SD	34.6 ± 13.2 vs 18.9 ± 9.7 ($p < 0.001$)
Management: medical / revision surgery planned, n (%)	17 (70.8) / 7 (29.2)

Discussion

This upcoming study from a medical institution in southern Iraq has demonstrated that 27.9% of patients treated with FESS due to CRS had a recurrent disease with an average follow-up of less than one year during which asthma, peripheral blood eosinophilia, a high Lund–Mackay CT score, and poor adherence to postoperative treatment were independent factors that lead to such recurrences [31]. These results correlate to worldwide studies which state that CRS, especially its forms associated with nasal polyps and eosinophils, is a chronic inflammatory disease that needs surgical treatment to change the anatomical conditions but does not resolve the problem entirely [32]. These findings provide regional information about the effectiveness of sinus surgery since there is very little published about this topic here.

The recurrence rate in this series lies within the wide range reported in the literature. DeConde and colleagues observed endoscopic polyp recurrence in about 35% of patients at six months and 40% at eighteen months, and studies with longer follow-up have reported much higher cumulative figures, approaching 80% at twelve years [33]. Lower rates of revision surgery, typically between

10% and 20% over several years, have been described in national audits and administrative databases, reflecting the fact that many patients with endoscopic recurrence are managed medically and never return to theatre. Our recurrence rate was somewhat lower than the 40% reported by DeConde at eighteen months, which is expected given our shorter follow-up and the inclusion of patients without polyps, who have a lower risk of recurrence. The proportion of our patients scheduled for revision surgery (8.1%) was also modest, but recurrence after FESS increases steadily with time, and the rates reported here should be regarded as early estimates that will almost certainly rise with longer observation. Variation between studies is further explained by differences in the definition of recurrence, the proportion of patients with polyps and asthma, and the extent of the original surgery [34].

As per the present study, one of the most significant determinants was asthma, with the odds of recurrence tripling in patients who had asthma. This finding is supported by a vast literature documenting that asthmatic patients with CRS present with more severe disease, a high eosinophilic burden, and less favorable surgical outcomes. Batra and coworkers observed that among patients who had asthma with nasal polyposis, the rates of recurrence were much higher. Loftus et al conducted a meta-analysis identifying asthma as one of the most important independent predictors of revision surgery in CRSwNP patients. Other studies have answered

whether asthma could be used as a predictor in terms of polyp recurrence. It should be noted that this relationship can be explained by the theory of the unified airway, suggesting that there is a specific type 2 inflammation process going on in the upper and lower airways, which is driven by interleukins 4, 5, and 13. The most extreme manifestation of this connection - AERD - was found to be associated with the highest recurrence rate in the sample examined (71.4%). This is consistent with the literature supporting the fact that AERD leads to fast recurrence of polyps and a need for revision surgeries in patients [35]. AERD was not included in the multivariable modeling because it was too similar to the concepts of asthma and nasal polyps, but its extremely high recurrence rate confirms the need for close follow-up and the use of adjunctive therapy in this patient group.

Blood eosinophilia was also an independent predictor, and tissue eosinophilia had a significant correlation with recurrence rate in patients with polyp disease. These findings are in agreement with those from studies performed in Asia and Europe. Lou et al. showed that tissue eosinophil count could be used as a predictor of polyp recurrence in a Chinese population; Vlaminck et al. found that local eosinophilia leads to worse prognosis three years after surgical procedure. Furthermore, in the Japanese JESREC study, blood eosinophilia was incorporated to the scoring system for identification of the patients suffering from refractory eosinophilic CRS. Moreover, Ho et al. showed that some systemic markers, including blood eosinophil count, could predict eosinophilic CRS with good accuracy [36]. In this regard, Brescia et al. used a combination of different factors, including blood eosinophilia, to reveal the patients at high risk of recurrence of the disease. Also, endotyping studies have demonstrated that eosinophil-dominated type 2 inflammation is associated with coexisting asthma and with recurrence of the disease, as well as with varying distribution of such endotypes in different populations. The significance of blood eosinophilia finding in our study is that blood test can be performed without high costs and at any hospital in Iraq, whereas tissue based methods need expensive instruments and cannot be used in general practice. Thus, the total eosinophil count before the surgery can be regarded as a simple marker of risk in regards to the disease.

Radiological disease severity, assessed based on the Lund-Mackay score, serves as the third independent predictor of recurrence. According to our findings, for each one-point increase in Lund-Mackay score, the odds of disease recurrence increase by around . Lund-Mackay score is a well-established and standardized diagnostic tool, and even though the correlation between CT score and symptoms intensity is weak, the higher level of Lund-Mackay score indicates a heavier burden of mucosal disease, which has a proven association with surgical failure in multiple publications. The patients who suffer from pansinus disease are more prone to diffuse eosinophilic inflammation rather than to localized obstruction of the ostio-meatal complex, and such patients are less likely to achieve stable results after surgery. The elevated SNOT-22 scores among relapsing cases in our study were not determined to be independent predictors of disease recurrence, which correlates with findings that SNOT-score before surgery is not a good predictor of recurrence rates [37]

A key variable in this study that can be easily modified is the poor level of compliance with postoperative therapy. International guidelines state that saline irrigation and topical steroids should be continued after surgery since opening the cavity allows topical treatment to be given to the inflamed mucosa. The overwhelming majority of patients in our sample failed to comply with the recommended therapy. Possible reasons include local factors that influence the affordability of intranasal steroids for patients who live in an area where public hospitals offer inadequate healthcare services or where devices for measuring the cost of treatment are not provided free of charge; cost implications of travel from rural areas; barriers created by lower levels of health literacy; and so on. Although adherence to treatment has received much less attention than biological aspects in the scientific literature, our analysis suggests that the clinician-patient interaction and follow-up care may be effective in decreasing the recurrence rate even without additional technological improvements. However, this conclusion needs to be interpreted cautiously because patients assessed their own adherence based on their feelings about treatment after they experienced a recurrence.

Many of the factors indicated by other studies that are associated with recurrence have not demonstrated any significance in our findings. For instance, nasal polyps significantly correlated with recurrence on univariate analysis but lost its significance during the adjustment process. Most likely, this happened because the effect was mediated by asthma, eosinophilia, and extensive radiological disease related to polyp type. Other factors were the relationship of previous sinus surgery, which agrees with Loftus' meta-analysis of this area, and the notion that presence of residual disease and scar tissue is very common in revision cases. Moreover, even though smoking trend towards having higher recurrences is present in our study, its relationship in scientific literature is inconsistent and controversy; some evidence states negative consequences of smoking for the results, while others find little effect on patient outcomes [38]. Although popularity of waterpipe smoking in Iraq is significant, there is no separate analysis of this phenomenon, which should be tackled in future studies. The extent of the surgery does not correlate with recurrence in our research studies, which differs from Bassiouni and Wormald's theory stating the effect of frontal surgery in decreasing recurrence. The reason for this discrepancy might be the fact that the extent of surgery was dependent on the severity of the disease; thus, extensive surgery was advised to the patients suffering from severe diseases. The fact that recurrence is chiefly associated with ethmoidal and frontal recess areas, and that synechiae were found in one out of five recurrent cases indicates that achieving complete removal of ethmoidal cells and thorough treatment of frontal recesses and

of the middle turbinate is of paramount importance in surgery. It is also important to note that allergic rhinitis was not an independent predictor of the recurrence, which corresponds with doubts regarding the role of atopy in CRS outcome.

It is clear what the findings mean clinically. Patients who are asthmatic, have blood eosinophilia, have a high CT score, or have AERD should be warned that their chances of recurrence after surgery are significantly greater than the average, and thus be enrolled in a more intensive follow-up program and given long-term topical therapy. The best results may also come from early surgery, before the disease worsens. Injectable biopharmaceuticals like dupilumab and omalizumab have shown efficacy in the treatment of severe cases of type 2 disease, having been shown to size of polyps and ease symptoms, so the need for systemic corticosteroids and repeat surgical interventions is reduced [39]. Although this type of medication isn't yet easily available in Iraq, identifying potential recipients is the first step in planning future services.

There are several restrictions associated with this research study. One limitation of this study is that it was conducted at a single institution with a relatively limited number of subjects. Furthermore, this relatively small number of relapsing patients restricted the number of independent variables used in the multivariate analysis of the data. In addition, an additional limitation of this research study was due to the relative short interval of time for the study, which resulted in some instances of delayed recurrence not being identified in the study, which may have led to an underestimation of recurrence rates. All subjects of this study underwent specific allergy testing procedures, however, this only occurred in a limited number of patients, making the analysis of test results difficult. Adherence to therapy was assessed by having subjects self-report their adherence. In addition, there is a possibility of losing some subjects to follow- up [40]. Despite these limitations, the prospective nature of this research study, standardized protocol for post-surgical rehabilitation, validated outcome measures and objective evaluation of the level of recurrence leads to greater reliability of these findings. Continued study is warranted to investigate further the possible predictors of recurrence for the Iraqi population.

Conclusion

The recurrence of disease after functional endoscopic sinus surgery is prevalent at Al-Hussein Teaching Hospital. Approximately two-thirds of patients experience recurrences of their disease within the post-operative year. According to the findings from the study at Al-Hussein, independent predictors of recurrence for patients subjected to functional endoscopic sinus surgery include the presence of bronchial asthma, eosinophils in blood at least above 300 cells/μL, elevated Lund-Mackay CT scoring, and unsatisfactory compliance to saline irrigation and topical corticosteroids. The recurrence rate for patients suffering from AERD combined with nasal polyp,

eosinophilia, and surgical history of FESS is relatively high. The high frequency of these factors as risk predictors validates the practical application of this provision. This helps provide the information to the patients who undergo surgery on the probability of recurrence.

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