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ORIGINAL RESEARCH

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Clinical feature-based diagnosis criteria of eosinophil and non-eosinophil chronic rhinosinusitis in Taiwan

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Abstract

Background: The prevalence of eosinophilic chronic rhinosinusitis (ECRS) has increased in Taiwan with a higher recurrence rate of nasal polyps after surgery. Therefore, we aimed to formulate the pre-operative diagnostic criteria for patients with ECRS in Taiwan.

Methods: This case–control study included patients diagnosed with CRS with nasal polyps (CRSwNP) who underwent functional endoscopic sinus surgery (FESS) at a tertiary hospital in Taiwan. The patients were classified into ECRS and non-eosinophilic CRS (NECRS) groups based on their histopathology. Demographic data, symptom severity scores, and computed tomography findings of the two groups were analyzed. We utilized receiver operating characteristic curve (ROC) analysis to evaluate parameters that could predict the diagnosis of ECRS.

Results: Total 408 CRSwNP patients were enrolled (ECRS group: 163; NECRS group: 245). ECRS group was strongly associated with asthma (6.1% vs. 2.0%, $p = .03$), higher blood eosinophil counts (4.3% vs. 2.7%, $p < .01$), higher serum IgE (285.3 vs. 50.2 IU/mL, $p = .02$), and higher 22-item Sino-Nasal Outcome Test (SNOT-22) score (40.5 vs. 36.7, $p = .03$). The ECRS criteria based on ROC curve included the SNOT-22 (>45, 2 points), serum eosinophil count percentage (>4%, 4 points), asthma (4 points), total serum IgE (>140 IU/mL, 4 points), Lund–Mackay score (>9.5, 4 points), and ethmoid-to-maxillary opacification ratio on CT (>1.5, 5 points). The cutoff score was 14 points (sensitivity, 70.2%; specificity, 93.3%).

Conclusions: Clinical-feature-based criteria may predict the diagnosis of ECRS before FESS in Taiwan.

Level of Evidence: Level 3.

KEYWORDS
chronic rhinosinusitis, eosinophil, nasal polyps, non-eosinophil

1 | INTRODUCTION

Chronic rhinosinusitis (CRS) is a common disease worldwide and has been defined as an inflammatory disease. The prevalence of CRS based on clinical diagnosis ranges from 5.5% to 28%.[1] According to data from Taiwan's Longitudinal Health Insurance database, the prevalence of CRS determined based on diagnosis by certified otolaryngologists with or without imaging tests is 25%.[2]

CRS is commonly subdivided according to clinical examination into CRS without nasal polyps (CRSsNP) and CRS with nasal polyps (CRSwNP).[3,4] However, various phenotypes of CRS have been mentioned in recent years and reported in the European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS2020).[1] The elucidation of endotypes and phenotypes based on imaging, pathology, and comorbidity analysis offers new possibilities in terms of the prediction of prognosis and risks of CRS and establishing guidelines for pharmacotherapy or surgical treatment of CRS.

Specialists have focused on patients with ECRS because of their poor prognosis and higher recurrent rate after appropriate maximal treatment or functional endoscopic sinus surgery (FESS).[5–7] Although the higher prevalence of ECRS may be due to a function of better training and more adept rhinologists who are paying attention to ECRS versus an actual increase in prevalence, ECRS has shown a trend of an escalated rate in Asian countries, such as Japan and Taiwan in recent years.[5–10]

Some studies have defined ECRS based on the number of definite eosinophilic counts or specific cytokine (IL-5) in operative tissue.[11,12] However, no global consensus has been established regarding the "pre-operative" diagnostic criteria for ECRS (Table 1).[1,13–15] Currently, existing criteria entirely utilize the biopsy or post-FESS pathologic eosinophil count reading for the ECRS diagnosis. However, not every pathologist has the time to interpret pathology slides in terms of the eosinophil count. Therefore, the aim of this study was to distinguish between ECRS and NECRS by analyzing the "pre-operative" features, including allergy characteristics, relevant clinical symptoms, laboratory data, and imaging results. Furthermore, we developed novel clinical feature-based diagnostic criteria for ECRS in Taiwan.

2 | METHODS

This single-center retrospective study included patients with CRSwNP (ICD-9 codes, 471.9 and 473.9) whose histopathological, allergic, and radiological assessment data were available and those who underwent functional endoscopic sinus surgery (FESS) at China Medical University Hospital (CMUH) between September 2015 and September 2020. CRSwNP was diagnosed according to the criteria established by EPOS2020. We retrieved patient's data from the "Taiwan National Health Insurance database" to further examine the medication history of patients in the 4 weeks prior to surgery, and patient exclusion criteria were as follows: (1) younger than 18 years old; (2) previous treatment with systemic or topical corticosteroids, or other immune-modulating drugs up to 1 month before surgery; and (3) conditions such as autoimmune disease, allergic fungal sinusitis, cystic fibrosis or immotile ciliary disease. This study was approved by the Institutional Review Board of CMUH (IRB #CMUH110--REC1-080) and funded by a grant from CMUH (DMR-109-041).

2.1 | Demographic

A total of 784 patients with CRSwNP were enrolled in this study. Demographic data (age and sex), lifestyle (cigarette smoking and alcohol consumption), comorbidities, nasal septum deviation, atopic status

TABLE 1 Commonly used guidelines for the diagnosis of ECRS in the world.

Guidelines	The diagnostic criteria for ECRS
American Academy of Otolaryngology-Head and Neck Surgery Foundation (AAO-HNSF) Clinical Practice Guideline.[13]	1. The presence of CRS symptoms and inflammation. 2. At least two of the following: (a) nasal polyps; (b) eosinophilic mucin; (c) >10 eosinophils per HPF on nasal biopsy; (d) elevated serum IgE.
European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS 2020).[1]	1. The presence of CRS symptoms and inflammation 2. >10 eosinophils per high-power field (HPF) in at least one biopsy of the middle meatus or evidence of nasal polyps.
Japanese Society of Allergology (JSA) Guidelines for Diagnosis and Treatment of Allergic Rhinitis.[14]	1. The presence of CRS symptoms and inflammation. 2. >10 eosinophils per HPF on nasal biopsy, and/or evidence of nasal polyps.
The Japanese Epidemiological Survey of Refractory Eosinophilic Chronic Rhinosinusitis (JESREC) scoring system in 2019.[15]	1. Bilateral lesion, 3 points; 2. The presence of nasal polyps, 2 points; 3. Blood eosinophil percent >2% – ≤5%, 4 points; >5 – ≤10%, 8 points; >10%, 10 points; 4. Ethmoid sinus dominant shadows in CT scans, 2 points. Total score ≥ 11 points and mucosal eosinophil count ≥70/high-power field (HPF).
Preoperative clinical feature-based criteria (this study).	1. Asthma history, 4 points, 2. SNOT-22 >45, 2 points, 3. Blood eosinophils count >4%, 4 points, 4. Total serum IgE >140 IU/mL, 4 points, 5. Lund–Mackay score >9.5, 4 points, 6. EM ratio >1.5, 5 points. Total score ≥14 points.

Abbreviations: CRS: chronic rhinosinusitis; ECRS: eosinophilic chronic rhinosinusitis; EM ratio: ethmoid-to-maxillary opacification ratio.

(allergic rhinitis, ectopic dermatitis, and asthma), allergy testing results, and severity of chronic rhinosinusitis (pre- and postoperative 22-item Sino-Nasal Outcome Test [SNOT-22] scores) were collected.[16] SNOT-22 score and mucociliary clearance time (MCT) were measured in 1 week before the FESS and 3 months after the surgery. The diagnosis of allergic rhinitis was based on Phadiatop results and determined according to the Clinical Practice Guideline of the American Academy of Otolaryngology.[17] Asthma was confirmed based on the clinical history with pulmonary function tests according to the Global Initiative for Asthma guidelines.[18]

2.2 | Diagnosis of ECRS and non-ECRS

Pathological specimens obtained during FESS were stained with hematoxylin and eosin. The patients were categorized into two groups based on histopathology: "ECRS" and "non-ECRS" (Figure 1). The "ECRS" had an absolute eosinophil count of >10 per 400× high-power field (HPF) and >10% tissue eosinophils in the total inflammatory cells.[5–7,10] The "NECRS" was diagnosed with CRSwNP but without an absolute eosinophil count of >10 per 400× high-power field (HPF) or >10% tissue eosinophils in the total inflammatory cells.

2.3 | Serologic profile

All blood examinations, including analysis of complete blood cell count, differential count, and total serum IgE levels, were performed within 1 week before surgery at our hospital. Atopic status was defined by total serum IgE levels, and aeroallergen sensitization was determined using the Phadiatop test. Positive allergy testing results were confirmed. The cutoff value of total serum IgE was 150 IU/mL according to the study of Bradley E. Chipps.[19] The patients avoided antihistamines and oral steroids for at least 4 weeks before the examinations.

2.4 | Image assessment

Nasal endoscopy and CT scans were performed before the operation during clinic visits in 1 month. We evaluated nasal polyps on each side and graded based on polyp size, resulting in scores of 0 to 4.[20] The paranasal sinuses were evaluated from the CT scan as serial images (0.4-mm slices) captured on coronal, axial, and sagittal views. Two senior investigators (Jia-Hung Ma and Bing-Han Hsieh) who were blinded to the patient data used the Lund–Mackay scoring system and ethmoid-to-maxillary opacification ratio (EM ratio) to evaluate the CT scan.[1,21–24] The statistical data results of two investigators were averaged and confirmed by a third investigator (Liang-Chun Shih).

2.5 | Statistical analyses

All statistical analyses were performed using SPSS version 24 (IBM Corp., Armonk, NY, USA). We statistically compared the ECRS group with the NECRS group using the chi-square test and *t*-test. Age has been presented as parametric and mean standard deviation. Statistical analyze were performed using the chi-square test to evaluate the associations between the groups and clinical allergy history. *T*-tests were used to evaluate the associations between ECRS and NECRS. Statistical significance was set at $p < .05$. Confidence intervals (95%)

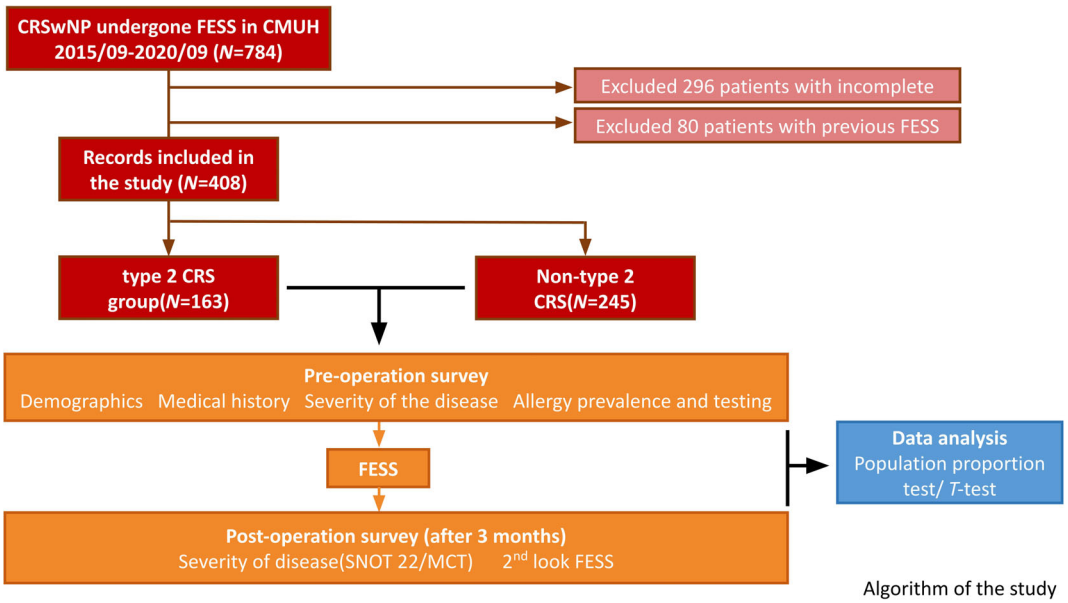

FIGURE 1 Algorithm of the study. CMUH, China Medical University Hospital; MCT, mucociliary clearance time; N, number; SNOT-22, Sinonasal Outcome Test (SNOT-22); *$p < .05$.

and odds ratios were calculated for each clinical parameter (Figure 1). The diagnostic potential of the domains for ECRS before was evaluated using a receiver operating characteristic (ROC) curve analysis.

3 | RESULTS

A total of 784 patients with CRSwNP who underwent FESS were included in the study. A total of 376 patients were excluded due to previous FESS or incomplete data; 163 and 245 patients were classified into the ECRS group and the non-ECRS group, respectively (Figure 1). The data we used tracked patients' postoperative revision rates up to the time of writing the paper, spanning a period of 2 years.

3.1 | Clinical characteristics

The mean age for the ECRS group was 51.50 ± 16.37 years, and the patient population was predominantly male (58.9%). For the NECRS group, the mean age was 49 ± 16.56 years, and the patient population was also predominantly male (54.3%). A total of 17.8% of smokers in the ECRS group and 21.6% in the NECRS group were identified. No significant differences were observed in terms of age, smoking rate, or drinking rate (Table 2).

Among all allergy histories, the prevalence of asthma was 3.7% in all patients with CRSwNP. The prevalence of asthma was classified as follows: 6.1% in ECRS and 2.0% in NECRS. A significant difference was observed in the incidence of asthma between ECRS and NECRS ($p = .031$), but no significant difference was observed between allergic rhinitis and atopic dermatitis.

Anatomical variations and severity of CRS were reported using nasal endoscopy and CT. No significant difference was observed in nasal polyp scores (4.03 vs. 3.89, $p = .239$) and septal deviation (19.6% vs. 19.6%, $p = .992$) between ECRS and NECRS groups. However, Lund–Mackay score (11.77 vs. 8.39, $p < .001$) and EM ratio (2.26 vs. 1.17, $p < .001$) both showed significant difference between the two groups (Table 2).

The serological results of our study showed no significant difference in preoperative white blood cell count between the two groups. Nevertheless, statistical analysis revealed a significant difference in eosinophil percentages from the differential count but not in basophils (eosinophils, 4.26% vs. 2.70%, $p < .001$; basophils, 0.87% vs. 0.67%, $p = .062$). Moreover, the mean total serum IgE proved a significant difference between the two groups (285.27 IU/mL vs. 50.15 IU/mL; $p = .018$) (Table 2).

In terms of the severity of clinical symptoms, the preoperative mean SNOT-22 score of patients with ECRS was significantly higher than that of patients without ECRS (40.53 vs. 36.68, $p = .034$). The SNOT-22 results significantly improved after surgery in both groups, and the difference was significant between ECRS and NECRS (15.81 vs. 12.61, $p = .034$). However, no significant difference was observed in the preoperative and postoperative mean MCT between ECRS and

TABLE 2 Demographics and clinical characteristics of patients with ECRS and NECRS.

		ECRS ($n = 163$)	NECRS ($n = 245$)	p value
Basic data	Mean age	51.5 ± 16.37	49 ± 16.56	.443
	Gender (F/M)	67/96	112/133	.358
Lifestyle	Smoking	29 (17.8%)	53 (21.6%)	.343
	Alcohol	22 (13.5%)	37 (15.1%)	.652
Comorbidity	Nasal septum deviation	32 (19.6%)	48 (19.6%)	.992
	Allergic rhinitis symptoms	47 (28.8%)	71 (29.0%)	.975
	Phadiatop positive ($n = 112,168$)	47 (42.0%)	70 (41.7%)	.961
	*Asthma	10 (6.1%)	5 (2.0%)	*.031
	Atopic dermatitis	5 (3.1%)	18 (7.3%)	.066
Image	Nasal polyp score	4.03	3.89	.239
	Lund–Mackay score	11.77	8.39	*<.001
	Ethmoid-to-maxillary opacification ratio	2.26	1.17	*<.001
Laboratory	White blood count ($n = 53,86$)	7790	7251	.124
	*Eosinophil count's percentage in WBC ($n = 53,86$)	4.26%	2.7%	*.001
	Basophil count's percentage in WBC ($n = 53,86$)	0.87%	0.67%	.062
	*IgE ($n = 46,57$)	285.27 IU/mL	50.15 IU/mL	*.018
Prognosis	Blood loss during surgery ($n = 162,242$)	282.03 mL	259.62 mL	.180
	Revision FESS during follow-up	52 (31.9%)	31 (12.6%)	*<.001
Pathology	*Average eosinophil count under 3 "400X HPF"	53.67	2.5	*<.001

Abbreviations: ECRS, eosinophilic chronic rhinosinusitis; F, female; FESS, functional endoscopic sinus surgery; HPF, high-power field; IgE, immunoglobulin E; M, male; N, number; NECRS, non-eosinophilic chronic rhinosinusitis; WBC, white blood cell.
*$p < .05$.

NECRS groups ($p = .225$ and $p = .111$, respectively) (Table 3). Furthermore, the revision FESS rate during follow-up was significantly higher in the ECRS group (31.9% vs. 12.6%, $p < .001$) (Table 2).

3.2 | Clinical-feature-based criteria for ECRS

Moreover, we calculated the significant differences between ECRS and NECRS patients using the area under the curve (AUC) of the receiver operating characteristic (ROC) curve. For ECRS diagnosis, the AUC value of the SNOT-22 score was 0.561, with a sensitivity of 42.90% and a specificity of 71.80%. The AUC value of the Lund–Mackay score was 0.685, with a sensitivity of 60.10% and a specificity of 67.80%. The EM ratio had the highest AUC of 0.744, with a sensitivity of 73.00% and a specificity of 62.40%. The AUC of mean total serum levels of IgE was 0.586, with a sensitivity of 34.80% and a specificity of 84.20%. The AUC of eosinophil percentages in the differential count was 0.632, with a sensitivity of 44.80% and a specificity of 82.80% (Figure 2). We pool the above data to establish clinical feature-based criteria (Table 4) for diagnosing pre-operative patients with ECRS. We added up all parameters' AUC and give each parameter a score based on the proportion of each parameter's AUC

TABLE 3 Symptom severity of patients with ECRS and NECRS based on the Sino-Nasal Outcome Test and mucociliary clearance time.

		ECRS ($n = 163$)	NECRS ($n = 245$)	p value
Pre-operation	*SNOT-22 ($n = 155,238$)	40.53	36.68	*.032
	MCT ($n = 140,223$)	1412.36 s	1497.31 s	.225
Post-operation 3 months	SNOT-22 ($n = 92,135$)	15.81	12.61	.061
	MCT ($n = 68,105$)	1189.11 s	1300.17 s	.111
Improvement	SNOT-22 ($n = 86,132$)	−25.08	−23.80	.307
	MCT ($n = 57,97$)	−208.86	−115.36	.237

Abbreviations: ECRS, eosinophilic chronic rhinosinusitis; MCT, mucociliary clearance time; N, number; NECRS, non-eosinophilic chronic rhinosinusitis; SNOT-22, Sinonasal Outcome Test (SNOT-22).
*$p < .05$.

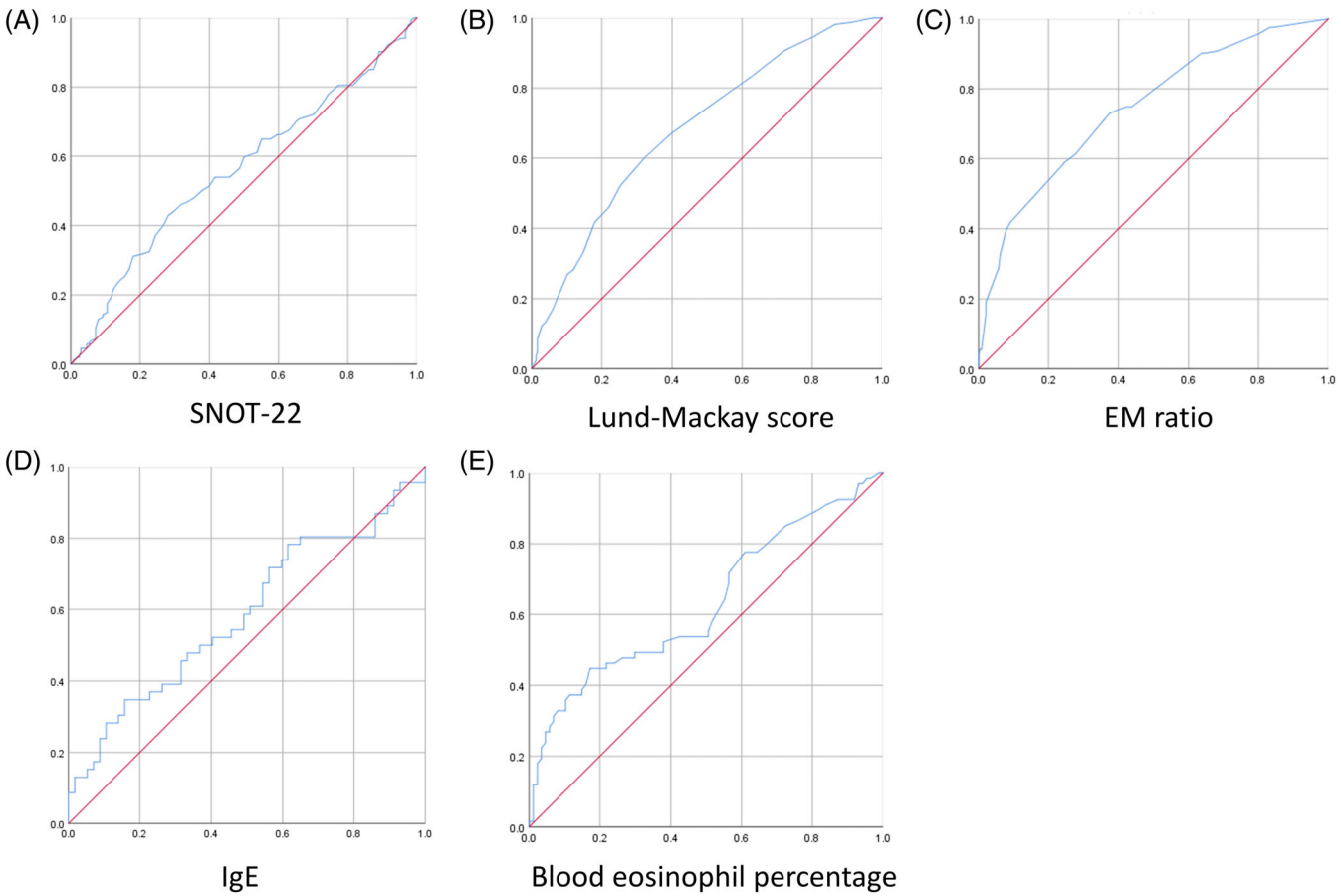

FIGURE 2 ROC curve analysis was used for discriminating patients with ECRS from those with CRSwNP. (A) SNOT-22, (B) Lund–Mackay score, (C) EM ratio, (D) IgE, and (E) blood eosinophil percentage.

(all parameters' AUC = 3.208, total parameter's point = 23, parameter's point = 23× parameter's AUC / total parameter AUC and rounding the number). Therefore, the criteria consist of SNOT-22 (>45, 2 points), asthma (4 points), percentage of blood eosinophil count (>4%, 4 points), total serum IgE levels (>140 IU/mL, 4 points), Lund–Mackay score (>9.5, 4 points), and EM ratio determined by CT scans (>1.5, 5 points). We verified different cutoff points and found that 14 were the most precise score for the ECRS diagnosis (Figure 3). This novel criterion had the best Youden index with a sensitivity of 70.20% and specificity of 93.30% from our patient database (Figure 4).

TABLE 4 Clinical-feature-based criteria for diagnosis of ECRS before surgery in Taiwan.

Parameter	Score
SNOT-22 >45	2
Asthma	4
Percentage of blood eosinophil count >4%	4
Total serum IgE >140 kU/L	4
Sinus CT	
Lund–Mackay score >9.5	4
EM ratio >1.5	5

Note: ECRS can be diagnosed when the total score is higher than **14** points.

4 | DISCUSSION

More than half of CRSwNP patients in Eastern Asia have non-eosinophilic inflammation, but the number of patients with ECRS has increased in recent years.[5–7,25] Rhinologists have focused on patients with ECRS because of the higher recurrence rate after surgery.[6,7] Most studies have used eosinophil counts in pathohistology to define ECRS after surgery, but it is difficult to distinguish patients with ECRS from other phenotypes of CRS before FESS.[11,12] In recent years, rhinologists have attempted to establish consistent criteria to distinguish

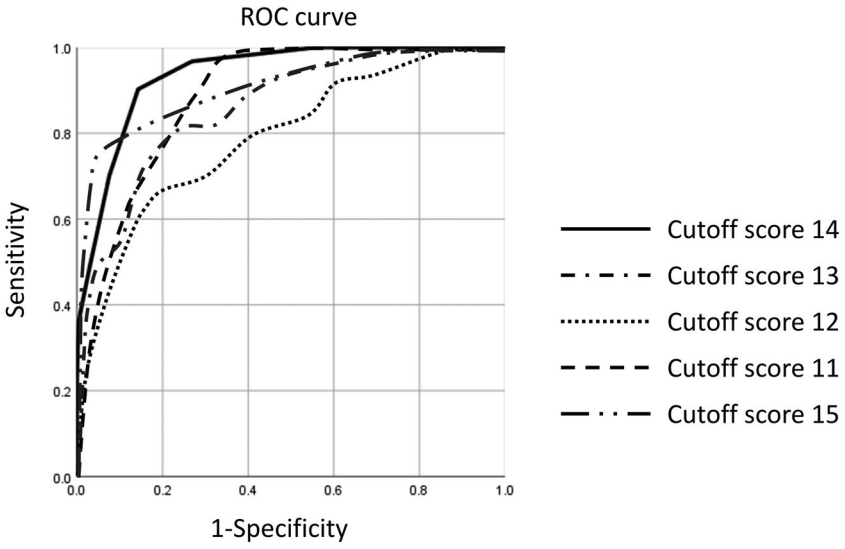

FIGURE 3 ROC curve analysis was used for different cutoff scores of our clinical-feature-based criteria.

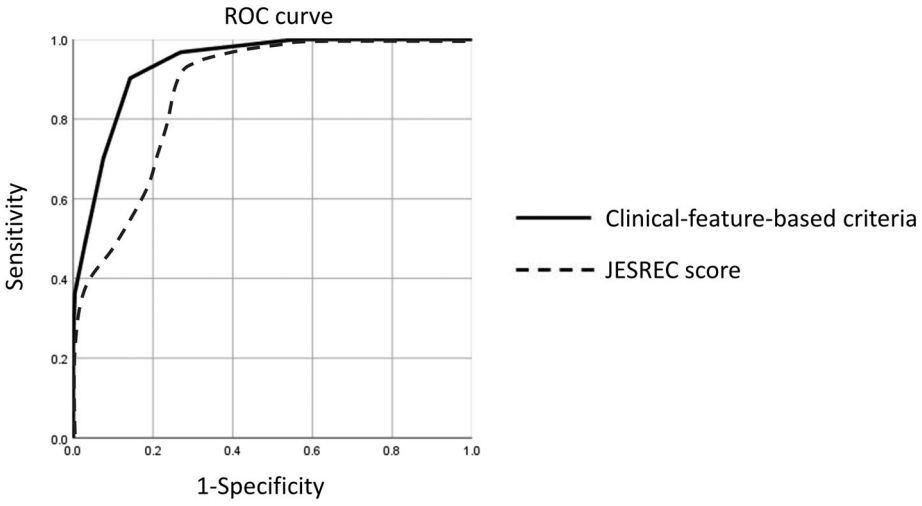

FIGURE 4 ROC curve of our clinical-feature-based criteria and JESREC score.

the type of CRS via epidemiology and pathophysiology, which can help clinicians predict and diagnose ECRS and NECRS before surgery.[1,9,12,22,26] Precise information and shared decision-making regarding advanced ESS or biologics may be provided to patient prior to standard surgery.

4.1 | Asthma prevalence in the Asian population with ECRS

Previous studies have attempted to analyze the relationship between ECRS and asthma.[5,8,11,12,27–29] Sella GCP et al. found that asthma and allergic rhinitis are frequently associated with eosinophilic and T2 responses in CRS, which are critical factors contributing to disease relapse.[30] Shah et al. found pathophysiology of ECRS was similar to asthma.[8] Andrea Matucci et al. found that upper and lower airway remodeling is the direct consequence of ongoing or cyclic inflammation and repair occurring in both asthma and CRS.[31]

We postulated that asthma was related to ECRS; however, race and geographic characteristics may influence the effect of asthma on CRS. EPOS 2020 has shown that most Caucasian patients with CRSwNP in Western countries demonstrate type 2-biased immune responses are characterized by upregulated production of local IgE and pronounced tissue eosinophilia.[1] Andrea Matucci et al. showed that asthma and CRS can coexist.[31] In our study, patients with ECRS demonstrated higher asthma rates than NECRS (6.1% vs. 2.0%, $p = .031$). We proved that asthma is an excellent preoperative predictor of ECRS in Asian populations.

4.2 | Symptom severity in patients with ECRS

Most reports have shown that the clinical symptoms were more severe in the ECRS population than in the non-ECRS patients, but only a few studies used objective data to analyze these findings.[5–7,11,22] Gitomer et al. used olfactory disability, asthmatics, and Lund–Mackay scores for evaluation.[32] Hu et al. used the VAS score to evaluate symptoms but failed to demonstrate a significant correlation between ECRS and NECRS.[10] In our study, we used the SNOT-22 score and found that the preoperative mean SNOT-22 score of patients with ECRS was significantly higher than that of patients with the non-ECRS group (40.53 vs. 36.68, $p = .034$). We hypothesized that patients with ECRS have more eosinophils in the tissue and blood for induction of type-2 inflammation, which further leads to extranasal rhinological symptoms, including nasal obstruction, loss of smell, and cough. Said et al. reviewed the pathogenesis of eosinophilic degradation and accumulation in ECRS and found that the release of cytokines and chemokines plays an important role in mucus production, which explains why the symptoms are more severe in patients with ECRS than in those with NECRS.[8]

Generally, for a given difference in mean values, the percentage of patients with outliers varies based on the mean values of the reference population. This phenomenon presents challenges in explaining mean differences in vulnerable populations and defining the Minimal Clinically Important Difference (MCID) in outcomes that are specific to certain mean values. Namely, we found significant differences in preoperative symptoms between the two groups in our study, but it is possible that these differences did not reach the MCID. However, we think that it is important to strike a balance between statistical significance and clinical relevance. While establishing statistical credibility is vital, findings must also be clinically meaningful to inform effective interventions and decisions. We believe that the differences in symptoms between ECRS and NECRS patients can also serve as a clinical indicator for distinguishing between the two groups. In the future, we intend to present additional research and evidence to validate the utility of the SNOT-22 questionnaire in aiding the diagnosis of ECRS.

4.3 | Radiology analysis of Asian patients with ECRS

Lund–Mackay CT scores have been accepted globally as predictors of eosinophilic CRSwNP. Tokunaga et al. showed that the predominance of ethmoid sinus inflammation on CT scans is one of the important risk factors for refractory CRS.[13] Meng et al. used an optimal cutoff value of >2.59 for the ethmoid-to-maxillary opacification ratio, and the results showed a sensitivity of 94% and specificity of 90% for predicting eosinophilic CRSwNP.[33] We also found similar results, a significant difference was observed between ECRS and non-ECRS (Lund–Mackay score: 11.77 vs. 8.39, $p < .001$; EM ratio: 2.26 vs. 1.17, $p < .001$). We postulate that the Lund–Mackay score and EM ratio may help identify ECRS preoperatively.

4.4 | Hematology test of Asian patients with ECRS

Ho et al. reviewed 345 ECRS patients and found that ECRS is associated with elevated blood eosinophil count, eosinophil ratio, and lower ESR than NECRS.[11] Hu et al.[10] and Sakuma et al.[12] found elevated blood eosinophil count and percentage in association with ECRS and proposed that blood eosinophil count and percentage could be used to predict ECRS in patients with CRSwNP. Our findings were consistent with the previous result that eosinophil count's percentage was significantly elevated in the ECRS group compared with the non-ECRS group (4.26% vs. 2.70%, $p < .001$). However, Gitomer et al.[32] and Asghari et al.[34] failed to demonstrate a significant association between peripheral eosinophilia and CRS. Lou et al. also hypothesized eosinophilia in blood cannot reflect tissue eosinophilia because eosinophil counts can be influenced by drug, autoimmune diseases, corticosteroid therapies, or allergies.[9] It needed more large studies to rule out the effects of drugs or these diseases in ECRS.

Hu et al. found eosinophilic CRSwNP patients had higher blood IgE levels than those with noneosinophilic CRSwNP.[10] In our study, patients with ECRS also demonstrated higher IgE levels than those without NECRS patients (285.27 vs. 50.15, $p = .018$). Gion et al. found that IgE-positive cells are increased due to an allergic

predisposition in ECRS, which activates strong antigen stimulation and the immune response, further increasing IgE levels.[35] We hypothesized that IgE can be utilized as a predictor of ECRS in CRSwNP.

4.5 | Clinical pre-operative diagnostic criteria of ECRS

A consensus regarding the diagnostic criteria for ECRS has not been established globally.[36–38] We listed the important guidelines of ECRS diagnosis from literature during the past 10 years (Table 1).[1,13–15] These criteria all included persistent or recurrent symptoms of CRS and the presence of eosinophilic inflammation according to the histopathologic examination. However, the specific cutoffs for tissue eosinophil counts may vary depending on the region and race. Second, these criteria lack objective parameters or specific numbers to evaluate patients with ECRS before surgery. Third, it is time-consuming and expensive to check the tissue eosinophil counts of each patient. Fourth, eosinophilic mucin was described in Western countries but it is extremely challenging because the presence of allergic mucin is rare in Asian patients.[39] Fifth, since the diagnosis depends on postoperative pathological investigation, it reduces the possibility of helping patients arrange precise surgical methods before surgery.

In 2011, the "Japanese Epidemiological Survey of Refractory Eosinophilic Chronic Rhinosinusitis study" used "The JESREC score" to define ECRS with nasal polyps, ethmoid-to-maxillary opacification ratio, and the peripheral blood eosinophil count. However, we used the JESREC score to diagnose ECRS in our patient database and calculated the Youden index, which was only 46.1% with a sensitivity of 68.70% and a specificity of 77.40%.[13,15] In addition, we hypothesized that the JESREC score focuses on the peripheral blood eosinophil counts and may decrease specificity in the diagnosis of the patients because the peripheral blood eosinophil counts may be influenced by autoimmune diseases or drugs.

In our study, we aimed to add subjective and objective parameters to help diagnose patients with ECRS "before" surgery, such as the SNOT-22 score, total serum IgE, blood eosinophil count, and history of asthma. In addition, we utilized Lund–Mackay score and EM opacification ratio from the sinus CT scans as the parameter. Each parameter represents a different score according to the AUC (Figures 2 and 3, and Table 4). These clinical-feature-based criteria consisted of SNOT-22 (>45, 2 points), eosinophil count's percentage (>4%, 4 points), asthma (4 points), total serum IgE (>140 IU/mL, 4 points), Lund–Mackay score (>9.5, 4 points), and Ethmoid-to-Maxillary opacification ratio on CT (>1.5, 5 points). The cutoff score was 14 points (sensitivity, 70.2%; specificity, 93.3%). This novel criterion had a better Youden index (63.5%) with a sensitivity of 70.20% and specificity of 93.30% in our patient database than the JESREC scoring system (Youden index: 46.1%) (Figure 4). Therefore, this criterion is convenient for diagnosing ECRS before surgery with high accuracy.

4.6 | Limitations

The limitations of this study must be addressed. First, a few parameters were not recorded for all patients, especially the differential count of white blood cells. Readers should be aware that the results might be underrepresented. Second, our single-institution study with limited case numbers may not reveal regional and racial effects. Third, retrospective chart review and image collection are limited by accessible data. Fourth, based on our existing data, we can observe significant differences in preoperative symptoms with SNOT-22. However, we are unable to provide evidence of whether these differences reach the level of minimal clinically important difference. Fifth, we were able to assess nasal polyp scores through endoscopic imaging in the collected historical data, but describing eosinophilic mucin was extremely challenging that the presence of allergic mucin is rare in Asian patients.[39] Finally, further endotype studies, such as specific allergen tests and cytokine identification, are necessary to formulate a classification of nasal polyp endotypes.

5 | CONCLUSION

In Taiwan, ECRS was strongly associated with asthma, higher blood eosinophil counts, higher serum IgE, higher SNOT-22 score, and higher revision FESS rate. To diagnose ECRS, novel criteria were devised, which consisted of SNOT-22 (>45, 2 points), percentage of blood eosinophil count (>4%, 4 points), asthma (4 points), total serum IgE levels (>140 IU/mL, 4 points), Lund–Mackay score (>9.5, 4 points), and EM opacification ratio observed on CT scan (>1.5, 5 points). The cutoff score was 14 points (sensitivity, 70.2%; specificity, 93.3%). These results may be used to predict ECRS before FESS in the Taiwanese population. Precise information and shared decision making may be provided to the patient prior to surgery.

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Jia-Hung Ma and Liang-Chun Shih involved with the conception of the work, contributed to protocol development and interpreted results. Jia-Hung Ma performed the data collection, data analysis, data interpretation and drafted the article. Jia-Hung Ma and Bing-Han Hsieh collected the data. Yung-An Tsou, Chia-Der Lin, and Chih-Jaan Tai provided critical feedback and direction for the manuscript and revision of the article. Liang-Chun Shih contributed to protocol development, interpreted the results and finalized the article. All authors gave final approval of the version to be published.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest relevant to this report.

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