

A Predictive Model for Recurrence After Endoscopic Sinus Surgery in Chronic Rhinosinusitis Without Nasal Polyps

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Abstract:

Objective: Recurrence of chronic rhinosinusitis without nasal polyps (CRSsNP) after endoscopic sinus surgery (ESS) remains a clinically important challenge, with reported rates varying widely across follow-up durations. This study aimed to identify clinical predictors of recurrence and develop a prognostic model to estimate recurrence risk at 3, 5, 10, and 15 years post-ESS.

Material and Methods: In this retrospective, single-institution cohort study, 106 CRSsNP patients who underwent ESS between January 1, 2002, and December 31, 2024, were included, and time-to-recurrence was analyzed. Candidate predictors, including age, sex, smoking, asthma, NSAIDs hypersensitivity, symptom duration, blood eosinophil count (BEC), Modified Lund-Kennedy (MLK) score, and Lund-Mackay (LM) score, were evaluated using a least absolute shrinkage and selection operator (LASSO)-pooled logistic model. A nomogram was constructed and assessed using time-dependent AUROC, Brier scores, calibration curves, internal validation with 1,000 bootstrap resamples, and decision curve analysis (DCA).

Results: Recurrence occurred in 17.9%. Smoking, asthma, BEC, and LM score were significant predictors. The nomogram showed good discrimination, with AUROCs of 0.759, 0.780, 0.773, and 0.742 at 3, 5, 10, and 15 years post-ESS, respectively, and low prediction error, with corresponding Brier scores of 0.137, 0.132, 0.108, and 0.097. Internal validation demonstrated stable performance. Calibration curves showed strong agreement between predicted and observed outcomes. DCA demonstrated a meaningful net benefit, particularly at the threshold probabilities of 0.2–0.7 for 3- and 5-year predictions and 0.1–0.6 for 10- and 15-year predictions.

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Conclusion: The LASSO-based pooled logistic nomogram provides a well-calibrated, robust, and clinically applicable tool for individualized long-term recurrence risk prediction in patients with CRSsNP after ESS.

Keywords: chronic rhinosinusitis without nasal polyps, endoscopic sinus surgery, LASSO-penalized pooled logistic regression model, nomogram, prognostic model, recurrence

Introduction

Chronic rhinosinusitis (CRS) is a common inflammatory disorder of the sinonasal mucosa, affecting 5–12% of the population and significantly impairing quality of life^{1–3}. CRS is broadly classified into CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP), with the latter accounting for approximately 80% of cases^{4–6}. Despite advances in pharmacotherapy and endoscopic sinus surgery (ESS), recurrence remains a significant clinical challenge. Up to 8.8% of patients experience recurrence within three years⁷, increasing to 16% at five years after ESS⁸, leading to revision surgery in 4.1% of cases at one year, 10.4% at three years⁹, and 15.5% at five years¹⁰. Notably, ESS is performed more frequently for CRSsNP (66.0%) than for CRSwNP (29.3%), with the remaining 4.8% undertaken for other indications¹¹. Accurate preoperative prediction of recurrence is therefore essential to guide individualized management strategies, including consideration of extended surgical approaches, optimized postoperative surveillance, and timely adjunctive therapies.

We hypothesized that routinely available preoperative clinical variables, including patient characteristics, comorbidities, endoscopic and imaging scores, and peripheral blood inflammatory cell counts, may help predict recurrence risk. Although these factors have been extensively evaluated in CRSwNP and mixed CRS populations^{8,12–22}, few studies have specifically examined CRSsNP, and their predictive value in this subgroup remains uncertain^{5,23,24}. Moreover, Asian patients with CRS often exhibit lower type 2 inflammation and a lower

prevalence of comorbid asthma, highlighting the need for population-specific predictors²⁵. Existing studies are further limited by mixed CRS populations, short follow-up durations (1–5 years), and statistical approaches that consider only recurrence rates without accounting for event timing.

To address these gaps, we conducted a long-term follow-up of up to 20 years to identify the preoperative predictors of recurrence after ESS in CRSsNP. Using least absolute shrinkage and selection operator (LASSO) –penalized pooled logistic regression within a discrete-time survival framework and tenfold cross-validation, we developed a model that selects key predictors, minimizes overfitting, and estimates time-dependent recurrence risk, providing a noninvasive tool to stratify high-risk patients and guide personalized postoperative management.

Material and Methods

Study population

All patients with CRSsNP who underwent ESS between January 1, 2002, and December 31, 2024, were eligible. Inclusion criteria were: (1) bilateral CRSsNP diagnosed clinically and confirmed by nasal endoscopy and sinus CT according to the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) criteria¹; (2) availability of a complete clinical database; and (3) a minimum follow-up of six months. Exclusion criteria were: allergic fungal rhinosinusitis, cystic fibrosis, congenital mucociliary disorders, autoimmune diseases (e.g., granulomatosis with polyangiitis), immunodeficiency, previous sinonasal surgery, unavailable preoperative computed tomography (CT), and

complete blood count within 3 months before surgery, or systemic corticosteroid use within 1 month prior to blood testing. The study protocol was approved by the Institutional Review Board (approval number 65507131).

Study design

This is a retrospective, single-institution cohort study. All patients initially received appropriate medical therapy, including regular use of intranasal corticosteroids (two sprays per nostril twice daily) and at least one 10–14-day course of oral antibiotics. ESS was performed for patients with persistent symptoms beyond three months. Surgical procedures included maxillary antrostomy and anterior and posterior ethmoidectomy; sphenoid and frontal sinusotomies were performed when indicated. Postoperatively, patients continued nasal corticosteroids and were followed up with nasal endoscopy according to a standardized schedule: weekly for the first month, monthly during months two and three, every 2–3 months up to one year, and biannually thereafter. Persistent symptoms or endoscopic findings prompted intensified therapy with corticosteroids and/or antibiotics.

Collection of clinical data

Demographic and clinical information, including age, sex, smoking status, sinonasal symptoms, comorbidities, and medication use, was recorded for each participant. Non-smoking was defined as having smoked fewer than 100 cigarettes during one's lifetime and not currently smoking. Symptom duration was defined as the interval from the patient's initial symptom onset to the date of surgery. NSAIDs hypersensitivity was defined by a history of asthma attacks triggered by nonsteroidal anti-inflammatory drugs. Asthma was diagnosed based on recurrent wheezing, shortness of breath, chest tightness, or nighttime cough, with a normal chest X-ray. Blood eosinophil count (BEC), nasal endoscopic findings based on the Modified Lund–

Kennedy (MLK) score, and paranasal sinus CT findings based on the Lund–Mackay (LM) score were recorded on the date closest to surgery. The MLK score and prescribed medications were documented at each follow-up visit.

Outcomes observed during the cohort

Recurrence was defined as the presence of diseased mucosa characterized by nasal polyps, mucopurulent secretions, and/or inflammation, identified on nasal endoscopy at least one month postoperatively, accompanied by ≥ 2 CRS symptoms (nasal obstruction, nasal discharge, facial pain/pressure, or reduction/loss of smell), one of which had to be nasal obstruction or discharge, each scoring ≥ 2 on a four-point scale (0=none, 1=mild, 2=moderate, 3=severe), persisting for at least one month after endoscopic confirmation, despite systemic treatment with oral antibiotics and/or corticosteroids during the symptomatic period.

Sample size calculations

Sample size was estimated using Schoenfeld's log-rank formula (two-sided $\alpha=0.05$, 80% power) with allocation proportions of $q_0=0.83$ (CRSsNP without asthma) and $q_1=0.17$ (CRSsNP with asthma) and a target hazard ratio of 5.54.¹⁷ Nineteen outcome events were required. Assuming a 5-year cumulative incidence of 16% under exponential hazards⁸, the pooled incidence was approximately 23.8%, yielding a minimal sample size of 80 participants. The Schoenfeld approximation was applied within a pooled logistic regression framework for discrete-time survival analysis.

Missing data

Patterns of missing data were assessed using `md.pattern`, and the missing-at-random assumption was evaluated with chi-squared and t-tests. When appropriate, multiple imputation with predictive mean matching was performed to generate five datasets, which were pooled

using Rubin's rules to obtain final estimates and standard errors²⁶.

Statistical analysis

Analyses were performed using R version 4.4.3 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were presented as mean (S.D.) or median (IQR) and compared using the Student's t-test or the Wilcoxon rank-sum test, as appropriate. Categorical variables were presented as counts (%) and compared using Pearson's χ^2 test or Fisher's exact test. A two-tailed p-value < 0.05 was considered statistically significant.

Model estimation

Predictor selection and model development followed the TRIPOD guidelines. Data were formatted in a person-period structure, treating each follow-up interval as a separate binary observation of recurrence, modeling the conditional probability of recurrence in each interval using standard logistic regression frameworks. Univariable pooled logistic regression evaluated individual predictors. A multivariable pooled logistic regression model penalized by the Least Absolute Shrinkage and Selection Operator (LASSO) was developed to enhance parsimony and reduce overfitting, with the penalty parameter (λ) optimized via 10-fold cross-validation. Model assumptions were assessed using deviance residuals for linearity, variance inflation factors for multicollinearity, DFBETA for influential observations, and deviance and standardized residuals for overall model fit. Discrimination was assessed using time-dependent area under the receiver operating characteristic curve (AUROC) at 3, 5, 10, and 15 years, with internal validation performed via 10-fold cross-validation.

Nomogram development

A nomogram was constructed by scaling each β coefficient from the LASSO-pooled logistic model to a 0–100 point scale. Individual predictor scores were summed to

generate a total score, which was mapped to the predicted probability of recurrence at 3, 5, 10, and 15 years.

Model performance and validation

Nomogram performance was evaluated by time-dependent AUROC, calibration curves, and Brier score. Internal validation with 1,000 bootstrap resamples assessed variability, optimism, and overfitting, confirming model stability and clinical reliability.

Decision curve analysis

Time-dependent decision curve analysis (DCA) evaluated the nomogram's clinical utility in predicting recurrence after ESS in CRSsNP patients. Net benefits across threshold probabilities demonstrated greater value when the nomogram's curves surpassed the 'treat-all' and 'treat-none' strategies.

Results

Study cohort characteristics

Of 112 CRSsNP patients who underwent ESS, 6 were excluded due to missing CT scans (n=2), incomplete endoscopy (n=1), or insufficient follow-up (n=3), resulting in 106 patients available for analysis. Baseline characteristics and clinical parameters stratified by recurrence status are summarized in Table 1. Overall, 17.9% of patients experienced recurrence. No significant differences were observed in age, sex, NSAIDs hypersensitivity, symptom duration, MLK score, or LM score between groups. However, recurrence was significantly associated with higher rates of smoking, asthma, and elevated BEC.

Prognostic factor analysis using univariable and LASSO-penalized pooled logistic regression

Candidate variables included age, sex, smoking status, NSAIDs hypersensitivity, asthma, symptom duration, BEC, MLK score, and LM score. In univariable analysis, smoking status, asthma, and BEC were significantly

Table 1 Baseline characteristics and clinical parameters of the two groups

Characteristics	Recurrence (n=19)	Non-recurrence (n=87)	p-value
Age, mean (S.D.), year	43.6 (18.5)	41.9 (12.6)	0.705 ^a
Sex, No. M/F	5/14	32/55	0.548 ^c
Smoking, No (%)	7 (36.8)	8 (9.2)	0.006 ^c
NSAID hypersensitivity, No (%)	1 (5.3)	1 (1.1)	0.328 ^c
Asthma, No (%)	6 (5.3)	1 (2.9)	<0.001 ^c
Duration, median (IQR), year	4.0 (2.5, 8.0)	2.0 (1.0, 9.3)	0.236 ^b
Blood eosinophil count, median (IQR), 1x10 ⁹ cells/L	0.40 (0.19, 0.65)	0.17 (0.09, 0.28)	<0.001 ^b
Modified Lund-Kennedy score, median (IQR)	6.0 (5.0, 6.0)	6.0 (5.0, 6.0)	0.243 ^b
Lund-Mackay score, median (IQR)	8.0 (4.5, 12.0)	6.0 (5.0, 6.0)	0.315 ^b

^a=Independent samples t-test; ^b=Wilcoxon Rank-Sum Test; ^c=Pearson's χ^2 test, F=female, IQR=interquartile range, L=liter, M=male, NSAID=non-steroidal anti-inflammatory drug, No=number; S.D.=standard deviation

Table 2 Univariable and LASSO-penalized pooled logistic regression model for recurrence

Characteristics	Univariable pooled logistic model		LASSO-pooled logistic model	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.01 (0.97, 1.04)	0.712	–	–
Sex (Male as ref.)	1.42 (0.54, 4.39)	0.507	–	–
Smoking, (Never as ref.)	4.37 (1.61, 10.96)	0.002	1.69 (0.55, 4.88)	0.339
NSAID hypersensitivity (Absence as ref.)	2.57 (1.42, 12.85)	0.362	–	–
Asthma (Absence as ref.)	7.83 (2.714, 20.17)	< 0.001	5.43 (1.78, 14.78)	0.001
Duration	1.02 (0.95, 1.09)	0.488	–	–
Blood eosinophil count	13.48 (3.63, 41.29)	< 0.001	7.78 (1.72, 29.96)	0.004
Modified Lund-Kennedy score	1.58 (0.89, 2.89)	0.131	–	–
Lund-Mackay score	1.09 (0.98, 1.19)	0.086	1.06 (0.94, 1.17)	0.278

CI=confidence interval, OR=odds ratio, LASSO=least absolute shrinkage and selection operator, NSAID=non-steroidal anti-inflammatory drug

associated with recurrence, with LM score showing a trend toward statistical significance (p-value=0.086). In the LASSO-pooled logistic model, smoking status, asthma, BEC, and LM score were retained as predictors, although smoking status and LM score were not statistically significant (Table 2).

Model estimation and performance

A predictive model was developed using LASSO-pooled logistic regression, with the linear predictor (LP) representing the log-odds of recurrence:

$$\text{logit}(P)=5.698+0.286\cdot\text{smoking status}+1.492\cdot\text{asthma}+1.920\cdot\text{BEC}+0.008\cdot\text{LM score}$$

The model demonstrated good discrimination, with time-dependent AUROCs of 0.815, 0.804, 0.809, and 0.808 at 3, 5, 10, and 15 years, respectively. Internal validation using 10-fold cross-validation produced slightly lower mean AUROCs of 0.752, 0.743, 0.736, and 0.739, with corresponding Brier scores of 0.146, 0.135, 0.111, and 0.100, indicating modest optimism and supporting the robustness and generalizability of the model.

Nomogram development

A prognostic nomogram was developed based on variables selected by the LASSO-pooled logistic model (Figure 1). Points were assigned to each variable proportional to its coefficient, enabling visual risk estimation and calculation of total scores corresponding to the predicted probability of recurrence at 3, 5, 10, and 15 years.

Performance evaluation and validation of the nomogram

The nomogram demonstrated good discriminative ability for predicting recurrence, with time-dependent AUROCs of 0.759, 0.780, 0.773, and 0.742 at 3, 5, 10, and 15 years, respectively (Figure 2), which were slightly lower than those of the original regression model, likely due to minor precision loss when converting coefficients into the nomogram format.

Calibration curves (Figure 3) display perfect calibration (dotted line), apparent calibration from training data (dashed line), and bootstrap-corrected calibration

(solid line), demonstrating good overall agreement between the predicted and observed recurrence probabilities. At 3 years, the bootstrap-corrected curve lies below the perfect line at the low predicted probabilities (0.1–0.3), indicating overestimation of recurrence risk, and above the line in the mid-range (0.3–0.7), reflecting underestimation. At 5 years, alignment improves but shows a similar pattern of minor overestimation at the low probabilities and underestimation in the mid-range. At 10 and 15 years, the curve increasingly lies above the perfect line across the mid-range, reflecting diminished calibration accuracy and greater underestimation over longer time horizons.

Time-dependent Brier scores were 0.137, 0.132, 0.108, and 0.097 at 3, 5, 10, and 15 years, respectively, reflecting stable and accurate predictions with the lowest error at 15 years. Internal validation using 1,000 bootstrap resamples confirmed consistent performance, yielding mean AUROCs of 0.736, 0.721, 0.734, and 0.743, supporting the model's robustness.

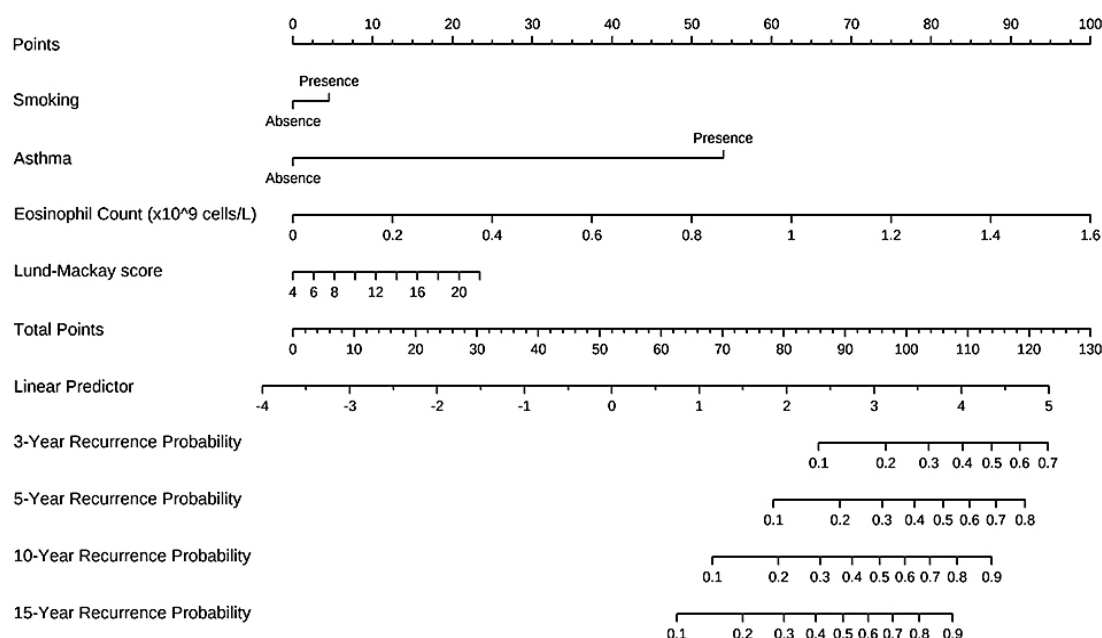


Figure 1 Least absolute shrinkage and selection operator (LASSO)-based pooled logistic nomogram for predicting 3-, 5-, 10-, and 15-year recurrence probabilities

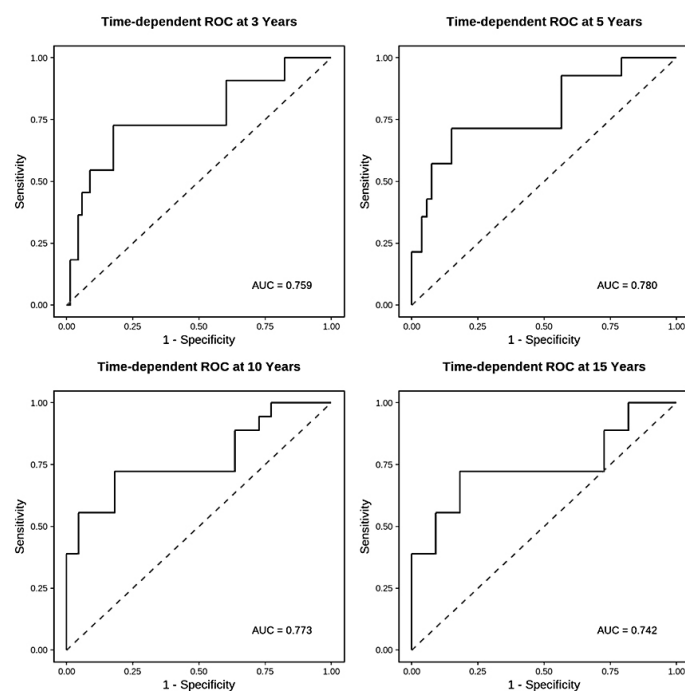


Figure 2 Time-dependent AUROCs of the least absolute shrinkage and selection operator (LASSO)-based pooled logistic nomogram for 3-, 5-, 10-, and 15-year recurrence probabilities

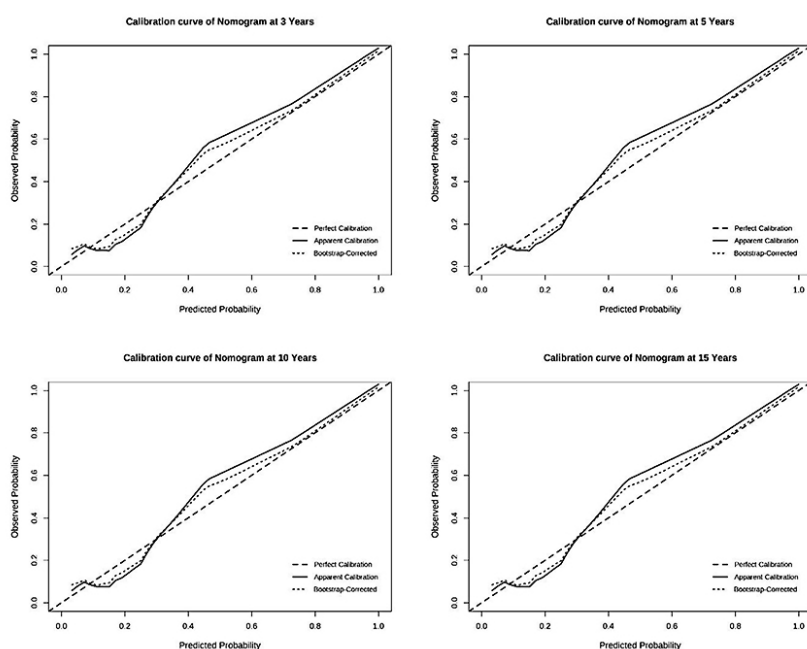


Figure 3 Calibration curves of the least absolute shrinkage and selection operator (LASSO)-based pooled logistic nomogram for 3-, 5-, 10-, and 15-year recurrence probabilities

Clinical utility of the nomogram

Decision curve analysis (Figure 4) demonstrated the nomogram's clinical utility in predicting survival at 3, 5, 10, and 15 years, with the model, the horizontal line at zero represents 'treat none,' the smooth downward-sloping curve represents 'treat all,' and the irregular curve represents the predictive model. At 3 and 5 years, benefit was greatest across the thresholds of 0.2–0.7 and remained superior beyond 0.7, whereas "treat all" was slightly outperformed at 0.1–0.2. At 10 and 15 years, the nomogram's advantage was the most pronounced at the thresholds of 0.1–0.6 and persisted beyond 0.6, with a modest plateau and minor superiority of "treat all" near 0.1. Overall, the net benefit remained stable over time, with minimal attenuation.

Discussion

This study developed a LASSO-penalized pooled logistic regression model using noninvasive, routinely

available preoperative variables to predict postoperative CRSsNP recurrence. Candidate predictors were selected based on clinical relevance, accessibility, and prior evidence. LASSO regularization enhanced model performance by reducing overfitting and prioritizing the most informative variables. Among the baseline characteristics (age, sex), comorbidities (asthma, NSAIDs hypersensitivity), behavioral risk factors (smoking), disease chronicity (symptom duration), and noninvasive inflammatory markers (BEC, MLK, and LM scores), four variables, smoking, asthma, BEC, and LM scores, were retained as independent predictors.

Elevated BEC was the strongest predictor ($OR=7.78$), reflecting systemic type 2 inflammation and its effects on epithelial barrier dysfunction, subepithelial fibrosis, and persistent local inflammation^{8,19,24,27,28}. Asthma was also strongly associated with recurrence ($OR=5.43$), as CRSsNP patients with asthma showed more severe sinonasal

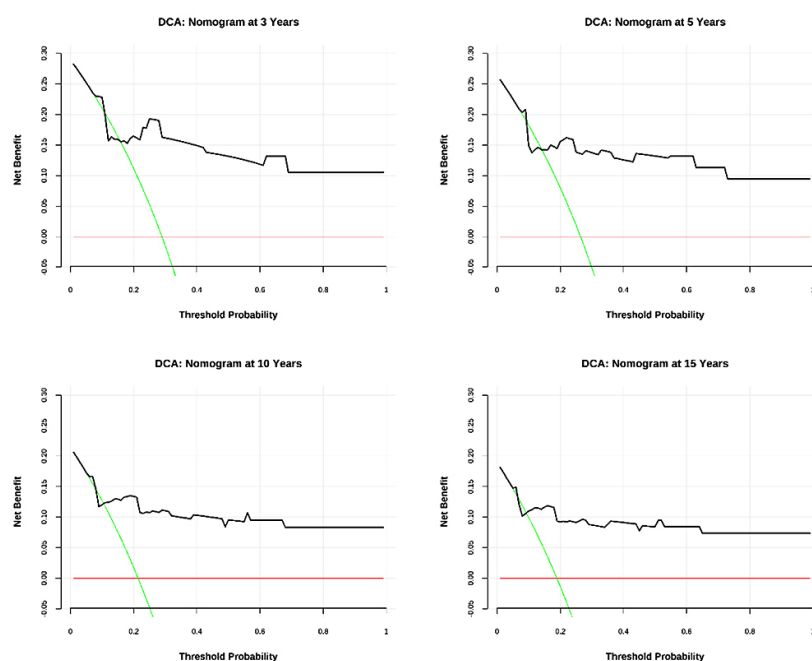


Figure 4 Decision curve analysis of the least absolute shrinkage and selection operator (LASSO)-based pooled logistic nomogram for 3-, 5-, 10-, and 15-year recurrence probabilities

inflammation, a higher eosinophil burden, and elevated type 2 cytokines, all of which contribute to the refractory disease state^{14,17,19,24,29}. Smoking and LM score provided incremental predictive value, despite modest independent effects. Smoking may exacerbate mucosal inflammation and impair repair via ciliary dysfunction, epithelial barrier disruption, biofilm formation, and microbiome alterations^{12,13,30–32}. Higher LM scores indicate more extensive disease and mucosal inflammation, increasing the risk of residual disease, surgical complexity, impaired postoperative drainage, and sustained local inflammation^{19,33–36}; thus, LM scores serve as both diagnostic and prognostic indicators. Other variables, including age, sex, NSAIDs hypersensitivity, symptom duration, and MLK score, were not significantly associated with recurrence, suggesting limited prognostic value compared with stronger inflammatory markers. Despite evidence suggesting slightly higher recurrence in younger patients due to more aggressive inflammation and lower recurrence in older patients related to immunosenescence, most studies find no significant association between age and postoperative outcomes³⁷. Similarly, sex was not predictive, consistent with prior studies showing mixed or null associations with disease severity or recurrence. Sex-related immunological differences may modulate inflammatory pathways, but their impact appears minor relative to type 2 inflammatory markers^{37,38}. NSAIDs hypersensitivity was not predictive in CRSsNP, likely due to its low prevalence, as it is more strongly associated with nasal polyps and type 2 inflammation^{20,36,39}. The heterogeneous, frequently non-type 2 inflammatory profile of CRSsNP further limits its prognostic value^{4,24}. Symptom duration was not a predictor of recurrence, likely because chronicity does not reliably reflect the underlying inflammatory activity. Patients with long-standing symptoms may have relatively milder diseases, whereas those with shorter histories can present with high-risk inflammatory profiles. However, some studies

have reported that prolonged symptoms are associated with worse outcomes, highlighting their limited predictive value.⁴⁰

Existing recurrence models in CRS have focused on CRSwNP or mixed cohorts, often with short follow-up, limited time-to-event analyses, and incomplete reporting of calibration, Brier score, or clinical utility metrics. By applying LASSO regularization and a pooled logistic regression framework, this study addressed these limitations, providing a robust and clinically applicable model. Using a discrete-time survival approach, the model estimated recurrence risk over follow-up intervals while handling censored data without assuming proportional hazards. The resulting nomogram demonstrated good discrimination (AUROC 0.742–0.780), low prediction error (Brier score 0.097–0.137), good calibration, and stability in internal validation with 1,000 bootstrap resamples at 3, 5, 10, and 15 years. DCA confirmed consistent net clinical benefit, supporting individualized, time-specific risk estimation.

Several limitations should be acknowledged. The relatively small number of recurrence events may have limited model stability and increased the risk of overfitting; therefore, external validation in larger cohorts is warranted. Although reliance on noninvasive variables enhances clinical practicality, the exclusion of molecular biomarkers such as IL-8 or TGF- β 1 may have reduced predictive accuracy. Additionally, the retrospective, single-center design introduces potential selection bias, and gradual temporal changes in surgical techniques, perioperative care, and treatment protocols over the extended study period may have introduced additional variability.

Conclusion

The LASSO-penalized nomogram, incorporating asthma, smoking status, blood eosinophil count, and Lund-Mackay score, demonstrated good discrimination and calibration, with stable internal validation. Low Brier

scores indicated minimal prediction error, and decision curve analysis confirmed consistent net clinical benefit. This model provides a practical tool for individualized prediction of recurrence risk in chronic rhinosinusitis without nasal polyps at 3, 5, 10, and 15 years after endoscopic sinus surgery.

Author contributions

Virat Kirtsreesakul: Conception and design of the project; data acquisition, analysis, and interpretation; drafting of the manuscript; critical revision; final approval of the version to be published; agreement to be accountable for all aspects of the work.

Paramee Thongsuksai: Conception and design of the project; data interpretation; critical revision; final approval of the version to be published; agreement to be accountable for all aspects of the work.

Nuttha Sanghan: Data acquisition and interpretation; critical revision; final approval of the version to be published; agreement to be accountable for all aspects of the work.

Chakapan Promsopa: Data acquisition; critical revision; final approval of the version to be published; agreement to be accountable for all aspects of the work.

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Data Availability

The data are not publicly available. Requests for data sharing can be directed to the corresponding author and will be considered in accordance with the regulations of Prince of Songkla University.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

The study protocol was approved by the Institutional Review Board of Prince of Songkla University (Approval REC No. 65507131).

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