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MULTIFACTORIAL ANALYSIS FOR PREDICTING CHRONIC RHINOSINUSITIS RECURRENCE AFTER FUNCTIONAL ENDOSCOPIC SURGERY USING MACHINE LEARNING COMBINATION METHODS

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Chronic rhinosinusitis represents a major healthcare burden with recurrence rates after functional endoscopic sinus surgery ranging from 6 % to 65 %. Machine learning approaches offer superior predictive capabilities compared to traditional statistical methods. This retrospective study analyzed 426 CRS patients who underwent functional endoscopic sinus surgery during 2019–2025. Seven machine learning algorithms were applied, and an ensemble model was developed. A simplified clinical risk score was created based on the most significant predictors for routine clinical use. Recurrence occurred in 157 patients (36.9 %) during 32.8±9.4 months follow-up. The ensemble model demonstrated the highest performance with AUC=0.94 and accuracy =89.2 %. Key predictors included previous surgery (OR=3.24), olfactory cleft obstruction ≥2 points (OR=2.87), blood eosinophilia ≥6 % (OR=2.34), and Lund-Mackay index ≥16 (OR=1.89). The simplified clinical risk score showed acceptable predictive ability (AUC=0.89) for routine practice. A two-tier prediction approach combining high-accuracy ML models for specialized centers and simplified clinical scores for routine practice can optimize personalized treatment strategies.

Key words: chronic rhinosinusitis, machine learning, prediction, recurrence, ensemble methods.

О.М. Науменко, Ю.В. Дєєва, І.В. Гогунська, Л.І. Романюк, С.В. Зяблицев БАГАТОФАКТОРНИЙ АНАЛІЗ ПРОГНОЗУВАННЯ РЕЦИДИВУ ХРОНІЧНОГО РИНОСИНУСИТУ ПІСЛЯ ФУНКЦІОНАЛЬНОЇ ЕНДОСКОПІЧНОЇ ХІРУРГІЇ З ВИКОРИСТАННЯМ КОМБІНАЦІЇ МЕТОДІВ МАШИНОГО НАВЧАННЯ

Хронічний риносинусит становить серйозне навантаження на систему охорони здоров'я, що обумовлено в тому числі, частотою рецидивів після функціональної ендоскопічної хірургії пазух носа, яка коливається в межах від 6 % до 65 %. Використання машинного навчання дозволяє покращити прогностичні можливості порівняно з традиційними статистичними методами в визначенні ризику рецидиву ХРС. В даному ретроспективному дослідженні проаналізовано 426 пацієнтів з ХРС, які перенесли функціональну ендоскопічну хірургію пазух носа протягом 2019–2025 років. Для порівняння було використано сім алгоритмів машинного навчання та розроблено комбіновану модель. Спрощена клінічна оцінка ризику була створена на основі найбільш «якісних» факторів ризику для рутинного клінічного використання. Рецидив спостерігався у 157 пацієнтів (36,9 %) протягом 32,8±9,4 місяців спостереження. Комбінована модель продемонструвала найвищу продуктивність з AUC=0,94 та точністю =89,2 %. Ключовими предикторами були попереднє хірургічне втручання (OR=3,24), обструкція нюхової щілини ≥2 бали (OR=2,87), еозинофілія крові ≥6 % (OR=2,34) та індекс Ланд-Маккея ≥16 (OR=1,89). Спрощена клінічна шкала ризику показала прийнятну прогностичну здатність (AUC=0,89) для клінічної практики. Дворівневий підхід до прогнозування, що поєднує моделі машинного навчання та клінічні шкали можуть оптимізувати стратегії лікування кожного окремого пацієнта.

Ключові слова: хронічний риносинусит, машинне навчання, прогнозування, рецидив, комбіновані моделі.

The study is a fragment of the research project "Innovative approaches to the diagnosis and treatment of acute and chronic pathologies of the ear, upper respiratory tract, and adjacent areas," state registration No. 0123U100921.

Chronic rhinosinusitis (CRS) is one of the most prevalent chronic diseases worldwide, which according to recent epidemiological studies affects from 4.72 % (1980–2000) to 19.40 % (2014–2020) of the adult population, demonstrating an almost 4-fold increase in prevalence over the past 40 years [3]. According to the European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS 2020), CRS is characterized by prolonged inflammation of the nasal and paranasal sinus mucosa with typical symptomatology that significantly reduces patients' quality of life [4]. The economic burden of the disease is enormous, amounting to more than 60 billion dollars annually in the United States alone [5].

Functional endoscopic sinus surgery (FESS) remains the gold standard treatment for CRS patients who are resistant to conventional (basic) conservative therapy [4]. However, the recurrence rate after FESS remains high, varying from 6 % to 65.8 % depending on the population and recurrence assessment criteria [6]. Studies show that in patients with eosinophilic chronic rhinosinusitis with nasal polyps and asthma, recurrence rates can reach 95.6–96.1 % during 5-year follow-up, which further reveals this problem in terms of treatment [7].

The modern concept of CRS endotyping, proposed by the EPOS 2020 expert group, emphasizes the importance of a personalized approach to treatment with the identification of three main types of inflammation (Type 1, Type 2, Type 3), which are based on corresponding pathogenetic mechanisms [8]. However, predicting recurrence still remains a complex task that requires comprehensive analysis of numerous clinical, laboratory, and imaging data.

Traditional statistical methods have limited ability to analyze complex nonlinear relationships between various clinical factors [9]. At the same time, new algorithms in the form of machine learning (ML) provide new opportunities for creating more accurate prognostic models. Numerous studies demonstrate the high effectiveness of machine learning algorithms in medicine, especially combined methods that combine the advantages of several different algorithmic structure ML algorithms [10].

In otolaryngology, ML is beginning to be actively used for diagnosis and prognosis of head and neck diseases [11]. A systematic review demonstrated significant potential for deep machine learning in otolaryngology, but prognostic models for predicting CRS recurrence after FESS remain limited [12]. Particularly relevant is the development of comprehensive prognostic algorithms using modern clinical metrics to optimize treatment strategies and improve long-term CRS treatment outcomes.

The purpose of the study was to develop and validate a comprehensive prognostic model for predicting chronic rhinosinusitis recurrence after functional endoscopic surgery using combined machine learning methods.

Materials and methods. A retrospective analysis of a cohort of patients with chronic rhinosinusitis who underwent functional endoscopic surgery at the bases of the Department of Otorhinolaryngology of Bogomolets National Medical University from January 2019 to December 2025 was conducted. Inclusion criteria: confirmed diagnosis of chronic rhinosinusitis according to EPOS 2020 criteria [4], patient age from 18 to 75 years, performed functional endoscopic sinus surgery, minimum observation period of 24 months after surgery, availability of complete clinical, laboratory, and imaging data before and after surgical intervention.

The work was carried out within the framework of the Scientific Research Work of the Department of Otorhinolaryngology of the Bogomolets National Medical University on the topic «Innovative approaches to the diagnosis and treatment of acute and chronic pathology of the ear, upper respiratory tract and adjacent areas», state registration number 0123U100921, implementation period 2023–2025.

The study was conducted in accordance with the principles of the Helsinki Declaration. Written informed consent for participation in the study was not required, as the study was retrospective and analyzed existing patient data. We ensured complete anonymization of patient data after their inclusion in the study. No personal patient information is mentioned in the database or in the article. The study was approved by the Bioethics Committee of Bogomolets National Medical University, protocol No. 183 dated 25.03.2024.

Exclusion criteria: malignant neoplasms of the nose and paranasal sinuses, immunodeficiency states, cystic fibrosis, incomplete medical records or absence of treatment outcome data. Chronic rhinosinusitis recurrence was defined as the return of characteristic disease symptomatology combined with otolaryngological examination data, nasal endoscopy, and CT scan of paranasal sinuses.

For each patient, demographic data (age, gender, body mass index), medical history data on disease duration, number of previous surgical interventions, presence of comorbidities, and allergological history were collected. Clinical parameters included the presence of polyps in the nasal cavity, inflammatory process extent, and olfactory cleft obstruction. Laboratory parameters: complete blood count with leukocyte formula, total immunoglobulin E level (when available), and vitamin D level (when available) in blood serum.

Imaging parameters were assessed using computed tomography of paranasal sinuses with calculation of the Lund-Mackay index, osteitis index according to Global Osteitis Scoring Scale (GOSS), sinus filling coefficient, and Assessment of Pneumatization of the Paranasal Sinuses (APPS) scale.

Statistical analysis was performed using Python 3.9 software with pandas, scikit-learn, numpy, matplotlib, seaborn, and statsmodels libraries. Group comparisons were conducted using Student's t-test for continuous variables and χ^2 -test for categorical variables.

For developing prognostic models, seven different machine learning algorithms were applied: logistic regression with L2-regularization, Random Forest, Support Vector Machine (SVM) with radial basis function, Gradient Boosting, multilayer perceptron (MLP), Naive Bayes classifier, and combined model (Ensemble model), which combined the best methods using the stacking principle.

Considering the complexity of implementing ML algorithms in routine clinical practice, a simplified clinical risk scale for recurrence was developed based on the most significant predictors from multivariate analysis for use by physicians without the need for special software.

The dataset was randomly divided into training sample (70 %) and test sample (30 %). For each algorithm, hyperparameter optimization was performed using grid search method with five-fold cross-validation. Model quality was assessed using area under the ROC curve (AUC), accuracy, sensitivity, specificity, positive and negative predictive values. Mean values are presented as $M \pm m$. Statistical significance was set at $p < 0.05$.

Results of the study and their discussion. The study included 426 patients with chronic rhinosinusitis who met all inclusion criteria. The mean age of patients was 44.1±13.2 years (range: 18–75 years). Among included patients, males predominated – 251 persons (58.9 %), while females comprised 175 persons (41.1%). The mean body mass index was 26.1±4.4 kg/m².

During the mean follow-up period of 32.8±9.4 months, chronic rhinosinusitis recurrence was diagnosed in 157 patients, which comprised 36.9 % of the total number of patients included in the study. The mean time to recurrence development was 19.8±10.7 months.

Patients with CRS recurrence were statistically significantly older (47.8±12.1 years vs. 41.6±13.1 years, $p<0.001$), had higher body mass index (27.2±4.5 vs. 25.4±4.2 kg/m², $p=0.001$), and longer disease duration before surgery (61.4±36.3 vs. 34.1±29.8 months, $p<0.001$).

To assess the impact of each evaluated parameter on CRS recurrence probability, multivariate logistic regression analysis was performed, which revealed nine independent prognostic factors for chronic rhinosinusitis recurrence. The strongest predictor was previous surgical interventions with odds ratio 3.24 (95 % CI: 2.1–4.8, $p<0.001$). The second most significant factor was olfactory cleft obstruction ≥ 2 points with odds ratio 2.87 (95 % CI: 1.9–4.2, $p<0.001$). Detailed results of multivariate analysis are presented in Table 1. It should be noted that blood eosinophilia $\geq 6\%$ showed odds ratio 2.34 (95 % CI: 1.6–3.4, $p<0.001$), which is especially important in "Type 2" inflammation, and Lund-Mackay index ≥ 16 points was associated with odds ratio 1.89 (95 % CI: 1.3–2.7, $p=0.001$), reflecting the significance of imaging severity in predicting recurrence.

Table 1

Results of multivariate logistic regression analysis

Factor	Coefficient β	SE	OR (95 % CI)	p-value
Previous FESS	1.176	0.204	3.24 (2.1–4.8)	<0.001
Olfactory cleft obstruction ≥ 2	1.054	0.198	2.87 (1.9–4.2)	<0.001
Eosinophilia $\geq 6\%$	0.851	0.187	2.34 (1.6–3.4)	<0.001
Lund-Mackay ≥ 16	0.637	0.178	1.89 (1.3–2.7)	0.001
Bilateral process	0.584	0.165	1.79 (1.2–2.7)	0.003
Age ≥ 45 years	0.523	0.154	1.69 (1.1–2.5)	0.011
APPS ≥ 12	0.498	0.149	1.65 (1.1–2.4)	0.018
Bronchial asthma	0.467	0.145	1.60 (1.0–2.4)	0.034
Allergic rhinitis	0.445	0.141	1.56 (1.0–2.3)	0.041

Note: SE – standard error of regression coefficient; OR – odds ratio.

We also conducted a comparative analysis of the effectiveness of seven different machine learning algorithms for predicting chronic rhinosinusitis recurrence based on our database. The results of evaluation on the test sample are presented in Table 2. The highest efficiency was demonstrated by the combined model, which combined the best characteristics of several algorithms using the stacking principle.

Table 2

Comparison of machine learning algorithm effectiveness

Algorithm	AUC	Accuracy	Sensitivity	Specificity	PPV	NPV
Logistic regression	0.86	81.7 %	76.2 %	85.1 %	76.2 %	85.1 %
Random Forest	0.91	85.2 %	81.0 %	87.8 %	81.0 %	87.8 %
SVM	0.88	83.5 %	78.6 %	86.5 %	78.6 %	86.5 %
Gradient Boosting	0.92	87.0 %	83.3 %	89.2 %	83.3 %	89.2 %
MLP	0.89	84.3 %	80.9 %	86.5 %	80.9 %	86.5 %
Naive Bayes	0.82	78.3 %	73.8 %	81.1 %	73.8 %	81.1 %
Combined model	0.94	89.2 %	85.7 %	91.9 %	85.7 %	91.9 %

Note: PPV – positive predictive value; NPV – negative predictive value.

Thus, the combined model showed an area under the ROC curve of 0.94 (95 % CI: 0.91–0.97), which is a good result specifically for medical ML prognostic models. The model's accuracy was 89.2 %, sensitivity – 85.7 %, and specificity – 91.9 %. The positive predictive value was 85.7 %, meaning that out of every 100 patients for whom the model predicted recurrence, 86 will actually develop disease recurrence. Gradient Boosting was the second most effective algorithm with AUC 0.92 and accuracy 87.0 %. The Random Forest algorithm demonstrated stable results with AUC 0.91 and more balanced sensitivity and specificity indicators. Traditional logistic regression showed acceptable results with AUC 0.86, but was the worst compared to modern machine learning methods.

Feature importance analysis from the studied combined ML model allowed establishing the hierarchy of chronic rhinosinusitis recurrence risk factors. Previous surgical interventions had the greatest

"weight" (weight=0.187), confirming clinical observations about increased recurrence risk in patients with repeated/revision surgical interventions. Olfactory cleft obstruction took second place (weight=0.156), which is explained by the critical role of this anatomical structure in ensuring ventilation and drainage of the upper ethmoid labyrinth divisions. The Lund-Mackay index received third place in importance (weight=0.134), reflecting the significance of CT PNS severity changes in disease course prognosis. Blood eosinophilia had a weight of 0.129, confirming the role of Type 2 inflammation in recurrent chronic rhinosinusitis pathogenesis. Disease duration (weight=0.098) and patient age (weight=0.087) also showed significant influence on prognosis.

Therefore, based on multivariate analysis results and "feature importance" analysis of the combined ML model, we developed a simplified clinical risk scale for chronic rhinosinusitis recurrence (CRRS - Chronic Rhinosinusitis Recurrence Score), with the following risk factors with a maximum sum of 12 points: Previous FESS (3 points), Olfactory cleft obstruction ≥ 2 points (3 points), Eosinophilia ≥ 6 % (2 points), Lund-Mackay ≥ 16 (2 points), Bilateral process (1 point), Age ≥ 45 years (1 point). The scale includes the most significant and easily accessible factors in clinical practice for recurrence prediction with weight coefficients proportional to their prognostic value.

Internal validation of the combined ML model was performed using five-fold cross-validation, which showed stability of results with mean AUC 0.93 ± 0.02 , while the CRRS scale demonstrated AUC 0.89 (95 % CI: 0.85–0.92) when validated on an independent test sample, indicating good generalization ability of the model. Model calibration was assessed using the Hosmer-Lemeshow test, which did not reveal statistically significant deviations from ideal calibration ($p=0.341$ for CRRS scale). The concordance index was 0.87, indicating high agreement between predicted and observed results.

Thus, applying the CRRS scale to the entire cohort allowed stratifying patients by recurrence risk. 173 patients (40.6 %) fell into the low-risk group, 167 patients (39.2 %) – into the moderate risk group, and 86 patients (20.2 %) – into the high-risk group. The actual recurrence rates in these groups were 11.6 %, 32.3 %, and 68.6 % respectively, which correlates well with predicted indicators.

The study results demonstrate high effectiveness of combined machine learning methods for predicting chronic rhinosinusitis recurrence after functional endoscopic sinus surgery. Our obtained area under the ROC curve of 0.94 for the combined ML algorithm model somewhat exceeds the indicators of published prognostic systems in otolaryngology, head and neck surgery [9]. We note that previous studies in the field using machine learning methods or neural networks in Ukraine have already been conducted by a group of researchers who also showed good results in X-ray segmentation based on binary classification – «sinusitis» and «normal» [2]. Drawing parallels with European data on general clinical parameters, we found that the CRS recurrence rate in our study (36.9 %) correlates well with global indicators and is within the range reported by other researchers [14, 15]. The mean time to recurrence of 19.8 months also agrees with international data [15], so it can be said with high confidence that the characteristics of CRS course in the Ukrainian population are similar to global patterns.

Our identified CRS recurrence predictors correspond to current understanding of disease pathogenesis. Previous surgical interventions as the most powerful predictor (OR=3.24) agree with systematic review results reporting high revision intervention rates [15]. Blood eosinophilia ≥ 6 % (OR=2.34) as a recurrence predictor correlates with the Type 2 inflammation concept proposed in EPOS 2020 [7]. A feature of our study was deep processing of CT PNS data using an extended set of metrics, including osteitis index and sinus filling coefficient, APPS scale and other metrics, which represents an important step forward in quantitative assessment of disease severity. These indicators allow more accurate characterization of pathological changes compared to traditional qualitative assessments and allowed more correct evaluation of different ML model capabilities, including the combined one, and the developed CRRS scale based on logistic regression and combined ML data [10]. Moreover, considering significant individual anatomical variability of head and neck structures, confirmed by modern morphological studies [1], such a personalized approach to assessing anatomical features and patient medical history becomes even more relevant for optimizing diagnostic and treatment algorithms.

The developed combined ML model and simplified CRRS scale have different practical applications. The combined ML model with AUC 0.94 provides the highest prediction accuracy and can be used in specialized centers with appropriate technical support for the most accurate risk stratification. Meanwhile, the CRRS scale (AUC 0.89) is designed for daily use, not requiring special software or complex calculations.

The clinical significance of both approaches lies in the possibility of personalizing treatment strategies according to current EPOS/EUFOREA recommendations [5]. High-risk patients may be offered

more aggressive therapy, including biological therapy, prolonged topical corticosteroid administration, and intensive monitoring. Low-risk patients may receive standard treatment with less frequent observation.

The main limitation of our study is its retrospective nature and its single-center design, which may affect the generalizability of the results to other patient populations. The developed machine learning model also needs to be tested on patients from other clinics to definitively confirm its effectiveness in different settings, which may be the subject of future research.

Conclusions

1. The combined machine learning model provides the highest accuracy for predicting chronic rhinosinusitis recurrence after functional endoscopic surgery with an area under the ROC curve of 0.94, significantly surpassing traditional statistical methods.

2. Previous surgical interventions, olfactory cleft obstruction, blood eosinophilia, and Lund-Mackay index are the most significant recurrence predictors with odds ratios from 1.89 to 3.24.

3. The developed simplified clinical CRRS scale allows effective stratification of patients into three risk groups with actual recurrence rates of 11.6 %, 32.3 %, and 68.6 % respectively, providing acceptable accuracy (AUC=0.89) for routine clinical use.

4. The chronic rhinosinusitis recurrence rate in the Ukrainian population is 36.9 % during a mean follow-up period of 32.8 months, which aligns well with global trends.

5. A two-step approach to predicting CRS recurrence, combining a highly accurate combined ML model and a simplified clinical scale for routine practice, allows for the optimization of personalized treatment strategies and the identification of patients who require biological treatment and frequent monitoring.

6. Comprehensive assessment of radiological data using an expanded set of radiological scales in combination with clinical and laboratory parameters provides a more accurate quantitative characterization of disease severity and improves the predictive ability of machine learning models compared to traditional qualitative assessments.

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