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ORIGINAL RESEARCH

Machine Learning Prediction of Residual and Recurrent High-Grade CIN Post-LEEP

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Purpose: This study aims to develop a machine learning (ML) model to predict the risk of residual or recurrent high-grade cervical intraepithelial neoplasia (CIN) after loop electrosurgical excision procedure (LEEP), addressing a critical gap in personalized follow-up care.

Methods: A retrospective analysis of 532 patients who underwent LEEP for high-grade CIN at Cangzhou Central Hospital (2016–2020) was conducted. In the final analysis, 99 women (18.6%) were found to have residual or recurrent high-grade CIN (CIN2 or worse) within five years of follow-up. Four feature selection methods identified significant predictors of residual or recurrent CIN. Eight ML algorithms were evaluated using performance metrics such as AUROC, accuracy, sensitivity, specificity, PPV, NPV, F1 score, calibration curve, and decision curve analysis. Fivefold cross-validation optimized and validated the model, and SHAP analysis assessed feature importance.

Results: The XGBoost algorithm demonstrated the highest predictive performance with the best AUROC. The optimized model included six key predictors: age, ThinPrep cytologic test (TCT) results, HPV classification, CIN severity, glandular involvement, and margin status. SHAP analysis identified CIN severity and margin status as the most influential predictors. An online prediction tool was developed for real-time risk assessment.

Conclusion: This ML-based predictive model for post-LEEP high-grade CIN provides a significant advancement in gynecologic oncology, enhancing personalized patient care and facilitating early intervention and informed clinical decision-making.

Keywords: cervical intraepithelial neoplasia, loop electrosurgical excision procedure, residual or recurrent, machine learning, predictive modeling

Introduction

Globally, cervical cancer ranks as the fourth most common and deadly cancer, with varying trends in incidence and mortality between developed and developing nations.[1,2] While developed countries are experiencing a decrease in cases, there is a concerning rise in China, with an estimated 110,000 new cases and 60,000 deaths projected by 2020.[3] This disparity underscores the critical need for structured screening programs to detect and intervene early in precancerous lesions, particularly cervical intraepithelial neoplasia (CIN2+), which is essential for preventing cervical cancer.

Cervical intraepithelial neoplasia (CIN), a significant precursor to invasive cervical cancer (ICC), has a significant impact on the gynecological health of women, especially those of reproductive age.[4,5] Left untreated, high-grade CIN can progress to ICC, highlighting the challenge of predicting lesion outcomes and emphasizing the need for effective surgical interventions like loop electrosurgical excision procedure (LEEP) and cold knife conization (CKC).[6] While these treatments are generally successful, a small percentage of cases (5% to 25%) may still be at risk of developing residual or recurrent high-grade lesions, increasing the likelihood of progression to ICC.[7]

Effective post-operative management is crucial for preventing residual or recurrent lesions after surgical interventions for high-grade CIN. Persistent high-risk human papillomavirus (HR-HPV) infection is a significant predictor for post-conization recurrence, making HPV testing alongside cytology essential in follow-up strategies.[8,9] The status of conization margins is equally important; positive margins often necessitate more intensive monitoring.[10] While research has identified additional risk factors such as age, menopausal status, smoking history, initial lesion severity, and

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immunosuppressive status, their relative importance remains debated due to inconsistencies in studies.[11–13] This underscores the need for comprehensive research to develop practical, refined risk assessment tools that can guide personalized post-operative management strategies.

Managing residual or recurrent dysplasia post-treatment requires carefully classifying patients based on their risk of recurrence. This classification is crucial for tailoring surveillance and determining future treatments. While many studies have tried to assess the risk of residual or recurrent CIN, accurately determining an individual patient's risk remains challenging. Additionally, current predictive models, while innovative, need more clinical utility due to their complexity and the need for extensive big data analytics, thus hindering their widespread adoption in clinical practice.[14]

The emergence of machine learning (ML) in medical diagnostics and treatment strategies has significantly improved patient care.[15] Recent efforts to develop ML-based predictive models for post-treatment residual or recurrent CIN highlight the importance of effective patient management and follow-up. Bogani et al[16,17] and Chen et al[18] have proposed models combining clinical and pathological factors, showing promising predictive accuracy. However, there is still untapped potential for advanced ML techniques to consider a wide range of risk factors and create a precise and clinically helpful model for predicting post-LEEP residual or recurrent high-grade CIN risk. Additionally, the integration of these models into daily clinical practice for guiding patient management decisions is an area that requires further development. Among the various treatment options available, LEEP conization is the preferred method for treating CIN due to its rapid procedure, minimal blood loss, quick recovery, minimal tissue damage, low complication rates, and lesser impact on fertility.[19] This research aims to leverage ML algorithms in conjunction with clinical and pathological information to create an innovative predictive model that will enhance the precision of forecasting the likelihood of residual or recurrent high-grade CIN after LEEP.

Methods

Study Design

This retrospective study analyzed the clinicopathologic data of 532 patients diagnosed with high-grade cervical intraepithelial neoplasia (CIN2/3) who underwent LEEP at Cangzhou Central Hospital between January 2016 and December 2020. Follow-up was conducted until December 2021, with ethical approval from the Ethics Committee of Cangzhou Central Hospital (2021–054-02) and a waiver for informed consent.

Eligibility Criteria

Inclusion criteria encompassed individuals with a CIN2/3 diagnosis confirmed by colposcopic multi-site cervical biopsy, undergoing LEEP, and agreeing to participate in follow-up procedures. Exclusion criteria ruled out individuals with concurrent reproductive tract illnesses, severe conditions affecting the respiratory or circulatory systems, liver and kidney dysfunctions, those who had undergone total hysterectomy, were diagnosed with ICC post-operation, had a history of cervical pathologies, were on hormone replacement therapy, had acute infectious diseases, or were pregnant.

Data Collection

Patient clinicopathological details were meticulously gathered from medical records, including age, gravidity, parity, menopausal status, results from TCT, HPV classifications, CIN severity, glandular involvement, and margin status from initial LEEP specimens.

Crucial Definitions

Surgical interventions, performed by specialized gynecologists, involved removing a cone-shaped section of the cervix's transformation zone. The excision depth and margins were tailored to the lesion's extent. Histological analysis of colposcopy-obtained tissue samples was used to detect residual or recurring disease. Residual disease was defined as lesions found within the first year post-LEEP; those found later were considered recurrent. For modeling, both types were grouped due to similar clinical implications.

Follow-Up Protocol

Patients had follow-up visits semiannually for 2 years, then annually. Positive HPV tests prompted colposcopy and biopsy. Lesion severity ranged from normal to various CIN stages, adenocarcinoma in situ, adenocarcinoma, or squamous cell carcinoma. HPV/TCT results from LEEP were analyzed. Procedures were done by experienced professionals. Diagnoses were verified by two pathologists and reviewed by seniors for ambiguity. Follow-up duration was from conization to residual/recurrent CIN detection, loss to follow-up, death, or study end.

Feature Selection

In our study, we utilized four advanced feature selection techniques to identify key predictors of post-conization high-grade CIN residual or recurrent: Least Absolute Shrinkage and Selection Operator (Lasso), Boruta, Recursive Feature Elimination (RFE), and Relief. Each method analyzed the dataset independently, with Lasso utilizing a cross-validation approach to fine-tune the penalty parameter and remove non-essential feature coefficients, thus simplifying the feature selection process.[20] The Boruta algorithm focused on identifying all relevant features by comparing the importance of original features with shadow features (random permutations of genuine features) to highlight significantly informative ones.[21] RFE systematically eliminated less critical features based on their impact on model performance,[22] while Relief evaluated each feature's ability to differentiate between neighboring instances of different classes.[23]

Model Establishment and Development

For model development and comparison, we employed eight algorithms: extreme gradient boosting (XGBoost), logistic regression (LR), random forest (RF), adaptive boosting, Gaussian naive Bayes, multilayer perceptron (MLP), support vector machine (SVM), and k-nearest neighbors (KNN). These models were implemented using Python 3.7, with "xgboost 2.0.1" for XGBoost and "sklearn 1.1.3" for the other models. A bootstrap resampling technique was utilized for training and validation, dividing patients into training and test sets with an 8:2 ratio. Model performance was evaluated using discrimination metrics such as the area under the receiver operating characteristic curve (AUROC), accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and F1 scores. Additionally, calibration curves were utilized to visually assess predicted outcomes compared to actual disease residual or recurrent.

Model Optimization and Evaluation

Model optimization involved fivefold cross-validation to assess predictive performance. The training set was divided into five parts, with four used for training and the fifth for validation. Model discrimination was evaluated using ROC curve analysis, calibration plots, and decision curve analysis (DCA). Feature importance was determined using the SHapley Additive exPlanations (SHAP) method, with higher SHAP values indicating a more significant impact on predictions. The relationship between feature values and predictions was also examined. An online prediction tool was developed to estimate the risk of high-grade CIN residual or recurrent based on key model features.

Statistical Analysis

Statistical analyses were performed using R (version 3.6.3) and Python's Scikit-Learn (version 1.1.3). Comparative analyses between patients with residual/recurrent disease and controls were conducted using chi-squared tests, with ROC differences evaluated through DeLong tests. Statistical significance was set at $p < 0.05$, following a two-tailed approach.

Results

Baseline Characteristics and Follow-Up

A total of 532 patients who underwent LEEP for high-grade CIN were included in the study. The baseline characteristics of the patients are summarized in Table 1. There were no significant differences in age, gravidity, parity, or glandular involvement between the groups with and without residual or recurrent disease (all $p > 0.05$). However, significant differences were observed in the distribution of pre-LEEP TCT results, HPV genotypes, CIN grades, menopausal status

Table 1 Baseline Characteristics of the Population

Patient Characteristic	No Residual/Residual CIN (n=433)	Residual/Residual CIN (n=99)	*P-value*
Age (years)	41.4 ± 9.9	42.9 ± 11.6	0.187
Gravidity, n (%)			0.350
<3	218 (50.3)	55 (55.6)	
≥3	215 (49.7)	44 (44.4)	
Parity, n (%)			0.435
<2	144 (33.3)	37 (37.4)	
≥2	289 (66.7)	62 (62.6)	
Menopause, n (%)			0.020
No	333 (76.9)	65 (65.7)	
Yes	100 (23.1)	34 (34.3)	
TCT, n (%)			<0.001
<ASC-H	280 (64.7)	36 (36.4)	
≥ASC-H	153 (35.3)	63 (63.6)	
HPV, n (%)			<0.001
No HR-HPV	10 (2.3)	3 (3.0)	
HPV16/18	225 (52.0)	78 (78.8)	
Other HR HPV	198 (45.7)	18 (18.2)	
Degrees of CIN, n (%)			<0.001
CIN2	320 (73.9)	26 (26.3)	
CIN3	113 (26.1)	73 (73.7)	
Glandular involvement, n (%)			0.148
No	287 (66.3)	58 (58.6)	
Yes	146 (33.7)	41 (41.4)	
Margin status, n (%)			<0.001
Negative	339 (78.3)	26 (26.3)	
Positive	94 (21.7)	73 (73.7)	

Note: Data are shown as mean±standard deviation or median (interquartile range) or percentage.
Abbreviations: CIN, cervical intraepithelial neoplasia; TCT, ThinPrep cytological test; ASC-H, atypical squamous cells cannot exclude high grade squamous intraepithelial lesion; HR-HPV, high-risk human papilloma virus. P value< 0.05 was considered significant.

and margin status between the two groups (all $p < 0.05$). Patients with residual or recurrent disease had a significantly higher proportion of postmenopausal women, High-Grade TCT results (ASC-H [Atypical Squamous Cells, cannot exclude High-grade squamous intraepithelial lesion]/HSIL [High-grade Squamous Intraepithelial Lesion]), HPV16/18 infections, CIN3 diagnoses, and positive margins compared to those without residual or recurrent disease.

The median follow-up time was 26 months (6–60 months), with 75% of patients being followed for more than 18 months. The overall rate of residual or recurrent high-grade CIN (CIN2 or worse) followed for five years after LEEP was 18.6%. The median time to patient residual/recurrent disease was 20 months (6–56 months).

Feature Selection and Comparison of Multiple Classification Models

To determine the factors that predict recurrent and residual cervical intraepithelial neoplasia post-LEEP conization, we identified vital variables presented in Table 1. By nullifying nine variable coefficients, the Lasso method indicated their minimal impact, as depicted in Figure 1a. The Boruta algorithm marked six variables as significant, assigning lesser importance to others (Figure 1b). Iterative processes in RFE and the Relief algorithm's neighbor-based approach similarly highlighted these variables' significance in prognosticating outcomes, as seen in Figure 1c and d. Collating results from these algorithms, we derived critical features for a predictive model: age, TCT, HPV classification, CIN severity, glandular involvement, and margin status. Comparative analysis of eight ML classification models for residual and recurrent CIN risk prediction in training and validation cohorts is summarized in Table 2 and Figure 2. Among these models, XGBoost

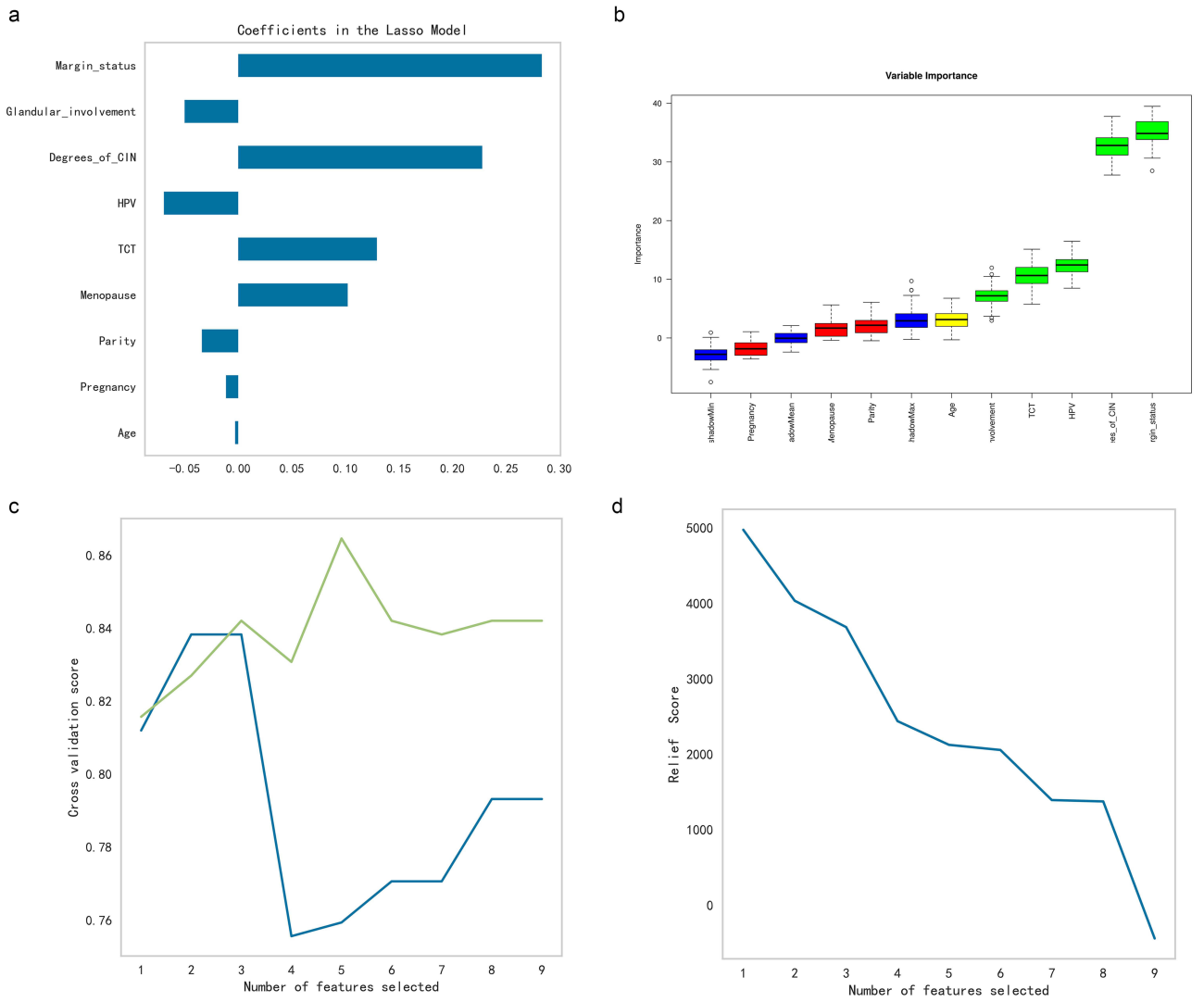

Figure 1 Comparison of feature screening methods for predictors of post-conization high-grade cervical intraepithelial neoplasia (CIN) residual or recurrent. (**a**) Lasso model coefficient plots demonstrating the magnitude of the coefficients for each predictor variable; (**b**) Variable significance plots of Boruta's method, as represented by the box plots; (**c**) Number of features versus cross-validation scores in the RFE method; and (**d**) Variation of feature scores in the Relief method.

outperformed others in predicting high-grade CIN post-LEEP, as evidenced in Figure 2a and b through ROC curve analysis. RF showed a tendency towards overfitting, while XGBoost demonstrated stability. Calibration plots (Figure 2c) evaluated the models' accuracy, and forest plots (Figure 2d) displayed the ROC results, including error bars representing the mean and standard deviation.

Model Optimization and Interpretation

Optimization of the XGBoost model involved auto-tuning its parameters using the six shortlisted variables. A fivefold cross-validation, dividing patients into five groups for testing and training, achieved AUC scores of 0.940, 0.865, and 0.827 in the training, validation, and test sets, respectively (Table 3 and Figure 3a–c). The model's learning curve (Figure 3d) indicated no overfitting and further accuracy assessments were conducted via calibration plots (Figure 3e). This model's decision curve analysis, shown in Figure 3f, demonstrated significant net benefit compared to extreme management plans at risk thresholds below 80%. For model interpretability, SHAP values, based on game theory's Shapley values, analyzed the XGBoost algorithm's outcomes. Feature importance, depicted in Figure 3g, and the summary plot in Figure 3h, showcased the influence of high and low feature values.

Table 2 Predictive Performance of the Eight Machine Learning Algorithms in the Training and Validation Sets for Post-LEEP High-Grade CIN Residual or Recurrent

Models	AUC	Accuracy	Sensitivity	Specificity	PPV	NPV	F1 score
Training set							
XGBoost	0.916	0.854	0.855	0.852	0.587	0.958	0.691
LR	0.884	0.820	0.830	0.820	0.509	0.951	0.631
RF	0.997	0.975	0.987	0.972	0.896	0.994	0.939
AdaBoost	0.887	0.825	0.820	0.829	0.510	0.949	0.628
GNB	0.884	0.818	0.792	0.828	0.510	0.943	0.616
MLP	0.451	0.488	0.640	0.461	0.173	0.854	0.269
SVM	0.836	0.795	0.741	0.811	0.470	0.928	0.573
KNN	0.924	0.895	0.907	0.812	0.739	0.925	0.809
Validation set							
XGBoost	0.836	0.813	0.813	0.792	0.514	0.924	0.624
LR	0.841	0.793	0.743	0.841	0.475	0.926	0.575
RF	0.781	0.796	0.793	0.706	0.491	0.862	0.602
AdaBoost	0.858	0.828	0.807	0.817	0.571	0.927	0.668
GNB	0.852	0.789	0.793	0.814	0.469	0.925	0.578
MLP	0.416	0.503	0.636	0.467	0.172	0.809	0.206
SVM	0.823	0.772	0.827	0.753	0.462	0.918	0.579
KNN	0.728	0.804	0.604	0.768	0.499	0.860	0.532

Abbreviations: CIN, cervical intraepithelial neoplasia; LEEP, loop electrosurgical excision procedure; AUC, area under the curve; PPV, positive predictive value; NPV, negative predictive value; XGBoost, extreme gradient boosting; LR, logistic regression; RF, random forest; GNB, Gaussian naïve Bayes; MLP, multilayer perceptron; SVM, support vector machine; KNN, k-nearest neighbor.

Kaplan–Meier Estimates

Finally, patient stratification efficacy was illustrated through Kaplan-Meier survival curves, differentiating high- and low-risk groups based on predicted outcomes (Figure 4). The significant p-value (< 0.0001) in the Log rank test confirmed the model's robust performance.

Model Presentation

Our finalized model is presented through an interactive web application based on Python designed for replicability and validation by other researchers (http://www.xsmartanalysis.com/model/list/predict/model/html?mid=14070andsymbol=11Ep7128501CU652KoHY). A general model screenshot is provided in Figure 5.

Discussion

Our study thoroughly examines the predictive factors for residual or recurrent high-grade CIN following LEEP and introduces a novel predictive model incorporating six preoperative and post-operative risk factors. This model represents a significant advancement in the field, providing a practical and cost-effective tool for identifying at-risk patients. It is also highly interpretable, utilizing SHAP values to demonstrate the impact of each variable transparently. The development of this model highlights the value of ML in improving prognostic assessments, offering a data-driven and patient-centered approach to post-operative care in cervical cancer prevention, especially in underserved regions. This empowers clinicians to make well-informed decisions and enhances personalized patient care. To facilitate the application of our research, we have created an online tool for risk prediction that streamlines the clinical decision-making process with its intuitive interface for rapid risk assessment and analysis.

Recently, the flexibility and accuracy of ML algorithms have made them increasingly popular in various medical fields, including cervical dysplasia management. These algorithms can identify complex relationships between input features and output data, enhancing prediction accuracy. To predict the risk of persistence or recurrence of CIN post-treatment, studies by Bogani et al[16,17] and Chen et al[18] have integrated clinical and pathological factors like CIN grade

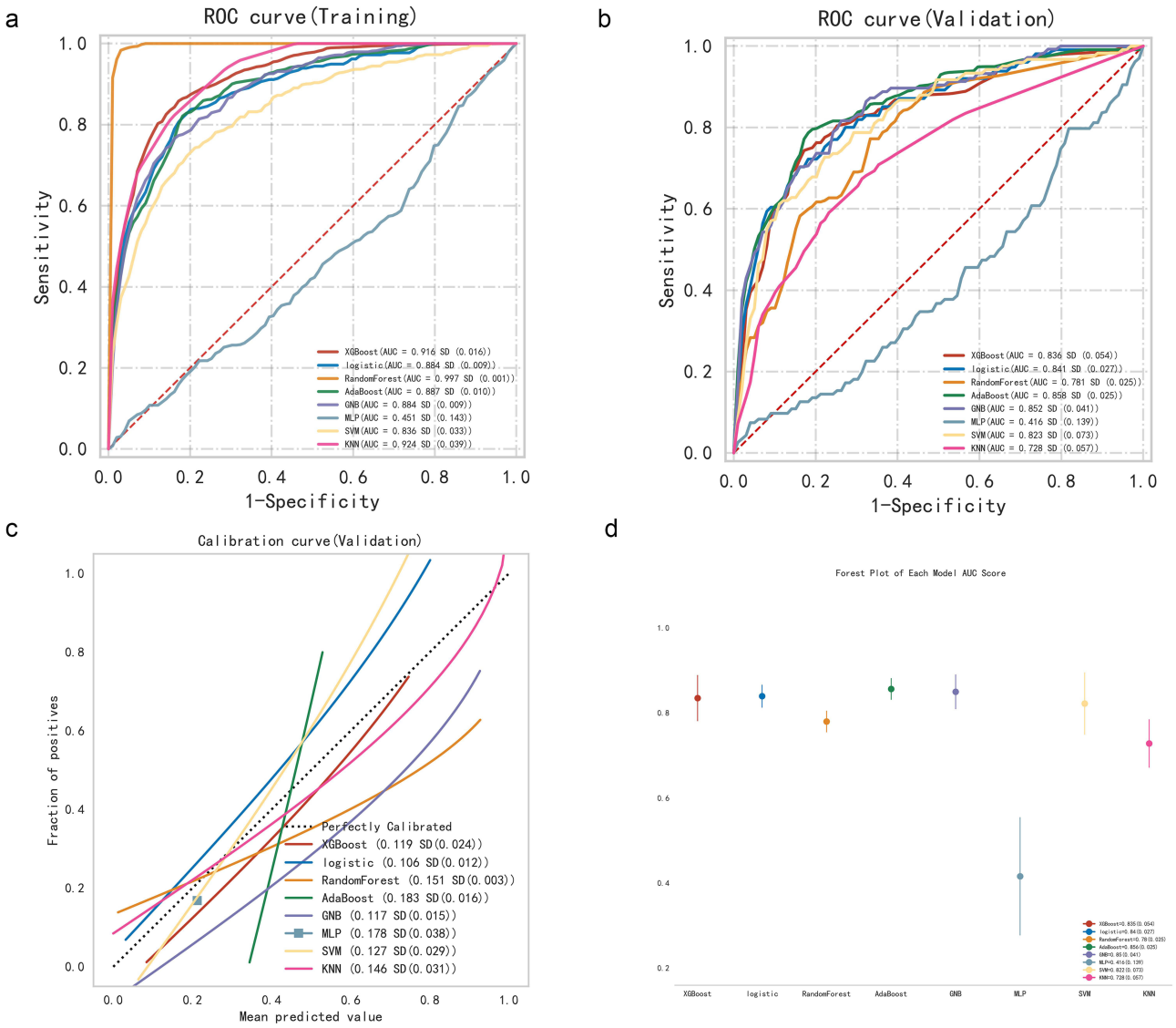

Figure 2 Construction and comparison of multiple machine learning models ROC curve analysis of machine learning algorithms for predicting residual/recurrent of high-grade cervical intraepithelial neoplasia (CIN) post-loop electrosurgical excision procedure (LEEP) in the train (**a**) and validation set (**b**). (**c**) Calibration plots for predicting residual/recurrent with various models and (**d**) Forest map of each model AUC score.

and HPV status into nomograms and machine learning models, achieving high C-indexes and AUCs. Our study builds on these research and introduces an optimized predictive model for high-grade CIN after conization. We identified six critical variables through machine learning algorithms, achieving an impressive AUC of 0.94. This model improves

Table 3 Diagnostic Performance of the XGBoost Model for the Prediction of Residual or Recurrent High-Grade CIN After LEEP

Model	Cut off	AUC	Accuracy	Sensitivity	Specificity	PPV	NPV	F1 score
Training set	0.308	0.940	0.855	0.912	0.840	0.565	0.972	0.697
Validation set	0.308	0.865	0.768	0.939	0.714	0.428	0.920	0.584
Test set	0.321	0.827	0.821	0.706	0.905	0.523	0.927	0.599

Abbreviations: CIN, cervical intraepithelial neoplasia; LEEP, loop electrosurgical excision procedure; AUC, area under the curve; PPV, positive predictive value; NPV, negative predictive value; XGBoost, extreme gradient boosting.

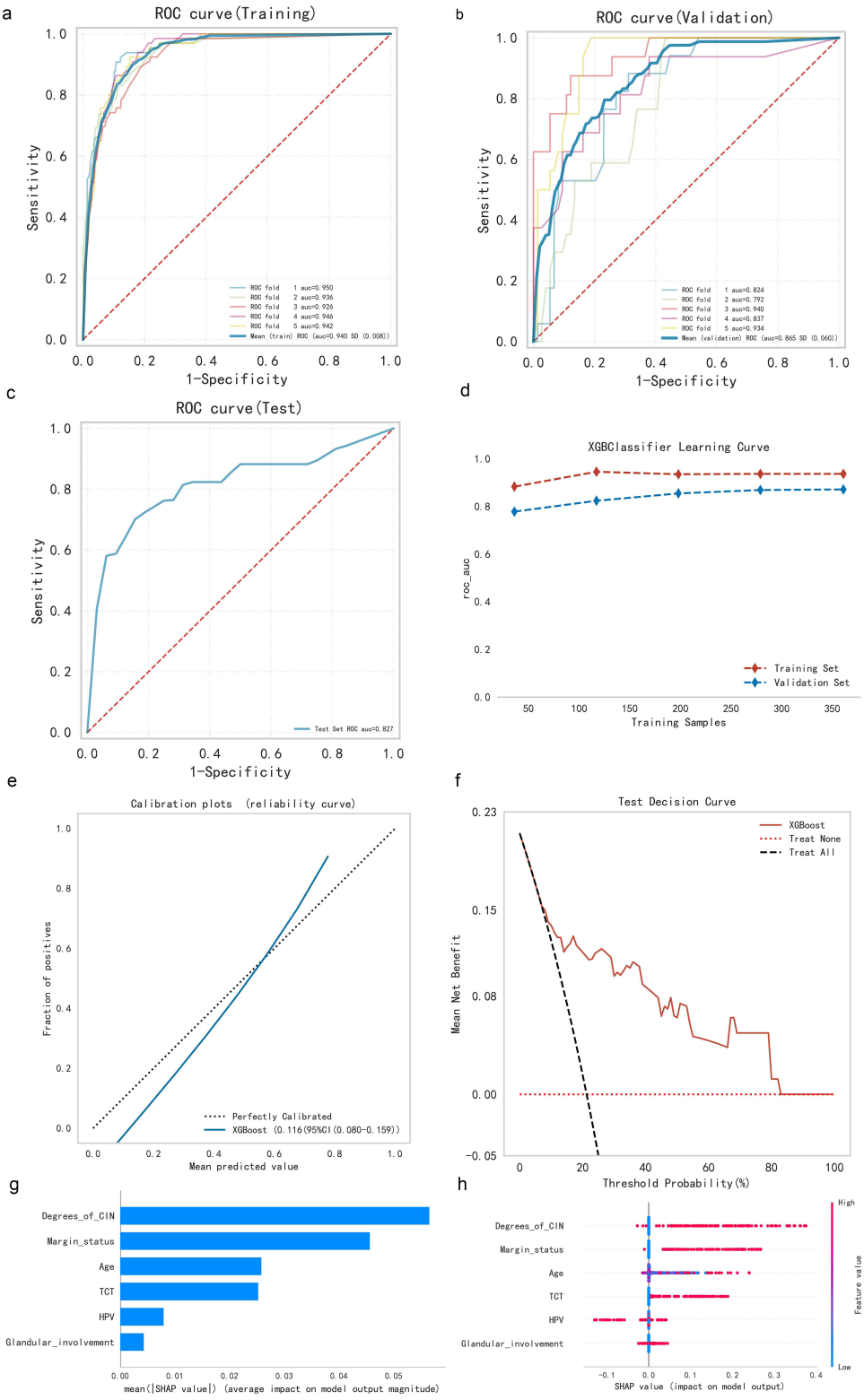

Figure 3 Construction and assessment of extreme gradient boosting (XGBoost) model. The ROC curves of XGBoost using the fivefold cross-validation on the training set (**a**), validation set (**b**), and test set (**c**). (**d**) Machine learning curve and (**e**) calibration plots for XGBoost. (**f**) Decision curve analysis graph showing the net benefit against threshold probabilities based on decisions from model outputs. Feature Importance SHAP summary chart and bar chart. (**g**) The bars on the left represent the importance of the variables and their overall contribution to the model predictions. (**h**) The right dot plot represents the direction of contribution of each value of each variable, with red representing larger values and blue representing lower values of each variable.

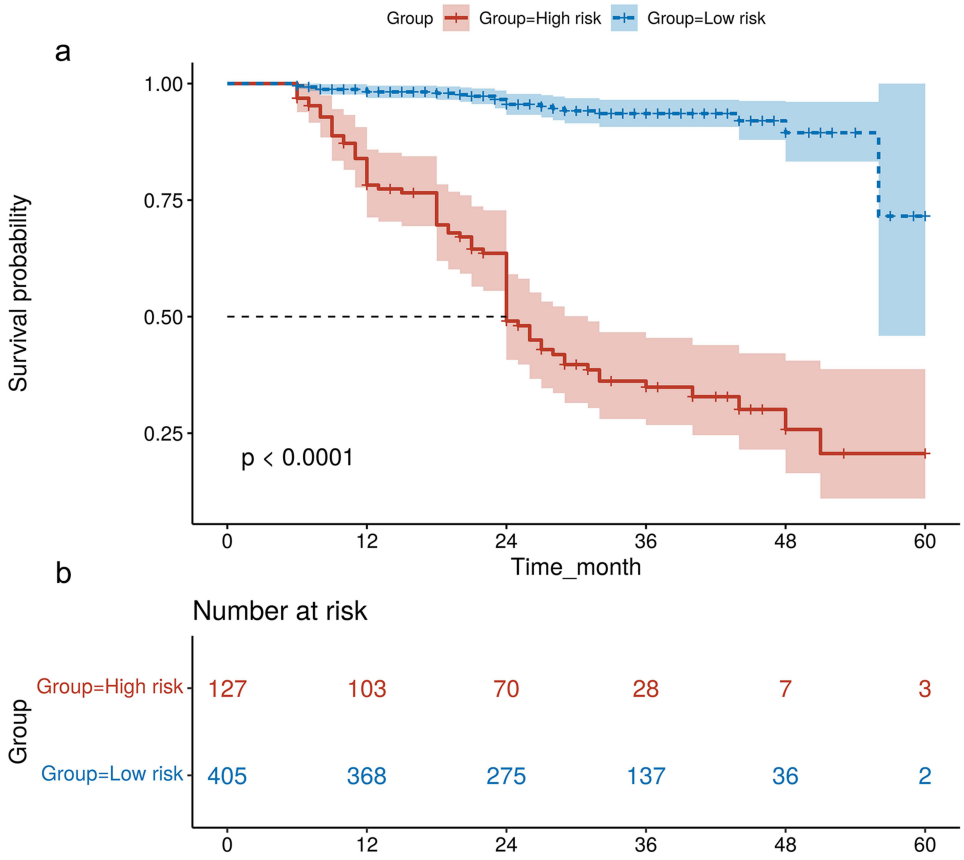

Figure 4 Kaplan-Meier survival curves for the risk of residual disease or recurrence in patients with high-grade cervical intraepithelial neoplasia (CIN) after conization, stratified into high-risk and low-risk groups based on a predictive model. (**a**) The Kaplan-Meier curve and (**b**) number at risk in residual/recurrent.

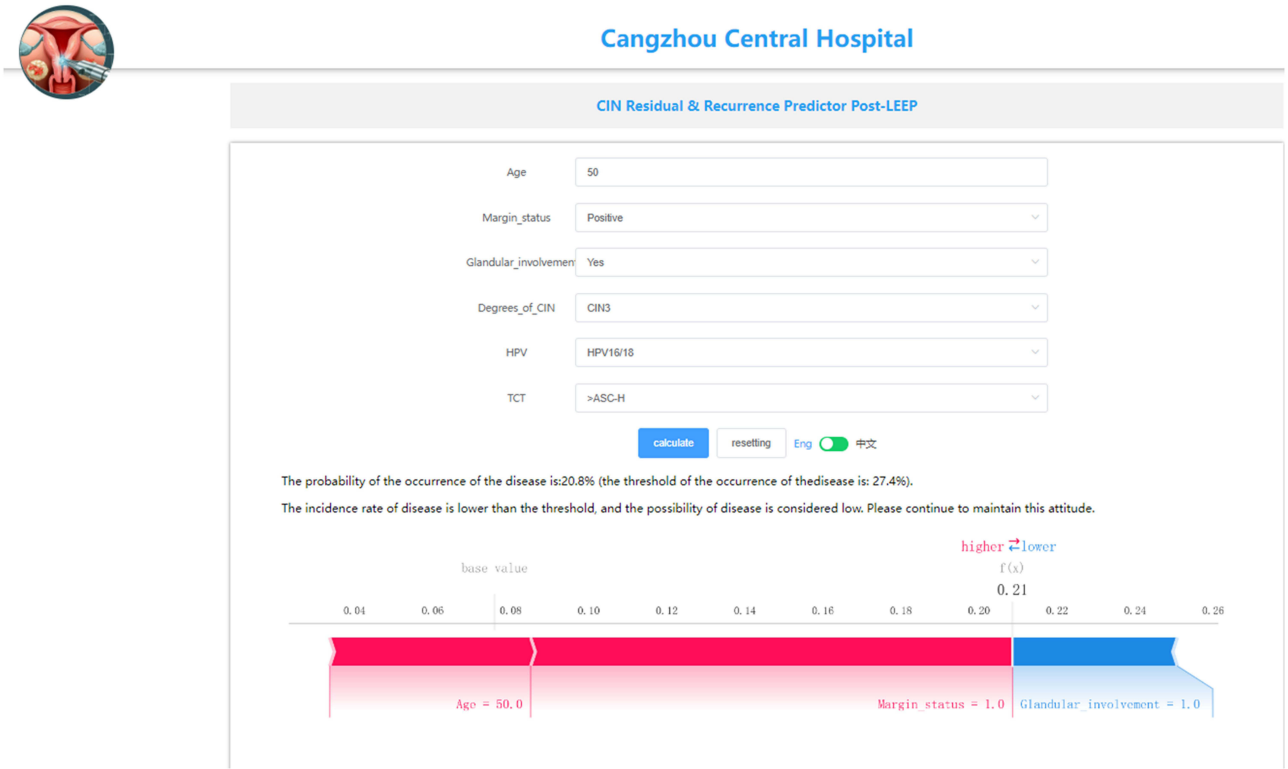

Figure 5 The web-based calculator for predicting the risk of residual/recurrent of cervical dysplasia.

predictive accuracy and enhances clinical decision-making, highlighting the potential of machine learning to optimize patient management and follow-up strategies in cervical dysplasia care.

Several factors have been identified as potential predictors of residual and recurrent disease following LEEP conization. These include positive surgical margins, which suggest incomplete lesion excision,[11] and persistent high-risk human papillomavirus (HR-HPV) infection, indicating ongoing viral activity that may drive disease progression.[24] Other factors such as smoking,[25] number of pregnancies,[26] and history of immunosuppression[26] have also been implicated, potentially due to their influence on the immune response and viral clearance. This study successfully identified six critical variables through feature selection for predicting residual and recurrent high-grade CIN after conization. The predictive model we established incorporates these variables and provides insight into patient prognosis post-surgery.

Utilizing advanced SHAP technology, our research has systematically examined and prioritized the importance of different predictors for the residual and recurrent of high-grade CIN post-Loop LEEP. Through the use of SHAP importance plots and summary charts, we found that the severity of CIN emerges as the most crucial predictive factor, followed by margin status, age, TCT results, HPV typing, and glandular involvement. This hierarchy reveals that higher CIN grade, positive margin status, age over 50 years, High-Grade TCT results (ASC-H/HSIL), and HPV16/18 genotypes are linked to a heightened risk of residual disease or recurrence.

In alignment with the bulk of extant research,[27,28] our analysis underscores the primacy of CIN severity as a pivotal predictor for the residual or recurrence of disease. This concordance among studies[12,29] reinforces the reliability of CIN severity as a prognostic marker. The escalated risk associated with higher-grade CIN lesions is likely due to the augmented probability of incomplete resection or the presence of multifocal disease. Moreover, our findings corroborate the significant prognostic value of margin status, ranking it the second most critical predictor. This aligns with the established correlation between positive surgical margins and heightened risk for residual or recurrent CIN.[30,31] Nevertheless, discrepancies exist within the literature regarding the paramountcy of margin status, potentially attributable to variances in definitions of margin positivity, methodologies employed in margin evaluation, and the prevalence of positive margins across different cohorts.[10] The incorporation of age as a considerable predictive factor in our model is supported by prior studies,[28,32,33] although the degree of its significance relative to other predictors varies. While specific studies have highlighted age as a foremost factor, others deem it less consequential, possibly influenced by the demographic composition of the study cohorts and the interplay of additional confounding variables.[34] Our analysis also identifies the outcomes of the TCT as a predictive element, aligning with existing literature.[35,36] However, the relative importance of TCT compared to factors such as CIN severity, margin status, and age has been less extensively examined. Our findings suggest that while TCT holds value in risk stratification, its predictive utility may be subordinate to the abovementioned variables. Furthermore, our study validates the role of HPV genotype classification as a predictor, mirroring findings from previous research.[10,11,37] Nevertheless, the significance attributed to HPV classification diverges across studies. This may be influenced by the prevalence of high-risk HPV genotypes in the populations studied and the methodologies applied for HPV detection. Lastly, glandular involvement is considered a lesser but pertinent predictive factor, consistent with prior study.[38,39] Its relative diminution in importance in our study might stem from the lower incidence of glandular involvement within our patient cohort or the dominance of other more impactful predictors.

In conclusion, utilizing SHAP values in our analysis provides a detailed and understandable assessment of risk factors for post-LEEP residual or recurrence in high-grade CIN, offering a solid foundation for further research and clinical interventions. Variations in the importance of these predictive factors in different studies can be attributed to various factors such as study design, patient demographics, treatment approaches, and analytical methodologies. Furthermore, the interaction between these factors and their potential combined effects may impact their relative significance in predicting residual or recurrent CIN.

The strength of our study is the development of a prognostic assessment model for HSIL patients, which uniquely combines preoperative and postoperative follow-up factors. Based on this machine learning predictive model, we propose clear risk thresholds and follow-up guidelines. For low-risk patients (predicted probability <10%), we recommend returning to routine 3-year screening intervals if co-testing is negative at 12 months, with the possibility of extending to 5-year intervals if results remain negative at 24 months. Moderate-risk patients (10–20%) should undergo co-testing every 6 months for the first year, with colposcopy at 12 months, and can return to routine screening if all tests are negative for 24 months. High-risk

patients (>20%) require colposcopy and biopsy at 6 and 12 months, quarterly co-testing for 24 months, and can transition to semi-annual follow-ups if three consecutive tests are negative thereafter. We propose that patients can transition from close post-treatment monitoring to routine screening when their predicted CIN3+ risk falls below 5% and they have two consecutive negative co-tests 12 months apart.

This stratified follow-up algorithm clearly differentiates between low and high-risk patients, allowing for resource optimization while ensuring adequate surveillance. It's important to note that any abnormal result during follow-up should prompt immediate colposcopy and biopsy if necessary, regardless of the risk category. While our model serves as a valuable supplement to standard post-operative co-testing and colposcopy, it is not intended to replace these procedures. For areas lacking comprehensive follow-up capabilities, the model's preoperative factors can be used for initial risk stratification, although we acknowledge that the performance of the preoperative prediction model still needs improvement. We recognize that these specific risk thresholds and follow-up protocols require validation in large-scale prospective studies.

While our model demonstrates improved predictive accuracy and patient-centered care, it is subject to several limitations and considerations. The retrospective, single-center design and lack of independent external validation constrain its generalizability across diverse populations and healthcare settings. Incomplete data and limited information on specific patient characteristics and emerging biomarkers (such as p16 and Ki-67) may impact the model's comprehensiveness. Moreover, our study does not fully account for the rapidly evolving landscape of cervical cancer prevention. As more women undergo multiple rounds of HPV-based screening and HPV vaccination becomes more prevalent, the risk profile for CIN3+ recurrence is likely to change. Earlier detection and treatment of smaller, less advanced lesions may lead to improved surgical outcomes and reduced recurrence rates, while the decreasing prevalence of high-risk HPV types 16 and 18 in vaccinated populations may alter the overall burden of high-grade CIN. These factors, along with potential changes in screening intervals and follow-up protocols, underscore the need for our model to be adaptable and regularly updated.

Conclusions

Our machine learning model, validated through metrics such as AUROC, accuracy, and SHAP analysis, provides accurate predictions for residual or recurrent high-grade cervical intraepithelial neoplasia post-LEEP. The integration of an accessible online prediction tool enhances its utility, particularly in resource-limited settings. This approach not only supports existing screening protocols but also showcases the transformative potential of machine learning in enhancing patient management and enabling personalized, early intervention strategies in cervical cancer prevention.

Data Sharing Statement

Some or all of the datasets generated and/or analyzed in the current study are not publicly available, but are available on reasonable request by the relevant authors.

Ethics

This study was approved by the Ethics Committee of Cangzhou Central Hospital (Approval No: 2021-054-02). The requirement for patient consent was waived due to the retrospective nature of the study, which involved anonymized data from medical records and posed minimal risk to the participants. The use of anonymized data ensured that individual privacy was protected. The study strictly adhered to the principles outlined in the Declaration of Helsinki, ensuring that all patient information was handled with confidentiality and used solely for research purposes.

Consent to Participate

Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

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Disclosure

The authors declare no competing interests.

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