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A machine learning-based risk prediction model for diabetic oral ulceration

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Abstract

Background Diabetic oral ulceration (DOU) is a prevalent and debilitating complication among diabetic patients, significantly impairing their quality of life and imposing substantial economic burdens. Studies indicate that over 90% of diabetic patients experience oral complications, with 45% suffering from oral ulcers. Clear diagnosis is crucial for effective clinical management and prognosis improvement. However, current diagnostic methods often fall short in early detection and intervention. Machine learning (ML) has shown promise in predicting disease development, yet no relevant predictive models for DOU have been established.

Methods This study aimed to develop an ML-based predictive model for DOU using oral examination, clinical, and socioeconomic data. The dataset included 324 diabetic patients, with 127 DOU features. One-hundred-fold cross-validation was employed for model optimization and feature selection. Data preprocessing involved handling missing values, scaling different range values, and feature selection using techniques such as Variance Threshold (VT), Mutual Information (MI), and Variance Inflation Factor (VIF). Four prediction models, Support Vector Machine Classifier (SVC), Multi-layer Perceptron (MLP), Logistic Regression Classifier (LogReg), and Perceptron, were established and evaluated.

Results The SVC model outperformed the other models, achieving an accuracy (ACC) of 0.95 and an area under the ROC curve (AUC) of 0.91. The top five features contributing to the model's predictions were the current number of oral ulcers, diminished oral functional capacity, number of decayed or missing teeth, possession of health insurance (commercial), and Low-Density Lipoprotein (LDL-C), accounting for 57.32% of the total importance. Oral examination indicators accounted for 46.46%, serum lipid markers for 6.93%, and sociodemographic factors, personal lifestyles, and cardiovascular diseases also played significant roles.

Conclusion The SVC model demonstrated superior performance and stability, making it suitable for predicting DOU occurrence and development in diabetic patients. This study's innovation lies in the comprehensive evaluation of multiple factors, including oral examinations, physiological indicators, self-management capabilities, and economic factors, to facilitate efficient DOU screening. The findings highlight the potential of ML in improving diagnostic accuracy and enabling timely interventions for DOU, ultimately contributing to better clinical management and

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patient outcomes. Future research should focus on validating the model across larger, multicenter cohorts and further exploring the long-term impact of ML-guided interventions on DOU management.

Keywords Diabetes, Oral ulcer, Machine learning, Predictive model

Introduction

Diabetic oral ulceration (DOU) refers to oral mucosal lesions and ulcers developing in patients with diabetes mellitus (DM) due to the disease itself and its associated complications. The oral cavity is particularly susceptible to the effects of chronic hyperglycemia [1]. Unlike skin tissue, the non-keratinized oral mucosa exhibits a weaker inflammatory response upon ulceration, resulting in a shorter self-repair process [2]. However, prolonged hyperglycemia disrupts immune homeostasis, leading to sustained inflammation, delayed wound healing, and recurrent ulcers with extended durations [3]. Ulcers, a common issue during the healing process, cause oral pain and dysphagia, significantly impacting the quality of life for individuals with DM [4]. Studies indicate that over 90% of DM patients experience oral complications [5], with a staggering 45% suffering from oral ulcer (OU) [6]. Furthermore, persistent hyperglycemia and immune imbalance increase the risk of oral infections and subsequent complications [7]. Despite the significance of DOU, current treatments remain expensive, complex, and often demonstrate low bioavailability, with potential for biotoxicity [8]. Given these limitations, early identification and intervention are crucial for effective DOU management.

OU is characterized by a persistent breach in oral epithelium integrity, often accompanied by varying degrees of underlying connective tissue damage, resulting in a crater-like appearance. While some OU types exhibit distinctive features, such as the stellate shape and well-defined margins of tuberculous ulcers or the easily identifiable location and morphology of traumatic ulcers [9], many others lack such distinct characteristics. This visual similarity poses significant challenges for accurate diagnosis and treatment [10]. The multifactorial nature of OU further complicates diagnosis, especially when the etiology is unclear or complex, and clinical presentations are atypical [9]. Chronic wounds are also associated with various systemic conditions, including gastrointestinal disorders, malignancies, and dermatological diseases [11], some of which share clinical features with DOU [9]. Notably, diabetic neuropathy can lead to oral sensory impairment and a general decline in well-being, potentially masking oral lesions in DM patients [12].

DM patients often seek medical attention after complications arise, significantly increasing their burden. Consequently, managing DM and its complications heavily relies on patient self-management [13]. This multifaceted concept encompasses physical, psychological, social, spiritual, and disease-related symptom or treatment changes [14]. Self-management strategies include dietary modifications, physical activity, blood glucose monitoring, adherence to medication regimens, effective problem-solving and coping skills, risk-reducing behaviors, and consistent self-care practices [13]. As a cornerstone of DM care, self-management profoundly impacts the quality of life for individuals with DM [15]. Notably, oral health serves as a crucial indicator of overall well-being [16]. Given the strong correlation between DM and OU, it can be hypothesized that effective DOU management hinges on robust self-management skills, potentially assessed through oral health, psychological well-being, and social determinants of health [16].

The visual similarities between DOU and other OU types pose significant challenges for accurate diagnosis. Machine learning (ML) has shown promise in improving the accuracy and efficiency of predicting oral disease development [17]. For example, ML models, including Support Vector Machine (SVM), Random Forest (RF), and Convolutional Neural Networks (CNN), have achieved high accuracy in detecting oral disease from radiographic images and clinical data [18]. These models can be incorporated into the diagnostic process, thereby enabling clinicians to maintain consistency in their diagnostic conclusions and effectively addressing challenges associated with insufficient clinical experience [19, 20]. By conducting a comprehensive assessment of oral examinations, physiological indicator changes, self-management capabilities, and economic factors, effective screening of DOU may be facilitated [21]. To date, according to our literature search in databases such as PubMed and Web of Science, no studies have specifically utilized ML for the risk prediction of DOU (search terms: "machine learning," "diabetes", "oral ulcer". The workflow of the paper screening process as per the PRISMA guidelines [22] is presented in Fig. 1). Therefore, this study aims to comprehensively evaluate the efficacy of ML-based methods in automatically predicting DOU.

The following null hypotheses were addressed:

1. To develop an ML-based predictive model for DOU recurrence using oral, clinical, and socioeconomic data.
2. To identify key risk factors and evaluate their contributions to DOU pathogenesis.
3. To provide actionable insights for integrating ML-driven predictions into clinical workflows, enabling personalized patient management.

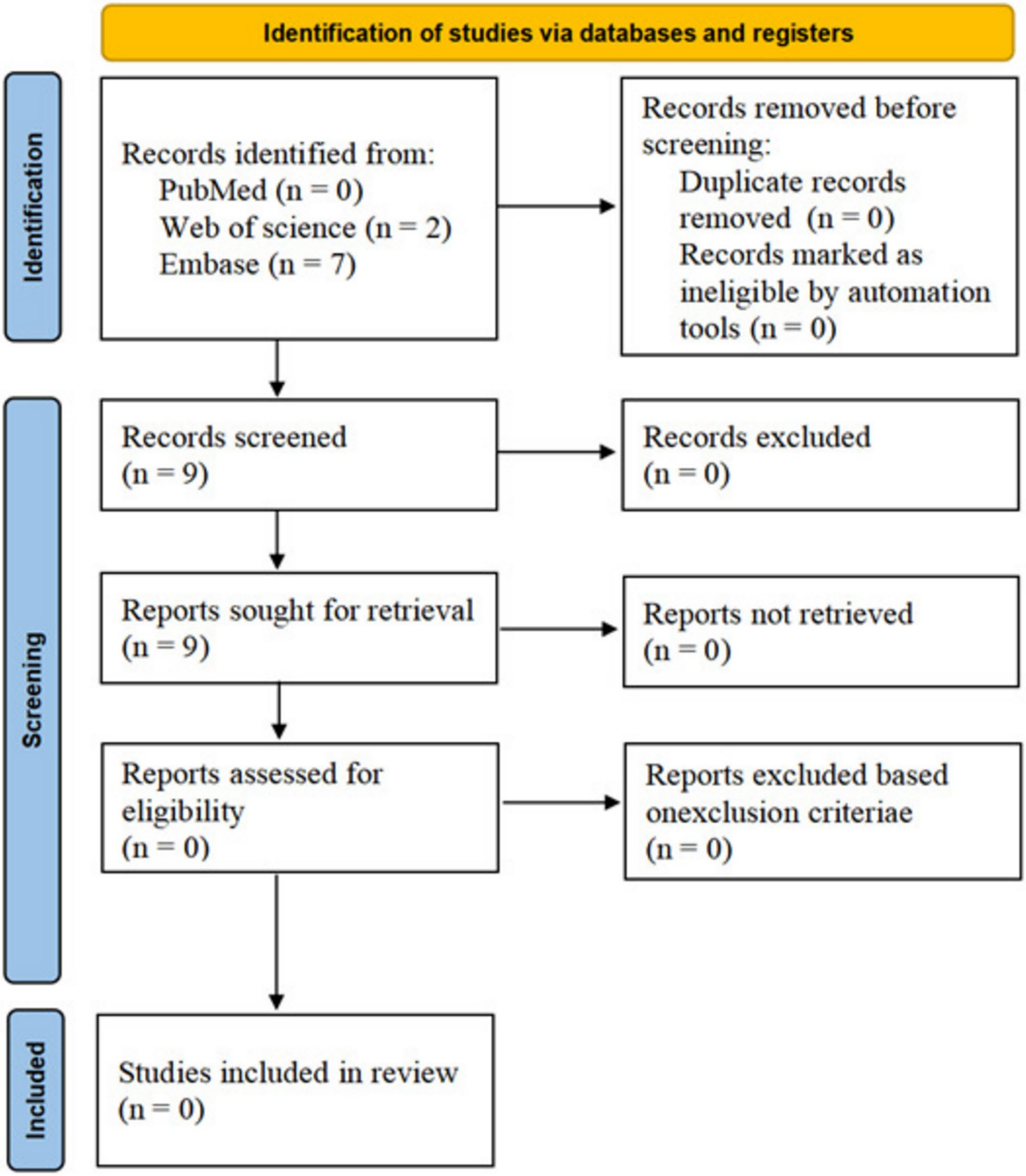

Fig. 1 Search strategy followed as described in PRISMA guidelines
*Criteria for considering studies for this study
The following inclusion criteria were used: (1) Main focus of the article must be, ML and its application to diabetic oral ulcer. (2) Studies reporting predictive and measurable outcomes. (3) Proper mention of the datasets used to assess a model
Following exclusion criteria were used: (1) Review articles, letters to editors, and case reports/conference abstracts.(2) The articles related to diagnosis use ML, but address the other oral issues.(3) Full-text articles, not available or accessible

Materials and methods

Participants

This study enrolled patients diagnosed with DM from the Endocrinology Department outpatient and inpatient services at Xinhua Hospital Affiliated with Shanghai Jiao Tong University School of Medicine, between April 2023 and July 2023. The study involved voluntary participation and informed consent from all participants. Patients with (i) severe liver or kidney disease or other critical illnesses (e.g., malignancies), (ii) incomplete or severely missing diagnostic information, or (iii) refusal to participate were excluded. Clinical information of participants, including self-management practices, local oral examinations, patient economic-related data, biochemical data, and 127 other risk indicators (detailed in Supplemental Table 1), was collected. The target feature column evaluated the inclusion sample based on "OU recurrence". Concurrently, reference categories for cross-validation were subgroup 0 (no recurrence) or subgroup 1 (recurrence present).

Cross-validation

This study utilized Repeated Stratified Random Sampling Cross-Validation as the validation scheme for model evaluation. This scheme combines the advantages of stratified sampling and repeated experiments to maintain the relative proportions of each class in the original dataset between training and testing sets, thereby enhancing the reliability and robustness of evaluation results. Specifically, In this study, we employed Repeated Random Subsampling Validation (also known as Monte Carlo Cross-Validation, MCCV) as the cross - validation scheme to evaluate the performance of various models. This method involves randomly dividing the dataset into training and testing sets 100 times independently (num_iterations = 100), with each division following an 80% training set and 20% testing set ratio (test_size = 0.2). Stratified sampling (stratify = y) was used to ensure the consistency of class distribution in both the training and testing sets. Compared to k - Fold Cross - Validation, this approach assesses model performance by repeatedly and randomly dividing the training and testing sets. Each time, the combination of training and testing data is new, thereby reducing the potential bias that may result from a single division.

In cases where there is sample imbalance between the training and validation sets during cross-validation, oversampling can be employed as a solution. Oversampling involves handling the divided training set separately during each cross-validation fold, followed by training the model on the oversampled dataset. This method involves analyzing minority class samples and artificially synthesizing new samples to add to the dataset. Specifically, Synthetic Minority Oversampling Technique (SMOTE) was used, generating a random point from minority class samples and including neighboring samples to construct new samples for computation [23].

Prediction models

Recognizing that combining multiple feature variables is more effective in DOU diagnosis than relying on a single indicator, this study aimed to evaluate the diagnostic capability of different feature combinations using machine learning techniques. Initially, t-Distributed Stochastic Neighbor Embedding (t-SNE) plots were used to examine the two-dimensional distribution of various indicators in the training and validation datasets, representing the potential combinations of indicators during the diagnostic process. Subsequently, correlation analysis among indicators in the training set confirmed significant positive or negative correlations, indicating synergistic or antagonistic roles of these indicators in diagnostic applications. Employing 100-fold cross-validation for model optimization and feature selection, t-SNE was used to reduce the dimensionality of feature variables, and a confusion matrix was constructed to build prediction models. Detailed information is presented in Figs. 2 and 3.

A range of machine learning algorithms were developed to mitigate the impact of algorithmic bias for each MC validation. Support Vector Machine Classifier (SVC), Multi-layer Perceptron (MLP), Logistic Regression Classifier (LogReg), and Perceptron were established as the optimal prediction models with minimal errors. Subsequently, each model commenced training using pre-processed training data that was randomly selected. Detailed parameters of each algorithmic model can be seen in Supplemental Table 2.

Data preprocessing

Handling missing values

Due to the presence of missing values in the dataset, features with more than 20% missing values were removed [24]. Features with less than 20% missing values were imputed using available data and their internal relationships to predict missing values [25], primarily using zero imputation and mean imputation, where missing values were replaced with zeros or the mean of corresponding feature observations [26].

Handling different range values

For features with different scales in the dataset, specifically varying in size or units, scaling was necessary to facilitate comparison and weighting across dissimilar features. This was achieved primarily through Min-Max normalization. Min-Max normalization linearly scales unnormalized data to a predefined range, typically between 0 and 1 or -1 and 1 [27].

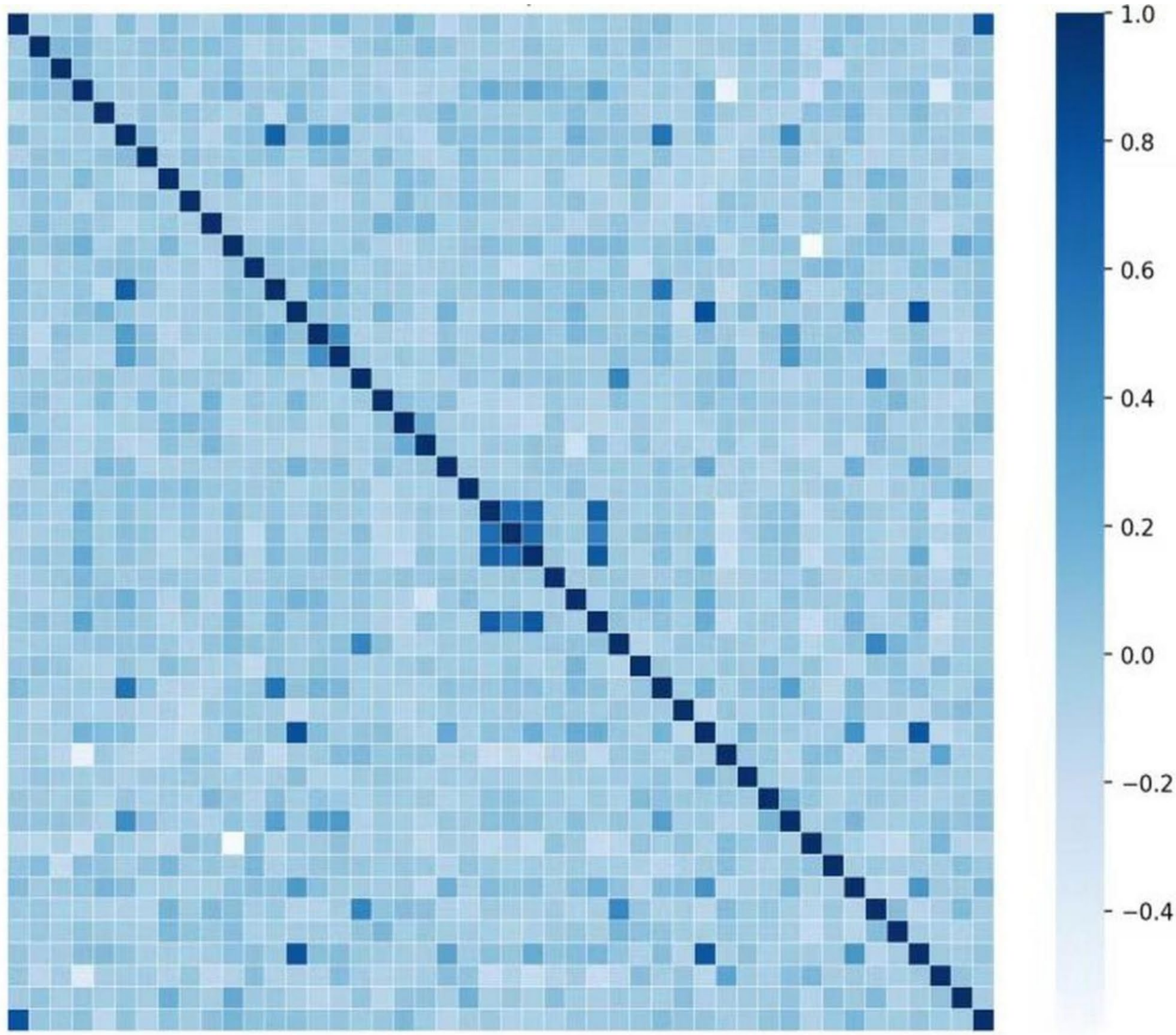

Fig. 2 Correlation matrix view of data: correlation values of 1 and – 1 represent 100% linear and inverse relationships between two features, respectively. Features with correlation values close to 0 are considered non-redundant

Feature selection

Feature Selection aims to discover the optimal feature set for constructing the model of interest. Effective feature selection can improve classification accuracy, whereas using too many features may lead to overfitting and be unsuitable for model construction. In this study, various feature selection techniques were employed, such as Variance Threshold (VT), Mutual Information (MI), and Variance Inflation Factor (VIF), to enhance model performance.

Variance threshold

Features with higher variance typically contain more useful information and should thus be retained in the ML model. VT filters and eliminates features with lower variance or those below a specific threshold. By default, features withzero variance, indicating no variation in sample feature values, are removed [24, 28].

Mutual information

MI is a measure of correlation used to assess the relevance between independent variables and the dependent variable. It selects features that are highly correlated with the label and have minimal redundancy with other features, typically achieved by selecting an appropriate threshold [29].

Variance inflation factor

Variance Inflation Factor (VIF) is a function used to detect multicollinearity, quantifying the extent to which the variance of regression coefficients increases when predictor variables are correlated. When predictor

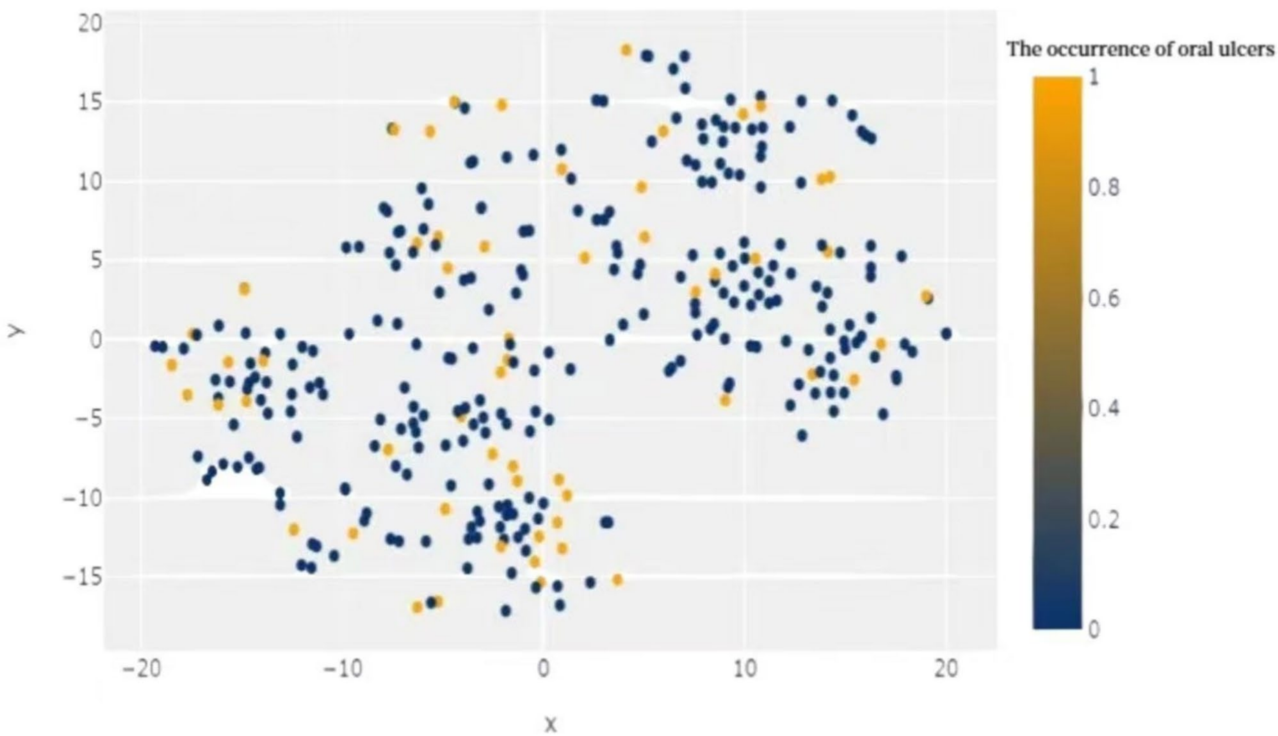

Fig. 3 t-Distributed stochastic neighbor embedding (t-SNE) visualization of data: samples are colored based on their respective label outcomes

Table 1 Cross-validation parameters, data balancing technique and feature selection criterias

Data Preprocessing	Strategy	Algorithm	Parameters
1	Imputation	Zero Imputation	-
2	Imputation	Mean Imputation	-
3	Scaling	Min-Max	-
4	Feature Selection	Variance Threshold	threshold = 0.02
5	Feature Selection	Mutual Information	Kept Top 60 features
6	Feature Selection	VIF	threshold = 10
7	Oversampling	SMOTE	-

variables are linearly related, VIF measures how much the variance inflation occurs compared to what it would be if predictors were orthogonal. A VIF value greater than 10 is commonly used as a robust indicator of multicollinearity. In cases where there is significant linear correlation among multiple variables, the standard errors of one or more individual regression coefficients may be overly inflated. To obtain more accurate results, variables with high VIF values can be removed from the model [30, 31].

These series of data preprocessing steps provide a reliable and standardized data foundation for subsequent analysis, ensuring the scientific rigor and accuracy of the study.

Details of Cross-Validation Parameters, Data Balancing Technique and Feature Selection Criterias can be Seen in Table 1.

Construction of prediction algorithms

To mitigate methodological biases and enhance prediction accuracy, four different prediction model algorithms were considered in this study: SVC, MLP, LogReg, and Perceptron. Each model will be comprehensively evaluated and compared in subsequent experiments to gain a thorough understanding of their performance on the current research problem.

Classifiers

Support vector machine classifier (SVC)

SVC is a classification algorithm based on support vector machines, aiming to find a hyperplane that effectively separates samples from different classes [32]. SVC exhibits strong expressive power. In this study, we chose the linear kernel as the kernel function for SVC. The linear kernel is suitable for handling linearly separable problems, performing inner product operations in high-dimensional space to linearly separate samples in that space.

Multilayer perceptron (MLP)

MLP is an artificial neural network composed of multiple layers of neurons trained using the backpropagation algorithm [33]. MLP utilizes non-linear activation functions at each neuron, capable of capturing complex non-linear relationships, making it suitable for complex classification tasks.

Logistic regression classifier (LogReg)

LogReg is a generalized linear model used for solving binary classification problems. It models the log-odds function and adjusts model parameters by maximizing likelihood estimation [34]. LogReg is widely applied in various fields due to its simple yet effective performance.

Perceptron

Perceptron is a simple linear classifier that classifies inputs by weighted summation and applying a threshold [34]. Despite lower performance compared to more complex models, Perceptron performs well in some straightforward classification tasks and has lower computational complexity.

Performance evaluation

In this study, we utilized Confusion Matrix analysis as the primary tool to evaluate the performance of the proposed models. A Confusion Matrix is a two-dimensional matrix used to compare the relationship between the model's predicted results and actual observations. Through the Confusion Matrix, multiple performance metrics can be computed, including but not limited to Accuracy (ACC), Sensitivity (SEN), Specificity (SPE), Positive Predictive Value (PPV), Negative Predictive Value (NPV), Occurrence (OCC), and F1 Score.

Accuracy (ACC)

ACC is the proportion of correctly predicted samples to the total number of samples. It is calculated as follows: ACC = (TP + TN) / (TP + TN + FP + FN). where TP is true positives, TN is true negatives, FP is false positives, and FN is false negatives.

Sensitivity (SEN)

SEN is also known as recall, represents the proportion of actual positives that are correctly predicted as positives. It is calculated as follows: SEN = TP / (TP + FN).

Specificity (SPE)

SPE is also known as recall, represents the proportion of actual positives that are correctly predicted as positives. It is calculated as follows: SPE = TN / (TN + FP).

Positive predictive value (PPV)

PPV is the proportion of predicted positives that are actually positive. It is calculated as follows: PPV = TP / (TP + FP).

Negative predictive value (NPV)

NPV is the proportion of predicted negatives that are actually negative. It is calculated as follows: NPV = TN / (TN + FN).

Occurrence (OCC)

Occurrence represents the weight ratio of various machine learning algorithms in cross-validation.

F1 score

F1 Score is a harmonic mean of precision and recall, used to measure the accuracy of binary classification models. It is calculated as follows: F1 Score = 2 × Precision × SEN / Precision + SEN. where F1 Score ranges from 0 (worst) to 1 (best), balancing precision and recall when evaluating model performance.

The F1 score primarily addresses the issue of the imbalance between precision and recall in model results. In practical evaluations, precision and recall of a model are often contradictory; that is, when precision is high, recall may be very low, and when recall is high, precision may be relatively low. When it is unclear whether to use precision or recall to evaluate a model, the F1 score can be considered.

Receiver Operating Characteristic curve (ROC) and Area Under Curve (AUC)

In addition to Confusion Matrix analysis, ROC curve and AUC were employed as evaluation metrics. ROC curve is a graphical tool illustrating the relationship between True Positive Rate (TPR) and False Positive Rate (FPR) at different thresholds. AUC quantifies the performance of the model across various thresholds, with values closer to 1 indicating better model performance. Through comprehensive analysis of these performance metrics, we gain a comprehensive understanding of the model's performance across different aspects and effectively evaluate its feasibility in practical applications.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD) or median, and categorical variables are presented as numbers and percentages (%). Mann-Whitney U test was used to analyze continuous variables, while chi-square test was used for categorical variables. Correlation regression analysis (Cor) was conducted to explore potential linear correlations among indicators in the training set, where $P < 0.05$ indicates statistical significance. t-SNE is a nonlinear dimensionality reduction algorithm in machine learning, used to visualize high-dimensional data and mitigate overfitting issues [35]. We employed t-SNE to visualize the results of indicators involved in routine laboratory tests.

Results

Characteristics of participants

A total of 324 DM patients with 51.5% ($n = 167$) males were included, aged 15 to 97 years (median: 66 years). The diabetes durations was ranged from 4 to 17 years (median: 11 years), among them, 48 were newly diagnosed DM [36]. We divided the data into a training group (267 cases with recurrent OU) and a validation group (113 cases without recurrent OU), from totally 127 features, 46 (82%) were identified as potential risk factors.

Evaluation of model performance

In our current study, we selected the best-performing algorithm among SVC, MLP, LogReg, and Perceptron using metrics such as AUC, ACC, SEN, PPV, NPV, and F1 Score. As shown in Fig. 4, the AUC values of the four classification algorithms ranged from 0.89 to 0.91, with SVC, LogReg, and Perceptron all having AUC values greater than or equal to 0.90. Table 2 shows that SVM performed the best among the four classification algorithms, with average scores in the training set under various evaluation criteria: AUC (0.91), Accuracy (0.95), Sensitivity (0.877), Specificity (0.977), PPV (0.85), NPV (0.97), and F1 Score (0.84). Standard deviations of performance metrics across different evaluation criteria are also provided in Table 3. Generally, standard deviation reflects the variability of model performance metrics across different cross-validation folds, indicating performance uncertainty. Although the AUCs of the four classification algorithms were similar, SVM showed the least variability in metrics such as ACC, PPV, SNS, F1 Score, and OCC, suggesting its performance stability relative to other classifiers. Overall, SVM exhibited the best performance and stability among the tested algorithms, with corresponding standard deviation scores of AUC (5.99), Accuracy (0.95), Sensitivity (0.877), Specificity (0.977), PPV (0.85), NPV (0.97), and F1 Score (0.84).

The performance of the SVC model in all MC-fold cross-validations was established through confusion matrix analysis, with an average AUC of 0.91 (CI: 90.49–91.71). See Figs. 5 and 6 for details.

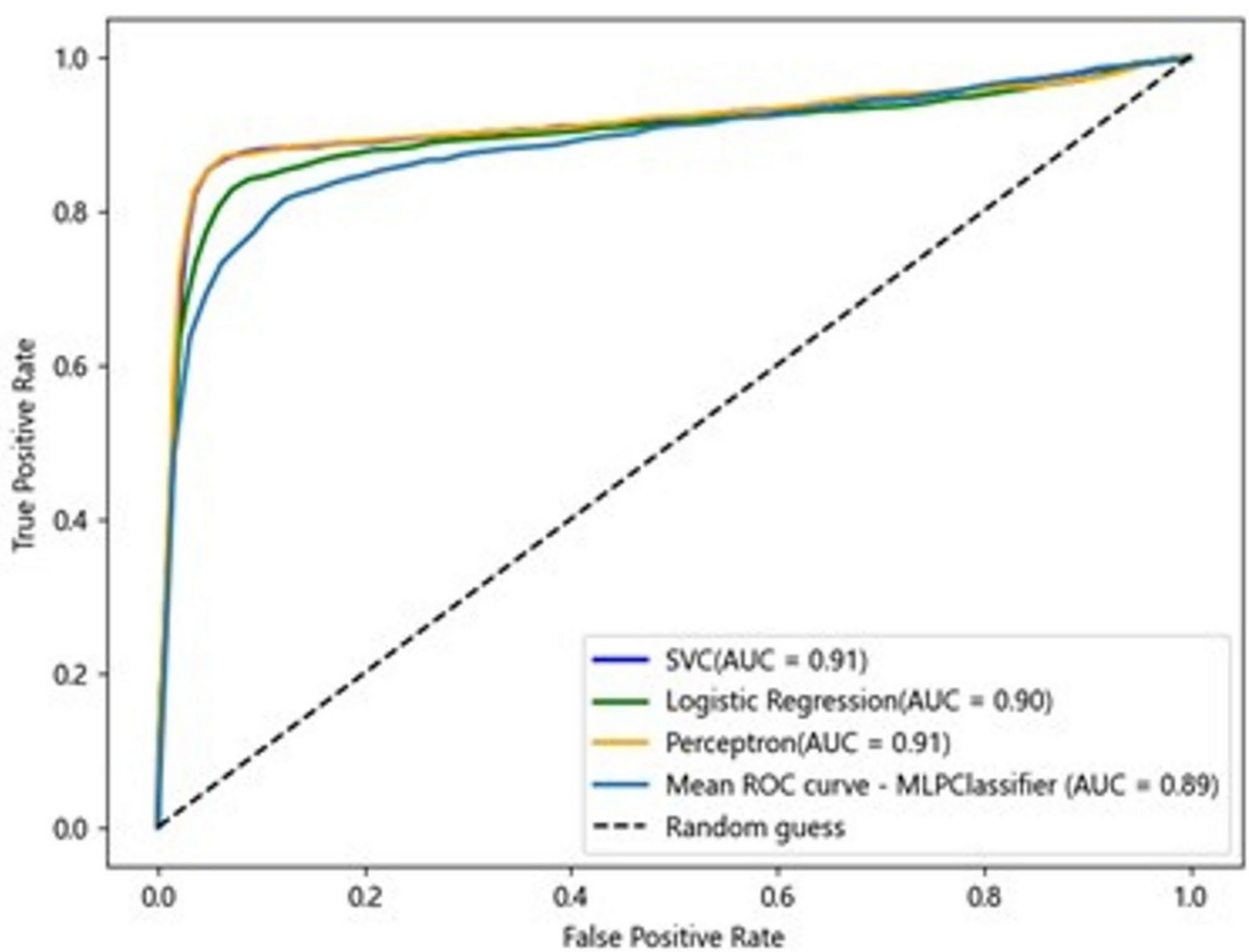

Fig. 4 Comparison of average ROC curves across 100 cross-validation folds for each model

Table 2 Average performance metrics matrix of each classification algorithm across 100 cross-validation folds

Mean(95%CI)	ACC	PPV	SNS	F1	AUC	OCC	NPV	SPC
SVC	94.74(94.28–95.20)	85.34(83.76–86.93)	84.09(81.98–86.20)	84.24(82.80-85.67)	91.11(89.93–92.29)	94.74(94.28–95.20)	96.91(96.52–97.29)	84.09(81.98–86.20)
MLP	90.77 (90.15–91.39)	73.00 (70.76–75.23)	75.55 (73.11–77.98)	73.41 (71.67–75.15)	89.27 (88.11–90.43)	90.77 (90.15–91.39)	93.87 (93.22–94.52)	75.55 (73.11–77.98)
LogReg	93.26 (92.75–93.77)	81.03 (79.12–82.94)	80.18 (77.83–82.54)	79.93 (78.35–81.51)	89.94 (88.77–91.12)	93.26 (92.75–93.77)	95.93 (95.45–96.40)	80.18 (77.83–82.54)
Perceptron	90.65 (88.85–92.44)	76.65 (73.06–80.24)	81.64 (78.86–84.41)	76.84 (74.23–79.45)	91.46 (90.30-92.63)	90.65 (88.85–92.44)	92.48 (90.25–94.71)	81.64 (78.86–84.41)

Abbreviations: ACC Accuracy, PPV Positive Predictive Value, SNS Sensitivity, F1 F1 Score, AUC Area Under the ROC Curve, OCC Occurrence, SPC Specificity, NPV Negative Predictive Value. Performance values are presented as percentages

Table 3 Standard deviation matrix of performance metrics for each model across 100 cross-validation folds

Standard Deviation(%)	ACC	PPV	SNS	F1	AUC	OCC	NPV	SPC
SVC	2.32	8.04	10.71	7.27	5.99	2.32	1.94	10.71
MLP	3.15	11.34	12.38	8.85	5.88	3.15	3.30	12.38
LogReg	2.58	9.68	11.95	8.04	5.99	2.58	2.41	11.95
Perceptron	3.22	20.82	21.85	21.00	6.06	3.22	1.55	21.85

Abbreviations: ACC Accuracy, PPV Positive Predictive Value, SNS Sensitivity, F1 F1 Score, AUC Area Under the ROC Curve, OCC Occurrence, SPC Specificity, NPV Negative Predictive Value. Performance values are presented as percentages

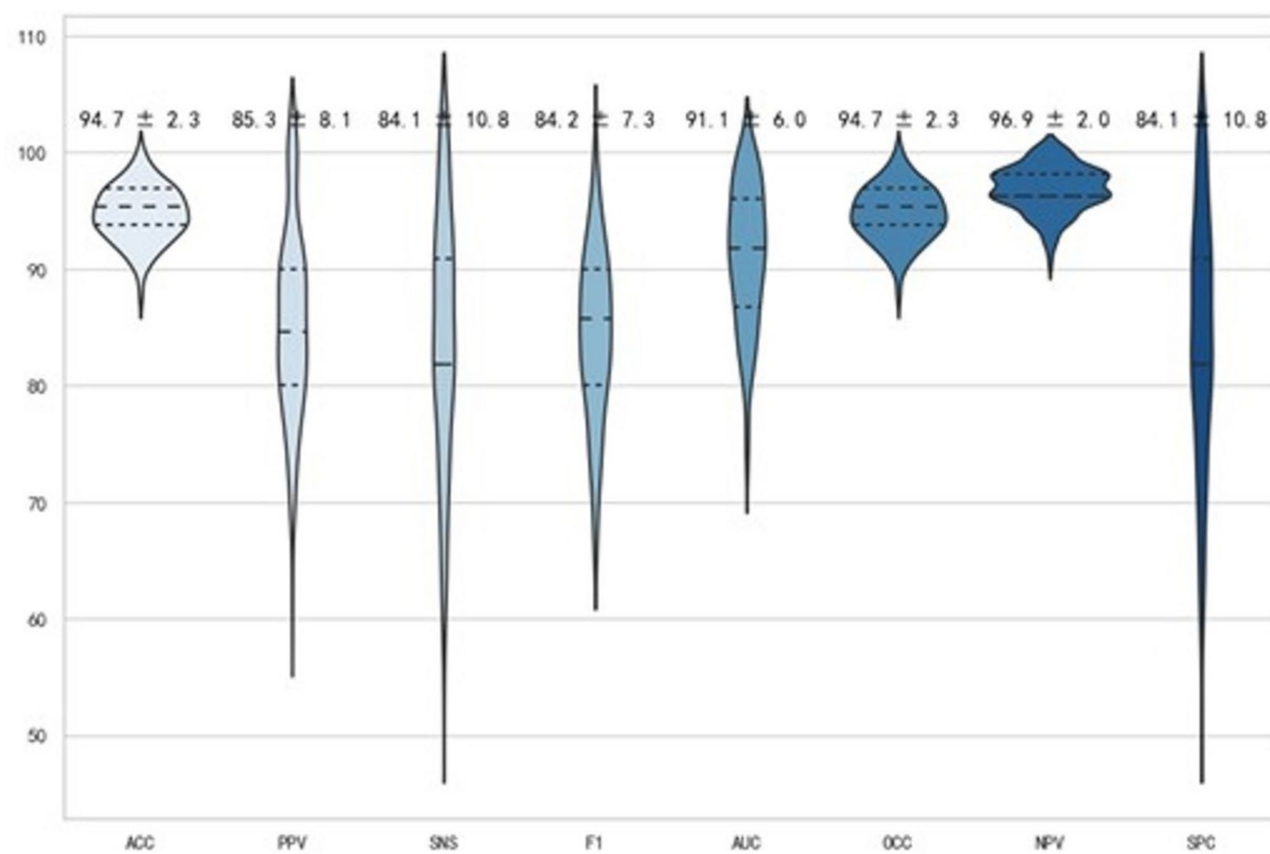

Fig. 5 Performance of SVC Model under 100 Cross-Validations. Abbreviations: ACC Accuracy, PPV Positive Predictive Value, SNS Sensitivity, F1 F1 Score, AUC Area Under the ROC Curve, OCC Occurrence, SPC Specificity, NPV Negative Predictive Value. Performance values are presented as percentages

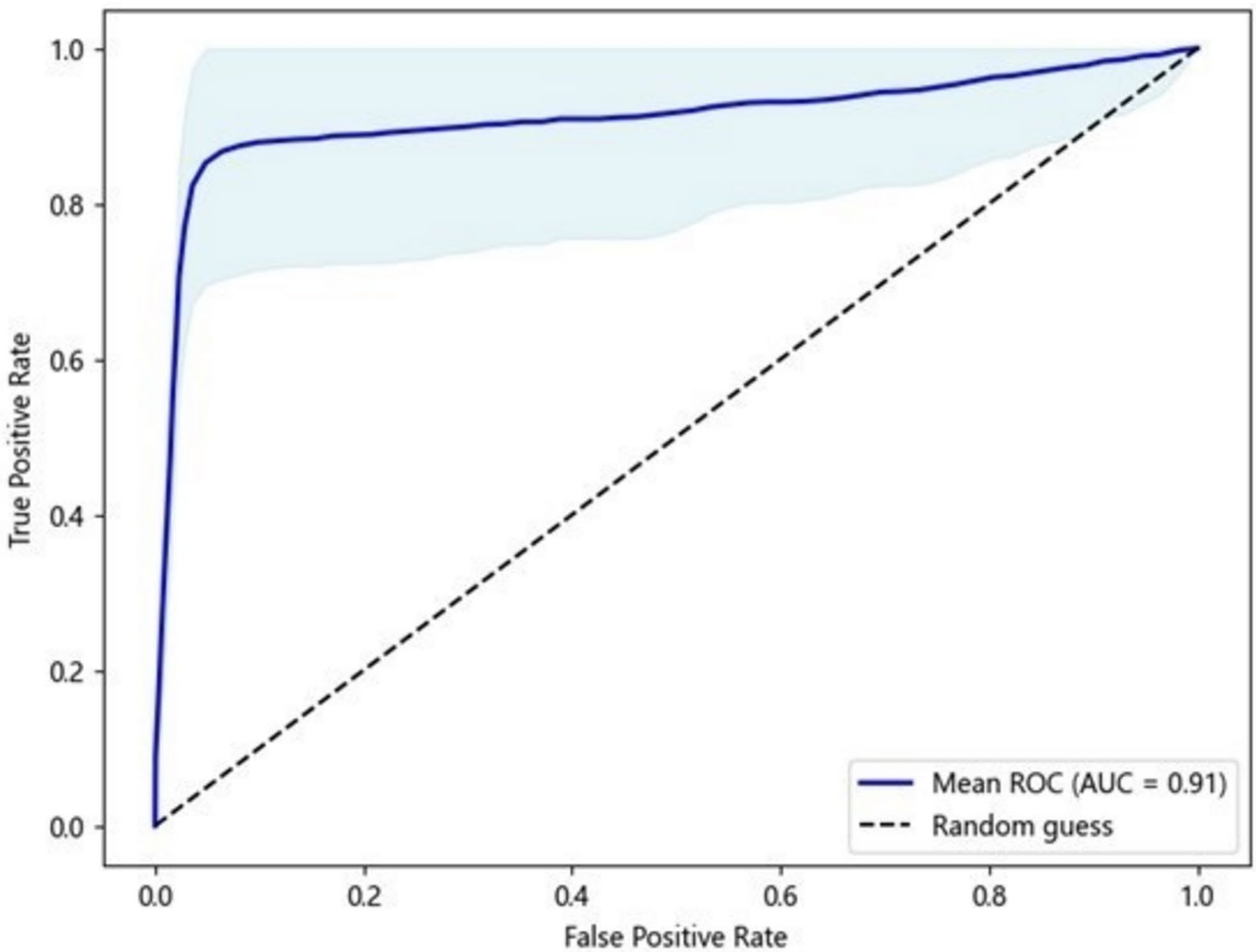

Fig. 6 Average receiver operating characteristic (ROC) curve for SVC model across 100 cross-validations

Feature weighting and distribution

Feature ranking and selection were performed as part of the data preprocessing steps for each fold (see preprocessing section). The final feature importance computation listed the top 30 features based on the average ranking across all features in MC folds. The final feature ranking is shown in Fig. 7. Through 100 Monte Carlo cross-validation folds involving 127 features, the top 30 features were identified based on average importance rankings. These encompassed oral examination findings, biochemical indicators, and epidemiological data. Analysis revealed several insights: Firstly, the top 5 highly ranked features included current number of oral ulcers, diminished oral functional capacity, number of decayed or missing teeth, possession of health insurance (commercial), and Low Density Lipoprotein (LDL-C), accounting for 57.32% collectively. Secondly, oral examination features, such as current number of oral ulcers, decayed or missing teeth, dental caries, loose teeth, and gingival texture, accounted for 46.46%. Thirdly, laboratory indicators including LDL-C, 2-hour postprandial blood glucose (2hPG), fasting blood glucose (FBG), and Triglyceride (TG) collectively contributed 6.93%. Lastly, sociodemographic factors (e.g., family support), personal lifestyle (e.g., preference for salty or vegetarian diet), and cardiovascular diseases (e.g., cerebrovascular disease, hypertension), while less contributing, also played a role in DOU prediction. The final feature ranking is shown in Fig. 7; Table 4.

Discussion

ML has demonstrated promising potential in enhancing the accuracy and efficiency of predicting the progression of oral diseases, particularly in early detection, disease identification, and the development of personalized treatment plans [37–39]. However, its application in the field of DOU remains limited. Our study reveals that the use of an ML ensemble algorithm, including SVC, MLP, LogReg, and Perceptron, for the prediction and identification of DOU yields excellent diagnostic performance. Further analysis of the model's predictions identified five key features influencing its performance: The damage

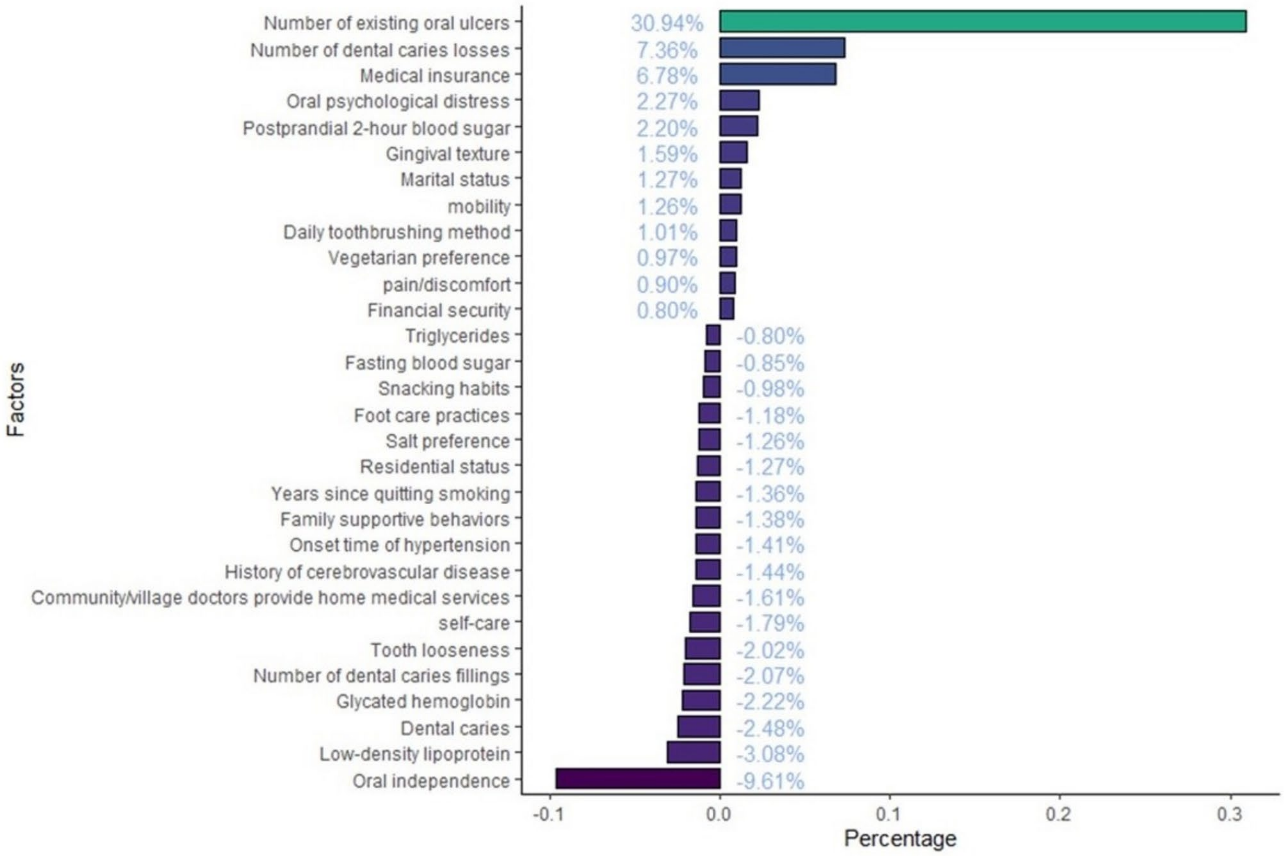

Fig. 7 Average feature importance ranking of SVC model across 100 cross-validation folds

status of oral mucosa and gingiva, the decline of oral functional capacity, oral health - related quality of life, the biochemical indicators related to diabetes or cardiovascular diseases, and the presence or absence of diabetes or cardiovascular diseases. These five factors accounted for 57.32% of the total importance. Our findings demonstrate that machine learning algorithms can effectively integrate multidimensional patient information, particularly for the prediction of DOU, a complex and variable condition, offering reliable support for clinicians and addressing the limitations of traditional diagnostic methods.

In this study, an ML ensemble algorithm employing SVC, MLP, LogReg, and Perceptron was utilized for DOU prediction and identification, demonstrating good diagnostic performance. The AUC values of all four algorithms were approximately 90%, indicating their reliable performance. However, SVC and Perceptron exhibited AUC values of 91%, with similar PPV, though SVC outperformed Perceptron in other metrics, boasting lower standard deviations in F1 score and AUC. Therefore, SVC emerged as the optimal performer. This suggests the feasibility of developing mobile applications based on the SVC model for clinical use, inputting patient-related risk factors to predict DOU occurrence and formulate personalized management strategies for precision treatment.

Oral examinations, which include the assessment of ulcer count, dental caries and tooth loss, dental caries, tooth mobility, and the fragility of gums, among others, significantly contribute to overall importance, accounting for as much as 46.46%. This underscores the necessity for a comprehensive oral examination that meticulously evaluates the lips, gums, oral mucosa, tongue, and pharynx, which is crucial for the definitive diagnosis of DOU. For patients with DM, changes in the oral environment often progress slowly [40], and potential neurological impairments may delay the patient's detection of these subtle changes, thereby affecting the timely implementation of necessary interventions [41]. Our study highlights that local oral changes have a decisive impact on the prediction and diagnosis of DOU. Furthermore, since local oral lesions have the highest weight in the DOU prediction model, this indicates that maintaining good oral hygiene is not only critical in reducing the risk of oral lesions but also in further mitigating the risk of DOU. It also emphasizes the necessity of adopting preventive local oral management measures to prevent DOU [42]. This depends on the patient's ability and willingness to

Table 4 Feature importance statistical table

Feature	Mean Ranking ± Dev	Min	Max	LQ	Median	UQ
Number of existing oral ulcers	30.49 ± 1.96	24.81	35.16	29.11	30.52	31.68
Oral independence	-9.61 ± 3.28	-16.82	-0.88	-11.66	-9.52	-7.55
Number of dental caries losses	7.36 ± 2.60	2.03	13.58	5.47	7.71	9.11
Medical insurance	6.78 ± 3.87	-0.27	14.28	4.65	7.87	9.11
Low-density lipoprotein	-3.08 ± 1.76	-7.51	1.14	-4.20	-3.17	-1.83
Dental caries	-2.48 ± 1.61	-7.76	1.38	-3.61	-2.38	-1.33
Oral psychological distress	2.27 ± 2.77	-4.38	9.21	0.33	2.07	4.12
Glycated hemoglobin	-2.22 ± 1.78	-7.06	1.24	-3.36	-2.09	-0.94
Postprandial 2-hour blood sugar	2.20 ± 1.92	-1.92	7.32	0.77	2.03	3.45
Number of dental caries fillings	-2.07 ± 1.48	-5.51	2.67	-2.90	-2.04	-1.21
Tooth looseness	-2.02 ± 1.06	-5.30	-0.07	-2.51	-2.01	-1.23
Self-care	-1.79 ± 1.42	-5.41	1.51	-2.61	-1.72	-1.10
Community/village doctors provide home medical services	-1.61 ± 1.27	-5.05	0.00	-2.44	-1.47	-0.58
Gingival texture	1.59 ± 0.86	-0.35	4.06	0.92	1.62	2.11
History of cerebrovascular disease	-1.44 ± 1.00	-4.85	0.19	-1.88	-1.36	-0.69
Onset time of hypertension	-1.41 ± 1.45	-4.57	1.56	-2.44	-1.41	-0.14
Family supportive behaviors	-1.38 ± 0.90	-3.63	0.04	-1.91	-1.28	-0.69
Years since quitting smoking	-1.36 ± 2.00	-7.00	2.02	-2.51	-0.91	0.01
Marital status	1.27 ± 1.50	-2.79	4.95	0.59	1.17	2.29
Residential status	-1.27 ± 2.25	-9.65	3.24	-2.11	-0.80	0.04
Mobility	1.26 ± 1.90	-3.47	5.49	0.18	1.22	2.62
Salt preference	-1.26 ± 1.15	-4.17	0.00	-2.07	-1.11	0.00
Foot care practices	-1.18 ± 1.05	-3.73	1.01	-1.89	-1.25	-0.33
Daily toothbrushing method	1.01 ± 0.58	-0.52	2.35	0.57	1.00	1.39
Snacking habits	-0.98 ± 0.75	-2.78	1.06	-1.42	-1.00	-0.46
Vegetarian preference	0.97 ± 1.59	-1.61	7.47	-0.19	0.81	1.77
Pain/discomfort	0.90 ± 1.37	-2.04	5.44	-0.10	0.71	2.03
Fasting blood sugar	-0.85 ± 1.45	-5.66	3.23	-1.99	-0.82	0.13
Financial security	0.80 ± 0.99	-1.31	3.56	0.08	0.81	1.51
Triglycerides	-0.80 ± 1.83	-6.52	3.42	-1.74	-0.60	0.38

establish and maintain a high standard of oral hygiene over the long term [43]. The high weight contribution of reduced independent ability in this prediction model (9.61%) supports the aforementioned conclusion and reflects that the current lack of oral independent ability in DOU patients is an urgent issue that needs to be addressed. A multidisciplinary team may be effective, but close collaboration between healthcare providers and patients is even more critical [44], taking into account the patient's skill level, knowledge, motivation, and values for personalized health education [45], while also teaching patients to correctly identify periodontal symptoms, such as gum bleeding during brushing or eating, tooth mobility, and gum pain, and to seek medical attention promptly [44]. This study also found that brushing methods are one of the predictive factors for DOU. This implies that specific guidance on brushing methods should be included in the health education intervention plan for DOU patients, including the specific selection of toothbrushes and toothpaste, as well as the timing and frequency of brushing [46]. However, relevant research is limited, and there is a lack of evidence-based clinical guidance. Future research can focus on filling this gap, generating high-quality evidence to enhance the efficiency of clinical practice guidance.

Oral health quality is a comprehensive metric that reflects not only an individual's oral and physical health status but also encompasses psychological and social health aspects. In this study, we found that factors such as commercial insurance ownership, economic status, oral psychological discomfort, and family support play significant roles in the prediction of DOU. Specifically, having commercial insurance may imply a higher income level and lower economic stress for patients, enabling them to access a richer array of medical resources, including more detailed screening and diagnostic services, which could potentially have a positive impact on oral health [47]. Oral issues such as ulcers, dental caries, and tooth loss not only lead to changes in oral structure but may also affect a patient's chewing, speech, and facial aesthetics [48], further exacerbating the psychological pressure of diabetic patients, triggering or worsening psychological discomforts such as tension, depression, and anxiety [49]. The non-healing ulcers caused by diabetes may prolong the treatment period, increase economic burdens, and further affect the psychological state of patients [50]. This psychological discomfort may, in turn, exacerbate the symptoms of DOU, creating a vicious cycle. Family support plays a role not only by directly assisting patients but also by improving their psychological discomfort and promoting the correction of self-behavior [51], ultimately affecting the occurrence and development of DOU. Additionally, we found that cerebrovascular diseases, hypertension, and living arrangements may also affect the occurrence and development of DOU. Although the number of related studies is currently limited and no definitive conclusions have been drawn, these factors may indirectly affect oral health quality through their impact on the ability to live independently. In summary, these characteristics together constitute the key dimensions for assessing oral health quality. The more relevant characteristics an individual has, the poorer their oral health quality may be, and correspondingly, the risk of DOU may increase. Therefore, developing predictive models based on big data analysis and creating more concise and effective oral health quality scales holds great potential. At the same time, the prediction results also indicate that interventions for DOU require close cooperation among multidisciplinary experts such as oral medicine, endocrinology, cardiology, and epidemiology to provide more comprehensive oral health services.

Interestingly, laboratory indicators such as LDL-C, FPG, 2hPG, and TG collectively accounted for approximately 8% of predictive contributions. In DM patients, changes in lipid biomarkers serve as critical indicators for DOU. Dyslipidemia is a characteristic feature of DM, with TG and LDL-C serving as serum biomarkers [52, 53]. Additionally, DM patients are more susceptible to oral mucosal lesions [54]. Studies demonstrate associations between oral health abnormalities and lipid metabolism disorders; a Korean study found significant correlations between periodontitis and High levels of LDL-C and Low levels of HDL-C in women's blood [55]. In a Brazilian study, tooth loss correlated positively with total cholesterol (TC), TG, and LDL-C levels and negatively with HDL-C levels [56]. Changes in cholesterol levels among DM patients may alter immune responses [57], increasing inflammatory responses and affecting resistance to oral infection bacteria [58].

The authors suggest that the mobile application, which is based on the SVC model from this study, could provide real-time risk scores. This feature would aid in identifying high-risk patients and facilitating timely interventions. Moreover. The formation of DOU involves multifaceted factors, including oral examinations, physiological indicator changes, self-support capabilities, and economic factors. Comprehensive assessment facilitates efficient DOU screening. This also implies that there is an objective need for the development of diagnostic procedure standards. The identification of specific lipid markers (such as LDL-C, TG) and sociodemographic factors (e.g., insurance status, family support) in this predictive model indicates that the establishment of these standards should take these aspects into account. Moreover, it requires the collaborative efforts of multidisciplinary experts, including endocrinologists, dentists, and cardiologists, to achieve this goal. Despite oral health professionals typically not being included in DM management teams [59], incorporating them into future DM system management is essential based on practical needs.

Our study has several limitations. Firstly, constructing predictive models requires a large sample base [60], yet our study had a limited sample size and was a single-center analysis, potentially introducing selection bias and limiting the generalizability of conclusions. To verify result reliability, multicenter large-sample studies are necessary. Secondly, the algorithms did not classify DOU, limiting predictive effectiveness across different DOU categories. Future multicenter studies could address this issue. Risk assessment and personalized medical strategies for DOU still require clinical involvement. Therefore, further research and development are needed to overcome these challenges.

Specifically, future research should prioritize the following aspects: (1) Categorizing DOU based on diabetes type may enhance the model's applicability and accuracy. It is essential to focus on the differences in external validation across diverse patient populations and continuously refine the model accordingly. (2) The long-term impact of machine learning - guided interventions (e.g., targeted oral hygiene education) on DOU should be assessed. (3) Collaboration across multiple centers will facilitate the achievement of the above - mentioned goals.

Conclusion

In conclusion, our study developed a DOU risk prediction model based on the SVM algorithm, demonstrating high accuracy and stability. This model can be used for DOU risk warning, allowing clinicians to identify high-risk DOU patients based on risk severity and implement precise interventions, thereby providing clinical guidance and assistance in preventing DOU for DM patients.

Abbreviations

2hPG	2-hour postprandial blood glucose
ACC	Accuracy
AUC	Area under the ROC curve
DM	Diabetes mellitus
DOU	Diabetic oral ulceration
FBG	Fasting blood glucose
HDL-C	High density lipoprotein cholesterol
LDL-C	Low density lipoprotein cholesterol
LogReg	Logistic Regression Classifier
MI	Mutual Information
ML	Machine learning

MLP	Multi-layer Perceptron
NPV	Negative Predictive Value
OCC	Occurrence
OU	Oral ulcer
PPV	Positive Predictive Value
ROC	Receiver Operating Characteristic curve
SD	Standard deviation
SEN	Sensitivity
SMOTE	Synthetic Minority Oversampling Technique
SPE	Specificity
SVC	Support Vector Machine Classifier
t-SNE	T-Distributed Stochastic Neighbor Embedding
TC	Total cholesterol
TG	Triglyceride
VIF	Variance Inflation Factor
VT	Variance Threshold

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions
Conceptualization, Writing - Original Draft and Funding acquisition: W. XL. Conceptualization and Software: Z.ZQ. Writing - Original Draft and Methodology: W.BQ. collected all of the data: L.W., CL.Y and X.F. Software and Funding acquisition: G.SY. data pre-processing and Data Curation: C.HB. Data analysis: JT.L. Writing - Review & Editing and Project administration: GY.T. Validation, Visualization, Writing - Review & Editing, Project administration and Formal analysis: J.W. All authors approved the final version of the manuscript.

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Data availability
Data cannot be published without patients' consent. Researchers who are interested for academic need could contact the corresponding authors.

Declarations

Ethics approval and consent to participate
No biospecimens were collected from patients in this study. The confidentiality of patients' privacy and identity information was guaranteed, and there was no commercial interest involved, so that this research met the conditions for exemption from informed consent. This study was supported by the Ethics Committee of Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine (XHEC-D-2024-200). The conduct of this study strictly adhered to the ethical principles established by the Declaration of Helsinki, ensuring compliance with key provisions such as informed consent of participants, protection of privacy, and minimization of risks.

Consent for publication
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Competing interests
The authors declare no competing interests.

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