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ORIGINAL RESEARCH

Support Vector Machine for Stratification of Cognitive Impairment Using 3D T1WI in Patients with Type 2 Diabetes Mellitus

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Purpose: To explore the potential of MRI-based radiomics in predicting cognitive dysfunction in patients with diagnosed type 2 diabetes mellitus (T2DM).

Patients and Methods: In this study, data on 158 patients with T2DM were retrospectively collected between September 2019 and December 2020. The participants were categorized into a normal cognitive function (N) group (n=30), a mild cognitive impairment (MCI) group (n=90), and a dementia (DM) group (n=38) according to the Chinese version of the Montréal Cognitive Assessment Scale-B (MoCA-B). Radiomics features were extracted from the brain tissue except ventricles and sulci in the 3D T1WI images, support vector machine (SVM) model was then established to identify the CI and N groups, and the MCI and DM groups, respectively. The models were evaluated based on their area under the receiver operating characteristic curve (AUC), Precision (P), Recall rate (Recall, R), F1-score, and Support. Finally, ROC curves were plotted for each model.

Results: The study consisted of 68 cases in the N and CI group, with 54 cases in the training set and 14 in the verification set, and 128 cases were included in the MCI and DM groups, with 90 training sets and 38 verification sets. The consistency for inter-group and intra-group of radiomics features in two physicians were 0.86 and 0.90, respectively. After features selection, there were 11 optimal features to distinguish N and CI and 12 optimal features to MCI and DM. In the test set, the AUC for the SVM classifier was 0.857 and the accuracy was 0.830 in distinguishing CI and N, while AUC was 0.821 and the accuracy was 0.830 in distinguishing MCI and DM.

Conclusion: The SVM model based on MRI radiomics exhibits high efficacy in the diagnosis of cognitive dysfunction and evaluation of its severity among patients with T2DM.

Keywords: cognitive dysfunction, radiomics, magnetic resonance imaging, support vector machine, diabetes mellitus, type 2

Introduction

Diabetes mellitus (DM), characterized by chronic hyperglycemia, is a group of metabolic disorders. According to a national survey carried out by the Endocrine Society of the Chinese Medical Association from 2015–2017, the prevalence of diabetes among Chinese adults aged 18 years and older was 11.2%, with Type 2 diabetes mellitus (T2DM) being the most common form while Type 1 diabetes and other forms were rare. T2DM is typically characterized by decreased insulin secretion and insulin resistance. Its primary risk factors include obesity and sedentary behavior.[1–3] Alongside this, mild cognitive impairment (MCI) is a common comorbidity that affects T2DM patients, with approximately 45% (21.8–67.5%) being estimated to suffer from it.[2] However, the mechanism for cognitive dysfunction in T2DM is still unclear at present. Some proposed theories include brain blood vessels and blood-brain barrier damage, amyloidβ (Aβ) deposition, excessive phosphorylation of tau protein, insulin resistance, and oxidative stress response.[4,5] It is important to accurately assess patients' cognitive function to mitigate risk stratification and prognosis evaluation of the

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disease. Given the growing attention to MCI as a crucial factor in the diagnosis and treatment of diabetes, clinicians must pay close attention to their patients' cognitive function in the diagnosis and treatment of T2DM.[6]

Cognitive function of patients is often assessed through neuropsychological tests such as The MoCA, MMSE, and CDR. However, these assessments may not fully capture the biological diversity present in patient populations. Techniques such as structural MRI, blood oxygen level-dependent (BOLD) functional MRI, and MRI cerebral perfusion imaging have been increasingly employed to assess cognitive function. Despite their growing use, these imaging modalities still suffer from a lack of specificity,[7,8] highlighting the need for more precise diagnostic tools in the field.

Radiomics is a novel research field that employs artificial intelligence (AI) methods to extract a vast amount of high-dimensional feature information from medical images. This involves image acquisition, segmentation of regions of interest (ROIs), feature extraction, and subsequent statistical analysis, leading to the construction of statistical models using machine learning (ML) or deep learning algorithms. Such models can provide non-invasive biomarkers for diagnosis, prognosis, and treatment response monitoring of various diseases.[9,10] Previous radiomics studies have primarily focused on Alzheimer's disease, with limited research conducted on the cognitive function of patients with T2DM.[11,12] In this study, we aim to establish a SVM model based on MRI images and explore its value in predicting the severity of cognitive dysfunction of T2DM patients.

Materials and Methods

General Information

Data on a total of 158 T2DM patients were retrospectively collected in the Center for Endocrine and Metabolic Diseases of our hospital between September 2019 and December 2020. T2DM diagnosis was based on a fasting plasma glucose (FPG) level ≥7.0 mmol/L or a 2-hour oral glucose tolerance test (OGTT) glucose level ≥11.1 mmol/L.[13] Eligible participants were aged >50 years with a primary school education or above, had no central nervous system or psychiatric diseases, no severe cardiovascular disease, kidney or liver disease, not taking any psychotropic or hormonal medication within 3 weeks, can complete MRI examination under the doctors' guidance, and were right-handed. Exclusive criteria included other types of diabetes, body mass index (BMI) >35 kg/m², contraindications of MRI examination, and poor quality of MRI images.

We conducted a comprehensive analysis of the health status of the study participants, utilizing both clinical and laboratory parameters. The clinical data collected encompassed several important factors, including age, gender, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), history of coronary heart disease (CHD), history of alcohol consumption, retinopathy, and intermittent claudication. On the other hand, the laboratory data comprised an array of parameters, such as Fasting blood-glucose (FBG), Glycosylated hemoglobin (HbA1c), gamma-glutamyltransferase (γ-GGT), aspartate transaminase (AST), alanine transaminase (ALT), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG), total cholesterol (TC), serum creatinine (SCr), blood urea nitrogen (BUN), and urine creatinine (UCr). The comprehensive evaluation of these data provided valuable information about the health condition of the participants, which played a vital role in our outcome analysis.

Cognitive Function Assessment and Grouping

The cognitive function of all participants underwent assessment through the Chinese version of the MoCA-B.[14] The MoCA-B is a measure overall cognitive function and comprises eight domains. These include visuospatial and executive function (5 points), naming (3 points), memory (0 point), attention (6 points), language (3 points), abstract reasoning (2 points), delayed recall (5 points), and orientation (6 points). The total score ranges from 0–30, with one point added for individuals with less than 12 years of education. A score of ≥26 was considered normal, whereas 19–25 indicated mild cognitive impairment (MCI), and ≤18 indicated moderate to severe cognitive impairment.

Based on their MoCA-B scores, participants were separated into the normal cognitive function (N) group or the cognitive impairment (CI) group. The CI group was further divided into the MCI and Dementia (DM) groups, and 38 cases from the MCI and DM groups were randomly selected to form the CI group. The N group comprised of 30 cases,

the MCI group comprised of 90 cases, and the DM group comprised of 38 cases. Machine learning models were established separately for the N and CI groups, as well as the MCI and DM groups.

MRI Scanning Technique

The sagittal high-resolution 3D T1WI sequence was collected from all subjects using the Achieva 3.0T superconducting MRI scanner from Philips in conjunction with an 8-channel head and neck coil. To accomplish this, the whole brain scan was performed under the following parameters: TR = 7.2 ms, TE = 3.3 ms, inversion Angle = 12°, slice thickness = 2 mm, slice spacing = 0mm, excitation times = 1, matrix = 256×256, FOV = 256 mm×256 mm. To minimize movement artifacts, the subject's head was stabilized with a foam pad as they lay supine with their eyes closed and attempt to remain awake to minimize any conscious thought. This process was closely monitored by two experienced radiologists, and the scan was terminated as soon as motion artifacts appeared or the subject's active suggestion was intolerable. The MRI scans were performed on the same day as the clinical cognitive assessments, following the completion of clinical history taking and laboratory tests within a 3-day period prior to the MRI scan, to maintain a standardized protocol.

Radiomics Analysis

The region of interest (ROI)delineation, radiomics feature extraction, feature selection and machine learning models building were established on the uAI Research Portal V1.1 (Shanghai United Imaging Intelligence, Co., Ltd.)[15] (Figure 1).

Image Segmentation

ROI segmentation in this study was conducted manually on T1WI MRI images by two radiologists with 12 and 8 years of cranial MRI diagnosis experience (Feng Gu and Lili Zhao), respectively. The ROIs of the entire brain tissue excluding ventricles and sulci were delineated, ensuring that our analysis captured the full spectrum of cognitive functions affected by T2DM (Figure 2). These regions included but were not limited to the precuneus, cerebral cortex, hippocampus and posterior cingulate cortex, as these were well-established areas implicated in cognitive function and were relevant to our study's objectives. Inter-observer reliability of the manual segmentation was assessed by selecting ROIs of 20 subjects at random and having them segmented by the two radiologists. Disagreements between the two radiologists were resolved by a third radiologist with 16 years of experience (Zhigao Xu). Inter-observer agreement of the delineated ROIs was calculated using interclass correlation coefficient (ICC). An ICC value greater than 0.75 was considered indicative of good agreement.

Radiomics Feature Extraction

These features were grouped into three categories. The first group comprised of 126 descriptors that quantitatively described basic metrics related to the distribution of voxel intensities in MRI images, and belonged to the first-order statistics. The second group contained 14 3D features that reflected the size and shape of the region-based features. The third group was calculated based on gray-level run-length and gray-level co-occurrence texture matrix, comprising 525 texture features. These could quantify regional heterogeneity differences.

Radiomics Feature Selection and ML Model Construction

To improve the performance of the model and minimize redundant features, we employed dimensionality reduction analysis. We first used the variance thresholding method, setting the threshold at 0.8 to remove features with variance less than 0.8. Next, we used analysis of variance (ANOVA), a univariate feature selection method, to analyze the relationship between features and classification results based on a p-value composition. We only retained features with $P < 0.05$. The minimum absolute shrinkage sum selection operator (LASSO) with 5-fold cross-validation was then used, with the L1 regularizer as the cost function and a maximum of 1000 iterations. We employed the same feature selection method in both models. Support Vector Machine (SVM) method was used for the CI and N groups, as well as MCI and DM groups based on the optimal features selected, respectively. Finally, we divided the data into a validation set and a training set in the ratio of 2:8 and 3:7, respectively.

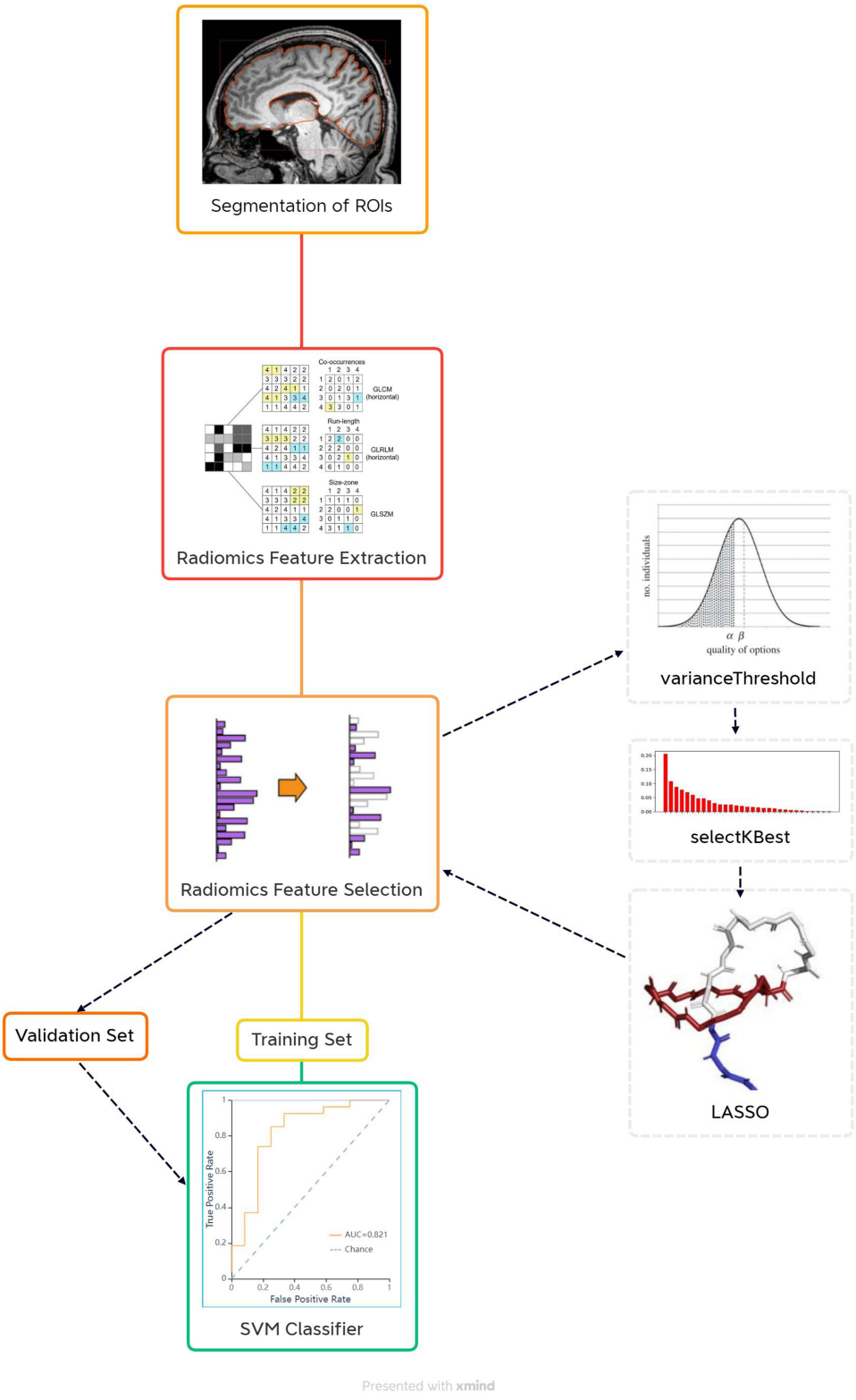

Figure 1 The workflow diagram of radiomics analysis.

Statistical Analysis

Statistical analyses were conducted on both clinical and laboratory data with SPSS version 22.0 (IBM Corp.). The Kolmogorov–Smirnov test was used to verify if the measurement data conformed to the normal distribution. Normally distributed continuous

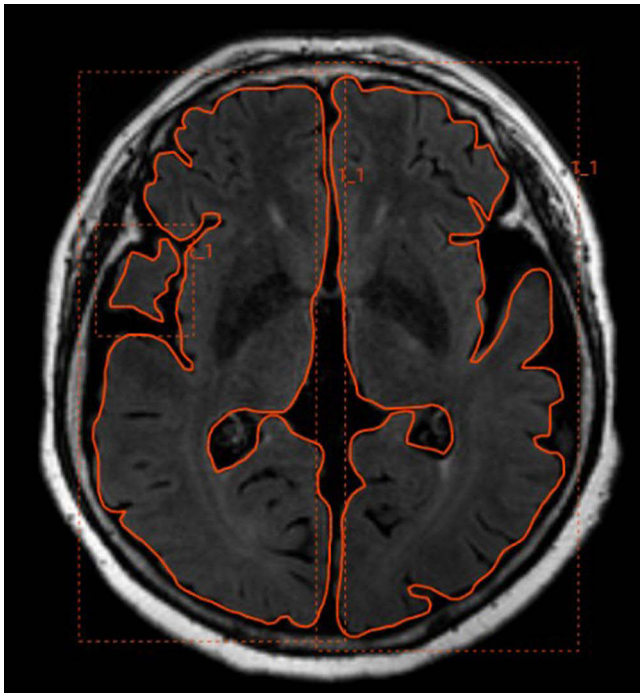

Figure 2 The ROIs on T1WI MRI images.

variables were expressed as the mean ± standard deviation ($\bar{x} \pm s$), whereas non-normally distributed variables were expressed as the median (interquartile range). The comparison of normally distributed variables between groups were tested using independent sample *t*-test and the non-parametric Kruskal–Wallis H-test were used for comparison between non-normally distributed variables. Categories variables were calculated as percentages and analyzed using the Chi-Square Test. All *P* values were 2-sided and $P < 0.05$ was considered statistically significant. Receiver operating characteristic (ROC) curves were then used to assess the predictive performance of classifiers in the training and validation sets, based on the area under the curve (AUC). And precision (*P*), recall®, F1 score, and support were also used to evaluate the models performance. Precision was calculated as true positive/(true positive + false positive), recall was defined as true positive/(true positive + false negative), the F1 score used the formula P*R*2/ (P+R), and the support metric represented the total number of observations within the test set.

Results

Comparison of General Information

In group CI compared to group N, significantly lower MoCA scores were observed ($P < 0.05$), furthermore, significantly higher age and MoCA scores were reported for the DM group in comparison to the MCI group ($P < 0.05$), which was in accordance with the clinical distribution characteristics of cognitive dysfunction.[16]

In group CI, the HbA1c and BUN levels were significantly higher than those in group N. However, no statistically significant differences were observed in systolic blood pressure, diastolic blood pressure, BMI, FBG, ALT, AST, BUA, SCr, TC, TG, HDL, LDL, T2DM duration, coronary heart disease, Malignant tumor, current or past drinking, concurrent retinopathy, or concurrent intermittent claudication when comparing the CI group with the N group or the DM group with the MCI group (all $P > 0.05$) (Table 1).

Radiomics Features Selection

We analyzed a total of 68 cases to identify the N and CI groups, comprising 54 and 14 cases in the training and validation sets, respectively. For ROI radiomic features that were manually segmented by two radiologists, the inter-group and intra-group intraclass correlation coefficients (ICCs) showed good agreement (0.86 and 0.90, respectively). We extracted 1409 radiomics features and selected 303 features based on variance threshold method (Figure 3). We then used the

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Table 1 Comparison of General Information

Characteristics	CI and N				MCI and DM			
	CI (n=38)	N (n=30)	t/c^2	*P*-value	MCI (n=90)	DM (n=38)	t/c^2	*P*-value
Age(years)	63.82±7.42	60.77±6.83	−1.71	0.09	62.12±6.94	65.18±7.20	−2.26	0.03
MoCA (scores)	19.79±4.43	26.73±0.98	8.89	0.00	21.74±2.13	14.79±2.95	14.96	0.00
BMI (Kg/m^2)	27.55±3.08	27.03±2.37	−0.76	0.45	27.45±3.19	27.41±3.45	0.07	0.95
Systolic blood pressure (mmHg)	123.00±13.59	126.87±13.10	1.16	0.25	124.02±14.23	120.95±15.94	1.08	0.28
Diastolic blood pressure (mmHg)	67.65±9.45	72.1±10.85	1.76	0.08	69.42±9.38	65.21±12.94	1.82	0.08
FBG (mmol/L)	9.06±3.32	8.26±2.31	−1.11	0.27	8.89±2.69	9.16±3.06	−0.49	0.63
HbA1c (mmol/mol)%	7.89±1.74	6.94±1.21	2.50	0.02	7.87±1.41	13.49±18.87	0.63	0.08
ALT (U/L)	26.44±17.44	27.11±12.85	0.17	0.86	31.63±20.05	31.22±21.37	0.1	0.92
AST (U/L)	22.45±10.65	21.45±6.58	−0.45	0.66	23.91±23.91	24.44±11.45	−0.24	0.81
BUN (mmol/L)	5.83±2.39	4.74±1.12	−2.37	0.02	5.15±1.35	6.34±6.97	−1.05	0.30
BUA (mmol/L)	308.71±87.40	314.70±69.92	0.30	0.77	315.32±84.91	303.46±84.14	0.72	0.47
SCr (μmol/L)	69.49±22.74	66.10±12.85	−0.72	0.47	68.21±16.80	62.51±13.30	1.86	0.07
TG (mmol/L)	1.86±1.10	2.77±2.33	1.93	0.06	2.00±1.06	2.07±1.26	−0.36	0.72
TC (mmol/L)	4.06±1.19	4.59±1.30	1.71	0.09	4.08±0.97	4.29±1.24	−1.02	0.31
LDL (mmol/L)	2.27±0.89	2.59±0.96	1.35	0.18	2.27±0.79	2.27±0.97	0.01	0.99
HDL (mmol/L)	1.06±0.29	1.08±0.22	0.29	0.77	1.05±0.30	1.14±0.29	−1.74	0.09
UCr (mmol/L)	6.65±5.13	6.66±9.81	0.45	0.65	7.58±6.10	5.75±3.54	2.12	0.04
Gender (Male)	11 (32.4%)	15 (50%)	2.06	0.15	39 (43.8%)	8 (20.5%)	6.34	0.01
Duration of T2DM (years)	12.67±9.23	9.64±6.02	−1.57	0.12	10.09±7.37	10.91±6.66	−0.59	0.56
Coronary heart disease	11 (32.4%)	8 (26.7%)	0.25	0.62	26 (29.2%)	7 (17.9%)	1.80	0.18
Malignant tumor	6 (17.6%)	10 (33.3%)	2.09	0.15	26 (29.2%)	9 (23.1%)	0.51	0.47
Drinking now	3 (8.8%)	6 (20.0%)	0.85	0.36	18 (20.2%)	4 (10.3%)	1.89	0.17
Drinking past	5 (14.7%)	10 (33.3%)	3.08	0.08	27 (30.3%)	7 (17.9%)	2.13	0.14
Concurrent retinopathy	3 (8.8%)	2 (6.7%)	0.00	1.00	3 (3.4%)	3 (3.4%)	0.00	1.00
Concurrent intermittent claudication	1 (2.9%)	0 (0%)	0.00	1.00	7 (7.9%)	3 (7.7%)	0.00	1.00

Abbreviations: MoCA, Montréal Cognitive Assessment Scale-B; BMI, body mass index; FBG, fast blood-glucose; HbA1c, Glycosylated hemoglobin; ALT, alanine transaminase; AST, aspartate transaminase; BUN, blood urea nitrogen; BUA, blood uric acid; SCr, serum creatinine; TG, triglyceride; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein; UCr, urine creatinine.

ANOVA method (Figure 4) to choose 92 features and the LASSO algorithm (Figure 5) to select 11 optimal feature (Table 2). Furthermore, to identify the MCI and DM groups, we analyzed a total of 128 cases with 90 cases in the training set and 38 cases in the validation set. We extracted 1409 radiomics features and selected 346 features based on variance threshold method (Figure 6). Then, we selected 197 features using the ANOVA method (Figure 7) and applied the LASSO algorithm (Figure 8) to select the 12 optimal feature values (Table 3).

The Utility of SVM Model for Predicting Cognitive Impairment in Patients With T2DM

The SVM classifier was utilized for training purposes in this study. The subsequent testing set evaluations revealed that the SVM classifier achieved an AUC of 0.857 for distinguishing between the N and CI groups, and an AUC of 0.821 when differentiating between the MCI and DM groups. Additionally, the classifier demonstrated an accuracy of 0.830 in both group comparisons. The ROC curve analysis illustrated these results, which are presented in Table 4, Figures 9, and 10. In addition, Table 5 displays the four metrics of the classifier used. These findings demonstrate the SVM classifier's usefulness in detecting the N and CI as well as distinguishing between the MCI and DM, as it provides an accurate and efficient methodology for stratifying the severity of cognitive dysfunction in patients with T2DM.

Discussion

Cognitive impairment is a common and significant complication of T2DM. In current clinical practice, cognitive function is often assessed by neuropsychiatric screening tests, such as MoCA, the Mini-Mental State Examination (MMSE) and the Clock Drawing Test (CDT). However, most cognitive tools were affected by age and education levels, as well most

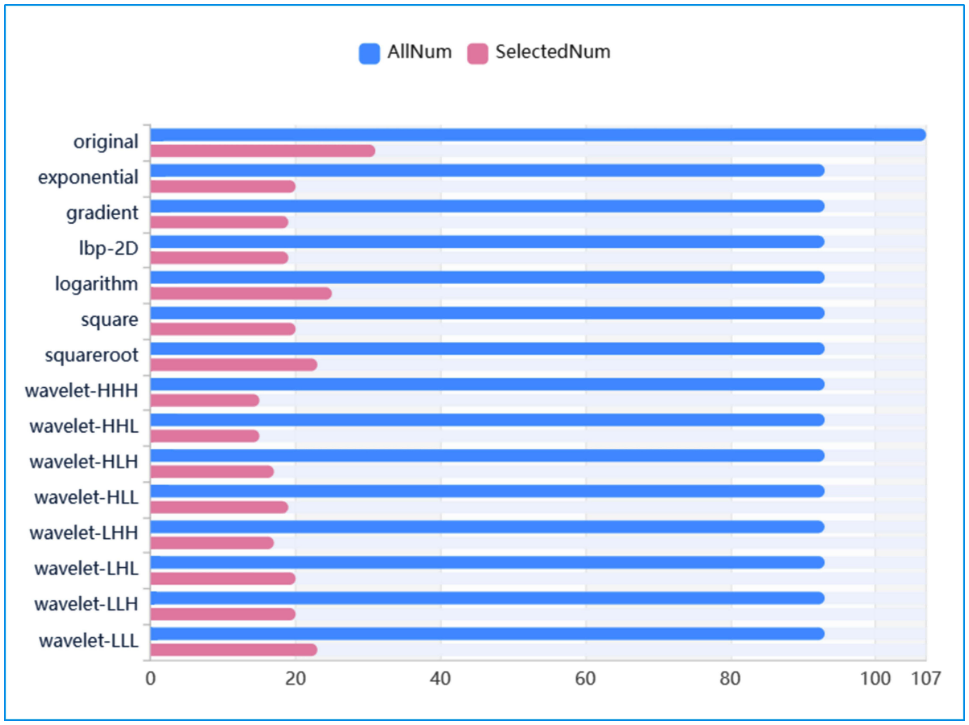

Figure 3 The groups of N and CI, Variance threshold method was used for feature selection. Variance threshold = 0.8, 303 radiomics features were selected from 1409 radiomics features.

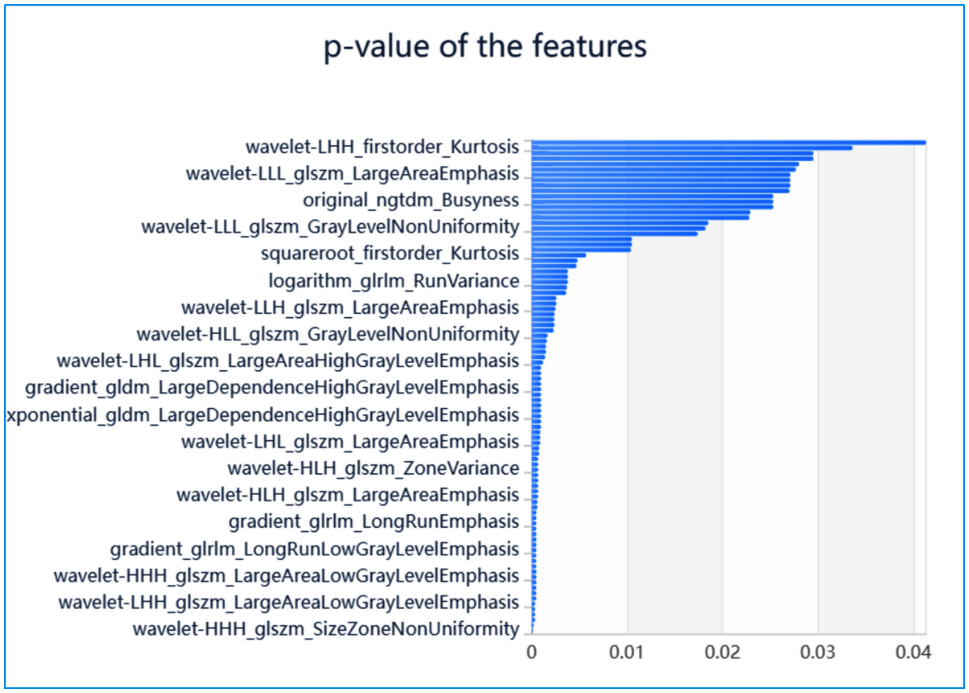

Figure 4 The groups N and CI, selectKbest method was used for feature selection, and 92 radiomics features were selected from 303.

tests needed to be administered by trained physicians and require extensive amount of time.[17] Additionally, optimal cut-off points need to be cautiously chosen while screening for MCI among different populations. To develop a more objective assessment method, we constructed a SVM model based on MRI radiomics to evaluate cognitive impairment and its severity in T2DM patients. Using high-dimensional radiomics features extracted from T1WI sequence, the SVM

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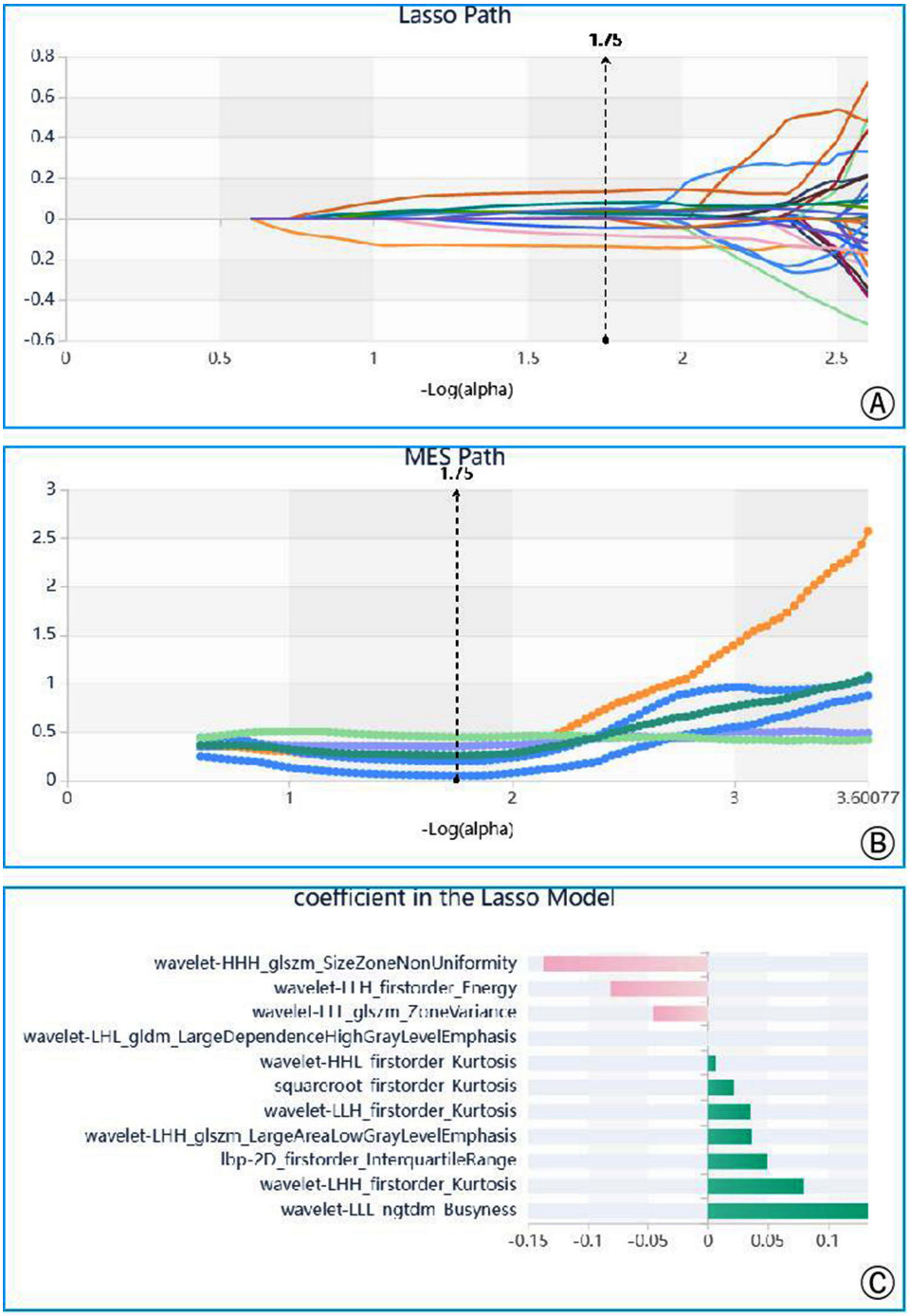

Figure 5 The groups of N and CI, Lasso method to select radiomics features. (**A**) Lasso path; (**B**) MSE path; (**C**) coefficients in the Lasso model. Using the Lasso model, 11 features with the best alpha values were selected.

model was able to detect cognitive impairment in T2DM patients and distinguish MCI from DM. These results demonstrate the potential of this ML model based on MRI-T1WI radiomics as a screening tool for risk stratification and clinical decision making.

Clinical Features Associated With Cognitive Dysfunction in T2DM Patients

The general data analysis revealed that the levels of HbA1c were higher in the CI group compared to the N group. According to MAAN's study, the increased HbA1c levels were found to be associated with cognitive impairment in

Table 2 Selected Radiomics Features and Their Associated Feature Types and Filters in the N and CI Groups

Radiomic Feature	Radiomic Class	Filter
SizeZoneNonUniformity	glszm	wavelet-HHH
SizeZoneNonUniformity	glszm	wavelet-HHH
LargeAreaLowGrayLevelEmphasis	glszm	wavelet-LHH
Busyness	ngtdm	wavelet-LLL
Kurtosis	firstorder	squareroot
Kurtosis	firstorder	wavelet-LLH
Energy	firstorder	wavelet-LLH
ZoneVariance	glszm	wavelet-LLL
InterquartileRange	firstorder	lbp-2D
LargeDependenceHighGrayLevelEmphasis	gldm	wavelet-LHL
Kurtosis	firstorder	wavelet-LHH

Abbreviations: N, normal cognitive function; CI, cognitive impairment.

T2DM patients, with oxidative stress reaction playing a significant role in hyperglycemia-induced ischemic injury and the exacerbation of glucose neurotoxicity.[18] The age of the DM group was significantly higher than that of the MCI group. Several studies have shown that T2DM is correlated with Alzheimer's disease (AD) and vascular dementia, both of which are significantly associated with age.[19,20] Furthermore, older patients with T2DM are more susceptible to developing MCI or DM than younger patients with T2DM.[5,21] Therefore, aging in combination with T2DM could potentially increase the likelihood of experiencing cognitive decline. However, other clinical and laboratory parameters did not show statistically significant differences between patients with cognitive impairment and healthy individuals in this study. This may be due to the small sample size, which limits the power to detect subtle differences. Vascular changes, lifestyle factors, and genetic predispositions are known risk factors for cognitive dysfunction.[1] Future studies should aim to recruit larger cohorts to better evaluate the impact of these clinical factors on cognitive impairment.

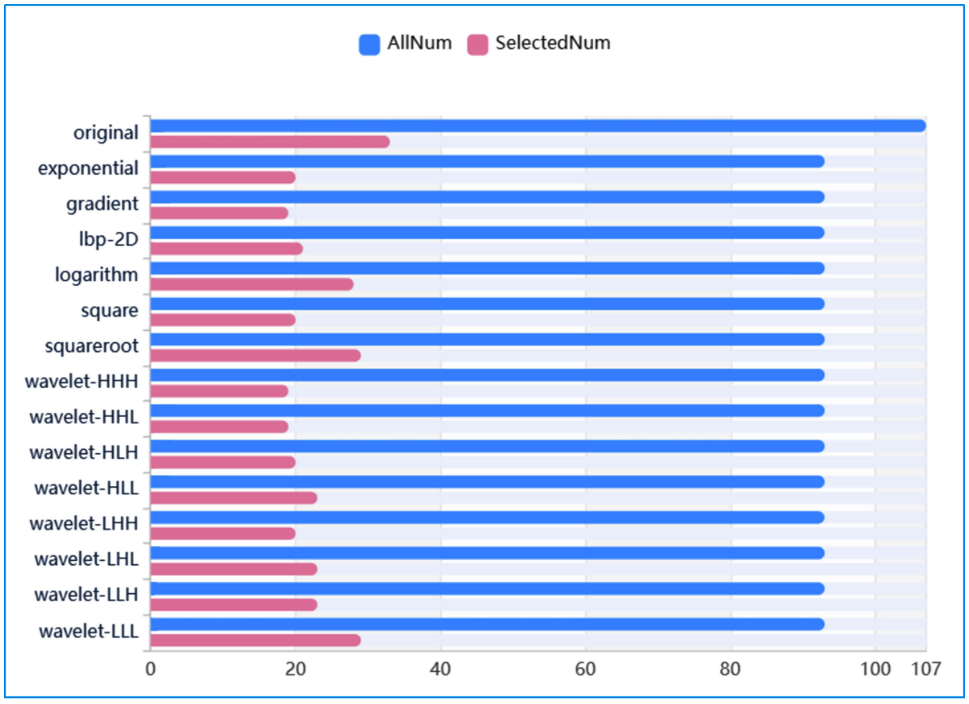

Figure 6 The groups of MCI and DM, Variance threshold method was used for feature selection. The variance threshold = 0.8, 346 radiomics features were selected from 1409 radiomics features.

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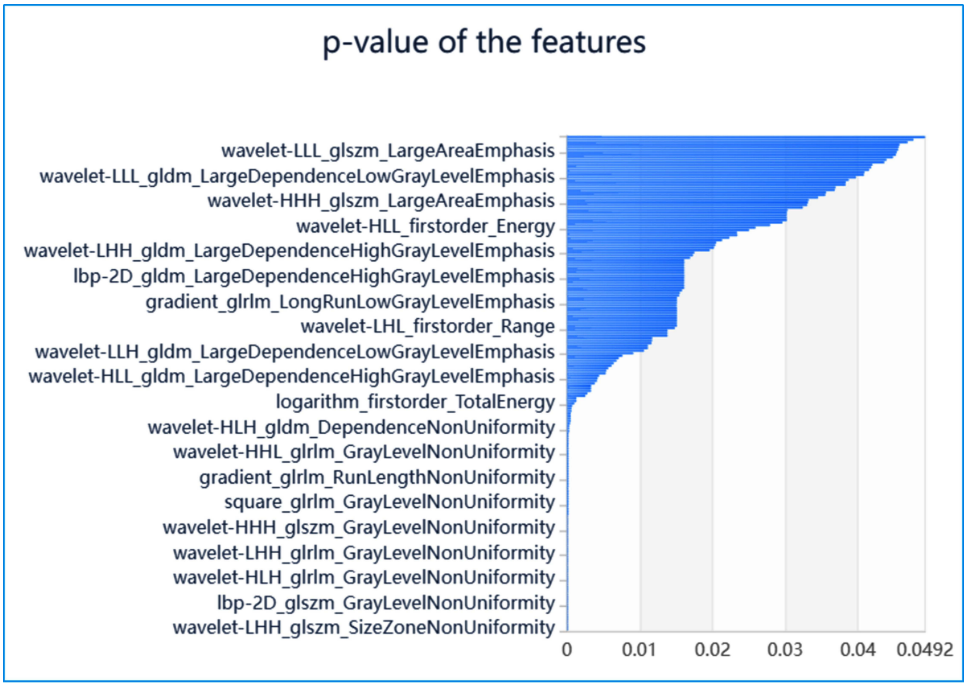

Figure 7 The groups of MCI and DM, selectKbest method was used for feature selection, and 197 radiomics features were selected from 346.

The Value of SVM Model Based on MRI Radiomics in Predicting Cognitive Impairs in T2DM Patients

T1WI has been identified to be effective in evaluating the brain structural abnormalities associated with dementia, with its brain atrophy and lesion index providing a means to quantify the impact of dementia on brain structure.[22] Additionally, MRI white matter hyperintensity, cerebral cortex, and hippocampus volume are considered biological markers of cognitive dysfunction. T2DM has been shown as a risk factor for brain atrophy and small vessel disease. Furthermore, patients with T2DM often exhibit abnormalities in brain metabolites that are associated with cognitive impairment.[23] Neuroimaging studies have found that microstructural lesions in both the gray and white matter of the brain in patients with diabetes are linked to cognitive impairment.[24] As such, changes in image features can reflect the destruction of normal tissue structure to some extent. Radiomics can extract abundant high-dimensional feature information from MRI and utilize artificial intelligence methods for analysis. Therefore, in order to better reflect the heterogeneity of brain tissue associated with cognitive impairment in patients with T2DM, T1-weighted whole-brain images were used for radiomic analysis in this study.

ML is a research field that employs statistical, probabilistic, and optimization techniques such as SVM, K-nearest neighbor (KNN), logistic regression (LR), decision trees (DT), artificial neural networks (ANN) and Random Forest (RF) to construct models that predict unknown data. Recently, ML algorithms have been extensively used in the recognition and grouping of medical images due to their ability to construct models using large and complex datasets.[25,26] Among the various ML techniques, SVM is particularly effective in maintaining the accuracy of the model while avoiding overfitting.[27] SVM is also proficient in identifying subtle information in complex datasets, leading to its application in solving practical problems such as those involving high dimensionality, non-linearity, and small sample data.[28] SVM has gained attention in the exploration of biological markers of mental disorders. Studies have shown that SVM performs favorably in the MRI-based detection and assessment of cognitive function in Alzheimer's disease patients.[29–31]

In our study, we selected the SVM for stratification of cognitive impairment in patients with T2DM using 3D T1-weighted imaging (T1WI). SVM's versatility and non-parametric approach make it an attractive choice for our study, as it does not assume a specific underlying data distribution, aligning well with the complexity of 3D T1WI data.[32] This aligns with the findings of other studies that have utilized SVM for similar applications in medical diagnostics.[33] In

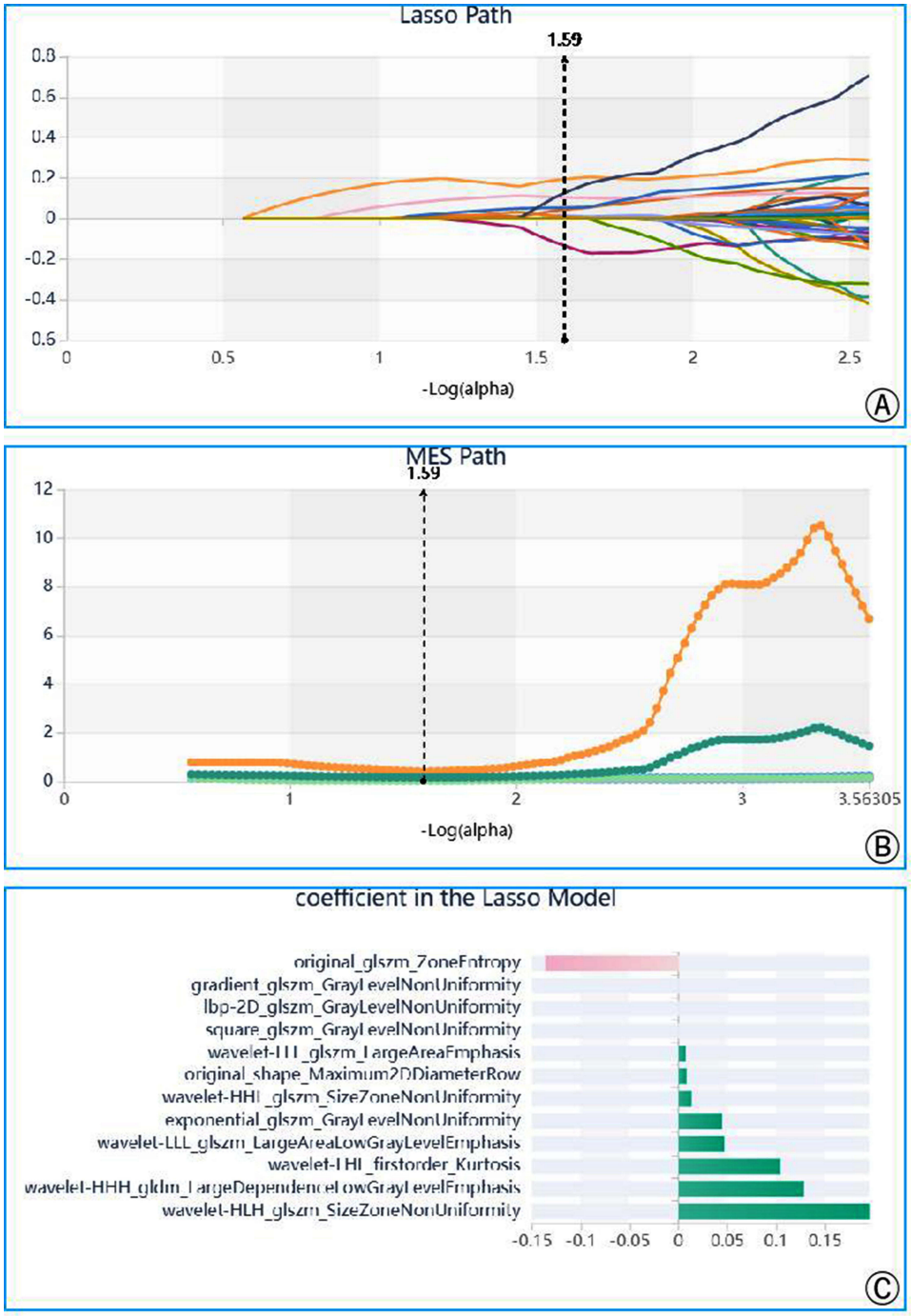

Figure 8 The groups of MCI and DM, selection of radiomics features by Lasso method. (**A**) Lasso path; (**B**) MSE path; (**C**) coefficients in the Lasso model. Using the Lasso model, 12 features with the best alpha values were selected.

conclusion, our decision to employ SVM was based on its strong performance in medical imaging, its aptitude for handling complex data sets like 3D T1WI, and its competitive standing against other machine learning models.

Our study's findings indicate that the SVM model based on MRI radiomics features demonstrates a high diagnostic accuracy in identifying cognitive impairment in T2DM patients. The AUC values of 0.857 and 0.821 for distinguishing between CI and N groups, and MCI and DM groups, respectively, are comparable to or exceed those reported in other studies employing different methodologies. For instance, Liu et al used SVM classifier to study the correlation between global brain network functional connectivity and cognitive dysfunction in T2DM patients. The results showed that the

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Table 3 Selected Radiomics Features and Their Associated Feature Types and Filters in MCI and DM Groups

Radiomic Feature	Radiomic Class	Filter
SizeZoneNonUniformity	glszm	wavelet-HLH
SizeZoneNonUniformity	glszm	wavelet-HHL
GrayLevelNonUniformity	glszm	exponential
GrayLevelNonUniformity	glszm	gradient
GrayLevelNonUniformity	glszm	square
GrayLevelNonUniformity	glszm	lbp-2D
Maximum2DDiameterRow	shape	original
ZoneEntropy	glszm	original
Kurtosis	firstorder	wavelet-LHL
LargeAreaEmphasis	glszm	wavelet-LLL
LargeAreaLowGrayLevelEmphasis	glszm	wavelet-LLL
LargeDependenceLowGrayLevelEmphasis	gldm	wavelet-HHH

Abbreviations: MCI, mild cognitive impairment; DM, dementia.

Table 4 Results of ROC Curve Analysis of SVM Classifier

Group of Groups	Data Set	AUC	95% CI	Sensitivity	Specificity
N and CI	Training set	0.991	0.940–1.000	0.960	0.960
	Set of tests	0.857	0.657–1.000	0.830	0.860
MCI and DM	Training set	0.990	0.925–1.000	0.870	0.920
	Set of tests	0.821	0.667–0.975	0.930	0.580

Abbreviations: ROC, receiver operating characteristic curve; SVM, support vector machine; AUC, area under the curve; CI, confidence interval; N, normal cognitive function; CI, cognitive impairment; MCI, mild cognitive impairment; DM, dementia.

accuracy of node centrality of precuneus and posterior cingulate cortex in SVM model to distinguish T2DM from normal control group was 97.56%.[34] Similarly, Shi et al developed a brain functional connectivity SVM model employing resting-state magnetic resonance imaging to assess cognitive function in patients with T2DM, with an AUC of 0.65–0.70 for identifying cognitive dysfunction.[35] Unlike these studies, this research applied radiomics research methods to extract features from conventional T1WI images, followed by radiomic feature selection using three feature dimensionality

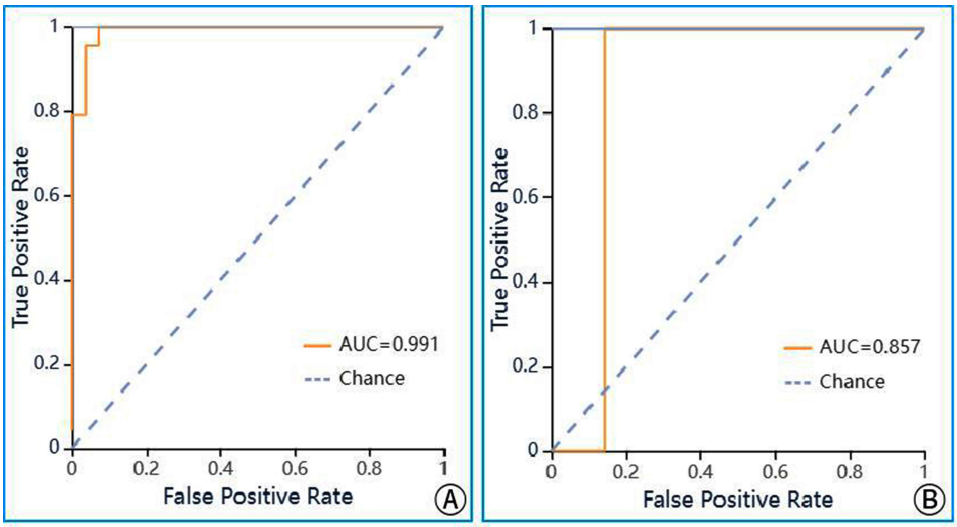

Figure 9 The ROC curves of SVM classifiers distinguishing between in N and CI groups. (**A**) The AUC for the N and CI groups in the training set was 0.991; (**B**) The AUC for the N and CI groups in the test set was 0.857.

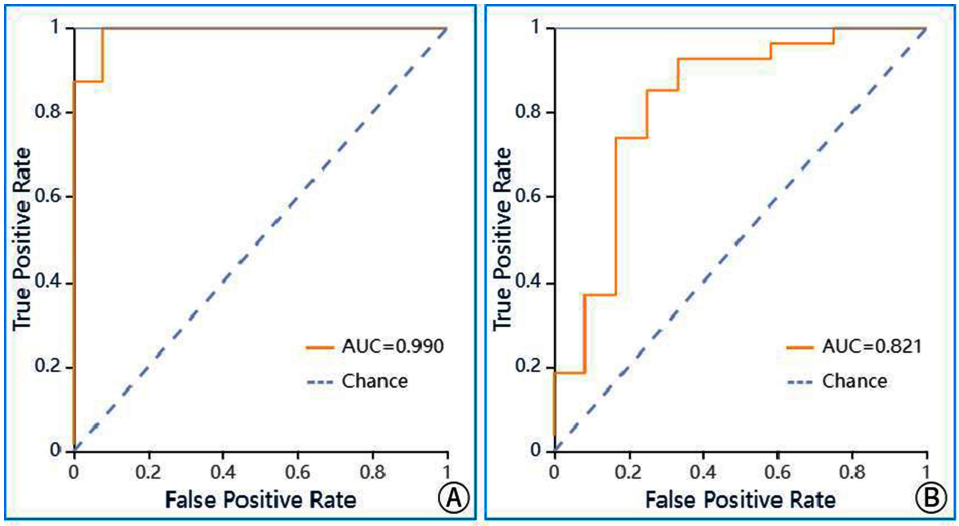

Figure 10 The ROC curve of SVM classifier distinguishing between MCI and DM groups. (**A**) The AUC for the MCI and DM group in the training set was 0.990; (**B**) The AUC for the MCI and DM in the test set was 0.821.

reduction methods: variance threshold, ANOVA and LASSO. From a total of eleven optimal features included in the model, six were first-order statistical features and five were texture features. These radiomics features reflect the characteristic differences in brain tissue dimensions between cognitive dysfunction and a normal cognitive state in T2DM patients.[36,37] Our approach of using SVM with radiomic features not only enhances the predictive power but also aligns with the trend of integrating machine learning with medical imaging data to improve diagnostic accuracy.[38] For example, a study by Avena-Koenigsberger et al highlighted the importance of network communication models in understanding brain network efficiency and resilience.[39] This underscores the potential of our model in advancing the field of cognitive impairment diagnostics, particularly in the context of T2DM.

Patients with DM commonly suffer from cognitive impairment, which significantly reduces their capacity to perform daily activities, learn, work, and communicate socially. The diagnosis of DM requires a comprehensive evaluation that includes medical history, general and neurological physical examination, neuropsychological evaluation, and laboratory and imaging examination results.[40] The combined machine learning model of both neuropsychological assessments and MRI data had the best performance for AD patients, with the Kernel Ridge Regression (KRR) model having an R2 of 0.874. Based on research, the possibility of MCI patients progressing to DM is 3–5 times greater than for normal individuals, and the annual rate of progression for the general population is estimated to be 12%, with high-risk individuals, such as those with diabetes and prediabetes, having rates as high as 20%.[41,42] Furthermore, Dove et al conducted research that found poor glycemic control and cardiovascular comorbidities to be important risk factors for cognitive impairment and progression in T2DM patients.[43] The SVM model was used in this study to evaluate the extent of cognitive impairment in T2DM patients. The analysis showed that the model had high power in distinguishing MCI

Table 5 Precision, Recall, F1 Score, and Support of the SVM Classifier

Group of Groups	Data Set	Precision	Sensitivity	F-score	Support
N and CI	Training set	0.960	0.960	0.960	24
	Set of tests	0.830	0.830	0.830	6
MCI and DM	Training set	0.960	0.870	0.920	63
	Set of tests	0.830	0.930	0.880	27

Abbreviations: N, normal cognitive function; CI, cognitive impairment; MCI, mild cognitive impairment; DM, dementia.

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from DM with an AUC of 0.821 (0.667–0.975) and an accuracy of 0.830. The findings suggest that the model is efficacious in evaluating the severity of cognitive dysfunction among patients with T2DM.

Comparison With Other Modalities for Predicting T2DM

In the field of diabetes research, a variety of diagnostic tools have been utilized to assess the risk and progression of T2DM. MRI-based methods, particularly those utilizing 3D-T1WI, have proven effective in evaluating brain structural abnormalities associated with dementia and cognitive decline. Functional MRI (fMRI) has been used to detect altered functional connectivity in patients with cognitive impairment in T2DM patient, and positron emission tomography(PET) was widely used to capture metabolic changes in the brain for early diagnosis, however, these high-precision brain imaging techniques have limited accuracy of less than 70.0%.[35,44] Furthermore, non-imaging-based prediction models, which rely on clinical parameters and biochemical markers, offer a more accessible and cost-effective alternative,[45] Marcisz's study shows that the addition of the T1-weighted MRI-based biomarker improves the quality of MCI detection.[46] However, these models often lack the sensitivity and specificity achieved by imaging-based methods.

Integrating machine learning algorithms into MRI-based methods has shown potential in enhancing predictive accuracy. Recently, the robustness and generalization capabilities of SVM have been well-documented in comparative studies, often outperforming other algorithms such as Naïve Bayes and Random Forest (RF) in disease prediction tasks.[47] While RF may show superior accuracy in some cases, SVM's margin maximization for classification is particularly beneficial when dealing with smaller datasets.[47] Comparing to RF model, the XGBoost algorithm performs better classification of subjects and better distinguishes between different types of neurodegenerative diagnoses.[48] Wu et al using the eXtreme Gradient Boosting(XGBoost) model achieved an accuracy of 87.91% in T2DM-MCI versus T2DM-NCI classification and 80% in T2DM-NCI versus NC classification,[44] the accuracy is roughly in line with our model. While each modality has its merits, the combination of radiomics with SVM offers a powerful tool for stratifying cognitive impairment in the context of T2DM, highlighting its potential for clinical application and further research.

Benefit to Practitioners

The incorporation of SVM with radiomic features extracted from 3D-T1WI MRI presents a multitude of practical advantages for clinicians and practitioners specializing in diabetes care. Firstly, the high accuracy and AUC values of our SVM model signify its potential for the early detection and stratification of cognitive impairment in patients with T2DM, which is essential for the timely initiation of interventions and optimized patient management. Secondly, our model serves as an objective assessment tool for cognitive function, reducing the susceptibility to variability and bias found in subjective clinical evaluations, thus fostering more standardized and dependable diagnosis of cognitive impairment in T2DM patients. Additionally, the precise differentiation between varying degrees of cognitive impairment facilitated by our model can guide treatment planning, enabling practitioners to make more informed decisions on therapeutic and management strategies for T2DM patients experiencing cognitive issues. Collectively, our study not only augments the current research on cognitive impairment in T2DM patients but also provides tangible benefits to practitioners through the provision of a dependable and precise diagnostic instrument, thereby enhancing the clinical relevance and significance of our findings.

The Shortcomings of This Study

Although the study provides valuable insights, several limitations hinder the generalizability of the findings. Firstly, as this retrospective analysis relied on sampled data, the potential selection bias may affect the reliability and repeatability of results. Therefore, continuous research and action are necessary to enhance the clinical practicability of the model. Secondly, for improved external validity, a larger scale, multicenter study is advised since this study was only conducted at one center. Secondly, although T1WI sequences were employed in this study, other MRI sequences may also contain useful information. Future studies will investigate the usefulness of these sequences to augment the current research findings. Furthermore, the present study utilized a single machine learning model, SVM, for its demonstrated effectiveness in high-dimensional medical imaging data. Future research may benefit from incorporating additional models to broaden the comparative analysis.

Conclusion

In this study, we developed two SVM models based on MRI radiomics features derived from 3D T1WI to stratify cognitive impairment in patients with T2DM. The models effectively differentiated between normal cognitive function and cognitive impairment, as well as between mild cognitive impairment (MCI) and dementia, highlighting the potential of our approach to provide a quantitative and objective assessment of cognitive dysfunction in T2DM patients. However, the relatively small sample size may pose a risk of overfitting. Future research should utilize larger datasets and multiple cross-validation methods to enhance model robustness and obtain more reliable accuracy estimates.

The radiomics-based SVM approach proposed here can be applied to both single-center and multi-center datasets, bridging the gap between group-level comparisons and individual patient outcomes. This method offers a promising tool for clinicians to facilitate early identification and intervention of cognitive impairment in T2DM patients. Further research is needed to validate the clinical application of these models.

Ethics Approval Statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Medical Ethics Committee of the Third People's Hospital of Datong (2022-01). Informed consent was not obtained, as it was waived by the Ethics Committee of the Third People's Hospital of Datong. The committee determined that this study, being observational in nature and posing minimal risk, did not require informed consent. Additionally, they assured that the privacy of the participants would not be compromised. We confirm that the data has been anonymized and is being maintained with the utmost confidentiality.

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Disclosure

The authors report no conflicts of interest in this work.

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