

Original Research

A Support Vector Machine Method With Correlation-Based Recursive Feature Elimination for the Early Diagnosis of Alzheimer's Disease

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Abstract

Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder where early diagnosis is critical. While magnetic resonance imaging (MRI) provides valuable structural information, most methods rely solely on imaging features, limiting clinical interpretability. **Methods:** A novel feature selection method using support vector machine with correlation factor-based recursive feature elimination and cross-validation (SVM_CF_RFECV) integrated correlation factors from mini-mental state examination (MMSE) scores into the feature weighting process is proposed for the early identification of Alzheimer's disease. This approach balances statistical discriminative power with clinical relevance and mitigates the local-optimum issue of traditional recursive feature elimination (RFE). **Results:** Using the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset, the proposed method achieved a peak accuracy of 87.5% in a single-split experiment and an average accuracy of 0.8489 ± 0.0330 across multiple random partitions, outperforming conventional SVM_RFECV. The selected 74 discriminative brain regions, including the hippocampus and cingulate cortex, align with established AD pathology. **Conclusions:** These findings demonstrate that SVM_CF_RFECV provides both accuracy and interpretability, supporting its potential as a clinically meaningful tool for early AD diagnosis.

Keywords: Alzheimer's disease; machine learning; feature selection; support vector machine

1. Introduction

Alzheimer's disease (AD) is a prevalent neurodegenerative disorder characterized by cognitive decline, memory impairment, and behavioral abnormalities [1,2,3]. With the acceleration of global aging, the incidence of AD has been increasing steadily. Recent studies project that by 2050, the prevalence of dementia will double in Europe and triple worldwide. When defined based on the biological criteria of AD, this estimate is expected to be even three times higher [4]. Given the rapid rise in AD cases, accurate diagnosis of AD and its early stage, mild cognitive impairment (MCI), is critical for timely intervention and potential disease progression delay.

In the diagnosis of AD, magnetic resonance imaging (MRI) serves as a non-invasive technique capable of capturing subtle structural and functional changes in the brain. It has become a crucial tool for both clinicians and researchers in diagnosing and monitoring AD. With advancements in computer-aided diagnosis (CAD), automated diagnostic methods based on MRI data have emerged as a key research focus [5]. In recent years, machine learning (ML) and deep learning (DL) techniques have been widely

applied to AD-related imaging analysis and classification tasks, significantly enhancing diagnostic efficiency and accuracy. These technologies enable researchers to extract critical features from complex imaging data and identify patterns, paving the way for more precise and efficient AD diagnosis [6,7,8,9,10].

Numerous studies have explored various feature extraction and machine learning techniques for AD classification. For instance, Abbas Saad Alatrany et al. [11] utilized data from the National Alzheimer's Coordinating Center (NACC), employed Support Vector Machine (SVM) for feature selection, and implemented rule-based explainability methods to enhance the transparency and reliability of Alzheimer's disease classification. Sheng et al. [12] proposed a method that integrates Fisher score and multimodal multi-task feature selection to enhance the classification of different stages of Alzheimer's disease by combining brain imaging and genetic data. This approach holds promise for improving the early diagnosis of the disease [12].

While deep learning methods [13,14], particularly graph convolutional networks (GCNs) and their variants, have achieved state-of-the-art classification accuracy



on Alzheimer's Disease Neuroimaging Initiative (ADNI) datasets, these approaches typically require large-scale data, substantial computational resources, and offer limited interpretability regarding which brain regions drive their decisions. In contrast, our work deliberately focuses on SVM-based feature selection, which provides explicit feature weights and direct links to individual brain regions, thereby offering greater clinical interpretability—a critical requirement for real-world diagnostic applications.

Among machine learning techniques, SVMs have been widely used in AD and other disease classifications [11,15,16]. SVM constructs an optimal hyperplane that maximizes the margin between different class data points in the feature space, enhancing classification generalization [17].

Recursive Feature Elimination (RFE) based on SVM (SVM-RFE), originally proposed by Guyon et al. [18], is a feature selection algorithm primarily used for cancer classification. It iteratively trains a model and removes the least important features, refining the feature subset [18]. SVM-RFE effectively reduces redundant information while preserving the most discriminative features, thereby improving model stability and generalization performance. In AD and other neurological disorder studies, RFE has been extensively applied to MRI imaging and biomarker data to extract critical features. Albashish et al. [19] introduced a Binary Biogeography-Based Optimization (BBO) and SVM-RFE feature selection method (BBO-SVM-RFE) to optimize feature selection in high-dimensional datasets. This method employs BBO for global search and integrates SVM-RFE within mutation operations, enhancing feature selection stability and classification accuracy. Richhariya et al. [20] proposed a Universum Support Vector Machine (USVM) based Recursive Feature Elimination (USVM-RFE) method for AD MRI image classification. By introducing Universum samples during the RFE process, their approach captures global data distribution, refining the feature selection strategy.

Furthermore, Recursive Feature Elimination with Cross-Validation (RFECV) has been widely adopted for feature selection [21,22]. Unlike traditional RFE, RFECV integrates cross-validation (CV) during feature elimination, automatically determining the optimal number of features while enhancing model stability and generalization capabilities.

The RFECV method iteratively eliminates the least relevant features at each step, following a traditional greedy algorithm. However, greedy algorithms focus solely on local optimization, which may lead to suboptimal solutions or solutions that are close to a local optimum. Furthermore, conventional feature selection methods prioritize classification accuracy while overlooking the contribution of clinical information, thereby reducing model interpretability.

To address these limitations, this study proposes a novel method, support vector machine with correla-

tion factor-based recursive feature elimination and cross-validation (SVM_CF_RFECV), based on SVM. This method enhances the traditional SVM-RFECV by incorporating a correlation factor (CF) that represents correlations with clinical measurements, thereby improving the model's understanding of disease progression. The introduction of the CF not only addresses the issue of local optimization but also improves feature selection stability and interpretability by integrating clinical data. Unlike conventional methods that neglect clinical information, SVM_CF_RFECV aligns the feature selection process with real-world clinical contexts, thus enhancing its practical relevance.

2. Materials and Methods

The specific workflow of this study consisted of three main stages: data processing, feature selection, and classification. Missing-value imputation and normalization were performed before the data were split. After data splitting, CF calculation and feature selection using the SVM_CF_RFECV method were conducted exclusively within each training fold. The selected feature subset was then used to train the classifier, while the corresponding testing fold was used only for model performance evaluation. The data used for CF calculation and feature selection were kept consistent with those used for classifier training to ensure the validity and generalizability of the results. The detailed workflow is illustrated in the Fig. 1:

2.1 Participants

All data were sourced from the ADNI database (<https://adni.loni.usc.edu/>), a landmark, global, multi-center, longitudinal study established to enhance the early diagnosis, progression tracking, and potential treatment development for Alzheimer's disease [23]. While ADNI collects an extensive range of data, including MRI, positron emission tomography (PET) imaging, and biomarker profiles, this research focuses specifically on MRI data [24]. The MRI dataset encompasses individuals with cognitively normal (CN), MCI, and AD, facilitating the discovery and validation of AD biomarkers and advancing early detection and therapeutic interventions. This initiative has become an essential resource, underpinning Alzheimer's disease research worldwide.

In this study, a total of 437 participants were selected from the ADNI database based on the following inclusion criteria: (1) availability of baseline T1-weighted MRI scans; (2) complete demographic and mini-mental state examination (MMSE) records at baseline; (3) clinical diagnosis of CN, MCI, or AD according to the standard ADNI diagnostic criteria; (4) no history of other neurological or psychiatric disorders. Subjects with excessive head motion or poor image quality were excluded. Based on these criteria, 170 CN individuals, 158 MCI patients, and 109 AD patients were included. Detailed information is shown in Table 1.

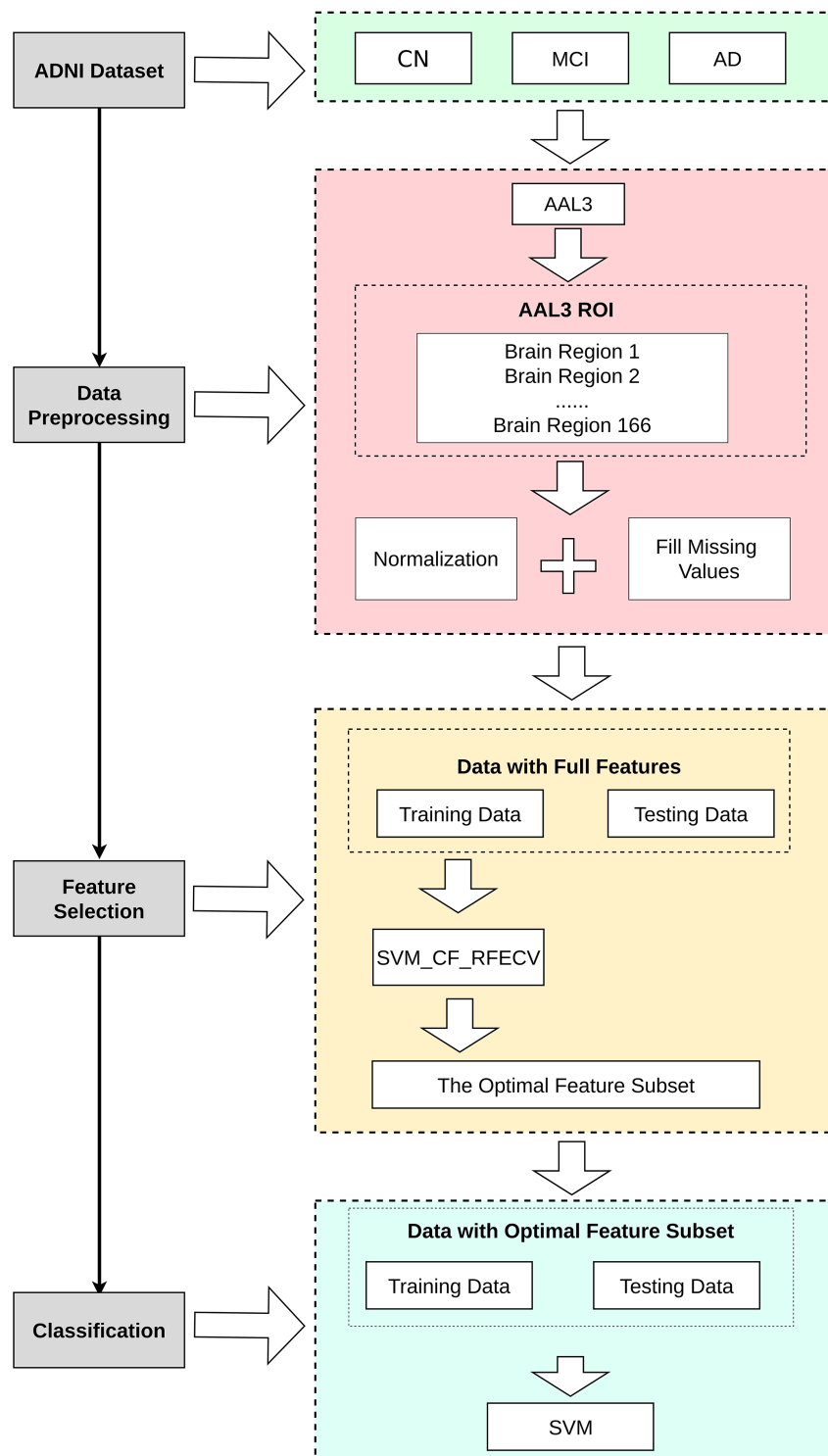


Fig. 1. Overall workflow of the research. ADNI, Alzheimer’s Disease Neuroimaging Initiative; CN, cognitively normal; MCI, mild cognitive impairment; AD, Alzheimer’s disease; AAL3, Automated Anatomical Labeling Atlas 3; SVM_CF_RFECV, support vector machine with correlation factor-based recursive feature elimination and cross-validation; SVM, Support Vector Machine.

In this study, a 10-fold stratified cross-validation strategy was employed to ensure consistent CN/MCI/AD class distributions across all training and test partitions. All data preprocessing steps, including missing-value imputation,

feature normalization, correlation factor (CF) calculation, and feature selection, were strictly implemented only within the training set in each fold. The statistical parameters and transformation rules learned from the training partition

Table 1. Detailed information of participants.

Category	Number	M/F	Age	MMSE
CN	170	78/92	72.6 ± 12.8	29.0 ± 5.0
MCI	158	96/62	70.1 ± 15.1	28.5 ± 4.5
AD	109	65/44	74.3 ± 18.7	23.1 ± 4.1

M, male; F, female; MMSE, mini-mental state examination.

were then directly applied to the held out test set without any recalculation. This strict separation eliminates data leakage and ensures unbiased evaluation of model generalization.

2.2 Data Preprocessing Based on AAL3

All raw structural MRI scans were preprocessed using standard protocols in FMRIB Software Library (FSL, V6.0, <https://fsl.fmrib.ox.ac.uk/fsl/docs/>) and Advanced Normalization Tools (ANTs, V2.6.2, <https://github.com/antsx/ants>). The preprocessing pipeline included: N4 bias field correction to correct intensity inhomogeneities, skull stripping to isolate brain parenchyma, non-linear spatial normalization to the MNI152 template, tissue segmentation into gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF), modulation with Jacobian determinants to preserve actual GM volume, smoothing with an 8 mm full-width at half-maximum (FWHM) Gaussian kernel, and intracranial volume (ICV) estimation as a covariate. Quality control was performed by visual inspection after each step; images with excessive motion artifacts or segmentation failures were excluded [25].

The Automated Anatomical Labeling Atlas 3 (AAL3) is an enhanced brain atlas designed for neuroimaging research, providing finer anatomical parcellation of brain regions. In AAL3, each region of interest (a total of 170 region labels) is defined as a network node. Through inverse transformations, the AAL3 atlas is registered from the standard Montreal Neurological Institute (MNI) space to the individual's native space to achieve precise anatomical localization. Due to the finer parcellation provided in AAL3, certain region numbers in AAL2 (such as those for the bilateral anterior cingulate cortex and thalamus) are left empty in AAL3. Consequently, AAL3 comprises 166 brain regions, with a maximum label number of 170. The mean gray matter volume was then extracted from each of the 166 regions as the structural feature. Finally, to strictly prevent data leakage, z-score normalization was performed dynamically within the cross-validation loop (mean and standard deviation computed from training folds only and applied to test folds).

2.3 Support Vector Machine Recursive Feature Elimination With Cross-Validation (SVM_RFECV)

In this study, the mean gray matter volume extracted from each of the 166 brain regions (based on the AAL3 atlas) was used as the feature vector. SVM-RFECV is a back-

ward feature elimination method that starts with the full set of features, calculates the weight of each feature, and iteratively removes the least relevant features in sequence. After removing each feature, the new subset of features is evaluated for model accuracy using Support Vector Machine Cross-Validation (SVM-CV). Features removed in the final iterations of SVM-RFECV, which are ranked highest, are considered the most important, whereas those removed in the initial iterations, ranked lowest, contribute the least information. After all iterations, the feature subset yielding the highest accuracy is selected as the final subset.

Compared to the traditional RFE method, RFECV offers significant advantages. RFECV automatically determines the optimal number of features through cross-validation during the feature selection process, eliminating the need for manual presetting and reducing subjectivity and trial-and-error efforts. Additionally, RFECV evaluates model performance through cross-validation at each iteration, selecting feature sets that perform consistently across different data splits. This approach effectively mitigates overfitting risks and enhances model generalizability. As a result, RFECV achieves higher accuracy and stability when the optimal number of features is uncertain, supporting the development of more precise predictive models. We acknowledge that RFECV introduces additional computational overhead. However, for the current sample size ($N = 437$), this overhead is acceptable. For future applications to larger datasets, potential optimizations include early stopping criteria and parallelized cross-validation.

However, the SVM-RFECV method still has its limitations. To address these, this study proposes an improved method, SVM_CF_RFECV, which incorporates the CF variable into the feature selection process. This method will be introduced in detail in the following section.

3. Proposed SVM_CF_RFECV Method

Many modern prediction methods tend to focus on processing image data while overlooking patients' clinical data, such as behavioral and cognitive test results. This leads to insufficient interpretability of the models, making clinical applications challenging. A lack of interpretability can undermine trust in the model's outcomes and hinder its adoption in real-world medical settings. To address this, our study incorporates the MMSE scores [26], which represent patients' clinical information and subjective cognitive functions.

Furthermore, the traditional RFECV method, which eliminates the least relevant feature at each step, follows a conventional greedy algorithm and is prone to local optima. To overcome this limitation, we propose an improved method based on the traditional SVM_RFECV, integrating the CF variable into the feature weight calculation process. This novel method, named SVM_CF_RFECV (support vector machine with correlation factor-based recursive feature elimination and cross-validation), optimizes the

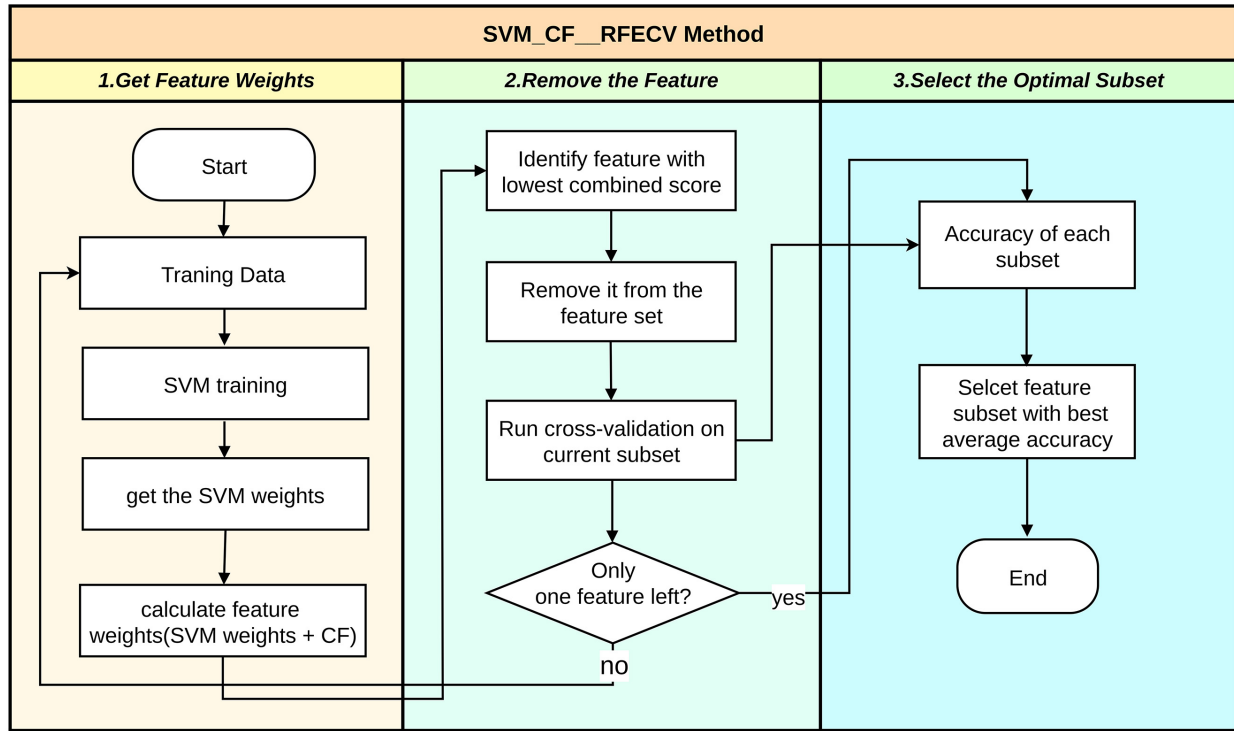


Fig. 2. Workflow of the SVM_CF_RFECV method.

feature selection process. The detailed workflow of this method is illustrated in Fig. 2.

The feature selection process in SVM_CF_RFECV follows an iterative elimination strategy. First, the raw dataset, including MRI-derived features and clinical information, is used as input. For each iteration, feature importance scores are computed by combining the absolute SVM coefficients with correlation factors derived from the association between features and MMSE scores. The feature with the lowest score is then removed, and the remaining subset is evaluated using k-fold stratified cross-validation with a linear SVM classifier. Model performance is assessed by accuracy and macro-F1 score at each step. This procedure is repeated until only one feature remains, and the subset yielding the highest cross-validation accuracy is selected as the optimal feature set.

3.1 Correlation Factor Variable

Traditional RFECV evaluates feature importance based solely on SVM-derived coefficients, which capture statistical discriminative power but ignore the clinical relevance of features. To address this limitation, we introduce CF that quantifies the association between each imaging feature and patients' MMSE scores.

Formally, for feature x_i , the CF is defined as the Pearson correlation coefficient with MMSE:

$$CF = \frac{\sum_{i=1}^n (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^n (x_i - \bar{x})^2} \sqrt{\sum_{i=1}^n (y_i - \bar{y})^2}} \quad (1)$$

Here, x_i represents data from different brain regions for various patients, and y_i corresponds to the patients' MMSE score.

By incorporating the CF variable, the model can account for patients' global cognitive performance as measured by the MMSE, enhancing its robustness and interpretability. This addition enables a better understanding of the relationship between brain features and cognitive function, improving the practical relevance of the model.

Notably, the Pearson correlation coefficients used to define the CF were computed exclusively within each training fold, rather than across the entire dataset. This ensures no information from the test partition influences feature weighting or feature selection, further preventing data leakage. MMSE scores are used only to compute correlation factors for feature weighting during feature selection and are not used as input features to the final classifier. All classification decisions are based solely on MRI-derived brain region features. To avoid the leakage of label or disease severity information, the correlation between each brain feature and MMSE is computed exclusively within the training fold, without access to test data.

3.2 Feature Weight Calculation Based on the CF Variable

Traditional RFECV methods remove the least relevant feature in each iteration, which is a classic greedy algorithm prone to local optima. To address this limitation, the proposed SVM_CF_RFECV method incorporates the CF variable into the feature weight calculation.

The decision function of a traditional SVM can be expressed as:

$$y = w_1x_1 + w_2x_2 + w_3x_3 + \dots + w_nx_n + b$$

$$= \sum_{i=1}^n w_i x_i + b \quad (2)$$

Here, w_i is the weight of feature i , obtained from SVM training; x_i is the i -th feature; and b is the bias term.

The weight array w_i contains coefficients corresponding to each feature, indicating the influence of each feature on the model. The importance of feature i is defined as:

$$I_i = |w_i| \quad (3)$$

The rationale for using the absolute value of SVM coefficients as a feature importance metric is rooted in the geometric interpretation of the linear SVM. In a linear SVM, the weight vector w defines the orientation of the decision hyperplane, and each component w_i directly reflects the contribution of the corresponding feature to the classification boundary. Features with larger w_i exert stronger influence on the decision function, making them more discriminative between diagnostic groups. This importance metric has been widely validated in gene selection and neuroimaging studies [18,20], where it effectively ranks features by their marginal contributions to class separation.

For SVM multi-class tasks (using one-vs-rest or one-vs-one strategies), each class has its own weight. Therefore, the total importance of feature i is typically calculated as the squared sum of weights across all classes:

$$I_i = \sum_{k=1}^K w_{ik}^2 \quad (4)$$

For multi-class classification tasks (CN, MCI, AD) using one-vs-rest or one-vs-one strategies, each class obtains a separate weight vector. The squared sum of weights across classes, as shown in Eqn. 4, provides a global importance score that aggregates discriminative power across all pairwise comparisons. This formulation penalizes features that are only discriminative for one class pair while favoring features that contribute consistently to separating multiple classes.

In Eqn. 4, we sum the squared weights across classes without additional normalization. This assumes that weight scales are comparable across the three one-vs-rest classifiers, which holds in our setting due to the same feature space, balanced class sizes (CN = 170, MCI = 158, AD = 109), and L2-regularized SVM. Nevertheless, we acknowledge that normalizing each class's weight vector (e.g., by its L2 norm) could further refine feature ranking, and we leave this as future work.

In the traditional SVM_RFECV method, feature importance is evaluated using the above formula. Features with the lowest importance are iteratively removed.

In contrast, the proposed SVM_CF_RFECV method introduces the CF variable into the importance evaluation formula, defined as:

$$I_i^{CF} = (1 - \alpha) \sum_{k=1}^3 |w_{ik}| + \alpha |corr_i| \quad (5)$$

Here, α represents the weight, and $corr_i$ is the correlation coefficient between feature i and the MMSE score. This coefficient captures the relationship between the feature and the patient's objective cognitive function.

Justification of the linear fusion strategy and selection of $\alpha = 0.1$:

The linear fusion strategy in Eqn. 5 was chosen for two reasons. First, it maintains the interpretability of feature importance as a weighted sum of two biologically meaningful components: discriminative power (w_i) and clinical relevance ($corr_i$). Second, it avoids the additional complexity and risk of overfitting associated with nonlinear fusion.

The weight α controls the trade-off between these two components. The optimal value $\alpha = 0.1$ was determined empirically by grid search over $\alpha \in [0, 1)$ with step size 0.1, using the average cross-validation accuracy on the training set as the selection criterion. As will be shown in Section 4.2, $\alpha = 0.1$ yields the highest accuracy and F1-score, while $\alpha = 0$ (pure SVM-based ranking) results in lower performance.

Traditional SVM-based importance ranks features solely by statistical discriminative power, which may ignore clinical relevance. Early AD diagnosis requires features that not only separate diagnostic groups but also track subtle cognitive decline. Eqn. 5 addresses this by incorporating the Pearson correlation ($corr_i$) between each imaging feature and MMSE scores, balancing two criteria: (i) discriminative power (w_i), and (ii) clinical relevance ($corr_i$). The hyperparameter α controls this trade-off.

This dual-criteria approach offers three advantages for early AD diagnosis: (1) it prioritizes features sensitive to early cognitive changes even when group-level discriminative power is modest; (2) it improves interpretability by selecting clinically relevant brain regions; (3) it enhances

robustness by down-weighting features with spurious discriminative power that lack clinical correlation.

By integrating the CF variable, SVM_CF_RFECV enhances the robustness and interpretability of the model by emphasizing features that are not only significant in classification but also clinically relevant to cognitive assessment.

3.3 Classification Methods and Performance Metrics

SVM has been proven to be one of the most effective machine learning methods for early classification of Alzheimer's disease. Therefore, this study primarily employs the SVM method for classification. Since the RFECV method requires the classifier to provide weights for each feature, SVM is implemented with a linear kernel.

The classification quality was evaluated using the following performance indices:

$$Accuracy = \frac{TP + TN}{TP + FP + FN + TN} \quad (6)$$

$$Precision = \frac{TP}{TP + FP} \quad (7)$$

$$Recall = \frac{TP}{TP + FN} \quad (8)$$

$$F1 \text{ score} = 2 \cdot \frac{Precision \cdot Recall}{Precision + Recall} \quad (9)$$

True Positive (TP), True Negative (TN), False Positive (FP), and False Negative (FN) represent the correctly identified positive cases, correctly identified negative cases, incorrectly identified positive cases, and missed positive cases, respectively. Accuracy reflects the overall correctness of the model's classification. Precision focuses on the proportion of true positive cases among all cases predicted as positive, while Recall measures the proportion of actual positive cases that were successfully identified. The F1-score, which is the harmonic mean of precision and recall, balances the two metrics and is particularly valuable when dealing with imbalanced class distributions. A comprehensive analysis of these metrics enables a thorough evaluation and optimization of the model's performance.

4. Results

In this section, the proposed SVM_CF_RFECV method is evaluated. We analyze the impact of different weights (α) on the model's performance and select the optimal weight value. Additionally, an ablation study is conducted to assess the contribution of the CF factor to the model, and comparisons are made with different feature

preprocessing methods in terms of results and processes. Furthermore, the most influential feature subset is identified. On this basis, various classifiers are employed to evaluate performance, and the proposed method is compared with recent early prediction methods for Alzheimer's disease. ROI-level feature extraction from MRI images is implemented using Statistical Parametric Mapping (SPM) version 12 (<https://www.fil.ion.ucl.ac.uk/spm/>), while the SVM_CF_RFECV algorithm is developed using the Scikit-learn [27].

4.1 Parameter Configuration

All missing values in the dataset were imputed using mean imputation, and all features were standardized. Cross-validation was uniformly conducted using 10-fold cross-validation. The SVM used a linear kernel for both feature selection and classification. For the comparison method, Principal Component Analysis (PCA)-based dimensionality reduction retained 95% of the variance.

All experiments were implemented using Python 3.10 with Scikit-learn version 1.4.2. SPM12 running on MATLAB R2020a (MathWorks, Natick, MA, USA) was used for image preprocessing. Missing values were imputed using Scikit-learn's Simple Imputer with strategy='mean'. Feature standardization was performed using StandardScaler (zero mean, unit variance). The SVM classifier used a linear kernel with default parameter $C = 1.0$. RFECV was configured with 10-fold stratified cross-validation and 'accuracy' as the scoring metric.

4.2 Impact of Different Weights on Results

In this section, we evaluate the impact of the weight (α) on the model's performance and select the optimal value based on experimental metrics.

According to the weight calculation formula introduced in the previous section, α can take values in the range $[0, 1)$. When $\alpha = 0$, CF is excluded from the model, making it equivalent to the original SVM_RFECV method. We set the step size of α to 0.1, divided the dataset uniformly, and calculated the influence of different weight values on the results. Metrics including the number of features, Accuracy, Precision, Recall, and F1-score were used to evaluate the performance, as shown in Table 2.

As illustrated in Table 2, when α is set to 0.1 or 0.2, the results outperform the original RFECV method ($\alpha = 0$) across various metrics. Specifically, when $\alpha = 0.1$, the model achieved the best performance, selecting 74 features with an accuracy of 87.5%, Precision of 86.89%, Recall of 87.66%, and F1-score of 86.68%. However, for $\alpha \geq 0.2$, the overall metrics fluctuated at levels generally below the peak observed at $\alpha = 0.1$, rather than changing monotonically. The optimal feature subset contained approximately 70 features. For all subsequent sections, the SVM_CF_RFECV method uses data obtained with $\alpha = 0.1$.

Table 2. Influence of different weight values on the results.

α	Feature number	Accuracy	Precision	Recall	F1-score
0	78	0.8295	0.8234	0.8320	0.8247
0.1	74	0.8750	0.8689	0.8766	0.8668
0.2	56	0.8409	0.8357	0.8365	0.8356
0.3	71	0.7955	0.7841	0.7812	0.7815
0.4	70	0.8068	0.8073	0.8159	0.8013
0.5	73	0.8068	0.7972	0.8011	0.7987
0.6	81	0.7727	0.7699	0.7764	0.7694
0.7	49	0.7727	0.7600	0.7689	0.7629
0.8	50	0.6932	0.6944	0.7107	0.6930
0.9	55	0.7841	0.7802	0.7821	0.7790

4.3 Ablation Study

This section presents an ablation study designed to validate the effectiveness of the key components of the proposed method, including the SVM classifier, the RFECV feature selection strategy, and the introduction of correlation-based feature weighting.

As shown in Table 3, removing the RFECV strategy and using only the SVM classifier led to a marked decline in model performance, highlighting the importance of recursive feature elimination for feature optimization. Similarly, removing the CF weights and using only the RFECV algorithm weakened the effectiveness of feature selection, demonstrating that incorporating domain knowledge can substantially enhance the model's discriminative ability.

To ensure consistency in the comparison process, the SVM algorithm was also evaluated using multi-fold cross-validation. Overall, the results of the ablation study indicate that the components of the proposed method work synergistically, collectively improving the effectiveness of early AD diagnosis.

Additionally, Fig. 3 illustrates the evaluation accuracy and the range of fold-wise accuracies during the feature elimination process on the training set for both algorithms (SVM_CF_RFECV and SVM_RFECV). It can be observed that, as the number of features is reduced from 166 to 74, the accuracy gradually increases to its peak, after which it decreases as the number of selected features further decreases. The optimal range of accuracy lies between 90 and 50 selected features.

Within this range, the SVM_CF_RFECV algorithm consistently outperforms the SVM_RFECV method, while the accuracies of both methods are generally similar outside of this range. This demonstrates that introducing the CF variable helps guide the feature selection process closer to a global optimum. Based on the comparisons above, we conclude that the proposed SVM_CF_RFECV method outperforms traditional RFECV on both the training and testing sets, making it better suited for early Alzheimer's disease prediction.

4.4 Comparison With Other Methods

To further validate the effectiveness of the proposed method, we compared its performance with several recent studies on Alzheimer's disease classification using SVM-based methods. The results are summarized in Table 4 (Ref. [11,19,20]). The proposed SVM_CF_RFECV achieved the highest accuracy of 0.8750, with balanced precision (0.8689), recall (0.8766), and F1-score (0.8668).

By comparison, Alatrany et al. [11] reported an accuracy of 0.8470 with similar precision and recall values. Among existing SVM-RFE variants, USVM-RFE achieved an accuracy of 0.8512 and BBO-SVM-RFE achieved 0.8426 in their respective original studies on the ADNI dataset. These comparisons demonstrate that the proposed SVM_CF_RFECV method consistently outperforms existing SVM-based feature selection approaches on the same dataset.

It is worth noting that deep learning methods in other studies have reported accuracies above 90%, but such models typically require large-scale data and offer limited interpretability. In contrast, our method achieves competitive performance while maintaining clear interpretability through feature selection guided by both imaging features and clinical correlation.

4.5 Discriminative Brain Regions Identified by SVM_CF_RFECV

To gain further insights into the neurobiological underpinnings of the classification results, we examined the brain regions selected by the proposed SVM_CF_RFECV method. Based on the AAL3 atlas, an initial set of 166 structural features was extracted, from which a representative subset of 74 discriminative regions was identified when α was set to 0.1.

Fig. 4 visualizes the spatial distribution of the selected regions on a standardized brain template. These regions are widely distributed across the temporal lobe, hippocampus, parietal cortex, cingulate cortex, default mode network, and cerebellum, many of which are known to be critically involved in AD-related neurodegeneration.

To provide more detailed information, the top 15 regions ranked by feature importance are summarized in Table 5, along with their weights, ranks, and primary functional roles. Notably, the hippocampus, cingulate cortex, and cerebellar subregions appear among the highest-ranked areas, suggesting that impairments in memory, executive control, and motor-cognitive integration play central roles in the early stages of AD.

4.6 Robustness Analysis

To further verify the stability of the proposed method, the optimal feature subset selected with $\alpha = 0.1$ contained 74 features and repeated the evaluation under 10 random train-test partitions. In each partition, all preprocessing steps (missing-value imputation, normalization, CF calcu-

Table 3. Ablation study.

Methods	Feature number	Accuracy	Precision	Recall	F1-score
SVM	166	0.7530	0.7599	0.7530	0.7505
SVM_RFECV	78	0.8295	0.8234	0.8320	0.8247
SVM_CF_RFECV	74	0.8750	0.8689	0.8766	0.8668

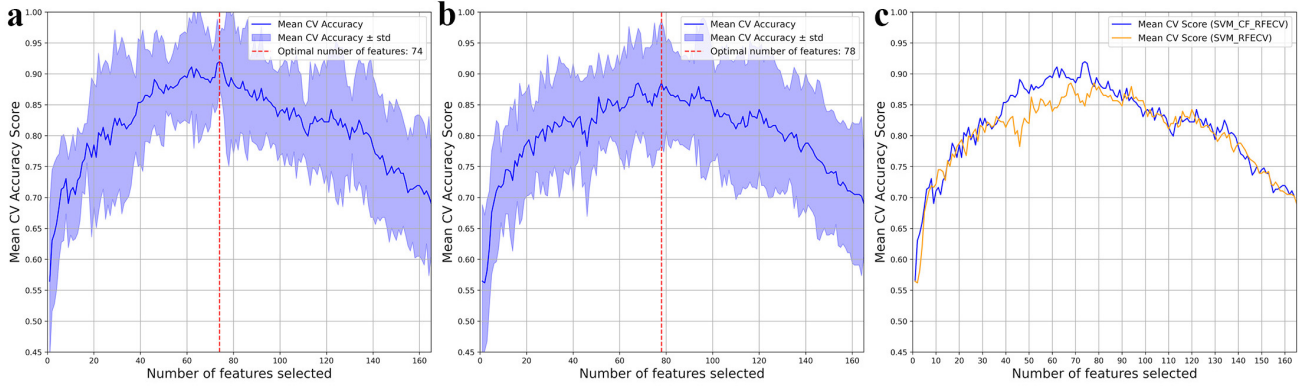


Fig. 3. Evaluation accuracy and the range of fold-wise accuracies during the feature elimination process. (a) SVM_CF_RFECV. (b) SVM_RFECV. (c) Comparison of classification accuracy between SVM_RFECV and SVM_CF_RFECV across different feature subset sizes.

Selected AAL3 Regions (Uniform Color)

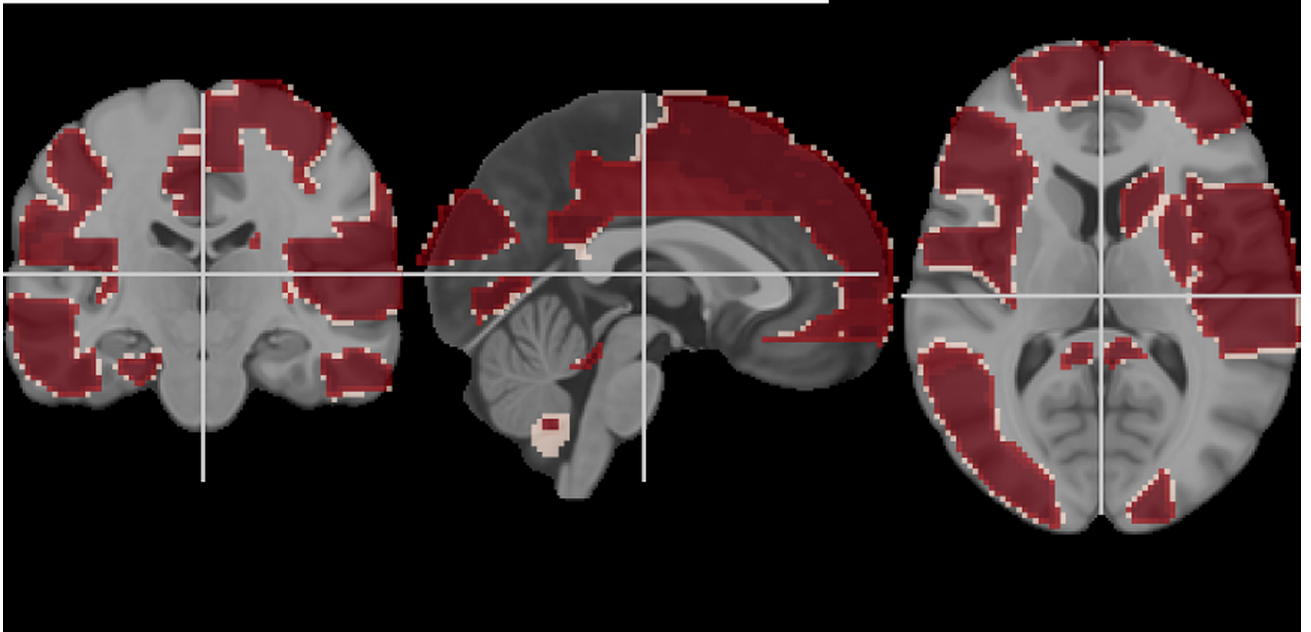


Fig. 4. Discriminative brain regions visualized based on SVM_CF_RFECV results. The red areas indicate the brain regions selected by the proposed SVM_CF_RFECV method.

lation, and feature selection) were performed only on the training set, and the learned parameters were applied to the test set without modification. Table 6 summarizes the averaged performance of the proposed SVM_CF_RFECV and the baseline SVM_RFECV across these runs. The proposed method achieved an accuracy of 0.8489 ± 0.0330 , which is consistently higher than the baseline accuracy of $0.8023 \pm$

0.0284 . Similar improvements were also observed in precision, recall, and F1-score. To statistically validate the superiority of the proposed method, paired two-tailed t -tests were conducted to compare cross-validation accuracies between SVM_CF_RFECV and SVM_RFECV across the 10 random partitions. SVM_CF_RFECV achieved an average accuracy of 0.8489 ± 0.0330 , significantly higher than the

Table 4. Comparison with SVM-based feature selection methods on the ADNI dataset.

Methods	Accuracy	Precision	Recall	F1-score
SVM_CF_RFECV	0.8750	0.8689	0.8766	0.8668
Alatrany et al. [11]	0.8470	0.8520	0.8470	0.8490
USVM-RFE [20]	0.8512	-	-	-
BBO-SVM-RFE [19]	0.8426	-	-	-
PCA+SVM	0.7386	0.7406	0.7386	0.7376

USVM-RFE, Universum Support Vector Machine based Recursive Feature Elimination; BBO-SVM-RFE, Binary Biogeography-Based Optimization and SVM-RFE feature selection method; PCA, Principal Component Analysis.

0.8023 ± 0.0284 of SVM_RFECV ($t = 3.86$, $df = 9$, $p = 0.003$). Significant improvements were also observed in precision, recall, and F1-score (all $p < 0.01$). These results confirm that the performance gain is statistically significant and not due to random chance.

In summary, the ablation study confirmed the effectiveness of each component of the proposed framework, while the comparison with other methods highlighted its superior performance under the single-split setting commonly adopted in prior studies. The robustness analysis presented here further demonstrates that the improvements are stable across different data partitions. Taken together, these findings confirm that the proposed SVM_CF_RFECV is both effective and reliable, offering a practical advantage for early AD diagnosis.

5. Discussion

This study proposed a novel feature selection method, SVM_CF_RFECV, which integrates correlation-based weighting into the SVM-RFECV framework. By embedding prior clinical knowledge into the feature ranking process, the method enhances both classification performance and interpretability for early AD prediction. Applied to a three-class classification task (CN, MCI, AD) using the ADNI dataset, the method achieved a peak accuracy of 87.5% under a single-split setting and an average accuracy of 0.8489 ± 0.0330 across multiple random partitions, significantly outperforming the baseline SVM_RFECV (0.8023 ± 0.0284). These findings confirm that the improvement is robust and not dependent on a particular partition.

As illustrated in Table 5, the hippocampus, cingulate cortices, and cerebellar subregions were among the most discriminative features identified by our method. The left hippocampus, a key region for memory formation and spatial navigation, ranked highest in importance, underscoring its critical role in AD-related cognitive impairment [28]. Notably, cerebellar regions such as Crus I and lobule VI also exhibited high weights, highlighting the cerebellum's involvement in cognitive regulation and motor coordination [29]. Both left and right middle cingulate

cortices, implicated in attention control and emotion regulation, contributed strongly, reflecting deficits in executive function and emotional processing frequently reported in AD [30]. In addition, regions associated with visual recognition and language processing—such as the fusiform gyrus, inferior temporal gyrus, supramarginal gyrus, and inferior frontal gyrus—showed strong diagnostic value, supporting the view that impairments in visual and language functions are integral to AD-related decline [31]. Importantly, left hemisphere regions (e.g., hippocampus, middle cingulate) generally exhibited higher weights than their right-hemisphere counterparts, and this hemispheric asymmetry was confirmed to be statistically significant by a binomial test (6 left-hemisphere vs. 9 right-hemisphere among the top 15 regions, $p < 0.05$), consistent with prior findings that left-lateralized deficits are more pronounced in early AD.

Overall, the selected regions overlap with established AD-related networks, including the temporal lobe, hippocampus, parietal cortex, default mode network, and limbic system [32]. The observed structural alterations and their associations with cognitive decline correspond closely to well-documented patterns of atrophy, hypometabolism, and disrupted connectivity [33]. This concordance reinforces the biological plausibility of the selected features and supports their potential as reliable neuroimaging biomarkers [34]. Importantly, compared with deep learning approaches that often act as black boxes, the proposed method provides interpretable feature weights directly linked to specific brain regions, offering both neuroscientific insight and clinical transparency.

6. Limitations

Despite these strengths, several limitations should be acknowledged. First, the computational scalability of the proposed method on larger datasets has not been systematically evaluated and remains a direction for future work. Second, although we performed strict subject-level cross-validation and fold-wise normalization to prevent data leakage, the atlas registration step (using the AAL3 atlas) was applied to the full dataset before cross-validation splitting, which may introduce a minor risk of data leakage. Third, external validation on independent datasets (e.g., the Australian Imaging, Biomarkers and Lifestyle Flagship Study of Ageing [AIBL] and the Open Access Series of Imaging Studies [OASIS]) was not conducted due to data constraints, limiting generalizability to broader populations. Fourth, this study was limited to cross-sectional MRI data; future work should incorporate longitudinal and multimodal imaging to evaluate predictive power for disease progression. Fifth, the use of MMSE scores in feature selection introduces dependence on clinical assessments, which may not be available in all clinical settings. Sixth, the ADNI dataset employs specific inclusion criteria (e.g., age range, comorbidity exclusions), which may bias results

Table 5. Brain regions selected by SVM_CF_RFECV with weights derived from SVM coefficients and correlations with MMSE scores.

Feature	Full name	Weight	Rank	Main functional descriptions
IHIP	Left Hippocampus	2.1782	1	Memory formation and consolidation, spatial navigation
rCERCRU1	Right Cerebellar Crus I	1.9745	2	Motor coordination, cognitive modulation
IMCC	Left Middle Cingulate Cortex	1.9707	3	Attention control, conflict processing, emotion regulation
rMCC	Right Middle Cingulate Cortex	1.4796	4	Attention control, conflict processing, emotion regulation
rFFG	Right Fusiform Gyrus	1.4369	5	Face recognition, visual processing
rHIP	Right Hippocampus	1.4075	6	Memory formation and consolidation, spatial navigation
rPreCG	Right Precentral Gyrus	1.3987	7	Motor control, motor planning
ISMG	Left Supramarginal Gyrus	1.3965	8	Language processing, spatial attention, working memory
rLING	Right Lingual Gyrus	1.3202	9	Visual processing, visual memory
IIFGtriang	Left Inferior Frontal Gyrus, Triangular Part	1.2739	10	Language production, executive function, cognitive control
IITG	Left Inferior Temporal Gyrus	1.2327	11	Visual recognition, semantic memory
IINS	Left Insula	1.1677	12	Emotion processing, visceral sensation, cognitive control
rCER6	Right Cerebellar Lobule VI	1.156	13	Motor coordination, cognitive function
rMFG	Right Middle Frontal Gyrus	1.1498	14	Working memory, executive control, cognitive flexibility
rMOG	Right Middle Occipital Gyrus	1.1385	15	Visual processing, spatial localization

Table 6. Robustness analysis.

Methods	Accuracy	Precision	Recall	F1-score
SVM_RFECV	0.8023 ± 0.0284	0.7943 ± 0.0277	0.7957 ± 0.0327	0.7926 ± 0.0303
SVM_CF_RFECV	0.8489 ± 0.0330	0.8419 ± 0.0360	0.8394 ± 0.0304	0.8384 ± 0.0334

toward a healthier, more homogeneous population and limit applicability to real-world clinical populations. Finally, clinical translation will require simplifying the selected 74 features into practical diagnostic tools, such as composite imaging scores or automated indices, to facilitate use in routine workflows.

7. Conclusions

This study proposed a novel feature selection method, SVM_CF_RFECV, which incorporates correlation-based weighting into the SVM-RFECV framework to enhance early prediction of Alzheimer's disease. Validated on the ADNI dataset, the method achieved a peak accuracy of 87.5% under a single-split setting and an average accuracy of 0.8489 ± 0.0330 across multiple random partitions, significantly outperforming traditional SVM_RFECV. These results demonstrate that the proposed approach effectively addresses challenges associated with high-dimensional feature selection and classification.

The final subset of 74 discriminative brain regions was largely distributed across areas strongly implicated in early AD pathology, including the hippocampal formation, temporal lobe, parietal cortex, default mode network, and limbic system. Their involvement is consistent with prior neuroimaging findings, supporting both the clinical relevance and neurobiological significance of the selected features.

In conclusion, SVM_CF_RFECV provides an effective and interpretable framework that not only improves classification performance but also yields insights aligned with established AD pathophysiology. These findings lay a solid foundation for MRI-based computer-aided diagnosis and biomarker discovery. Future work should extend this approach to multimodal and longitudinal datasets, and translate the selected features into practical tools such as imaging scores or automated indices to further confirm their stability and clinical utility in disease prediction and progression monitoring.

Availability of Data and Materials

Data used in preparation of this article are obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) (<http://adni.loni.usc.edu>). Additional information can be provided by the corresponding authors upon reasonable request.

Author Contributions

JS designed the project and supervised the overall research; HZ collected data, performed experiments and analysis; QZ and ZG designed the research; RZ, ZS, XZ, and YC participated in data collection or analysis. HZ and JS wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Protocols and procedures were approved by the institutional review board (IRB) at Hangzhou Dianzi University (IRB-2020001) and the ethics committee at Beijing Hospital (2022BJYYEC-375-01). Patient consent was waived due to the anonymization of all sensitive information in the collected data.

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Conflicts of Interest

The authors declare no conflicts of interest.

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