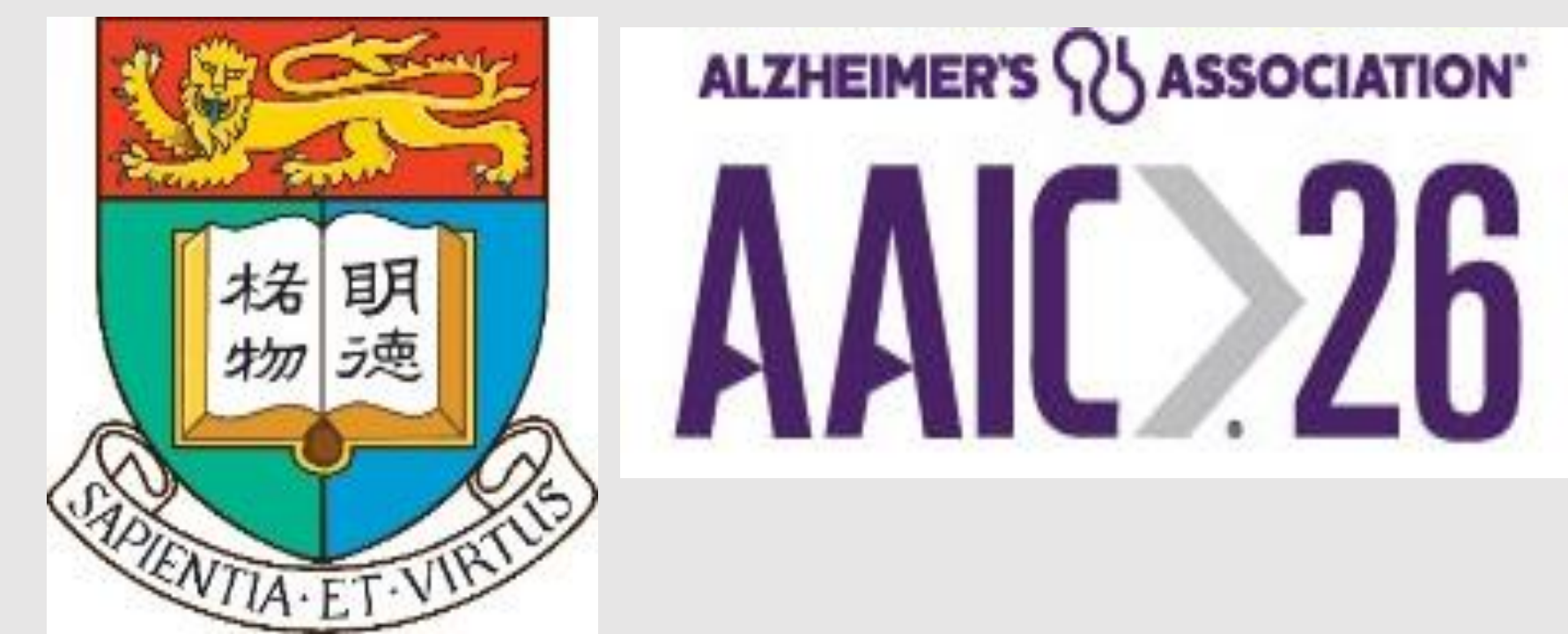


Cutoff Identification For Centiloid, WMH, and MoCa In Cognitive Syndromes: A Clinically Driven Decision Tree

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Background

Accurate differentiation of dementia-related clinical syndromes remains challenging due to overlapping symptoms and mixed pathologies. While advanced machine learning models exist, many lack transparency and are difficult to integrate into clinical workflows. This study aimed to develop a clinically interpretable model using Centiloid, white matter hyperintensity (WMH), and HK-MoCA scores to classify seven cognitive syndromes: Alzheimer's disease (AD), AD with MCI (ADMCI), mild cognitive impairment (MCI), mixed dementia (MD), vascular dementia with MCI (VDMCI), vascular dementia (VD), and subjective cognitive decline (SCD).

Participants

	Cohort 1	Cohort 2
AD	19	11
ADMCI	8	1
MCI	5	12
MD	16	3
VDMCI	10	5
VD	21	8
SCD	11	2

Imaging, Biomarker acquisition and processing

MRI: T1-weighted magnetization-prepared rapid gradient echo images (MPRAGE), T2-weighted images and 3D Fluid attenuated inversion recovery (FLAIR) were acquired. The MPRAGE images were used to retrieve the WMH with the FreeSurfer software package (<http://surfer.nmr.mgh.harvard.edu/version 7.1>). The FLAIR images were used to correlate with the result obtained from FreeSurfer software. The volume of WMH was obtained.

Amyloid PET imaging: 18F-Flutemetamol was used as radiotracer for amyloid PET. The amyloid PET/CT was processed using REST version 1.2 software. The mean standard uptake value (SUV) of the relevant brain regions in the AAL brain mask were calculated. The SUV of the whole cerebellum was used as the reference for the calculation of SUVR based on the equation: $SUVR = \frac{SUV_{VOI}}{SUV_{Whole\ cerebellum}}$. To standardize the Standard Uptake Value ratio (SUVR) among the three radiotracer, all SUVR obtained were converted to the 100-point Centiloid Level (CL), with reference to the procedure suggested by the Klunk et al study.

MoCA Test: HK Version were performed for all participants

Method

Model Building, Validation and Testing

The model was built using features from 70% of Cohort 1 participants and was validated by 30% of Cohort 1 participants. The numeric values of Centiloid scores, WMH volume and MoCA Score were input into the decision tree algorithms complied by R (Ihaka and Gentleman; V.4.0.5) with rattle and RGtk2 package for building the decision tree model for seven cognitive syndromes: Alzheimer's disease (AD), AD with MCI (ADMCI), mild cognitive impairment (MCI), mixed dementia (MD), vascular dementia with MCI (VDMCI), vascular dementia (VD), and subjective cognitive decline (SCD). The model was tested using local Cohort II. Classification accuracy, sensitivity, specificity, F1 score, and clinical interpretability were assessed. Confusion matrices and decision pathways were analysed to evaluate model performance and practical utility.

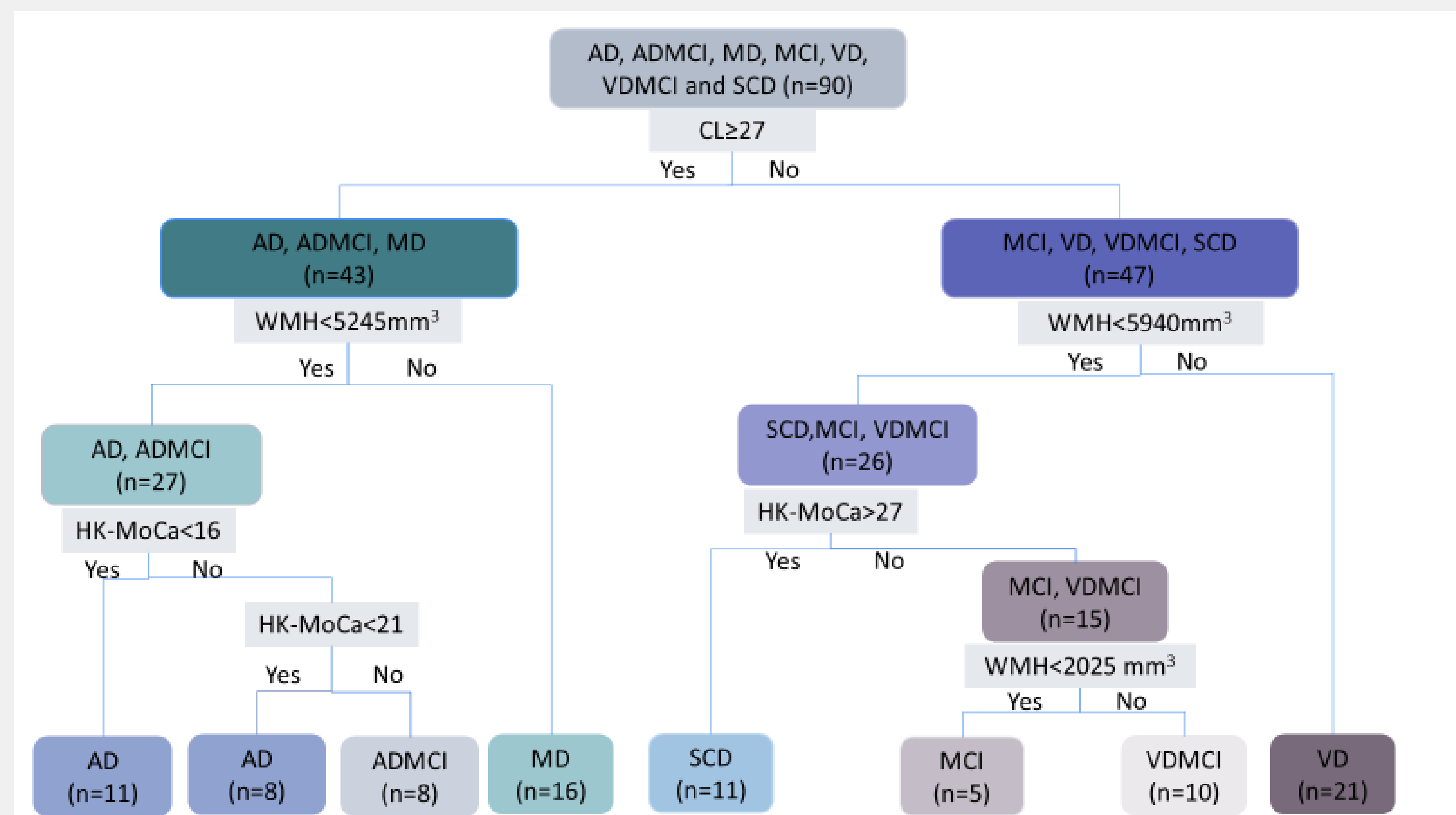
Cross validation

To improve the generalizability on the built models, 10-fold cross-validation was employed in the validation and testing process. All data within the group were divided into ten groups with an equal number of samples. During model building, the first decision tree training was trained by the initial nine groups, and the rest group was used as model validation. The training continued for 10 times which maximize the use of all groups of data. In validation and testing stage, the performance of each model was the average of the results computed in these 10 times of training.

Data Analysis

The overall performance and subgroup analysis performance of the decision tree model were assessed by the overall accuracy, confusion matrix, sensitivity, specificity, precision, F1 score and receiver operating characteristic (ROC) curves.

Result



Validation using Cohort II achieved 76.2% accuracy, 70% precision, 65% sensitivity, and 70% F1 score.

Conclusion

This clinically intuitive model demonstrates moderate but meaningful classification performance and offers a transparent, practical tool to support real world dementia diagnosis.