

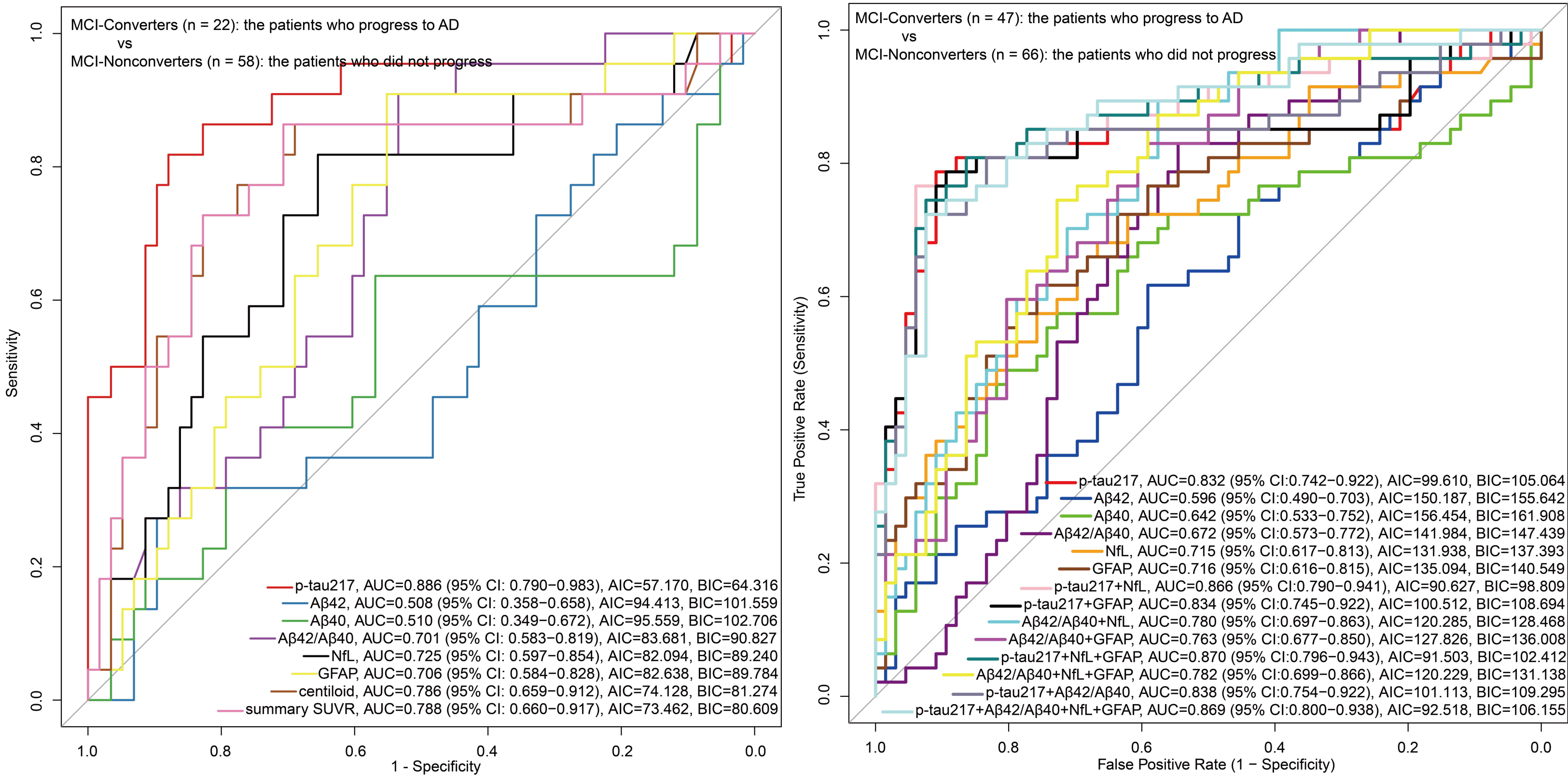
Plasma p-tau217 as a Potential Independent Biomarker for Predicting the Progression from MCI to AD Dementia

Sunday-1155

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1. Plasma p-tau217 achieves comparable discriminative performance to Aβ-PET and multi-biomarker panels for differentiating MCI patients who progressed to AD dementia from those who did not.
2. p-tau217 shows the most significant inter-group difference and strongest associations with Aβ pathology and longitudinal cognitive decline among all plasma biomarkers.
3. A two-cut-point p-tau217 risk stratification model accurately stratifies MCI patients with distinct cognitive trajectories and amyloid status, achieving 100% positive predictive value for Aβ positivity in the high-risk group (low-risk stratum: ≤0.185 pg/mL, moderate-risk stratum: 0.185–0.324 pg/mL, high-risk stratum: >0.324 pg/ mL).

INTRODUCTION		regression models, DeLong tests, Akaike information criterion, Bayesian information criterion, Cox proportional hazards models, Spearman correlations, and linear mixed-effects models (LMM) were applied to evaluate inter-group differences, discriminative performance, conversion risk, and associations of plasma biomarkers with Aβ-PET measures (centiloid, summary SUVR) and longitudinal cognitive decline. Risk stratification analyses were further conducted using LMM after categorizing participants into low-, moderate-, and high-risk strata according to a p-tau217-based two-cut-point approach.		associations with cognitive decline and Aβ-PET (<i>p</i> < 0.001). High-risk participants showed the steepest cognitive decline (<i>p</i> < 0.001), with a positive predictive value (PPV) of 100% for Aβ-PET amyloid positivity and a PPV of 82.2% for MCI-Converters. Low-risk participants showed a negative predictive value (NPV) of 78.3% for Aβ-PET amyloid negativity and an NPV of 84.9% for MCI-Nonconverters.		Figure 1	
Alzheimer's disease (AD) is the leading cause of dementia. Mild cognitive impairment (MCI) represents a critical stage for the early prevention and treatment of AD. Multiple plasma biomarkers, including phosphorylated tau 217 (p-tau217), have shown predictive potential for AD at the MCI stage. However, the comparative predictive performance of p-tau217 and Aβ-PET for AD remains uncertain. Furthermore, whether multi-biomarker plasma panels can improve clinical utility for AD prediction is unclear. Accordingly, this study aimed to assess whether plasma p-tau217 could serve as an alternative to Aβ-PET and multi-biomarker plasma panels for predicting AD in MCI individuals.		RESULTS		CONCLUSIONS			
		p-tau217 demonstrated the most significant inter-group difference (<i>p</i> < 0.001) and the highest Cox hazard ratio (7.88 [95% CI: 4.38-14.19]), and best distinguished MCI-Converters from MCI-Nonconverters (AUC = 0.886 [95% CI: 0.790-0.983]), with its discriminative performance comparable to that of Aβ-PET measures and multi-biomarker plasma models (DeLong <i>p</i> > 0.05) (Figure 1). p-tau217 exhibited the strongest		p-tau217 is the optimal plasma biomarker with the potential to serve as an alternative to Aβ-PET and multi-biomarker panels for predicting conversion from MCI to AD dementia, thereby facilitating plasma biomarker-based prediction of MCI-to-dementia conversion.			
METHODS		FUNDING		CONTACT			
Using follow-up diagnostic information, we included 47 MCI-Converters (patients who progressed to AD) and 66 MCI-Nonconverters (patients who did not progress) from the Alzheimer's Disease Neuroimaging Initiative. Wilcoxon rank-sum tests, five-fold cross-validated logistic		1.STI2030-Major Projects (No. 2021ZD0201802); 2.National Nature Science Foundation of China (No. 82471450); 3.Xicheng District Science and Technology Special Project (No. XCSTS-SD2024-02); 4.Shandong Medical and Health Science and Technology Project (No. 202403070166); 5.Haiyou Health High-Caliber Talent Project (No. 202412)		 *Corresponding author: Cuibai Wei Email:weicb@xwhosp.org ORCID: 0009-0004-7380-7451 ALZHEIMER'S ASSOCIATION 			