Comparative Evaluation of NIA-AA 2018 and 2024 Research Criteria for Alzheimer's Disease Diagnosis in a Real-World Clinical Cohort

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Objectives

To compare the diagnostic performance of the NIA-AA 2018 and NIA-AA 2024 research criteria for Alzheimer's disease (AD) against a clinical gold standard. We aimed to determine sensitivity, specificity, predictive values, overall accuracy, likelihood ratios, and to characterize misclassified cases in a real-world cohort.

Materials and methods

We retrospectively analyzed 138 consecutive patients (73 with clinical AD, 65 non-AD) referred to the Centro Disturbi Cognitivi e Demenze (CDCD) at the Policlinico di Bari. Data collected included demographics, Mini-Mental State Examination, and cerebrospinal fluid (CSF) biomarkers: A-beta42, total tau, and p-Tau-181. Clinical AD diagnosis was established by consensus among neurologists according to DSM-5 criteria. NIA-AA 2018 classified biomarker positivity as both A+ (abnormal A-beta42) and T+ (abnormal p-Tau). NIA-AA 2024 employed an expanded "core biomarker" definition (A+T+ or A+T+N+). Performance metrics—sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy, positive and negative likelihood ratios (LR+, LR–), and Youden Index—were calculated for each criterion. False negative (FN) and true positive (TP) groups under NIA-AA 2018 were compared using Welch's t-tests on age, sex distribution, MMSE, A-beta42, total tau, and p-Tau levels.

Results

For NIA-AA 2018 vs. clinical AD, sensitivity was 79.5%, specificity 98.5%, PPV 98.3%, NPV 81.0%, accuracy 88.4%; LR+ 51.6, LR– 0.21, Youden Index 0.78. NIA-AA 2024 showed improved sensitivity (90.4%), perfect specificity (100%), PPV 100%, NPV 90.3%, accuracy 94.9%; LR+ infinite (specificity 100%), LR– 0.10, Youden Index 0.90. Under NIA-AA 2018, 15 of 73 clinically diagnosed AD patients were FN. Compared with 58 TP patients, FN cases had significantly lower CSF total tau (358 ± 247 vs. 682 ± 320 pg/mL; p = 0.0015) and non-significantly higher A-beta42 (427 ± 345 vs. 454 ± 167 pg/mL; p = 0.80), with no differences in age (70.9 ± 6.2 vs. 72.1 ± 5.8 years; p = 0.48), sex ratio, or MMSE (24.6 ± 4.1 vs. 22.8 ± 5.1; p = 0.19). Similar patterns were observed when using NIA-AA 2024 as reference: FN cases (n = 7) under NIA-AA 2018 had lower A-beta42 (279 ± 68 vs. 454 ± 167; p < 0.0001) and total tau (403 ± 297 vs. 682 ± 320; p = 0.05).

Discussion

NIA-AA 2024 outperforms the 2018 framework by enhancing sensitivity without sacrificing specificity, thereby capturing a broader spectrum of AD biomarker profiles. The 2018 criteria, whilst highly specific, tend to miss patients with milder amyloid and tau abnormalities.

Comparison	NIA-AA 2018	NIA-AA 2024
Sensitivity	79.5 %	90.4 %
Specificity	98.5 %	100 %
Positive Predictive Value (PPV)	98.3 %	100 %
Negative Predictive Value (NPV)	81.0%	90.3%
Diagnostic Accuracy	88.4 %	94.9 %
Positive Likelihood Ratio (LR +)	51.6	∞
Negative Likelihood Ratio (LR –)	0.21	0.10

Comparison using NIA-AA 2024 as reference:

	False Negative (FN) mean+SD	True Positive (TP) mean+SD	P value
CSF A-beta42	279 ± 68	454 ± 167	p < 0.0001
CSF Total tau	403 ± 297	682 ± 320	p = 0.05
CSF P-Tau 181	51 ± 15	117±59	p = 0.0001

Conclusions

Implementation of NIA-AA 2024 criteria in clinical and research settings is recommended to improve early and accurate detection of Alzheimer's disease.

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