

Renal Function Influences Blood-based Alzheimer's Disease Biomarkers In A Disease-stage-dependent Manner: The Pumch Dementia Cohort

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Kidney function matters when interpreting plasma AD biomarkers.
Lower eGFR is strongly associated with higher plasma NfL across diagnostic groups.
The effect of eGFR on plasma p-tau217 is disease-stage dependent and attenuates in AD dementia.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Blood-based biomarkers are increasingly used for the detection, differential diagnosis, and monitoring of Alzheimer’s disease (AD), offering a less invasive and more scalable alternative to CSF and PET biomarkers [1]. Plasma p-tau217, NfL, GFAP, and Aβ-related measures capture complementary aspects of AD pathology, neuroaxonal injury, and glial activation, and are moving toward broader clinical implementation [1,2]. However, circulating biomarker concentrations may be affected by systemic comorbidities, particularly renal dysfunction, which can alter biomarker clearance and potentially confound interpretation [3]. Whether the influence of renal function differs across biomarkers and disease stages remains insufficiently understood. Therefore, we examined the association between eGFR and plasma AD-related biomarkers across cognitively unimpaired, non-AD dementia, and AD dementia groups in the PUMCH dementia cohort.	We examined associations between estimated glomerular filtration rate (eGFR) and plasma biomarkers, including p-tau217, NfL, GFAP, and Aβ42, in a real-world clinical cohort derived from the Peking Union Medical College Hospital (PUMCH) dementia cohort. Multivariable linear regression models with log-transformed biomarker levels were adjusted for age, sex, education, and APOE genotype, with effect sizes scaled per 10 mL/min/1.73 m² difference in eGFR. Disease-stage-dependent effects were evaluated using interaction models by diagnostic group (cognitively unimpaired, non-AD dementia, and AD dementia). The study was approved by the local institutional review board and registered at ClinicalTrials.gov (NCT05023564).	Associations between renal function and blood-based biomarkers differed substantially across biomarkers and disease stages. Lower eGFR was strongly associated with higher plasma NfL levels across all diagnostic groups, with the steepest association observed in cognitively unimpaired individuals and progressive attenuation in non-AD and AD dementia groups. For p-tau217, lower eGFR was associated with higher plasma levels in cognitively unimpaired and non-AD individuals, whereas this association was markedly attenuated and directionally reversed in AD dementia. Formal interaction analyses confirmed significant disease-stage-dependent heterogeneity for p-tau217, indicating that the relationship between renal function and p-tau217 is modified by disease stage. In contrast, no significant eGFR-by-diagnostic group interactions were observed for GFAP or Aβ42.	Renal function shows biomarker-specific and disease-stage-dependent effects on blood-based Alzheimer’s disease biomarkers. Nonspecific neuroaxonal injury markers such as NfL are strongly influenced by kidney function, particularly in preclinical stages. In contrast, associations between renal function and p-tau217 are attenuated or altered in AD dementia, suggesting that disease-related pathological burden and clinical severity increasingly dominate circulating p-tau217 levels at later stages. These findings emphasize the importance of accounting for kidney function when interpreting blood biomarkers, especially in non-demented and early disease stages.	1. Hansson O, Edelmayer RM, Boxer AL, et al. The Alzheimer's Association appropriate use recommendations for blood biomarkers in Alzheimer's disease. <i>Alzheimers Dement</i>. 2022;18(12):2669-2686. doi:10.1002/alz.12756 2. Hampel H, Hu Y, Cummings J, et al. Blood-based biomarkers for Alzheimer's disease: Current state and future use in a transformed global healthcare landscape. <i>Neuron</i>. 2023;111(18):2781-2799. doi:10.1016/j.neuron.2023.05.017 3. Janelidze S, Barthélemy NR, He Y, Bateman RJ, Hansson O. Mitigating the Associations of Kidney Dysfunction With Blood Biomarkers of Alzheimer Disease by Using Phosphorylated Tau to Total Tau Ratios. <i>JAMA Neurol</i>. 2023;80(5):516-522. doi:10.1001/jamaneurol.2023.0199 CONTACT  Yunfan You Department of Neurology, Peking Union Medical College Hospital Email: 1036941848@qq.cn ALZHEIMER'S ASSOCIATION AAIC>26