Total Aβ\textsubscript{42}/Aβ\textsubscript{40} ratio in plasma predicts amyloid-PET status, independent of clinical AD diagnosis

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Study objective and summary result
This study tested the hypothesis that lower plasma ratio of total amyloid-β-42 (Aβ\textsubscript{42}) to total amyloid-β-40 (Aβ\textsubscript{40}) is a reliable predictor of amyloid-PET positivity, and the results showed that lower total plasma Aβ\textsubscript{42}/Aβ\textsubscript{40} ratio is found in individuals with amyloid-PET positivity.

Classification of evidence
Class II.

What is known and what this paper adds
PET is an important tool suggesting the presence of cortical amyloid pathology, but it is expensive. This investigation’s results indicate that assessments of plasma Aβ\textsubscript{42}/Aβ\textsubscript{40} ratio can serve as a cheaper proxy measure.

Participants and setting
The investigators analyzed data from individuals who participated in the Australian Imaging, Biomarkers and Lifestyle (AIBL) study, which began in 2006. The AIBL participants selected for these analyses included 130 healthy controls, 24 individuals with mild cognitive impairment, and 22 individuals with Alzheimer disease.

Design, size, and duration
The AIBL participants provided blood samples and underwent PET with Pittsburgh compound B at 18-, 36-, and 54-month timepoints. The investigators used ELISA-based methods to quantify the plasma levels of Aβ\textsubscript{42} and Aβ\textsubscript{40} and examined the PET data to categorize the participants as positive or negative for amyloid-PET positivity. The personnel who analyzed plasma had no access to clinical data. The investigators then used receiver operating characteristic (ROC) analyses to determine whether the plasma Aβ\textsubscript{42}/Aβ\textsubscript{40} ratio is consistent with amyloid-PET positivity.

Main results and the role of chance
Relative to the individuals without amyloid-PET positivity, those with amyloid-PET positivity had lower total plasma Aβ\textsubscript{42}/Aβ\textsubscript{40} ratios at all timepoints (p < 0.0001). Total plasma Aβ\textsubscript{42}/Aβ\textsubscript{40} ratios reliably distinguished patients with and without amyloid-PET positivity, with the timepoint-specific areas under the ROC curves ranging from 0.880 at 36 months to 0.913 at 54 months.

Bias, confounding, and other reasons for caution
The sample size was small, and the plasma levels of Aβ\textsubscript{42} and Aβ\textsubscript{40} varied considerably. Patients did not have autopsy-confirmed Alzheimer disease pathology.

Generalizability to other populations
The present study’s reliance on data from Australia may limit the generalizability of the results to dissimilar countries.

Study funding/potential competing interests
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