

Predictors of Future Amyloid-Positive Conversion in Initially Amyloid-Negative Non-demented Individuals

P1-001

Han Kyu Na, MD¹, Yeeun Sun, MD¹, Yun Young Choi, MD¹, Jung Hyun Lee, MD¹, Seok Jong Chung, MD, PhD¹, Young H. Sohn, MD, PhD¹, Chul Hyoung Lyoo, MD, PhD², Hanna Cho², Phil Hyu Lee, MD, PhD^{1,*}

Correspondence:
Phil Hyu Lee (phlee@yuhs.ac)

¹ Dpt of Neurology, Yonsei University College of Medicine, Seoul, Korea; ² Dpt of Neurology, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

KEY TAKE AWAY: Among individuals with initially A β -negative (A β -) PET scans, APOE genotype, baseline cognitive status, subthreshold A β burden, and regional deposition patterns serve as robust predictors of future A β -positive (A β +) conversion

INTRODUCTION

Conversion from A β - to A β + status represents a critical inflection point that triggers the pathological cascade of AD biomarkers.

Given that anti-A β immunotherapy is most likely to be efficacious when administered before substantial neurodegeneration take place, prediction of impending A β + conversion has become increasingly important for timely therapeutic intervention.

OBJECTIVE: We sought to identify potential risk factors predictive of future A β + conversion in a non-demented population with baseline A β - PET findings.

METHODS

PARTICIPANTS: 168 non-demented individuals with A β - PET scans (SCD, n=56; MCI, n=112) who underwent follow-up A β imaging.

STATISTICAL ANALYSES:

(1) **Logistic regression analysis:** Identifying potential predictive factors associated with conversion from A β - to A β + status

(2) **Cox regression analysis:** Time to dementia conversion was further examined using Cox proportional hazards models

RESULTS

Over a median follow-up of 4.6 yrs, 48 of 168 participants (28.6%) showed A β + conversion, with a median time to conversion of 3.9 yrs

Potential predictors of A β + conversion: Global A β burden, regional A β positivity, APOE ϵ 4 carrier, baseline cognitive status

- Higher global amyloid burden on the Centiloid scale (OR 1.10 per unit increase; 95% CI, 1.04-1.17), regionally positive but globally negative amyloid PET patterns (OR 23.07; 95% CI, 5.68-93.62), APOE ϵ 4 carrier status (OR 5.05; 95% CI, 1.80-14.15), and baseline MCI status relative to subjective cognitive decline (OR 2.94; 95% CI, 1.02-8.47) were independently associated with future amyloid-positive conversion (predictive performance = 0.889; 95% CI, 0.837-0.941).
- In survival analysis, amyloid-positive converters exhibited a significantly elevated risk of subsequent dementia conversion (HR 2.79; 95% CI, 1.26-6.20).

CONCLUSION

Among individuals with initially A β - PET scans, APOE genotype, baseline cognitive status, subthreshold A β burden, and regional deposition patterns serve as robust predictors of future A β -positive conversion. These findings provide a clinically relevant risk stratification framework that may facilitate early identification of individuals along the AD pathological trajectory and support timely initiation of disease-modifying anti-amyloid therapies.