

Machine Learning Prediction Of ARIA-H Development In Amyloid-positive Subjects

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In 846 amyloid-positive A4 participants, an interpretable L2-penalized logistic model predicted 6-year ARIA-H conversion from baseline multimodal markers (AUC = 0.734, well-calibrated). The risk signature was CAA-aligned: baseline CMB location, regional WMH burden, APOE-ε4, and structural asymmetry.

INTRODUCTION	
• Anti-amyloid monoclonal antibodies are transforming Alzheimer’s disease treatment, but ARIA-H remains a major safety concern. • Baseline identification of high-risk individuals may support personalized monitoring and safer treatment planning.	
OBJECTIVE:	
To determine whether baseline MRI, plasma, cognitive, and clinical features can predict 6-year conversion to ARIA-H positivity.	
METHODS	
We enrolled 846 amyloid-positive A4 participants with baseline SWI/T2* imaging, ≤1 hemorrhagic lesion at baseline, and follow-up MRI at 6 years. ARIA-H was defined as ≥2 cerebral microhemorrhages and/or superficial siderosis on follow-up imaging.	
RESULTS	
An L2-penalized logistic regression was the best-performing model in nested 10×10 cross-validation, achieving 0.734 ± 0.091 AUC with 0.073 Brier score, indicating well-calibrated risk probabilities. At a recall-oriented threshold, the model reached 0.615 sensitivity and 0.752 specificity, favouring converter detection.	
CONCLUSIONS	
Baseline multimodal markers can stratify 6-year ARIA-H conversion risk prior to treatment. The strongest predictors were vascular and genetic in nature (baseline CMB location, regional WMH burden, and APOE-ε4) with structural asymmetry adding a complementary signal. These findings support MRI-informed risk assessment to identify patients who may require closer monitoring for ARIA during anti-amyloid therapy.	
REFERENCES	
Roytman, Michelle, et al. "Amyloid-related imaging abnormalities: an update." <i>American Journal of Roentgenology</i> 220.4 (2023): 562-574.	
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