

Title Page

Screening and predicting progression from high-risk mild cognitive impairment to Alzheimer's disease

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Supplementary Table S1.

Hazard ratio (95%) of cox proportional hazards analysis based on ADAS-13 predictive dataset.

Predictors	A1	A1+baseline MRI	A2	A2+baseline MRI	A2+ΔMRI
Age	0.96 [0.93, 1.00]	0.95 [0.91, 0.99] *	0.96 [0.92, 1.00] *	0.95 [0.91, 1.00] *	0.92 [0.86, 0.98] *
Gender	1.20 [0.69, 2.08]	1.47 [0.65, 3.33]	0.86 [0.46, 1.59]	1.19 [0.49, 2.90]	0.68 [0.31, 1.49]
Marital status=2	0.45 [0.15, 1.34]	0.19 [0.05, 0.71] *	△	0.28 [0.07, 1.11]	0.24 [0.04, 1.34]
Marital status=3	0.82 [0.37, 1.83]	0.93 [0.42, 2.08]	△	1.09 [0.47, 2.68]	2.39 [0.68, 8.40]
ApoEε4	1.14 [0.66, 1.97]	1.69 [0.95, 3.00]	1.19 [0.67, 2.14]	1.19 [0.62, 2.29]	1.29 [0.60, 2.79]
ADAS-13_bl	1.06 [1.00, 1.12] *	1.14 [1.07, 1.21] ***	1.09 [1.02, 1.16] **	1.14 [1.06, 1.23] ***	1.13 [1.03, 1.24] **
MMSE_bl	0.89 [0.77, 1.04]	0.84 [0.71, 0.99] *	0.91 [0.76, 1.11]	0.88 [0.73, 1.07]	0.80 [0.62, 1.02]
CDRSB_bl	-	1.56 [1.23, 1.97] ***	2.05 [1.53, 2.72] ***	2.06 [1.53, 2.77] ***	1.70 [1.20, 2.40] **
CDRSB_bl1	△	-	-	-	-
Hippocampus_bl(cm ³)	-	0.83 [0.54, 1.28]	-	0.80 [0.52, 1.22]	-
WholeBrain_bl(cm ³)	-	1.00 [0.99, 1.01]	-	1.00 [0.99, 1.01]	-
Entorhinal_bl(cm ³)	-	0.90 [0.53, 1.51]	-	1.30 [0.75, 2.27]	-
ΔADAS-13	-	-	1.09 [1.03, 1.17] **	1.09 [1.00, 1.18] *	1.01 [0.91, 1.11]
ΔMMSE	-	-	0.95 [0.80, 1.12]	1.00 [0.84, 1.18]	0.81 [0.63, 1.03]
ΔCDRSB	-	-	2.08 [1.59, 2.72] ***	2.08 [1.54, 2.80] ***	2.41 [1.62, 3.58] ***
ΔHippocampus (cm ³)	-	-	-	-	1.91 [0.27, 13.4]
ΔWholeBrain (cm ³)	-	-	-	-	0.95 [0.91, 0.99] *
ΔEntorhinal(cm ³)	-	-	-	-	0.17 [0.04, 0.85] *

Notes. A1: ADAS-13 baseline Prognosis Model; A2: ADAS-13 longitudinal Prognosis Model; M1: MMSE baseline Prognosis Model; M2: MMSE longitudinal Prognosis Model. ADAS-13_bl, Alzheimer Disease Assessment Scale Cognitive 13 items at Baseline; MMSE_bl, Mini mental state examination at Baseline; CDRSB_bl, Clinical Dementia Rating Sum of Boxes at Baseline; ΔADAS-13, (ADAS-13_M12 – ADAS-13_bl) /1 year; ΔMMSE, (MMSE_M12 – MMSE_bl)

/1 year; Δ CDRSB, (CDRSB_M12 – CDRSB_bl) /1 year; Hippocampus_bl, The Total Volumes of The Hippocampus at Baseline; WholeBrain_bl, Whole Brain at Baseline; Entorhinal_bl, Entorhinal Cortex at Baseline; Δ Hippocampus, (Hippocampus_M12 – Hippocampus_bl) /1 year; Δ WholeBrain, (WholeBrain_M12 – WholeBrain_bl) /1 year; Δ Entorhinal, (Entorhinal_M12 – Entorhinal_bl) /1 year. Δ : stratified variable. *p-value*: ***: $P < 0.001$; **: $P < 0.01$; *: $P < 0.05$.

Supplementary Table S2.

Hazard ratio (95%) of cox proportional hazards analysis based on MMSE predictive dataset.

Variables	M1	M1+baseline MRI	M2	M2+baseline MRI	M2+ Δ MRI
Age	0.96 [0.92, 1.00]	0.93 [0.88, 0.98] **	0.96 [0.92, 1.01]	0.94 [0.88, 0.99] *	0.93 [0.86, 1.01]
Gender	0.90 [0.49, 1.67]	0.67 [0.26, 1.71]	0.97 [0.48, 1.93]	0.72 [0.28, 1.89]	0.55 [0.23, 1.34]
Marital status=2	0.80 [0.25, 2.50]	0.40 [0.10, 1.55]	0.61 [0.18, 2.02]	0.34 [0.08, 1.39]	0.21 [0.03, 1.30]
Marital status=3	1.13 [0.42, 3.03]	2.16 [0.77, 6.07]	0.72 [0.25, 2.06]	1.58 [0.53, 4.71]	1.33 [0.28, 6.30]
ApoE ϵ 4	0.97 [0.53, 1.78]	1.44 [0.76, 2.70]	1.01 [0.53, 1.92]	1.10 [0.54, 2.21]	0.99 [0.36, 2.70]
ADAS-13_bl	1.07 [1.02, 1.13] **	1.14 [1.07, 1.21] ***	1.10 [1.04, 1.17] **	1.16 [1.08, 1.24] ***	1.19 [1.07, 1.32] **
MMSE_bl	1.06 [0.89, 1.28]	0.94 [0.77, 1.16]	1.00 [0.80, 1.23]	1.00 [0.79, 1.26]	0.88 [0.65, 1.19]
CDRSB_bl	-	1.88 [1.39, 2.53] ***	-	2.07 [1.49, 2.89] ***	2.03 [1.33, 3.09] ***
CDRSB_bl1	Δ	-	Δ	-	-
Hippocampus_bl(cm ³)	-	0.82 [0.54, 1.24]	-	0.83 [0.53, 1.29]	-
WholeBrain_bl(cm ³)	-	1.00 [0.99, 1.01]	-	1.00 [0.99, 1.01]	-
Entorhinal_bl(cm ³)	-	0.87 [0.51, 1.49]	-	0.98 [0.56, 1.70]	-
Δ ADAS-13	-	-	0.97 [0.79, 1.18] **	1.09 [1.00, 1.18] *	1.06 [0.96, 1.17]
Δ MMSE	-	-	1.10 [1.03, 1.17]	1.14 [0.92, 1.41]	1.11 [0.82, 1.48]
Δ CDRSB	-	-	1.66 [1.25, 2.21] ***	1.79 [1.30, 2.47] ***	2.26 [1.42, 3.60] ***
Δ Hippocampus (cm ³)	-	-	-	-	1.43 [0.17, 12.0]
Δ WholeBrain (cm ³)	-	-	-	-	0.97 [0.92, 1.01]
Δ Entorhinal(cm ³)	-	-	-	-	0.29 [0.06, 1.47]

Notes. A1: ADAS-13 baseline Prognosis Model; A2: ADAS-13 longitudinal Prognosis Model; M1: MMSE baseline Prognosis Model; M2: MMSE longitudinal Prognosis Model. ADAS-13_bl, Alzheimer Disease Assessment Scale Cognitive 13 items at Baseline; MMSE_bl, Mini mental state examination at Baseline; CDRSB_bl, Clinical Dementia Rating Sum of Boxes at Baseline; Δ ADAS-13, (ADAS-13_M12 – ADAS-13_bl) /1 year; Δ MMSE, (MMSE_M12 – MMSE_bl)

/1 year; Δ CDRSB, (CDRSB_M12 – CDRSB_bl) /1 year; Hippocampus_bl, The Total Volumes of The Hippocampus at Baseline; WholeBrain_bl, Whole Brain at Baseline; Entorhinal_bl, Entorhinal Cortex at Baseline; Δ Hippocampus, (Hippocampus_M12 – Hippocampus_bl) /1 year; Δ WholeBrain, (WholeBrain_M12 – WholeBrain_bl) /1 year; Δ Entorhinal, (Entorhinal_M12 – Entorhinal_bl) /1 year. Δ : stratified variable. *p-value*: ***: $P < 0.001$; **: $P < 0.01$; *: $P < 0.05$.

Supplementary Table S3.

The performance of ADAS-13 and MMSE prognosis models validated by bootstrap, as indicated by Optimism-corrected concordance index (Optimism-corrected C-index) (B=500).

Model	Apparent	Bootstrap	Test	Optimism	Optimism. corrected	Optimism-corrected concordance index
A1	0.484	0.507	0.403	0.104	0.380	0.690
A1+baseline MRI	0.556	0.617	0.509	0.108	0.448	0.724
A2	0.650	0.689	0.618	0.071	0.579	0.790
A2+baseline MRI	0.701	0.621	0.544	0.078	0.623	0.812
A2+ Δ MRI	0.772	0.799	0.686	0.113	0.659	0.830
M1	0.503	0.528	0.425	0.103	0.400	0.700
M1+baseline MRI	0.590	0.663	0.554	0.109	0.481	0.741
M2	0.602	0.652	0.549	0.102	0.500	0.750
M2+baseline MRI	0.704	0.677	0.578	0.100	0.604	0.802
M2+ Δ MRI	0.725	0.748	0.606	0.142	0.583	0.792

Notes. A1: ADAS-13 baseline Prognosis Model; A2: ADAS-13 longitudinal Prognosis Model; M1: MMSE baseline Prognosis Model; M2: MMSE longitudinal Prognosis Model.