



Mortality of early-onset dementia in a Thai cohort at Siriraj Hospital, Thailand

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Early-onset dementia (EOD), defined as onset before age 65, significantly increases mortality risk compared to the general population

Objectives: We followed EOD cohort to determine the mortality rate. We investigated biological and characteristically mortality risk factor of EOD cohort.

Method: 151individuals with EOD at EOD clinic and memory clinic at Siriraj hospital were follow up for 15 years. Baseline subject characteristics and blood (68) or cerebrospinal fluid (CSF) (82) biomarkers were recorded. MRI brain volume analysis had only performed only 59 subjects, the rest were waiting for the results.

Results: Among151EOD patients, 94 were Alzheimer disease (AD) dementia, 57 were non-AD dementia. After the diagnosis, 21 was transferred to manage at hospitals where the patients live. Mean follow up time was 8.13 years. At the last hospital visit or telephone follow up call in 2025, 98 are alive, and 53 were dead (35.09%). Mean survival after the diagnosis was 8.13 years. Mean survival time for AD group was 14.03 years while mean survival time fornnon-AD group was 10.99 years (p=0.101).There were no statistically significant differences between those who are alive and those who were dead in age at onset, gender, duration after the diagnosis, ApoE4 status, AD or non-AD diagnosis, baseline (BL) Thai mental state exam (TMSE), BL neuropsychiatric problems, BL blood pTau217, BL blood AB42/40, and interim brain volume analysis. Those who presenting with social history issues (namely having a positive familial history of YOD, fear of having dementia, financial problems, jobloss, relationship problems, work problems, or worries from caregivers) have ORs of 2.94 (p=0.047) for death risk. There were significant difference at BL between the alive group and the dead group in blood BL CSF AB42 (p=0.008, OR=0.996), CSF total Tau(p=0.041, OR=0.001), BL activity of daily living scale scores(ADL)(p=0.007,OR=1.067), BL functional assessment questionnaire (FAQ) (p=0.005,OR=1.057), BL verbal fluency from ACE iii R (p=0.020, OR=0.817), TMSE at the 5th year follow up (p=0.017, OR=0.925). There was a trend of BL GFAP to be mortality risk (p=0.051, OR=1.006). Having family history of either EOD or LOD (Goldman score 1 or 2 or 3 or 3.5 vs 4) is also indicate mortality risk (p=0.002, OR=3.554). Limitations of our study are small cohort and single center. Multicenter study with data exploring health disparity should be included in future study.

Conclusion: Our study revealed that verbal fluency, clinical function, neuroinflammation, and global cognition at the 5th year were mortality risk in our EOD cohort.

Table 2. Binary logistic analysis showed predicted probability of membership for death

Predicted Probability is of Membership for Dead								
Variable	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
Goldman_score	0.523	0.207542	6.355466	1	0.012	1.687	1.123	2.534
Family history (Have)	-1.385	0.4	11.978	1	<.001	0.25	0.114	0.548
GFAP	0.006	0.003	3.799	1	0.051	1.006	1	1.012
AB_CSf	-0.004	0.001	7.201	1	0.007	0.996	0.993	0.999
Total_tau	0.001	0	4.491	1	0.034	1.001	1	1.002
TMSEfuYEAR_5	-0.078	0.033	5.738	1	0.017	0.925	0.868	0.986
Addenbrook_fluen	-0.201	0.088	5.252	1	0.022	0.818	0.689	0.971
SumADL	0.065	0.024	7.361	1	0.007	1.067	1.018	1.119
SumFAQ	0.055	0.02	7.942	1	0.005	1.057	1.017	1.098

Table 3. Presenting symptoms: Odds ratios of death

Presenting symptoms	Alive		Dead		p-value	Odds Ratio
	Presence	Absence	Presence	Absence		
Cognitive	86 (87.8%)	12 (12.2%)	48 (90.6%)	5 (9.4%)	0.789	1.34
Affective	27 (27.6%)	71 (72.4%)	11 (20.8%)	42 (79.2%)	0.434	0.689
Behavioral	21 (21.4%)	77 (78.6%)	16 (30.2%)	37 (69.8%)	0.241	1.586
Vascular	3 (3.1%)	95 (96.9%)	0 (0%)	53 (100%)	0.552	-
Gait disturbance	7 (7.1%)	91 (92.9%)	3 (5.7%)	50 (94.3%)	1.000	0.78
Weight and appetite	5 (5.1%)	93 (94.9%)	0 (0%)	53 (100%)	0.163	-
Social	75 (76.5%)	23 (25.5%)	48 (90.6%)	5 (9.4%)	0.047	2.944
Daily fuction	14 (14.3%)	84 (85.7%)	8 (15.1%)	45 (84.9%)	1.000	1.067
Data are presented as number (%).						
P-value corresponds to Chi-square test or Fisher's exact test.						

Figure 1. Survival analysis: AD vs non-AD

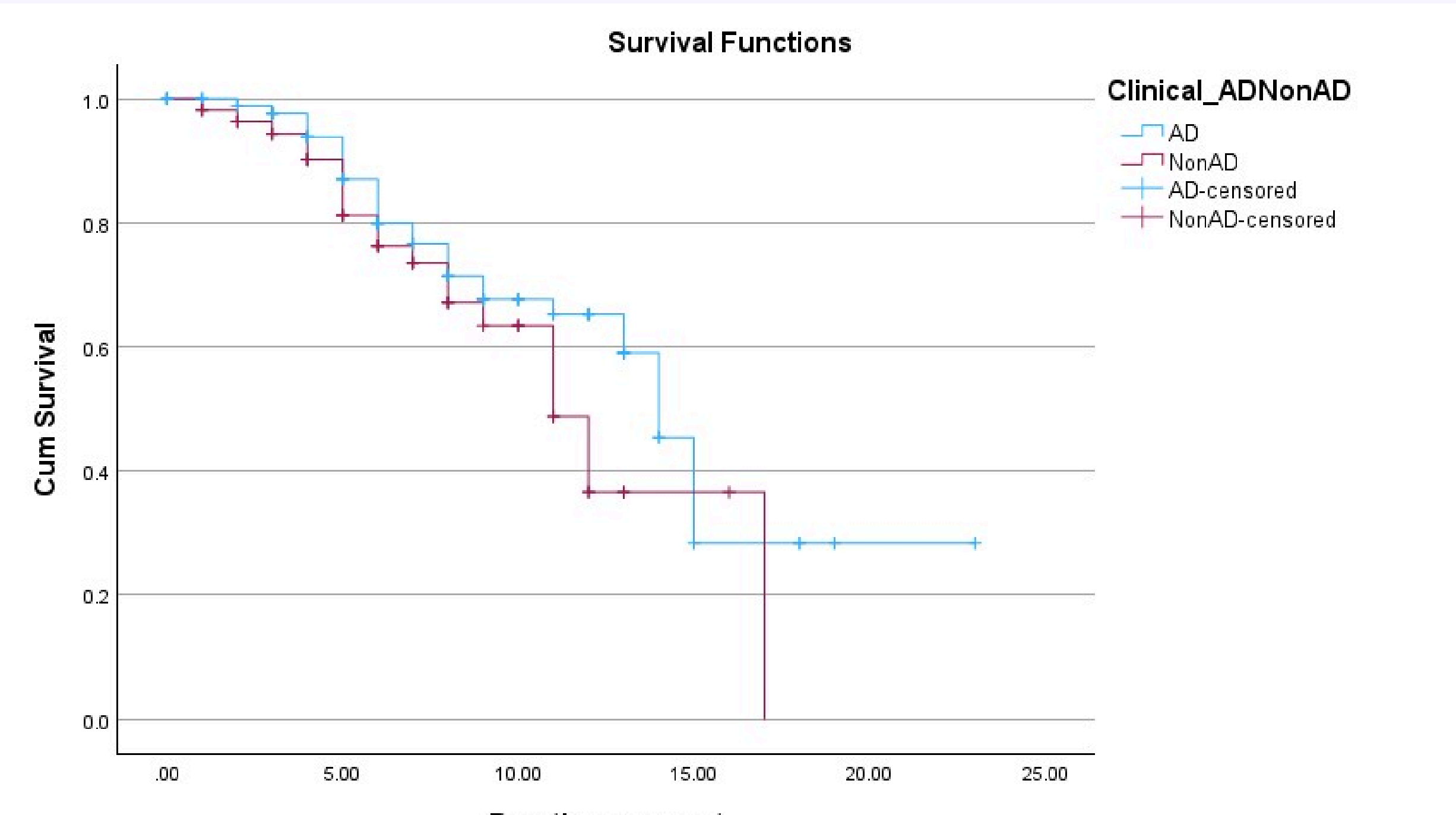


Table 1. Subject characteristics

Characteristics	AD n=94	Non AD n=57	p-value
Age (onset)	59.5 (56-62.25)	60 (55-65)	0.343
Education (years)	13.0 (6-16)	13 (4.75-16)	0.740
Duration follow up (years)	9.0 (4-12)	8 (4.5-11)	0.763
Sex (Female %)	62 (66%)	31 (54.4%)	0.171
Family history (have)	37 (42.5%)	19 (35.2%)	0.479
Status			
Alive	63 (67%)	35 (61.4%)	0.488
Dead	31 (33%)	22 (38.6%)	
APOE			
E4 homozygous	15 (18.1%)	2 (4.7%)	<0.001
E4 heterozygous	28 (33.7%)	5 (11.6%)	
E4 non-carrier	40 (48.2%)	36 (83.7%)	
Hometown			
Bangkok	48 (51.1%)	32 (56.1%)	0.615
Others	46 (48.9%)	25 (43.9%)	
Blood Biomarkers			
ptau217	1.28 ±0.64	0.84 ±0.60	0.034
ptau181	37.5 (27.65-50.675)	33.3 (21.5-49.1)	0.278
AB42:40	0.0490 (0.0435-0.0547)	0.058 (0.0461-0.0642)	0.176
NFL	32.0 (23.2-47.9)	44.1 (24.7-77)	0.098
GFAP	136.0 (95.6-222)	103 (67.2-194)	0.091
CSF			
AB_CSf	365.0 (249.5-440.25)	573.5 (346-850.25)	<0.001
P_tau	66.0 (49.25-92.75)	48 (39-61.5)	0.028
Total_tau	400.5 (270.75-654.5)	268.5 (167.25-642.5)	0.087
BL_TMSE	22.0 (14.5-25)	20 (14-26)	0.864
fuYEAR_1	20.0 (11.5-24.5)	19 (11.5-26)	0.886
fuYEAR_2	20.0 (9-25)	14 (6-23)	0.119
fuYEAR_3	18.0 (6.75-25.25)	12 (0-23)	0.89
fuYEAR_4	16.0 (0.5-24.75)	15 (0-23.5)	0.669
fuYEAR_5	21.0 (4-24)	9 (0-21.5)	0.282
MOCA	15.73 ±7.81	15.58 ±6.70	0.937
Addenbrook_attention	9.0 (7-15)	10 (7-16)	0.705
Addenbrook_memory	9.0 (5-14)	8 (5-16)	0.941
Addenbrook_fluency	7.12 ±3.61	4.44 ±3.76	0.006
Addenbrook_language	21.0 (16-24)	16 (12-24)	0.328
Addenbrook_visospatio	12.0 (4-15)	9 (4-15)	0.35
Addenbrook_total	55.61 ±23.92	52.04 ±24.17	0.568
SumADL	6.0 (1-14)	7 (0-18)	0.949
SumFAQ	9.5 (2-20)	10 (1-20)	0.791
NPI_Sum	1.5 (0-3)	2 (0-4)	0.599

Data are presented as number (%), mean ± standard deviation (SD), or median (interquartile rang P-values were calculated using the independent t-test, Mann-Whitney U test, Chi-square test, or Fisher's exact test, as appropriate.