

Association between Early Cognitive Impairment and Short-Term Functional Outcome in Acute Ischemic Stroke

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Supplementary Table 1. Age- and sex-adjusted ORs of PSCI and PreSD vs. normal cognition for poor functional outcome (mRS 3–6) by category of stroke-related factor in the acute care phase

Stroke-related factor category	PSCI					PreSD				
	No. of subjects	No. of events	OR	(95% CI)	<i>P</i> -heter.	No. of subjects	No. of events	OR	(95% CI)	<i>P</i> -heter.
Previous stroke										
No	672	154	3.67	(2.40-5.63)	0.38	633	140	3.47	(2.07-5.82)	0.80
Yes	120	34	9.80	(3.39-28.34)		133	40	6.49	(2.60-16.21)	
NIHSS score										
≤4	625	93	2.27	(1.34-3.87)	0.04	594	88	2.36	(1.27-4.38)	0.94
>4	167	95	7.29	(3.16-16.78)		172	92	3.21	(1.52-6.75)	
Stroke subtype										
Non-cardioembolic	658	147	3.60	(2.30-5.65)	0.21	647	144	3.22	(1.96-5.26)	0.04
Cardioembolic	134	41	6.65	(2.89-15.31)		119	36	9.96	(3.61-27.50)	
Laterality of stroke										
Left hemisphere										
No	394	98	3.74	(2.02-6.94)	0.38	400	101	3.06	(1.62-5.74)	0.12
Yes	398	90	5.19	(3.05-8.81)		366	79	5.70	(3.08-10.56)	
Right hemisphere										
No	487	109	4.33	(2.60-7.20)	0.68	469	101	4.10	(2.33-7.20)	0.84
Yes	305	79	3.87	(2.11-7.09)		297	79	4.00	(1.97-8.10)	
Location of stroke										
Cortex										
No	507	119	3.12	(1.83-5.32)	0.16	481	107	3.00	(1.58-5.71)	0.16
Yes	285	69	7.26	(3.87-13.61)		285	73	7.30	(3.71-14.34)	
Basal ganglia										
No	362	76	4.21	(2.32-7.63)	0.78	360	76	3.72	(1.96-7.05)	0.40
Yes	430	112	4.26	(2.52-7.21)		406	104	5.10	(2.72-9.57)	
Brainstem/cerebellum										
No	600	138	4.08	(2.62-6.34)	0.45	577	136	4.67	(2.83-7.71)	0.31
Yes	192	50	5.73	(2.35-13.98)		189	44	2.74	(1.08-6.96)	
Reperfusion therapy										
No	731	178	4.37	(2.92-6.53)	0.52	697	165	4.39	(2.77-6.95)	0.70
Yes	61	10	2.37	(0.25-22.42)		69	15	1.88	(0.41-8.60)	

mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; *P*-heter., *P* for heterogeneity; and PSCI, post-stroke cognitive impairment.

Supplementary Table 2 Age- and sex-adjusted ORs of PSCI and PreSD vs. normal cognition for poor functional outcome (mRS 3–6) by category of stroke-related factor in the rehabilitation phase

Stroke-related factor category	PSCI					PreSD				
	No. of subjects	No. of events	OR	(95% CI)	<i>P</i> -heter.	No. of subjects	No. of events	OR	(95% CI)	<i>P</i> -heter.
Previous stroke										
No	320	57	2.92	(1.56-5.45)	0.50	293	60	6.74	(3.27-13.92)	0.11
Yes	66	18	2.57	(0.76-8.69)		68	20	2.78	(0.83-9.30)	
NIHSS score										
≤4	263	31	2.35	(1.01-5.46)	0.49	245	30	3.53	(1.37-9.15)	0.90
>4	123	44	1.88	(0.84-4.22)		116	50	4.12	(1.67-10.15)	
Stroke subtype										
Non-cardioembolic	311	59	3.14	(1.65-5.96)	0.70	300	60	4.16	(2.08-8.34)	0.07
Cardioembolic	75	16	2.69	(0.81-8.95)		61	20	18.60	(4.01-86.14)	
Laterality of stroke										
Left hemisphere										
No	197	39	4.47	(1.89-10.62)	0.36	200	44	5.89	(2.45-14.16)	0.86
Yes	189	36	2.30	(1.06-4.95)		161	36	5.53	(2.28-13.40)	
Right hemisphere										
No	233	40	2.18	(1.04-4.57)	0.33	212	42	5.42	(2.38-12.31)	0.94
Yes	153	35	4.43	(1.85-10.67)		149	38	5.99	(2.30-15.60)	
Location of stroke										
Cortex										
No	253	49	3.18	(1.53-6.62)	0.64	234	42	3.78	(1.54-9.28)	0.26
Yes	133	26	2.71	(1.08-6.78)		127	38	7.71	(2.97-20.04)	
Basal ganglia										
No	163	26	3.66	(1.46-9.20)	0.49	156	30	6.73	(2.42-18.70)	0.61
Yes	223	49	2.65	(1.29-5.43)		205	50	5.54	(2.45-12.56)	
Brainstem/cerebellum										
No	292	58	2.25	(1.20-4.21)	0.10	271	65	5.20	(2.63-10.29)	0.66
Yes	94	17	6.88	(2.00-23.61)		90	15	8.41	(1.84-38.47)	
Reperfusion therapy										
No	358	67	3.22	(1.80-5.73)	0.83	330	69	6.33	(3.33-12.04)	0.66
Yes	28	8	2.19	(0.06-76.27)		31	11	1.18	(0.08-18.03)	

mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; *P*-heter., *P* for heterogeneity; and PreSD, pre-stroke dementia.

Supplementary Table 3. Age- and sex-adjusted ORs of PSCI and PreSD vs. normal cognition for poor functional outcome (mRS 3–6) by category of vascular risk factor in the acute care phase

Vascular risk factor category	PSCI					PreSD				
	No. of subjects	No. of events	OR	(95% CI)	<i>P</i> -heter.	No. of subjects	No. of events	OR	(95% CI)	<i>P</i> -heter.
Age (sex-adjusted)										
<73 y	433	70	6.46	(3.36-12.41)	0.12	410	56	5.43	(2.25-13.10)	0.54
≥73 y	359	118	3.39	(2.10-5.47)		356	122	4.06	(2.50-6.57)	
Sex (age-adjusted)										
Men	495	97	4.12	(2.44-6.97)	0.78	473	92	5.09	(2.80-9.25)	0.44
Women	297	91	4.20	(2.34-7.52)		293	88	2.98	(1.57-5.66)	
Hypertension										
No	137	32	16.67	(5.72-48.52)	0.02	135	25	6.25	(2.14-18.27)	0.87
Yes	655	156	3.23	(2.11-4.95)		631	155	3.81	(2.34-6.19)	
Diabetes mellitus										
No	533	126	5.25	(3.26-8.46)	0.09	515	116	3.97	(2.31-6.83)	0.81
Yes	259	62	2.62	(1.30-5.25)		251	64	4.03	(1.90-8.55)	
Dyslipidemia										
No	340	76	5.54	(3.07-9.98)	0.32	342	80	5.81	(3.14-10.74)	0.29
Yes	452	112	3.32	(1.96-5.59)		424	100	3.00	(1.57-5.72)	
Coronary heart disease										
No	711	167	3.73	(2.46-5.66)	0.29	697	166	3.68	(2.33-5.82)	0.44
Yes	81	21	17.58	(4.00-77.20)		69	14	14.86	(2.73-80.79)	
Current smoking										
No	550	141	3.47	(2.20-5.48)	0.07	541	145	4.10	(2.49-6.77)	0.55
Yes	231	46	7.27	(3.32-15.94)		211	33	5.28	(2.00-13.92)	
Current alcohol intake										
No	398	116	4.55	(2.73-7.58)	0.73	397	114	3.35	(1.95-5.76)	0.11
Yes	382	71	3.67	(1.98-6.80)		353	64	7.07	(3.18-15.70)	

Age was dichotomized with a median (73).

mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; p-heter., *P* for heterogeneity; and PSCI, post-stroke cognitive impairment.

Supplementary Table 4. Age- and sex-adjusted ORs of PSCI and PreSD vs. normal cognition for poor functional outcome (mRS 3–6) by category of vascular risk factor in the rehabilitation phase

Vascular risk factor category	PSCI					PreSD				
	No. of subjects	No. of events	OR	(95% CI)	<i>P</i> -heter.	No. of subjects	No. of events	OR	(95% CI)	<i>P</i> -heter.
Age (sex-adjusted)										
<73 y	186	19	4.72	(1.63-13.63)	0.31	176	17	5.62	(1.67-18.81)	0.85
≥73 y	200	56	2.45	(1.30-4.62)		185	63	6.50	(3.22-13.09)	
Sex (age-adjusted)										
Men	238	40	2.17	(1.02-4.60)	0.34	145	38	4.24	(1.75-10.26)	0.60
Women	148	35	3.91	(1.70-8.98)		216	42	6.70	(2.86-15.72)	
Hypertension										
No	68	13	9.18	(1.90-44.26)	0.49	61	11	9.96	(1.88-52.67)	0.88
Yes	318	62	2.44	(1.32-4.49)		300	69	4.81	(2.43-9.49)	
Diabetes mellitus										
No	267	50	2.93	(1.50-5.71)	0.85	244	53	6.38	(2.91-14.00)	0.67
Yes	119	25	2.46	(0.89-6.79)		117	27	4.35	(1.56-12.11)	
Dyslipidemia										
No	162	32	2.80	(1.21-6.48)	0.77	155	38	6.72	(2.81-16.07)	0.42
Yes	224	43	2.43	(1.19-4.96)		206	42	4.41	(1.80-10.78)	
Coronary heart disease										
No	339	68	2.44	(1.36-4.41)	0.14	324	76	5.13	(2.72-9.68)	0.35
Yes	47	7	30.72	(2.28-413.16)		37	4	19.15	(1.17-312.78)	
Current smoking										
No	280	57	3.15	(1.67-5.97)	0.61	267	63	5.71	(2.82-11.53)	0.98
Yes	102	17	1.92	(0.59-6.29)		89	16	5.77	(1.51-21.99)	
Current alcohol intake										
No	209	53	2.80	(1.42-5.53)	0.64	201	58	4.44	(2.12-9.26)	0.21
Yes	172	21	3.00	(1.11-8.11)		154	21	10.03	(3.17-31.67)	

Age was dichotomized with a median (73).

mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; *P*-heter., *P* for heterogeneity; and PreSD, pre-stroke dementia

Supplementary Table 5. Quality parameters of logistic regression model in Table 2

	Model 1	Model 2	Model 3
Acute care phase (n=923)			
Cox & Snell R ²	0.14	0.28	0.29
Nagelkerke R ²	0.21	0.40	0.41
AUC	0.74	0.84	0.85
Rehabilitation phase (n=460)			
Cox & Snell R ²	0.16	0.22	0.24
Nagelkerke R ²	0.23	0.33	0.36
AUC	0.77	0.80	0.82

AUC, area under the curve

Supplementary Table 6. Variance inflation factor for all variables in the multivariable analysis

Variables	VIF	Tolerance (1/VIF)
PSCI	1.20	0.83
PreSD	1.38	0.73
Age	1.48	0.68
Men	1.29	0.77
Stroke-related clinical factors		
Previous stroke	1.06	0.95
NIHSS score	1.37	0.73
Cardioembolic stroke	1.35	0.74
Laterality of infarction		
Left hemisphere, n (%)	2.83	0.35
Right hemisphere, n (%)	2.68	0.37
Location of infarction		
Cortex, n (%)	2.99	0.33
Basal ganglia, n (%)	2.92	0.34
Brainstem/cerebellum, n (%)	1.98	0.50
Reperfusion therapy, n (%)	1.12	0.89
Vascular risk factors		
Hypertension, n (%)	1.05	0.95
Diabetes mellitus, n (%)	1.08	0.92
Dyslipidemia, n (%)	1.10	0.91
Coronary heart disease, n (%)	1.04	0.83
Current smoking, n (%)	1.26	0.79
Current alcohol intake, n (%)	1.21	0.83

NIHSS, National Institutes of Health Stroke Scale; PreSD, pre-stroke dementia; and PSCI, post-stroke cognitive impairment; VIF, Variance inflation factor.

Supplementary Table 7. Association of cognitive state and poor functional outcome (mRS 3–6) at the end of acute care phase in patients discharged from acute care units and patients transferred to rehabilitation units

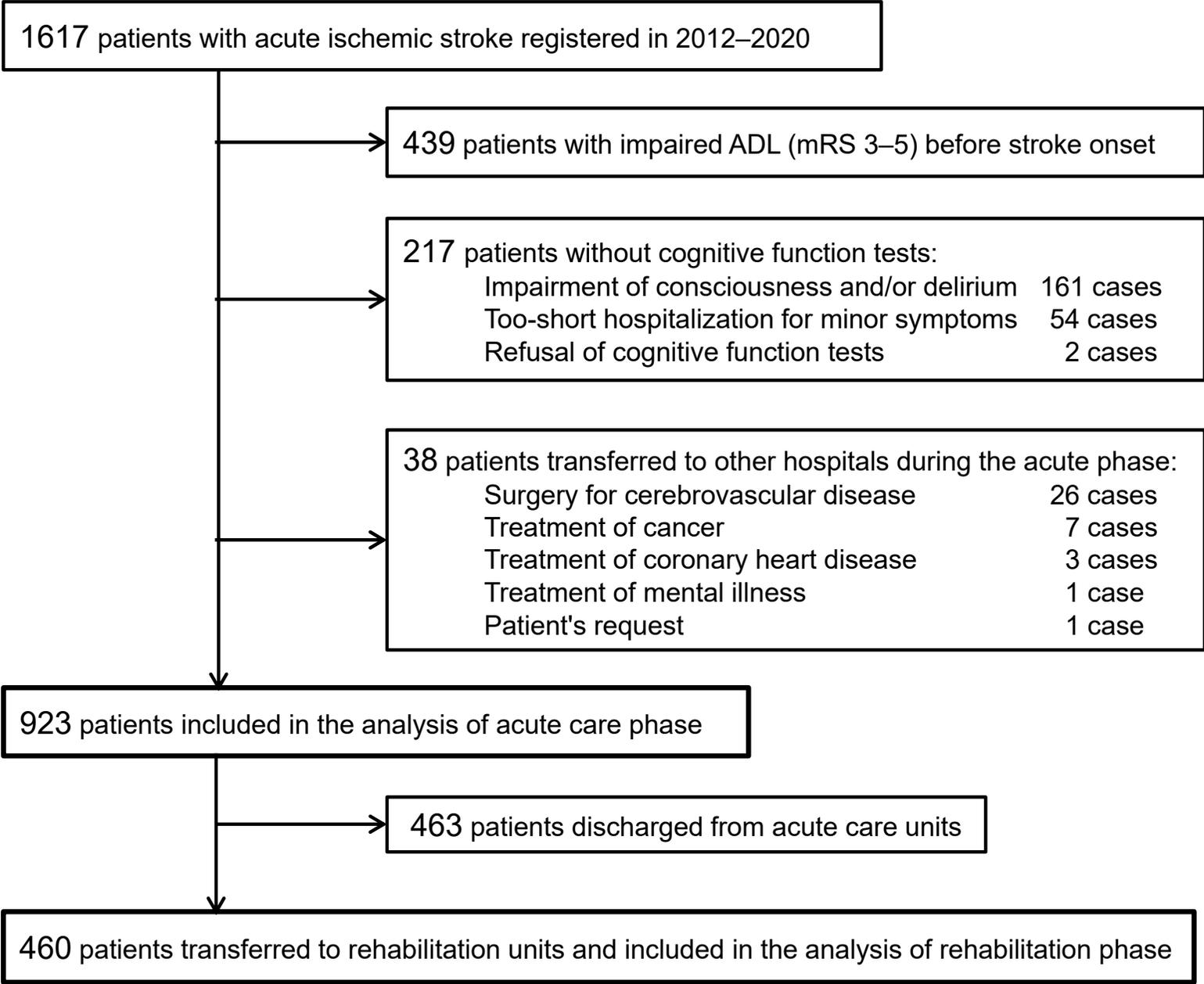
	No. of events (%)	Model 1		Model 2		Model 3	
		OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value
Patients discharged from acute care units							
Normal cognition (n=348)	9 (2.6)	1.00 (reference)		1.00 (reference)		1.00 (reference)	
PSCI (n=58)	11 (19.0)	7.58 (2.90-19.85)	<0.001	9.32 (3.10-28.04)	<0.001	7.81 (2.39-25.53)	<0.001
PreSD (n=57)	18 (31.6)	13.67 (5.06-36.92)	<0.001	8.80 (2.58-29.95)	<0.001	8.47 (2.26-31.77)	<0.01
Patients transferred to rehabilitation units							
Normal cognition (n=287)	99 (34.5)	1.00 (reference)		1.00 (reference)		1.00 (reference)	
PSCI (n=99)	69 (69.7)	3.51 (2.11-5.84)	<0.001	2.66 (1.49-4.78)	<0.01	2.84 (1.56-5.16)	<0.001
PreSD (n=74)	54 (73.0)	4.67 (2.02-6.64)	<0.001	2.13 (1.08-4.19)	<0.05	2.24 (1.11-4.51)	<0.05

mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; PreSD, pre-stroke dementia; and PSCI, post-stroke cognitive impairment.

Model 1 was adjusted for age and sex.

Model 2 was adjusted for the variables included in model 1 and previous stroke, NIHSS score, stroke subtype, laterality of infarction, location of infarction, and intravenous thrombolysis.

Model 3 was adjusted for the variables included in model 2 and hypertension, diabetes mellitus, dyslipidemia, coronary heart disease, current smoking, and current alcohol intake.



Supplementary Methods

Assessment of Stroke-related Factors

Previous stroke was defined as a history of hemorrhagic or ischemic stroke. The neurologic severity was scaled by attending physicians using the National Institutes of Health Stroke Scale (NIHSS) score. Index ischemic stroke was classified into 4 subtypes—cardioembolic stroke, atherothrombotic infarction, lacunar infarction, and unclassified infarction—on the basis of the diagnostic criteria of the Trial of Org 10172 in Acute Stroke Treatment (TOAST) Study [1]. The infarct lesions and laterality were evaluated by neurologic findings and brain CT and/or MRI including diffusion-weighted imaging. Brain MRI was performed in 908 patients (98.4%). The location of lesions was classified into the cortex, basal ganglia, and brainstem/cerebellum. Reperfusion therapy was defined as intravenous thrombolysis with recombinant tissue plasminogen activator administered in the hyperacute phase of the stroke.

Assessment of Vascular Risk Factors

Blood samples were collected within 24 h of admission. Hypertension was defined as blood pressure $\geq 140/90$ mmHg or a medical history of hypertension. A diagnosis of diabetes mellitus was determined by the diagnostic criteria of the Japan Diabetes Society before stroke onset or during hospitalization [2]. Dyslipidemia was defined as either a low-density lipoprotein-cholesterol level ≥ 3.62 mmol/L, high-density lipoprotein-cholesterol level < 1.03 mmol/L, triglycerides ≥ 1.69 mmol/L, or current treatment with a cholesterol-lowering drug. Atrial fibrillation was diagnosed based on electrocardiographic findings on admission or during hospitalization. Coronary heart disease was defined as a previous history of angina pectoris, myocardial infarction, percutaneous coronary intervention, or coronary artery bypass graft surgery. Information on smoking habits and alcohol intake was obtained by use of a standardized questionnaire.

Supplementary References

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2. Committee of the Japan Diabetes Society on the Diagnostic Criteria of Diabetes Mellitus, Seino Y, Nanjo K, Tajima N, Kadowaki T, Kashiwagi A, Araki E, Ito C, Inagaki N, Iwamoto Y, et al. Report of the committee on the classification and diagnostic criteria of diabetes mellitus. *J Diabetes Investig* 2010;1:212–228.

Supplementary Figure Legend

Supplementary Fig 1. Flow chart of participants

Abbreviations: ADL, activities of daily living; and mRS, modified Rankin scale.