Supplemental material

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SUPPLEMENTARY FILE

Chelune formula

Raw test scores were converted to a Reliable Change Index (RCI) with the Chelune formula that takes measurement errors and practice effects into account (equation 1).

(1)

$$RCI = \frac{(X_2 - X_1) - (\overline{X}_{C2} - \overline{X}_{C1})}{SE_{diff}}$$

X_1 and X_2 denote individual test scores measured at baseline and follow-up, respectively. $\overline{X}_{C1}$ and $\overline{X}_{C2}$ denote mean test scores from the control group, at baseline and follow-up, respectively.

SE_{diff} denotes the standard error of the difference score, calculated by equation 2:

(2)

$$SE_{diff} = \sqrt{2s_1^2(1 - r_{12})}$$

r_{12} denotes test-retest reliability in the control group and s_1 denotes the standard deviation of the baseline score in the control group.

Supplementary Table 1 Baseline characteristics of the study population and patients who only completed a baseline assessment.

	Baseline and follow-up assessment completed (n=393)	Only baseline assessment completed (n=205)	P value
Median age at index event, years (IQR)	44.3 (38.4-47.2)	44.5 (38.4-47.6)	0.787
Men, N (%)	198 (50.4)	113 (55.1)	0.271
Median time to assessment BL, days (IQR)	80 (54-114)	89 (60-126)	0.026*
Median education level (IQR)	5 (5-6)	5 (5-6)	0.034*
Median NIHSS score at admission (IQR)	2 (1-5)	3 (1-5)	0.010*
Median NIHSS score at discharge (IQR)	1 (0-2)	1 (0-2)	0.070
Barthel Index good outcome (BI≥85), N (%)	367 (97.9)	185 (93.9)	0.014*
mRS good outcome (mRS 0-1), N (%)	257 (67.6)	121 (61.7%)	0.158
MINI- symptoms of depression present, N (%)	37 (9.7)	18 (9.0)	0.788
Mean CIS-20R-fatigue severity (SD)	33.0 (11.8)	32.6 (12.2)	0.676
TOAST, N (%)			0.134
Atherothrombotic	12 (3.1)	13 (6.3)	
Likely atherothrombotic	40 (10.2)	30 (14.6)	
Small vessel disease	55 (14.0)	30 (14.6)	
Cardioembolic	70 (17.8)	27 (13.2)	
Rare causes	85 (21.6)	39 (19.0)	
Multiple causes	28 (7.1)	9 (4.4)	
Cryptogenic	103 (26.2)	57 (27.8)	
Vascular risk factors, N (%)			
Hypertension	145 (36.9)	79 (38.5)	0.694
Diabetes mellitus	32 (8.1)	23 (11.2)	0.277
Dyslipidemia	249 (63.4)	143 (69.8)	0.118
Obesity	51 (13.0)	27 (13.2)	0.947
Morbid obesity	24 (6.1)	8 (3.9)	0.256
Alcohol	22 (5.6)	12 (5.9)	0.898
Cognitive impaired at baseline, N (%)			
Episodic memory	76 (19.5)	49 (24.4)	0.173
Processing speed	108 (27.6)	68 (33.8)	0.118
Visuoconstruction	129 (34.1)	81 (42.2)	0.059
Executive functioning	26 (6.6)	19 (9.3)	0.236
Visual neglect	1 (0.5)	2 (0.5)	1.000
Language deficits	40 (20.8)	66 (17.5)	0.335
Attention and working memory	19 (5.0)	12 (6.2)	0.547

Education category 5, i.e. middle school / secondary vocational training. IQR: interquartile range; NIHSS: National Institutes of Health Stroke Scale; MINI: Mini International Neuropsychiatric Interview; CIS-20R: Checklist Individual Strength; TOAST: Trial of ORG 10172 in Acute Stroke Treatment.

* indicates significant P values (p<0.05).

Missing data in patients with only baseline assessment completed: Barthel Index 8 (3.9%); mRS 9 (4.4%); MMSE 5 (2.4%); MINI - symptoms of depression 6 (1.5%); CIS-20R-fatigue 47 (22.9%); Cognitive impaired: Episodic memory 4 (2.0%); Processing speed 4 (2.0%); Visuoconstruction 13 (6.3%); Executive functioning 1 (0.5%); Visual neglect 5 (2.4%); Language deficits 13 (6.3%); Attention and working memory 11 (5.4%).

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Supplementary Table 2 Multivariable Linear regression analysis of cognitive domain specific predictors for the Z-scores at follow-up

Predictor	Episodic memory		Processing speed		Visuoconstruction		Executive functioning		Language deficits		Attention and working memory	
	Beta Coefficient (β)	p-value	Beta Coefficient (β)	p-value	Beta Coefficient (β)	p-value	Beta Coefficient (β)	p-value	Beta Coefficient (β)	p-value	Beta Coefficient (β)	p-value
Z-score at baseline (same domain as outcome)	0.653	**<0.001***	0.827	**<0.001***	0.471	**<0.001***	0.591	**<0.001***	0.391	**<0.001***	0.775	**<0.001***
Age at event, year	-	-	0.002	0.916	-	-	-	-	0.016	**0.003***	-	-
Gender [a]	-	-	-	-	-	-	-	-	-	-	-0.075	0.367
Education [b]												
Middle (5)	-0.010	0.960	-0.139	0.607	-0.291	**0.039***	-0.070	0.632	-	-	-0.087	0.401
High (6-7)	-0.290	**0.009***	-0.135	0.205	-0.186	**0.047***	-0.140	0.142	-	-	-0.069	0.401
NIHSS at admission	-0.025	0.054	-0.002	0.916	-	-	-0.007	0.430	-0.016	0.065	-	-
NIHSS at discharge	0.017	0.693	0.010	0.916	-	-	<-0.001	0.997	-0.009	0.631	-	-
CIS-20R - fatigue severity at baseline	-0.005	0.275	-	-	-	-	-0.005	0.156	-	-	-	-
MINI symptoms of depression at baseline [c]	-	-	-	-	-	-	-0.160	0.251	-	-	-	-
Lesion location [d]												
Right supratentorial	0.106	0.426	0.012	0.916	-	-	-	-	-	-	-	-
Bilateral supratentorial	-0.015	0.960	0.049	0.916	-	-	-	-	-	-	-	-
Infratentorial	0.172	0.275	-0.015	0.916	-	-	-	-	-	-	-	-
Unilateral supratentorial and infratentorial	0.011	0.960	-0.063	0.916	-	-	-	-	-	-	-	-
Bilateral supratentorial and infratentorial	0.426	0.180	-0.103	0.916	-	-	-	-	-	-	-	-
Discharge to [e]												
Clinical rehabilitation	-0.253	0.219	-0.146	0.647	-	-	-0.015	0.978	-	-	0.003	0.962
Outpatient rehabilitation	-0.076	0.693	-0.059	0.916	-	-	0.029	0.898	-	-	0.075	0.401
Nursing home	NA	NA	NA	NA	-	-	NA	NA	-	-	-1.372	**0.016***
Different	-0.540	0.140	-0.124	0.916	-	-	-0.305	0.251	-	-	-0.146	0.401
Lesion Volume on MRI, mL	-	-	<-0.001	0.916	-	-	-	-	-	-	-	-
Adjusted R-squared	0.478		0.754		0.216		0.487		0.274		0.595	

Education category 5 , i.e. middle school/ secondary vocational training. NIHSS: National Institutes of Health Stroke scale; CIS-20R: Checklist Individual Strength; MINI: Mini International Neuropsychiatric Interview. [a] Reference category Gender: Male. [b] Reference category Education level: Low(1-4). [c] Reference category MINI symptoms of depression: No. [d] Reference category Lesion location: Left supratentorial. [e] Reference category Discharge to: Home. Variables that were not statistically significant in univariable analysis were excluded from the multivariable regression model and are represented as '-' in the table. Variables that were

not statistically significant in any univariable analysis were omitted from the table.
Numbers with * and bold indicates significant p-values after FDR-correction.