

Functional Outcome Prediction in Japanese Patients with Nonsurgical Intracerebral Hemorrhage: The FSR ICH Score

Kiyohara, Takuya

Department of Medicine and Clinical Science, Graduate School of Medical Sciences, Kyushu University

Matsuo, Ryu

Department of Health Care Administration and Management, Graduate School of Medical Sciences, Kyushu University

Irie, Fumi

Department of Medicine and Clinical Science, Graduate School of Medical Sciences, Kyushu University

Nakamura, Kuniyuki

Department of Medicine and Clinical Science, Graduate School of Medical Sciences, Kyushu University

他

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Supplementary Materials

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Takuya Kiyohara, Ryu Matsuo, Fumi Irie, Kuniyuki Nakamura, Jun Hata,
Yoshinobu Wakisaka, Takanari Kitazono, Masahiro Kamouchi, Tetsuro Ago,
Investigators for Fukuoka Stroke Registry

Supplementary Methods

Supplementary References

Appendix

Supplementary Figures

Supplementary Figure 1. Flow chart of patient selection

Supplementary Figure 2. Comparison of the C statistics between the FSR ICH score and max-ICH score for predicting poor functional outcome at 3 months

Supplementary Tables

Supplementary Table 1. Age- and sex-adjusted and fully OR (95% CI) for the development of poor functional outcome

Supplementary Methods

Study participants

A total of 1,324 patients with ICH who were hospitalized within 7 days after onset and did not undergo neurosurgical treatment were consecutively registered in the FSR database. Among them, 44 patients with secondary causes of ICH, namely moyamoya disease, arteriovenous malformation, intratumoral hemorrhage, cerebral venous sinus thrombosis, ruptured aneurysm, cavernous hemangioma, arteriovenous fistula, subarachnoid hemorrhage, or trauma, were excluded. Additionally, 172 patients with impaired activities of daily living (modified Rankin Scale score, 3–5) before the ICH onset, 69 patients who underwent neurosurgical treatment during hospitalization, and 22 patients for whom data on functional status were unavailable during 3-month follow-up after the onset were excluded. The patient selection process is shown as a flowchart in online suppl. Figure 1.

Assessment of Risk Factors

Hypertension was defined as blood pressure $\geq 140/90$ mmHg in the chronic stage or a medical history of hypertension. Diabetes mellitus was diagnosed based on the criteria of the Japan Diabetes Society, either before stroke onset or during hospitalization [1]. 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. Pre-stroke dementia was defined as any type of dementia that was present prior to the index ICH. The assessment of cognitive and functional status before stroke onset was based on a clinical interview with a knowledgeable informant. Pre-stroke dementia was diagnosed by attending physicians according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition Text Revision criteria [2]. Previous stroke was defined as a history of hemorrhagic or ischemic stroke. Coronary artery 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 (previous or current cigarette smoking) and alcohol intake (previous or current drinking) was obtained using a standardized questionnaire. Oral anticoagulation was defined as current treatment with any oral anticoagulants, including vitamin K antagonists and non-vitamin K antagonist oral anticoagulants. Antiplatelet medication was defined as the current use of any antiplatelet drugs, such as aspirin, clopidogrel, cilostazol, beraprost sodium, sarpogrelate and dipyridamole. Time from onset to admission was determined based on the patient's medical history as assessed by the attending physicians and divided into four groups (≤ 1 hr; > 1 hr and ≤ 6 hr; > 6 hr and ≤ 24

hr; >24 hr). Blood pressure on admission was measured by trained nurses in the supine position using either an automated cuff, a mercury sphygmomanometer, or an aneroid sphygmomanometer. Plasma glucose levels were assessed using blood samples on admission. The severity of the stroke on admission was evaluated based on the Japan Coma Scale [3] and National Institutes of Health Stroke Scale (NIHSS) score. The location of the ICH was categorized into three groups: lobar (cortex and cortical–subcortical junction), deep (basal ganglia, thalamus, internal capsule, and deep periventricular white matter), and infratentorial (cerebellar and brain stem), following the classification from previous reports [4, 5].

Multivariable analysis

In the fully adjusted multivariable model, systolic blood pressure and Japan Coma Scale were not used for the variable selection because of their strong correlation with pulse pressure (Pearson's correlation coefficient, $r=0.74$ for systolic blood pressure) and NIHSS score (Spearman's rank correlation coefficient $r=0.68$ for Japan Coma Scale), respectively. Regarding the factors of ICH location, we selected only the deep location for inclusion in the fully adjusted multivariable model based on the results of the age- and sex-adjusted model.

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Appendix

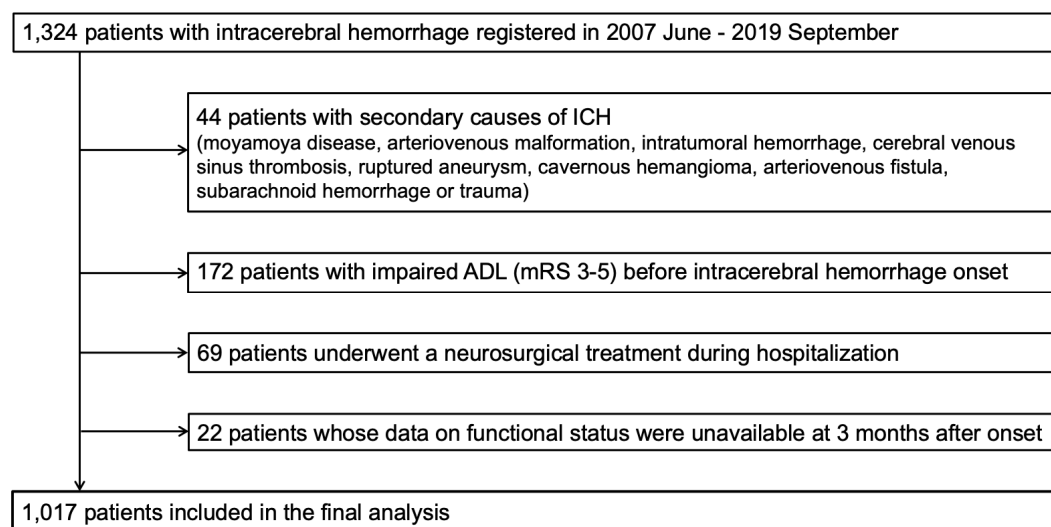
Steering Committee and Research Working Group Members:

Takao Ishitsuka, MD, PhD (Fukuoka Mirai Hospital, Fukuoka, Japan); Setsuro Ibayashi, MD, PhD (Chair, Seiai Rehabilitation Hospital, Onojo, Japan); Kenji Kusuda, MD, PhD (Seiai Rehabilitation Hospital, Onojo, Japan); Kenichiro Fujii, MD, PhD (Japan Seafarers Relief Association Moji Ekisaikai Hospital, Kitakyushu, Japan); Tetsuhiko Nagao, MD, PhD (Safety Monitoring Committee, Seiai Rehabilitation Hospital, Onojo, Japan); Yasushi Okada, MD, PhD (Vice-Chair, National Hospital Organization Kyushu Medical Center, Fukuoka, Japan); Masahiro Yasaka, MD, PhD (Fukuoka Neurosurgical Hospital, Fukuoka, Japan); Hiroaki Ooboshi, MD, PhD (Fukuoka Dental College Medical and Dental Hospital, Fukuoka, Japan); Takanari Kitazono, MD, PhD (Principal Investigator, Kyushu University, Fukuoka, Japan); Katsumi Irie, MD, PhD (Hakujuji Hospital, Fukuoka, Japan); Tsuyoshi Omae, MD, PhD (Imazu Red Cross Hospital, Fukuoka, Japan); Kazunori Toyoda, MD, PhD (National Cerebral and Cardiovascular Center, Suita, Japan); Hiroshi Nakane, MD, PhD (National Hospital Organization Fukuoka-Higashi Medical Center, Koga, Japan); Masahiro Kamouchi, MD, PhD (Kyushu University, Fukuoka, Japan); Hiroshi Sugimori, MD, PhD (National Hospital Organization Kyushu Medical Center, Fukuoka, Japan); Shuji Arakawa, MD, PhD (Steel Memorial Yawata Hospital, Kitakyushu, Japan); Kenji Fukuda, MD, PhD (St Mary's Hospital, Kurume, Japan); Tetsuro Ago, MD, PhD (Kyushu University, Fukuoka, Japan); Jiro Kitayama, MD, PhD (Fukuoka Red Cross Hospital, Fukuoka, Japan); Shigeru Fujimoto, MD, PhD (Jichi Medical University, Shimotsuke, Japan); Shoji Arihiro, MD (Japan Labor Health and Welfare Organization Kyushu Rosai Hospital, Kitakyushu, Japan); Junya Kuroda, MD, PhD (National Hospital Organization Fukuoka-Higashi Medical Center, Koga, Japan); Yoshinobu Wakisaka, MD, PhD (Kyushu University Hospital, Fukuoka, Japan); Yoshihisa Fukushima, MD (St Mary's Hospital, Kurume, Japan); Ryu Matsuo, MD, PhD (Secretariat, Kyushu University, Fukuoka, Japan); Fumi Irie, MD, PhD (Kyushu University, Fukuoka, Japan); Kuniyuki Nakamura, MD, PhD (Kyushu University Hospital, Fukuoka, Japan); and Takuya Kiyohara, MD, PhD (Kyushu University Hospital, Fukuoka, Japan).

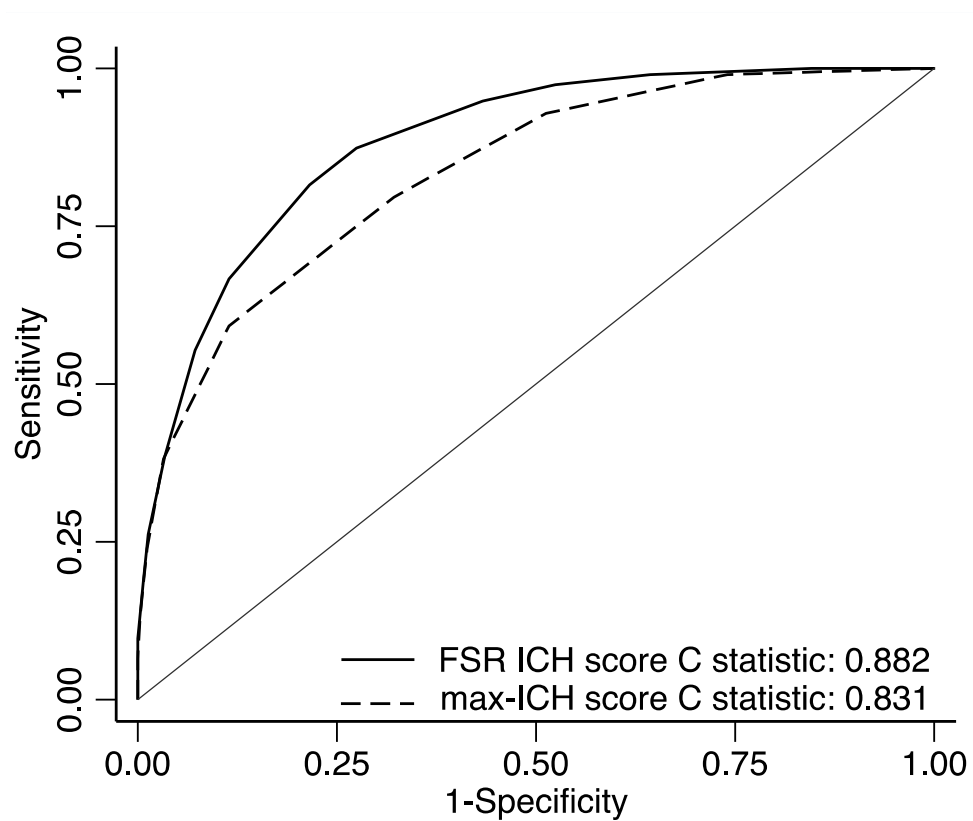
Supplementary Figures

Supplementary Figure 1. Flow chart of patient selection

ICH, intracerebral hemorrhage; ADL, activities of daily living; mRS, modified Rankin Scale.



Supplementary Figure 2. Comparison of the C statistics between the FSR ICH score and max-ICH score for predicting poor functional outcome at 3 months



Supplementary Table 1. Age- and sex-adjusted and fully OR (95% CI) for the development of poor functional outcome

		Numbers of events/at risk (%)	Age- and sex-adjusted		Fully adjusted	
			OR (95% CI)	<i>P</i> Value	OR (95% CI)	<i>P</i> Value
Age (years)						
	≤59	50/252 (19.8)	1.00 (Ref.)		1.00 (Ref.)	
	60-69	65/267 (24.3)	1.30 (0.86-1.97)	0.22	1.21 (0.71-2.06)	0.48
	70-79	108/289 (37.4)	2.40 (1.62-3.56)	<0.001	3.52 (2.01-6.16)	<0.001
	≥80	100/209 (47.9)	3.68 (2.41-5.63)	<0.001	5.53 (2.84-10.79)	<0.001
Sex						
	Women	141/398 (35.4)	1.00 (Ref.)		1.00 (Ref.)	
	Men	182/619 (29.4)	0.98 (0.74-1.31)	0.93	1.05 (0.66-1.68)	0.84
Hypertension						
	No	10/38 (26.3)	1.00 (Ref.)		1.00 (Ref.)	
	Yes	313/979 (32.0)	1.51 (0.71-3.20)	0.29	2.17 (0.73-6.46)	0.16
Diabetes mellitus						
	No	244/796 (30.7)	1.00 (Ref.)		1.00 (Ref.)	
	Yes	79/221 (35.8)	1.33 (0.96-1.84)	0.09	1.84 (1.11-3.07)	0.02
Dyslipidemia						
	No	213/637 (33.4)	1.00 (Ref.)		1.00 (Ref.)	
	Yes	110/380 (29.0)	0.83 (0.62-1.10)	0.20	1.24 (0.83-1.85)	0.29
Pre-stroke dementia						
	No	262/910 (28.8)	1.00 (Ref.)		1.00 (Ref.)	
	Yes	49/90 (54.4)	1.94 (1.22-3.09)	0.005	3.05 (1.57-5.95)	0.001
Previous stroke						
	No	272/862 (31.6)	1.00 (Ref.)		1.00 (Ref.)	
	Yes	51/155 (32.9)	1.00 (0.68-1.45)	0.99	1.13 (0.65-1.97)	0.66
Coronary artery disease						
	No	283/919 (30.8)	1.00 (Ref.)		1.00 (Ref.)	
	Yes	40/98 (40.8)	1.24 (0.80-1.93)	0.33	1.51 (0.76-3.03)	0.24
Smoking						
	No	158/468 (33.8)	1.00 (Ref.)		1.00 (Ref.)	
	Yes	165/549 (30.1)	1.09 (0.78-1.52)	0.62	1.32 (0.84-2.08)	0.23
Drinking						
	No	216/600 (36.0)	1.00 (Ref.)		1.00 (Ref.)	
	Yes	107/417 (25.7)	0.73 (0.54-1.00)	0.05	0.67 (0.44-1.02)	0.06
Oral anticoagulation						
	No	287/916 (31.3)	1.00 (Ref.)		1.00 (Ref.)	
	Yes	36/101 (35.6)	0.96 (0.62-1.51)	0.87	0.60 (0.30-1.19)	0.15
Antiplatelet medication						
	No	253/831 (30.5)	1.00 (Ref.)		1.00 (Ref.)	
	Yes	70/186 (37.6)	1.10 (0.78-1.55)	0.61	1.17 (0.67-2.04)	0.58
Time from onset to admission						
	≤1 hr	113/267 (42.3)	1.00 (Ref.)		1.00 (Ref.)	
	>1 hr and ≤6 hr	133/376 (35.8)	0.65 (0.46-0.91)	0.01	0.87 (0.57-1.35)	0.54
	6 hr and ≤24 hr	55/229 (24.0)	0.35 (0.23-0.52)	<0.001	0.80 (0.45-1.44)	0.46
	>24 hr	22/145 (15.2)	0.17 (0.10-0.29)	<0.001	0.77 (0.36-1.64)	0.49

Systolic blood pressure (mmHg)						
≤159	69/260 (26.5)	1.00 (Ref.)				
160-179	72/249 (28.9)	1.27 (0.85-1.90)	0.24			
180-199	82/244 (33.6)	1.58 (1.06-2.34)	0.02			
≥200	100/264 (37.9)	2.02 (1.37-2.97)	<0.001			
Diastolic blood pressure (mmHg)						
≤89	91/286 (31.8)	1.00 (Ref.)		1.00 (Ref.)		
90-99	60/196 (30.6)	1.05 (0.70-1.58)	0.80	1.21 (0.70-2.11)	0.50	
100-109	69/217 (31.8)	1.37 (0.92-2.05)	0.12	1.02 (0.58-1.79)	0.94	
≥110	103/317 (32.5)	1.70 (1.17-2.49)	0.006	1.52 (0.89-2.58)	0.13	
Pulse pressure (mmHg)						
≤64	76/260 (29.2)	1.00 (Ref.)		1.00 (Ref.)		
65-79	77/263 (29.3)	0.94 (0.64-1.38)	0.75	0.95 (0.56-1.60)	0.84	
80-94	72/251 (28.7)	0.88 (0.59-1.31)	0.53	0.49 (0.29-0.84)	0.01	
≥95	98/242 (40.5)	1.38 (0.94-2.02)	0.10	0.91 (0.53-1.55)	0.73	
Plasma glucose (mg/dL)						
<112	84/327 (25.7)	1.00 (Ref.)		1.00 (Ref.)		
112 ≤ and <139	114/343 (33.2)	1.46 (1.04-2.06)	0.03	1.12 (0.71-1.79)	0.63	
≥140	125/346 (36.1)	1.79 (1.27-2.52)	0.001	0.86 (0.51-1.46)	0.58	
Japan Coma Scale						
0	39/431 (9.1)	1.00 (Ref.)				
1-3	157/371 (42.3)	7.18 (4.83-10.67)	<0.001			
10-30	88/169 (52.1)	11.59 (7.31-18.35)	<0.001			
100-300	39/46 (84.8)	60.35 (24.49-148.68)	<0.001			
NIHSS score						
0-2	8/243 (3.3)	1.00 (Ref.)		1.00 (Ref.)		
3-6	34/275 (12.7)	4.51 (2.02-10.06)	<0.001	3.91 (1.69-9.04)	0.002	
7-13	104/251 (41.4)	28.09 (13.02-60.60)	<0.001	23.56 (10.20-54.42)	<0.001	
≥14	177/246 (72.0)	106.05 (48.28-232.92)	<0.001	88.46 (35.81-218.50)	<0.001	
ICH location						
Lobar						
No	279/835 (33.4)	1.00 (Ref.)				
Yes	44/182 (24.2)	0.49 (0.33-0.72)	<0.001			
Deep						
No	74/306 (24.2)	1.00 (Ref.)		1.00 (Ref.)		
Yes	249/711 (35.0)	2.00 (1.45-2.74)	<0.001	1.00 (0.62-1.63)	0.99	
Infratentorial						
No	290/891 (32.6)	1.00 (Ref.)				
Yes	33/126 (26.2)	0.75 (0.49-1.16)	0.19			
Intraventricular hemorrhage						
No	179/777 (23.0)	1.00 (Ref.)		1.00 (Ref.)		
Yes	143/237 (60.3)	4.94 (3.60-6.78)	<0.001	2.91 (1.90-4.44)	<0.001	
Hematoma volume (ml)						
<10	141/613 (23.0)	1.00 (Ref.)		1.00 (Ref.)		
10 ≤ and <30	118/301 (39.2)	2.56 (1.87-3.50)	<0.001	1.07 (0.69-1.64)	0.77	
≥30	61/93 (65.6)	6.32 (3.90-10.24)	<0.001	2.39 (1.20-4.76)	0.01	

ICH, intracerebral hemorrhage; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio.