Predictors for Functional Outcome in Patients with Aneurysmal Subarachnoid Hemorrhage Who Completed In-Hospital Rehabilitation in a Single Institution

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Background: Although many studies evaluated independent prognosis factors of functional outcome in patients with subarachnoid hemorrhage (SAH) at a suitable time point, some patients take a long time to get functional improvement. The purpose of this study is to evaluate predictors for functional outcome in SAH patients who underwent surgical clipping and in-hospital rehabilitation in our single institution using Modified Rankin Scale (MRS) and Barthel Index (BI). *Methods:* Two-hundred fifty-one SAH patients were admitted to our hospital from January 2008 to December 2017. Of them, 144 patients who diagnosed aneurysmal SAH, underwent surgical clipping within 72 hours, and completed subsequent in-hospital rehabilitation were included in this study. We explored their clinical variables and evaluated the relationships between those factors and functional outcome using MRS and BI. *Results:* In multivariate analysis, independent prognostic factors of both MRS and BI were age, World Federation of Neurologic Surgeons grade, and symptomatic vasospasm. *Conclusions*: We suggest that age, SAH severity, and symptomatic vasospasm are associated with functional outcome in patients with aneurysmal SAH who completed surgical clipping and in-hospital rehabilitation.

Key Words: Aneurysmal subarachnoid hemorrhage—predictor for functional outcome—clipping—Barthel Index—Modified Rankin Scale

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Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) is one of the most serious diseases and has life-threatening complication.[1,2] There have been several reports that studied for independent prognostic factors of functional outcome in patients with aSAH, and many of them used a single scale, evaluated at a suitable time point that was determined such as 3, 6, and 12 months after onset.[3-12] However, as some patients take a longer time to get functional improvement,[13] times required for getting "stable" conditions may be different in each SAH patient.

In stroke clinical trials, Modified Rankin Scale (MRS) and Barthel Index (BI) are established scales to assess the functional outcome.[14] It has commonly reported that those 2 scales had generally good correlation with each other,[15] whereas there are not a few reports that pointed out the differences between them.[15-19] Therefore, it would be better if the patients after stroke can be assessed by their functional outcome using both evaluations.

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In this study, we evaluated independent prognosis factors of outcome in patients with aSAH who completed surgical clipping and in-hospital rehabilitation in our single institution using MRS and BI.

Materials and Methods

Patient and Clinical Variables

Two-hundred fifty-one aSAH patients were admitted to our neurosurgical hospital from January 2008 to December 2017. Ten patients who needed endovascular treatment for their ruptured aneurysm (AN) were excluded because they should be transferred to other hospitals. In addition, the patients who did not undergo surgical clipping within 72 hours after SAH onset due to preoperative death, observation for some reasons including fatal SAH and unknown origin, and who underwent other surgical treatments such as trapping were also excluded. Then, 26 patients who were dead or transferred to other hospitals to treat systemic complications after surgical clipping were also excluded. Finally, 144 patients with aSAH who underwent surgical clipping within 72 hours and subsequent in-hospital rehabilitation were included in this study, and the patients discharged from our hospital after completion of in-hospital rehabilitation. Of the patients, we explored their background, neurological and radiological findings on admission, clinical course, and evaluated the relationships between those factors and 2 assessment tools using MRS and BI (Fig 1).

Baseline demographic and clinical data included age, gender, World Federation of Neurologic Surgeons (WFNS) grade, Hunt and Kosnik (H&K) grade, Glasgow coma scale (GCS), ruptured AN size, and interval from ictus to surgery. All patients underwent surgical clipping within 72 hours. Surgical clipping were done via appropriate standard craniotomy. If necessary, we performed additional treatments such as superficial temporal artery-middle cerebral artery bypass, suction decompression technique, anterior clinoidectomy, ventricular or lumber drainage, external decompression, and urokinase administration for washing out the subarachnoid blood. Postsurgery, all patients underwent normal water balance managements (normovolemia, normotension, and normohemodilution) to prevent delayed cerebral ischemia. Other perioperative managements were followed past reports and guidelines. Rehabilitation for the patients started from the next day after the operation. Complications included angiographic vasospasm, symptomatic vasospasm, cerebral infarction, surgical management for normal pressure hydrocephalus, and transient systemic complication such as meningitis, pneumonia, cardiovascular disease, and gastrointestinal bleeding. Functional outcome was assessed at discharge using MRS and BI, and unfavorable outcome was defined as MRS greater than 3 and BI less than 60.

Radiological Variables

The amount of SAH blood and intraventricular hematoma (IVH) on admission computed tomography (CT) was scored using Hijdra score.[26] Midline shift on admission CT was defined as a positive if the deviation from midline was more than 5 mm. We measured maximum size of the ruptured AN on admission 3-dimensional CT angiography. Symptomatic vasospasm was defined as follows[27]: (1) the presence of neurological worsening including focal deficit, decrease level of consciousness, and motor paresis; (2) no other identifiable cause (intracranial

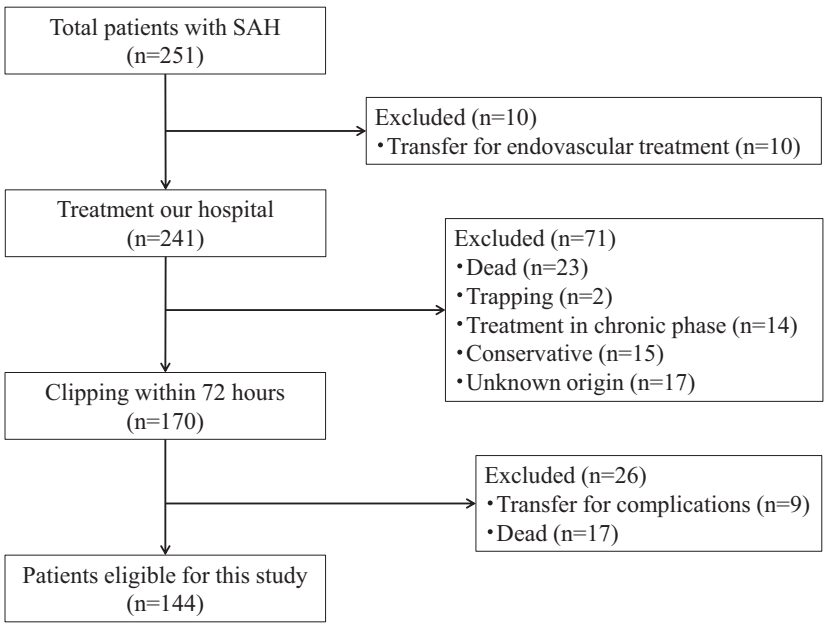

Figure 1. *Flow diagram outlining the inclusion and exclusion criteria. Abbreviation: SAH, subarachnoid hemorrhage.*

disorder and systemic complication) regarding neurological worsening; and (3) angiographic vasospasm in major trunk of internal carotid artery, anterior cerebral artery (A1), middle cerebral artery (M1), posterior cerebral artery (P1), and basilar artery; angiographic vasospasm was defined as 66% or less diameter on postoperative 7-10 days 3-dimensional CT angiography in comparison with the findings on admission one. Cerebral infarction was evaluated by diffusion-weighted image of magnetic resonance imaging on postoperative 10-14 days.

Statistical Analysis

Statcel software (OMS publication, Saitama, Japan), Ekuseru-Tokei 2012 statistical software (Social Survey Research Information Co, Ltd, Tokyo, Japan), and Graphpad Prism version 8 for Mac (Graphpad Software, San Diego, CA) were used for the statistical analysis. To analyze in a dichotomy, we set the threshold based on previous appropriate reports as follows: age (≥65 or <65),[28] WFNS and H&K grade (I-III or IV-V),[29-33] GCS (14-15 or 3-13),[34] SAH Hijdra score (0-19 or 20-30),[35] midline shift (≤5 mm or >5 mm),[36-39] AN size (≥7 mm or <7 mm),[40,41] Interval from ictus to surgery (≤24 hours or >24 hours),[42-46] MRS (0-3 or 4-5),[20-23] and BI (65-100 or 0-60).[9,20,24,25] According to the IVH Hijdra score and the length of hospital stay, we decided their thresholds based on receiver-operating characteristic analysis and set as follows: IVH Hijdra score (0-1 or 2-12) and length of hospital stay (≤70 days or >70 days in MRS and ≤78 days or >78 days in BI).

Chi-squared test was used for the univariate analysis. A logistic regression analysis was used to evaluate the multivariate effect of the parameters on unfavorable prognosis factors of MRS and BI, respectively. $P < .05$ was considered significant.

Results

Clinical Characteristic

The baseline characteristics of the 144 patients are shown in Table 1. The average age of the patients was 65.7 years, 108 (75.0%) were female and 36 (25.0%) were male. WFNS grades I-III were 112 (77.8%), H&K grades I-III were 129 (89.6%), and GCS 14-15 were 108 (75.0%) cases. SAH Hijdra scores 0-19 were 84 (58.3%) and IVH Hijdra scores 0-1 were 79 (54.9%) cases. Midline shift positive findings on admission CT (>5 mm) were 13 (9.0%) cases. The average length of hospital stay was 59.6 days. MRS 0-3 were 98 (68.1%) and 4-5 were 46 (31.9%) cases. BI 65-100 were 98 (68.1%) and 0-60 were 46 (31.9%) cases (Table 1).

Table 1. *Baseline characteristics in the 144 patients*

Characteristic	Category	Value Mean (Min-Max)/ N (%)
Age (yr)		65.7 (29-96)
	≥65	76 (52.8)
Gender	Female	108 (75.0)
WFNS grade	I-III	112 (77.8)
	IV, V	32 (22.2)
Hunt and Kosnik grade	I-III	129 (89.6)
	IV, V	15 (10.4)
GCS	14, 15	108 (75.0)
	3-13	36 (25.0)
SAH Hijdra score	0-19	84 (58.3)
	20-30	60 (41.7)
IVH Hijdra score	0-1	79 (54.9)
	2-12	65 (45.1)
Midline shift		13 (9.0)
Location	ACA	59 (41.0)
	ICA	40 (27.8)
	MCA	33 (22.9)
	VA-BA	12 (8.3)
AN size (mm)		5.9 (2.4-16.1)
Interval from ictus to surgery (h)		24.3 (3-72)
Angiographic vasospasm		33 (22.9)
Symptomatic vasospasm		28 (19.4)
Cerebral infarction		70 (48.6)
Systemic complication		74 (51.4)
Surgery for NPH		47 (32.6)
Length of hospital stay (d)		59.6 (17-211)
MRS		2.52 (0-5)
	0-3	98 (68.1)
	4,5	46 (31.9)
BI		70.2 (0-100)
	65-100	98 (68.1)
	0-60	46 (31.9)

Abbreviations: ACA, anterior cerebral artery; AN size, aneurysm size; aSAH, aneurysmal subarachnoid hemorrhage; BI, Barthel Index; ICA, internal carotid artery; GCS score, Glasgow coma scale; IVH, intraventricular hematoma; MCA, middle cerebral artery; MRS, Modified Rankin Scale; N, number of patients; NPH, normal pressure hydrocephalus; VA-BA, vertebrobasilar artery; WFNS, World Federation of Neurological Surgeons; SVS, symptomatic vasospasm; ICH, intracranial hemorrhage; CI, cerebral infarction.

Data are presented as mean (Min-Max) or number of patients (%).

Prognostic Factors of MRS and BI in Univariate Analysis

Age, WFNS grade, H&K grade, GCS score, SAH and IVH Hijdra score, midline shift, AN size, symptomatic vasospasm, cerebral infarction, systemic complications, surgery for normal pressure hydrocephalus, and length of hospital stay were correlated with unfavorable prognosis factors of MRS in univariate analysis (Table 2). These correlated variables regarding unfavorable prognosis factors of MRS were completely matched in comparison with those of BI in univariate analysis (Table 3).

Table 2. *Univariate analysis of characteristics in the patients regarding MRS*

Variables	Category	MRS		*P* value
		0-3 N (%)	4,5 N (%)	
Age (yr)	≥65	41 (41.8)	35 (76.1)	<.001
	<65	57 (58.2)	11 (23.9)	
Gender	Female	71 (72.4)	37 (80.4)	.302
	Male	27 (27.6)	9 (19.6)	
WFNS grade	I-III	93 (94.9)	19 (41.3)	<.001
	IV, V	5 (5.1)	27 (58.7)	
Hunt and Kosnik grade	I-III	97 (99.0)	32 (69.6)	<.001
	IV, V	1 (1.0)	14 (30.4)	
GCS	14, 15	89 (90.8)	19 (41.3)	<.001
	3-13	9 (9.2)	27 (58.7)	
SAH Hijdra score	0-19	66 (67.3)	18 (39.1)	.001
	20-30	32 (32.7)	28 (60.9)	
IVH Hijdra score	0-1	65 (66.3)	14 (30.4)	<.001
	2-12	33 (33.7)	32 (69.6)	
AN size (mm)	≥7	19 (19.4)	19 (41.3)	.005
	<7	79 (80.6)	27 (58.7)	
Midline shift	Yes	2 (2.0)	11 (23.9)	<.001
	No	96 (98.0)	35 (76.1)	
Interval from ictus to surgery (h)	>24	35 (35.7)	10 (21.7)	.091
	≤24	63 (64.3)	36 (78.3)	
Angiographic vasospasm	Yes	26 (26.5)	7 (15.2)	.132
	No	72 (73.5)	39 (84.8)	
Symptomatic vasospasm	Yes	10 (10.2)	18 (39.1)	<.001
	No	88 (89.8)	28 (60.9)	
Cerebral infarction	Yes	31 (31.6)	39 (84.8)	<.001
	No	67 (68.4)	7 (15.2)	
Systemic complication	Yes	34 (34.7)	40 (87.0)	<.001
	No	64 (65.3)	6 (13.0)	
Surgery for NPH	Yes	17 (17.3)	30 (65.2)	<.001
	No	81 (82.7)	16 (34.8)	
Length of hospital stay (d)	≥70	21 (21.4)	35 (76.1)	<.001
	<70	77 (78.6)	11 (23.9)	

Abbreviations were indicated in Table 1.

Prognostic Factors of MRS and BI in Multivariate Analysis

Before logistic regression analysis, we set the appropriate number of the variables as follows. First, we chose the variables of significant differences in the univariate analysis. Among them, we selected some parameters according to the previous reports that demonstrated significant correlations with prognosis such as age,[4-8,11,9,32] WFNS grade,[7,11,47,48] AN size,[4,5] and SAH Hijdra score.[7,8,49-51] Furthermore, the similar parameters including evaluating SAH severity on admission (H&K grade, GCS, and WFNS grade)[52] and delayed ischemic neurological deficit (cerebral infarction (CI) and symptomatic vasospasm (SVS)) were chosen 1 parameter between them.[53-55] Finally, we selected age, WFNS grade, SAH Hijdra score, AN size, and SVS as the variables in logistic regression analysis.

Independent unfavorable prognostic factors of MRS in multivariate analysis were age (odds ratio [OR] = 3.57), WFNS grade (OR = 22.2), and SVS (OR = 5.46; Table 4). Moreover, independent unfavorable prognostic factors of BI in multivariate analysis were also age (OR = 0.22), WFNS grade (OR = 0.08), and SVS (OR = 0.18; Table 5).

Discussion

Each SAH patient shows different conditions during the perioperative and rehabilitation period. In fact, Klein et al[13] reported that a SAH patient took 30 weeks to get functional improvement, and also, a SAH survivor showed favorable behavioral outcome at 22 weeks after rehabilitation. The findings encouraged us to examine the predictors of functional outcome in the SAH patients who completed surgical clipping and in-hospital rehabilitation. In this study, we analyzed independent prognosis factors for functional outcome in patients with aSAH who completed surgical clipping and in-hospital rehabilitation in our single institution using MRS and BI. We were

Table 3. *Univariate analysis of characteristics in the patients regarding BI*

Variables	Category	BI		*P* value
		65-100 N (%)	0-60 N (%)	
Age (yr)	≥65	40 (40.8)	36 (78.3)	<.001
	<65	58 (59.2)	10 (21.7)	
Gender	Female	70 (71.4)	38 (82.6)	.149
	Male	28 (28.6)	8 (17.4)	
WFNS grade	I-III	91 (92.9)	21 (45.7)	<.001
	IV, V	7 (7.1)	25 (54.3)	
Hunt and Kosnik grade	I-III	96 (98.0)	33 (71.7)	<.001
	IV, V	2 (2.0)	13 (28.3)	
GCS	14, 15	87 (88.8)	21 (45.7)	<.001
	3-13	11 (11.2)	25 (54.3)	
SAH Hijdra score	0-19	64 (65.3)	20 (43.5)	.013
	20-30	34 (34.7)	26 (56.5)	
IVH Hijdra score	0-1	62 (63.3)	17 (37.0)	.003
	2-12	36 (36.7)	29 (63.0)	
AN size (mm)	≥7	20 (20.4)	18 (39.1)	.017
	<7	78 (79.6)	28 (60.9)	
Midline shift	Yes	2 (2.0)	11 (23.9)	<.001
	No	96 (98.0)	35 (76.1)	
Interval from ictus to surgery (h)	>24	33 (33.7)	12 (26.1)	.36
	≤24	65 (66.3)	34 (73.9)	
Angiographic vasospasm	Yes	25 (25.5)	8 (17.4)	.28
	No	73 (74.5)	38 (82.6)	
Symptomatic vasospasm	Yes	10 (10.2)	18 (39.1)	<.001
	No	88 (89.8)	28 (60.9)	
Cerebral infarction	Yes	31 (31.6)	39 (84.8)	<.001
	No	67 (68.4)	7 (15.2)	
Systemic complication	Yes	34 (34.7)	40 (87.0)	<.001
	No	64 (65.3)	6 (13.0)	
Surgery for NPH	Yes	19 (19.4)	28 (60.9)	<.001
	No	79 (80.6)	18 (39.1)	
Length of hospital stay (d)	≥78	17 (17.3)	34 (73.9)	<.001
	<78	81 (82.7)	12 (26.1)	

Abbreviations were indicated in Table 1.

convinced that the present study contained 2 significant novelties. First, our study was to clarify the predictors for the functional outcome in SAH patients based on similar clinical course in-hospital in a single institution. Our SAH patients underwent similar surgical treatments and perioperative managements in our criteria, and also discharged from our hospital after completion of in-hospital rehabilitation. Therefore, we thought that there were less confounding factors to analyze functional outcome in SAH patients. Second, to our knowledge, we for the first time examined predictors for functional outcome of SAH patients using both MRS and BI. Both of them are widely

Table 4. *Multivariate analysis of independent prognostic factors of MRS in the patients*

Variables	*P* value	OR	95% confidence interval	
			Lower	Upper
Age (≥65)	.015	3.566	1.277	9.964
WFNS grade (IV, V)	<.001	22.23	6.789	72.77
SAH Hijdra score (≥20)	.137	2.089	0.791	5.520
AN size (≥7)	.317	1.740	0.589	5.141
Symptomatic vasospasm	.003	5.463	1.730	17.25

Abbreviations were indicated in Table 1.

Table 5. *Multivariate analysis of independent prognostic factors of BI in the patients*

Variables	*P* value	OR	95% confidence interval	
			Lower	Upper
Age (≥65)	.003	0.224	0.083	0.599
WFNS grade (IV, V)	<.001	0.083	0.028	0.243
SAH Hijdra score (≥20)	.526	0.742	0.296	1.862
AN size (≥7)	.606	0.760	0.267	2.159
Symptomatic vasospasm	.003	0.179	0.058	0.546

Abbreviations were indicated in Table 1.

used to evaluate functional outcome in clinical stroke studies.

In the stroke clinical trials, MRS and BI are known as established scales to assess stroke outcome.[20] However, De Haan et al and Peter and Rachelle mentioned that BI was detectable for minimum physiological changes and more sensitive scale to reflect activities of daily living (ADL) degree after stroke than MRS,[14,56,57] whereas MRS was more sensitive scale to reflect functional disorder degree after stroke than BI.[15] Therefore, we intended to evaluate functional outcome at discharge in our SAH patients using MRS and BI, respectively. According to our result, the independent unfavorable prognostic factors of MRS were completely matched in comparison with those of BI. In other words, age, WFNS, and symptomatic vasospasm were correlated with both fixed ADL and long-lasting functional disorder in our SAH patients. First, it has reported that age was one of the poor prognostic factors in SAH patients.[16,17] These reports and our study suggest that aged patients have relatively low ADL and low plasticity against brain injuries on admission, and those factors may resist the effect of medical treatments and rehabilitation compared with younger ones. Second, it was reported that WFNS grade that reflects the SAH severity on admission was the most important prognostic factors in patients with SAH.[1,19] Therefore, this result suggests that initial brain damage (early brain injury) after SAH is a significant factor for long-lasting functional disorder. Third, symptomatic vasospasm is known to induce ischemic complications with long-lasting neurological deficit.[3,58] To summarize previous reports, independent unfavorable prognostic factors of functional outcome in SAH patients can be summarized the following 3 groups[3-12]: first group are caused by the patients' background such as age, gender, and AN size.[3-12] Second group are caused by the mass effect and/or increased intracranial pressure by intracranial hemorrhage, acute hydrocephalus, and subarachnoid hematoma.[3-5,7,8,10] Third group are caused by ischemic pathophysiology such as cerebral infarction and cerebral vasospasm.[3,5,7,10,12] Taken together, the 3 factors were obvious predictors for functional outcome in aSAH patients and physicians should consider the appropriate term of in-hospital rehabilitation for the SAH patients with those factors.

There are some limitations in this study. First, there is a possibility that had not made valid adaptation of cut off (e.g., SAH and IVH in Hijdra score) and also we did not assess the threshold using ROC analysis. Second, the present study did not evaluate all prognostic factors that had ever reported as the significant factors, such as the case of rerupture and acute hydrocephalus.[3-12,18] In the multivariate analysis, we could not set enough variables due to the small number of cases. Third, as the present study was retrospectively performed in a single institution, it might be involved in information and selection bias. Fourth, it is standard to evaluate the functional prognosis of SAH patients at 3 or 6 months and those findings may give us other significant information. To confirm more reliable evidence with regard to functional outcome in SAH patients, a meta-analysis using large-scale retrospective studies should be needed. However, our valuable study clarified predictors for functional outcome in the patients with aSAH who completed surgical clipping and in-hospital rehabilitation in our single institution.

Conclusion

In this study, we evaluated predictors for functional outcome in SAH patients who completed in-hospital rehabilitation after surgical clipping in our hospital. Our study revealed that the independent unfavorable prognostic factors of both MRS and BI were age, WFNS, and symptomatic vasospasm.

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