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Original Article

Predictors of Outcomes Six Months after Endovascular Coil Embolization of Poor-Grade Aneurysmal Subarachnoid Hemorrhage

Taisuke Akimoto,[1] Makoto Ohtake,[1,2] Takafumi Kawasaki,[1,2] Shuto Fushimi,[1] Wataru Shimohigoshi,[1] Hiroshi Manaka,[1] Takashi Kawasaki,[1] Katsumi Sakata,[1] Ichiro Takeuchi,[2] and Tetsuya Yamamoto[3]

Objective: To identify factors associated with the outcome and prognosis of coil embolization for poor-grade aneurysmal subarachnoid hemorrhage (aSAH).

Methods: We retrospectively reviewed 118 patients with World Federation of Neurosurgical Societies (WFNS) grade IV or V subarachnoid hemorrhage at our institute between January 2010 and December 2020. Outcomes were assessed using modified Rankin Scale (mRS) scores at discharge and at six months after aSAH onset. In addition, patient background, aneurysm characteristics, and treatment outcome were compared between patients showing favorable (mRS scores: 0–2) and unfavorable (mRS scores: 3–6) outcomes at six months. Factors for change of mRS during follow-up were explored, and cut off values were calculated for age using the receiver operating characteristic analysis.

Results: Endovascular treatment was performed in 51 of the 118 enrolled patients. Data were analyzed for 43 of these patients who underwent coil embolization of ruptured aneurysms and had complete datasets. The mean age was 61.7 years and 24 (55.8%) patients had WFNS grade V aSAH. Coil embolization-related complications were observed in three patients. There were no treatment-related deaths; however, eight patients (18.6%) died at three months. Multivariate analysis showed that the maximum diameter of the aneurysm (p=0.041) and the postoperative dual antiplatelet therapy (DAPT) (p=0.040) were associated with unfavorable and favorable outcomes, respectively. Older age (p=0.033) was independently associated with mRS score deterioration following discharge. Age 72 years and older was the cut off value for mRS deterioration.

Conclusion: Aneurysm size and postoperative DAPT might be associated with outcomes at 6 months. Moreover, we identified older age as an independent factor that influences mRS deterioration following discharge; thus, especially in cases of elderly patients over 72 years of age, it is highly likely that long-term care to prevent disuse and regular follow-up on imaging will be necessary.

Keywords WFNS grade IV–V, poor-grade subarachnoid hemorrhage, endovascular treatment, dome–neck aspect ratio, stent-assisted technique

[1]Department of Neurosurgery, Yokohama City University Medical Center, Yokohama, Kanagawa, Japan
[2]Department of Emergency and Critical Care, Yokohama City University Medical Center, Yokohama, Kanagawa, Japan
[3]Department of Neurosurgery, Yokohama City University Graduate School of Medicine, Yokohama, Kanagawa, Japan

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Corresponding author: Makoto Ohtake. Department of Neurosurgery, Yokohama City University Medical Center, 4-57, Urafunecho, Minato-ku, Yokohama, Kanagawa 232-0024, Japan
Email: makoctnu@yokohama-cu.ac.jp

Introduction

Poor-grade aneurysmal subarachnoid hemorrhages (aSAHs), including those classified as World Federation of Neurosurgical Societies (WFNS) grades IV or V, comprise 20–30% of all aSAHs.[1,2] Patients with poor-grade aSAHs are considered to have a poor prognosis.[3]

In recent decades, endovascular coiling has provided a viable alternative to surgical aSAH treatment. Case series have shown that early endovascular treatment (EVT) of poor-grade aSAH is a feasible and appropriate option,[2,4,5] and an increasing number of patients with poor-grade aSAHs undergo EVT. In contrast, over-indication of coil embolization may lead to poorer outcomes in patients with poor-grade aSAHs.[2,6]

To the best of our knowledge, no studies have focused on modified Rankin Scale (mRS) score changes in the chronic phase and predictors of poor outcomes after coil embolization for poor-grade aSAH. Predicting outcomes of EVT for poor-grade aSAH may help determine which patients benefit from EVT and help to identify those who need to be more strictly followed up with after discharge. However, conditions that render EVT unsuitable for poor-grade aSAH remain unclear. Hence, we retrospectively reviewed aneurysm characteristics, endovascular procedures, and clinical features of consecutive patients with ruptured aneurysms to explore independent risk factors for EVT in patients with poor-grade aSAH. In addition, we focused on changes in mRS scores from discharge to six months after aSAH onset to explore medium-term prognostic factors after EVT.

Materials and Methods

Study design and participants

The study protocol was reviewed and approved by the Ethics Committee of our institute. Due to the retrospective study design, the Ethics Committee waived the requirement for written informed consent, offering participants an opt-out option, according to Personal Information Protection Law and National Research Ethics Guidelines in Japan. The study procedures were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. This single-center, retrospective cohort study evaluated 194 consecutive patients who presented with intrinsic subarachnoid hemorrhage (SAH) at our institute between January 2010 and December 2020. Cases of SAH due to trauma, infection, or iatrogenic causes were excluded. Poor-grade SAH was defined as a WFNS grade IV or V. Only cases with cerebral aneurysms were analyzed. Cases in which cardiopulmonary arrest (CPA) occurred at the time of visit or while waiting for treatment, and cases in which bilateral pupils were dilated on arrival could not be surgically treated and were excluded from this study. Data regarding demographic, clinical, radiological, and treatment-related information included sex, age, history of hypertension, diabetes mellitus, hyperlipidemia, SAH status, aneurysm localization, aneurysm size, dome–neck aspect ratio, volume embolization ratio, presence of rebleeding, surgical complications (bleeding and infarction, among others), presence of vasospasm, preoperative mRS score, and mRS scores at discharge and after six months. The aSAH diagnosis was verified by a neurosurgeon using CTA or DSA. Aneurysms with dissection at this point were categorized as dissection. If the bleeding source could not be detected by initial contrast imaging investigations, the patient was categorized as unknown. Cases for which contrast evaluation could not be performed due to a general fatal condition or some other reason were categorized as others. All aSAH cases that did not meet the exclusion criteria were included in this study, irrespective of the clinical management and treatment of the patient.

Treatment protocol

Microsurgical clipping and endovascular coiling were the main methods used for the treatment of intracranial aneurysms. In addition, the operative timing in this study was not limited and included interventions at early time points, as well as those after the end of the spasm phase. We reviewed patients with intracranial aneurysm-induced SAH with poor neurological condition during admission. EVT was performed under general anesthesia in this group of patients due to their poor condition. Patients with large intracerebral hematomas or ischemia, extensive midline shift or brainstem damage on CT, or unstable vital signs and those with a poor angiographic filling of cerebral vessels did not undergo EVT. Regarding choosing between coiling and clipping, coiling was generally the first choice, except for aneurysms of the middle cerebral artery (MCA). When coiling was not feasible, clipping was the treatment of choice. Clipping was the first treatment choice for hematoma-forming aSAH and MCA aneurysms, with coiling being the preferred option in situations wherein clipping was difficult. These decisions were consensually made by two or more neurosurgeons.

On the contrary, regarding the adjuvant technique for EVT, a balloon catheter was often on standby on the table when balloon assist was not selected. In addition, stents were used only when coiling was difficult without a stent or when used in emergencies. In cases where stents were used, antiplatelet agents were loaded, and dual antiplatelet drug therapy was continued thereafter for more than six months.

Outcome measures

The outcome measures were mRS scores at discharge and six months after aSAH, and complications (bleeding and infarction) during the perioperative and follow-up periods. Furthermore, the outcome was dichotomized as favorable (mRS score of 0–2) or unfavorable (mRS score of 3–6).

The status at six months after SAH onset was assessed by telephone, letters, outpatient appointments, or using the electronic medical records.

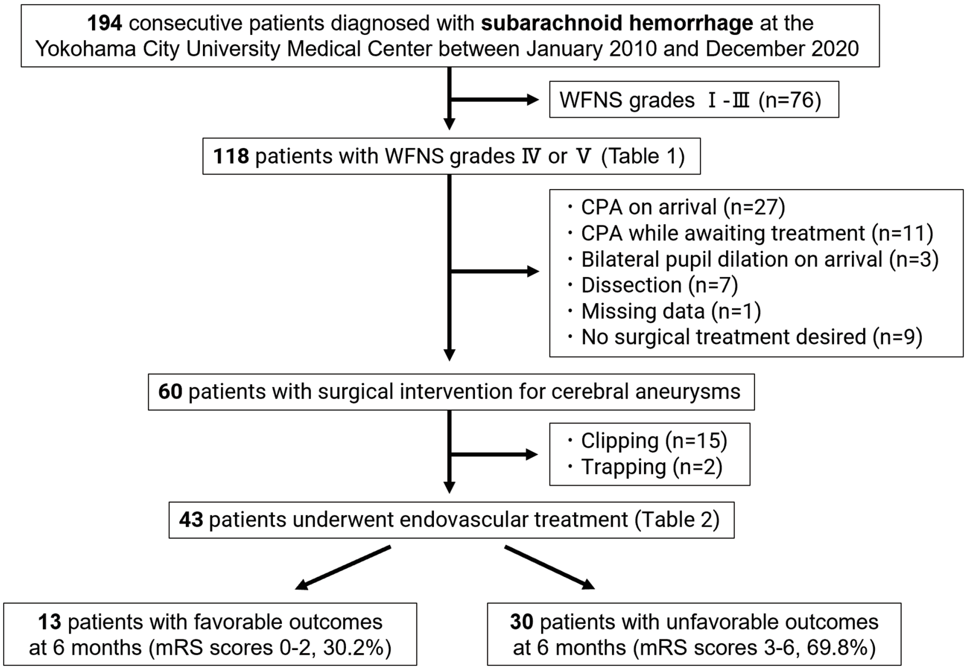

Fig. 1 Flowchart of patient inclusion. CPA: cardiopulmonary arrest; mRS: modified Rankin Scale; WFNS: World Federation of Neurosurgical Societies

Clinical outcomes were assessed by an independent neurosurgeon who was not involved in the treatment of patients, using the mRS scores at six months after onset.

Additionally, patients were grouped according to the change in the mRS score from the time of discharge to six months later: patients whose mRS scores improved by 1 or more points were in the improvement group, whereas patients whose mRS scores decreased by 1 or more points were in the deterioration group.

Statistical analysis

First, we analyzed all patients with poor-grade SAH and subsequently focused on those with ruptured aneurysms who underwent coil embolization. To account for biases, the analysis was performed after the study period had been completed. The results are presented as the mean and standard deviation for quantitative data and as frequencies (percentages) for categorical data. Data were not normalized because of the limited number of enrolled patients. For comparisons between groups, Pearson Chi-square test/Fisher's exact test for bivariate relationships and the Wilcoxon test for continuous variables were performed. A multivariate regression model was used to determine significant differences in clinical variables and aneurysm parameters between the favorable and unfavorable outcome groups. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. The area under the receiver operating characteristic curve was used to test the predictive ability of the model. An area under the receiver operating characteristic curve of 0.70–0.79 was regarded as average discrimination, 0.80–0.89 was regarded as good discrimination, and 0.90–1.00 was regarded as excellent discrimination. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using JMP 15 software (SAS Institute, Cary, NC, USA).

Results

Patient characteristics

Between January 2010 and December 2020, we retrospectively recruited 194 patients with SAH admitted to our hospital (**Fig. 1**). Except for 76 cases of WFNS grades I–III, there were 118 cases of grades IV–V. Of these 118 patients, 17 underwent clipping or trapping and 50 did not undergo surgical intervention for the following reasons: CPA on arrival (n = 27), CPA within 24 hours while awaiting treatment (n = 11), bilateral pupil dilatation on arrival (n = 3), or the patient's family refused surgical treatment (n = 9) (**Table 1**). Endovascular treatment was performed in the remaining 51 cases. One case with missing data and seven cases with dissection were excluded as we categorized ruptured aneurysms and dissection separately due to different treatment strategies. Finally, 43 patients with ruptured aneurysms who had undergone coil embolization and had complete datasets were included for further analysis.

Table 1 Poor-grade SAH characteristics

	Total (n = 118)	At discharge		p value
		mRS 0–2 (n = 18)	mRS 3–6 (n = 100)	
Mean age ± SD (years)	62.7 ± 14.9	60 ± 12.5	63.1 ± 15.4	0.243
Sex (%)				0.751
Female	76 (64.4)	11 (61.1)	65 (65.0)	
Male	42 (35.6)	7 (38.9)	35 (35.0)	
WFNS grade (%)				0.016
IV	37 (31.4)	10 (55.6)	27 (27.0)	
V	81 (68.4)	8 (44.4)	73 (73.0)	
Fisher grade (%)				0.758
1	0	0	0	
2	1 (0.8)	0	1 (1.0)	
3	115 (97.5)	18 (100)	97 (97.0)	
4	2 (1.7)	0	2 (2.0)	
Causes of SAH (%)				0.162
Aneurysm	89 (75.4)	16 (88.9)	73 (73.0)	
Dissection	7 (6.0)	2 (11.1)	5 (5.0)	
Unknown	3 (2.5)	0	3 (3.0)	
Others	19 (16.1)	0	19 (19.0)	
Treatment (%)				<0.001
EVT	51 (43.2)	15 (83.3)	36 (36.0)	
Clipping	17 (14.4)	2 (11.1)	15 (15.0)	
Nonsurgical intervention	50 (42.4)	1 (5.6)	49 (49.0)	
Reasons for nonsurgical intervention (%)	Total (n = 50)			
CPA on arrival	27 (54.0)	0	27 (54.0)	
CPA while awaiting treatment	11 (22.0)	0	11 (22.0)	
Bilateral pupil dilation	3 (6.0)	0	3 (6.0)	
Family members did not consent to surgical treatment	9 (18.0)	1 (5.6)	8 (8.0)	

Data are presented as number (%) or mean ± standard deviation. CPA: cardiopulmonary arrest; EVT: endovascular treatment; SAH: subarachnoid hemorrhage; SD: standard deviation; WFNS: World Federation of Neurological Surgeons

In the 118 cases of poor-grade SAH, WFNS grade **V** (favorable vs. unfavorable outcome: 8/18 [44.4%] vs. 73/100 [73.0%]; p = 0.016) was associated with an unfavorable outcome, and the surgical intervention group (favorable vs. unfavorable outcome: EVT 15/18 [83.3%] vs. 36/100 [36.0%], clipping 2/18 [11.1%] vs. 15/100 [15.0%], and non-surgical intervention 1/18 [5.6%] vs. 49/100 [49.0%]; p<0.001) was associated with the outcome at discharge (**Table 1**).

Univariate and multivariate analyses of unfavorable outcome predictors

Patients with poor-grade aSAH who underwent coil embolization had a mean age of 61.7 ± 15.2 years (range, 30–86 years) and comprised 19 (44.2%) patients with WFNS grade IV and 24 (55.8%) with WFNS grade V; 30 patients (69.8%) were women. Among the 43 patients included in the further analysis, 27 (62.8%) had a single aneurysm and 16 (37.2%) had multiple aneurysms. The mean number of days from onset to the hospital visit was 0.12 ± 0.39 days (range, 0–2 days), and the mean number of days from onset to EVT was 1.86 ± 3.68 days (range, 0–16 days). Four cases underwent EVT after the end of the spasm period, all of whom could not be treated due to their poor condition at the time of their visit. The mean number of days until discharge was 44.0 ± 30.3 days (range, 11–93 days). Post-EVT rebleeding was observed in two patients although both survived. The clinical characteristics did not differ between the favorable outcome (mRS scores of 0–2) and unfavorable outcome (mRS scores of 3–6) groups, except for age. Approximately 51.1% of the patients had underlying comorbidities, such as diabetes mellitus (3, 7.0%), hypertension (20, 46.5%), hyperlipidemia (8, 18.6%), and polycystic kidney disease (1, 2.3%; **Table 2**). The results of the univariate analysis for unfavorable outcomes among patients with ruptured aneurysms with coil embolization are presented in **Table 2**. The analysis of the six-month mRS score showed that age (56.3 ± 10.3 vs. 64.0 ± 2.7 years; p = 0.043), improvement in the mRS score (76.9% vs. 13.3%; p <0.001), maximum aneurysm diameter

Table 2 Univariate analysis of unfavorite outcome (mRS 3–6) at 6 months after onset

	Total (n = 43)	Univariate analysis		
		mRS 0–2 (n = 13)	mRS 3–6 (n = 30)	p value
Clinical characteristics				
Mean age ± SD (years)	61.7 ± 15.2	56.3 ± 10.3	64.0 ± 2.7	0.043
Sex, female (%)	30 (69.8)	8 (61.5)	22 (73.3)	0.439
Past history (%)				
Hypertension	20 (46.5)	6 (84.6)	14 (46.6)	0.975
Diabetes mellitus	3 (7.0)	1 (7.6)	2 (6.6)	0.999*
Hyperlipidemia	8 (18.6)	1 (7.6)	7 (23.3)	0.399*
Polycystic kidney disease	1 (2.3)	0	1 (3.3)	0.999*
Previous SAH	4 (9.3)	0	4 (13.3)	0.297*
Pretreated medications (%)				
Anticoagulants	2 (4.6)	0	2 (6.6)	0.999*
Anti-platelet agents	3 (7.0)	1 (7.6)	2 (6.6)	0.999*
Characteristics of SAH				
WFNS grade (%)				0.864
IV	19 (44.2)	6 (84.6)	13 (43.3)	
V	24 (55.8)	7 (53.8)	17 (56.6)	
Fisher grade (%)				0.999*
3	42 (97.7)	13 (100)	29 (96.6)	
4	1 (2.3)	0	1 (3.3)	
Multiple cerebral aneurysms (%)	16 (37.2)	6 (84.6)	10 (33.3)	0.424
Aneurysm location (%)				0.399
ICA	12 (27.9)	2 (15.3)	10 (33.3)	
Acom	11 (25.6)	7 (53.8)	4 (13.3)	
ACA	2 (4.6)	0	2 (6.6)	
MCA	7 (16.3)	1 (7.6)	6 (20)	
VBA	11 (15.5)	3 (23)	8 (26.6)	
Maximum diameter of An Mean ± SD (mm)	6.45 ± 1.08	4.67 ± 1.27	7.22 ± 3.76	0.034
Dome–neck ratio (%)	2.66 ± 0.49	1.92 ± 0.96	2.98 ± 1.72	0.031
Complications (%)				
Pulmonary edema	7 (16.3)	3 (23)	4 (13.3)	0.655*
Cerebral vasospasm	22 (51.1)	5 (38.4)	17 (56.6)	0.272
Hydrocephalus	9 (20.9)	1 (7.6)	8 (26.6)	0.237*
Cerebral infarction	6 (14.0)	2 (15.3)	4 (13.3)	0.999*
Characteristics of EVT				
Delayed EVT (after spasm period) (%)	4 (9.3)	1 (7.6)	3 (10)	0.999*
Heparinization (%)	39 (90.7)	11 (84.6)	28 (93.3)	0.366
Number of coils (%)	8.1 ± 1.8	6.3 ± 4.7	8.9 ± 6.0	0.174
VER (%)	37.6 ± 15.1	37.7 ± 15.2	37.6 ± 15.1	0.665
Embolization assessment				0.982
Body filling	3 (7.0)	1 (7.6)	2 (6.6)	
Neck remnant	16 (37.2)	5 (38.4)	11 (36.6)	
Complete occlusion	24 (55.8)	7 (53.8)	17 (56.6)	
Treatment technique (%)				0.025*
Simple	34 (79.1)	9 (69.2)	25 (83.3)	
Stent assist	5 (11.6)	4 (30)	1 (3.3)	
Others	4 (9.3)	0	4 (13.3)	
Perioperative complications (%)	8 (18.6)	3 (23)	5 (16.6)	0.619
Postoperative DAPT (%)	5 (11.6)	4 (30)	1 (3.3)	0.024*
EVT for spasm (%)	2 (4.6)	1 (7.6)	1 (3.3)	0.518*
Improvement in the mRS score	14 (32.6)	10 (76.9)	4 (13.3)	<0.001*
Retreatment after coil embolization (%)	5 (11.6)	3 (23)	2 (6.6)	0.153*

*Fisher's exact test. Data are presented as the number (%) or the mean ± standard deviation. ACA: anterior cerebral artery; Acom: anterior communicating artery; An: aneurysm; DAPT: dual antiplatelet therapy; EVT: endovascular treatment; ICA: internal carotid artery; MCA: medial cerebral artery; mRS: modified Rankin Scale; SAH: subarachnoid hemorrhage; SD: standard deviation; VBA: vertebral basilar artery; VER: volume embolization ratio; WFNS: World Federation of Neurological Surgeons

Table 3 OR for unfavorable outcome

	6 months mRS					
	Univariate analysis			Multivariate analysis		
	OR	95% CI	p value	OR	95% CI	p value
Advanced age (65 years or older)	1.82	0.48–6.8	0.37	0.9	0.4–1.9	0.760
Maximum diameter, larger than 7 mm (vs. smaller)	10.5	1.2–91.2	0.013	3.8	1.3–21.5	0.041
Dome neck ratio <2.0	0.68	0.1–2.7	0.58	1.1	0.5–2.7	0.700
Postoperative DAPT	0.08	0.01–0.8	0.01	0.2	0.04–0.7	0.040

CI: confidence interval; DAPT: dual antiplatelet therapy; mRS: modified Rankin Scale; OR: odds ratio

(4.67 ± 1.27 vs. 7.22 ± 3.76 mm; p = 0.034), dome–neck ratio (1.92 ± 0.96 vs. 2.98 ± 1.72; p = 0.031), treatment technique (simple technique 69.2% vs. 83.3%, stent-assisted technique 30% vs. 3.3%, and other techniques 0% vs. 13.3%; p = 0.025), and postoperative dual antiplatelet therapy (DAPT) (30% vs 3.3%; p = 0.010) were associated with unfavorable outcomes. Since the only postoperative DAPT cases were those with stent-assisted coiling, only the factor of DAPT underwent multivariate analysis. In the multivariate logistic analysis, a maximum diameter of >7 mm (OR, 3.8; 95% CI, 1.3–21.5; p = 0.041) and postoperative DAPT (OR, 0.2; 95% CI, 0.04–0.7; p = 0.04) were independently associated with unfavorable and favorable outcomes, respectively (**Table 3**). In the acute phase, eight patients died after coil embolization. The cause of death was CPA in two cases and extensive cerebral infarction in six cases. No coil embolization-related deaths were observed. Most of the acute deaths occurred in the first postoperative week. Two of the eight patients had some underlying disease, and the size (3 mm to 14 mm) and location of the aneurysms varied.

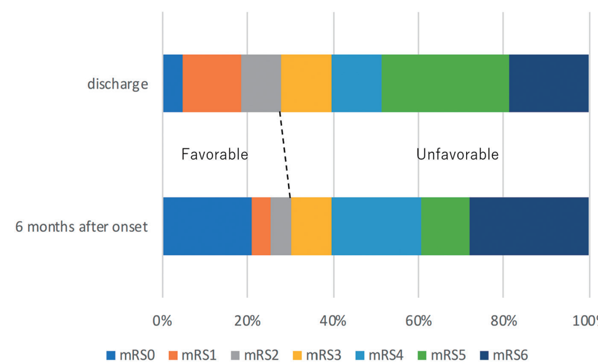

Fig. 2 Distribution of mRS scores at discharge and six months after SAH. mRS = modified Rankin Scale; SAH: subarachnoid hemorrhage

Factors associated with mRS score deterioration from discharge to six-month follow-up

The mRS score distributions were significantly different at six months (mRS 0, 20.9%; mRS 1, 4.6%; mRS 2, 4.6%; mRS 3, 9.3%; mRS 4, 20.9%; mRS 5, 11.6%; and mRS 6, 27.9%; p <0.001) compared with those at discharge (mRS 0, 4.6%; mRS 1, 13.9%; mRS 2, 9.3%; mRS 3, 11.6%; mRS 4, 11.6%; mRS 5, 30.2%; and mRS 6, 18.6%; **Fig. 2**).

A favorable outcome (mRS scores of 0–2) was achieved by 27.9% of patients at discharge and by 30.2% at six months after onset. The group with a very good prognosis (mRS scores of 0–1) comprised 18.0% of patients at discharge, increasing to 25.5% after six months. From discharge to six months, only one case changed from the favorable to unfavorable group (mRS 2 to 3), and two cases changed from the unfavorable to favorable group (mRS 3 to 0 and 4 to 2). All other cases varied within the same group. The percentage of patients with mRS 6 increased from 18.6% at discharge to 27.9% after six months. The percentage of participants with mRS 5 decreased from 30.6% at the time of discharge to 11.6% after six months, and the percentage representing the mRS 2 group similarly decreased from 9.3% to 4.6% after six months. All patients who died after 6 months had an mRS score of 5 at discharge.

The results of the univariate and multivariate analyses for the change in the mRS score from the time of hospital discharge to six months are presented in **Table 4**. According to the univariate analysis, age (59.1 ± 15.0 vs. 77.6 ± 4.1 years; p <0.001) was associated with mRS score deterioration. All patients with mRS score deterioration were over 65 years of age. In addition, the cut-off values associated with age-related mRS deterioration were determined using the receiver operating characteristic analysis. Age showed good discrimination, with an area under the curve of 0.885. The cutoff value for age was 72 years, and the unit OR was 1.18; the sensitivity and specificity were 1.00 and 0.76, respectively. In contrast, only postoperative DAPT (p = 0.032) was associated with mRS score improvement. The OR for improvement in the mRS score after treatment with postoperative DAPT was 11.2 (95% CI, 1.1–112.5; p = 0.019).

Table 4 Univariate analysis of changes in 6 months mRS scores from the time of hospital discharge

	Univariate analysis			Univariate analysis		
	Non-deterioration of mRS (n = 37)	Deterioration of mRS (n = 6)	p value	Non-improvement of mRS (n = 29)	Improvement of mRS (n = 14)	p value
Mean age ± SD (years)	59.1 ± 15.0	77.6 ± 4.1	<0.001	62.3 ± 17.2	60.6 ± 11.4	0.508
Sex, female (%)	24 (64.9)	6 (100.0)	0.155*	21 (72.4)	9 (64.3)	0.587
WFNS grade V	22 (59.5)	2 (33.3)	0.380*	17 (58.6)	7 (50.0)	0.594
Maximum diameter, mean ± SD (mm)	6.2 ± 3.2	7.7 ± 4.6	0.623	7.0 ± 3.8	5.4 ± 2.3	0.233
Dome neck ratio (%)	2.52 ± 1.34	3.48 ± 2.76	0.648	2.92 ± 1.74	2.11 ± 1.15	0.120
Postoperative DAPT	5 (13.5)	0	0.999*	1 (3.5)	4 (28.6)	0.032*
Delayed EVT (after spasm period) (%)	2 (5.4)	2 (33.3)	0.087*	3 (10.3)	1 (7.1)	0.999*
Complications						
Pulmonary edema	6 (16.2)	1 (16.7)	0.999*	5 (17.2)	2 (14.3)	0.999*
Cerebral vasospasm	19 (51.4)	3 (50.0)	0.999*	17 (58.6)	5 (35.7)	0.159
Hydrocephalus	6 (16.2)	3 (50.0)	0.095*	7 (24.1)	2 (14.3)	0.457
Perioperative complications	8 (21.6)	0	0.571*	6 (20.7)	2 (14.3)	0.999*
Retreatment after coil embolization	4 (10.8)	1 (16.7)	0.547*	3 (10.3)	2 (14.3)	0.999*

*Fisher's exact test. Data are presented as mean ± standard deviation. DAPT; dual antiplatelet therapy; EVT: endovascular treatment; mRS: modified Rankin Scale; SD: standard deviation; WFNS: World Federation of Neurological Surgeons

Discussion

This was a retrospective, single-center, observational study of consecutive patients undergoing endovascular therapy. Since the data were from a single center, we were able to follow the patients closely, and there was only one case with missing data. Postoperative DAPT might lead to favorable outcomes, whereas larger aneurysms were associated with unfavorable outcomes. Older age also contributed to the deterioration of the mRS score 6 months after coil embolization. The mean age of the 6 patients with mRS deterioration was 77.6 ± 4.1 years (range, 72–83 years), 4 of whom died from infections due to progressive disuse after 6 months and the remaining 2 had worsening symptoms due to hydrocephalus.

A poor-grade aSAH on admission is a well-known negative prognostic factor for outcomes in patients with SAH.[7–9] All poor-grade cases were hospitalized until the second day of onset, and none of the cases visited the hospital during the spasm period. This was thought to be due to the fact that all cases were of high severity and were immediately transported to the hospital. The most severe cases of poor-grade SAH present with CPA and bilateral dilatation of the pupils, and are difficult to treat because of their poor prognosis. In previous reports, the frequency of SAH with CPA was reported to be 3%–11% of all SAH.[10–12] In our study, CPA occurred in 38 of 194 patients (19.6%) within 24 hours of their visit, which was a slightly higher incidence than previously reported. This was attributed to the fact that our facility was an advanced emergency medical center for the most severe cases. According to a recent systematic literature review, the mortality rate in patients with WFNS grade IV or V is 60%, and approximately 29% of these cases die before undergoing any treatment for aneurysms.[13] In our study, approximately 60% of patients with SAH had poor status on admission (WFNS grade IV or V). The mortality rate without treatment was as high as 80% in our study; however, it was 18.6% at discharge, even in the treated group. Although the mortality rate remains high, the percentage of patients surviving aSAH in good clinical condition has increased in recent years, and survival rates continue to rise.[14,15] In our study, 13 out of 43 patients (30.2%) who underwent EVT were in good clinical condition (mRS 0–2) after 6 months. This is largely due to the development of EVT.[14] Therefore, future advances in EVT technology may further improve outcomes in patients with poor-grade aSAH.

We found that the maximum diameter of the aneurysm and postoperative DAPT might be outcome predictors. Patient age, WFNS grade, aneurysm size, aneurysms with wider necks, and thick cisternal and ventricular blood are well-known factors that influence the outcome after aSAH.[16–18] In addition, it has been suggested that incomplete occlusion may be a risk factor for poor prognosis.[18] Incomplete occlusion of aneurysms increases the risk of postoperative rebleeding.[18,19] Roh et al. showed that ruptured wide-necked aneurysms could be effectively and safely treated with the stent-assisted technique, and this technique in combination with DAPT may be a viable option even in acute SAH.[20] In addition, the use of stents has been reported to predominantly lower the risk of aneurysm recurrence, with large and giant aneurysms being predominantly at risk of recurrence.[21] Thus, aneurysm size might contribute to the risk of recurrence and incomplete occlusion. However, in the present study, rebleeding occurred in 2 of 43 patients during the 6 months follow-up, both of whom had aneurysms less than 10 mm (1.9 and 8.1 mm). Retreatment was performed in 5 cases, and there was no significant difference in aneurysm size (6.7 ± 3.5 vs 4.9 ± 2.2 mm; $p = 0.306$), indicating that the size of the aneurysm did not clearly increase the risk of rebleeding or retreatment. In contrast, there were no cases of retreatment in any of the 5 stent assisted cases, and complete occlusion was achieved in 4 of them. Thus, the use of stent in our study might be associated with lower risks of incomplete occlusion and recurrence. Several observational studies have reported results of DAPT for vasospasm after SAH. Some reports suggest that DAPT reduces symptomatic vasospasm.[22] On the other hand, some reports indicate that it increases the risk of bleeding; thus, its effectiveness is not constant.[23] In this study, only one patient had asymptomatic vasospasm among the DAPT cases. The stent-assisted cases and the DAPT cases were identical, and it was not possible to determine which was the more meaningful factor in this study. However, since DAPT (the use of stents) was associated with improved mRS at 6 months, we inferred that DAPT contributed more to improved prognosis than the use of stents, since DAPT was continued after 6 months, and recurrence and rebleeding had no impact on prognosis in this study. Thus, further studies are required to explore this association.

In the International Subarachnoid Aneurysm Trial, a subgroup analysis of elderly patients showed that in patients with internal carotid and posterior communicating artery aneurysms, coil embolization achieves a more favorable outcome than clipping, and many patients had good preoperative grades and relatively small-sized aneurysms.[24] In this subgroup analysis, elderly patients were defined as those aged ≥65 years at ictus, and similarly, we compared two groups of patients with an age cutoff of 65 years. In our study, advanced age was not associated with unfavorable outcomes in patients who underwent coil embolization. However, increased age was associated with mRS score deterioration in the chronic phase, and increased age affected the acute phase and the chronic phase, resulting in adverse long-term outcomes.

This study has several limitations. First, this was a single-center retrospective analysis. Our hospital is an advanced emergency medical center, and we mainly treat patients with severe SAH. Thus, factors, such as clinical conditions, aneurysm complexity, delayed referral, and decisions by patients and their families, may have led to selection bias. Second, our sample size was small, which may have limited the ability to detect existing differences. Third, procedures were performed by multiple surgeons, and surgical techniques varied over time. In severe cases, the diagnosis of symptomatic vasospasm is difficult to make based on clinical symptoms because of the strong disturbance of consciousness. In addition, it is difficult to determine whether the low-absorption areas on CT or other imaging are caused by spasm or brain damage at the time of aneurysm rupture. In the present study, the stent-assisted technique was used for rescue purposes, and the safety of stent use in the acute phase is not insured. Nevertheless, further studies are needed to determine the usefulness of stent-assisted techniques and the long-term effects of DAPT in this patient population.

Conclusion

We found that larger aneurysms might be associated with unfavorable outcomes and that postoperative DAPT might be associated with favorable outcomes at 6 months. Furthermore, we found that older age was an independent factor that influences mRS deterioration following discharge. We recommend long-term care to prevent disuse and regular follow-up on imaging, especially in patients aged 72 years and older.

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Disclosure Statement

The authors declare that they have no personal, financial, or institutional interest in any of the drugs, materials, or devices in the article.

References

1) Hutchinson PJ, Seeley HM, Kirkpatrick PJ. Factors implicated in deaths from subarachnoid haemorrhage: are they avoidable? *Br J Neurosurg* 1998; 12: 37–40.

2) Bergui M, Bradac GB. Acute endovascular treatment of ruptured aneurysms in poor-grade patients. *Neuroradiology* 2004; 46: 161–164.
3) Ransom ER, Mocco J, Komotar RJ, et al. External ventricular drainage response in poor grade aneurysmal subarachnoid hemorrhage: effect on preoperative grading and prognosis. *Neurocrit Care* 2007; 6: 174–180.
4) Weir RU, Marcellus ML, Do HM, et al. Aneurysmal subarachnoid hemorrhage in patients with Hunt and Hess grade 4 or 5: treatment using the Guglielmi detachable coil system. *AJNR Am J Neuroradiol* 2003; 24: 585–590.
5) Bracard S, Lebedinsky A, Anxionnat R, et al. Endovascular treatment of Hunt and Hess grade IV and V aneurysms. *AJNR Am J Neuroradiol* 2002; 23: 953–957.
6) Zheng K, Zhong M, Zhao B, et al. Poor-grade aneurysmal subarachnoid hemorrhage: risk factors affecting clinical outcomes in intracranial aneurysm patients in a multi-center study. *Front Neurol* 2019; 10: 123.
7) Konczalla J, Seifert V, Beck J, et al. Outcome after Hunt and Hess Grade V subarachnoid hemorrhage: a comparison of pre-coiling era (1980-1995) versus post-ISAT era (2005-2014). *J Neurosurg* 2018; 128: 100–110.
8) Suzuki S, Jahan R, Duckwiler GR, et al. Contribution of endovascular therapy to the management of poor-grade aneurysmal subarachnoid hemorrhage: clinical and angiographic outcomes. *J Neurosurg* 2006; 105: 664–670.
9) Wostrack M, Sandow N, Vajkoczy P, et al. Subarachnoid haemorrhage WFNS grade V: is maximal treatment worthwhile? *Acta Neurochir (Wien)* 2013; 155: 579–586.
10) Skrifvars MB, Parr MJ. Incidence, predisposing factors, management and survival following cardiac arrest due to subarachnoid haemorrhage: a review of the literature. *Scand J Trauma Resusc Emerg Med* 2012; 20: 75.
11) Vergouwen MD, Fang J, Casaubon LK, et al. Higher incidence of in-hospital complications in patients with clipped versus coiled ruptured intracranial aneurysms. *Stroke* 2011; 42: 3093–3098.
12) Toussaint LG 3rd, Friedman JA, Wijdicks EF, et al. Survival of cardiac arrest after aneurysmal subarachnoid hemorrhage. *Neurosurgery* 2005; 57: 25–31; discussion, 25–31.
13) de Oliveira Manoel AL, Mansur A, Silva GS, et al. Functional outcome after poor-grade subarachnoid hemorrhage: a single-center study and systematic literature review. *Neurocrit Care* 2016; 25: 338–350.
14) Inamasu J, Sadato A, Oheda M, et al. Improvement in patient outcomes following endovascular treatment of WFNS grade V subarachnoid haemorrhage from 2000 to 2014. *J Clin Neurosci* 2016; 27: 114–118.
15) Zhao B, Fan Y, Xiong Y, et al. Aneurysm rebleeding after poor-grade aneurysmal subarachnoid hemorrhage: predictors and impact on clinical outcomes. *J Neurol Sci* 2016; 371: 62–66.
16) Osawa M, Hongo K, Tanaka Y, et al. Results of direct surgery for aneurysmal subarachnoid haemorrhage: outcome of 2055 patients who underwent direct aneurysm surgery and profile of ruptured intracranial aneurysms. *Acta Neurochir (Wien)* 2001; 143: 655–663; discussion 663–664.
17) Mocco J, Ransom ER, Komotar RJ, et al. Preoperative prediction of long-term outcome in poor-grade aneurysmal subarachnoid hemorrhage. *Neurosurgery* 2006; 59: 529–538; discussion, 529–538.
18) Zhao B, Yang H, Zheng K, et al. Preoperative and postoperative predictors of long-term outcome after endovascular treatment of poor-grade aneurysmal subarachnoid hemorrhage. *J Neurosurg* 2017; 126: 1764–1771.
19) Fleming JB, Hoh BL, Simon SD, et al. Rebleeding risk after treatment of ruptured intracranial aneurysms. *J Neurosurg* 2011; 114: 1778–1784.
20) Roh H, Kim J, Bae H, et al. Comparison of stent-assisted and no-stent coil embolization for safety and effectiveness in the treatment of ruptured intracranial aneurysms. *J Neurosurg* 2020; 133: 814–820.
21) Li H, Gao BL, Li CH, et al. Endovascular retreatment of cerebral aneurysms previously treated with endovascular embolization. *J Neurol Surg A Cent Eur Neurosurg* 2020; 81: 207–212.
22) Scullen T, Amenta PS, Nerva JD, et al. Commentary: predicting long-term outcomes after poor-grade aneurysmal subarachnoid hemorrhage using decision tree modeling. *Neurosurgery* 2020; 87: E293–E295.
23) Darkwah Oppong M, Gembruch O, Pierscianek D, et al. Post-treatment antiplatelet therapy reduces risk for delayed cerebral ischemia due to aneurysmal subarachnoid hemorrhage. *Neurosurgery* 2019; 85: 827–833.
24) Ryttlefors M, Enblad P, Kerr RS, et al. International subarachnoid aneurysm trial of neurosurgical clipping versus endovascular coiling: subgroup analysis of 278 elderly patients. *Stroke* 2008; 39: 2720–2726.