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Original Article

Outcomes of Endovascular Therapy versus Microsurgical Treatment for Aneurysmal Subarachnoid Hemorrhage in Patients ≥70 Years of Age

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Purpose: This retrospective research aimed to compare the efficacy of endovascular therapy (EVT) versus microsurgical treatment (MST) for elderly patients with aneurysmal subarachnoid hemorrhage (aSAH).
Methods: Elderly (>70 years) patients with aSAH who underwent aneurysm obliteration during 2007–2017 were selected from our hospital database and enrolled in this retrospective study. We reviewed each patient's background, the severity of the aSAH, and aneurysmal characteristics that compelled EVT or microsurgery treatment and then compared the two treatment groups. A favorable primary outcome was defined by a modified Rankin scale (mRS) score of 0–3 at hospital discharge. The 78 patients formed two cohorts (39 patients each) based on their propensity scores for EVT or MST. We estimated the adjusted odds ratio, followed by a sensitivity analysis of the original 201 patients (118 with EVT and 83 with MST).
Results: In the propensity score-matched cohorts, favorable outcomes were observed in 33.3% and 7.7% of patients in the EVT and MST groups, respectively ($p = 0.01$). Results of the sensitivity analysis were similar to the main results.
Conclusion: The clinical outcomes for the elderly aSAH patients were better in the EVT group than in MST group.

Keywords▶ elderly, endovascular therapy, intracranial aneurysm, microsurgical treatment, subarachnoid hemorrhage

Introduction

As the population ages, a significant number of elderly patients are admitted to hospital with aneurysmal subarachnoid hemorrhage (aSAH).[1] Several studies have reported that elderly patients with aSAH who have undergone microsurgical treatment (MST) have a poor prognosis.[2–4] Hence, endovascular therapy (EVT) for elderly patients with aSAH has been suggested because it is less invasive than MST. Other reports, however, found that outcomes with EVT for aSAH in elderly patients are similar to those achieved with MST, rendering the effectiveness of EVT versus MST for aSAH unclear. Therefore, we planned to compare the effectiveness of EVT versus MST in elderly patients with aSAH.

Materials and Methods

Study design

A total of 600 consecutive patients with aSAH were admitted to our hospital between January 2007 and January 2017. Among them, the 201 patients who were >70 years of age and had undergone aneurysm obliteration (EVT or MST) were included in this study. Patients were identified retrospectively using a neurovascular database of our hospital. The primary outcome was good functioning (defined as a modified Rankin scale [mRS] score of 0–3 at hospital discharge). The secondary outcomes were rebleeding, hemorrhagic and ischemic complication due to EVT and MST, symptomatic cerebral vasospasm, and secondary normal-pressure hydrocephalus (sNPH) requiring shunt surgery. These outcomes were compared between the EVT and MST groups.

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Patient population

Patients' characteristic included their age, sex, history of smoking; presence of hypertension, diabetes mellitus, dyslipidemia, and baseline mRS. The severity of aSAH was evaluated using the Hunt and Kosnik grading system in which severe aSAH was defined as grade IV–V. On computed tomography (CT) scans, the SAH bleeding severity was assessed according to the Fisher classification. The presence of intracerebral hemorrhage (ICH) and acute subdural hemorrhage (ASDH) was also sought on CT scans and the aneurysms' features were determined using digital subtraction angiography (DSA) and three-dimensional rotation angiography. The aneurysms were subdivided according to (1) their location—that is, internal carotid artery (ICA), anterior communicating artery and anterior cerebral artery (Acom+ACA), middle cerebral artery (MCA), vertebral and basilar arteries (VA+BA); and (2) their size—that is, <6 mm vs ≥6 mm.

Aneurysm obliteration, SAH management, and outcome measurement

Treatment of the aneurysmal sac was carried out under general anesthesia almost all within 24 hours of aneurysmal rupture. No standard selection criteria were used for treatment assignment. The neurovascular interdisciplinary team (interventional neuroradiologists and vascular neurosurgeons) jointly discussed the obliteration procedure for each aneurysm according to the patient's clinical condition, the aneurysm's characteristics, comorbidities, and the background of the patient. The obliteration procedure (EVT or MST) was then chosen. If acute hydrocephalus was confirmed on CT scans, external ventricular drainage was performed after EVT or during MST. Hemorrhagic and ischemic complication was evaluated in the perioperative period. Hemorrhagic complication was defined as subarachnoid hemorrhage and ICH due to microsurgical and endovascular procedure. Ischemic complication was defined as aphasia, paralysis of limbs and face due to ischemic lesion or cerebral artery occlusion associated with microsurgical and endovascular procedure. Following treatment of the aneurysm, all patients underwent routine medical treatment for SAH, which entailed postoperative monitoring in the intensive care unit or stroke care unit for at least 14 days after aneurysm rupture. In principle, DSA was performed on days 7–10 and magnetic resonance angiography on day 14 to detect possible cerebral vasospasm. If symptomatic cerebral vasospasm had occurred and magnetic resonance imaging showed that cerebral infarction was not complete, the patient was given a selective intraarterial injection of fasudil hydrochloride. Alternatively, percutaneous transluminal angioplasty of the target vessel was carried out. During the course of hospitalization, we monitored the patient for the presence of aneurysmal rebleeding, symptomatic cerebral vasospasm, and sNPH. If sNPH occurred, a ventriculoperitoneal shunt was performed. At the time of discharge, mRS and duration of hospitalization were recorded.

Statistical analysis

Statistical analysis was carried out using JMP software (version 14.0.0; SAS Institute, Inc., Cary, NC, USA). Categorical variables are presented as numbers and percentages. They were compared using Pearson's χ^2 test or Fisher's exact test. Continuous variables ware expressed as medians and the interquartile range. Continuous variables were compared based on their distributions using the Wilcoxon rank-sum test.

Because the selection of EVT or MST for elderly aSAH patients was determined by each physician based on the patient's background, SAH severity, and aneurysmal characteristics, the patient's characteristics were presumed to be highly different between the groups. We therefore developed propensity score-matched cohorts. We used a logistic regression model to develop the propensity score for the choice of EVT, with nine independent variables relevant to making this choice. The variables for the propensity score included the following: (1) patient's age; (2) Hunt and Kosnik grade; (3) aneurysm location (ICA, MCA, Acom+ACA, VA+BA); (4) preoperative mRS score; (5) presence of ICH, ASDH, or acute hydrocephalus requiring external ventricular drainage. These variables were selected, as they had previously been associated with aSAH outcomes or were deemed a priori to be important demographic characteristics. After propensity score generation, cohort and treatment groups underwent 1:1 nearest-neighbor matching with a caliper width of 0.25 of the standard deviation of the propensity score.[5–7] Matching was performed without replacement treatment, and control units not meeting the matching criteria were excluded. We used the standardized difference to measure the covariate balance.[5] Imbalance was defined as absolute values greater than $1.96 \times \sqrt{(2/n)}$. The primary and secondary end points were compared between the EVT and MST groups in the propensity score-matched cohorts using McNemar's test. We also constructed multivariable logistic regression models for all enrolled patients as sensitivity analyses to access the

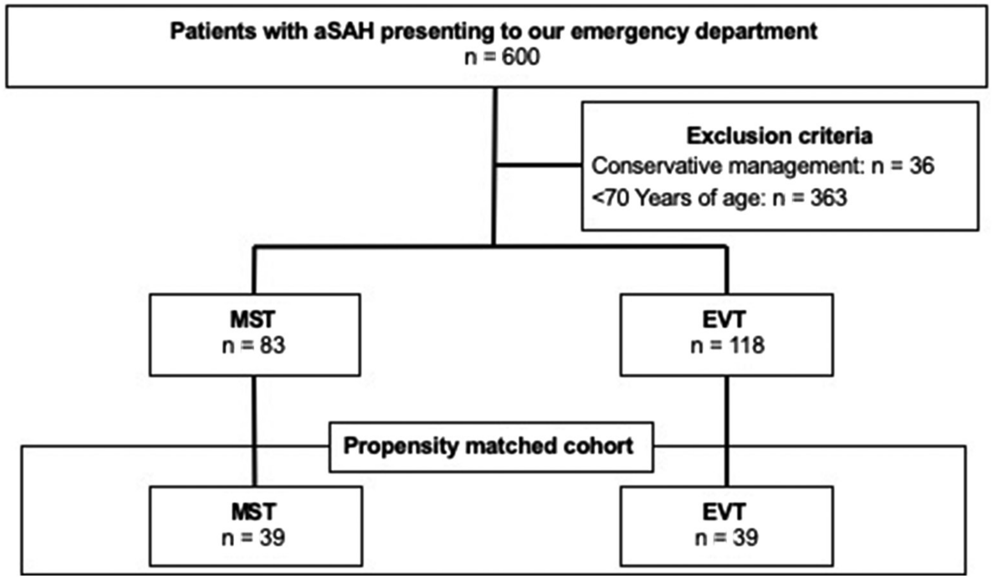

Fig. 1 Patient's flowchart for current analysis. aSAH: aneurysmal subarachnoid hemorrhage; EVT: endovascular therapy; MST: microsurgical treatment

robustness of the models. $p < 0.05$ was considered to indicate statistical significance.

Results

Patients' characteristics

Among the 564 aSAH patients who had undergone aneurysmal obliteration, 201 were >70 years of age. Among them, 118 (59%) underwent EVT, and 83 (41%) underwent MST (**Fig. 1**).

Table 1 shows the patients' baseline characteristics. In the univariate analysis, there was no significant difference between the EVT and MST groups regarding sex, history of smoking, hypertension, diabetes mellitus, dyslipidemia, baseline mRS 0–2, Fisher group 3, anterior communicating artery and anterior cerebral artery (Acom+ACA) location, or aneurysm size. More elderly patients were selected for EVT than for MST ($p < 0.01$). More severe aSAH (Hunt and Kosnik grade IV–V) patients tended to be selected for EVT than for MST ($p = 0.03$). There were more ICA ($p = 0.03$) and VA+BA ($p < 0.01$) aneurysms in the EVT group and more MCA aneurysms ($p < 0.01$) in the MST group. Acute hydrocephalus requiring external ventricular drainage was more common in the EVT group ($p = 0.01$) and ICH or ASDH in the MST group ($p < 0.01$).

Outcomes

In the original cohort before matching, there was no difference between EVT and MST groups regarding outcomes and duration of hospitalization (**Table 2**). The standard deviation of the propensity score was 0.31. Thus, a caliper width was set at 0.08, and equal numbers of EVT and MST patients (39 per group) were matched (**Table 3**). There was no difference in characteristics between the two groups. Because there were 39 patients in each group, the cutoff value of the absolute standardized difference for imbalance was 0.44. Across the baseline covariates, the absolute standardized differences ranged from a low of 0 to a high of 0.41, indicating that the means and prevalence of continuous and dichotomous variables were similar in the two treatment groups in the matched sample (**Table 3**).

In the propensity score-matched cohorts, the favorable outcome, defined by mRS 0–3 at discharge, was observed in 33.3% and 7.7% of the EVT and MST groups, respectively ($p = 0.01$) (**Table 4**). There was no difference between the two group regarding secondary outcomes (i.e., rebleeding, hemorrhagic and ischemic complication, symptomatic cerebral vasospasm, and sNPH requiring shunt surgery). Duration of hospitalization was longer in MST group than EVT group.

Sensitivity analysis

In the original cohort (201 patients), a favorable outcome was observed in 22.9% and 19.3% of the EVT and MST groups, respectively ($p = 0.54$). The adjusted odds ratio of the favorable outcomes of EVT relative to MST groups was 9.78 (95% confidence interval 2.55–37.46, $p < 0.01$), which was similar to the main results (**Table 5**). The secondary findings were also similar to the main results.

Table 1 Baseline characteristics in 201 patients >70 years of age treated for ruptured cerebral aneurysms

Characteristics	EVT (n = 118)	MST (n = 83)	p
Age, y; median (IQR)	79 (75–83)	76 (73–80)	<0.01
Female sex, n (%)	102 (86.4)	69 (83.1)	0.55
History of smoking, n (%)	10 (8.5)	12 (14.5)	0.25
Comorbidities, n (%)			
Hypertension	65 (56.4)	45 (54.2)	0.96
Diabetes mellitus	8 (6.8)	8 (9.6)	0.6
Dyslipidemia	23 (19.5)	16 (19.3)	1.0
Baseline mRS 0–2, n (%)	103 (87.3)	76 (91.5)	0.37
Fisher group 3, n (%)	105 (89.0)	73 (88.0)	0.83
Hunt & Kosnik grade, n (%)			
I	10 (8.5)	11 (13.3)	0.35
II	15 (12.7)	15 (18.1)	0.32
III	14 (11.9)	15 (18.1)	0.23
IV	23 (19.5)	21 (25.3)	0.39
V	56 (47.5)	21 (25.3)	<0.01
IV–V[a]	79 (66.9)	42 (50.6)	0.03
Aneurysm location, n (%)			
Internal carotid artery	50 (42.3)	22 (26.5)	0.03
Acom+ACA	36 (30.5)	20 (24.1)	0.34
Middle cerebral artery	5 (4.2)	36 (43.3)	<0.01
Vertebral and basilar artery	26 (22.0)	4 (4.8)	<0.01
Aneurysm size ≥6 mm (%)	60 (50.8)	44 (53.0)	0.78
Acute hydrocephalus (EVD), n (%)	30 (25.4)	9 (10.8)	0.01
Presence of ICH or ASDH, n (%)	16 (13.6)	31 (37.4)	<0.01

[a]Severe aSAH. ACA: anterior cerebral artery; Acom: anterior communicating artery; aSAH: aneurysmal subarachnoid hemorrhage; ASDH: acute subdural hemorrhage; EVD: external ventricular drainage; EVT: endovascular therapy; ICH: intracranial hemorrhage; IQR: interquartile range; mRS: modified Rankin scale; MST: microsurgical treatment

Table 2 Outcomes before matching

Outcomes	EVT (n = 118)	MST (n = 83)	p
Re-rupture, n (%)	14 (11.9)	12 (14.5)	0.67
Hemorrhagic complication, n (%)	10 (8.5)	10 (12.1)	0.48
Ischemic complication, n (%)	13 (11.0)	5 (6.0)	0.32
Symptomatic vasospasm, n (%)	12 (10.2)	11 (13.3)	0.51
sNPH requiring shunt surgery, n (%)	20 (17.0)	16 (19.3)	0.71
Duration of hospitalization, days; median (IQR)	39 (16–56)	44 (20–63)	0.21
mRS 0–3 at discharge	27 (22.9)	16 (19.3)	0.60

EVT: endovascular therapy; IQR: interquartile range; mRS: modified Rankin scale; MST: microsurgical treatment; sNPH: secondary normal-pressure hydrocephalus

Discussion

The outcome at discharge for the elderly aSAH patients in this retrospective study was better in the EVT group than in MST group. Previous reports could show (1) no overall difference between EVT and MST for treating elderly aSAH patients and (2) no superior effectiveness of EVT over MST in these patients.[3,8,9] In the subgroup analysis of elderly patients in the International Subarachnoid Aneurysm Trial (ISAT), the EVT group had better outcomes than the MST group if the analysis was limited to ICA aneurysms,[8] suggesting that EVT for elderly aSAH patients has a more positive effect than MST in specific cases. In the same study, the EVT group had fewer seizures, infections, and episodes of pulmonary edema and a shorter hospital stay than the MST group. The overall conclusion of ISAT subgroup study was that the EVT was a better treatment for elderly aSAH patients as in our study.

Although better outcomes could have been expected by performing EVT in more of the patients with aSAH in this study, it is sometimes difficult to perform EVT in elderly aSAH patients in clinical practice. For example, it is difficult to reach the aneurysm with the catheter because of severe arteriosclerotic changes in the vessel. There is also a higher risk of embolic complications in elderly patients,[10–12] and coil embolization is not always safe or easy in elderly patients. In the ISAT subgroup study, which compared the outcomes of elderly patients with aSAH after EVT versus MST, when the analysis was confined to only MCA aneurysms the MST group had better outcomes than the EVT

Table 3 Baseline characteristics in patients >70 years of age treated for ruptured cerebral aneurysms: matched cohorts

Characteristics	EVT (n = 39)	MST (n = 39)	p	SD
Age, y; median (IQR)	77 (73–80)	77 (74–82)	0.55	0.04
Female sex, n (%)	35 (87.2)	34 (87.2)	0.74	0.08
History of smoking, n (%)	6 (15.4)	3 (7.7)	0.32	0.24
Comorbidities, n (%)				
Hypertension	20 (51.3)	19 (48.7)	0.79	0.05
Diabetes mellitus	2 (5.1)	4 (10.3)	0.41	0.19
Dyslipidemia	7 (18.0)	2 (5.1)	0.06	0.41
Baseline mRS 0–2, n (%)	38 (97.4)	35 (89.7)	0.18	0.32
Fisher group 3, n (%)	34 (87.2)	37 (94.9)	0.26	0.27
Hunt and Kosnik grade, n (%)				
I	4 (10.3)	4 (10.3)	1.00	0
II	8 (20.5)	6 (15.4)	0.56	0.13
III	8 (20.5)	6 (15.4)	0.53	0.13
IV	7 (18.0)	12 (30.8)	0.13	0.30
V	12 (30.8)	11 (28.2)	0.81	0.06
IV–V[a]	19 (48.7)	23 (59.0)	0.35	0.21
Aneurysm location, n (%)				
Internal carotid artery	14 (35.9)	15 (38.5)	0.80	0.05
Acom+ACA	16 (41.0)	13 (33.3)	0.49	0.16
Middle cerebral artery	4 (10.3)	6 (15.4)	0.32	0.15
Vertebral and basilar artery	4 (10.3)	4 (10.3)	1.00	0
Aneurysm size ≥6 mm, n (%)	20 (51.3)	18 (46.2)	0.67	0.10
Acute hydrocephalus (EVD), n (%)	7 (18.0)	6 (15.4)	0.78	0.07
Presence of ICH or ASDH, n (%)	11 (28.2)	10 (25.6)	0.81	0.06

[a]Severe aSAH. ACA: anterior cerebral artery; Acom: Anterior communicating artery; aSAH: aneurysmal subarachnoid hemorrhage; ASDH: acute subdural hemorrhage; EVD: external ventricular drainage; EVT: endovascular therapy; ICH: intracranial hemorrhage; IQR: interquartile range; mRS: modified Rankin scale; MST: microsurgical treatment; SD: standard deviation

Table 4 Outcomes after 1:1 matching by propensity score

Outcomes	EVT (n = 39)	MST (n = 39)	p
Primary outcome			
mRS 0-3 at discharge	13 (33.3)	3 (7.7)	0.01
Secondary outcomes			
Re-rupture, n (%)	3 (7.7)	5 (12.8)	0.41
Hemorrhagic complication, n (%)	3 (7.7)	7 (18.0)	0.16
Ischemic complication, n (%)	6 (15.4)	4 (10.3)	0.48
Symptomatic Vasospasm, n (%)	5 (12.8)	5 (12.8)	1.00
sNPH requiring shunt surgery, n (%)	6 (15.4)	8 (20.5)	0.56
Duration of hospitalization, days; median (IQR)	35 (16–50)	52 (23–68)	0.04

EVT: endovascular therapy; IQR: interquartile range; MST: microsurgical treatment; mRS: modified Rankin scale; sNPH: secondary normal-pressure hydrocephalus

Table 5 Sensitivity analysis

Outcomes	EVT (n = 118)	MST (n = 83)	Crude OR (95% CI)	p	Adjusted OR (95% CI)	p
Primary outcome						
mRS 0-3 at hospital discharge, n (%)	27 (22.9)	16 (19.3)	1.24 (0.62–2.49)	0.54	9.78 (2.55–37.46)	<0.01
Secondary outcomes						
Re-rupture, n (%)	14 (11.9)	12 (14.5)	0.80 (0.35–1.82)	0.59	0.56 (0.18–1.75)	0.32
Hemorrhagic complication, n (%)	10 (8.5)	10 (12.1)	0.68 (0.27–1.71)	0.41	0.35 (0.10–1.18)	0.09
Ischemic complication, n (%)	13 (11.0)	5 (6.0)	1.93 (0.66–5.64)	0.23	2.66 (0.65–10.83)	0.17
Symptomatic Vasospasm, n (%)	12 (10.2)	11 (13.3)	0.74 (0.31–1.77)	0.50	0.65 (0.21–2.12)	0.48
sNPH requiring shunt surgery, n (%)	20 (17.0)	16 (19.3)	0.85 (0.41–1.77)	0.67	0.76 (0.30–1.94)	0.56

CI: confidential interval; EVT: endovascular therapy; mRS: modified Rankin scale; MST: microsurgical treatment; OR: odds ratio; sNPH: symptomatic normal pressure hydrocephalus

group.[8)] Thus, we should think of EVT as a first choice for elderly aSAH patients overall; however, it is not appropriate to suggest that EVT is always better for them.

In this study, factors that affected the prognosis of patients with aSAH included the appearance of rebleeding, hemorrhagic and ischemic complication, symptomatic cerebral vasospasm, and sNPH requiring shunt surgery,[9,13,14] with no differences between the EVT and MST groups. Hence, we could not determine why EVT provided better outcomes. Past studies have offered several considerations for why EVT was more effective than MST in elderly patients with aSAH. It was thought that EVT was superior to MST in the following ways. (1) With EVT, there is no brain parenchymal damage due to intraoperative brain traction or venous injury. Awakening and respiratory withdrawal was therefore rapid, leading to early postoperative ambulation and prevention of disuse syndrome.[14,15] (2) With EVT, there are fewer incidence of postoperative pneumonia, heart failure, pulmonary edema, or seizures.[8] In this research, shorter hospitalization in EVT may be related to early postoperative ambulation and fewer incidents of systemic complications. In future research, it will be necessary to investigate factors such as seizures and systemic complications regarding whether they are associated with the prognosis.

There were several limitations in this study. First, the short duration and dispersion of the follow-up period occurred because we adopted evaluation of mRS at discharge as the primary outcome. Because most severe elderly aSAH patients are ultimately transferred to a long-term care medical institution. They therefore cannot come to our hospital for follow-up, so it was difficult to follow their prognosis and the missing values increased. We then had no choice but to choose mRS at discharge as the primary outcome in this study. Second, the study was retrospective. Because there were no selection criteria for the treatment method and the treatment was selected in each case by the cerebrovascular team, selection bias may exist. Third, our treatment outcome was poor compared to past reports because there were many elderly patients with severe aSAH in our study. In some past reports of treatment outcomes of elderly aSAH patients, good outcomes were attained in 36.4%– 65.0% of the MST group and 33.3%–78.7% of the EVT group.[1–4,8–12,15–19] In this study, we achieved good outcomes in 19.3% of the MST group and 22.9% of the EVT group, with each of these outcomes poorer than in past reports. Because our hospital is an emergency and critical care center, the proportion of elderly patients with severe aSAH (Hunt and Kosnik grade IV–V) was very high (IV: 19.5% and V: 47.5% in the EVT group, IV: 25.3% and V: 25.3% in the MST group). We believe that it explains why our treatment outcomes data were poor. In the future, it will be necessary to (1) design a study with as little bias as possible when comparing the therapeutic effect between EVT and MST; (2) determine why EVT delivered results superior to those from MST for elderly aSAH patients; (3) evaluate which treatment is more effective for which patient group and which type of aneurysm.

Conclusions

The clinical outcomes for the elderly aSAH patients were better in the EVT group than in MST group. The elderly aSAH patients might have more favorable outcomes depending on the treatment modality.

Disclosure Statement

The authors declare that they have no conflicts of interest.

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