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Original Article

Vasospasm and Hydrocephalus Following Subarachnoid Hemorrhage Are Less Frequent in Coil Embolization Than in Clipping

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Objective: The effects of treatment methods for ruptured aneurysms on the incidence of vasospasm and normal pressure hydrocephalus (NPH) following subarachnoid hemorrhage (SAH) are controversial. We retrospectively examined the Nagasaki SAH registry data, and the complication rates of symptomatic vasospasm and NPH were analyzed based on the treatment methods.

Methods: Between January 2015 and December 2017, 800 SAH patients were registered from 18 hospitals, and their age, sex, World Federation of Neurological Societies (WFNS) grade, Fisher group, size and location of cerebral aneurysms, treatment methods, incidence of symptomatic vasospasm and shunt-dependent hydrocephalus, and prognosis (discharge or 3 months later) were retrospectively analyzed. The effects of treatment methods for the ruptured aneurysm on the incidence of symptomatic vasospasm and shunt-dependent hydrocephalus were then statistically analyzed.

Results: The mean age was 66.2 years old. There were 245 (30.6%) male patients and 555 (69.3%) female patients. Cerebral aneurysms were identified in 708 patients (87.5%) and surgical treatments were performed for 620. Neck clipping was employed in 416 patients (67.1%) and coil embolization was employed in 180 (29.0%). Symptomatic vasospasm developed in 118 (28.4%) in the clipping group and 30 (16.7%) in the coiling group (P = 0.0024). NPH developed in 148 (35.6%) in the clipping group and 42 (23.3%) in the coiling group (P = 0.0032). Vasospasm was listed as a major factor for an unfavorable outcome in 23 patients (8.9%) and as a minor factor in 33 (13.3%). NPH was listed as a major factor for an unfavorable outcome in 19 patients (3.5%) and as a minor factor in 46 (18.5%).

Conclusions: The multicenter registry study demonstrated lower incidences of both symptomatic vasospasms and NPH in the coiling group than in the clipping group. This superiority may result in better outcomes in the coiling group.

Keywords ▶ subarachnoid hemorrhage, clipping, coiling, vasospasm, hydrocephalus

Introduction

The Nagasaki Subarachnoid Hemorrhage (SAH) Registry is a multicenter cooperative study by Nagasaki University and its affiliated institutions. It was initiated in 1989. Approximately 300 patients per year were registered. The data were collected every year to investigate the annual status of treatment. Previously, we reported patients with severe SAH and elderly patients with SAH based on the analytical data.[1,2] In Nagasaki Prefecture, coil embolization of cerebral aneurysms was introduced in 1999, and a large-scale study revealed that this procedure yielded better outcomes than those of clipping.[3] Thus, coil embolization has been routinely performed. In this study, we analyzed the data to examine the incidences of cerebral vasospasm and normal pressure hydrocephalus (NPH) after SAH as treatment-related complications.

Materials and Methods

Patients with SAH were retrospectively registered from 18 Nagasaki University-affiliated institutions involving the

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department of neurosurgery. The data were registered after the study protocol was approved by the ethics review board of each institution. An Excel file regarding the patient age, sex, World Federation of Neurological Societies (WFNS) grade, Fisher's CT classification, size of the cerebral aneurysm (≥25 mm, 10–24 mm, 5–9 mm, or <5 mm), site (anterior cerebral artery, distal anterior cerebral artery, internal carotid artery, middle cerebral artery, basilar artery, vertebral artery, and others), surgical treatment (cervical clipping of cerebral aneurysms, coating, coil embolization of cerebral aneurysms, trapping, and others), cerebral vasospasm (reversible or irreversible), hydrocephalus requiring cerebrospinal fluid shunt, complications, outcome after 3 months or at discharge (modified Rankin Scale [mRS] score), and factors for a poor outcome (the most important factors that influenced the outcome; primary factors, other factors that influenced the outcome; secondary factors) was prepared and provided to each institution. After the data were input in each institution, they were accumulated/analyzed at Nagasaki University. When there was an omission or incompatible input, the corresponding institution was requested to revise it. The data from 800 patients registered between January 2015 and December 2017 were collected and analyzed.

Concerning cerebral vasospasm, transient cerebral vasospasm with ≥50% stenosis on imaging was regarded as reversible, whereas persistent cerebral vasospasm was regarded as irreversible. Furthermore, hydrocephalus was defined as that requiring cerebrospinal fluid shunting.

We compared the incidences of reversible or irreversible cerebral vasospasm after SAH and hydrocephalus requiring cerebrospinal fluid shunting between clipping and coil embolization. Furthermore, we examined the influence of the respective procedures on the outcome.

For statistical analysis, we used JMP10.0 software (SAS Institute, NC, USA). Analysis was conducted using the chi-square and Fisher's exact tests. A p value of 0.05 was regarded as significant.

Results

The number of patients registered from the 18 institutions ranged from 1 to 114. The mean age was 66.2 years. The subjects consisted of 245 males (30.6%) and 555 females (69.3%). According to Fisher's CT classification, 19 patients (2.4%) were classified as Group 1, 99 (12.4%) as Group 2, 531 (66.7%) as Group 3, 66 (8.3%) as Group 4, and 81 (10.2%) as Group 3+4. The WFNS grade on admission was evaluated as I in 220 patients (27.6%), II in 188 (23.6%), III in 29 (3.6%), IV in 116 (14.6%), and V in 243 (30.5%). Cerebral aneurysms were observed in 708 patients (87.5%). Aneurysm assessment was impossible in 44 patients. Aneurysms were not able to be identified despite examination (unknown SAH) in 44 patients. The aneurysm size was ≥25 mm in 5 patients (0.7%), 10–24 mm in 101 (14.3%), 5–9 mm in 325 (45.9%), and <5 mm in 273 (38.6%). The aneurysmal sites consisted of the anterior communicating artery in 168 patients (23.7%), internal carotid artery in 239 (33.8%), middle cerebral artery in 145 (20.5%), distal anterior cerebral artery in 35 (4.9%), basilar artery in 46 (6.5%), and vertebral artery in 43 (6.1%).

Surgery was performed on 620 patients (87.5%): clipping, 416 patients (67.1%); coil embolization, 180 (29.0%). Other treatments, such as trapping and coating, were carried out for 24 patients. At three institutions, coil embolization was more frequent than clipping. The mean age of patients who underwent clipping was 65.3 ± 13.9 years and that of those who underwent coiling was 65.1 ± 16.2 years. In the clipping group, the WFNS grade was evaluated as I in 135 patients (32.5%), II in 111 (26.7%), III in 16 (3.8%), IV in 81 (19.5%), and V in 73 (17.5%). In the coil embolization group, it was evaluated as I in 48 patients (26.7%), II in 56 (31.1%), III in 9 (5.0%), IV in 19 (10.6%), and V in 48 (26.7%). Regarding selection, there were no age- or SAH-grade-related differences in treatment. The selection of treatment with respect to the aneurysmal site and size is shown in **Table 1**. To treat middle cerebral artery and distal anterior cerebral artery aneurysms, clipping was performed in 127 (96.9%) and 27 (87.5%) patients, respectively. To treat basilar artery aneurysms, coil embolization was performed in 26 patients (81.3%). There were no aneurysm-size-related differences.

Reversible cerebral vasospasm was observed in 72 patients (17.3%) in the clipping group and in 10 (5.6%) in the coil embolization group. Irreversible cerebral vasospasm was noted in 46 (11.1%) and 20 (11.1%) patients, respectively. A total of 118 (28.4%) and 30 (16.7%) patients developed cerebral vasospasm, respectively; the incidence was significantly lower in the coil embolization group (P = 0.0024). Fasudil hydrochloride was administered to 378 patients (90.9%) in the clipping group and to 115 (63.9%) in the coil embolization group. Ozagrel hydrochloride was administered to 200 patients (48.1%) in the clipping group and to 119 (66.1%) in the coil embolization group. Cerebrospinal fluid shunting for hydrocephalus was performed in 148 patients (35.6%) in the clipping group and in 42 (23.3%)

Table 1 Location and sized of cerebral aneurysm in treatment methods

	Clipping (%)	Coiling (%)	Others (%)	Total
Aneurysm	416 (67.1)	180 (29.0)	24 (3.9)	620
Location				
ACA	91 (62.3)	55 (37.7)	0 (0)	146
Distal ACA	28 (87.5)	4 (12.5)	0 (0)	32
ICA	145 (67.4)	66 (30.7)	4 (1.9)	215
MCA	127 (96.9)	3 (2.3)	1 (0.8)	131
BA	6 (18.8)	26 (81.3)	0 (0)	32
VA	8 (21.6)	18 (48.6)	11 (29.7)	37
Others	11 (40.7)	8 (29.6)	8 (29.6)	27
Size				
25 mm <	1 (100)	0 (0)	0 (0)	1
10–24 mm	44 (57.9)	31 (40.8)	1 (1.3)	76
5–9 mm	194 (64.9)	93 (31.1)	12 (4)	299
5 mm >	177 (72.5)	56 (23)	11 (4.5)	244

ACA: anterior cerebral artery; BA: basilar artery; ICA: internal carotid artery; MCA: middle cerebral artery; VA: vertebral artery

in the coil embolization group; the percentage was significantly lower in the latter (P=0.0032).

Concerning the outcome at discharge or after 3 months, the mRS score was 0 in 211 patients (26.5%), 1 in 94 (11.8%), 2 in 64 (8.1%), 3 in 70 (8.8%), 4 in 80 (10.1%), 5 in 112 (14.0%), and 6 in 164 (20.6%). The relationship between the treatment methods and outcome is shown in **Fig. 1**. Among the WFNS grade 1 and 2 patients, clipping was performed in 244. The mRS score was 0 to 2 in 170 (70.0%) (**Fig. 1A**). Among the WFNS grade 1 and 2 patients, coil embolization was performed in 103. The mRS score was 0 to 2 in 79 (77.0%) (**Fig. 1B**); the outcome was slightly better in the coil embolization group, but there was no significant difference (P=0.184).

Primary factors for a poor outcome included initial hemorrhage in 351 patients (65.0%), cerebral vasospasm in 23 (8.9%), rebleeding in 36 (6.7%), surgery-related complications in 33 (6.1%), hydrocephalus in 19 (3.5%), and concomitant hematomas in 18 (3.3%). Secondary factors included hydrocephalus in 46 patients (18.5%), initial hemorrhage in 43 (17.3%), hematomas in 39 (15.7%), cerebral vasospasm in 33 (13.3%), surgery-related complications in 15 (6.0%), and rebleeding in 13 (5.2%).

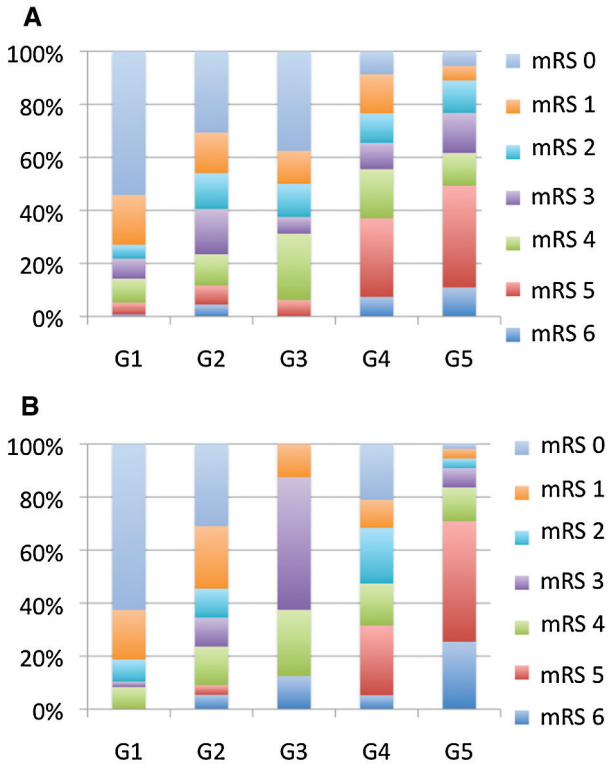

Fig. 1 Relationship of WFNS grade and prognosis in the clipping group (**A**) and coil embolization group (**B**). WFNS: World Federation of Neurological Societies

Discussion

A large-scale randomized study previously demonstrated the superiority of coil embolization of ruptured cerebral aneurysms. This procedure has also been increasingly selected in Japan.[3] In this study, the rate of patients who underwent coil embolization was approximately 30%, although there was a gradual increase. Each institution was responsible for the selection of treatment. At 3 of the 18 institutions, coil embolization was selected as a first-choice procedure. There were no aneurysm-size- or severity-related differences in the selection of treatment. Regarding the aneurysmal site, clipping was frequently performed to treat middle cerebral artery and distal anterior cerebral

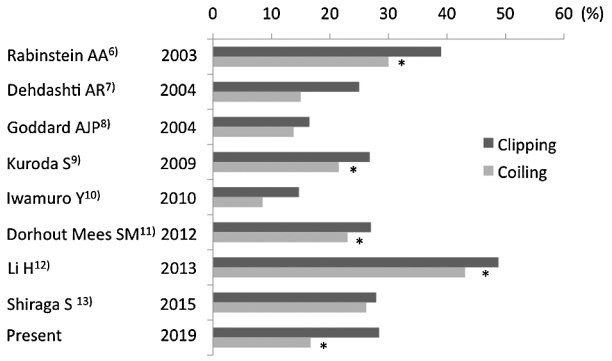

Fig. 2 Previous reports on complication ratio of cerebral vasospasm following neck clipping and coil embolization for ruptured cerebral aneurysms. *significant.

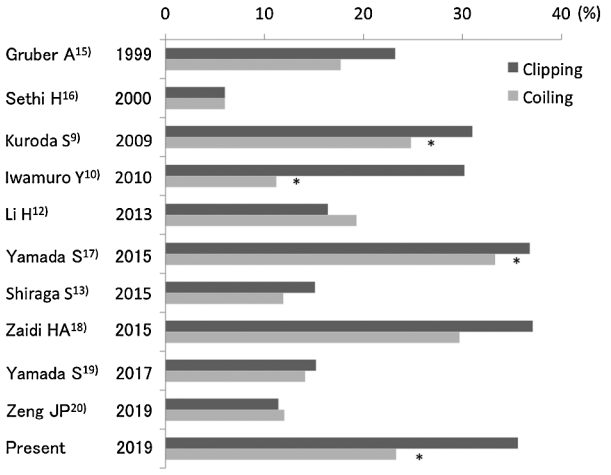

Fig. 3 Previous reports on the complication ratio of NPH following neck clipping and coil embolization for ruptured cerebral aneurysms. *significant. NPH: normal pressure hydrocephalus

artery aneurysms. Coil embolization was frequently conducted to treat basilar artery aneurysms.

Many drugs have been developed and neuroendovascular treatment is applied to treat cerebral vasospasm. However, it is still an important factor that influences the course of SAH.[4] It is frequent in patients with severe SAH and the timing of treatment is important.[5] Treatment ≥5 days after onset increases the incidence. The incidence of cerebral vasospasm after clipping or coil embolization in previous studies is shown in **Fig. 2.**[6–13] The definition of cerebral vasospasm varies among studies: symptomatic, asymptomatic, changes on imaging, reversible, and irreversible. Its incidence ranges from approximately 10% to 50%, but most studies reported that the incidence of cerebral vasospasm after coil embolization was lower than that after clipping. In half of the studies, there were significant differences. A study regarding the superiority of clipping emphasized that hematomas can be removed during surgery. On the other hand, intraoperative cerebrovascular injury, injury of the cerebral parenchyma, or systemic inflammation may cause cerebral vasospasm.[14]

Shiraga et al. reported that the incidence of cerebral vasospasm was significantly lower in the coil embolization group among patients with severe SAH, suggesting that arachnoid exfoliation for craniotomy plays a role in delayed hematoma elimination in severe-status patients, leading to cerebral vasospasm.[13] In coil embolization, cerebrospinal fluid circulation is preserved, which may promote the washout of hematomas.[8]

Reports on the incidence of conventional-treatment-related hydrocephalus are presented in **Fig. 3.**[9,10,12,13,15–20] The definition of hydrocephalus also varies: symptomatic, imaging findings, and hydrocephalus requiring surgery. Its incidence ranges from approximately 10 to 40%, but hydrocephalus after coil embolization is less frequent than after clipping. There were significant differences in 4 of 12 articles, including this study. As for why hydrocephalus after clipping is less frequent than after coil embolization, one study suggested that craniotomy during which hematomas can be removed is more advantageous, as the incidence of hydrocephalus is higher at a larger SAH volume.[20] Furthermore, another study proposed that ventricle-cistern communication through the lamina terminalis opening prevents hydrocephalus.[19] On the other hand, as for why clipping can induce hydrocephalus, arachnoid opening during surgical operations may promote arachnoid cicatrization and fibrous thickening after surgery, leading to closure of the subarachnoid space.[19] In clipping, elimination is primarily promoted through cisternal drainage, whereas it is promoted through lumbar vertebral drainage during coil embolization in many cases; involvement of the postoperative recumbency period and cisternal drainage is suggested.[19] Iwamuro et al.[10] reported that the incidence of hydrocephalus was significantly higher in the clipping group consisting of elderly patients. Initially, coil embolization was indicated for patients with severe SAH related to ruptured posterior circulation cerebral aneurysms. However, posterior circulation and severe SAH are independent factors for hydrocephalus. This was considered to be the reason why the incidence of hydrocephalus after coil embolization was high.[19,20] Following advances in devices for coil embolization, this procedure is increasingly indicated for patients with anterior circulation aneurysms or mild SAH. This may have led to a decrease in the incidence of hydrocephalus after coil embolization.[19]

In this study, the outcome after coil embolization was slightly better than that after clipping in mild-status patients. Cerebral vasospasm was the second most frequent primary factor for a poor outcome, following initial hemorrhage; it may have influenced the outcome. Furthermore, hydrocephalus was the most frequent secondary factor for a poor outcome. These are considered important complications. Kuroda et al.[9] also reported cerebral vasospasm and hydrocephalus as factors for a poor outcome.

As the limitations of this study, this was a multicenter, retrospective registration study, and treatment strategies/methods were selected based on the physicians' evaluation at each institution; there were aneurysm-site-related differences in the selection of clipping or coil embolization. In addition, the prevention and treatment of cerebral vasospasm and hydrocephalus differed among the institutions. In comparison with other articles, the definitions of cerebral vasospasm and hydrocephalus vary,[14] and the timing of evaluation differs[9]; therefore, these factors may have influenced the results. In studies involving a large-scale database or volunteer registration, there may be omissions, making the calculation of incidences inaccurate through a sampling bias.[10] In this study, concerning omissions, documents were returned to the registrants to promote filling-in, facilitating more accurate examination. The results of meta-analysis may also be influenced by a large database. In randomized studies, institutions reaching a specific level can participate, thus the results may not reflect the actual status. Of 9559 patients with SAH, the ISAT study involved 2143 with aneurysms in whom both clipping and coil embolization were possible; the results were compared in only a portion.[3] Furthermore, severe-status patients accounted for 4% of the subjects, demonstrating dissociation from the actual status.[3] A sub-analysis of the study also involved only a portion and the results are not universal.[11] In a report from a single institution, there was a significant bias related to institutional strategies and it referred to a high-volume center; the actual situation is not reflected. A registration study involving a core hospital and its affiliated institutions, such as this study, is possible due to the Japan-specific medical system. The results of a prospective registration study involving 836 patients with SAH during a period of 5 years in Hokkaido University and 7 major affiliated institutions were previously published.[9] The rate of severe-status patients was high, similar to that in this study. Concerning treatment methods, clipping was performed in 548 patients (79.5%) and coil embolization was performed in 121 (17.6%); there was a deviation.[9] This study involved 18 institutions, and the number of patients per institution ranged from 1 to 114; small-scale to core institutions were comprehensively registered. The number of physicians responsible for treatment was large and there was only a relatively small deviation in the treatment methods. Therefore, this study may reflect the actual status accurately.

Conclusion

This multicenter registration study revealed that the incidences of symptomatic cerebral vasospasm and hydrocephalus requiring cerebrospinal fluid shunting after coil embolization of ruptured cerebral aneurysms were lower than those after clipping. Respective conditions accounted for a specific rate as factors for a poor outcome of SAH; they may have led to the treatment-related differences in the results.

Disclosure Statement

The authors declare no conflict of interest.

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