Results of Endovascular Treatment in 295 Elderly Patients with Unruptured Cerebral Aneurysms in Comparison with Non-elderly Patients in a Single Institution

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Objective: To explain the results of endovascular treatment for unruptured cerebral aneurysms in elderly patients, we divided patients with unruptured cerebral aneurysms who underwent endovascular treatment in our hospital into three groups: elderly (75 years and older), pre-elderly (65–74 years), and young (65 years and younger) groups, and compared the treatment results.

Subjects and Methods: In our hospital, 646 patients (elderly: 53, pre-elderly: 242, young: 351) with unruptured cerebral aneurysms underwent initial endovascular treatment between April 2007 and December 2015. We retrospectively compared aneurysmal factors, treatment methods, and treatment results (complications, results of embolization immediately after surgery, and results of follow-up imaging).

Results: The mean ages of the subjects in the aforementioned groups were 77.8 ± 2.45 (75–84 years), 69.2 ± 2.93 (65–74 years), and 53.3 ± 8.64 (26–64 years) years. Mean volume embolization ratios (VERs) of the elderly and pre-elderly groups were significantly lower when compared with that of the young group. Complete occlusion (Raymond Scale [RS] 1) was found in 48 (94.1%), 210 (87.5%), and 316 (91.6%) patients in the elderly, pre-elderly, and young groups, respectively, using digital subtraction angiography. Complications were noted in 8 (15.4%), 23 (9.5%), and 27 (7.7%) patients in the elderly, non-elderly, and young groups, respectively. In the elderly group, the incidence of embolic complications was slightly, although not remarkably, higher. On the final follow-up imaging, RS 1 was achieved in 40 (80.0%), 196 (83.1%), and 295 (86.5%) patients in the elderly, pre-elderly, and young groups, respectively; these differences did not rise to the level of statistical significance. Recanalization was achieved in 9 (18.0%), 31 (13.1%), and 39 (11.4%) patients in the elderly, pre-elderly, and young groups, respectively. Additional treatment was required for 1 (2.0%), 5 (2.1%), and 4 (1.2%) patients, in the elderly, pre-elderly, and young groups, respectively, showing no significant between-group differences.

Conclusion: The results of endovascular treatment for unruptured cerebral aneurysms in both the elderly and pre-elderly groups were similar to those in the young group. After due consideration of all known indications and treatment methods, endovascular treatment should be considered a feasible management for elderly patients.

Keywords: unruptured cerebral aneurysms, elderly patients, coil embolization

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Introduction

With a rapidly aging population, opportunities for treating elderly patients with subarachnoid hemorrhage (SAH) and ruptured or intact cerebral aneurysms have increased. Advanced age is a prognostic factor for ruptured cerebral aneurysms.\(^1,2\) In the treatment of unruptured cerebral aneurysms for rupture prevention, it is necessary to maintain a more healthy status and avoid a severe condition at the time of rupture. For elderly patients, endovascular treatment is increasingly selected as a first-line procedure, considering its invasiveness. However, the prognosis for recovery remains unfavorable\(^3\) because of gerontological issues, such as life expectancy and other unexpected complications.\(^4\) It is difficult to determine the indication for surgery, considering the incidence of aneurysmal rupture.\(^5-7\) Several studies examined the relationship between the results of treatment for unruptured cerebral aneurysms and age, establishing 60 or 65 years of age as a border.\(^8,9\) However, with recent changes in the social background, a study evaluated the results by assigning subjects aged 65–74 years to the pre-elderly group and those aged 75 years and older to the elderly group.\(^10\) Methodological issues exist with some previous studies that variously compared two groups, obtained data from a small number of patients, or merged the results obtained over multiple study centers. This study was a single-center, retrospective analysis of treatment outcomes of patients divided into three groups (elderly, pre-elderly, and young groups). All patients exhibited unruptured cerebral aneurysms and underwent endovascular treatment.

Subjects and Methods

Subjects

The subjects were 646 patients with unruptured saccular cerebral aneurysms who underwent initial endovascular treatment in our hospital between April 2007 and December 2015. Patients were assigned to the “elderly” group (aged 75 years and older; 53 patients), the “pre-elderly” group (aged 65–74 years; 242 patients), or the “young” group (aged 64 years and younger; 351 patients). The results of treatment were compared among the three groups.

Criteria for inclusion

In our hospital, treatment is generally indicated for aneurysms with a maximum diameter of ≥5 mm or irregularly shaped aneurysms with a bleb formation. Additionally, treatment is recommended to patients with a family history of aneurysms or those with changes in the aneurysm shape, even if observation therapy was initially selected. To treat these aneurysms, we consider two techniques: clipping and endovascular treatment, based on patients’ wishes. Only patients who were able to understand the potential risks and complications, as well as the morbidity and mortality rates associated with treatment were considered treatment candidates, and an informed consent form was obtained from them.

In patients for whom treatment was not indicated or those who did not consent to treatment, follow-up imaging was conducted every 6 months to 1 year. When a change was noted, treatment was recommended.

Methods

Coil embolization was performed for all patients under general anesthesia. A single aneurysm was treated per session. A femoral artery puncture was basically performed, and a radial or brachial artery puncture was selected in accordance with the vascular state. Surgeons were responsible for the selection of approaches or coils.

As antiplatelet therapy, aspirin at 100 mg/day and clopidogrel at 75 mg/day were orally administered from 1 week before surgery, as a rule, when using the single-catheter method. Patients aged 70 years and older received oral aspirin at 100 mg/day and clopidogrel at 50 mg/day. From the day after surgery, the same dose of clopidogrel alone was continuously administered for at least 1 month. During surgery, systemic heparinization was performed after puncture, and the activated coagulation time was controlled, targeting 2- to 2.5-fold of the preoperative value.

Evaluation

The aneurysm site, shape, maximum diameter, dome/neck ratio (D/N ratio), and volume were evaluated as aneurysmal factors. The shapes of aneurysms with bleb formations were regarded as irregular. We retrospectively compared the treatment methods (single-catheter method, adjunctive technique [balloon-assisted or double catheter techniques], and stent-assisted techniques), treatment results immediately after surgery, follow-up results, volume embolization ratio (VER), changes in the modified Rankin Scale (mRS) score before and after admission, and postoperative complications among the elderly, pre-elderly, and young groups. The angiographic results were evaluated with the Raymond grading system as follows: complete occlusion (Raymond Scale [RS] 1), residual neck (RS2), and residual aneurysm (RS3). As a rule, follow-up angiography was
performed 6 months and 1 year after surgery. Subsequently, follow-up MRA was performed. When a patient’s general condition was not adequate for angiography, or when it was difficult to obtain consent, follow-up was performed using MRA alone. Recanalization was defined as deterioration of the RS.

Statistical analysis
For statistical analysis, JMP Pro 12 software (SAS Institute Inc., Cary, NC, USA) was used. For detection of differences among the three groups, we tested significance using the Tukey–Kramer HSD test. For percentage comparisons, Fisher’s exact test was used. A p-value of 0.05 was regarded as significant.

Results

Patient background/aneurysm descriptions
The patient background and aneurysms descriptions in each group are shown in Table 1. The results of endovascular treatment were compared among the three groups. Of the 53, 242, and 351 patients in the elderly, pre-elderly, and young groups, respectively, 46 (86.8%), 200 (82.6%), and 270 (76.9%) patients were women. There were no gender differences among the three groups. The mean ages were 77.8 ± 2.45 (75–84 years) for patients in the elderly, 69.2 ± 2.93 (65–74 years), and 53.3 ± 8.64 (26–64 years) years for patients in the elderly, pre-elderly, and young groups, respectively. There were no differences in the aneurysm site, shape, or rate of aneurysm location among the three groups. Concerning aneurysm size, the mean aneurysm neck diameters were 4.48 ± 1.50 (elderly), 4.17 ± 1.36 (pre-elderly), and 3.82 ± 1.30 mm (young). The mean maximum aneurysm diameters were 7.19 ± 2.48 (elderly), 6.57 ± 2.40 (pre-elderly), and 6.39 ± 2.55 mm (young). The mean D/N ratios were 1.66 ± 0.53 (elderly), 1.62 ± 0.43 (pre-elderly), and 1.73 ± 0.55 (young). The mean aneurysm volumes were 181.9 ± 245.4 (elderly), 131.0 ± 232.3 (pre-elderly), and 136.8 ± 351.6 mm³ (young). The average aneurysm neck diameters for patients in the elderly and pre-elderly groups were significantly larger than those observed in the young group (p <0.01). The D/N ratio of the pre-elderly group was significantly lower than that observed in the young group (p = 0.030). There were no significant differences in the maximum aneurysm diameter; however, slight age-related increases were observed.

Procedures
The aneurysm was unable to be accessed in one patient in the elderly group. Endovascular procedures are shown in Table 2. In the elderly group (52 patients), the single-catheter method was used in 20 (38.5%), the adjunctive technique in 29 (55.8%), and the stent-assisted technique in 3 (5.8%) patients. In the pre-elderly and young groups, the single-catheter method was used in 61 (25.2%) and in 73 (20.8%) patients, respectively. Thus, it is observed that more patients in the elderly group underwent endovascular treatment using the single-catheter method compared to the young group (p <0.01).

Treatment results
Endovascular treatment results are shown in Table 3. Treatment failures occurred in one patient in the elderly...
group due to catheter instability related to marked arteriosclerosis. In the young group, treatment failures occurred in two patients due to coil protrusion. Intraoperative rupture caused termination of simple coil embolization in two and four patients in the pre-elderly and in the young groups, respectively. In these patients, the procedure was switched to craniotomy, excluding one patient with parent vessel occlusion in the young group. Among patients in whom treatment could be accomplished using endovascular treatment alone, the mean VERs were 34.4 ± 8.0 and 34.7 ± 8.7% in the elderly and pre-elderly groups, respectively, lower than in the young group (37.0 ± 8.2%). There was a significant difference between the pre-elderly and young groups (p <0.01). Using digital subtraction angiography, RS 1 was achieved in 48 (94.1%), 210 (87.5%), and 316 (91.6%) patients in the elderly, pre-elderly, and young groups, respectively; the results were similar among all the three groups.

Complications

Complications were noted in 8 (15.4%), 23 (9.5%), and 27 (7.7%) patients in the elderly, pre-elderly, and young groups, respectively. Although there were no significant differences, the incidence of complications slightly higher in the elderly groups. Breeding complications, such as SAH and intracerebral hemorrhage, and embolic complications occurred in 1 and 6 patients (1.9% and 11.3%), in the elderly group, in 6 and 15 patients (2.5% and 6.2%), in the pre-elderly group, and in 10 and 2 patients (2.8% and 0.6%), in the young group. In the elderly and pre-elderly groups, the incidence of embolic complications was slightly higher. In the young group, the incidence of hemorrhagic complications was slightly higher.

Of patients with embolic complications in the elderly (n = 6), pre-elderly (n = 12), and young (n = 2) groups, 5 (9.4%), 10 (4.1%), and 2 (0.6%) patients in the elderly,
pre-elderly, and young groups, respectively, were symptomatic. However, symptom relief was achieved before discharge in 1 and 4 patients in the elderly and pre-elderly group, respectively.

Of the patients with hemorrhagic complications, treatment was accomplished using coil embolization alone in 1 (1.9%), 4 (1.7%), and 6 (1.7%) patients in the elderly, pre-elderly, and young groups, respectively. Of the patients with hemorrhagic complications in the elderly group, postoperative computed tomography scan revealed slight SAH around the aneurysm; however, it was asymptomatic. We observed asymptomatic hemorrhagic complications in 2 (0.8%) and 4 (1.1%) patients in the pre-elderly and young groups, respectively. To treat hemorrhagic complications, parent vessel occlusion was performed in addition to coil embolization in 1 (0.3%) patient in the young group. In 2 (0.8%) and 3 (0.9%) patients in the pre-elderly and young groups, respectively, the procedure was switched to craniotomy. The above-mentioned patients who underwent parent vessel occlusion and in whom the procedure was switched to craniotomy died; all patient fatalities were in the young group (0.9%).

Due to these complications, the mRS scores on discharge were poorer than that on admission in 4 (7.6%) patients with embolic complications in the elderly group, in 11 (4.6%) patients, including 6 with embolic complications and 4 with hemorrhagic complications, in the pre-elderly group, and in 12 (3.4%) patients, including 2 with embolic complications and 6 with hemorrhagic complications, in the young group. No significant differences were noted. Of these, 1 (1.9%), 5 (2.1%), and 5 (1.4%) in the elderly, pre-elderly and young groups, respectively, required hospital transfer for rehabilitation. The patient in the elderly group discharged to home following 2 month’s rehabilitation.

Follow-up results
The follow-up results are shown in Table 4. Of patients who were successfully treated, follow-up imaging was possible in 50 (98.0%) patients in the elderly group, with a mean period of 21.2 ± 10.7 months, in 236 (98.3%) patients in the pre-elderly group, with a mean period of 23.8 ± 14.8 months, and in 341 (98.8%) patients in the young group, with a mean period of 24.6 ± 15.1 months. On the final follow-up imaging, RS 1 was achieved in 40 (80.0%), 196 (83.1%), and 295 (86.5%) patients in the elderly, pre-elderly, and young groups, respectively. Recanalization was achieved in 9 (18.0%), 31 (13.1%), and 39 (11.4%) patients in the elderly, pre-elderly, and young groups, respectively. In the elderly group, the recanalization rate was slightly higher, but no significant differences were observed when compared with the other two groups. In the elderly group, additional treatment was performed due to hemorrhage in one (2.0%) patient. This patient did not wish to undergo additional treatment despite deterioration of RS. In the young group, additional treatment was required in four (1.2%) patients. In the pre-elderly group, additional treatment was performed in five (2.1%) patients. The additional treatment rates were similar among the three groups.

Discussion
Natural history of unruptured cerebral aneurysms
In Japan, the number of elderly persons has increased. With the recent widespread use of magnetic resonance imaging and positive utilization of health checkups, the detection rate of unruptured cerebral aneurysms in elderly persons has increased. Cerebral aneurysms cause serious diseases, such as SAH and intracerebral hemorrhage, at the time of rupture. They are asymptomatic in the absence of aneurysm-related compression; therefore, treatment for unruptured cerebral aneurysms is preventive in nature. Concerning unruptured cerebral aneurysms, large-scale studies, such as the International Study of Unruptured Intracranial Aneurysms (ISUIA)11) and Unruptured Cerebral Aneurysm Study in Japan (UCAS Japan),7) have been conducted. The ISUIA indicated that, in elderly patients, the incidence of complications after clipping was higher than after endovascular treatment, suggesting that endovascular treatment should be recommended for elderly patients. In the UCAS Japan, risk factors for rupture included advanced age (80 years and older), and the incidence of surgical complications was high in the elderly group. This suggests that the necessity of

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Table 4 Follow-up result

<table>
<thead>
<tr>
<th></th>
<th>Elderly (n=50)</th>
<th>Pre-elderly (n=236)</th>
<th>Young (n=341)</th>
<th>P value</th>
</tr>
</thead>
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<tr>
<td>Recanalization</td>
<td>8 (15.7%)</td>
<td>31 (13.1%)</td>
<td>39 (11.4)</td>
<td>0.559</td>
</tr>
<tr>
<td>Raymond scale at the final follow-up</td>
<td>1</td>
<td>40 (80.0%)</td>
<td>196 (83.1%)</td>
<td>295 (86.5%)</td>
</tr>
<tr>
<td>2</td>
<td>8 (16.0%)</td>
<td>30 (12.7%)</td>
<td>41 (12.0%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2 (4.0%)</td>
<td>10 (4.2%)</td>
<td>5 (1.5%)</td>
<td></td>
</tr>
<tr>
<td>Re-treatment</td>
<td>1 (2.0%)</td>
<td>5 (2.1%)</td>
<td>4 (1.4%)</td>
<td>0.519</td>
</tr>
</tbody>
</table>

*Statistical difference: <0.05. Recanalization, Raymond scale at the final follow-up, Re-treatment; Fisher’s exact test.
surgical indication should be carefully determined. Especially in elderly patients, it is important to evaluate the general pretreatment condition of each patient. This condition includes activities of daily living (ADLs), systemic complications, and prognosis.\textsuperscript{6,6}\textsuperscript{1}

**Therapeutic strategies**

In patients with unruptured cerebral aneurysms, it is still impossible to accurately predict rupture.\textsuperscript{12} Therefore, anxiety is a common factor among patients. In elderly patients, this anxiety is more marked, and many patients report this anxiety as mental stress.\textsuperscript{13–15}\textsuperscript{2}

Sah with ruptured cerebral aneurysm more frequently leads to a serious condition in elderly patients, making it difficult to maintain pretreatment ADLs after rupture;\textsuperscript{12} in addition to the characteristics of Sah, protracted-bedrest-related cognitive dysfunction or disuse progression\textsuperscript{16,17}\textsuperscript{3} may affect subsequent recovery in elderly patients.\textsuperscript{18–20}\textsuperscript{4}

In many cases, the treatment indication for unruptured cerebral aneurysms in non-elderly patients is evaluated based on the location, size, and shape of aneurysms. These factors should therefore be sufficiently reviewed.

In our hospital, only elderly patients at high risk with unruptured cerebral aneurysms are treated. Coil embolization is not recommended for all patients of advanced age. In these cases, coil embolization or clipping is selected, as performed in non-elderly patients. Therefore, it is important that these complications be comprehensively explained to elderly patients. Only patients who understand the natural history of the disease, consider follow-up options, and still request treatment should be treated.

**Procedures**

The single-catheter method was more frequently selected in patients within the elderly group compared with the young and pre-elderly groups. This may have been associated with problems accessing the aneurysms, including vascular torsion and arteriosclerosis, or adjunctive-technique-related increases in the risks of complications. In the elderly patients, a single-catheter method included a single-catheter procedure with a distal access catheter, direct cervical puncture, and radial artery approach; it was necessary to devise treatment methods comparable to those used with young patients. Concerning the aneurysm size, the aneurysm neck diameter in the patients in the pre-elderly group was greater than the patients in the young group, and the D/N ratio was lower; wide-neck aneurysms may have been positively treated by adopting adjunctive techniques or stent-assisted procedures. On the other hand, in the elderly group, wide-neck aneurysms were treated, but treatment was indicated for aneurysms in which the single-catheter method was available based on the D/N ratio. Furthermore, the maximum aneurysm diameter was larger, and aneurysms with a high risk of rupture were treated.

**Treatment results: State of aneurysm embolization**

The results of this study showed that the VERs in the patients in the elderly and pre-elderly groups were lower than that in the young group. On the other hand, there were no differences in the number of patients with RS 1 on imaging. Concerning the association between a high VER and a reduction in the recanalization rate, a previous study reported that a VER of 25% was required to reduce the recanalization rate.\textsuperscript{21} Based on the results of this study, even the elderly group with the lowest mean VER, the VER exceeded 25% (34.4 ± 8.0%); sufficient embolization was achieved, and this may have contributed to the absence of differences in the complete occlusion.

During long-term follow-up after treatment, the postoperative recanalization rate in the elderly group was slightly higher than in the young group. However, the rate of patients requiring additional treatment was similar.

These results suggest that, in our hospital, patient selection based on the D/N ratio and aneurysm size, and single-catheter-based treatment selection, involving the use of intermediate catheters are useful for preventing the rupture of aneurysms.

According to Oishi et al., the results of endovascular treatment in elderly patients have improved with recent advances in the instruments and techniques using for endovascular treatment; therefore, there may be no differences in the results of treatment if inclusionary criteria are sufficiently considered in patients aged 65 years and older.\textsuperscript{10} The results of this study were also consistent with their findings. In our study, the treatment results in the elderly and pre-elderly groups were similar to those in the young group, suggesting that coil embolization is effective for cerebral aneurysms when considering inclusionary criteria, regardless of age.

**Treatment results: Complications**

Based on previous studies, perioperative complications may occur in the presence of underlying diseases in elderly patients.\textsuperscript{41} In particular, arteriosclerosis is associated with advanced age; consequently, thrombotic and embolic complications must be considered.\textsuperscript{22–24} However, the other hand, another
study indicated that advanced age did not influence the morbidity rate. In this study, the incidence of perioperative complications was high in the elderly group; among these complications, thrombotic complications were more frequent than in the young group. However, the incidence of declines in ADLs, complications that make discharge difficult, was not high. The incidence of complications that influence ADLs in elderly patients may be similar to those in young patients by reviewing aneurysmal factors, such as the aneurysm diameter and D/N ratio, procedures, and access routes before treatment.

Limitations of this study
This was a retrospective study. In outpatient care, patients are evaluated based on their general condition, rather than strict inclusion/exclusion factors, despite the necessity to treat based on aneurysmal factors; the results of this study do not reflect the whole picture of unruptured cerebral aneurysms in elderly patients. Treatment for elderly patients should be established from the viewpoint of life-span prolongation. We cannot conclude that treatment prolongs the lifespan based on the results of this study; however, it may contribute to its prolongation. When determining treatment in our hospital, we evaluate the patient’s age and treatment tolerance. As indicated earlier, it may be impossible to standardize treatment criteria based on age alone. The results of this study suggest that elderly patients can achieve treatment results similar to those observed in young patients by performing endovascular treatment after reviewing indication criteria based on the patient’s general condition.

Conclusion
In both the pre-elderly and elderly groups, the results of treatment for unruptured cerebral aneurysms were similar to those in the young group. After due consideration of indications and treatment methods, endovascular treatment should be considered a feasible management for elderly patients.

Disclosure Statement
There is no conflict of interest for the main author and coauthors.

References


