

## Does Age Affects the Surgical Outcome in Patients with Unruptured Cerebral Aneurysms? A 2-Year Retrospective Study from a Single Center in Japan

### Abstract

**Background:** The management of unruptured cerebral aneurysms (UCA) in elderly population is a challenge. With a very high life expectancy and high risk of rupture in Japan, the need for identifying the best treatment modality is essential to help the patients in decision-making. **Methods:** This was a 2-year single-center retrospective comparative analysis of the outcomes of surgical clipping (SC) in patients aged above 75 and <75 years. The modified Rankin score was used to stratify the patients and to analyze the functional outcome. Functional status at discharge was the primary end point. **Results:** There were 224 patients with 239 aneurysms. About 12.5% of the patients were more than 75 years with a mean age of 77.85. The mean age of patients <75 years was 60.96, and it was statistically significant. The overall male-to-female ratio was 1:3.3. The most common location was the middle cerebral artery followed by internal carotid artery at the posterior communicating and ophthalmic segments, and 22 patients had aneurysms of the posterior circulation. Nearly 77% of the aneurysms were <6 mm. There was no significant difference in size of the aneurysm as the age increased to more than 75 years. There were complications in 6 patients, and there was no mortality in the study population. There was no statistically significant difference in the outcome between the groups. **Conclusions:** SC can be considered a safe option for UCA in the aging population.

**Keywords:** Age, outcome, unruptured cerebral aneurysms

### Introduction

The management of elderly patients with unruptured cerebral aneurysms (UCA) is challenging. The world's highest life expectancy is seen in Japan and hence there is an increasing incidence of identifying UCA's. The decision to perform surgery on this group of patients is complex. We must consider the life expectancy, risk from surgery, risk of rupture, and the ensuing poor prognosis. The annual rate of rupture for all aneurysms is approximately 1.6%.<sup>[1]</sup> However, the risk of rupture of an unruptured aneurysm is high in Japan and it is approximately 2.3% per year.<sup>[2]</sup> The Unruptured Cerebral Aneurysm Study of Japan (UCAS Japan) enrolled 5720 patients and 27.6% of the patients were older than 70 years.<sup>[3]</sup> There are a few studies which have demonstrated that increasing age is a poor prognosticator for all forms of treatment.<sup>[4-6]</sup> Elderly aneurysmal subarachnoid hemorrhage patients are more likely to experience symptomatic vasospasm which translates to worse

outcomes.<sup>[7]</sup> Hence, in this retrospective study, we analyzed our data of UCA's who underwent surgical treatment from October 2014 to September 2016.

### Methods

#### Patients

We included all the patients who underwent surgical treatment for UCA at our hospital during the period from October 2014 to September 2016. The treatment modality was decided by the patient on the basis of the recommendation of the treating physician. All patients older than 20 years and size of the aneurysm >3 mm, who underwent surgery were included in the study. We excluded the patients if there was any unknown cause for intracranial hemorrhage before the treatment. We divided the patients into 2 groups based on the age. Since the life expectancy is high in Japan, we considered the cutoff age as 75. All the patients who were 75 years and above were grouped and compared with

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the patients who were <75 years of age. Only patients with unruptured aneurysms were enrolled in this study to specifically look into the short-term outcomes of surgery. We used the modified Rankin score (mRS) to stratify the patients and to analyze the functional outcome. A score of 0 indicates that there is no disability, 1 indicates slight symptoms, 2 indicates slight disability, 3 indicates moderate and 4 indicates moderately severe disability, 5 indicates severe disability, and 6 indicates death.

### Data collection

This was a retrospective chart review study. Informed consent was obtained from all the patients for enrollment in the study and for publishing the data. The study was approved by the institutional review board. All the data were collected from the hospital information system and data were tabulated on an Excel sheet. We did not collect the data of the patients who underwent other forms of treatment or patients who refused any form of treatment. The patient's clinical characteristics, aneurysm morphology, and the treatment were recorded. The admitting mRS and the discharge mRS were used for the comparison of the outcomes. Functional status at discharge was the primary end point.

### Objective

The objective of this study was to compare clinical and functional outcomes between 2 age groups ( $\geq 75$ , <75 years) and to determine whether age is an independent predictor of outcome.

It is anticipated that these data will be helpful in the informed clinical decision-making of older individuals with aneurysms.

### Statistical analysis

The data were collected for 2 years. Student's *t*-test was used to analyze normally distributed data and Chi-square test for independence was applied for two categorical variables in the patient population. Kruskal–Wallis H test was used to determine if there are statistically significant differences between the groups of an independent variable. All analysis was performed using Statistical Package for the Social Sciences (SPSS, IBM Corporation, New York, United States) software package v 2015.

### Results

During the study period, as per the inclusion criteria, we identified 224 patients with 239 aneurysms. Twelve patients had multiple aneurysms. All the patients were having only mild symptoms such as headache or dizziness. None of the patients had even a slight disability before the treatment. Based on the age, patients were divided into two groups, more than 75 years and <75 years. There were 28 patients (12.5%) who were more than 75 years and 196 patients were <75 years. The mean age of the

patients in more than 75 years group was 77.85 and 60.96 in <75 years group which was statistically significant with  $P = 0.001$ . The mean age of the entire study population was 69.42 years. Nearly 76.8% of the study population were women. The overall male-to-female ratio was 1:3.3 and it doubled after 75 years to 1:6. The characteristics of the patients and aneurysms are shown in Table 1.

The various locations of the aneurysms are shown in Table 1. The most common location was the middle cerebral artery followed by internal carotid artery at the posterior communicating and ophthalmic segments. Twenty-two patients had aneurysms of the posterior circulation. The sizes of the aneurysms were grouped into 3–4 mm, 4.1–6 mm, 6.1–9 mm, and more than 9.1 mm. Most of the aneurysms (77%) were <6 mm. The mean size of the aneurysm in more than 75 years group was  $5.87 \pm 2.187$  and  $5.58 \pm 2.94$  in <75 years group. There was no significant difference in size of the aneurysm as the age increased to more than 75 years. Clipping was the most common treatment modality in all groups (96.02%), 7 patients underwent wrapping of the aneurysms and two patients underwent bypass and trapping of the aneurysms.

**Table 1: Characteristics of the patients and aneurysms**

Demographic characteristics (n=224)	Number of patients
Age	
>75	28 (12.5)
<75	196 (87.5)
Gender	
Male	52 (23.2)
Female	172 (76.8)
Location of aneurysm	
A1	3
A2-3	13
AComm	27
BA top	7
BA-SCA	5
IC-Acho	10
IC-Bi	9
IC-fusiform	1
IC-Oph	31
IC-PC	33
MCA	75
P2-3	1
PICA	1
VA-PICA	8
Size of aneurysm	
3-4 mm	89 (39.7)
4.1-6 mm	84 (37.50)
6.1-9 mm	29 (13)
9.1 and more	21 (9.8)
Type of treatment	
Bypass, trapping	2 (0.88)
Clipping	215 (96.02)
Wrapping	7 (3.1)

There was no mortality in the study population. We encountered complications in 6 patients. The complications and the location of the aneurysms are shown in Table 2.

The mRS was used for assessing the functional outcome of the patients at discharge. The mRS at admission in both the groups was same and was not statistically significant. The mean mRS at discharge in patients more than 75 years was  $1.07 \pm 0.37$  and  $1.03 \pm 0.23$  in patients <75 years. This difference was not statistically significant with  $P = 0.495$ . In patients more than 75 years, we compared the admission mRS and discharge mRS, and it was not statistically significant with  $P = 0.326$ . In patients <75 years, the mRS at admission and discharge was statistically significant with  $P = 0.034$ . There was no statistically significant difference in outcome in male sex. In female sex, the mRS at admission and discharge was statistically significant with  $P = 0.032$ .

## Discussion

There has been an increase in the detection and treatment of UCA's in Japan due to the advances in medical technology and increasing quality of health care. According to the WHO, data published in 2015 life expectancy in Japan for males is 80.5, females is 86.8, and total life expectancy is 83.7, which gives Japan a world life expectancy ranking of 1. This also contributes to the increasing number of patients who are diagnosed with the UCA's. The annual rupture rate of UCA in Japan is 0.95%/year by UCAS Japan,<sup>[3]</sup> and 3 times easier to rupture than Western countries due to PHASES score.<sup>[8]</sup> Age more than 80 is by itself an independent risk factor<sup>[9]</sup> for rupture and the prognosis of the patients with ruptured aneurysms is poor when compared to patients with UCA.<sup>[7]</sup> In this study, we analyzed the outcomes following surgical clipping (SC) in two groups of patients in the same center, operated by a single surgeon. This is essential in the decision-making process of elderly patients with UCA's, as they have a host of comorbid factors and it is considered a risk for performing any major surgery.

In UCA patients, in general, as per the International Subarachnoid Aneurysm Trial (ISAT) study, endovascular coiling (EC) has been associated with lower rates of

complications, mortality and morbidity rate than SC, with overall 30-day morbidity and mortality rates of 1.8%–13.7%, respectively, in patients who underwent SC and 2.0%–9.3%, respectively, in patients receiving EC.<sup>[9]</sup> According to the Japan Standard Stroke Registry Study, the poor outcome rates according to the ISAT criteria were 18.3%–24.2% in the SC and EC groups, respectively. These rates were superior to the ISAT data (36.4% for SC and 25.4% for EC).<sup>[10]</sup>

There have been only few studies which have examined the outcomes following clipping and coiling in elderly patients. The ISAT subgroup analysis involved 278 elderly patients with subarachnoid hemorrhage, and of them, 39.9% treated with EC were dependent or dead at 1 year when compared to 43.9% in the surgical group.<sup>[5]</sup> This study also demonstrated that the outcome after surgery for middle cerebral artery aneurysm was better than EC, but for internal carotid artery and posterior communicating artery aneurysms, EC was superior to SC. Hence, there was an overall benefit of EC in this subgroup analysis. The United States National Inpatient Sample Study on UCA's concluded that older patients had significantly less morbidity and mortality when treated with EC than SC.<sup>[4]</sup>

It is very important to note that in our study, there was no mortality in both the groups following SC and there was no significant difference in the outcomes between the groups after surgery.

In a long-term follow-up of unruptured intracranial aneurysms repaired in California, there was no survival benefit between EC and SC.<sup>[11]</sup> In a study of UCA's in New York state, coiling produced good outcome when compared to clipping but did not change the overall patient outcome.<sup>[12]</sup> This study also emphasized the need for centralization of the care for better outcomes.<sup>[12]</sup> In a study by McDonald *et al.*<sup>[13]</sup> Where a commercial database was used to assess the comparative effectiveness of EC and SC, there was no survival benefit from either treatment during the initial hospitalization, although there was an association between clipping and an unfavorable discharge.

The limitation of the study was the retrospective nature of the analysis. Our study included all the patients who underwent SC and there was no significant difference in the outcomes as age progresses.

## Conclusions

The future of the Japanese healthcare system will revolve around caring for an aged population to include the high cost of treating chronic illness and adapting new systems to fill the gap caused by societal changes. Based on our study, we conclude that SC can be considered as a safe option for UCA's in the aging population.

**Table 2: Complications following aneurysms**

Complication	Location	Age	mRS admission	mRS discharge
Hydrocephalus	Acomm	70	1	2
Visual deficit-inferior quadrant	IC-oph	60	1	3
Transient weakness	IC-PC	72	1	2
Transient III nerve palsy	BA-top	53	1	2
Visual loss	IC-oph	58	1	3
Weakness	BA top	78	1	3

mRS – Modified Rankin score

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## Conflicts of interest

There are no conflicts of interest.

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