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# Clinical Outcomes of Clipping and Coiling in Elderly Patients with Unruptured Cerebral Aneurysms: a National Cohort Study in Korea

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## ABSTRACT


**Background:** We aimed to analyze outcomes of clipping and coiling in treating unruptured intracranial aneurysms (UIAs) in elderly patients and to identify the age at which perioperative risk increases based on national cohort data in South Korea.

**Methods:** The incidence of perioperative intracranial hemorrhage (ICRH), perioperative cerebral infarction (CI), mortality, and moderate to severe disability data of the patients who underwent coiling or clipping for UIAs were retrieved. Estimated breakpoint (EBP) was calculated to identify the age at which the risk of treatment increases.

**Results:** A total of 38,207 patients were treated for UIAs. Among these, 22,093 (57.8%) patients underwent coiling and 16,114 (42.2%) patients underwent clipping. The incidence of ICRH, requiring a secondary operation, within 3 months in patients  $\geq 65$  years that underwent coiling and clipping was 1.13% and 4.81%, respectively, and that of both groups assessed were significantly higher in patients  $\geq 75$  years (coiling,  $P = 0.013$ , relative risk (RR) 1.81; clipping,  $P = 0.015$ ) than younger patients. The incidence of CI within 3 months in patients aged  $\geq 65$  was 13.90% and 9.19% in the coiling and clipping groups, respectively. The incidence of CI after coiling in patients aged  $\geq 75$  years ( $P < 0.001$ , RR 1.96) and after clipping in patients aged  $\geq 70$  years ( $P < 0.001$ , RR 1.76) was significantly higher than that in younger patients. The mortality rates within 1 year in patients with perioperative ICRH or CI were 2.41% and 3.39% for coiling and clipping groups, respectively, in patients  $\geq 65$ . These rates increased significantly at age 70 in the coiling group and at age 75 for the clipping group ( $P = 0.012$  and  $P < 0.001$ , respectively).

**Conclusion:** The risk of treatment increases with age, and this risk increases dramatically in patients aged  $\geq 70$  years. Therefore, the treatment decisions in patients aged  $\geq 70$  years should be made with utmost care.


**Keywords:** Cerebral Infarction; Intracranial Aneurysm; Intracranial Hemorrhages

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#### Disclosure

The authors have no potential conflicts of interest to disclose.

#### Author Contributions

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## INTRODUCTION

Intracranial aneurysms (IAs), which may lead to subarachnoid hemorrhage (SAH), are estimated to affect approximately 2% of the population worldwide.<sup>1-3</sup> According to a report published by United Nations, the world's population is growing older, and the number of individuals  $\geq 65$  years is snowballing.<sup>4</sup> In Japan, 23% of the total population was aged  $\geq 65$  years in 2019. It has been estimated that, by 2030, one in every three people will be  $\geq 65$  years, and one in five people will be  $\geq 75$  years. The increased elderly population is likely to play a major role in the increased prevalence of unruptured IAs (UIAs).<sup>1,5,6</sup> Moreover, the widespread availability of non-invasive imaging has further increased the detection of UIAs.<sup>6,7</sup> The management of UIAs in elderly patients is controversial because the treatment risk in patients with UIAs increases with advanced age and the presence of medical comorbidities.<sup>1</sup> Elderly patients are particularly prone to postoperative complications due to comorbidities, high anesthetic risk, and slow recovery rates. However, the development of newer endovascular devices and increased surgical experience have reduced procedure-related risks associated with UIA treatment. Consequently, the age of treatment in elderly patients has also changed.

Several studies have assessed the treatment of UIA in elderly patients.<sup>8-18</sup> However, only a few studies have compared the results of treatment by subdividing the age until the late old age, and a small number of studies have reported the cut-off point of age at which the perioperative risk of clipping and coiling increases. Therefore, we conducted a nationwide cohort study using Korea's National Health Insurance Service (NHIS) data that contains age-specific UIA clipping and coiling outcomes in early and late elderly patients to identify the age at which the perioperative risk of treatment increases.

## MATERIALS AND METHODS

### Data source

We conducted a retrospective cohort study using the National Health Claim Database, which was availed to us by the NHIS to investigate outcomes in patients who underwent clipping or coiling for UIA between 2004 to 2016. The NHIS is a nationwide universal insurance system in Korea responsible for the nation's health care and medical bills. The database consists of hospital records for 98% of the Korean population. Further, the NHIS operates a Severe Disease Registration System for which strict diagnostic criteria must be met for registration that supports patient's medical expenses. Accordingly, the NHIS database, which covers a single-ethnicity population of 50 million people, is well suited for this epidemiological study. We extracted data exclusively from tertiary referral general hospitals, general hospitals, and semi-hospitals to increase confidence in the medical data. Data from other medical institutions that were not clear were excluded.

### Study population and cohort design

Using the International Classification of Diseases, 10th Revision (ICD-10) diagnostic codes, we collected data from patients with UIAs. We identified patients with UIA throughout the assessment period using I67.1 ICD code. Patients diagnosed with UIA were classified based on whether they underwent clipping or coiling. Clipping was specified using Korean Classification of Diseases procedure codes S4641 and S4642, and coiling was indicated using codes M1661 and M1662. Patients who had been diagnosed with brain trauma (e.g., S06-S09), brain tumor (e.g., C41.0, C75.2, C71, C79.3, D32.9-D333, D35.3, or D44.4), stroke

(e.g., I60–I63), or experienced morbidity during the preceding 3-year period at any clinic or hospital were excluded to accurately identify and classify cases with new complications such as intracranial hemorrhage (ICRH) or cerebral infarction (CI) that occurred after clipping or coiling. To ensure a 5-year washout period (2004–2008) within the total period (2004–2016), we used data starting from 2009. Thus, the total period of assessment for the reconstructed cohort was 8 years (2009–2016). We assessed changes in the distribution according to the age of the patients and in treatment results over time by aggregating patients in the outcomes cohort into two time blocks. Each group that underwent clipping or coiling was reclassified into group 1, which included patients treated between 2009 and 2012, and group 2, which included patients treated between 2013 and 2016. These time blocks were established because the characteristics of patients do not change noticeably on a yearly basis and the assumption that outcomes might change due to changes in experience and technology.

### Outcomes and study variables

According to operation year, both the clipping group and the coiling group were reclassified into group 1 and group 2. Patients aged < 60 were classified into individuals < 50 years old and those 50–59 years old. Patients  $\geq 60$  were classified within age groups defined using 5-year intervals. We defined “elderly” as the age of 65 years old or older, which was further separated into “early elderly” as those between 65 through 74 years old and “late elderly” as those over 75 years old.<sup>19–23</sup>

To analyze perioperative complication incidence, the ICRH (e.g., I60–I62) such as intracerebral hemorrhage (ICH), SAH, subdural hematoma (SDH) or epidural hematoma (EDH), and CI (e.g., I63) within the 3-month period that followed surgery was analyzed according to treatment group and age. Regarding postoperative ICRH, only cases that underwent additional surgery for ICRH that involved hematoma drainage, craniotomy, or craniectomy, and those defined using the following codes: N0321–N0324, S4621, S4622, and N0333, were included in order to exclude clinically insignificant bleeding. To confirm the results one year postoperatively in these patients with perioperative ICRH or CI, the mortality rate and the moderate to severe disability rates during the 1-year period following surgery were analyzed. In Korea, patients with moderate to severe disabilities with a modified Rankin Scale (mRS) of  $\geq 3$  are assigned a disability rating. If patients have a disability rating, they receive significant financial support. Therefore, most patients with disabilities have a disability rating, and, therefore, accurate data regarding disability could be confirmed.

### Data analysis

Data manipulation and extraction were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA). All statistical analyses were performed by a biostatistician from the Medical Research Collaborating Center in Seoul National University Bundang Hospital using R statistical software, version 2.8.1. Based on the 2009 demographic structure, the population distribution by age and gender from 2009 to 2016 was standardized to correct for demographic bias of the cohort relative to the structure of the national population. To compare each group, either a chi-square test or Fisher's exact test was used, and values of  $P < 0.05$  were considered significant. The estimated breakpoint (EBP) was calculated using segmented regression analysis to identify the inflection point of the incidence rate according to age. In cases with insignificant EBP values, we noted the ages at which the incidence of complications was significantly higher than those in the younger age group. Only ages that were  $\geq$  EBP were included to identify the age at which the incidence of complications rapidly increases.

### Ethics statement

This study was approved by Institutional Review Board at Seoul National University Bundang Hospital (X-1810/498-903), which waived the requirement for informed consent due to the retrospective nature of this study.

## RESULTS

Throughout an eight-year period, a total of 38,207 patients were treated for UIA. Among these, 22,093 (57.8%) patients underwent coiling and 16,114 (42.2%) patients underwent clipping procedures. Among patients who underwent coiling, the proportion of patients over 70 years of age increased from 19.2% in group 1 to 21.3% in group 2. The proportion of patients over 70 years of age who underwent clipping increased from 12.2% to 15.3%. The proportion of patients over 75 years of age increased from 7.3% to 9.5% in patients who underwent coiling and increased from 3.3% to 4.7% in patients who underwent clipping (**Table 1**).

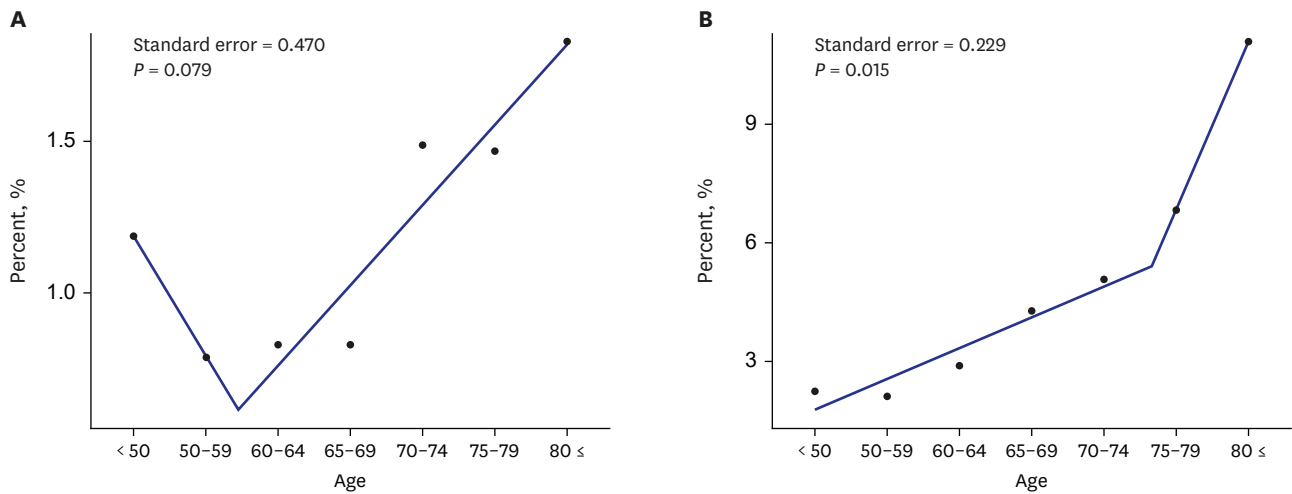
### Postoperative ICRH

The incidence of ICRH, requiring a secondary operation, within 3-month patients who underwent coiling and clipping within group 2 was 0.99% and 2.99%, respectively. Among these, the ratio of SAH or ICH-related ICRH was 95.7% in the coiling group and 62.9% in the clipping group. On the other hand, only SDH or EDH occurred in 4.3% and 37.1% of patients, respectively. These values were significantly greater after clipping for patients of age groups except those aged  $\geq 80$  years. In group 2, the incidence of ICRH was 1.13% and 4.81% in patients aged  $\geq 65$  years that underwent coiling and in those that underwent clipping, respectively. The incidence of ICRH was 1.65% and 7.44%, respectively, in those aged  $\geq 75$  years (**Table 2**). The EBP of the incidence of ICRH in patients that underwent clipping was 75 years, and the incidence of ICRH significantly increased in patients aged  $\geq 75$  years ( $P = 0.015$ , standard error [SE] 0.229). Similarly, the EBP of the incidence of SAH or ICH-related ICRH in patients who underwent clipping was 75 years ( $P = 0.028$ , standard error (SE) 0.305). The incidence of SDH or EDH without SAH or ICH after clipping was significantly higher in patients aged  $\geq 75$  years than that in younger patients ( $P < 0.001$ , relative risk (RR) 3.56, 95% CI 2.18–5.54) despite non-significant EBP. Even though the EBP was determined to be non-significant ( $P = 0.079$ , SE 0.470) in the coiling group, the incidence of ICRH in patients aged  $\geq 75$  years was significantly higher than that in younger patients ( $P = 0.013$ , RR 1.81, 95% CI 1.12–2.89). In addition, the incidence of SAH or ICH in patients aged  $\geq 75$  years was also significantly higher than that in younger patients ( $P = 0.039$ , RR 1.57, 95% CI 1.00–2.36) (**Fig. 1A and B**). On comparing groups 1 and 2, we found no significant difference in the incidence of ICRH in the coiling group and the clipping group (**Table 3**).

**Table 1.** Total number of patients underwent coiling and clipping for unruptured intracranial aneurysms

Age	Coiling		Clipping	
	Group 1 (%)	Group 2 (%)	Group 1 (%)	Group 2 (%)
Total	8,107	13,986	7,023	9,091
< 50	1,477 (18.22)	2,457 (17.57)	1,277 (18.18)	1,349 (14.84)
50–60	2,663 (32.85)	4,394 (31.42)	2,535 (36.10)	3,247 (35.72)
60–64	1,274 (15.71)	2,287 (16.35)	1,273 (18.13)	1,753 (19.28)
65–69	1,133 (13.98)	1,869 (13.36)	1,081 (15.39)	1,355 (14.90)
70–74	972 (11.99)	1,649 (11.79)	623 (8.87)	957 (10.53)
75–79	461 (5.69)	964 (6.89)	197 (2.81)	359 (3.95)
80 $\leq$	127 (1.57)	366 (2.62)	37 (0.53)	71 (0.78)

Unruptured Cerebral Aneurysms in Elderly Patients



**Fig. 1.** The EBP of the incidence of ICRH in patients that underwent clipping was 75 years, and the incidence of ICRH significantly increased in patients aged  $\geq 75$  years ( $P = 0.015$ ; **B**). However, there was no significant EBP determined for patients of the coiling group ( $P = 0.079$ ; **A**). EBP = estimated breakpoint, ICRH = intracranial hemorrhage.

**Table 2.** The comparison of treatment outcomes for unruptured intracranial between coiling and clipping

Outcomes	Age	Group 1			Group 2		
		Coiling (%)	Clipping (%)	P value	Coiling (%)	Clipping (%)	P value
ICRH	Total	96 (1.18)	231 (3.29)	< 0.001	138 (0.99)	272 (2.99)	< 0.001
	< 50	16 (1.08)	30 (2.35)	0.015	31 (1.26)	29 (2.15)	0.049
	50-59	28 (1.05)	64 (2.52)	< 0.001	28 (0.64)	58 (1.79)	< 0.001
	60-64	13 (1.02)	34 (2.67)	< 0.001	24 (1.05)	53 (3.02)	< 0.001
	65-69	14 (1.24)	51 (4.72)	< 0.001	11 (0.59)	53 (3.91)	< 0.001
	70-74	17 (1.75)	34 (5.46)	< 0.001	22 (1.33)	47 (4.91)	< 0.001
	75-79	4 (0.87)	13 (6.60)	< 0.001	17 (1.76)	25 (6.96)	< 0.001
	80 $\leq$	4 (3.15)	5 (13.51)	0.028	5 (1.37)	7 (9.86)	0.060
CI	Total	957 (11.80)	557 (7.93)	< 0.001	1,406 (10.05)	628 (6.91)	0.108
	< 50	112 (7.58)	77 (6.03)	0.126	166 (6.76)	75 (5.56)	0.168
	50-59	249 (9.35)	169 (6.67)	< 0.001	339 (7.72)	173 (5.33)	< 0.001
	60-64	145 (11.38)	100 (7.86)	0.215	227 (9.93)	128 (7.30)	0.004
	65-69	165 (14.56)	109 (10.08)	0.002	218 (11.66)	101 (7.45)	< 0.001
	70-74	169 (17.39)	62 (9.95)	< 0.001	216 (13.10)	90 (9.40)	0.003
	75-79	81 (17.57)	32 (16.24)	0.764	163 (16.91)	52 (14.48)	0.328
	80 $\leq$	36 (28.35)	8 (21.62)	0.547	77 (21.04)	9 (12.68)	0.145
Mortality	Total	93 (1.15)	93 (1.32)	0.362	162 (1.16)	78 (0.86)	0.033
	< 50	7 (0.47)	7 (0.55)	0.996	9 (0.37)	2 (0.15)	0.347
	50-59	12 (0.45)	12 (0.47)	1.000	24 (0.55)	9 (0.28)	0.110
	60-64	6 (0.47)	9 (0.71)	0.113	12 (0.52)	7 (0.40)	0.730
	65-69	16 (1.41)	21 (1.94)	0.419	20 (1.07)	13 (0.96)	0.896
	70-74	25 (2.57)	22 (3.53)	0.340	38 (2.30)	18 (1.88)	0.519
	75-79	17 (3.69)	13 (6.60)	0.151	37 (3.84)	21 (5.85)	0.151
	80 $\leq$	10 (7.87)	9 (24.32)	0.016	22 (6.01)	8 (11.27)	0.123
Disability (mRS $\geq 3$ )	Total	48 (0.59)	50 (0.71)	0.415	53 (0.38)	49 (0.54)	0.091
	< 50	3 (0.20)	4 (0.31)	0.711	6 (0.24)	9 (0.67)	0.085
	50-59	22 (0.83)	18 (0.71)	0.025	16 (0.36)	17 (0.52)	0.382
	60-64	8 (0.63)	3 (0.24)	0.756	5 (0.22)	12 (0.68)	0.043
	65-69	6 (0.53)	14 (1.30)	0.093	8 (0.43)	5 (0.37)	1.000
	70-74	7 (0.72)	9 (1.44)	0.247	7 (0.42)	6 (0.63)	0.569
	75-79	2 (0.43)	2 (1.02)	0.587	8 (0.83)	0 (0.00)	0.117
	80 $\leq$	0 (0.00)	0 (0.00)	1.000	3 (0.82)	0 (0.00)	1.000

CI = cerebral infarction, ICRH = intracranial hemorrhage, mRS = modified Rankin Scale.

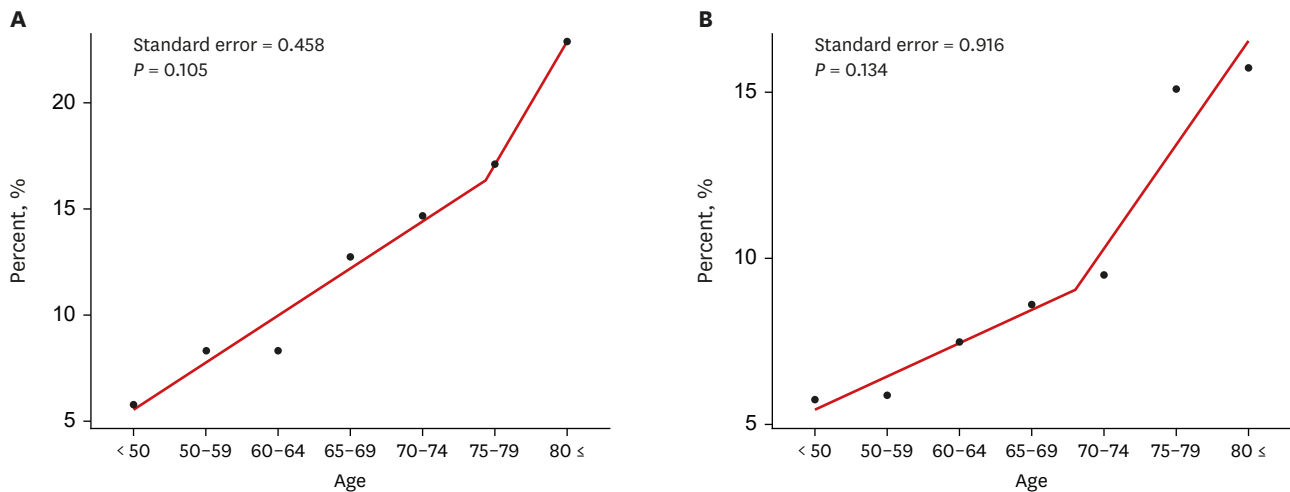
**Table 3.** The comparison of treatment outcomes for unruptured intracranial between group 1 and group 2

Outcomes	Age	Coiling			Clipping		
		Group 1 (%)	Group 2 (%)	<i>P</i> value	Group 1 (%)	Group 2 (%)	<i>P</i> value
ICRH	Total	96 (1.18)	138 (0.99)	0.189	231 (3.29)	272 (2.99)	0.303
	< 50	16 (1.08)	31 (1.26)	0.728	30 (2.35)	29 (2.15)	0.831
	50–59	28 (1.05)	28 (0.64)	0.078	64 (2.52)	58 (1.79)	0.065
	60–64	13 (1.02)	24 (1.05)	0.135	34 (2.67)	53 (3.02)	0.644
	65–69	14 (1.24)	11 (0.59)	0.092	51 (4.72)	53 (3.91)	0.380
	70–74	17 (1.75)	22 (1.33)	0.496	34 (5.46)	47 (4.91)	0.653
	75–79	4 (0.87)	17 (1.76)	0.281	13 (6.60)	25 (6.96)	1.000
	80 ≤	4 (3.15)	5 (1.37)	0.214	5 (13.51)	7 (9.86)	0.748
CI	Total	957 (11.80)	1,406 (10.05)	< 0.001	557 (7.93)	628 (6.91)	0.015
	< 50	112 (7.58)	166 (6.76)	0.360	77 (6.03)	75 (5.56)	0.666
	50–59	249 (9.35)	339 (7.72)	0.018	169 (6.67)	173 (5.33)	0.037
	60–64	145 (11.38)	227 (9.93)	0.000	100 (7.86)	128 (7.30)	0.617
	65–69	165 (14.56)	218 (11.66)	0.024	109 (10.08)	101 (7.45)	0.026
	70–74	169 (17.39)	216 (13.10)	0.003	62 (9.95)	90 (9.40)	0.695
	75–79	81 (17.57)	163 (16.91)	0.814	32 (16.24)	52 (14.48)	0.667
	80 ≤	36 (28.35)	77 (21.04)	0.117	8 (21.62)	9 (12.68)	0.351
Mortality	Total	93 (1.15)	162 (1.16)	0.993	93 (1.32)	78 (0.86)	0.005
	< 50	7 (0.47)	9 (0.37)	0.799	7 (0.55)	2 (0.15)	0.100
	50–59	12 (0.45)	24 (0.55)	0.708	12 (0.47)	9 (0.28)	0.312
	60–64	6 (0.47)	12 (0.52)	0.283	9 (0.71)	7 (0.40)	0.369
	65–69	16 (1.41)	20 (1.07)	0.508	21 (1.94)	13 (0.96)	0.060
	70–74	25 (2.57)	38 (2.30)	0.764	22 (3.53)	18 (1.88)	0.053
	75–79	17 (3.69)	37 (3.84)	1.000	13 (6.60)	21 (5.85)	0.867
	80 ≤	10 (7.87)	22 (6.01)	0.599	9 (24.32)	8 (11.27)	0.136
Disability (mRS ≥ 3)	Total	48 (0.59)	53 (0.38)	0.031	50 (0.71)	49 (0.54)	0.197
	< 50	3 (0.20)	6 (0.24)	1.000	4 (0.31)	9 (0.67)	0.311
	50–59	22 (0.83)	16 (0.36)	0.016	18 (0.71)	17 (0.52)	0.462
	60–64	8 (0.63)	5 (0.22)	0.518	3 (0.24)	12 (0.68)	0.141
	65–69	6 (0.53)	8 (0.43)	0.905	14 (1.30)	5 (0.37)	0.019
	70–74	7 (0.72)	7 (0.42)	0.468	9 (1.44)	6 (0.63)	0.158
	75–79	2 (0.43)	8 (0.83)	0.515	2 (1.02)	0 (0.00)	0.125
	80 ≤	0 (0.00)	3 (0.82)	0.573	0 (0.00)	0 (0.00)	1.000

CI = cerebral infarction, ICRH = intracranial hemorrhage, mRS = modified Rankin Scale.

### Postoperative CI

For patients in group 1, the incidence of CI during the post-treatment 3-month period was significantly higher among patients that underwent coiling (11.8%) than clipping (7.9%) ( $P < 0.01$ ). In group 2, however, patients that underwent coiling (10.1%) experienced CI more frequently than those who underwent clipping (6.91%); however, the difference was not significant ( $P = 0.110$ ). In group 2, the incidence of CI in those aged  $\geq 65$  years was 13.90% and 9.19% in the coiling group and clipping group, respectively. These values were higher than the 8.01% and 5.92% incidence rates determined for those aged  $< 65$  years in the coiling group and clipping group, respectively. The incidence of CI in patients aged  $\geq 75$  years in group 2 of the coiling group and clipping group was 18.05% and 14.19%, respectively. In most patients that were less than 75 years of age, coiling was associated with an increased incidence of CI when compared with clipping. However, in patients aged  $\geq 75$  years, the incidence of CI in patients that underwent clipping increased and did not significantly differ from those that underwent coiling (Table 2). The EBP of the incidence of CI was 75 years of age ( $P = 0.105$ , SE 0.458) in patients who underwent coiling and 70 years of age ( $P = 0.134$ , SE 0.916) in those who underwent clipping. However, neither value was statistically significant (Fig. 2A and B). The incidence of CI after coiling in patients aged  $\geq 75$  years ( $P < 0.001$ , RR 1.96, 95% CI 1.72–2.23) and after clipping in patients aged  $\geq 70$  years ( $P < 0.001$ , RR 1.76, 95% CI 1.47–2.10) was significantly higher than that in younger patients. The incidence of CI after



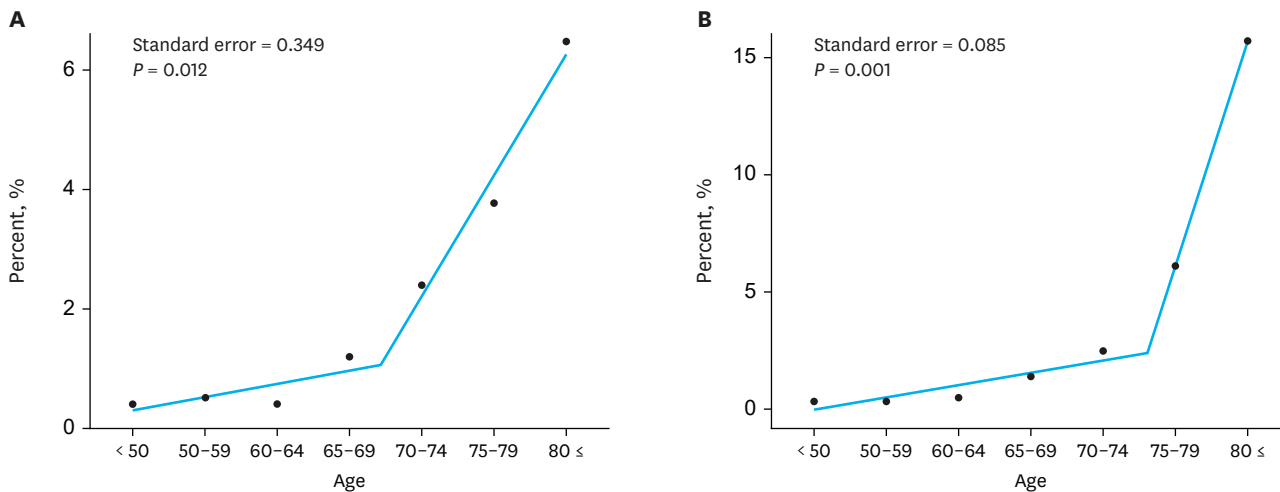
**Fig. 2.** The estimated breakpoint of cerebral infarction incidence was determined to be 75 years old ( $P = 0.105$ ; **A**) in patients who underwent coiling and 70 years old ( $P = 0.134$ ; **B**) in patients who underwent clipping; however, the value was not statistically significant.

both coiling and clipping was significantly reduced in group 2 compared to group 1 (coiling,  $P < 0.001$ ; clipping,  $P = 0.010$ ). Moreover, the incidence of CI tended to be lower in group 2 compared to group 1 among patients of all ages (Table 3).

### Postoperative mortality and disability

Mortality within the 1-year period that followed treatment in patients with perioperative ICRH or CI did not show a significant difference between the coiling group (1.15%) and clipping group (1.32%) in group 1. However, clipping (0.86%) was determined to be associated with significantly lower mortality than coiling (1.16%) in group 2. The mortality rates for coiling groups and clipping groups in patients aged  $\geq 65$  were 2.41% and 3.39%, respectively. Mortality rates in patients aged 75–79 years who underwent coiling and clipping were 3.84% and 5.85%, respectively ( $P = 0.151$ ). For those aged  $\geq 80$ , mortality rates associated with coiling and clipping were 6.01% and 11.27%, respectively ( $P = 0.123$ ). Although not statistically significant, the mortality rates tended to be higher in patients aged  $< 75$  years in the coiling group than those in the clipping group. In contrast, the mortality rates tended to be higher in patients aged  $\geq 75$  years in the clipping group than those in the coiling group (Table 2). No significant difference was observed in mortality among patients that underwent coiling between group 1 and group 2. However, mortality after clipping was significantly reduced ( $P = 0.010$ ) (Table 3). EBP analysis revealed that mortality increased in patients that underwent coiling in patients aged  $\geq 70$  years ( $P = 0.012$ , SE 0.349) and in patients that underwent clipping aged 75 years ( $P < 0.01$ , SE 0.085) (Fig. 3A and B).

The rate of disability among patients with perioperative ICRH or CI at a level of mRS 3 or greater in group 2 was 0.38% for patients that underwent coiling and 0.54% for patients that underwent clipping, and no significant difference was observed between the two groups ( $P = 0.091$ ). In patients aged  $\geq 65$  years, disability rates were 0.54% and 0.40% for the coiling group and the clipping group, respectively (Table 2). Additionally, when rates of disability in group 1 and group 2 were examined individually, the disability rate was significantly lower in group 2 for patients that underwent coiling ( $P = 0.031$ ), while disability tended to decrease in patients that underwent clipping. However, the difference was not significant ( $P = 0.200$ ) (Table 3).



**Fig. 3.** Estimated breakpoint analysis for disability revealed elevated values in patients who underwent coiling among those aged 70 years or older ( $P = 0.012$ ; **A**). The same type of analysis revealed elevated values in patients who underwent clipping among those aged 75 years or older ( $P < 0.001$ ; **B**).

## DISCUSSION

Several papers have reported outcomes of clipping and coiling in elderly patients with UIA.<sup>8-18,24</sup> However, the ages of elderly individuals in these studies have not been consistent, and large-scale studies assessing outcomes stratified by age are rare.<sup>8,11,16</sup> This study assessed treatment outcomes stratified according to population age, including the late elderly, and revealed trends associated with outcomes of UIA over time. Most importantly, EBP values were calculated to identify the appropriate age at which the risk of treatment for UIA rapidly increases.

Most studies to date have classified those individuals aged  $\geq 65$  years as elderly patients. In previous studies, the incidence of ICRH in patients aged  $\geq 65$  years was reported to be 0.3–3.9% among patients who underwent coiling and 0.2–5.1% among patients who underwent clipping.<sup>8,12,14,17</sup> Although the incidence of ICRH was elevated in patients aged  $\geq 65$  years compared with patients aged  $< 65$  years, the difference was not statistically significant.<sup>8</sup> We identified 75 years of age in the coiling and clipping groups as the age at which ICRH incidence increased significantly. The incidence of ICRH was significantly higher than that noted in younger individuals above the age of 75.

Similar to the results of our study (coiling, 13.90%; clipping, 9.19%), a previous study determined that the incidence of CI in elderly patients aged  $\geq 65$  years was 2.9–8.9% among patients who underwent coiling and 2.2–10.3% among patients who underwent clipping. Differences between the incidence of CI in the two groups were conflicting.<sup>8,12-14,17,18</sup> However, it was reported that CI occurred significantly more frequently in older individuals ( $\geq 65$ ) than those who were younger ( $< 65$ ).<sup>8,17,18</sup> Despite the non-significant EBP in our study, the incidence of CI in patients whose age was above the EBP age (age  $\geq 75$  years in coiling group and age  $\geq 70$  years in clipping group) was significantly higher than that in patients in younger age groups. The relatively high incidence of CI observed in this study was likely because the study included both patients with major infarction and those with minor infarction that exhibited mild symptoms, as evident from the low mortality rate and disability (mRS  $\geq 3$ ) rate compared to the high incidence of CI.



Previous studies have shown that mortality rates within one year of treatment in patients aged  $\geq 65$  were 7.6–10% for those who underwent coiling and 5.9% for patients who underwent clipping.<sup>10,13</sup> Mortality rates within 30 days were reported to be 0–1.9% for patients who underwent coiling and 0.2–3.2% for patients who underwent clipping.<sup>8-10,12,17,18</sup> For those over 80, the mortality rates were 2.4% and 6.3–21.4% for coiling and clipping, respectively.<sup>8,15</sup> There was no significant difference between prior and current findings. However, as a key finding of this study, mortality rates were found to increase dramatically and significantly after the age of 70 in patients who underwent coiling and after the age of 75 in patients who underwent clipping.

Post-treatment neurological deficits in elderly patients aged  $\geq 65$  years who underwent coiling were 3.0–5.6% and 2.8–17.3% in patients who underwent clipping. The values rose to 9.8% and 33.5% in patients aged  $\geq 80$  years who underwent coiling and clipping, respectively. When rates of deficit in older individuals were compared to individuals aged  $< 65$  years, it was demonstrated that rates in patients of advanced age were significantly elevated.<sup>8,11,13,15,17</sup> We analyzed the incidence rate of moderate to severe disability (mRS  $\geq 3$ ). However, it is likely that our statistical analysis was limited by the low number of treatments performed in very old aged individuals relative to incidence. Further, as evident from our study results, mortality is high compared to very low cases of disability at age  $\geq 75$  years. Accordingly, it is assumed that the disability rate at age  $\geq 75$  could have been underestimated because moderate to severe disability can lead to mortality when ICRH or CI occurs at age  $\geq 75$ .

A nationwide study conducted during 2000–2010 in the United States of America found that the number of elderly patients aged 65–74 years who underwent coiling or clipping for UIA had increased by 47.4%.<sup>9</sup> Furthermore, a comparison of a group that received treatment between 2001 and 2003 with the group that received treatment between 2008 and 2010 revealed that both 30-day mortality and complication rates decreased over time, with the same results also being observed in elderly patients.<sup>9</sup> In our study, when comparing group 1 and group 2, the number of patients over 70 years of age who underwent coiling or clipping treatment for UIA had increased by 91.0% and 61.5%, respectively. Similar to the results from previous studies, ICRH, CI, and mortality rates appeared to decrease among patients in group 2 than those in group 1. Notably, the incidence of postoperative CI after coiling and clipping, the mortality rate after clipping, and disability rate after coiling were significantly decreased.

In summary, the likelihood of experiencing complications including ICRH, CI, mortality, and disability increases significantly with age. Furthermore, ICRH, CI, and mortality rates begin to increase rapidly at 70 or 75 years. Based on these findings, when deciding the treatment of elderly patients aged  $\geq 70$  years with UIA, the risk of treatment should be carefully compared with the spontaneous rupture rate. Moreover, because the risk of treatment shows a decreasing trend over time, which is likely due to advancements in the performance of endovascular techniques, general improvements in postprocedural care, and increased past-year clipping and coiling volumes, it is estimated that in the future, the age range eligible for UIA will have to be further increased.<sup>25,26</sup>

A limitation of this study is that the NHIS data did not contain information regarding the location and size of UIA or the use of stent or antiplatelet drugs, which are associated with the incidence of ICRH and CI. Moreover, the nature of the NHIS data meant that if the underlying diseases were to be included as variables, the number of study subjects, especially the number of late elderly patients, would significantly decrease. Therefore, a population

analysis was performed to sufficiently assess late elderly patients, for which variables other than age and sex were excluded. However, the data used in the study comprised 98% of the total population, and, therefore, it may be considered valuable in evaluating the treatment outcomes in practice. Another limitation was the lack of information regarding the accuracy of measurements such as mRS for neurological disorders that occurred during the long-term patient follow-up. Although moderate to severe sequelae (mRS  $\geq$  3) were identified with mortality and disability levels, no information regarding the occurrence of mild level neurologic deficit was available. In addition, although most patients with severe disabilities are enrolled in the disability registration system, there is a possibility that the incidence of disability is slightly underestimated because a small number of patients are occasionally omitted. Therefore, a large-scale multicenter prospective study will be necessary to analyze the natural course of UIA and treatment outcomes in elderly patients.

In conclusion, the risk of treatment in elderly patients diagnosed with UIA increases with age, and this also increases dramatically in patients aged  $\geq$  70 years. Therefore, the eligibility for treatment among patients aged  $\geq$  70 years should be determined carefully after considering the following factors: the natural course of UIA, the patient's general condition, preoperative comorbidities, and the patient's life expectancy. In addition, more attention and focus are required throughout the surgical processes, including administration of anesthesia and postoperative management.

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