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Treatment Strategy of Unruptured Intracranial Aneurysms in Octogenarian Patients: A Single-Institution Experience

Byul Hee YOON[1], Yung Ki PARK[1], Jong Hyun KIM[2], Yong Seok PARK[3], Wonhyoung PARK[4], Jung Cheol PARK[4], Jae Sung AHN[4], Joonho BYUN[2]

[1]Uijeongbu Eulji Medical Center, Eulji University School of Medicine, Department of Neurosurgery, Uijeongbu, Korea
[2]Korea University Guro Hospital, Korea University College of Medicine, Department of Neurosurgery, Seoul, Korea
[3]Asan Medical Center, University of Ulsan College of Medicine, Department of Anesthesiology, Seoul, Korea
[4]Asan Medical Center, University of Ulsan College of Medicine, Department of Neurosurgery, Seoul, Korea

Corresponding author: Joonho BYUN ✉ drjunho2@gmail.com

ABSTRACT

AIM: To share our clinical insights into octogenarian patients with unruptured intracranial aneurysms (UIAs) and evaluate the treatment strategies for this demographic.

MATERIAL and METHODS: A retrospective analysis was conducted on data from 134 patients with a follow-up exceeding 6 months, all enrolled in this study. We assessed the incidence rates (IRs) of aneurysm growth and rupture, along with potential predictors of aneurysm growth.

RESULTS: Among the 134 patients, 99 (73.9%) underwent conservative management, 25 (18.7%) received coiling, and 10 (7.5%) underwent clipping. The mean age of the cohort was 81.8 years. The middle cerebral artery was the most common location for aneurysms. The mean aneurysm size was 4.9 mm, with sizes significantly larger in the treatment groups (coiling and clipping) compared to the observation group (4.4 mm in the observation group; 5.9 and 7.4 mm in the coiling and clipping groups, respectively). The proportion of aneurysms with a daughter sac was higher in the treatment groups compared to the observation group (6.1% vs. 44% [coiling] and 50% [clipping]). The IR of aneurysm growth was 5.9 per 100 person-years, and that of aneurysm rupture was 0.8 per 100 person-years. No factors were statistically significant for aneurysm growth.

CONCLUSION: Age alone, especially in individuals over 80 years old, may not be a contraindication for UIA treatment. We recommend considering treatment in octogenarians with high-risk aneurysm features, such as a large aneurysm and the presence of a daughter sac, as the complication rates are low.

KEYWORDS: Octogenarians, Unruptured aneurysms, Intracranial aneurysms, Treatment

ABBREVIATIONS: AcomA: Anterior communicating artery, **CT:** Computed tomography, **CTA:** Computed tomography angiography, **GOS:** Glasgow Outcome Scale, **IR:** Incidence rate, **MCA:** Middle cerebral artery, **MRA:** Magnetic resonance angiography, **MRI:** Magnetic resonance imaging, **PcomA:** Posterior communicating artery, **UIA:** Unruptured intracranial aneurysm

Byul Hee YOON : 0000-0002-4986-1173
Yung Ki PARK : 0000-0002-4925-5333
Jong Hyun KIM : 0000-0002-8300-9486
Yong Seok PARK : 0000-0002-3752-2211
Wonhyoung PARK : 0000-0002-9977-0595
Jung Cheol PARK : 0000-0001-6677-455X
Jae Sung AHN : 0000-0001-6134-6214
Joonho BYUN : 0000-0003-0687-3286

INTRODUCTION

The prevalence of unruptured intracranial aneurysms (UIAs) in the general population is 2% (13), and the annual rupture rate is reported to be 0.95% according to the Unruptured Cerebral Aneurysm Study of Japan (18). With an increase in life expectancy in South Korea and a rise in the use of brain imaging studies, such as computed tomography (CT) and magnetic resonance imaging (MRI), in clinical practice, healthy octogenarian patients with UIAs are becoming more common in outpatient clinics.

Despite suggested indications for UIA treatment, the question of imposing an age limitation on treatment remains contentious (7,15,17). The treatment guideline for UIAs from the Journal of the Korean Neurosurgical Society recommends intervention for patients expected to live over 10 years (15). However, decision-making for treatment in older patients, especially octogenarians, is intricate due to various medical and social considerations. Furthermore, the incidence of post-treatment complications is notably high in octogenarians. While our institute has primarily adopted a conservative approach for octogenarian patients, we do not categorize age alone as a contraindication to treatment. The rates of aneurysm rupture and growth serve as crucial factors in determining the appropriate course of action for patients aged over 80 years diagnosed with UIAs. Therefore, this study aimed to present our institutional experience with octogenarian patients having UIAs and to assess the treatment strategy for UIAs in this specific age group.

MATERIAL and METHODS

Patient Population

The study protocol and retrospective review of medical records received approval from the institutional review board of our institute (approval no. 2020-0466). A total of 754 patients aged over 80 years visited the neurosurgical clinic for UIA between 2000 and 2019 (Figure 1). Exclusions were made for patients diagnosed with UIA before the age of 80 years and those with fusiform aneurysms, petrous and cavernous internal carotid artery aneurysms, extradural aneurysm locations, subarachnoid hemorrhage, accompanying other vascular diseases (arteriovenous malformation or dural arteriovenous fistula), and brain neoplasms. Among them, 288 patients did not revisit the clinic. Consequently, only data from 134 patients with follow-up exceeding 6 months were included in the analysis of the incidence rates (IRs) of aneurysm growth and rupture, as well as the predictors of aneurysm growth.

In the treatment group, follow-up evaluations comprised physical examinations and assessments of functional outcomes at hospital discharge, and at 1, 3, 6, and 12 months post-treatment. The conservative management group underwent CT angiography (CTA) or magnetic resonance angiography (MRA) at 6 months post-initial imaging assessment and annually thereafter.

Aneurysm size was defined as the maximal aneurysmal dome size on CTA or MRA. To minimize measurement errors, each aneurysm's size was measured three times by three different board-certified neurosurgeons at diagnosis, and the mean value was recorded. Functional status was assessed using the Glasgow Outcome Scale (GOS) before and after treatment. Additionally, the PHASES score was analyzed for each group. The risk of aneurysm rupture in Korean people was assumed to be similar to that in Japanese people, assigning three points for geographical region. The PHASES risk scores were dichotomized into two levels based on rupture risk (high risk, ≥ 10; intermediate and low risk, < 10). Furthermore, aneurysm growth was determined through visual comparison between CTA and MRA (Figure 1).

Statistical Analysis

The follow-up period was defined as the interval between the dates of initial treatment and the last brain imaging (CTA or MRA) evaluation. Subgroup analysis was conducted using one-way analysis of variance and linear-by-linear association.

Potential predictors of aneurysm growth, including sex, aneurysm size, aneurysm location (anterior circulation, posterior communicating artery, and posterior circulation), presence of a daughter sac, and use of antiplatelet and anticoagulant drugs, were analyzed using Cox proportional hazard model regression.

IR was calculated as the number of cases divided by 100 person-years. The confidence interval of IR was calculated using the exact method for the Poisson mean. To identify risk factors for aneurysm growth, a univariate Cox proportional hazard model was utilized. The proportional hazard assumption was tested using Schoenfeld's test and was determined to be satisfied for all potential risk factors considered in the study. All analyses were performed using R 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

A total of 134 patients, with a follow-up duration of ≥ 6 months and brain imaging (CTA or MRA) evaluations, were included in the analysis of IRs and predictors. Compared to the overall population of 754 patients aged over 80 years, the enrolled 134 patients showed no significant differences in sex (χ^2= 0.578, df = 1, p=0.447) and age (p=0.976). In these patients, 99 (73.9%), 25 (18.1%), and 10 (7.5%) were categorized into the conservative management, coiling, and clipping groups, respectively. The mean age of the patients was 87 years, with the most common aneurysm location being the middle cerebral artery, followed by the posterior communicating artery, anterior communicating artery, and paraclinoid segment of the internal carotid artery.

The mean aneurysm size was 4.9 mm, significantly larger in the treatment (coiling and clipping) groups than in the observation group (4.4 mm in the observation group; 5.9 and 7.4 mm in the coiling and clipping groups, respectively). The proportion of aneurysms with a daughter sac was also higher in the treatment groups than in the observation group (6.1% vs. 44% [coiling group] and 50% [clipping group]). Significant differences in aneurysm size and the proportion of aneurysms

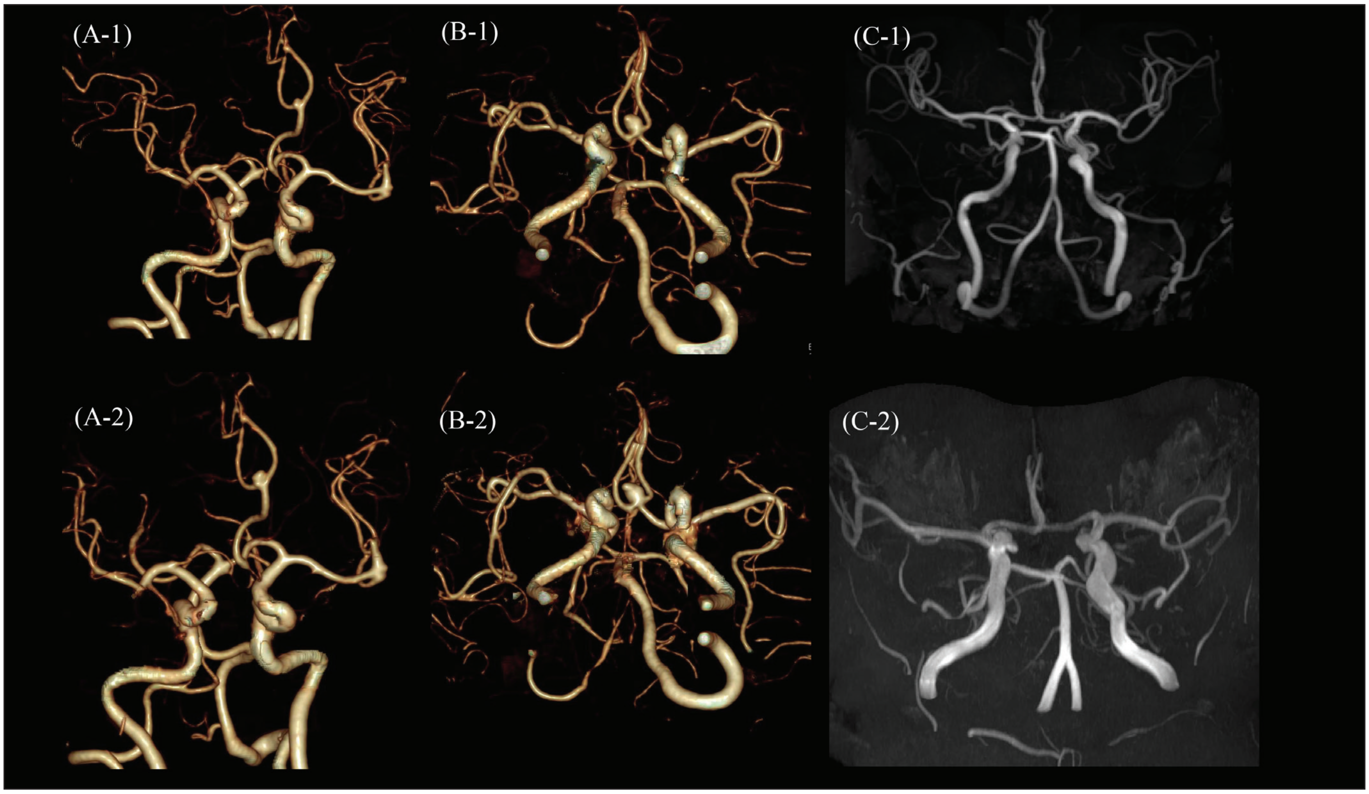

Figure 1: Three cases of aneurysm growth in octogenarian patients with unruptured intracranial aneurysm **(A-1, A-2)** Case of an 81-year-old female patient with a distal anterior cerebral artery (ACA) aneurysm in the azygos ACA. **(A-1)** Initial brain computed tomography angiography (CTA) showing a 2 mm aneurysm in the distal ACA. **(A-2)** Annual brain CTA image at the 2-year follow-up, revealing aneurysm growth (from 2 to 4 mm). The patient underwent clipping surgery. **(B-1, B-2)** Case of an 80-year-old male patient with an anterior communicating artery (AcomA) aneurysm. **(B-1)** Brain CTA revealing a 6 mm AcomA aneurysm. **(B-2)** Patient opted for conservative management. In the 1-year follow-up CTA, aneurysm growth (from 6 to 8 mm) was noted. Treatment was recommended, but the patient refused to proceed with the treatment. **(C-1, C-2)** Case of an 82-year-old female patient with a right paraclinoid aneurysm. **(C-1)** Initial brain magnetic resonance angiography showing a 2 mm right paraclinoid aneurysm. **(C-2)** Conservative management was recommended. Follow-up imaging after 2 years revealed aneurysm growth (from 2 to 4 mm). Coiling was recommended, but the patient refused the treatment.

with a daughter sac were found among the conservative management, coiling, and clipping groups (p<0.01) at our institute.

The proportions of patients with Karnofsky performance status score ≥ 70, combined hypertension, diabetes, medical comorbidities, and the use of antiplatelet and anticoagulant medications did not show significant differences among the groups. During the follow-up period in the conservative management group, two cases of rupture and 13 cases of aneurysm growth occurred. No aneurysm rupture or recurrence was observed in patients in the treatment groups. Postoperative complications were reported only in the endovascular treatment group (three cases out of the total). No general medical complications, major postoperative infarction, or hemorrhage were found.

Our data showed that the group of patients selected for treatment based on the presence of a daughter sac and the aneurysm size corresponded to the high-risk group according to the PHASES score (p<0.01). The median follow-up period for all enrolled patients was 18 months, and treatment-related complications were confirmed through GOS evaluation at 6 months. The mean duration of hospital stay for clipping surgery was 8.2 days, and endovascular surgery was 5.3 days. Detailed patient characteristics are presented in Table I.

We analyzed the IRs of aneurysm growth and rupture in the 134 patients followed up for ≥ 6 months with CTA or MRA. During this period, 13 patients experienced aneurysm growth, and two patients experienced aneurysm rupture. In the two patients with aneurysm rupture, the GOS score was 2 in one patient and 4 in the other. The IR of aneurysm growth was 5.9 per 100 person-years, and that of aneurysm rupture was 0.8 per 100 person-years (Table II). We also analyzed potential risk factors for aneurysm growth in octogenarian patients, including sex, aneurysm location (anterior circulation, posterior communicating artery, and posterior circulation), aneurysm size (> 7 mm), presence of a daughter sac, and use of antiplatelet and anticoagulant medications. However, none of the patient data showed any statistically significant result.

Table I: Basal Characteristics of Enrolled Patients

Treatment decision making	Conservative [n=99 (73.9%)]	Coiling [n=25 (18.7%)]	Clipping [n=10 (7.5%)]	Total [n=134]	p-value
Age (mean, years)	81.5 (80-91)	82.6 (80-93)	82.2 (80-85)	81.9 (80-93)	0.1
Sex					
Male	70 (22.9)	6 (24)	2 (20)	37 (27.6)	1.00
Female	29 (77.1)	19 (76)	8 (80)	97 (72.4)	
Location					0.36
MCA	38 (38.4)	6 (24)	7 (70)	51 (38.1)	
PcomA	22 (22)	7 (28)	1 (10)	30 (22.4)	
AchoA	2 (2)			2 (1.5)	
AcomA	16 (16.2)	6 (24)		22 (16.4)	
Paraclinoid	11 (11.1)		1 (10)	12 (9)	
Basilar tip	1 (1)	2 (8)		3 (2.2)	
SCA	2 (2)			2 (1.5)	
PICA	0 (0)			0 (0)	
VA	1 (1)			1 (0.7)	
Distal ACA	1 (1)	2 (8)	1 (10)	4 (3.0)	
AICA	3 (3)			3 (2.2)	
ICA bifurcation	1 (1)	1 (4)		2 (1.5)	
Proximal ACA	1 (1)			1 (0.7)	
PCA	0 (0)			0 (0)	
Basilar trunk	1 (1)			1 (0.7)	
Single aneurysm	86 (86.9)	22 (88)	8 (80)	116 (86.6)	0.80
Multiple aneurysm	13 (13.1)	3 (12)	2 (20)	18 (13.4)	
Size of aneurysm (Mean, mm)	4.4 (2-10)	5.9 (3-12)	7.4 (4-12)	4.9 (2-12)	**0.001**
Daughter sac	6 (6.1%)	11 (44)	5 (50)	22 (16.4)	**0.001**
History of SAH	1 (1)	1 (4)	0	2 (1.5)	0.5
Family history of SAH	1 (1)	0	0	1 (0.7)	0.83
Hypertension	71 (71.7)	16 (64)	10 (100)	97 (72.4)	0.1
DM	19 (19.2)	6 (23.1)	2 (18.2)	27 (20.1)	0.87
Co-morbidity (heart, lung, liver, kidney, endocrine)	54 (54.5)	9 (36)	2 (20)	65 (48.5)	0.04
Smoking	6 (6.1)	3 (12)	0	9 (6.7)	0.63
Medication					
Antiplatelet	30 (30.3)	4 (16)	3 (30)	37 (27.6)	0.36
Anticoagulant	10 (10.1)	3 (12)	0	11 (8.2)	0.54
Karnofsky performance scale ≥ 70	88 (88.9)	24 (96)	10 (100)	122 (91)	0.32
Rupture during observation	2 (2)	NA	NA	2 (1.5)	NA
Growth of aneurysm	13 (13.1)	NA	NA	13 (9.7)	NA
PHASES score					
high risk (≥10)	4 (4.1)	6 (24)	5 (50)	16 (11.9)	**0.001**
low risk (<10)	94 (95.9)	19 (76)	5 (50)	118 (88.1)	
Treatment-related complication	NA	3 (12)	0	3 (2.2)	NA
Neurological complications	NA	3/3	0	0	NA
Medical complications	NA	0	0	0	NA
Recurrence	NA	0	0	0	NA

Table I: Cont.

Treatment decision making	Conservative [n=99 (73.9%)]	Coiling [n=25 (18.7%)]	Clipping [n=10 (7.5%)]	Total [n=134]	p-value
6 months GOS	NA 18 months				NA
5		25 (100)	10 (100)		
4					
3					
2					
1					
Mean hospital stay		5.3	8.2		
Follow-up period (median, months)	27.5 (1-116)	22.1 (1-107)	11.3 (6-14)	18 (0-116)	

***MCA:** Middle cerebral artery, **PcomA:** Posterior communicating artery, **AchoA:** Anterior choroidal artery, **AcomA:** Anterior communicating artery, **SCA:** Superior cerebellar artery, **PICA:** Posterior inferior cerebellar artery, **VA:** Vertebral artery, **ACA:** Anterior cerebral artery, **AICA:** Anterior inferior cerebellar artery, **ICA:** Internal carotid artery, **PCA:** Posterior cerebral artery, **SAH:** Subarachnoid hemorrhage, **DM:** Diabete mellitus, PHASES (predict risk of rupture for asymptomatic intracranial aneurysms).*

Table II: Incidence Rate of Aneurysm Growth and Rupture

Total n=134	Incidence rate	95% confidence interval
Aneurysm growth (n=12)	5.9 of 100 person-year	0.03-0.1
Aneurysm rupture (n=2)	0.8 of 100 person-year	0.001-0.031

DISCUSSION

In South Korea, the recent increase in life expectancy and improved access to medical care has led to a rise in octogenarian patients with UIAs. Life expectancy for Koreans increased by 3 years between 2011 and 2020, reaching 86.5 years for women in 2020, with a projected rise to nearly 90 years by 2030 (www.kostat.go.kr). Enhanced accessibility to medical services, including brain MRI coverage for symptoms such as headache and dizziness, contributes to the growing encounters with independent-living octogenarians with UIA.

The decision-making process for UIA treatment in octogenarians is complex (15,17). Previous guidelines recommended treating UIA in patients with an estimated life expectancy of over 10 years, excluding octogenarians due to their age (15). Furthermore, numerous prior studies on UIA in older patients were conducted among individuals aged 65 years and older (4,8,12). The lack of evidence and difficulty in estimating life expectancy in this age group led to individualized decisions. Even for aneurysmal subarachnoid hemorrhage in patients aged over 80 years, limited studies have reported the risk/benefit ratio of treatment, and only a restricted use of endovascular surgery has been recommended based on individual circumstances (16). The unique characteristic of higher refusal rates for treatment and follow-up in octogenarians further complicates the establishment of treatment guidelines. Currently, there is no consensus on age limitations for UIA treatment, necessitating a re-evaluation of treatment guidelines.

While the need for UIA treatment is established (9,18), the decision becomes intricate for octogenarians. Though endovascular coiling and microsurgical clipping show comparable outcomes (14), age-related risks, including higher complication rates, add complexity (3,10). Conservative management is often recommended, considering the natural history of small unruptured aneurysms. However, for healthy octogenarians with high-risk features, such as large aneurysm size or the presence of a daughter sac, treatment decisions pose challenges.

At our institute, age over 80 is not considered a contraindication for UIA treatment. Interventions are guided by intuitive indications, treating high-risk features. While large aneurysm size and the presence of a daughter sac are considered indications for treatment, the PHASES score provides a reasonable basis for identifying the high-risk group. Factors like Karnofsky performance status score, hypertension, diabetes, medical comorbidities, and use of antiplatelet and anticoagulant medications did not significantly influence the decision to treat the aneurysm. Moreover, our postoperative complication rate was 0.9%, which is comparable to that reported by Moroi et al. (mortality rate of 0.6% and morbidity rate of 0.3% for all age groups) (11). In general, the complication rate of both clipping and coiling is higher in older patients than in younger patients (2,14). This emphasizes the careful selection of patients and postoperative caution in this high-risk octogenarian group. However, we did not encounter significant post-treatment complications following either clipping or coiling in octogenarian patients, though it is essential to note that our results may not be broadly applicable due to the limited number of treated patients. It is important to exercise caution when interpreting our low complication rate, as the outcomes may vary in different study settings. We applied treatment to unruptured aneurysms in carefully selected patients within this older age group. It is crucial to interpret our low complication rate in the context of delicately selected patients and specialized postoperative care.

Observational studies on octogenarian patients with UIA are scarce, and, to our knowledge, the IR of aneurysm growth and rupture in this population has not been reported in the literature. While rupture is more likely in aneurysms with a large diameter, some types can rupture without a significant increase in size. Additionally, the time interval between aneurysm growth and rupture has not been thoroughly investigated to date (1,6). Our study's aneurysm rupture rate (0.8 per 100 person-years) is comparable to that reported by the International Study of UIA Investigators (rupture rate, 0.5%) (5). However, our findings are insufficient to explain the association between the risk/benefit of treatment in octogenarians and the rates of aneurysm rupture or growth. Nonetheless, active treatments are recommended since our experience indicates a low postoperative complication rate.

Several factors must be considered regarding the treatment of UIA in octogenarian patients. Atherosclerotic changes in arteries, tortuosity of intracranial arteries, weak and adhesive dura, and atrophic brain changes can make both coiling and clipping challenging (2). However, given the IRs of aneurysm growth (5.9 per 100 person-years) and aneurysm rupture (0.8 per 100 person-years), age over 80 years should not be a contraindication for UIA treatment. It is important to note that a significant proportion of patients who underwent conservative management were lost to follow-up, possibly due to the socio-medical characteristics of extremely old-aged patients. This follow-up loss could indicate that the actual aneurysm growth or rupture rate in this population may be higher than reported in this study, emphasizing the potential need for UIA treatment in the octogenarian age group.

Despite the challenges in evaluating the natural history of UIA in octogenarian patients due to a high rate of follow-up loss, considering the possibilities of aneurysm rupture, the poor prognosis of subarachnoid hemorrhage, advanced medical management, and surgical techniques, we argue that age alone may not be a sole contraindication. Extended evaluation of the necessity of UIA treatment in this extremely old age group should be considered in future studies.

However, our study has some limitations. It is a retrospective study with only 134 patients in the statistical analysis, limiting meaningful multivariate analysis of outcomes or predictors. The study period of 10 years may have seen advancements in surgical techniques and endovascular instruments. The evaluation of functional status depended on individual clinicians' opinions, and there may be selection bias given the highly selective surgical indication. Many patients were lost to follow-up, reflecting the social characteristics of old-aged patients. Despite these limitations, our data, although subject to attrition, does not show statistically significant differences between the baseline sample and follow-up. With the aging population, future research may prove statistical significance and contribute to the evolving treatment strategy for elderly patients over age 80. This study is meaningful as it suggests favorable considerations in the treatment strategy for this age group, considering advanced surgical techniques and devices. Future research could explore IRs by age, account for low attrition, and delve into the natural history of UIA.

CONCLUSION

Judicious decision-making is essential when considering the treatment of UIAs in octogenarian patients. The findings of this study suggest that advanced age alone should not be deemed a contraindication for UIA treatment in this age group. We advocate for the consideration of UIA treatment in octogenarians, particularly in cases involving large aneurysms or those with a daughter sac, both of which are identified as high-risk features. This recommendation stems from the well-established knowledge that the prognosis of subarachnoid hemorrhage in extremely old patients is notably poor.

Disclosure and conflicts of interest

The authors have no conflicts of interests to declare and this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

Ethical approval

This retrospective study was approved by the appropriate ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments Institutional review board of Asan Medical Center, approval no. 2020-0466). For this type of study, formal consent is not required.

Informed consent

This type of study does not require informed consent.

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AUTHORSHIP CONTRIBUTION

Study conception and design: JHK, JB
Data collection: YSP, JB
Analysis and interpretation of results: BHY, WP, JB
Draft manuscript preparation: BHY
Critical revision of the article: JB
Other (study supervision, fundings, materials, etc...): YKP, JCP, JSA, JB
All authors (BHY, YKP, JHK, YSP, WP, JCP, JSA, JB) reviewed the results and approved the final version of the manuscript.

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