Unruptured intracranial aneurysms (UIAs) in older adults present unique challenges due to distinct treatment considerations. The increasing age of the global population necessitates a deeper understanding of the natural history and rupture risks of UIAs in older adults, as well as special considerations relevant to this demographic group. Furthermore, determining the optimal treatment strategy in older adults remains challenging due to factors such as reduced life expectancy, comorbidities, and frailty. Conservative management may be appropriate for low-risk aneurysms, while endovascular treatments offer advantages in selected cases. Microsurgical clipping remains a viable option, although it may pose higher perioperative risks in older patients. In this review, we provide a comprehensive understanding of UIAs in older adults. A tailored approach considering age, comorbidities, and aneurysm characteristics can optimize treatment outcomes.

Keywords: Aneurysm; Aged; Microsurgery; Endovascular; Complication

Introduction

Unruptured intracranial aneurysms (UIAs) are prevalent in 1% to 3% of the general population [1–4]. Several studies have reported on the appropriate treatment modalities and general management guidelines for UIAs. However, the optimal management strategy for elderly patients is yet to be established. Owing to the limited life expectancy in the elderly population, along with the complexity of various comorbidities and treatment considerations not seen in younger patients. As such, the expected outcomes of treatment are uncertain.

The populations of developed countries are aging, with that in South Korea aging rapidly. However, advancements in societal culture and qualitative improvements in healthcare have increased life expectancy. It is predicted that by 2030, the life expectancy at birth for South Korean women will exceed 86.7 years, with a probability of 90% [5]. Advancements in non-invasive diagnostic examinations have led to an increase in the diagnosis of UIAs in elderly patients. With this, neurosurgeons may encounter challenges in determining treatment strategies for elderly patients with UIAs. A precise understanding of the natural course, review of possible treatment outcomes, and consideration of complex scenarios that may arise in the elderly are essential for making knowledgeable and evidence-based decisions regarding the management and treatment of elderly patients diagnosed with UIAs. This article will review the challenges of UIAs in the elderly and provide information on treatment.

Natural History

Prevalence

The prevalence of cerebral aneurysms vary in the literature, ranging from 1% to 3% to as high as 7% in the general population. However, these figures pertain to the overall population, and unruptured cerebral aneurysms may be more prevalent in the elderly [2,6–8]. In a study by Taylor et al. [9], UIAs were prevalent in S$4 per 100,000 (0.06%) among 20,767 hospitalized elderly patients. This significant difference compared to the general population implies that many elderly patients may remain undiagnosed for un-
ruptured aneurysms. There are autopsy studies supporting this assertion. Inagawa and Hirano [1] reported a higher incidence of unruptured aneurysms in patients aged ≥ 60 years, particularly noting the highest incidence in those in their 70s. In a study by Iwamoto et al. [10], which involved 1,230 autopsies, the peak incidence was observed in individuals in their 40s and 60s, with the prevalence of unruptured aneurysms increasing with advancing age. In contrast, a meta-analysis of 68 studies involving 94,912 patients and 1,450 UIAs revealed that the prevalence of aneurysms was influenced by factors such as autosomal dominant polycystic kidney disease, family history, age, and sex. However, when compared with that in patients aged 80 years and above, statistically significant lower prevalence was only observed in patients aged under 30 years, with no significant differences found in other age groups [2].

Natural history and rupture risk of UIAs
Evaluating the annual rupture risk of aneurysms is crucial in determining the appropriate treatment modality for cerebral aneurysms in elderly patients. The International Study of Unruptured Intracranial Aneurysms (ISUIA), one of the largest prospective studies addressing the natural history and rupture risk of unruptured cerebral aneurysms, indicated a higher rupture risk for aneurysms larger than 7 mm and those located in the posterior circulation. However, there was no mention of age-specific natural history or rupture risk of aneurysms. Instead, it reported a higher risk associated with treatment in the elderly [11]. The Unruptured Cerebral Aneurysm Study of Japan (UCAS), one of the largest prospective studies addressing the natural history and rupture risk of unruptured cerebral aneurysms, indicated a higher rupture risk for aneurysms larger than 7 mm and those located in the posterior circulation. However, there was no mention of age-specific natural history or rupture risk of aneurysms. Instead, it reported a higher risk associated with treatment in the elderly [11]. The Unruptured Cerebral Aneurysm Study of Japan (UCAS), one of the largest prospective studies addressing the natural history and rupture risk of unruptured cerebral aneurysms, indicated a higher rupture risk for aneurysms larger than 7 mm and those located in the posterior circulation. However, there was no mention of age-specific natural history or rupture risk of aneurysms. Instead, it reported a higher risk associated with treatment in the elderly [11].

In a comprehensive study combining three prospective studies from the Japan group, including UCAS, a total of 1,896 patients with 2,227 aneurysms were longitudinally observed over an average period of 802.7 days [12]. The study reported that along with age over 80 years, aneurysm size larger than 7 mm and location in the posterior communicating artery were independent risk factors for rupture. Similar trends were observed in a systematic review of 51 studies [13] where the overall prevalence of subarachnoid hemorrhage (SAH) was 9 per 100,000 person-years. Meanwhile, it was 26.2 per 100,000 person-years in the population aged 75 to 85 years and 31.3 per 100,000 person-years in those aged ≥ 85 years, indicating an increase in rupture rate with increased age.

Special Considerations in Elderly Patients
Treatment decision considering age and reduced life expectancy
Medically, old age is commonly defined as being 65 years or older. However, this is based not on a biological definition, but rather on cultural and customary definitions. Literature also defines old age variably, ranging from 65 years to as high as 80 years and above. Therefore, determining old age should take into consideration the patient’s country of origin, culture, and level of healthcare.

In Korea, alongside the continuous increase in life expectancy over the past 20 years, there has been a consistent trend of increasing healthy life expectancy among the elderly. As of 2020, life expectancy is estimated to reach approximately 85 years [14,15]. Moreover, healthy life expectancy, which encompasses disability-free, disease-free, health-adjusted, and quality-adjusted life expectancies, has also been consistently increasing. Despite heterogeneity across studies, it is generally around age 70 years [16–19]. One study conducted a risk-benefit analysis of preventive treatment based on prospective data from the ISUIA. The results showed a benefit to surgery, excluding anterior circulation aneurysms smaller than 7 mm without a history of SAH, for individuals with a life expectancy of < 15 to 35 years or 45 to 70 years [20]. However, given that approximately 20 years have passed since this study, current life expectancy may be higher. Additionally, considering age along with the size and shape of aneurysms, there is a need to critically evaluate and cautiously accept such conclusions.

There are scoring systems designed to assess the natural course of aneurysms or guide their treatment. Among them, the PHASES score is one of the widely used scores to predict the rupture risk of aneurysms. Contrary to the PHASES score [21], which adds points for rupture risk in individuals aged ≥ 75 years, the Unruptured Intracranial Aneurysm Treatment Score assigns fewer points for treatment as age increases among the elderly [22]. Therefore, clinicians must consider life expectancy as a crucial factor in determining whether to treat UIAs.

Comorbidity and frailty
Elderly patients not only experience an increase in chronological age due to the aging process but may also have various accompanying conditions, leading to a decrease in physiological reserve and delayed postoperative recovery, making them more prone to experiencing postoperative complications. There are several comprehensive and abstract factors that contribute to the increased incidence of postoperative complications in elderly patients. Key factors include chronological age, comorbidity, and frailty. However, because individual health and physiological status vary, simple chronological age alone is inadequate in predicting outcomes. Ac-
According to some studies [23,24], frailty, defined as a concept distinct from chronological age and characterized by decreased physiological reserve, may be more effective in predicting worse outcomes in neurosurgical conditions than chronological age alone [24,25].

In addition to the aging process and the resulting decrease in physiological reserve, elderly patients may also have comorbidities, and these comorbidities can influence postoperative outcomes. There are surrogate predictors such as the Charlson comorbidity index, neurovascular comorbidities index, and Karnofsky performance scale. After risk stratification, high-risk patients should be prioritized for management such as intensive care unit admission or pharmacological therapy rather than surgical management [26,27].

Cognitive function

Cognitive function and quality of life are decreased following SAH caused by ruptured cerebral aneurysms, and non-ruptured cerebral aneurysms themselves can also increase anxiety and depression, leading to psychiatric issues [28]. In addition, cerebrovascular injury and parenchymal injury accompanying cerebral aneurysm treatment, as well as complications associated with treatment such as infarction, can lead to changes in cognitive function. From a therapeutic perspective, maintaining cognitive function is crucial for maintaining independence and improving compliance with medication and treatment in the elderly. Microsurgical clipping of non-ruptured cerebral aneurysms itself does not have a significant impact on cognitive function [29,30]. There is no significant difference in cognitive function before and after endovascular treatment, as well as microsurgical clipping [31]. Additionally, treatment in elderly patients with asymptomatic UIAs does not impair cognitive function but rather reduces anxiety [32].

However, according to the ISUIA, approximately 3% to 5% of patients with unruptured aneurysms experience impairment in cognitive function. Further, cognitive function impairment is more frequent in the open surgery group among patients treated for unruptured aneurysms. Open surgery is associated with a possibility of microvascular injury or traction injury. Inoue et al. [33] reported a significant association between changes in T2 images and decreased cognitive function after clip surgery. Moreover, hyperintensities in the deep white matter are a risk factor for decreased postoperative cognitive function [34]. In a study investigating the age and surgical approach based on the location of an aneurysm among 43 patients aged ≥ 65 years with anterior communicating artery aneurysms, 17 patients experienced a decline in cognitive function following microsurgical clipping [35]. This can be attributed to frontal lobe retraction; rectus gyrus resection; and damages to the anterior hypothalamus, nucleus accumbens, and basal nucleus of Meynert, which are commonly supplied by anterior communicating artery perforators [36–39]. Additionally, advanced age ( > 65 years) [11,40,41], interhemispheric approach [35], operative time > 5 hours [41], and presence of preoperative brain damage [33] are risk factors for postoperative cognitive impairment. However, there is a paucity of prospective studies evaluating cognitive function after surgery for unruptured aneurysms in the elderly population. Furthermore, owing to the heterogeneity in analysis methods, evaluation criteria, and definitions of cognitive impairment across studies, study findings should be critically evaluated. Cognitive function should be thoroughly assessed in patients with multiple risk factors before making treatment decisions.

Complication of antiplatelet medication (gastrointestinal bleeding)

The efficacy of dual antiplatelet therapy (DAPT) medication in neurointervention has been demonstrated, and DAPT is commonly used medication perioperatively to reduce ischemic complications during endovascular treatment of aneurysms [42–44]. Furthermore, in elderly patients, the frequent occurrence of tortuous vasculature and wide-necked aneurysms often necessitates the use of stents, leading to the need for the maintenance of antiplatelet medication postoperatively. An increasing number of elderly patients are being prescribed antiplatelet medication. However, the use of antiplatelet drugs can lead to several complications in elderly patients, the most common of which includes a life-threatening complication of gastrointestinal (GI) bleeding [45,46].

Approximately 3% of the elderly population die from GI bleeding [46], making it an important issue that cannot be overlooked as it prolongs hospitalization and incurs significant societal and economic costs. A meta-analysis reported that low-dose aspirin monotherapy increased the risk of GI bleeding (odds ratio, 1.55; 95% confidence interval, 1.27–1.90) [47]. When DAPT was initiated, the risk of GI bleeding within 30 days was 1.3% [48,49]. Moreover, coronary intervention studies have shown that patients taking DAPT who also take warfarin have a higher risk of major bleeding [50]. Efforts to mitigate GI bleeding include the use of H2 antagonists and proton pump inhibitors (PPIs). Yeomans et al. [51] reported that PPIs are superior to H2 antagonists in suppressing gastric acid, preventing ulcers, and promoting healing. Therefore, PPIs are recommended as for preventing GI bleeding [52]. In the cardiovascular field, the concomitant use of DAPT and PPIs significantly reduces GI bleeding without increasing ischemic complications [53].

Whether prophylactic acid-suppressive therapy is justified for elderly patients who require antiplatelet medication for a certain
period needs to be clarified. The risk of complications such as GI bleeding can be increased based on the patient’s baseline risk. Therefore, physicians prescribing antiplatelet medication must assess the individual risk factors of GI complications for each patient and should always inquire about symptoms and check for them during follow-up visits to the clinic.

**Treatment Modality**

**Conservative management**

The benefit of treatment considering the short life expectancy may be limited in cases where the size of the aneurysm is stable or small, and the rupture risk is deemed low. Owing to the high procedure-related morbidity associated with aging and various comorbidities, conservative treatment may be preferred over preventive treatment. Animal model study suggests that aspirin lowers the risk of aneurysm rupture by inhibiting COX-2 [54], which indirectly indicates that aneurysms enlarge and rupture due to inflammation [55]. One preliminary study found a reduced activity of COX-2 in human aneurysm biopsies from individuals taking aspirin [56]. However, there are still uncertainties regarding the actual effectiveness of aspirin in preventing aneurysmal SAH, and some findings suggest that it does not significantly influence aneurysm rupture [57]. Subsequent prospective, multicenter observational studies have reported the safety of aspirin use in patients with small unruptured aneurysms who experienced stroke, showing a relatively low risk of aneurysm rupture [58]. Since then, there have also been reports suggesting that aspirin can prevent aneurysm rupture [59–62]. A meta-analysis also reported that aspirin can reduce the risk of aneurysm rupture [63–65].

Aspirin has also been reported to help prevent aneurysm growth. A prospective study of 272 patients followed up within 48 months reported a lower increase in aneurysm size in the aspirin group [66]. In addition, statins, which have pleiotropic effects, also prevent aneurysm growth, but their role and effects remain unclear. A prospective study conducted in China [67,68] reported that statins helped prevent an increased aneurysm size, but the study’s design was criticized for potential selection bias as it was not randomized.

Given the high prevalence of comorbidities in elderly patients, the use of aspirin and statins is common. Among elderly patients with aneurysms with low rupture risk, management through such medication may be considered. However, aspirin use can increase the risk of bleeding in the elderly [69,70], and its safety for primary prevention has not been established [71]. Therefore, the use of aspirin for conservative treatment of unruptured cerebral aneurysms in the elderly should be carefully decided upon with a critical perspective.

**Follow-up radiologic surveillance and considerations for elderly patients**

There is limited knowledge regarding the radiologic growth rate of aneurysms or the associated risks in elderly patients. Kubo et al. [72] reported that female sex is a risk factor for UIA growth in elderly patients. Meanwhile, Huang et al. [73] reported an overall growth risk of 4.2% during a follow-up period of 1,025 person-years in elderly patients, highlighting the significance of multiplicity and the presence of blebs in aneurysm growth. Infarction due to diagnostic cerebral angiography can occur in elderly patients [74,75], with aging-related atherosclerotic changes and complex vasculature potentially increasing neurological complications following diagnostic angiography.

Therefore, invasive diagnostic cerebral angiography should be cautiously considered. Additionally, radiologic surveillance should consider the possibility of rupture, presence of comorbidities, and potential benefits of preventive treatment. However, the lack of large-volume, prospective studies in the elderly makes it difficult to justify long-term robust radiological surveillance. Unless the lesion poses a high risk of rupture, non-invasive tests are more appropriate. Considering factors identified in previous studies that contribute to aneurysm growth in the elderly, or even in elderly patients with factors known to increase aneurysm size in the general population, non-invasive tests may be considered within reasonable limits.

**Endovascular treatment**

Endovascular treatment for unruptured cerebral aneurysms offers advantages over microsurgical aneurysm clipping, including shorter procedure times, reduced bleeding, and shorter recovery periods. These factors make endovascular treatment preferable for elderly patients. According to the International Subarachnoid Aneurysm Trial and its subgroup analyses involving patients with ruptured aneurysm, endovascular treatment is slightly more favorable in elderly patients with anterior circulation aneurysms [76,77]. However, the advantages of endovascular treatment in elderly patients with unruptured aneurysms remain unclear.

Stiebel et al. [78] reported morbidity and mortality rates of approximately 4% in a retrospective study involving 70 patients with a mean age of 75 years, advocating that endovascular treatment can be safely performed in elderly patients. However, a point of concern in this study is that patients treated with adjuvant techniques such as balloons or stents exhibited a higher complication rate. Similarly, a single-center report on the safety of endovascular treatment in elderly patients showed technical success in the majority
of cases (95.9%) and observed procedure-related complications in only 4.1% of cases, with no permanent deficits reported [79]. However, it is important to note that only less than 10% of patients were treated with stents, and the authors also emphasized the significance of technical complications in elderly patients. As mentioned earlier, the use of DAPT medication may pose issues such as GI bleeding and other hemorrhagic complications. Thus, the use of adjunctive devices in elderly patients should be carefully considered not only because it may potentially lead to problems on its own, but also because of issues arising from concomitant medications.

The vascular curvature becomes more tortuous with aging [80], and wide neck aneurysms are more common in the elderly [81]. Hence, performing endovascular treatment via simple coiling without adjunctive devices is extremely challenging. Owing to the tortuous vasculature and decreased navigability in elderly patients, as well as limited catheter stabilization, achieving complete coil embolization may be difficult. Consequently, the recanalization rate could increase, and retreatment rates also range from 5.7% to 17.4% in the treatment of cerebral aneurysms in the elderly [78,82–84]. Given the relatively limited life expectancy in elderly patients, the extent to which such recanalization is acceptable has not been studied, and this aspect should be thoroughly considered by both physicians and patients.

Flow diverters are primarily used for large to giant aneurysms, but they are also gradually found to be safe and effective in the treatment of small- to medium-sized aneurysms [85]. However, there is no prospective research on the safety of flow diversion in the treatment of unruptured aneurysms in elderly patients. A meta-analysis also reported higher morbidity in elderly patients [86]. Technical challenges due to tortuous vasculature in elderly cases may make it difficult to achieve appropriate wall apposition and flow diversion. Thus, surgical ligation may be preferable over flow diversion in some cases [87,88]. The safety of Woven EndoBridge (WEB), used in the treatment of wide neck bifurcation aneurysms, has not yet been established in elderly patients. However, Pierot et al. [89] reported a morbidity of 3.1% and a 15.6% rate of thromboembolic events in a multicenter preliminary study involving 33 patients. Notably, among the six patients aged ≥ 65 years in their study, 3 (50%) patients experienced thromboembolic events. Although all patients had a favorable modified Rankin scale score of 0 at 1 month, elderly patients should be cautiously evaluated for thromboembolic events when using WEB.

**Microsurgical clipping**

Recent studies have reported a decreased incidence of complications following surgery for UIA. This is attributed to advancements in microscopy and the use of endoscopes, as well as the introduction of indocyanine green angiography, microvascular Doppler, intraoperative monitoring, and preservation of the sylvian vein and improvement in neurosurgeon skills. In general, aneurysm clipping offers advantages over endovascular treatment in elderly patients. Aneurysm clipping does not require consideration of aortic arch tortuosity, proximal vessel tortuosity, atherosclerotic changes, catheter stabilization, and other factors. Jang et al. [90] reported that the outcomes of microsurgical treatment in elderly patients were non-inferior to those of endovascular treatment and that advanced age did not act as a limiting factor. In a study by Bekelis et al. [91] involving 8,705 elderly patients, there was no significant difference in 1-month and 1-year mortality between the clipping and coiling groups. However, the length of hospital stay was significantly higher, and the rate of discharge to a short- or long-term care facility was higher in patients who underwent coiling than in those who underwent clipping (5% [n = 308] vs. 19.3% [n = 500]).

Microsurgical clipping is associated with a longer hospitalization period than endovascular coiling [91,92]. This is because microsurgical treatment typically involves longer surgical times, higher blood loss, and longer recovery times due to pain. The long-term durability of microsurgical treatment tends to favor its application in relatively younger patients. Conversely, endovascular treatment may be more favorable than microsurgical clipping in elderly patients with a shorter life expectancy. A large-scale study addressing the treatment of unruptured cerebral aneurysms in 5,635 elderly patients reported higher in-hospital mortality rates (2.2% vs. 0.9%) and perioperative stroke rates (10.3% vs. 3.5%) for clipping surgery compared to those for coiling [93]. The authors advocated that, when appropriate, endovascular coiling or conservative observation is a favorable option. One possible reason for this may be the detrimental effects of vascular aging in elderly patients. As the aging process progresses, vascular aging can occur, accompanied by processes such as mechanical stress on elastin, endothelial dysfunction, and glycation of elastin. These processes can lead to vascular calcification, atherosclerotic changes, and other related alterations in the vasculature [94].

Such findings may be present at the neck or dome of a cerebral aneurysm, and atherosclerotic plaques may predispose patients to ischemic complications during microsurgical clipping [95,96]. In cases of such atherosclerotic aneurysms, surgeons may unavoidably resort to incomplete clipping and may even opt for wrapping alone in some instances. Sakarunchai et al. [97] have reported on techniques aimed at reducing ischemic complications in such aneurysms by avoiding the use of temporary and permanent clips in the yellowish area. Another consideration, related to the aging pro-

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cess of vessels in the elderly, is the difficulty in achieving proximal control. This phenomenon is particularly crucial in surgeries involving distal internal carotid artery (ICA) aneurysms (e.g., posterior communicating artery aneurysms, anterior choroidal artery aneurysms, and paraclinoid ICA aneurysms). ICA calcification occurs more frequently in the elderly, and in such cases, intracranial ICA temporary clips may fail to achieve proximal control altogether (Fig. 1), potentially leading to vessel injury (Fig. 2) [98]. Therefore, there may be cases in which additional neck dissection is performed, leading to increased surgical time and inevitable wounds in the neck area. This can potentially result in complications such as vocal cord palsy, neck hematoma, and airway compromise [99]. Methods such as induced cardiac arrest through adenosine injection or proximal control via endovascular balloon occlusion can be employed. However, given the high prevalence of comorbidities and frailty in elderly patients, careful consideration of their stability is essential before making decisions regarding these techniques.

**Conclusion**

The prevalence of unruptured cerebral aneurysms in the elderly and the necessity for their treatment are increasing owing to population aging and increased life expectancy. However, despite these, the paucity of prospective, randomized trials targeting the elderly population has resulted in unclear treatment guidelines and standards. Compared to younger patients, elderly patients require special considerations. Surgeons must carefully consider the characteristics of the elderly population to minimize potential treatment-related complications associated when deciding on the need for treatment, type of surgery, and medical treatment.

**Conflicts of interest**

No potential conflict of interest relevant to this article was reported.

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**REFERENCES**

56. Hasan D, Hashimoto T, Kung D, et al. Upregulation of cyclooxygenase-2 (COX-2) and microsomal prostaglandin E2 synthase-1 (mPGES-1) in wall of ruptured human cerebral aneurysms: pre-
Unruptured intracranial aneurysms in older adults


