



Research Article

## Outcomes of Atherosclerotic Cerebral Aneurysm Surgery in Advanced Age Patients

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### Abstract

**Background:** The advanced age of patients usually increases the incidence of atherosclerotic cerebral aneurysm. The risk of treating this type of aneurysm by surgical clipping is development of a thromboembolic event. We would like to know the exact rate of ischemic event and the risk factors associated with embolic stroke by treatment of this aneurysm in elderly patients.

**Methods:** This is a retrospective cohort study in patients older than 70 years who were diagnosed as unruptured atherosclerotic cerebral aneurysm and underwent microsurgical clipping between January 2012 and August 2014. We compared the ischemic events and factors associated with embolic stroke with a younger group of patients (70 years old). The endpoint was the incidence of cerebral infarction evaluated by brain imaging and discharge modified Rankin Scale (mRS) score. A statistical analysis of the factors associated with embolic stroke was done by Fisher's exact tests in each group.

**Results:** Among 30 atherosclerotic cerebral aneurysms of older group of patient, only 2 patients (6.7%) were associated with postoperative cerebral infarction. There were no factors associated with ischemic outcome. In the younger age group, only 1 patient (1.4%) developed cerebral infarction and the number of clips was associated with ischemic outcome ( $P = 0.01$ ).

**Conclusions:** The older patients had an increasing trend of cerebral infarction after surgery compared with the younger patients. No independent risk factors were associated with cerebral infarction after atherosclerotic cerebral aneurysm surgery in the greater than 70-year-old group.

### Keywords

Advanced age; Atherosclerotic cerebral aneurysm; Ischemic event; Thromboembolism

## Introduction

The number of incidental findings of unruptured intracranial aneurysms (UIAs) has increased due to the advantages of non-invasive imaging technology. According to the higher prevalence of chronic hypertension, diabetes mellitus, hypercholesterolemia and smoking, a higher prevalence of atherosclerotic or calcified aneurysms are found,

especially in patients of advanced age [1]. No previous study focused on the incidence or the exact data of atherosclerotic aneurysms in older patients who were older than 70 years. They reported only that the atherosclerotic type of aneurysm was related with a poor outcome after surgery which was more than 7.8 times higher when compared with patients who had non-atherosclerotic aneurysms [2]. The role of surgery in atherosclerotic aneurysm should be concerned because it can shower emboli during manipulation or the placement of the clip especially it can break the unstable local plaque resulting in distal arterial occlusion that leads to brain infarction. Therefore, the outcome for this type of aneurysm treatment may not be satisfactory. Since there are no previous studies on the incidence of ischemia and factors associated with thromboembolic events after treatment with surgical clipping in the old patient, the aim of this study is to review the ischemic events of atherosclerotic aneurysm clipping and the associated factors for embolic stroke after clipping an aneurysm in patients >70 years old and perform a comparison with younger patients 70 years old.

## Materials and Methods

A retrospective cohort study was performed at a university hospital. The study was approved by the ethics committee of Fujita Health University and each patient signed an informed consent before receiving the treatment between January 2012 and August 2014. All patients were operated on by a senior neurosurgeon (Y.K.) and the operative video records of each patient were reviewed. The baseline characteristics of the patients (i.e., demographic, radiographic, intraoperative and postoperative data) were noted and we classified the patients into two groups based on age: the older group (>70 years old) and the younger group (>70 years old). The eligibility criteria were a diagnosis of unruptured atherosclerotic cerebral aneurysm. The ineligibility criteria were ruptured cerebral aneurysm and developed the clinical condition of cerebral infarction prior surgery.

All patients were operated on under standard techniques. After they were diagnosed as unruptured cerebral aneurysm from 3-dimensional (3D) CT angiography (CTA), an informed consent was obtained from them and their relatives before surgery was scheduled. Intraoperative physiologic monitoring such as motor evoked potential (MEP) or somatosensory evoked potential (SSEP) was applied in selected cases who had a risk of injury to small perforating arteries during surgery that could lead to a neurological deficit. The standard fronto-temporal transylvian approach was selected for internal carotid artery (ICA), posterior communicating artery (PCoA), anterior communicating artery (ACoA), and middle cerebral artery (MCA) aneurysms. The other approach was the frontal interhemispheric approach for distal anterior artery (ACA) or high position ACoA aneurysms. Indocyanine green-video assist (ICG-VA) with FLOW-800 software generated with infrared (Zeiss, OPMI Pentero, Germany) was used in all patients before and after clipping to check the anatomical architecture of the aneurysm and associated arteries such as the parent and perforating arteries. The patency of these arteries and the completeness of aneurysmal obliteration can be checked with this device. Endoscope-assisted microsurgery was used for anatomical safety to check before and after aneurysm clipping in case the neck or small perforator arteries were invisible. Doppler

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ultrasonography was used to determine the characteristics of the blood flow after clipping of the aneurysmal sac and identification of unintentional injury to small perforating or parent arteries. Postoperative magnetic resonance imaging (MRI) of the brain was routinely performed within 24 hours to check for complications of infarction. The outcome evaluation was estimated by the modified Rankin scale (mRS) score on the discharged day.

Ischemia was defined either as symptomatic or asymptomatic. Symptomatic ischemia referred to a neurological deterioration after the operation and all of these proved by MRI of the brain showing evidence of restriction of the signal for DWI in the distribution of a vascular territory (Figure 1). Asymptomatic ischemia or silent ischemia in this study was a diagnosis by imaging of the brain and the patient did not have any symptoms. A neurological deficit from direct injury during surgery and not related with embolic infarction was excluded from the definition of ischemia. We measured the outcome of cerebral infarction by using the discharge mRS score which is classified into clinical symptoms with 0 to 6 points [3]. Atherosclerotic is defined as the detection of yellowish plaque located at the dome and/or neck of an aneurysm and/or the parent artery (Figure 2). A filling defect area is compatible with yellowish plaque also detected by ICG-VA for confirmation of diagnosis. The classification of the location of atherosclerotic change is designated and described (Table 1). The location of atherosclerotic change might influence the effect of embolic stroke during manipulation or adjustment of the clip force around this area. The demographic data included age, sex, underlying disease, smoking history, and symptoms of the patient. Radiographic data included the location, size (small: <7 mm, medium: 7 to 12 mm, large: 13 to 25 mm, giant: >25 mm), and the number of aneurysms. Operative data included the area of the atherosclerotic plaque, number and location of clippings, application of temporary occlusion, adjustments of the clip during operation, and time duration of the operation. Post-operation data on the day before discharge were mRS score (good: 0-2, fair: 3-4, and poor: 5-6), the neurological deficit and the imaging of the brain were obtained (Table 2). A statistical analysis was performed to evaluate the demographic and radiographic data, procedural and post-procedural variable parameters. The data were interpreted by median  $\pm$  interquartile range (IQR) in ordinal data and analyzed using the R program. The Wilcoxon Rank-sum test and Fisher's exact test were used to analyze for non-parametric ordinal scale and nominal scale, respectively, to find the risk factors associated with ischemic outcome. Statistical significance was defined as  $P < 0.05$ .

## Results

A total of 103 patients were included in this study. The numbers of patients in the older and younger age groups were 30 and 73 patients, respectively. More than half of the older patients had a comorbidity of high blood pressure. Both groups of patients presented with asymptomatic aneurysm and the majority of the patients were diagnosed from image screening tests. PCoA aneurysms were found in most patients and the average mean aneurysmal size was less than 7 mm. Parent vessel was the most common location of atherosclerotic change. Only 3 cases (2.9%) developed ischemia after the operation and the MRI of the brain showed evidence of cerebral infarction. Among the three infarction patients, the first case was diagnosed with an anterior communicating artery aneurysm (ACoA) aneurysm. This 73-year-old female patient underwent aneurysm clipping and developed cerebral infarction in the right side of frontal lobe and hemiparesis was observed. Finally, the patient's neurological deficit improved. In the second case, a 77-year-old female was diagnosed with

a MCA aneurysm and clipping was performed. She developed cerebral infarction post-operatively but she later had reversible hemiparesis. The last case was a 66-year-old male patient diagnosed with a M1 aneurysm and at post-aneurysm clipping he developed weakness at his contralateral side. He still has a permanent neurological deficit (mRS score 3). There was no statistical significance for the factors associated with ischemic symptoms in the older age group but the number of clips had statistical significance of the factors associated with infarction in the younger patients.

## Discussion

This is the first series review investigating the outcome of treatment in unruptured atherosclerotic cerebral aneurysm in the aged patients, especially the risk of thromboembolism in an ischemic event. Thirty and 73 atherosclerotic aneurysms of older and younger age groups, respectively, were analyzed for factors associated with an ischemic event after undergoing an operation. We found very few ischemic events and vascular atherosclerotic risk factors of both groups of patients and there were no independent risk factors associated with embolic stroke outcome in the older age group. There was also no increase in the incidence of ischemia despite the location of the atherosclerotic plaque, size of aneurysm, frequency of

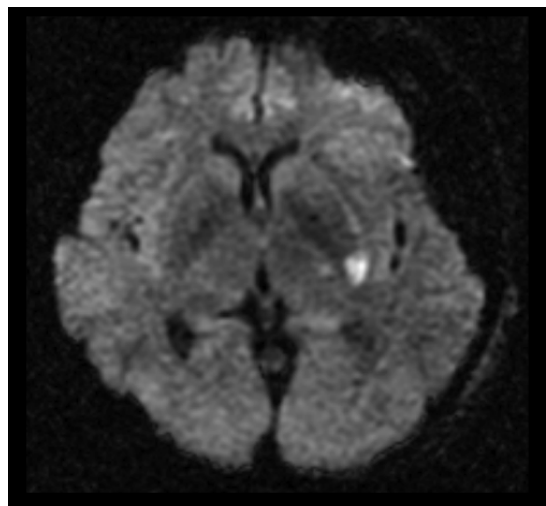


Figure 1: Illustration of the restriction signal from MRI brain that represented to infarction after clipping.



Figure 2: Illustrations of atherosclerotic change at dome of aneurysm.

**Table 1:** Classification of atherosclerotic change locations.

Part of atherosclerosis	Definition*
Dome	Sclerotic changes in the aneurysmal sac just beyond the neck at least 1 mm
Neck	Sclerotic changes in the neck of the aneurysm not involving the aneurysmal sac or parent vessel more than 1 mm.
Parent artery	Sclerotic changes in the parent vessel not far away from the neck more than 5 mm and it doesn't involve the neck

Abbreviation: mm = millimeters

\*Plus the filling defect lesion after ICG-VA administration

**Table 2:** Demographic, radiographic, procedural, and post-procedural data and univariate analysis for factors associated with infarction outcome in each age group.

Characteristic	Age 70 year-old		Age >70 year-old	
	Number (%)	P Values	Number (%)	P Values
<b>Age (year) (mean)</b>	63 (30,69)	0.589	74 (70,79)	0.780
<b>Sex</b>				
Male	26 (57.4)		14 (74.5)	
Female	47 (60.9)		16 (74)	
<b>Underlying disease</b>				
Diabetes mellitus	2 (2.7)	1	1 (3.3)	1
Hypertension	34 (46.6)	1	20 (66.7)	1
Dyslipidemia	8 (11)	1	7 (23.3)	0.4
Smoking	26 (35.6)	1	7 (23.3)	1
Symptomatic	10 (13.7)	0.14	4 (13.3)	1
<b>Location of aneurysm</b>				
PCoA	20 (27.4)	1	12 (40)	1
MCA bifurcation	17 (23.3)	1	8 (26.7)	0.95
MCA M1	3 (4.1)	0.06	0 (0)	-
ACoA	11 (15.1)	1	5 (16.7)	0.31
Distal ACA	6 (8.2)	1	2 (6.7)	1
Posterior circulation	0 (0)	-	0 (0)	-
Other ICA (Ophthalmic, AntChoroidal)	16 (21.9)	1	3 (10)	1
<b>Size of aneurysm</b>	51 (69.9)	0.66	19 (63.3)	1
Small (<7 mm)	18 (24.7)	1	10 (33.3)	1
Medium (7-12mm)	4 (5.5)	0.07	1 (3.3)	1
Large (13-25mm)	0 (0)	-	0 (0)	-
Giant (>25mm)	1 (1,1)	1	1 (1,1)	1
<b>Location of atherosclerotic change</b>				
Neck of aneurysm	31 (42.5)	0.42	17 (56.7)	0.18
Dome of aneurysm	38 (52.1)	1	17 (56.7)	1
Parent artery of aneurysm	43 (58.9)	1	19(63.3)	1
Neck & Dome of aneurysm	8 (11)	1	6(20)	1
Neck & Parent artery of aneurysm	7 (9.6)	1	4(13.3)	1
Dome & Parent artery of- aneurysm	8 (11)	1	3(10)	1
Neck & Dome & Parent artery of- aneurysm	8 (11)	0.11		1
<b>Number of clips (median)</b>	1 (1,2)	0.01	1(1,2)	1
<b>Readjusted clips (times)</b>	6 (8.2)	0.08	2(6.7)	1
<b>Location of clipping</b>				
Dome	24 (32.9)	0.33	6(20)	1
Neck	61 (83.6)	1	28(93.3)	1
<b>Temporary artery occlusion (Yes)</b>		0.66	4(13.3)	1
<b>Discharge mRS score</b>				
Good (0-2)	72 (98.6)		30(30)	
Fair (3-4)	1 (1.4)		0(0)	
Severe (5-6)	0(0)			
<b>Neurological deficit</b>	1 (1.4)		2(6.7)	
<b>MRI brain (ischemia)</b>	1 (1.4)		2(6.7)	

median : (interquartile range = IQR)

readjusting the clip, and the location of the clipping. These parameters usually increase the risk of infarction but in this study they did not. The statistical analysis determined that the number of clips were the independent risk factors of an ischemic outcome in the younger aged patients. However, a critical interpretation of these results is needed because of the small number of patients who developed an infarction after surgical clipping.

In patients who have a background of chronic hypertension, the pathophysiology leads to intima thickening and necrosis of the tunica media. The composition of the matrix changes and the internal elastic lamina degenerates resulting in a weakening of the arterial wall that develops into an aneurysm [4,5]. There is still debate on the optimal treatment of UIAs because of a lack of prospective randomized controlled trials [4,6]. According to our knowledge, the atherosclerotic plaque of an aneurysm enhances the risk of generating a shower of thrombi to the distal vascular territory that results in cerebral infarction [7]. This is a serious sequela and complication after atherosclerotic aneurysm treatment especially when we replace the clip and manipulate around the yellow plaque or thickened wall area that might squeeze the atheromatous plaque allowing it to migrate to a distal vascular area. In some situations, if the booster clip technique is used at the neck of the aneurysm, it will protrude the atheromatous thrombi and showered them and cause blockage in a distal area. Most reports usually mentioned stroke events related to surgical clipping in only non-atherosclerotic aneurysm [7-9]. Due to this poor outcome, some authors have suggested an alternative technique to firstly remove atheroma or sclerotic plaque and then directly repair the wall of the aneurysm with a micro-suture. After that, the clip was used to close the neck which also decreased thromboembolic events [10]. Some aneurysms have limitations such as atherosclerotic plaque located at the neck and clip placement cannot be done in this area. Suitable clipping terminology was introduced to place the clip at the aneurysmal sac or dome and then wrap the neck to avoid a poor outcome of ischemia from showering the emboli [11]. They found not only a poor outcome after treatment of atherosclerosis or calcified aneurysm but it was also difficult to adequately place the clip. The clip needed readjustment or it was sometimes necessary to use multiple clips for reconstruction of the neck or formation of the parent artery or dome. That meant it probably increased the risk of injury to the small perforator arteries which were located adjacent to the aneurysm and led to cerebral infarction [2].

Therefore, it is very difficult to judge how to suitably place the clip to prevent emboli migration and obtain maximal exclusion of the aneurysm. Unstable plaque is very weak and easily migrates due to the force of the clip compression or manipulation around the plaque. In some cases, since the location of the plaque is incorporated in the neck and dome and there is no area for placement of the clip, it becomes necessary to perform a dome clip to decrease the risk of rupture in the future. We should leave some part of the yellowish plaque because the risk of aneurysmal growth in this area is very low. This is the strategic treatment of this type of aneurysm.

The older age group (70 years) more frequently has atherosclerotic risk factors than the younger age group. This result indicates that the impact of atherosclerotic risk factors on cerebral aneurysm can be the cause of ischemic outcome after surgical clipping.

## Conclusions

The incidence of atherosclerotic aneurysm is increasing especially in the older age group of patients. An atherosclerotic plaque aneurysm

is difficult to judge for treatment. The worse complication of surgical clipping is cerebral infarction from showering of the emboli. A technique for clipping was introduced to avoid placing a clip in the yellow area to decrease the incidence of ischemia and leave some areas of yellow plaque. We prefer this technique for treatment of this type of aneurysm especially in the older age group to decrease adverse events from an embolic event.

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