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Early postoperative angiography after clipping of intracranial aneurysms: Clinical value of angiography and predisposing factors for aneurysm remnants

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Directed by Professor Yong Bae Kim

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<TABLE OF CONTENTS>

LIST OF FIGURES

LIST OF TABLES

ABSTRACT

Early postoperative angiography after clipping of intracranial aneurysms: clinical value of angiography and predisposing factors for aneurysm remnants

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Aneurysm remnants after microsurgical clipping have a risk of regrowth and rupture and have not been validated in the era of 3-dimensional angiography. Although computed tomography angiography (CTA) is currently preferred for evaluating aneurysmal clipping results, it cannot completely rule out postoperative remnant occurrence. Furthermore, there is no concrete evidence supporting its superior accuracy to digital subtraction angiography (DSA). Therefore, this study aimed to (1) evaluate the clinical value of angiography in diagnosing remnants, (2) determine the rate of remnants, and (3) identify the predictors for remnants after microsurgical clipping. Between January 2014 and May 2017, 200 aneurysms in 154 patients, treated via microsurgical clipping, were considered eligible for the present study. Among them, 139 aneurysms in 106 patients were finally selected for evaluation. The results of microsurgical clipping were evaluated within 7 days to predict the remnant development risk using DSA based on the classification, and clinical features of the patients and characteristics of treated aneurysms. The rate of aneurysm remnants, including intentional remnants, was 29.5%, and retreatments were needed in 6.5% of such cases. Neck size (cut-off: 5.68 mm; sensitivity, 66.7%; specificity, 96.2%) and maximum diameter (cut-off: 7.03 mm; sensitivity, 66.7%; specificity, 89.2%) of aneurysms were independent predisposing factors for the occurrence of aneurysm remnants that need retreatment (OR: 2.30; $p < 0.001$; OR: 1.38; $p < 0.001$, respectively). Postoperative DSA may identify remnants after microsurgical clipping. Aneurysms with larger neck size and maximum diameter have a higher risk of aneurysmal remnants after clipping.

Key words: intracranial aneurysm, clipping, remnants, angiography, predictor, retreatment

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I. INTRODUCTION

After Guglielmi detachable coils were first introduced in 1991[1], endovascular treatment became the primary modality for the treatment of intracranial aneurysms, and the trend increased after the publication of the results of the International Study of Unruptured Intracranial Aneurysms Investigators in 1998[2] and the International Subarachnoid Aneurysm Trial in 2002[3]. Although endovascular treatment is not superior to microsurgical clipping in terms of occlusion and recurrence rates, the result of endovascular treatment can be evaluated immediately and intuitively. To prevent the growth and rupture of remnants after endovascular treatment, physicians tend to follow patients closely and frequently via plane X-ray, magnetic resonance angiography (MRA), and conventional angiography.

Unlike endovascular treatment, the result of microsurgical clipping might depend on the judgment of the operator, in spite of intraoperative indocyanine green (ICG) angiography and endoscopic inspection. Moreover, MRA or computed tomography angiography (CTA) is inadequate to completely rule out remnants after microsurgical clipping. The annual hemorrhage risk of remnants after microsurgical clipping is higher than the annual rupture risk of untreated aneurysms[2,6] at 0.5 – 1.9%[4,5], thus indicating the need to focus on remnants after clipping.

The rate of remnants after microsurgical clipping ranges from 1.6% to 42%[7-11], and the risk factors include location of aneurysms and complexity of aneurysm morphology[7,11,12]. Several studies have analyzed the angiographic results of aneurysmal clipping before the development of 3-dimensional (3D) rotational digital subtraction angiography (DSA). Although CTA is currently the primary modality used to evaluate the results of aneurysmal clipping, to the best of our knowledge, there is no concrete evidence that CTA is superior to DSA in terms of accuracy[13,14].

This study aimed to (1) evaluate the clinical value of angiography in diagnosing remnants, (2) determine the rate of remnants, and (3) identify the predictors for remnants after microsurgical clipping in the endovascular era.

II. MATERIALS AND METHODS

1. Patients

Between January 2014 and May 2017, 200 aneurysms (from 154 patients) clipped by one neurosurgeon (YBK) with more than 10-year experience were eligible for the present study. Among them, 139 aneurysms in 106 patients were finally enrolled after satisfying the following criteria: 1) intracranial aneurysms treated via microsurgical clipping; 2) DSA with 3D rotational imaging was performed within 7 days after surgery. Informed consent was waived under permission of institutional review board because of retrospective study based on de-identified data.

2. Follow-up angiography and data interpretation

All patients with ruptured or unruptured intracranial aneurysms were managed based on the latest guideline[15,16]. Preoperative DSA was required to diagnose intracranial aneurysms and to determine the treatment modality. Postoperative DSA was performed on postoperative day 6 or 7 for unruptured aneurysms or within two weeks for ruptured aneurysms according to institutional guidelines.

All DSAs were performed in the biplane angiography using Artis zee biplane, (Siemens Healthcare GmbH, Erlangen, Germany), while postoperative DSAs were performed only for the target vessel using 3D-rotational reconstruction.

The collected data of the enrolled patients included sex, age, and medical history (hypertension, diabetes mellitus, dyslipidemia, and previous stroke).

Based on 3D-rotational images, the neck size, height, depth, and width of the aneurysms were measured, and the maximal diameter was defined as the greatest value among these parameters. Moreover, the location of the aneurysm was categorized into 4 groups: middle cerebral artery, internal carotid artery including posterior communicating artery, anterior cerebral artery, and posterior circulation. In addition, the ratio by which the aneurysmal neck encases the parent artery was dichotomized as over 50% and under 50%.

The result of postoperative DSA was evaluated and the remnants after microsurgical clipping were classified by one neurosurgeon (JJK) and one neuroradiologist (SHS) based on the Sindou classification[17], which categorizes remnants from grades I to V:

Grade I: remnant is less than 50% of the neck size.

Grade II: remnant is more than 50% of the neck size.

Grade III: residual sac of a multilobulated aneurysm

Grade IV: residual sac is less than 75% of the aneurysmal dome.

Grade V: residual sac is more than 75% of the aneurysmal dome.

Grade 0 was defined as “no remnant at all.” All enrolled and classified aneurysms were dichotomized into 2 groups of those who needed and did not need retreatment to identify the predictors of aneurysm remnants after clipping. Group A (no retreatment group) comprised patients with completely clipped aneurysms and remnants of grade 0, I, II, and III, while Group B (retreatment group) comprised patients with remnants of grade IV and V.

3. Statistical analysis

All variables were analyzed with binary logistic regression model, and p value ≤ 0.05 was considered significant. If continuous variables were identified to be significant, cut-off values were calculated on the receiver operating characteristic (ROC) curve using Youden’s index. All statistical analyses were performed using IBM SPSS Statistics (version 23.0, IBM Analytics)

III. RESULTS

The mean patient age was 56.6 years (range, 21-75 years) and 69% were women. Eighteen aneurysms (13%) were ruptured at the time of treatment, and the mean interval between clipping and DSA was 7.4 days (range, 2-18 days). The characteristics of the patients and the aneurysms are described in Table 1.

Table 1. Patient Characteristics

Parameter	Value
Mean age, years	56.6 ± 10.6
Women (%)	96 (69.1%)
Location	
MCA	45 (32.4%)
Posterior Circulation	5 (3.6%)
ICA	55 (39.6%)
ACA	34 (24.4%)
Multiplicity (%)	75 (54.0%)
Parent artery encasement (>50%)	41 (29.5%)

Number of clips	1.8 ± 1.0
Mean neck size (mm)	3.46 ± 1.62
Mean maximum diameter (mm)	5.17 ± 2.83
Aspect ratio	1.2 ± 0.7

Abbreviations: MCA, middle cerebral artery; ICA, internal carotid artery; ACA, anterior cerebral artery

Based on 3D rotational images of postoperative DSA, 41 clipped aneurysms (29.5%) were identified as remnants (Table 2).

Table 2. Postoperative angiographic results based on Sindou classification

Sindou classification	Number (%)	Remnants (%)[1]	Group (%)[2]
No remnants	98 (70.5%)	98 (70.5%)	130 (93.5%)
Grade I	20 (14.4%)	41 (29.5%)	
Grade II	8 (5.8%)		
Grade III	4 (2.9%)		
Grade IV	5 (3.6%)		9 (6.5%)
Grade V	4 (2.9%)		

[1] Remnants was calculated in group of "No Remnants" and "grade I to V".

[2] Group was calculated in groups of grade 0-III and grade IV, V.

The demographic data of the patients in Group A and B are shown in Table 3. The neck size and maximum diameter of aneurysms were significantly different between Group A and Group B (neck size: 3.3±1.3 mm versus 6.3±2.9 mm, p=0.013; maximum diameter, 4.9±2.6 mm versus 8.7±4.4 mm, p=0.035, respectively). Meanwhile other variables including ratio of parent artery encasement, aspect ratio, and location of aneurysms did not show any significant difference.

Table 3. Demographic data of 2 groups

Parameters	Group A (Sindou grades 0 to III; N=130)	Group B (Sinou grades IV and V; N=9)	p value*
Unruptured (%)	113 (86.9%)	8 (88.9%)	1.000
Sex, Female (%)	88 (67.7%)	8 (88.9%)	0.338
Mean age[1], years	56.2 ± 10.6	62.3 ± 9.5	0.096
Location[2]			0.371
MCA	43 (33.1%)	2 (22.2%)	
Posterior circulation	4 (3.1%)	1 (11.1%)	
ICA	50 (38.5%)	5 (55.6%)	
ACA	33 (25.4%)	1 (11.1%)	
Multiplicity	71 (54.6%)	4 (44.4%)	0.805
Parent artery encasement (>50%, %)	36 (27.7%)	5 (55.6%)	0.163
Number of clips			0.394
1	59 (45.4%)	5 (55.6%)	
2	42 (32.3%)	0 (0.0%)	
3	21 (16.2%)	3 (33.3%)	
4	7 (5.4%)	1 (11.1%)	
6	1 (0.8%)	0 (0.0%)	
Neck size[1] (mm)	3.3 ± 1.3	6.3 ± 2.9	0.013
Maximum diameter[1] (mm)	4.9 ± 2.6	8.7 ± 4.4	0.035
Aspect Ratio[1]	1.2 ± 0.7	1.2 ± 0.4	0.994

* p value < 0.05 means statistically significant difference between two group.

[1] Value described in average ± standard deviation.

[2] MCA: middle cerebral artery, ICA: internal cerebral artery, ACA: anterior cerebral artery

Binary logistic regression analysis of all variables was performed in a step-wise manner to identify the independent predictors of clip remnants that need re-treatment (Sindou classification IV and V). The results showed that neck size (OR: 2.30; 95% CI: 1.50–3.52; $p<0.001$) and maximum diameter (OR: 1.38; 95% CI: 1.14–1.67; $p=0.001$) of aneurysms were associated with occurrence of clip remnants. Multivariate logistic regression model was not possible due to the multicollinearity of 2 variables (Table 4).

Table 4. Logistic regression analyses

Predictors of remnants after clipping that need retreatment (Sindou grades IV and V)	Odds ratio (95% CI[1])	p Value†
Age	1.08 (0.99-1.17)	0.098
Location – Posterior circulation	5.38 (0.40-73.01)	0.21
Ratio of encasement (>50%)	3.26 (0.83-12.84)	0.091
Neck size* (mm)	2.30 (1.50-3.52)	<0.001
Maximum diameter* (mm)	1.38 (1.14-1.67)	0.001
Aspect ratio	0.99 (0.38-2.64)	0.994

* Multivariate logistic regression was not possible due to their multicollinearity
† p value < 0.05 means statistically significant.

[1] CI: confidence interval

Hence, the ROC curves of these continuous variables were made individually to define the cutoff value. Both ROC curves revealed adequate value of neck size (AUC: 0.826) and maximum diameter (AUC: 0.753) to be predictive of clip remnants that need retreatment. Further, the cut-off value for neck size and maximum diameter was measured as 5.68 mm (sensitivity, 66.7%; specificity, 96.2%) and 7.03 mm (sensitivity, 66.7%; specificity, 89.2%) (Figure 1).

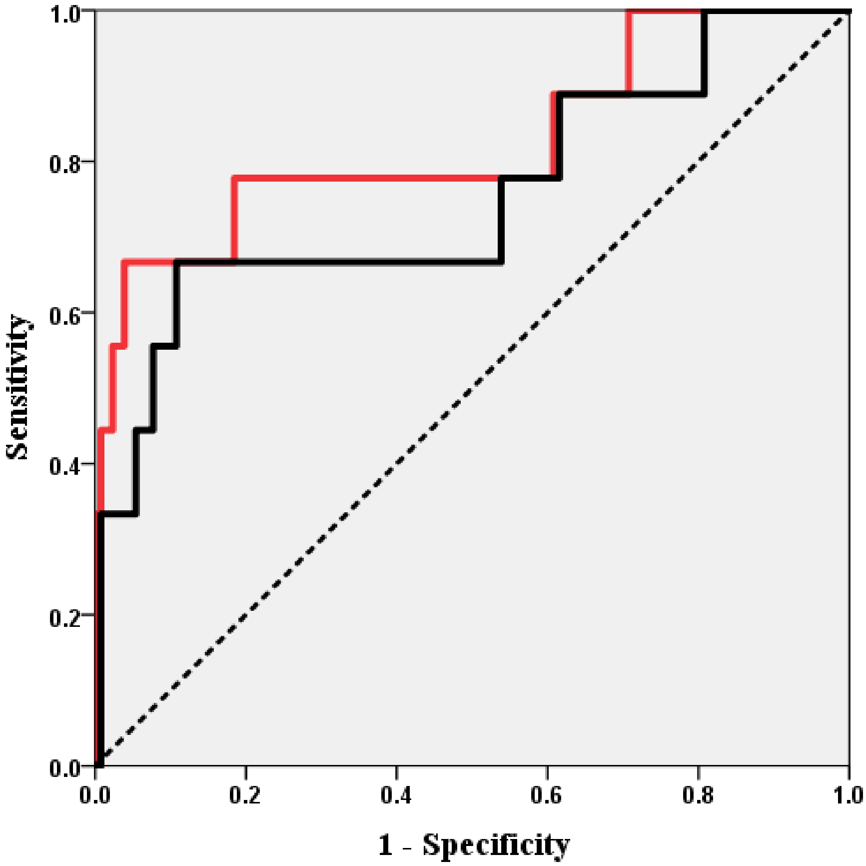

Figure 1. ROC curve of neck size and maximum diameter of aneurysm to predict the occurrence of remnants that need to be re-treated. Both ROC curves revealed adequate value of neck size (red line; AUC 0.826) and maximum diameter (black line; AUC 0.753) to predict the clip remnants that need re-treatment. The cut-off value for neck size and maximum diameter were 5.68 mm (sensitivity, 66.7%; specificity, 96.2%) and 7.03 mm (sensitivity, 66.7%; specificity, 89.2%)

IV. DISCUSSION

In this study, we attempted to evaluate the clinical value of angiography in diagnosing remnants, determine the rate of remnants, and identify the predictors for remnants after microsurgical clipping in the endovascular era. Even though the occlusion rate of microsurgical clipping is higher than that of endovascular coiling, it may not be possible to completely clip all aneurysms. The rate of remnants after microsurgical clipping ranges from 1.6% to 42% and it tends to increase in the era of 3D angiography[9,18]. In the current study, the overall rate of remnants after microsurgical clipping was 29.5%, which was considerably higher than we expected.

The overall rate could be attributed to the following reasons. First, several patients with clipped aneurysms were excluded from the analyzed cohort. A total of 41 patients with 61 aneurysms were not assessed via postoperative DSA because of patients' refusal, risk of renal insufficiency, and surgeon's decision. Among them, there was no evidence of recurrence or re-bleeding on follow-up images but further follow-up should be necessary. Second, the motion artifact of 3D rotational angiography was attributed to the rate of remnants of Sindou Grade II. In cases of paraclinoid aneurysms, clips were positioned parallel to the parent artery and the motion of the clip blades left their traces on dual-volume reconstructed images of 3D-DSA. Third, the 5 aneurysms in Group B were incompletely clipped by intention due to severe atherosclerotic wall degeneration and the involvement of major perforators or branches from the aneurysmal wall, among others. For example, a 64-year-old female patient underwent microsurgical clipping of unruptured basilar bifurcation aneurysm with the neck measuring 11.2 millimeter (mm) and a maximal diameter of 14.1 mm (Figure 2). During the operation, the aneurysm and perforators from the top of the basilar artery were not visualized, and we partially clipped the aneurysm to facilitate succeeding endovascular treatment of simple coiling. If these 5 aneurysms were excluded from the analyses, the overall rate of remnants after microsurgical clipping would be 23.7%, and the rate of remnants that need to be retreatment (Group B) would be 2.9%.

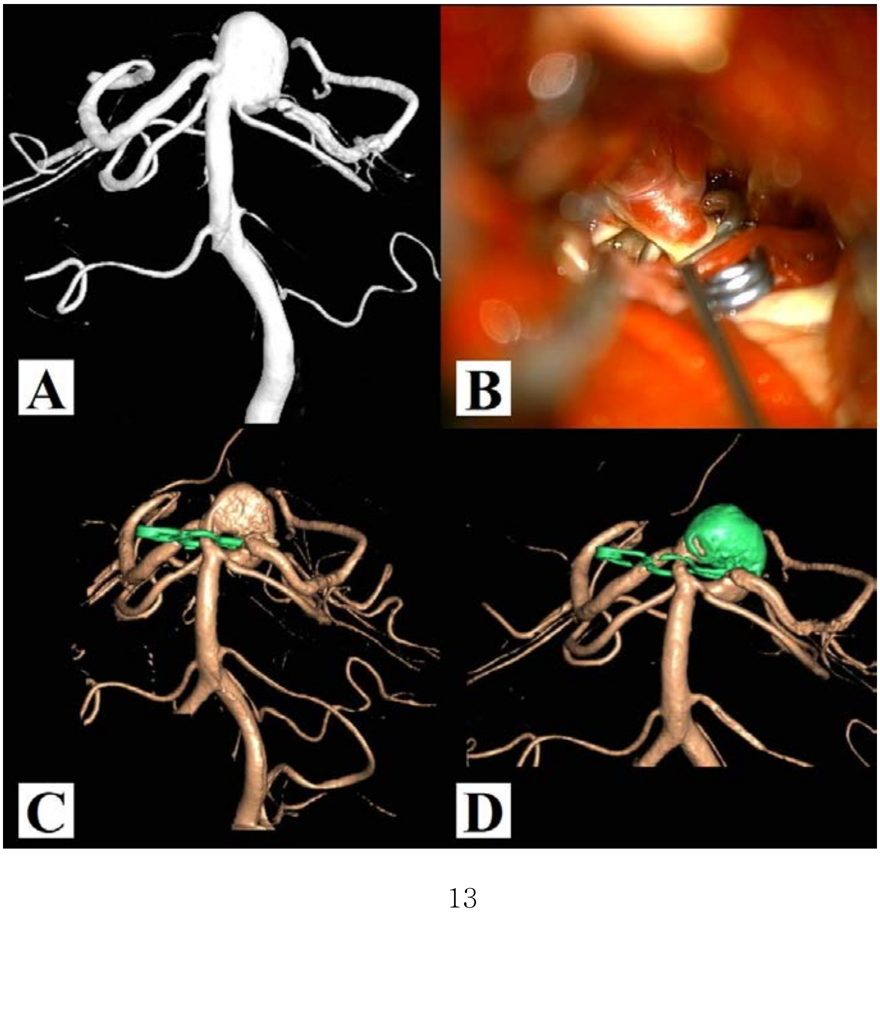

FIGURE 2. Illustrative case for intentional remnant after microsurgical clipping. A 64-year-old female patient underwent microsurgical clipping of unruptured basilar bifurcation aneurysm with the neck measuring 11.2 mm and a maximal diameter of 14.1 mm. (A) During the operation, the entire aspect of the aneurysm and perforators from the top of the basilar artery were not visualized, (B) and we intentionally partially clipped the aneurysm to facilitate suceeding endovascular treatment of simple coiling (C, D).

In contrast to endovascular treatment, the angiographic result of microsurgical clipping is difficult to confirm. In our institute, we utilize intraoperative ICG angiography, and endoscopic inspection during microsurgical clipping, but these modalities are inadequate to ensure the completeness of clipping in techniques resulting in smaller surgical corridor, such as the lateral supraorbital approach. In addition, intraoperative DSA was not applied in the current study.

Previous studies reported that the predictors of remnants after microsurgical clipping are the location and the complexity of aneurysms[7,11,12]. In the current study, the neck diameter and maximal diameter of aneurysms showed significant correlation with the occurrence of remnants after microsurgical clipping (OR: 2.30; 95% CI: 1.50–3.52; $p<0.001$; OR: 1.38; 95% CI: 1.14–1.67; $p=0.001$). By contrast, we measured the ratio of encasement of parent artery and found no significant correlation with the occurrence of remnants (OR: 3.26; 95% CI: 0.83–12.84; $p=0.091$). This result might be attributed to the ambiguous setting of the cut-off value, and the ratio of encasement of the parent artery should have been classified into 3 groups as 0%–25%, 25%–50%, and >50%. Additionally, in contrast to the results of previous studies, the location of aneurysms showed no significance (p=0.21). Most previous studies showed a high rate of remnants after clipping among aneurysms located at the ACA or anterior communicating artery[7, 11, 12]. On the ROC curves of neck size (AUC: 0.826) and maximum diameter (AUC: 0.753) of aneurysms, the cut-off value for neck size and maximum diameter were 5.68 mm (sensitivity, 66.7%; specificity, 96.2%) and 7.03 mm (sensitivity, 66.7%; specificity, 89.2%), respectively.

Recent studies based on nationwide data showed that the treatment of aneurysms have markedly increased in the past decade[19-21]. In general, the result of microsurgical clipping has been judged by the surgeon in the operative field. Although intraoperative ICG angiography, endoscopic inspection, and other assistive modalities are helpful for complete clipping, the reported rate of remnants are not negligible. Moreover, the roles of microsurgical clipping are highlighted in the era of endovascular treatment to manage complex aneurysms[22]. The result of microsurgical clipping might need to be evaluated and validated angiographically. Despite the accessibility and improved accuracy of CTA, DSA has remained the gold standard for diagnosis with low complication rate[23]. In the current study, we performed postoperative DSA only for the targeted vessel to reduce the amount of contrast and radiation dose without any complications.

This study has several limitations. The main limitation is the retrospective design and selection bias derived from the low inclusion rate (139 of 200 aneurysms). Although the enrollment of patients was limited to one surgeon to minimize the difference in surgical techniques, the patients may not reflect the characteristics of the general patient population. In addition, the duration and modality of postoperative image acquisition was based on the clinical guidelines of our institute; thus, the clinical course was similar during the hospitalization. Second, there was no protocol for reconstruction of the postoperative DSA in 3D; thus, the width and depth of images were heterogeneous. Over- or underestimation of the remnants after microsurgical clipping was possible. Third, long-term follow-up data were insufficient because most patients were treated within 3 years. To determine and evaluate the risk of hemorrhage and growth, further evaluation and long-term follow-up of the cohort are needed.

V. CONCLUSION

In conclusion, postoperative DSA may be useful to identify remnants after microsurgical clipping. In the current study, DSA diagnosed a considerable rate of remnants. The neck size and the maximum diameter of aneurysms were independent predictors of the occurrence of remnants after microsurgical clipping.

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ABSTRACT(IN KOREAN)

뇌동맥류 결찰 후 초기 혈관조영술의 임상적 의미와 잔여 뇌동맥류에 대한 예측인자

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연세대학교 대학원 의학과

김 정 재

뇌동맥류 결찰 후 발생하는 잔여 뇌동맥류는 재성장과 파열의 위험성이 있으나, 이에 대한 3차원 뇌혈관조영술을 이용한 검증은 제대로 이루어지지 않았다. 본 연구에서는 3차원 뇌혈관조영술을 이용하여 결찰 후 발생하는 잔여 뇌동맥류의 위험인자를 분석하여 뇌혈관조영술의 임상적 의미에 대해 고찰해보고자 한다. 뇌동맥류 결찰을 시행한 후 2주 이내 뇌혈관조영술을 시행한 환자들을 대상으로 하였으며, 환자들의 특성 및 치료한 뇌동맥류의 특성 그리고 수술 후 시행한 3차원 뇌혈관조영술을 토대로한 잔여 뇌동맥류를 분석하였다. 총 106명 환자의 139개의 뇌동맥류를 대상으로 분석하였고, 41개의 뇌동맥류가 잔여 뇌동맥류로 확인되었다. (29.5%) 통계적인 분석을 통해 뇌동맥류의 목 길이 (승산비 2.30)와 최대 직경(승산비 1.38)이 뇌동맥류 결찰 후 치료가 필요한 뇌동맥류 발생의 독립적인 예측인자임을 확인하였다. 본 연구를 통해 뇌동맥류 결찰 후 초기 시행한 혈관조영술이 잔여 뇌동맥류를 진단하는데 유용함을 확인하였으며, 수술 전 뇌동맥류의 목 길이와 최대 직경이 재치료가 필요한 잔여 뇌동맥류 발생의 예측인자임을 알 수 있다.

핵심되는 말: 뇌동맥류, 결찰술, 잔여뇌동맥류, 뇌혈관조영술, 예측인자, 재치료