Original Article

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Comparison of Stent-Assisted Coil Embolization Versus Coil Embolization Alone for Ruptured Cerebral Aneurysms with Mild Symptoms: A Single-Clinic Experience

경미한 증상을 가지는 파열 뇌동맥류의 치료에 있어서 스텐트를 이용한 코일 색전술과 단순 코일 색전술의 비교: 단일 병원 경험

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Purpose To evaluate the safety and efficacy of stent-assisted coil embolization (SAC) in acutely ruptured cerebral aneurysms without severe symptoms, and thus, the usefulness of the stent itself in patients with subarachnoid hemorrhages.

Materials and Methods From January 2017 to June 2019, 118 patients were treated with coil embolization for acutely ruptured cerebral aneurysms without severe symptoms (Hunt & Hess grade ≤ 3). The periprocedural complications, six-month modified Rankin scores (mRS), and six-month radiologic outcomes were compared between 56 patients with SAC and 62 patients without SAC (non-SAC).

Results The rate of good clinical outcomes (mRS ≤ 2), as well as the rate of hemorrhagic and ischemic complications, showed no significant difference between the SAC and non-SAC groups. Moreover, compared to the non-SAC group, the SAC group showed a lower recanalization rate on the six-month follow-up angiogram (20% vs. 39.3%, $p = 0.001$).

Conclusion Although stent use was not significantly associated with clinical outcomes in coil embolization of ruptured cerebral aneurysms with non-severe symptoms (Hunt & Hess grade ≤ 3), it significantly decreased the rate of recanalization on follow-up cerebral angiograms.

Index terms Aneurysm, Ruptured; Subarachnoid Hemorrhage; Stents

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INTRODUCTION

Stent-assisted coil embolization (SAC) is an endovascular treatment option for intracranial aneurysms. It is well known that using a stent makes coiling easier, especially for aneurysms with wide necks. The recurrence rate of coiled aneurysms with SAC has been found to be less than that of coiled aneurysms without a stent in follow-ups (1).

However, the use of stents for treating acutely ruptured aneurysms is controversial because stent deployment increases the complexity of the procedure and the risk of thromboembolism. It also increases the possibility of rebleeding after coiling due to the antithrombotic agents used alongside the stent (2). In addition, it elevates the risk of hemorrhagic complications if additional surgical intervention is required, such as decompressive craniectomy or external ventricular drain (EVD).

In recognition of this, the 2012 American Heart Association/American Stroke Association (AHA/ASA) and 2018 Korean Practice Guidelines for the management of Aneurysmal Subarachnoid Hemorrhages (SAH) suggest that SAC should be used carefully in limited cases for which no alternative treatment is available (3, 4).

Detailed studies, such as those based on the patients' initial symptoms, may be needed to derive more reliable guidelines for the use of stents in ruptured aneurysm. Previous studies have focused on the safety of stents for all ruptured aneurysms without considering patients' initial symptoms (5-7).

The purpose of this study is to investigate the safety and efficacy of stent-assisted coiling on ruptured aneurysms in patients presenting only mild symptoms (Hunt & Hess grade $\leq$ 3).

MATERIALS AND METHODS

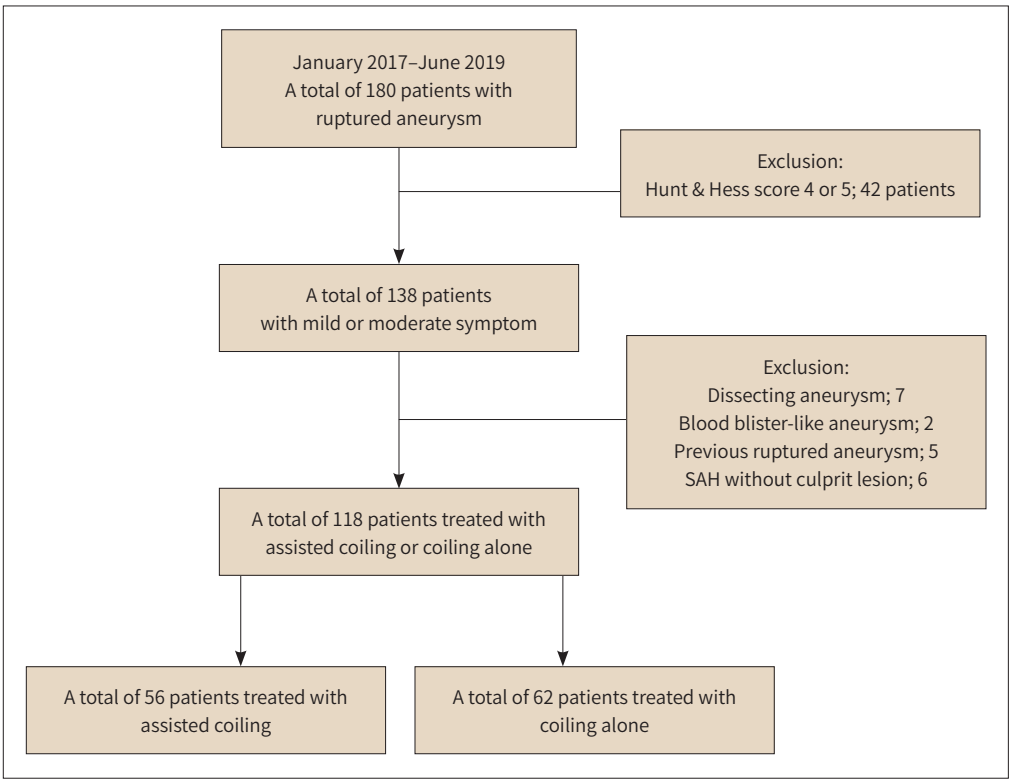
PATIENT POPULATION

From January 2017 to June 2019, we retrospectively identified 180 patients with acutely ruptured aneurysms who were underwent endovascular treatment. Among the 180 patients, 42 patients with severe symptoms (Hunt & Hess grade 4 or 5) at onset were excluded. Seven patients with dissecting aneurysms, five patients with previously ruptured aneurysms, six patients without culprit aneurysms, and two patients with blood-blister-like aneurysms were excluded. Finally, 118 patients with mild symptoms (Hunt & Hess grade $\leq$ 3) were included in our study. Among those patients, 56 were treated with SAC and 62 were treated without the use of a stent (Fig. 1). We conducted a retrospective comparative analysis of the two groups (SAC vs. non-SAC) following approval from the our Institutional Review Board (IRB No. 2020-03-052). Informed consent was waived for its retrospective study.

PROCEDURAL TECHNIQUE AND MEDICATIONS

Two neurointerventionists, both with about 15 years of experience, performed all endovascular treatment. All procedures were performed using general anesthesia with a trans-femoral approach. To reduce the risk of thromboembolic complications during the procedure, heparinization mixed with coaxial catheter-flushing saline at a concentration of 5U of heparin per 1 mL of saline was maintained in the patients. In order to achieve a target activated

Fig. 1. Flowchart showing the inclusion of 118 patients with acute SAH with mild symptoms who were treated with SAC or non-SAC.



SAC = stent-assisted coil embolization, SAH = subarachnoid hemorrhage

clotting time of 250–300 seconds or 2–2.5 times the activated clotting time level at baseline during the procedure, the drop rate of catheter-flushing saline was controlled.

A 7-Fr., 80 cm guiding sheath (Super Arrow-Flex PSI set; Arrow International, Inc., Reading, PA, USA) was inserted into the common carotid artery or subclavian artery and then a 6-Fr. guiding catheter or intermediate catheter was inserted into the distal internal carotid artery or distal vertebral artery through the 7-Fr. guiding sheath, as appropriate. All microcatheters, stents, and coils were delivered through this 6-Fr. catheter. Stents and coils were deployed according to standard procedure, as recommended by the manufacturer. If acute thrombosis occurred during the procedure, a glycoprotein IIb/IIIa inhibitor (tirofiban) was delivered through microcatheter.

The decision to perform SAC was based on the geometry of the aneurysm. The use of stents was indicated for wide-necked aneurysms (> 4 mm or aspect ratio < 1.5) or as a rescue method when coils herniated into the parent artery. Various types of stents were used in this study. Atlas (n = 28), low-profile visualized intraluminal support (LVIS) (n = 13), Solitaire AB (n = 8) and Enterprise (n = 7) were used, respectively. Aneurysms were embolized with various bare platinum coils according to the operator's preference.

When the SAC technique was used, aspirin (100 mg) and clopidogrel (300 mg) were immediately administered postoperatively. Dual-antiplatelet agents (100 mg aspirin and 75 mg clopidogrel) were administered daily for three to six months, and followed by 100 mg aspirin daily, which was continued indefinitely. Postoperative antiplatelet therapy was not given in

any of the patients who received coiling without stenting.

Additionally, surgical procedures including lumbar drain, EVD, and other procedures (decompressive craniectomy and/or hematoma evacuation) were performed according to each patient's clinical situation.

CLINICAL AND ANGIOGRAPHIC FOLLOW-UP

All the patients underwent the first clinical follow-up at discharge, and the surviving patients were advised to undergo both clinical and radiologic follow-ups 3, 6, and 12 months after initial treatment and once annually thereafter. At six months, a radiologic follow-up was performed with digital subtraction angiography (DSA).

The clinical outcome evaluations were based on modified Rankin score (mRS). Good outcomes were defined as a mRS score between zero and two, and poor outcomes as a mRS score between three and six. Complications were defined as intraprocedural rupture and thrombosis, postprocedural hemorrhages and infarction, coil escape, and surgical procedure-related hemorrhagic events were recorded (6).

Efficacy was analyzed in terms of degree of aneurysm obliteration by using the modified Raymond-Roy occlusion classification system (1, complete obliteration; 2, residual neck; 3, residual aneurysm) and recurrence rate (2). The angiographic follow-ups using DSA were classified into four categories when compared with the degree of immediate embolization: 1) occluded, defined as no contrast material filling into the aneurysm sac, 2) improved, defined as decreased contrast material filling into the aneurysm sac, 3) stable, defined as unchanged contrast material filling into the aneurysm sac, or 4) recanalized, defined as increased contrast material filling into the aneurysm sac. Any aneurysm that displayed an increased contrast filling in its neck or body was considered a recurrence regardless of the need for retreatment (2).

STATISTICAL ANALYSIS

Data are presented as mean standard deviations for continuous variables, and as frequencies and percentages for categorical variables. Statistical analysis was performed by using the independent-samples *t* test, chi-square test, Fisher's exact test, and logistic regression analysis. Univariate analysis and logistic regression were performed to determine risk factors for poor clinical outcomes (mRS $\geq$ 3) with the following variables: age, sex, Hunt & Hess grade, choice of stent-assisted technique, ischemic or hemorrhagic complications, amount of SAH, and EVD. The univariate analysis cutoff for inclusion in the logistic regression analysis was $p < 0.20$ and demographic variables such as age and sex were also included. A p value of < 0.05 was considered statistically significant. All analyses in the present study were performed using Statistical Analysis Software (SAS version 8.0, SAS Institute Inc., Cary, NC, USA).

RESULTS

Clinical and radiological variables and outcomes of SAC and non-SAC groups at 6 months are shown in Tables 1 and 2. In the SAC group, 87.5% (49 of 56) of patients showed a good clinical outcome (mRS $\leq$ 2) and 83.9% (52 of 62) of patients showed a good clinical outcome in the

non-SAC group (87.5% vs. 83.9%, p = 0.583). There was one death in each of the two groups. One patient from the SAC group died due to bacteremia and septic condition, and the other patient in the non-SAC group died due to heart failure following cardiac arrest. The died pa-

Table 1. Comparison of Clinical Variables and Outcomes Between the SAC and Non-SAC Groups

Variables	SAC Group (n = 56)	Non-SAC Group (n = 62)	p-Value
Female	24 (42.9)	21 (33.9)	0.322
Age, years	55.5 ± 10.3	56.2 ± 12.0	0.731
Hunt & Hess grade			0.174
I	5	8	
II	29	37	
III	22	17	
Complications			
Ischemic	17 (30.4)	15 (24.2)	0.454
Hemorrhagic	6 (10.7)	5 (8.1)	0.623
mRS score			0.582
0–2	49 (87.5)	52 (83.9)	
3–6	7 (12.5)	10 (16.1)	
Mortality	1 (1.8)	1 (1.6)	1.000
EVD	9 (16.0)	8 (12.9)	0.109
Hemorrhage from EVD	3 (33.3)	0 (0)	0.124

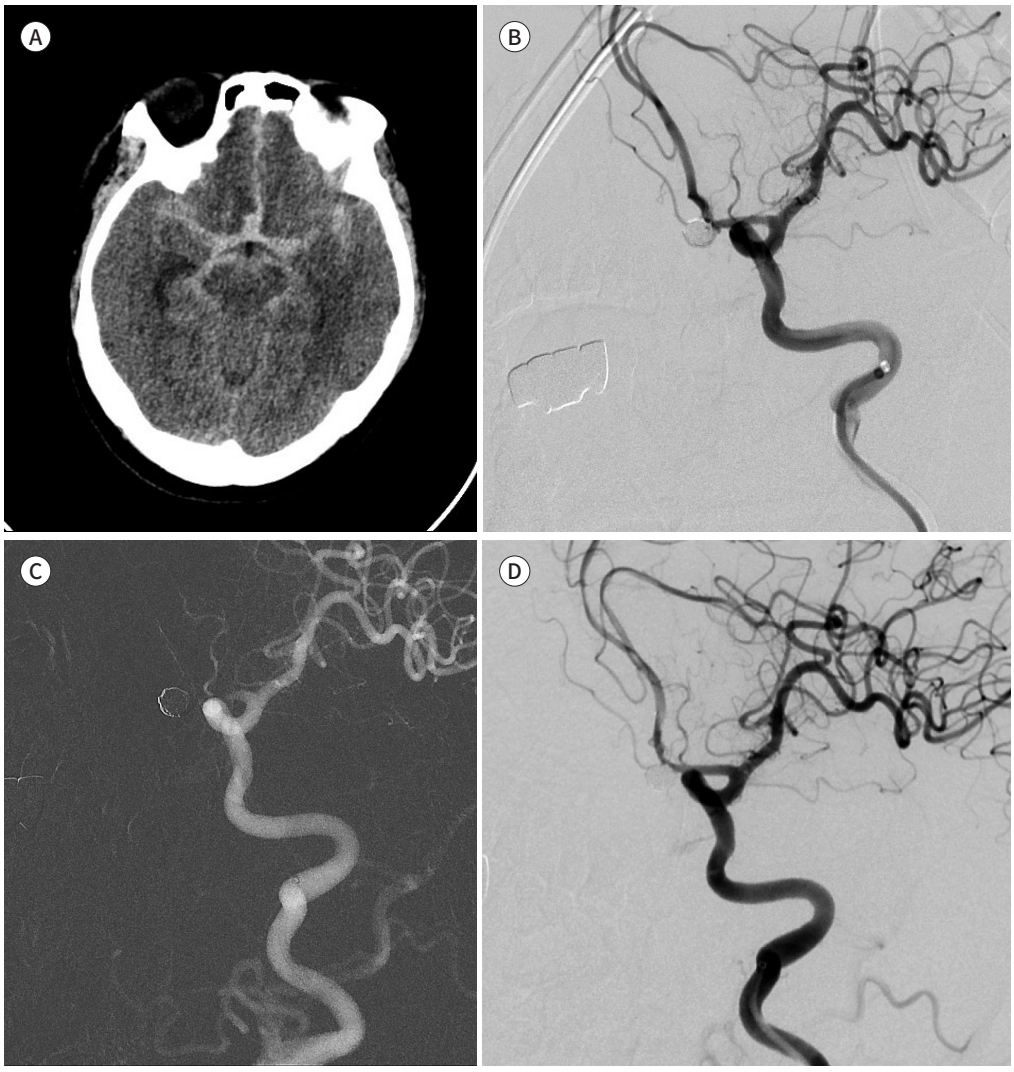
Data are presented as the number of patients (%) or mean ± standard deviation, unless otherwise indicated.
EVD = external ventricular drain, mRS = modified Rankin score, SAC = stent-assisted coil embolization

Table 2. Comparison of Radiologic Variables Between the SAC and Non-SAC Groups

Variables	SAC Group (n = 56)	Non-SAC Group (n = 62)	p-Value
Modified Fisher score			0.221
1–2	28 (50.0)	24 (38.7)	
3–4	28 (50.0)	38 (61.3)	
Neck, mm	3.83 ± 2.32	3.76 ± 1.96	0.859
Dome/neck ratio	1.17 ± 0.30	1.61 ± 0.68	0.0001
Aneurysm size, mm	5.49 ± 3.43	6.70 ± 3.96	0.079
Location			0.277
ICA	5 (8.9)	2 (3.2)	
P-Com.	9 (16.1)	17 (27.4)	
ACA	4 (7.1)	3 (4.8)	
A-Com.	21 (37.5)	23 (37.1)	
MCA	11 (19.6)	15 (24.2)	
PC	6 (10.7)	2 (3.2)	
Number of 6 months DSA	50 (89.3)	56 (90.3)	0.277
Recanalization on 6 months DSA	10 (20.0)	22 (39.3)	0.001

Data are presented as the number of patients (%) or mean ± standard deviation, unless otherwise indicated.
ACA = anterior cerebral artery, A-Com. = anterior communicating artery, Aneurysm size = maximum diameter of aneurysm, DSA = digital subtraction angiography, ICA = internal carotid artery, MCA = middle cerebral artery, PC = posterior circulation, P-Com. = posterior communicating artery, SAC = stent-assisted coil embolization

Fig. 2. A 55-year-old female who underwent a non-SAC procedure for ruptured aneurysm (Hunt & Hess grade 3).
A. The CT scan shows diffuse subarachnoid hemorrhage with modified Fisher grade IV.
B. The digital subtraction angiogram shows an embolized ruptured anterior communicating artery aneurysm using the non-SAC method.
C. Six hours later, the left A1 is occluded.
D. After intra-arterial thrombectomy with a stent retriever, left A1 and A2 are recanalized.
SAC = stent-assisted coil embolization

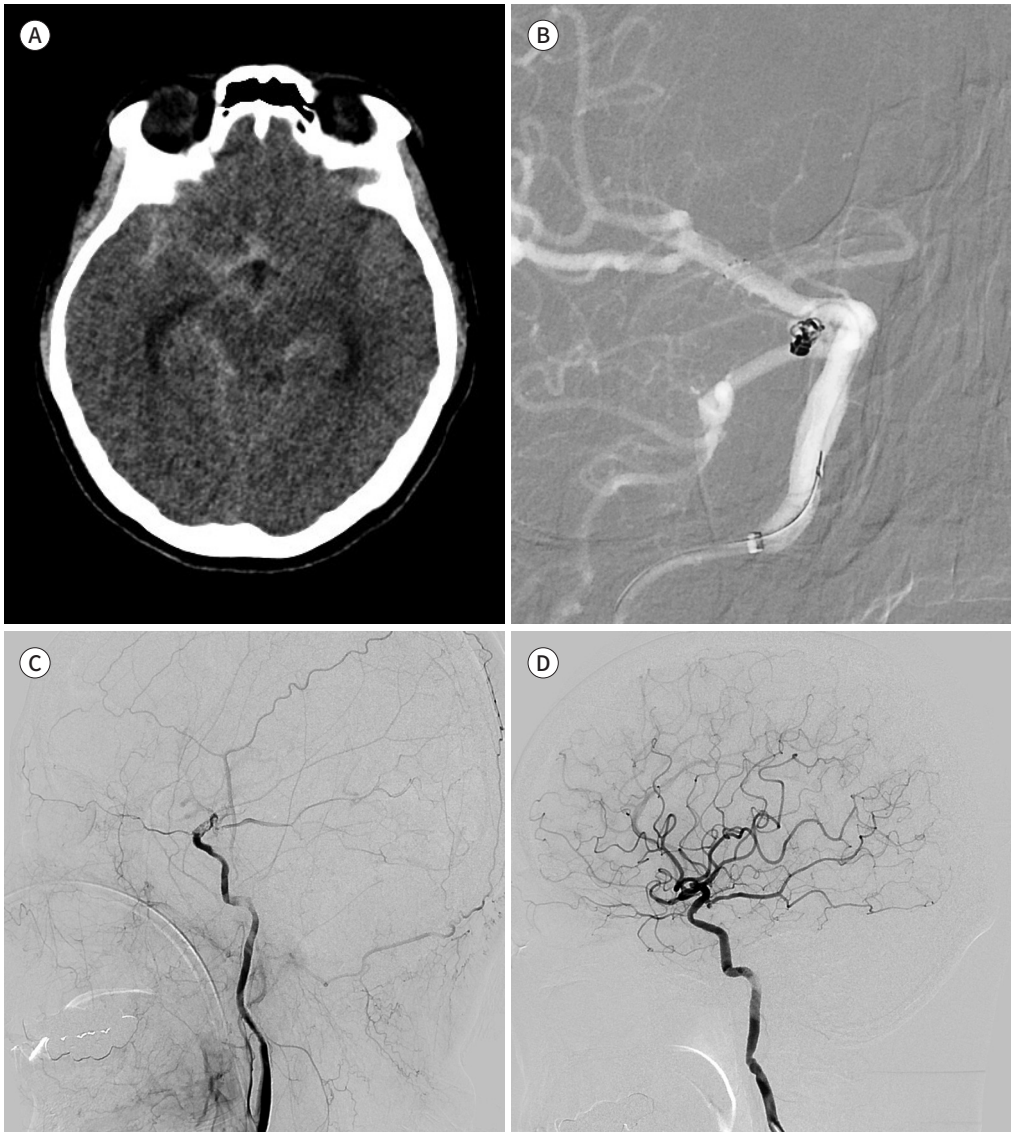


tient in the non-SAC group suffered an occlusion in the parent artery six hours after the coiling procedure and experienced recanalization after IA thrombectomy (Fig. 2).

In the SAC group, one case of total occlusion of parent artery was also occurred immediately after the procedure. We performed revascularization quickly and the outcome was good (6 months mRS was 1) (Fig. 3).

The rate of ischemic complications showed no significant difference (30.4% vs. 24.2%, p = 0.452). Neither did the rate of hemorrhagic complications show a significant difference (10.7% vs. 8.1%, p = 0.621). EVD was performed 9 patients (16.0%) in SAC group and 8 patients (12.9%) in non-SAC group (Table 1). A total of 3 EVD-related hemorrhage were ob-

Fig. 3. A 44-year-old female who underwent a SAC procedure for ruptured aneurysm (Hunt & Hess grade 3).
A. The CT scan shows diffuse subarachnoid hemorrhage with modified Fisher grade I.
B. The digital subtraction angiogram shows an embolized ruptured posterior communicating artery aneurysm using the SAC method.
C. Ninety minutes later, the right distal internal carotid artery is occluded.
D. After intra-arterial thrombolysis, the right internal carotid artery is recanalized.
SAC = stent-assisted coil embolization



served only in the SAC group, and all were asymptomatic.

In radiologic analysis, there was no significant difference in the amount of SAH according to modified Fisher score (Table 2). A six-month follow-up DSA was performed on about 90% of all patients, and the recurrence rate of coiled aneurysms was significantly lower in the SAC-treated group vs. the non-SAC treated group in spite of wide neck aneurysms: 20.0% vs. 39.3% ($p = 0.001$).

Table 3. Logistic Regression Model Assessing Risk Factors of Poor Clinical Outcomes (Modified Rankin Score ≥ 3)

Variables	Univariate Analysis			Multivariate Analysis		
	Odds Ratio	95% Confidence Interval	*p*-Value	Odds Ratio	95% Confidence Interval	*p*-Value
Age	1.068	1.017–1.120	0.008	1.054	0.994–1.118	0.077
Sex	0.867	0.297–2.534	0.794			
Hunt & Hess grade	1.249	0.544–2.872	0.600			
Stent	0.743	0.262–2.105	0.576	0.443	0.114–1.721	0.240
Complications						
Ischemic	6.984	2.314–21.079	0.001	9.187	2.321–36.368	0.002
Hemorrhagic	10.473	2.740–40.028	0.001	13.540	2.360–77.664	0.004
Modified Fisher score (3–4)	2.943	0.898–9.643	0.075	3.704	0.848–16.175	0.082
EVD	0.332	0.041–2.684	0.301			

EVD = external ventricular drain

RISK FACTORS FOR POOR CLINICAL OUTCOME

In a univariate analysis, age, hemorrhagic complications, and ischemic complications showed significance (Table 3). In a binary logistic regression analysis (multivariate analysis), only hemorrhagic and ischemic complications were independent predictors of poor clinical outcomes, whereas SAC and age were not.

DISCUSSION

Even though many studies have suggested that SAC has not been a significant risk factor for poor clinical outcome, the usefulness and safety of SAC has always been a critical issue in the coiling of ruptured aneurysms (7). Patients with ruptured aneurysms experience high mortality and permanent disability (8). Thirty-day case fatality rates range from 32% to 42%, and the dependency rate is approximately 50% among survivors. Therefore, the severity of the disease complicates the discussion of the safety of the stent itself in treating ruptured aneurysm. If patients with severe symptoms of Hunt & Hess grade 4 or 5 are included, it may be more difficult to predict the correct outcome of stents. In order to minimize the distortion of stent safety due to the high mortality of the condition, only patients with mild symptoms were included in this study.

Roh et al. (2), who studied the safety and usefulness of stents in ruptured aneurysm, found that stents were safe and useful even in mild symptoms below Hunt & Hess grade 3. However, a smaller number of cases were included and only discussed through subgroup analysis in the study.

Our study, which included only patients with mild symptoms, showed that there were no statistically significant differences in periprocedural ischemic or hemorrhagic complication, and clinical outcomes at 6 months between the SAC group and the non-SAC group. At 6 months DSA, the recurrence rate was lower in the SAC group. In multivariate analysis, hemorrhagic and ischemic complications were independent predictors of poor clinical outcomes, whereas SAC and age were not.

Our results suggest that ruptured aneurysm with mild symptom can be safely and feasibly

treated with SAC compared with non-SAC.

Although the use of dual antiplatelet agents is essential for SAC, there have been many issues on the administration of antiplatelet agents. The first issue is when to use antiplatelet agents, and the second issue is whether dual antiplatelet therapy is suitable for subsequent surgery such as EVD or decompression craniotomy.

Administration of antiplatelet agents before the procedure might reduce the risk of thromboembolism in SAC for ruptured aneurysms (9-14). Amenta et al. (9) loaded clopidogrel through a naso-gastric tube before procedures for patients with acutely ruptured aneurysms. The incidence of thromboembolism during surgery was 7.7% (5 patients), and the secondary bleeding rate following the administration of antiplatelet agents was also 7.7% (5 patients), of which 3 patients had fatal hemorrhage. In contrast, Choi et al. (7) loaded antiplatelet agents following the procedure. The rate of procedural thromboembolisms was 25.5%, and the rate of hemorrhagic complications was 9.1% in the SAC group. Despite a high rate of procedural thromboembolisms in patients who were given antiplatelet agents after the coiling, Choi et al. (7) reported that the proper use of tirofiban during procedure resulted in successful recanalization without subsequent hemorrhagic complications. Yoon et al. (15) found that either intra-arterial (IA) or intravenous (IV) tirofiban was useful in the treatment of thromboembolisms during coiling for ruptured aneurysms. However, the study also mentioned that the use of tirofiban may be dangerous for patients with intracerebral hematomas. Since ruptured aneurysms with mild symptoms are less likely to be associated with intracerebral hematomas, tirofiban may be safe to use for these aneurysms.

Since thromboembolisms can be safely resolved using IA tirofiban during the procedure, we suggest administering dual antiplatelet agents immediately after stent deployment rather than prior to the procedure.

However, in rare cases, delayed in-stent thrombosis may occur in SAC of ruptured aneurysm (Fig. 3). To prevent this, it is necessary to perform delayed angiography 10 to 20 minutes after SAC or to carefully observe the patient for at least 4 hours after administration of dual antiplatelet agents. EVD-related hemorrhages were more frequently reported in the SAC group than in the non-SAC group for acute ruptured aneurysms (16). EVD was performed in fewer patients in our study with mild symptoms than other studies that included all acute ruptured aneurysms. In a study by Roh et al. (2) that included all ruptured aneurysms, EVD was performed in approximately 26.7% of patients, but in our study, it was performed in only 14.4% (17/118) of patients. Most cases of ventricular drainage were performed via lumbar drainage in our study. In terms of EVD-related hemorrhage, SAC is considered safe in mild acute ruptured aneurysms compared to patients with severe symptoms, due to the reduced frequency of EVD.

There were several limitations in this study. First, the follow-up period of our study was 6 months, which is too short. This may not capture the additional complication related to stent use. Second, this study was limited by its retrospective design and single-clinic experience with a relatively small sample. Third, we did not compare the outcomes of ruptured aneurysms with mild symptoms against all ruptured aneurysm cases treated at our clinic, which would include cases with severe symptoms.

In this study, the use of stent was not significantly related with clinical outcomes in coil

embolization of ruptured cerebral aneurysms with mild symptoms (Hunt & Hess grade $\leq$ 3). The use of stent significantly decreased the rate of recanalization on follow-up cerebral angiograms.

Author Contributions

Conceptualization, S.S.H., K.S.C.; data curation, L.G., P.B.; formal analysis, L.G.; investigation, L.G., S.S.H.; methodology, S.S.H., P.B.; software, L.G.; supervision, S.S.H.; validation, L.T.Y., K.W.; visualization, L.G.; writing—original draft, S.S.H., L.G.; and writing—review & editing, L.T.Y., K.W.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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경미한 증상을 가지는 파열 뇌동맥류의 치료에 있어서 스텐트를 이용한 코일 색전술과 단순 코일 색전술의 비교: 단일 병원 경험

임가영[1] · 신상훈[1*] · 이태영[1] · 권운정[1] · 박병수[2] · 권순찬[3]

목적 심각한 증상이 없는 파열된 급성뇌동맥류에서 스텐트를 이용한 코일 색전술 기법의 안전성과 유효성을 평가하고, 지주막하출혈 환자에서 스텐트 자체의 유용성을 평가해 보고자 한다.

대상과 방법 2017년 1월부터 2019년 6월까지 심한 증상이 없는(헌트 앤드 헤스 등급 3 이하) 파열된 뇌동맥류에 대해 코일 색전술로 치료받은 118명의 환자를 대상으로 하였다. 스텐트를 사용한 56명과 스텐트를 사용하지 않은 62명에 대해 시술 이후 합병증, 6개월 수정 랜킨 척도, 6개월 영상의학적 결과에 대해 비교하였다.

결과 스텐트를 사용한 군과 스텐트 사용하지 않은 군에서 좋은 임상 결과의 비율(수정 랜킨 척도 2 이하)과 출혈성 및 허혈성 합병증의 비율은 유의한 차이를 보이지 않았다. 그러나 스텐트를 사용한 군은 6개월 추적 뇌혈관조영술에서 재개통률이 낮았다(20.0% 대 39.3%, p = 0.001).

결론 심한 증상이 없는(헌트 앤드 헤스 등급 3 이하) 파열된 뇌동맥류의 코일 색전술에서 스텐트의 사용은 임상 결과와 유의한 관련성이 없었다. 스텐트를 사용함으로써 추적 뇌혈관조영술에서 재개통률이 감소하였다.

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