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Original Article

Stent-Assisted Coil Embolization Using Only a Glycoprotein IIb/IIIa Inhibitor (Tirofiban) for Ruptured Wide-Necked Aneurysm Repair

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Objective : The aim of this study was to evaluate the safety and efficacy of stent-assisted coil embolization using only a glycoprotein IIb/IIIa inhibitor (tirofiban).

Materials and Methods : We retrospectively reviewed patients with a subarachnoid hemorrhage due to ruptured wide-necked intracranial aneurysms who were treated by stent-assisted coil embolization. In all patients, the glycoprotein IIb/IIIa inhibitor tirofiban was administered just before stent deployment. Electronic medical records for these patients were reviewed for peri-procedural complications and extra-ventricular drainage catheter related hemorrhage, as well as Glasgow outcome scale (GOS) at discharge, 3 months, and 6 months follow-up were recorded.

Results : Fifty-one aneurysms in 50 patients were treated. The mean patient age was 64.9 years. Eighteen patients (36%) received a World Federation of Neurosurgical Societies grade of 4 or 5. The mean aneurysm size was 9.48 mm and mean dome-to-neck ratio was 1.06. No intraoperative aneurysm ruptures occurred, although five (10%) episodes of asymptomatic stent thrombosis did occur. Three patients experienced a delayed thrombo-embolic event and two a delayed hemorrhagic event. Immediate radiologic assessment indicated a complete occlusion in 29 patients, a residual neck in 19, and a residual sac in 3. Four patients (8%) died. Sixteen patients (32%) experienced a poor GOS (< 4). Two aneurysms were recanalized during the follow-up period (mean, 19 months for clinical and 18 months for angiographic follow-up).

Conclusion : Treatment of ruptured wide-necked intracranial aneurysms via stent-assisted coil embolization with a glycoprotein IIb/IIIa inhibitor alone was found to be relatively safe and efficient.

Keywords Aneurysm, Subarachnoid hemorrhage, Endovascular procedures, Platelet Aggregation Inhibitors, Tirofiban, Stents

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INTRODUCTION

Endovascular treatment for aneurysm repair has become a widely used method since the publication of results from the International Subarachnoid Aneurysm Trial (ISAT).[23] The ISAT demonstrated the safety and

efficacy of this technique for the treatment of aneurysms. In wide-necked aneurysms and those with a smaller dome to neck ratio, endovascular coil embolization has some limitations and obstacles to overcome. These include an unstable coil loop and/or coil herniation from the aneurysm to a parent artery or distal arterial branch. Various attempts at overcoming this problem have included, for example, balloon-assisted coil embolization,[1)21)22)24)25)] the double catheter technique,[17)] and stent-assisted coil embolization (SAC).[2-5)12)18)20)27)28)] Among them, use of an intracranial stent to treat ruptured intracranial aneurysms is controversial. Complications resulting from the use of an intracranial stent in the setting of acutely ruptured aneurysm repair include transient or permanent thromboembolic event provocation. To prevent these thromboembolic events, peri- procedural antiplatelet, heparin, or glycoprotein IIb/IIIa inhibitors are typically administered. Antiplatelet/anticoagulant administration in the setting of an acutely hemorrhagic state may lead to additional hemorrhagic complications including aneurysm re-bleeding, extra-ventricular drainage (EVD)-related hemorrhage. Currently, there are no publicly-available guidelines for the use of peri-procedural antiplatelet/anticoagulant medications, nor have any randomized controlled trials evaluated the proper administration of these medications in this context. Many studies[2-5)12)14)18)20)27)28)] have examined the use of aspirin, clopidogrel, heparin, or glycoprotein IIb/IIIa inhibitors as peri-procedural medications. However, to the best of our knowledge, there are no studies of glycoprotein IIb/IIIa inhibitor administration alone as a prophylactic for thromboembolic events following the SAC of ruptured aneurysm (in the three known studies[12)19)28)] where a glycoprotein IIb/IIIa inhibitor has been used, heparin was also used). There are, however, several randomized controlled trials[10)11)13)26)30)] that have evaluated glycoprotein IIb/IIIa inhibitor use in ischemic disease (e.g., cerebral infarction and myocardial infarction). There are currently no studies examining whether glycoprotein IIb/IIIa inhibitor use is suitable in the SAC of ruptured aneurysms. In this study, a glycoprotein IIb/IIIa inhibitor, tirofiban, was used alone to prevent thromboembolic events. Tirofiban is a nonpeptide tyrosine derivative that acts as a platelet glycoprotein IIb/IIIa receptor antagonist.[9)] Our aim here was to evaluate the safety and efficacy of SAC of ruptured wide-necked intracranial aneurysms using only a glycoprotein IIb/IIIa inhibitor.

MATERIALS AND METHODS

Patients

We retrospectively reviewed all patients with a subarachnoid hemorrhage due to a ruptured wide-necked intracranial aneurysm, treated by SAC from April 2012 to March 2016 at our institution. We defined wide-necked aneurysms as those with a as neck size > 4 mm or with a dome-to-neck (D/N) ratio > 1.4. Fifty patients with a collective total of 51 aneurysms were enrolled. Ruptured dissecting aneurysm cases were excluded. Subarachnoid hemorrhage was measured according to Hunt and Hess (H-H) grade, the Fisher scale, and World Federation of Neurosurgical Societies (WFNS) grade. Aneurysms characteristics included location, sub-location, maximal diameter, neck size, and D/N ratio. After appropriate consultation, neurosurgeons and neuro-interventionists decided on either coil placement or surgical repair. Endovascular treatment (EVT), rather than clip placement, was preferred when the aneurysm affected posterior circulation or when the patient's medical condition was poor.

Procedure

EVT was performed by two experienced neuro-interventionists upon patient diagnosis with subarachnoid hemorrhage due to ruptured aneurysm. A unilateral or bilateral transfemoral approach was used. All EVTs were performed under general anesthesia. Neither pre-procedural nor intra-procedural antiplatelet, systemic heparinization agents were administered. Coil packing technique was determined based on the location and shape of the

aneurysm, size of dome, size of neck, and D/N ratio, although EVT was primarily performed via the double catheter technique.[17] A 7-F or 6-F guiding catheter was placed in a parent artery (internal carotid artery or vertebral artery) with continuous flushing with 5,000 U heparin per liter normal saline solution. Procedures were generally performed as follows. The most appropriate microcatheter and microwire were chosen for each individual case. When an initial frame was formed by first inserting a coil into the aneurysm sac, an additional microcatheter was placed in the aneurysm sac. Following this, the aneurysm sac was packed with the coil via the double catheter technique. In cases where this technique posed a challenge, however, the aneurysm was packed via the triple catheter technique. If there remained a high probability of coil herniation or migration to a parent artery or distal branch after coil packing, a stent was deployed through the aneurysm to adequately cover the aneurysmal neck. At the time of stent placement, the rupture point of the aneurysm was secured. After deployment of the stent, any remaining remnant aneurysmal sac area was packed with additional coil via the semi-jailing technique. Stents (Enterprise, LVIS Jr., LVIS, Solitare) were selected by neuro-interventionists on a case-by-case basis.

Peri-procedural glycoprotein IIb/IIIa inhibitor medication

Tirofiban was administered just before stent deployment in all cases. A loading dose (0.4 μg/kg/min) was maintained for 30 minutes. A maintenance dose (25 μg/kg) was then maintained for 23.5 hours for a total tirofiban administration time of 24 hours. Six hours prior to tirofiban administration cessation, aspirin (100 mg) and clopidogrel (75 mg) were administered via nasogastric tube or orally. Daily aspirin (100 mg) and clopidogrel (75 mg) were then maintained in all patients.

EVD

EVD catheters were placed prior to endovascular treatment, immediately upon detection of hydrocephalus via initial brain computed tomography (CT) and relatedly impaired consciousness. Following SAC, post-operative CTs were taken for all patients. In patients who did not initially undergo EVD catheter insertion, evidence of progressive hydrocephalus upon post-operative CT indicated EVD catheter insertion. EVD catheter insertion was also performed without cessation of tirofiban. No hemostatic agents such as tranexamic acid or vitamin K were used.

Outcomes and follow-up

Peri-procedural complications and EVD-related hemorrhage were retrospectively detected by electronic medical record (EMR) review. Clinical outcome was assessed via patients' EMR-reported Glasgow outcome scale (GOS) scores at discharge and 3 and 6 months post-discharge. Radiologic follow-up was conducted at 6 months, 1 year, and 2 years post-discharge. Follow-up imaging studies were retrospectively reviewed via a picture archiving and communication system. Follow-up imaging modalities included magnetic resonance angiography or transfemoral cerebral angiography. We evaluated the recurrence of aneurysm (major or minor) using the Raymond scale.

RESULTS

Patients demographics

Fifty-one aneurysms in 50 patients were treated between April 2012 and March 2016. Among them, nine patients were male (18%) and 41 were female (82%) (Table 1). Mean patient age was 64.9 years (range, 16-89). Four patients (8%) presented with a Hunt-Hess grade I, 23 (46%) with a grade II, four (8%) with a grade III, 11 (22%) with a grade IV, and eight (16%) with a grade V. Four patients (8%) presented with a Fisher grade I, seven (14%) with a grade II, 11 (22%) with a grade III, and 28 (56%) with a grade IV. Twenty-three patients (46%) presented with a WFNS grade I, eight (16%) with a grade II, one (2%) with a grade III, four (8%) with a grade IV, and 14 (28%) with a grade V (Table 2). Twenty-four patients (48%) had a history of hypertension, two (4%) a history of

diabetes, and 10 (20%) a history of dyslipidemia. Six patients (12%) reported smoking while seven (14%) reported drinking (Table 1).

Aneurysm characteristics

Diameter, neck size, and D/N ratio of aneurysms were measured. The mean maximal diameter of the aneurysms was 9.48 mm (range, 3-23). Mean aneurysm neck size was 5.43 mm (range, 3-10). The mean D/N ratio was 1.06 (range, 0.42-3.82) and the most common aneurysm location was in the anterior circulation (anterior circulation 82%, posterior circulation 18%) (Table 3).

Complications

We divided reported complications between two groups: procedure-related and delayed. We defined procedure-related complications as an aneurysm rupture during SAC, hemorrhagic events, or thromboembolic events. When a thromboembolic event occurred during the procedure, intra-arterial glycoprotein IIb/IIIa inhibitor injection or observation were performed on a case-by-case basis. No intra-procedural aneurysm ruptures or hemorrhagic events were reported. However, 5 asymptomatic in-stent thrombosis events (10%) were reported. Delayed complications were defined as hemorrhagic and thromboembolic events following the procedure. Five patients suffered from delayed complications (Table 3). These included 2 hemorrhagic events and 3 thromboembolic events.

EVD-related hemorrhage

Seventeen cases involved EVD catheter insertion. EVD catheters were inserted in 11 cases prior to SAC and in 6 after SAC. Four (23.5%) EVD-related hemorrhagic events occurred, though all were asymptomatic and none resulted in neurologic deficits. Two of the 4 EVD-related hemorrhage cases underwent EVD insertion before SAC and the other 2 underwent EVD insertion after SAC (Table 4).

A complicated case

Among all the cases studied here, one was particularly complex and deserves specific attention. A 53-year-old man was admitted for treatment of subarachnoid hemorrhage. He was initially reported to have a mental state indicative of coma (WFNS grade V). CT angiography revealed a 15 mm anterior communicating artery aneurysm with bleb. After SAC was performed, thrombosis formation in Enterprise stent and delayed filling of left A2 segment were detected. Intra-arterial tirofiban was administered and vessel patency restored. Ten days post-operation, the patient experienced upper gastro-intestinal bleeding. Follow-up angiography 6 months later showed major recanalization of the previously coiled aneurysm. Retreatment of the recanalized aneurysm was performed (Fig. 1).

Table 1. Patients demographics

Characteristic	Value
Age (years)	64.9 (16-89)
Sex (M/F)	9:41
Comorbidity	
HTN	24 (48)
DM	2 (4)
Dyslipidemia	10 (20)
Smoking	6 (12)
Alcohol	7 (14)

Values are presented as mean (range) or number (%).
M = male; F = female; HTN = hypertension; DM = diabetes mellitus.

Table 2. SAH grade on admission at emergency room

	I	II	III	IV	V
H-H grade	4 (8)	23 (46)	4 (8)	11 (22)	8 (16)
Fisher scale	4 (8)	7 (14)	11 (22)	28 (56)	
WFNS grade	23 (46)	8 (16)	1 (2)	4 (8)	14 (28)

Values are presented as number (%).
SAH = subarachnoid hemorrhage; H-H grade = Hune-Hess grade; WFNS grade = World Federation of Neurosurgical Societies grade.

Table 3. Clinical characteristics and complication of patients and aneurysms

No.	Age/ sex	H-H grade	Fisher scale	Sub-location of Aneurysm	Maximal diameter	Neck size	D/N ratio	Thromboembolic event	Delayed thromboembolic event	Bleeding event	GOS at discharge
1	80/F	3	3	PComA	9.0	5.0	1.4	-	-	-	5
2	64/F	2	3	PComA	10.0	5.9	1.5	-	-	-	5
3	65/F	2	3	PCA	13.0	9.0	1.3	-	-	-	5
4	79/F	2	2	ICA-PARACLINOID	14	5.5	3.8	-	Embolic infarction at POD 11	ICH	5
5	70/M	4	4	PCA	6.55	3.9	0.7	-	-		4
6	16/F	3	4	A2/3 Jx.	7.1	3.4	2.1	-	-		3
7	81/F	4	4	PComA	12	7.5	0.9	-	-		2
8	48/M	1	2	AComA	6	3.1	1.0	In stent thrombosis	-		5
9	47/F	2	3	A2	5.0	2.5	0.6	-	Embolic infarction at POD 1		4
10	64/M	2	4	AComA	6.1	3.7	1.2	-	-		2
11	56/F	2	4	VA	7.4	7.8	0.6	-	-		5
12	89/F	4	4	PComA	12.3	9.1	0.8	-	-		3
13	56/F	2	4	AComA	7	3.7	0.7	-	-		5
14	58/F	2	1	MCAB	11	6.7	1.3	-	-		5
15	77/F	2	4	MCAB	7	4.9	0.5	-	-		1
16	45/M	2	4	AComA	11	7.1	0.9	-	-		4
17	67/F	2	4	PComA	11	5.6	0.8	In stent thrombosis	-		4
18	76/F	4	4	ICA	23	7.6	1.3	In stent thrombosis	-		1
19	60/F	2	4	PComA	17	11.3	1.0	-	-		4
20	74/F	5	4	ICA-ACHA	8.0	3.8	1.0	-	-		2
21	71/F	2	3	BAbif	11.0	6.5	1.1	-	-		5
22	86/F	2	1	AComA	6	4.6	0.6	-	-		5
23	77/F	2	4	AComA	5.2	2.6	1.1	-	-		2
24	53/M	4	3	AComA	15	8.3	1.0	In stent thrombosis	-	UGI bleeding	4
25	57/M	4	4	AComA	14	7.8	1.0	-	-		1
26	44/F	5	4	AComA	12	7.0	1.1	-	-		5
27	44/F	4	4	PICA	10	6.0	1.1	In stent thrombosis	-		5
28	56/F	4	4	AComA	12.9	6.3	1.9	-	-		4
29	77/F	4	4	ICA-PARACLINOID	17.0	7.1	1.3	-	-		1
				ICA-PARACLINOID	5.0	2.8	1.3	-	-		
30	80/F	3	4	AComA	7	4.1	0.7	-	-		3
31	47/F	2	3	BAbif	9.21	4.1	1.7	-	-		5
32	70/F	4	4	AComA	12	6.4	0.6	-	-		3
33	48/F	2	2	PComA	11	5.2	0.9	-	-		5
34	56/M	2	2	BAbif	4.4	2.6	1.2	-	-		5
35	78/F	2	2	MCAB	5.1	3.5	0.5	-	-		5
36	80/F	5	4	A2/3 Jx.	13	6.4	1.1	-	-		2
37	41/F	3	3	ICA-PARACLINOID	6.1	4.8	0.7	-	Embolic infarction at POD 14		3
38	82/F	2	1	AComA	11	6.8	0.9	-	-		5
39	70/F	5	4	AComA	5.1	2.9	0.9	-	-		4
40	57/F	1	1	A2/3 Jx.	10.5	4.6	0.9	-	-		5
41	59/M	1	2	AComA	8.5	4.6	1.1	-	-		4
42	69/M	5	4	AComA	5.03	2.8	1.0	-	-		4
43	63/F	5	4	AComA	6.1	3.9	1.0	-	-		5
44	87/F	4	3	PICA	3.3	3.3	0.4	-	-		3
45	60/F	2	3	AComA	5.1	4.2	0.7	-	-		5
46	77/F	2	2	PComA	10.2	6.0	1.2	-	-		5
47	59/F	5	4	BAbif	12.0	7.8	1.1	-	-		5
48	77/F	2	4	AComA	7.1	4.4	1.1	-	-		4
49	85/F	1	4	AComA	10.0	6.2	0.6	-	-		3
50	53/F	5	3	PComA	10.1	5.5	1.2	-	-		5

H-H grade = Hunt-Hess grade; D/N ratio = dome to neck ratio; GOS = Glasgow outcome scale; F = female; PComA = posterior communicating artery; PCA = posterior cerebral artery; ICA = internal carotid artery; POD = post-operative day; ICH = intracerebral hemorrhage; M = male; Jx. = junction; AComA = anterior communicating artery; VA = vertebral artery; MCAB = middle cerebral artery bifurcation; ACHA = anterior choroidal artery; BAbif = basilar artery bifurcation; UGI bleedin = upper gastr-intestinal bleeding; PICA = posterior inferior cerebellar artery.

Table 4. EVD related hemorrhage

No. of EVD cath. insertion	EVD cath. insertion before SAC	Hemorrhage in EVD cath. insertion before SAC	EVD cath. insertion after SAC	Hemorrhage in EVD cath. insertion after SAC
17	11	2	6	2

EVD = extra-ventricular drainage; cath. = catheter; SAC = stent-assisted coil embolization.

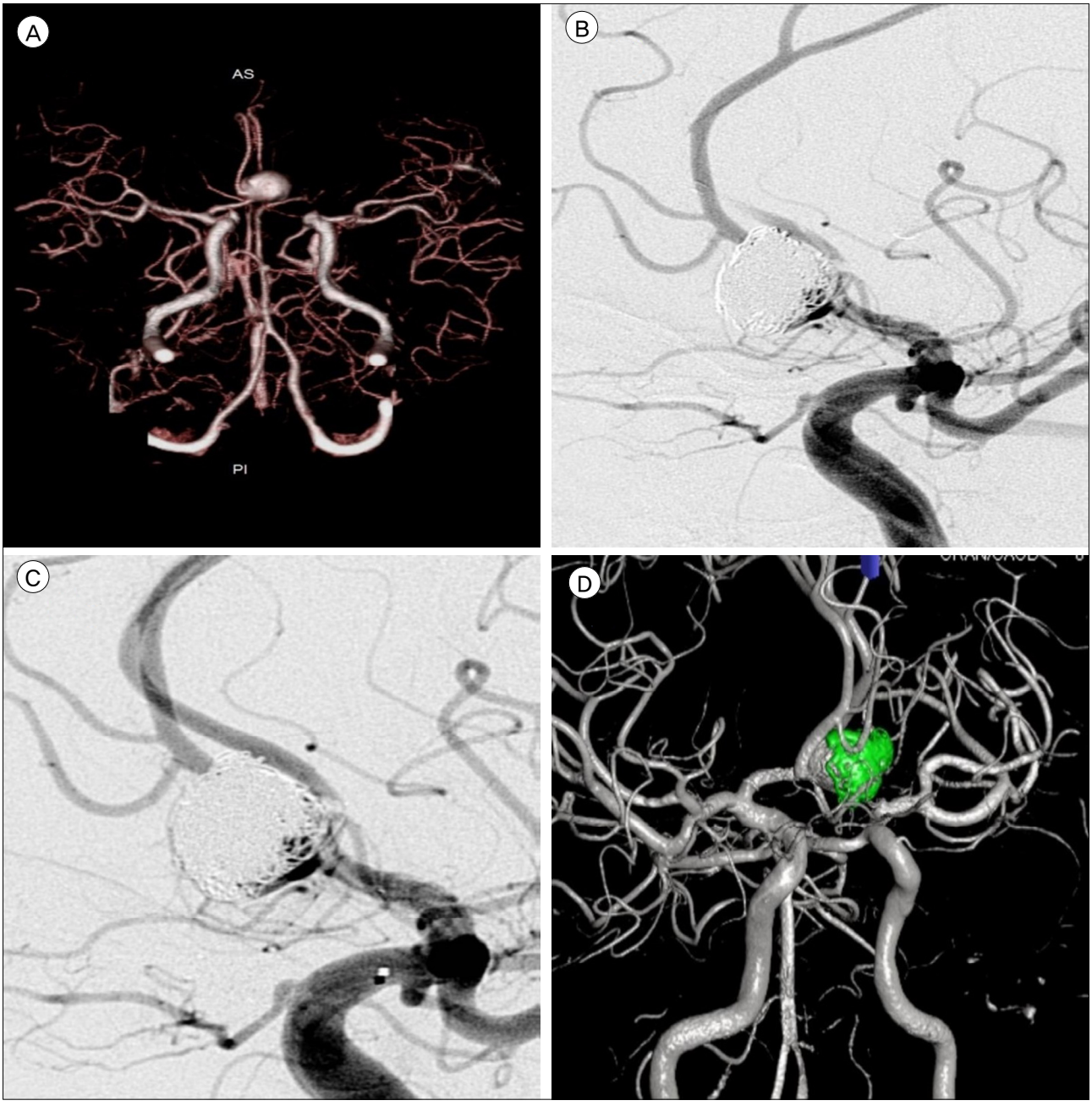

Fig. 1. 53-year-old man was admitted with subarachnoid hemorrhage. His initial mentality was coma (WFNS Gr V). (A) CTA showed 15mm sized AcomA aneurysm with bleb. (B) After SAC was performed, thrombosis formation in Enterprise stent and delayed filling left A2 was detected. (C) IA Tirofiban was administered and patency of the vessel was restored. At postoperative 10 days, He suffered UGI bleeding. (D) Follow-up angiography 6 months later showed major recanalization of previous coiled aneurysm. Retreatment of recanalized aneurysm was done. WFNS Gr = World Federation of Neurosurgical Societies grade; CTA = computed tomography angiography; AComA = anterior communicating artery; SAC = stent-assisted coil embolization; IA = intra-arterial; UGI bleeding = upper gastro-intestinal bleeding.

Immediate angiographic results and clinical outcomes

The Raymond scale was used to evaluate angiographic results. Twenty-nine patients received a Raymond scale I (complete occlusion) rating, 19 a Raymond scale II (residual neck), and 3 a Raymond scale III (residual sac). The mortality rate was 8% (four patients). Three patients died due to malignant brain swelling and one patient due to pneumonia. Sixteen (32%) patients had a poor GOS (<4) (Table 5).

Follow-up

The mean duration to final clinical follow-up was 19 months (41 patients). The other nine patients were lost to follow-up due to death or transfer to another hospital. During the follow-up period, eight patients experienced improved GOS (Table 5). The mean duration to angiographic follow-up was 18 months (31 patients). Recanalization of coiled aneurysms was required for two patients upon follow-up. One of these was a minor recanalization while the other was more significant. Retreatment was performed for this major recanalization case.

DISCUSSION

The publication of the randomized controlled ISAT[23] established EVT as a safe and effective therapeutic option. Therefore, treatment of aneurysms by EVT experienced increased popularity. However, when performing EVT, the catheter may act as a contact activator of the coagulation cascade, leading to thromboembolic events and significant thromboembolic risk.[8] The same is true of cases of subarachnoid hemorrhage due to a ruptured aneurysm. In the acute phase of subarachnoid hemorrhage, a hypercoagulable state occurs.[27] Unlike in EVT of unruptured aneurysms, pre-procedure antiplatelet medications are not administered to these patients, leading to an elevated risk of thromboembolic events. The use of stents in the treatment of wide-necked aneurysms increases the likelihood of thromboembolic events, such as in-stent thrombosis formation. Multiple studies[2-5)7)12)18)20)27)28] of the peri-procedural administration of aspirin, clopidogrel, heparin, or a glycoprotein IIb/IIIa inhibitor

Table 5. Clinical and radiologic outcome

No.	GOS at discharge	GOS at 3 months	GOS at 6 months	Raymond grade
1	5	5	5	N
2	5	5	5	N
3	5	5	5	C
4	5	5	5	C
5	4	5	5	C
6	3	Follow-up loss	Follow-up loss	C
7	2	Follow-up loss	Follow-up loss	C
8	5	5	5	C
9	4	5	5	C
10	2	2	2	C
11	5	5	5	C
12	3	3	3	C
13	5	5	5	S
14	5	5	5	C
15	1	1	1	C
16	4	5	5	C
17	4	5	5	N
18	1	1	1	C
19	4	5	5	N
20	2	Follow-up loss	Follow-up loss	C
21	5	5	5	C
22	5	5	5	S
23	2	Follow-up loss	Follow-up loss	C
24	4	5	5	N
25	1	1	1	C
26	5	5	5	N
27	5	5	5	N
28	4	4	4	N
29	1	1	1	N C
30	3	Follow-up loss	Follow-up loss	N
31	5	5	5	N
32	3	Follow-up loss	Follow-up loss	N
33	5	5	5	N
34	5	5	5	C
35	5	5	5	N
36	2	Follow-up loss	Follow-up loss	N
37	3	4	4	C
38	5	5	5	C
39	4	4	4	C
40	5	5	5	N
41	4	5	5	N
42	4	4	4	N
43	5	5	5	C
44	3	Follow-up loss	Follow-up loss	C
45	5	5	5	C
46	5	5	5	C
47	5	5	5	S
48	4	5	5	C
49	3	Follow-up loss	Follow-up loss	C
50	5	5	5	N

GOS = Glasgow outcome scale; C = complete occlusion; N = residual neck; S = residual sac.

during EVT to prevent the occurrence of a thromboembolic event have been conducted, but there are no established guidelines for the use of these drugs in this surgical context. In most studies, systemic heparinization was performed with pre and/or intra-procedural aspirin and clopidogrel for the prevention of thromboembolic events. Glycoprotein IIb/IIIa inhibitors have also been used systemically to prevent thromboembolic events.[12)19)28)] Bruening et al.[5)] describe intravenous or intra-arterial injection of glycoprotein IIb/IIIa inhibitors upon the occurrence of thromboembolic events such as in-stent thrombosis or defective parent artery filling. However, as far as are aware, the present study was the first to examine tirofiban administration in SAC without pre- or intra-procedural aspirin, clopidogrel, or systemic heparinization. Although Liang et al.[19)] reported on the safety and efficacy of tirofiban administration in coil embolization of ruptured aneurysms, they included single coiling without stent deployment. The present study examines only coil embolization with stent deployment. Furthermore, in the present study there was no pre- or intra-procedural aspirin or clopidogrel administration. Tirofiban was loaded just before stent deployment and its administration was maintained for 24 hours. Tirofiban loading and procedures such as stent deployment, additional coil packing were simultaneously performed. Since onset time of tirofiban is rapid, it seems to be enough to prevent the thromboembolic event with tirofiban. While intra-procedural administration of tirofiban may reduce thromboembolic events, it seems likely to increase the likelihood of intra-procedural rupture. However, in the present study, there were no intra-procedural aneurysm ruptures reported. When bleeding occurs due to an aneurysm rupture, platelets aggregate and form a thrombus at the aneurysm rupture site which can stop bleeding. A platelet-rich thrombus might dissolve upon tirofiban administration when the aneurysm is not secured as tirofiban acts to break the dihydrogen sulfate bonds between platelets.[29)] This eventually contributes to an increased risk for aneurysm re-bleeding. To avoid this potentially catastrophic outcome, in the present study, tirofiban was loaded just prior to stent deployment but after the coil was packed in the rupture site to ensure against re-bleeding. As such, we concluded that no intra-procedural ruptures of aneurysms occurred in our cohort of patients because of tirofiban inhibitor loading prior to securing of aneurysms. If tirofiban had been administered prior to this, aneurysm re-bleeding would have occurred. On the other hand, if tirofiban was administered late, thromboembolic event would have occurred. Tirofiban has some practical advantages over other preventive medications. When used as pre-procedural medications, antiplatelet agents (aspirin and clopidogrel) have to be administered enterally. Alert, conscious patients can take an antiplatelet agent orally, though this requires consumption of a small amount of water. Consumption of any foods or liquids prior to receiving general anesthesia, which can lead to vomiting during intubation or extubation, is associated with an increased risk of aspiration pneumonia. However, if the procedure is delayed to allow for sufficient fasting time before general anesthesia administration, aneurysm re-bleeding risk increases. Additionally, to achieve intra-procedural administration of these drugs, an additional, troublesome nasogastric tube must be inserted. In unconscious patients, nasogastric tube insertion prior to the procedure is necessary for administration of an antiplatelet agent. Nasogastric tube insertion induces the gag reflex and consequently increases blood pressure and intracranial pressure. This also leads to an increased risk of aneurysm re-bleeding. Unlike the difficulties faced in administering these drugs, tirofiban can be simply and conveniently administered intravenously. The short, 1.5-hour half-life of tirofiban[9)16)] provides an additional practical advantage over other, longer-lived antiplatelet and anticoagulant agents. Should hemorrhagic complications occur during or after the procedure, this shorter half-life allows for decreased exacerbation of hemorrhagic complications. When thromboembolic complications do occur, there

is an advantage in applying the same substance previously infused intravenously via intra-arterial injection to treat thromboembolisms. Alurkar et al.[2] previously reported two cases with intra-procedural, in-stent thrombosis treated by intra-arterial injection of glycoprotein IIb/IIIa inhibitor without any resultant neurologic deficits. Cho et al.[6] and Kim et al.[15] have also reported on the safety and efficacy of intra-arterial tirofiban injection to treat thromboembolic events during EVT of ruptured aneurysms. Likewise, when intra-procedural thromboembolic events occurred in the present study cohort, we also obtained good results from the use of intra-arterial tirofiban injection—only five cases of intra-procedure thromboembolic events despite tirofiban use were identified. All of these events comprised in-stent thrombosis, where intra-arterial glycoprotein IIb/IIIa inhibitor injection was done on a case-by-case basis. When delayed contrast filling occurred due to thrombosis formation in one patient, vessel patency was restored with intra-arterial injection of tirofiban. Although just one case, this evidences the safety and efficacy of intra-arterial injection of tirofiban.

While there were no cases of intra-procedural aneurysm rupture reported here, it is critical to note that hemorrhagic complications beyond aneurysm re-bleeding may occur with anticoagulant use. Extra-cranial hemorrhagic complication such as complicated hematoma or gastro-intestinal bleeding may occur. In the present study, there were no cases of complicated hematoma, though one case of upper gastro-intestinal bleeding and one case of delayed intracerebral hemorrhage which was not related to aneurysm were reported. Despite the concern that tirofiban use in the acute phase of SAH may lead to intra-procedural rupture of aneurysms, tirofiban proved to be a relatively safe and efficacious medication for the prevention of thromboembolic complications.

This study has several limitations. First, it uses a retrospective design and is therefore subject to selection bias. Second, it results from data collected at a single center study with a relatively small patient population which does not provide the power to ensure the broader safety and efficacy of tirofiban. Finally, this study faces the limitation that it contains no true control group as all patients were prescribed tirofiban, as is dictated by best clinical practice guidelines at our institution. While other medical centers may use a glycoprotein IIb/IIIa inhibitor, centers cannot universally treat patients identically as various procedural and clinical factors (e.g., endovascular procedure technique used, neuro-interventionist competence and experience, etc.) will differ.

CONCLUSION

There is concern about the exclusive use of tirofiban to prevent thromboembolic events in stent-assisted coil embolization. However, in the present study, we report the outcomes of ruptured wide-necked intracranial aneurysms treated with SAC with tirofiban alone and conclude that its use is both relatively safe and therapeutically efficient.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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