



Full length article

Impact of antithrombotic treatment on clinical outcomes after craniotomy for unruptured intracranial aneurysm



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ABSTRACT

Objective: Patients receiving antithrombotic treatment occasionally undergo craniotomy. We aimed to explore the impact of perioperative use of antithrombotic agents on the occurrence of surgical complications and clinical outcomes in patients with unruptured intracranial aneurysm (UIA).

Patients and methods: We retrospectively analyzed 401 consecutive patients who had undergone craniotomy for UIA at our institution between January 2006 and December 2016. Patients were divided into two groups: those who received oral antiplatelet and/or anticoagulant agents during the perioperative period (antithrombotic treatment group, $n = 45$); and those who did not (no antithrombotic treatment group, $n = 356$). In the antithrombotic treatment group, 40 patients received antiplatelet alone, 2 received anticoagulant alone, and 3 received antiplatelet plus anticoagulant.

Results: The two groups showed no significant differences in mortality, morbidity, or occurrence of symptomatic brain infarction, but intracranial hemorrhage was more frequent in the antithrombotic treatment group than in the no antithrombotic treatment group ($p = 0.0187$). Multivariate analysis revealed posterior location of the aneurysm (odds ratio (OR), 8.10; 95% confidence interval (CI), 2.77–23.68; $p = 0.0001$) and surgical procedure (OR, 5.48; 95%CI, 1.68–17.86; $p = 0.0048$) as significantly correlated with severe morbidity, and intracranial hemorrhage as correlated significantly with antithrombotic treatment (OR, 3.83; 95%CI, 1.36–10.76; $p = 0.0110$).

Conclusions: This study provides important information about the occurrence of intracranial hemorrhage and clinical outcomes in patients undergoing antithrombotic treatment during the perioperative period of craniotomy for UIA.

1. Introduction

Patients with cardiovascular disease are increasing worldwide [1], and some patients harboring unruptured intracranial aneurysms (UIAs) require antithrombotic treatment for cerebrovascular or cardiovascular risks. The use of antithrombotic agents may make subarachnoid hemorrhage lethal during conservative management, and can increase the risk of hemorrhage associated with craniotomy or endovascular management. Temporary interruption of antithrombotic agents during periprocedural period may reduce bleeding complications, but can also induce thromboembolic complications. Rates of mortality, morbidity, and intracranial hemorrhage or ischemic stroke in craniotomy for UIA in patients undergoing perioperative antithrombotic treatment remain

unclear.

The present study was therefore undertaken to explore the impact of the perioperative use of antithrombotic agents on the occurrence of surgical complications and clinical outcomes in patients with UIA.

2. Patients and methods

2.1. Patients

We retrospectively included consecutive patients with UIAs who were treated surgically between January 2006 and December 2016 at our institution. All surgeries were performed by experienced vascular neurosurgeons. Clinical data on patients were obtained by retrospective

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chart review including age, sex, medical history, perioperative use of antithrombotic agents, location and size of aneurysm, multiplicity of aneurysm, operative procedure, postoperative neurological and imaging findings, and modified Rankin scale (mRS) at admission and discharge. Patients were divided into two groups: patients taking oral antiplatelet or anticoagulant for cerebrovascular or cardiovascular risks during the perioperative period of UIA surgery (antithrombotic treatment group) and those who were not (no antithrombotic treatment group).

2.2. Adverse events

Mortality was defined as any-cause death within 30 days after surgery. Morbidity was evaluated at discharge. Severe morbidity was defined as a decrease in mRS score ≥ 2 , and minor morbidity as a decrease in mRS score of 1. Postoperative intracranial hemorrhage was defined as any intracerebral or subarachnoid hemorrhage, or symptomatic epi- or subdural hematoma revealed by computed tomography on the day of or the day after surgery. Symptomatic brain infarction was defined as any newly developed neurological symptom with a hyperintense lesion apparent on postoperative diffusion-weighted imaging. Mortality, morbidity, intracranial hemorrhage, and symptomatic brain infarction were considered as adverse events.

2.3. Statistical analysis

Statistical analysis was performed using JMP (JMP version 13; SAS Institute, Cary, NC). Continuous data are expressed as mean \pm standard deviation. Mean ages of patients in the antithrombotic and no antithrombotic treatment groups were compared using Student's *t*-test. Pearson's chi-square test or Fisher's exact test were used to compare categorical variables. Logistic regression models were used to evaluate independent associations between variables and severe morbidity or intracranial hemorrhage. Values of $p < 0.05$ were considered statistically significant.

3. Results

3.1. Patient characteristics

Overall, 401 patients (281 women, 120 men) were enrolled in this study, with a mean age of 61.8 ± 10.2 years (range, 28–83 years) (Table 1). Forty-five patients (11.2%) received oral antiplatelet and/or anticoagulant agents during the perioperative period (antiplatelet, $n = 40$; anticoagulant, $n = 2$; antiplatelet plus anticoagulant, $n = 3$). No patients received dual antiplatelets. Mean pre-hospitalization mRS was 0.25 ± 0.67 in the no antithrombotic treatment group and 0.51 ± 0.83 in the antithrombotic treatment group ($p = 0.0200$). The underlying cause of antiplatelet treatment was prior brain infarction (58.1%), followed by coronary disease (27.9%), transient ischemic attack (4.7%), internal carotid artery stenosis (4.7%), hypertrophic cardiomyopathy (2.3%), and unknown (2.3%). Anticoagulation was administered for chronic atrial fibrillation (40.0%), paroxysmal atrial fibrillation (20.0%), prior brain infarction (20.0%), or unknown cause (20.0%). The CHA₂DS₂-VASc score [2] in patients with atrial fibrillation was 3, 3, or 5. Aspirin was the most commonly used antiplatelet, followed by clopidogrel and cilostazol. Warfarin was used for all 5 patients who received anticoagulant. In these anticoagulated patients, bridging anticoagulation with heparin was used during the perioperative period. Mean duration of preoperative interruption of warfarin was 5.6 ± 1.5 days, and mean duration of bridging anticoagulation was 9.4 ± 7.1 days. Mean PT-INR just before starting bridging anticoagulation was 2.09 ± 0.14 . Antiplatelets were temporarily interrupted at a mean of 5.6 ± 3.0 days before surgery in 28 of the 43 patients receiving antiplatelet treatment. Antiplatelets were discontinued after surgery in three patients. One patient who did not take

Table 1

Baseline characteristics in patients with unruptured intracranial aneurysm by perioperative antithrombotic treatment.

	Overall (n = 401)	Antithrombotic treatment (n = 45)	No antithrombotic treatment (n = 356)	P
Age, mean (SD)	61.8 (10.2)	67.6 (6.0)	61.1 (10.4)	< 0.0001
Female	281 (70.1%)	34 (75.6%)	247 (69.4%)	0.3861
Medical history				
Brain infarction	35 (8.7%)	25 (55.6%)	10 (2.8%)	< 0.0001
TIA	5 (1.3%)	4 (8.9%)	1 (0.28%)	0.0003
ICA stenosis	3 (0.8%)	2 (4.4%)	1 (0.28%)	0.0221
MCA occlusion	6 (1.5%)	4 (8.9%)	2 (0.56%)	0.0011
Coronary disease	16 (4.0%)	12 (26.7%)	4 (1.1%)	< 0.0001
Chronic Af	2 (0.5%)	2 (4.4%)	0	0.0030
Paf	2 (0.5%)	1 (2.2%)	1 (0.28%)	0.1732
HCM	2 (0.5%)	2 (4.4%)	0	0.0030
Valvular disease	3 (0.8%)	1 (2.2%)	2 (0.56%)	0.3072
DVT	0	0	0	
Hypertension	233 (58.1%)	38 (84.4%)	195 (54.8%)	< 0.0001
Diabetes mellitus	24 (6.0%)	9 (20.0%)	15 (4.2%)	0.0005
Dyslipidemia	100 (24.9%)	22 (48.9%)	78 (21.9%)	0.0002
Cancer	21 (5.2%)	5 (11.1%)	16 (4.5%)	0.0933
End-stage RF	3 (0.8%)	1 (2.2%)	2 (0.56%)	0.3072
FH of aneurysm	38 (9.5%)	1 (2.2%)	37 (10.4%)	0.0399
History of SAH	8 (2.0%)	1 (2.2%)	7 (2.0%)	0.9079

Values are expressed as number (percentages) unless otherwise indicated.

TIA, transient ischemic attack; ICA, internal carotid artery; MCA, middle cerebral artery; Af, atrial fibrillation; Paf, paroxysmal atrial fibrillation; HCM, hypertrophic cardiomyopathy; DVT, deep vein thrombosis; RF, renal failure; FH, family history; SAH, subarachnoid hemorrhage.

any antiplatelet before surgery was started on antiplatelet treatment after surgery. Mean duration of perioperative interruption of antiplatelets was 10.6 ± 7.9 days.

3.2. Aneurysm characteristics

Overall, the most common aneurysm location was the MCA, followed by the internal carotid artery and anterior communicating artery (Table 2). Thirty-nine aneurysms (9.7%) were located in the posterior circulation, while 362 (90.3%) were located in the anterior circulation. The most frequent aneurysm size was 5–6 mm, followed by 3–4 mm and 7–9 mm. Ninety-four patients (23.4%) presented with multiple aneurysms. A total of 165 aneurysms (41.2%) had a daughter sac. No significant difference in aneurysm location or size was evident between groups.

3.3. Procedure

Overall, 372 aneurysms were treated by clipping (92.8%) with or without assist bypass, 20 (5.0%) by trapping with bypass, 5 (1.2%) by trapping alone, and 2 (0.5%) by bypass with coiling. Two aneurysms were not treated by clipping nor trapping. More than one aneurysm was treated simultaneously in 6.5% of patients. No significant difference in the use of surgical procedures was evident between groups ($p = 0.2618$).

3.4. Adverse events

The overall mortality rate within 30 days after surgery was 0.25% (Table 3). Rates of severe and minor morbidity at discharge were 4.5% and 9.0%, respectively. No significant difference in mortality and morbidity rates was seen between groups. Symptomatic brain infarction

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