Journal of Clinical Neuroscience xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Case study

Clinical outcomes after craniotomy for unruptured intracranial aneurysm in patients with coronary artery disease

Akira Nakamizo *, Toshiyuki Amano, Satoshi Matsuo, Yuhei Michiwaki, Yutaka Fujioka, Yousuke Kawano

Departments of Neurosurgery, Clinical Research Institute, National Hospital Organization, Kyushu Medical Center, Japan

ARTICLE INFO

Article history:
Received 19 May 2017
Accepted 14 August 2017
Available online xxxx

Keywords:
Intracranial aneurysm
Coronary artery disease
Antiplatelet agents
Outcomes
Craniotomy

ABSTRACT

Background: Coronary artery disease (CAD) patients receiving antiplatelet agents occasionally undergo craniotomy. We aimed to clarify clinical outcomes after craniotomy for unruptured intracranial aneurysm (UIA) in patients with CAD. We also aimed to identify the possible predictive factors for morbidity and surgical complications in patients on antiplatelet treatment.

Methods: We retrospectively analyzed 401 consecutive patients who had undergone craniotomy for UIA at our institution between January 2006 and December 2016. Forty-three patients (10.7%) received antiplatelet agents during the perioperative period. The underlying reasons for antiplatelet treatment were CAD in 12 patients and other diseases in 31 patients.

Results: Severe morbidity and intracranial hemorrhage occurred more commonly and symptomatic brain infarction occurred less frequently in patients with CAD compared to patients with other underlying diseases (16.7% versus 3.2%, 16.7% versus 9.7%, and 8.3% versus 16.1%, respectively), though differences between the two groups were not significant. Univariate analysis revealed that a low preoperative baseline platelet count was significantly correlated with the occurrence of intracranial hemorrhage (cutoff value, $16.5 \times 10^4/\mu L$; odds ratio (OR), 46.67; 95% confidence interval (CI), 3.88–561.95; $p = 0.0005$), and a high baseline platelet count tended to correlate with severe morbidity (cutoff value, $29.8 \times 10^4/\mu L$; OR, 11.33; 95% CI, 0.88–145.52; $p = 0.0550$).

Conclusions: Our results suggest that surgical complications and clinical outcomes after craniotomy may depend on the underlying reason for antiplatelet treatment. Moreover, a preoperative platelet count can be useful in predicting the occurrence of intracranial hemorrhage and severe morbidity after craniotomy in patients receiving antiplatelet agents.

1. Introduction

The 2017 Heart Disease and Stroke Statistics update of the American Heart Association recently reported that 16.5 million persons in the Unites States have coronary heart disease (CHD), and the prevalence increases with age for both women and men, but mortality of patients with CHD has declined [1]. The number of patients with coronary artery disease (CAD) undergoing cardiac or non-cardiac surgery has increased over time. After percutaneous coronary intervention (PCI), 4%–8% of patients undergo surgery within 1 year and 23% within 5 years [2].

In patients with CAD managed by antiplatelet agents, defining the fine balance between ischemic and hemorrhagic risk remains a challenge in patients undergoing non-cardiac surgery [3]. A consensus document from Italian cardiology, surgery, and anesthesiology societies in 2014 classifies the hemorrhagic risk of common surgical interventions as low, intermediate, and high, where neurosurgery for intracerebral tumors and intraparenchymal hemorrhage is classified as a surgery with high hemorrhagic risk [4]. In this category, elective surgery for patients with low risk of thromboembolism is recommended to be performed after discontinuation of the antiplatelet agent, and surgery for patients with intermediate or high risk of thromboembolism is recommended to be postponed.

We hypothesized that the rates of morbidity and surgical complications after craniotomy depend on the underlying reason for the antiplatelet treatment. Therefore, we aimed to clarify the occurrence of surgical complications and clinical outcomes after craniotomy for UIA in patients with CAD by comparing them with complications and outcomes in patients taking antiplatelet agents for other underlying diseases. We also aimed to identify possible

* Corresponding author at: Department of Neurosurgery, Clinical Research Institute, National Hospital Organization, Kyushu Medical Center, 1-8-1, Jigyohama, Chuo-ku, Fukuoka 810-8563, Japan.
E-mail address: nakamizo@ns.med.kyushu-u.ac.jp (A. Nakamizo).

http://dx.doi.org/10.1016/j.jocn.2017.08.043
0967-5868/

predictive factors for surgical complications and morbidity in patients receiving antiplatelet agents during the perioperative period.

2. Methods

2.1. Patients

We retrospectively analyzed 401 consecutive patients with UIAs who were treated surgically between January 2006 and December 2016 at our institution. Of these, 43 patients receiving antiplatelet agents during the perioperative period were enrolled in this study. This study was approved by a formally constituted research ethics committee. Patients' clinical data were obtained by retrospective chart review. Patients were divided into two groups: those taking oral antiplatelet agents for CAD and those taking them for other underlying diseases. Perioperative continuation or interruption of antiplatelet agents in patients with CAD was determined by cardiologists.

2.2. Surgical complications and adverse events

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 was defined as any-cause death within 30 days after surgery. Morbidity was evaluated at discharge. Severe morbidity was defined as an increase in modified Rankin scale (mRS) score of $\geq$2 points [6–8]. Mortality, morbidity, intracranial hemorrhage, and symptomatic brain infarction were considered as adverse events.

2.3. Statistical analysis

Statistical analysis was performed using JMP statistical software (JMP version 13; SAS Institute, Cary, NC). Continuous data are expressed as mean ± standard deviation. Mean ages of patients, days of antiplatelet interruption, baseline platelet count, and estimated functional newly formed platelet count were compared between the two groups using Student's *t*-test or the unpaired *t*-test. Pearson's chi-square test or Fisher's exact test was used to compare categorical variables. Logistic regression models were used to evaluate independent associations between variables and severe morbidity or intracranial hemorrhage. To determine the platelet count cutoff values capable to predict the occurrence of intracranial hemorrhage or severe morbidity, receiver operating characteristics (ROC) analysis was performed, and the areas under the curve (AUC) were calculated. Values of $p < 0.05$ were considered statistically significant.

3. Results

3.1. Patient characteristics

Overall, 32 women and 11 men were enrolled in this study, with a mean age of 67.3 ± 6.0 years (range, 53–83 years). The most frequent medical history was hypertension, followed by prior brain infarction, dyslipidemia, coronary heart disease, and diabetes mellitus. No patients with CAD had experienced brain infarction or transient ischemic attack, while no patients with other underlying disease had experienced CHD ($p < 0.0001$). No significant differences between the two groups were noted in age, sex, or other comorbidities including transient ischemic attack, atrial fibrillation, hypertension, diabetes mellitus, dyslipidemia, chronic kidney disease, or cancer. Overall, aspirin was the most commonly used antiplatelet agent, followed by clopidogrel and cilostazol (Table 1). No patients received dual antiplatelet therapy. The rate of aspirin use tended to be higher in patients with CAD than in patients with other diseases. Antiplatelet agents were temporarily interrupted in 75.0% of patients with CAD and in 61.3% of patients with other diseases ($p = 0.3892$), and the mean durations of interruption were 7.2 ± 2.6 days and 4.9 ± 0.6 days before surgery, respectively ($p = 0.0497$). Baseline platelet count analyzed on the day of or the day before interruption of antiplatelet therapy was $22.9 \times 10^4/\mu L$ in patients with CAD and $24.0 \times 10^4/\mu L$ in patients with other diseases ($p = 0.5157$). Estimated number of newly formed functional platelets (calculated by 0.1 × baseline platelet count × number of days of antiplatelet interruption) [9] was $11.5 \times 10^4/\mu L$ in patients with CAD and $5.9 \times 10^4/\mu L$ in patients with other diseases ($p = 0.0304$).

3.2. Aneurysm characteristics

Overall, the most common aneurysm location was the middle cerebral artery, followed by the internal carotid artery and anterior communicating artery. No patients with CAD had an anterior communicating artery aneurysm, while 8 (25.8%) patients with other diseases did ($p = 0.0246$). The most frequent aneurysm size was 7–9 mm, followed by 3–4 mm and 5–6 mm. No significant differences in aneurysm size, multiplicity, presence of daughter sac, or performed procedure were evident between the two groups.

3.3. Surgical complications and adverse events

The overall mortality rate within 30 days after surgery was 0% (Table 2). Rate of severe morbidity at discharge was 7.0%. Rates of symptomatic brain infarction and intracranial hemorrhage were 14.0% and 11.6%, respectively. Three patients (7.0%) required evacuation of hematoma. Severe morbidity and intracranial hemorrhage occurred more commonly and symptomatic brain infarction occurred less frequently in patients with CAD compared to patients with other diseases (16.7% versus 3.2%, 16.7% versus 9.7%, and 8.3% versus 16.1%, respectively), though differences between the two groups were not significant ($p = 0.5340$, $p = 0.1461$, and $p = 0.4892$, respectively). In the context of antiplatelet agent interruption, symptomatic brain infarction occurred in 1 of 9 (11.1%) CAD patients with interruption, none of 3 CAD patients with continuation, 2 of 19 (10.5%) other disease patients with interruption, and 3 of 12 (25.0%) other disease patients with continuation. Intracranial hemorrhage occurred in 1 of 3 (33.3%) CAD patients with continuation, 1 of 9 (11.1%) CAD patients with interruption, 2 of 12 (16.7%) other disease patients with continuation, and 1 of 19 (5.3%) other disease patients with interruption. Prior brain infarction was the underlying reason for antiplatelet treatment in all of the patients with other diseases who experienced symptomatic brain infarction.

A cutoff baseline platelet count value $<16.5 \times 10^4/\mu L$ was detected as the most reliable value to predict intracranial hemorrhage (AUC = 0.78684, sensitivity 80.0%, specificity 92.1%; $p = 0.0174$). Baseline platelet count $\geq 29.8 \times 10^4/\mu L$ was detected as a cutoff value to predict severe morbidity (AUC = 0.6667, sensitivity 66.7%, specificity 85.0%; $p = 0.2432$). Estimated functional platelet count $<3.99 \times 10^4/\mu L$ was detected as a cutoff value to predict intracranial hemorrhage (AUC = 0.67105, sensitivity 80.0%, specificity 60.5%; $p = 0.1925$). Estimated functional platelet count $\geq 12.3 \times 10^4/\mu L$ was detected as a cutoff value to predict severe morbidity (AUC = 0.6250, sensitivity 66.7%, specificity 77.5%; $p = 0.5994$). In univariate analysis, the occurrence of intracranial

Please cite this article in press as: Nakamizo A et al. Clinical outcomes after craniotomy for unruptured intracranial aneurysm in patients with coronary artery disease. J Clin Neurosci (2017), http://dx.doi.org/10.1016/j.jocn.2017.08.043