The Safety and Efficacy of Triple Antiplatelet Therapy after Intracranial Stent-Assisted Coil Embolization

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Background: Stent-assisted coil embolization is effective for intracranial aneurysms, especially for wide-necked aneurysms; however, the optimal antiplatelet regimens for postoperative ischemic events have not yet been established. We aimed at determining the efficacy and safety of a triple antiplatelet therapy regimen after intracranial stent-assisted coil embolization. *Methods:* We retrospectively evaluated patients who underwent stent-assisted coil embolization for unruptured intracranial aneurysms or during the chronic phase of a ruptured intracranial aneurysm (≥4 weeks after subarachnoid hemorrhage onset). We recorded the incidence of ischemic and bleeding events 140 days postoperatively. *Results:* We assessed 79 cases in patients who received either dual (n = 51) or triple (n = 28) antiplatelet therapy. The duration of triple antiplatelet therapy was 49 ± 29 days. Seven patients in the dual group experienced postoperative ischemic events. Compared to the dual group, the triple group had a similar incidence of postoperative bleeding events but a significantly lower incidence of postoperative ischemic events ($P < .05$). *Conclusions:* Triple antiplatelet therapy had a significantly lower incidence of postoperative ischemic events and a similar incidence of postoperative bleeding events 140 days postoperatively. **Key Words:** Intracranial aneurysm—stent-assisted coil embolization—ischemic event—antiplatelet therapy.

Introduction

Stent-assisted coil embolization for intracranial aneurysms increases packing density and decreases the coil deviation rates of the parent artery,[1] and it is especially useful for wide-necked aneurysms.[2,3] However, this procedure is associated with thromboembolic events.[4-7] In earlier studies, dual antiplatelet agents were used for periods of 3 weeks to 6 months postoperatively followed by the administration of a single antiplatelet agent intended to be administered for the rest of the patients' lives.[4-7] A postoperative ischemic event is more likely to occur relatively soon after the operation, and its occurrence is likewise associated with the cessation of dual antiplatelet therapy.[5,7,8] However, the administration of multiple antiplatelet agents increases the risk of a hemorrhagic event.[9,10]

The optimal antiplatelet agent regimen for patients who have undergone intracranial stent-assisted coil embolization has not yet been established.[7,8] For coronary intervention, the safety and efficacy of triple antiplatelet therapy compared with dual antiplatelet therapy after

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percutaneous coronary intervention were reported.[11-13] These results led to the hypothesis that triple antiplatelet therapy may effectively prevent thromboembolic events in intracranial stent-assisted endovascular treatment. Kono et al[14] reported that the triple antiplatelet therapy for Y-stents assisted in coiling for cerebral aneurysm cases, and while triple antiplatelet therapy for Y-stents may not prevent thromboembolic events, no postprocedural or late hemorrhagic events occurred. We previously proposed a new antiplatelet agent regimen: triple antiplatelet therapy administered 6 weeks postoperatively followed by dual antiplatelet therapy.[15] Therefore, the present study evaluated the safety and efficacy of this triple antiplatelet therapy regimen for preventing postoperative ischemic events during the early period of stent-assisted coil embolization.

Methods

Between July 2010 and May 2014, we retrospectively collected data on patients at the Fukuoka University Chikushi Hospital with unruptured intracranial aneurysms or during the chronic phase of ruptured intracranial aneurysms (≥4 weeks after subarachnoid hemorrhage onset). Patients were included if they were treated by intracranial stent-assisted coil embolization and if a follow-up assessment by a neurologist or neurosurgeon was performed at least 5 months postoperatively. This study protocol was approved by the ethics committee of the Fukuoka University Chikushi Hospital.

In this study, the patients were divided into 2 groups depending on the antiplatelet agents administered preoperatively: a dual antiplatelet therapy group (aspirin plus clopidogrel or aspirin plus cilostazol, or clopidogrel plus cilostazol) and a triple antiplatelet therapy group (aspirin plus clopidogrel plus cilostazol). The selection of the kinds and the amounts of the antiplatelet drugs depended on each doctor's decision. The preoperative minimum antiplatelet agent dose for each antiplatelet agent was as follows: 200 mg for aspirin, 300 mg for clopidogrel, and 100 mg for cilostazol. The maintenance dose for each antiplatelet agent was 81-100 mg/day for aspirin, 75 mg/day for clopidogrel, and 200 mg/day (dual group) or 100-200 mg/day (triple group) for cilostazol. Our typical postoperative follow-up evaluation included magnetic resonance imaging (MRI) and/or digital subtraction angiography (DSA), which were performed 3-10 months postoperatively. Subsequently, we prescribed single antiplatelet therapy. If stroke-like symptoms occurred, we monitored the symptoms and performed MRI and/or DSA evaluations. The Enterprise VRD (Codman Neurovascular, Raynham, MA) was used in 53 cases, and the Neuroform stent (Stryker Neurovascular, Fremont, CA) was used in 26 cases. The patients were treated under general anesthesia. During the operation, heparin was administered to the patients before stent insertion.

To assess the efficacy between the dual and triple antiplatelet therapies for preventing early-stage postoperative ischemic stroke events, we recorded the postoperative ischemic and bleeding events 140 days postoperatively, because in the present study, the maximum duration of triple antiplatelet therapy was 137 days postoperatively.

Study Definitions and Evaluation Techniques

The records of cerebrovascular risk factors and history were dependent on the patients' self-reporting, but the final records were left to the physician's discretion after he/she comprehensively reviewed the patients' self-report and in-hospital examination results. We used standard multiprojection cerebral angiography, three-dimensional DSA, MRI, and time-of-flight magnetic resonance angiography for the preoperative morphologic evaluations and measurements.

Postoperative ischemic events primarily consisted of cerebral infarction, transient ischemic attack (TIA), or eye symptoms. A postoperative ischemic event was defined as a cerebral infarction if the persisted neurologic deterioration or the additional imaging abnormality–defined cerebral infarction (ie, new high-intensity area of diffusion-weighted and T2-weighted MRI examination) was detected after the ischemic event. If a brief episode of neurologic dysfunction without additional imaging abnormality–defined cerebral infarction was detected after the ischemic event, it was defined as a TIA. In the case of eye symptoms, a detailed examination, including the eye ground, was performed by ophthalmologists for confirmation. A bleeding event was defined as any intracranial bleeding, bleeding requiring blood transfusion, or any other clinically relevant bleeding as judged by the study investigator.

Statistical Analysis

The Mann–Whitney *U* test was used to determine significant differences in age, aneurysmal size, diameter of the parent artery, and operation time. Fisher exact test was used for assessing all other parameters. Each hypothesis was tested using 2-tailed analyses. A *P* value less than .05 was considered statistically significant.

Results

The study flow chart is shown in Figures 1, 2, and 3. Of the 231 patients treated with endovascular procedures for unruptured intracranial aneurysms or for the chronic phase of ruptured intracranial aneurysms during a 45-month period, we retrospectively enrolled 105 patients (106 cases) who underwent intracranial stent-assisted coil embolization. We excluded 27 cases from this study, which included 8 cases treated with 2 stent constructs (Y configuration and coaxial) or the waffle corn