



Perioperative Antiplatelet Therapy for the Stent-Assisted Coil Embolization: Results of the Questionnaire Survey

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Objective: This study aimed to determine the status of perioperative antiplatelet therapy in stent-assisted coil embolization (SAC) in Japan.

Methods: The questionnaire consisted of 13 questions and used Google forms, and was sent to institutions where endovascular specialists were employed. The results were analyzed.

Results: The responses from 307 centers indicated that the timing of initiation of antiplatelet therapy was 14 days–1 month before treatment in half of centers, and 7–14 days before treatment in the other half. Platelet function tests were performed at 165 centers (56.2%), of which 136 centers (46.3%) performed these tests for all patients, with the VerifyNow system being the most widely used tool. The duration of postoperative dual antiplatelet therapy was 6, 3, and 12 months in 169 (57.7%), 70 (23.5%), and 42 (14.3%) centers, respectively. The antiplatelet agents used for monotherapy were P2Y12 receptor antagonists or aspirin, with a postoperative period of up to 12 months in 139 centers (47.3%), 24 months in 68 centers (23.1%), and longer than 24 months in 50 centers (17%).

Conclusion: Current antiplatelet therapy for SAC in Japan varies widely among institutions. Moreover, each center has its own empirical rules for SAC. Therefore, the findings of this survey suggest the need to establish guidelines for optimal periprocedural antiplatelet therapy for SAC.

Keywords ▶ unruptured aneurysm, stent-assisted coil embolization, flow diverter, antiplatelet therapy

Introduction

Endovascular coil embolization for unruptured intracranial aneurysms (UIAs) is performed worldwide. A nationwide survey in Japan showed that the number of coil embolizations for UIAs has been increasing¹⁾ and now exceeds the number of clippings. The number of Japanese Society for Neuroendovascular Therapy (JSNET) specialists is also increasing, and treatments are expected to continue to increase further in the future. Assist stents and flow diverters (FDs), which have been approved in Japan since 2010 and 2015, respectively,

have contributed to expanding the treatment options for wide-neck aneurysms. The difficulty associated with using simple coiling to manage wide neck aneurysms has primarily caused the increase in the number of endovascular treatments. All the endovascular treatments have the potential risk of thromboembolism, which can be 3% or 10% after stent-assisted coil embolization (SAC) or FD embolization, respectively.^{2,3)}

To prevent periprocedural thromboembolic complications, dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 inhibitor is widely used during SAC or FD embolization.^{2,3)} However, preoperative platelet reactivity to prescribed antiplatelet agents is associated with periprocedural hemorrhagic and ischemic complications.⁴⁾ Therefore, preoperative evaluation of platelet reactivity using platelet function testing, such as light transmission aggregometry (LTA) or VerifyNow (Accumetrics, San Diego, CA, USA), is essential for determining the risk of perioperative complications. Adjusting the drug or dosage according to the results of these tests may reduce the risk of complications; however, its clinical efficacy has not been proven.

There is no evidence regarding the duration of postoperative antiplatelet therapy. Therefore, this study aimed to

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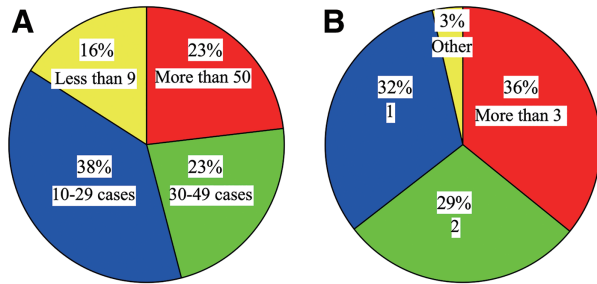


Fig. 1 Information about the centers of the JSNET members. (A) The number of treatments per year and (B) the number of JSNET specialists per institution. JSNET: Japanese Society for Neuroendovascular Therapy

assess the current status of perioperative antiplatelet therapy in Japan, and the current article discusses the optimal duration and selection of antiplatelet therapy based on the results of the study.

Materials and Methods

We developed a questionnaire consisting of 13 questions using Google forms, regarding information about centers and perioperative antiplatelet therapy for SAC or FD embolization. This questionnaire was sent to institutions belonging to the JSNET specialists in June 2021; the responses to the questionnaire were collected in October 2021. The responses were obtained from a total of 307 centers, and the results were analyzed. The questions were divided into the following three sections: information about the center (**Fig. 1**), preoperative antiplatelet therapy (**Fig. 2**), and postoperative antiplatelet therapy (**Fig. 3**).

In this study, the total duration from the operation to the termination of antiplatelet therapy (including DAPT and single antiplatelet therapy [SAPT]) was described as “total duration.”

The institutional review board’s approval was not required for the study as the data were obtained through an anonymous online survey.

Results

Information about the center

The number of endovascular treatments for UIAs per year was ≥ 30 in 46% of the centers (141 centers, **Fig. 1A**). The number of JSNET specialists was more than three in 36% (110 centers), two in 29% (88 centers), and only one in 32% (98 centers, **Fig. 1B**) of the centers.

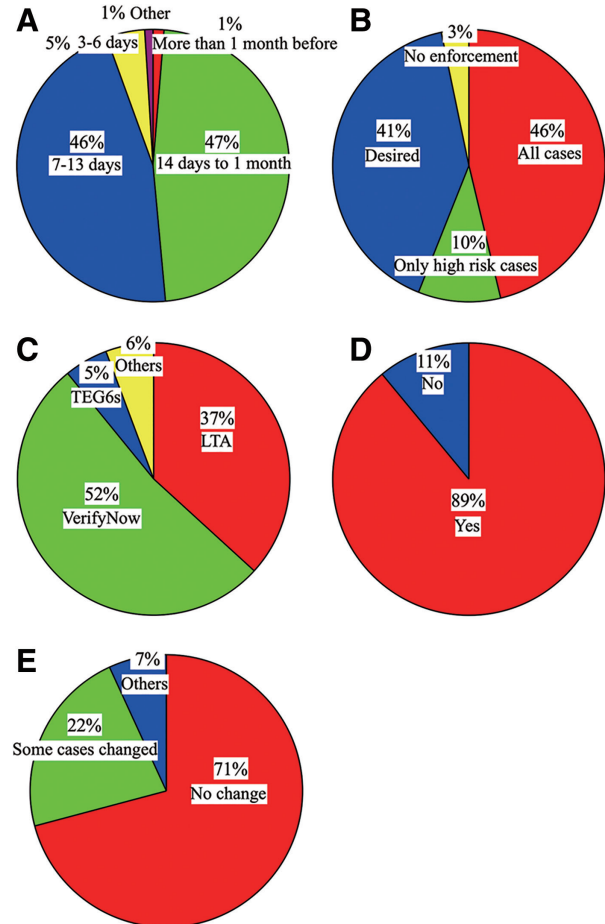


Fig. 2 Preoperative APT. (A) The timing of initiation of APT, (B) the preoperative platelet function test, (C) the types of the platelet function test, (D) the preoperative drug adjustment according to the platelet function test results, and (E) operation day changes made according to the platelet function test results. APT: antiplatelet therapy; LTA: light transmission aggregometry

Preoperative antiplatelet therapy

Figure 2A presents details regarding the timing of the initiation of antiplatelet therapy, which was 14 days–1 month before the treatment in 47% (145) and start 7–13 days before the treatment in 46% (141) of the centers.

Preoperative platelet function tests were performed in 56% (172) of the centers. A total of 142 centers were involved in all cases, and 20 centers in only high-risk cases. Forty-one percent (125 centers) did not perform; however, they indicated that they would like to perform such cases if possible (**Fig. 2B**). The platelet function test results are shown in **Fig. 2C**. VerifyNow was the most widely used tool (52%), followed by LTA (37%). Preoperative drug adjustment according to the platelet function test was performed in 89% of the centers (**Fig. 2D**). However, several centers (71%, 124 centers) did not change the operation day according to the platelet function tests (**Fig. 2E**).

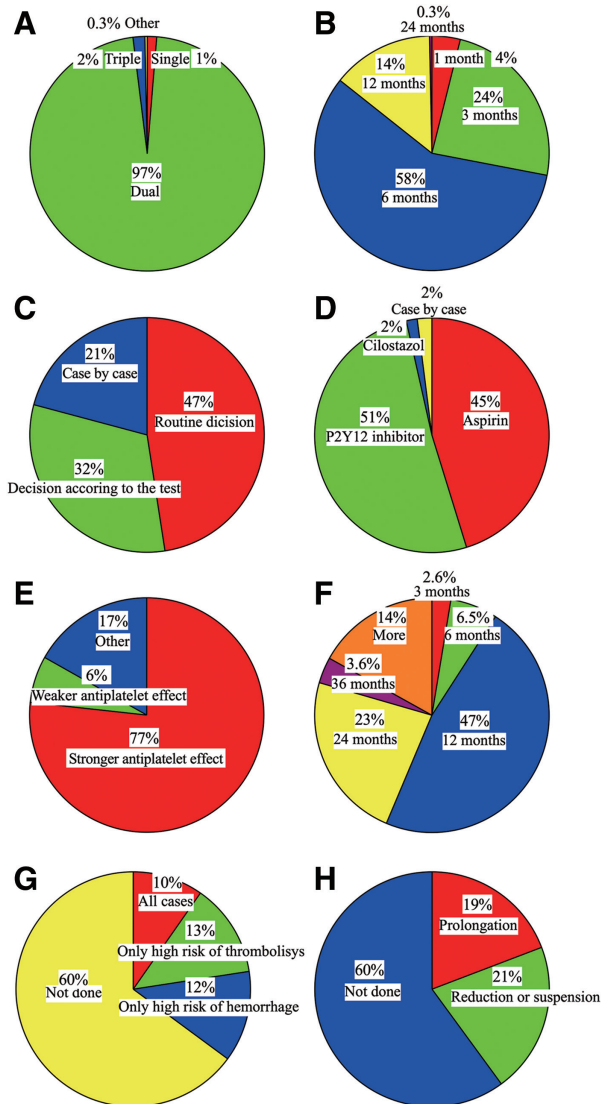


Fig. 3 Postoperative APT. (A) The number of postoperative antiplatelet drugs, (B) the average period of DAPT, (C) the selection of SAPT, (D) the types of SAPT, (E) the policy for determining of SAPT, (F) the average period of the duration from the operation to the termination of antiplatelet therapy, (G) the postoperative platelet function test results, and (H) the postoperative drug adjustment according to the platelet function test results. APT: antiplatelet therapy; DAPT: dual antiplatelet therapy; SAPT: single antiplatelet therapy

Postoperative antiplatelet therapy

The number of postoperative antiplatelet therapies administered is shown in **Fig. 3A**. Almost all of the centers (97%) used DAPT. The duration of postoperative DAPT is shown in **Fig. 3B**. DAPT was most often maintained for 6 months (58%, 177 centers), followed by 3 months (24%, 74 centers) and 12 months (14%, 43 centers). Details of the antiplatelet agents used for postoperative SAPT and the total duration from the operation to the termination of antiplatelet therapy are shown in **Fig. 3C–3F**. The same

antiplatelet agent was routinely selected for SAPT in 47% (146) of the centers and for platelet function testing in 32% (97) of the centers. For postoperative SAPT, P2Y12 receptor inhibitors were most frequently used (51%) and were followed by aspirin (45%, **Fig. 3D**). Several centers in which SAPT was selected by platelet function testing showed stronger antiplatelet reactivity (77%, 155 centers) and weaker antiplatelet activity was rare (6%, 13 centers, **Fig. 3E**). The most common total duration reported (**Fig. 3F**) was 12 months (47%, 145 centers), followed by 24 months (23%, 71 centers). Several centers (65%, 207 centers) did not perform postoperative platelet function tests (**Fig. 3G**) and did not adjust the dose or period according to the results of the platelet function test (60%, 197 centers, **Fig. 3H**).

Discussion

The following were the most common responses to the questionnaire about perioperative antiplatelet therapy: 1) started within 1 month preoperatively, 2) started within 6 months of DAPT, and 3) had a total duration of 12-months. Several centers performed platelet function tests to determine platelet reactivity before treatment and formulated tailor-made antiplatelet therapy based on the test results. This survey showed that the current antiplatelet therapy for SAC varied widely among centers based on each center's empirical rules.

Preoperative antiplatelet therapy is essential for preventing periprocedural thrombotic and hemorrhagic complications.⁴⁾ Previous reports have shown that thromboembolic lesions following coil embolization for unruptured aneurysms are associated with adjunctive techniques⁵⁾ and pretreatment platelet function tests.^{4,6)} Delgado Almandoz et al. reported that postoperative P2Y12 reaction unit values on VerifyNow were associated with major thromboembolic and hemorrhagic complications after FD placement, and that a P2Y12 reaction unit (PRU) of <60 or >240 was an independent predictor of major thromboembolic and hemorrhagic complications.⁴⁾ In this survey, the JSNET members were highly interested in preoperative antiplatelet therapy. Platelet function tests were performed in 172 out of the 307 centers, and preoperative drug adjustment according to the results was managed in most centers. These management strategies may contribute to a reduction in perioperative complications.

Postoperative antiplatelet remains controversial, even in the field of percutaneous coronary intervention (PCI). Several reports have shown that short-term DAPT after PCI

was not associated with thrombotic events.⁷⁻⁹⁾ In the Noboli Dual Antiplatelet Therapy As Appropriate Duration study, the rate of onset of postprocedural adverse events was compared between 6 and 18 months of DAPT, and shorter duration of DAPT was not associated with postoperative adverse events.⁷⁾ Another report showed that a shorter duration of DAPT after PCI (1 month) resulted in a significantly lower rate of cardiovascular and bleeding events than a longer DAPT (12 months).⁸⁾ Recently, the optimal management of antithrombotic therapy after PCI has been established by these clinical evidences⁷⁻⁹⁾ and other guidelines.¹⁰⁾

Multiple reports have been made on postoperative antiplatelet therapy in the neurointerventional field.^{4,11-14)} These studies have demonstrated the importance of postoperative platelet function tests. Kim et al. examined the optimal duration of postoperative DAPT. They dichotomized the DAPT duration at 9 months and noted that long-term DAPT (>9 months DAPT) delayed the occurrence of delayed thromboembolic events; however, it did not decrease their incidence.¹⁴⁾ Caroff et al. reported a national survey of anti-thrombotic therapies for neurointerventional surgery in France, in which DAPT was continued for 6 months in 53% of centers and SAPT was prescribed for 12 months in 63% of centers after FD placement.¹²⁾ These results are similar to those of the present study. Therefore, antiplatelet therapy may be the primary treatment method used worldwide after SAC or FD embolization. Shoda et al. reported that preoperative platelet reactivity was associated with not only periprocedural but also delayed complications.¹³⁾ Although the rate of postoperative platelet function tests was lower than the preoperative rate; it may be necessary to focus on postoperative platelet function tests. Furthermore, it is necessary to establish guidelines for the use of perioperative antiplatelet therapy in neurointervention therapy.

This study had some limitations. This study was an online questionnaire survey that was answered by one representative physician per center. Therefore, the results cannot be generalized to all physicians.

Conclusion

An online questionnaire survey was conducted to determine the current status of using perioperative antiplatelet therapy for SAC or FD embolization in Japan. The findings show that the use of perioperative antiplatelet therapy for SAC or FD widely varied among institutions. The results of this survey suggest the need for further research and guidelines on the optimal regimen for preprocedural and

postprocedural antiplatelet therapy for the endovascular treatment of UIAs.

Disclosure Statement

Yukiko Enomoto received research grants from Sysmex. The other authors declare no conflicts of interest.

References

- 1) Satow T, Ikeda G, Takahashi JC, et al. Coil embolization for unruptured intracranial aneurysms at the dawn of stent era: results of the Japanese Registry of Neuroendovascular Therapy (JR-NET) 3. *Neurol Med Chir (Tokyo)* 2020; 60: 55–65.
- 2) Narata AP, Amelot A, Bibi R, et al. Dual antiplatelet therapy combining aspirin and ticagrelor for intracranial stenting procedures: a retrospective single center study of 154 consecutive patients with unruptured aneurysms. *Neurosurgery* 2019; 84: 77–83.
- 3) Farrokh S, Owusu K, Lara LR, et al. Neuro-interventional use of oral antiplatelets: a survey of neuro-endovascular centers in the United States and review of the literature. *J Pharm Pract* 2021; 34: 207–215.
- 4) Delgado Almandoz JE, Crandall BM, Scholz JM, et al. Last-recorded P2Y12 reaction units value is strongly associated with thromboembolic and hemorrhagic complications occurring up to 6 months after treatment in patients with cerebral aneurysms treated with the pipeline embolization device. *AJNR Am J Neuroradiol* 2014; 35: 128–135.
- 5) Takigawa T, Suzuki K, Sugiura Y, et al. Thromboembolic events associated with single balloon-, double balloon-, and stent-assisted coil embolization of asymptomatic unruptured cerebral aneurysms: evaluation with diffusion-weighted MR imaging. *Neuroradiology* 2014; 56: 1079–1086.
- 6) Pötin M, Blanc R, Spelle L, et al. Stent-assisted coiling of intracranial aneurysms: clinical and angiographic results in 216 consecutive aneurysms. *Stroke* 2010; 41: 110–115.
- 7) Nakamura M, Iijima R, Ako J, et al. Dual antiplatelet therapy for 6 versus 18 months after biodegradable polymer drug-eluting stent implantation. *JACC Cardiovasc Interv* 2017; 10: 1189–1198.
- 8) Watanabe H, Domei T, Morimoto T, et al. Effect of 1-month dual antiplatelet therapy followed by clopidogrel vs 12-month dual antiplatelet therapy on cardiovascular and bleeding events in patients receiving PCI: the STOPDAPT-2 randomized clinical trial. *JAMA* 2019; 321: 2414–2427.
- 9) Natsuaki M, Morimoto T, Yamamoto E, et al. One-year outcome of a prospective trial stopping dual antiplatelet therapy at 3 months after everolimus-eluting cobalt-chromium

- stent implantation: short and optimal duration of dual antiplatelet therapy after everolimus-eluting cobalt-chromium stent (STOPDAPT) trial. *Cardiovasc Interv Ther* 2016; 31: 196–209.
- 10) Nakamura M, Kimura K, Kimura T, et al. guideline focused update on antithrombotic therapy in patients with coronary artery disease. *Circ J* 2020; 84: 831–865.
 - 11) Ospel JM, Brouwer P, Dorn F, et al. Antiplatelet management for stent-assisted coiling and flow diversion of ruptured intracranial aneurysms: a DELPHI consensus statement. *AJNR Am J Neuroradiol* 2020; 41: 1856–1862.
 - 12) Caroff J, Aubert L, Lavenu-Bomblé C, et al. Antithrombotic therapies for neurointerventional surgery: a 2021 French comprehensive national survey. *J Neurointerv Surg* 2022 Mar 28. [Epub ahead of print]
 - 13) Shoda K, Enomoto Y, Egashira Y, et al. Long-term complications after stent assist coiling dependent on clopidogrel response. *BMC Neurol* 2021; 21: 247.
 - 14) Kim T, Kim CH, Kang SH, et al. Relevance of antiplatelet therapy duration after stent-assisted coil embolization for unruptured intracranial aneurysms. *World Neurosurg* 2018; 116: e699–e708.