Management of Antithrombotic Drugs before Elective Spine Surgery: A Nationwide Web-Based Questionnaire Survey in Japan

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Abstract:

Introduction: The number of patients on antithrombotic drugs for coronary heart disease or cerebrovascular disease has been increasing with the aging of society. We occasionally need to decide whether to continue or discontinue antithrombotic drugs before spine surgery. The purpose of this study is to understand the current perioperative management of antithrombotic drugs before elective spine surgery in Japan.

Methods: In 2021, members of the Japanese Society for Spine Surgery and Related Research (JSSR) were asked to complete a web-based questionnaire survey that included items concerning the respondents' surgical experience, their policy regarding discontinuation or continuation of antithrombotic drugs, their reasons for decisions concerning the management of antithrombotic drugs, and their experience of perioperative complications related to the continuation or discontinuation of these drugs.

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Results: A total of 1,181 spine surgeons returned completed questionnaires, giving a response rate of 32.0%. JSSR board-certified spine surgeons comprised 75.1% of the respondents. Depending on the management policy regarding antithrombotic drugs for each comorbidity, approximately 73% of respondents discontinued these drugs before elective spine surgery, and about 80% also discontinued anticoagulants. Only 4%-5% of respondents reported continuing antiplatelet drugs, and 2.5% reported continuing anticoagulants. Among the respondents who discontinued antiplatelet drugs, 20.4% reported having encountered cerebral infarction and 3.7% reported encountering myocardial infarction; among those who discontinued anticoagulants, 13.6% reported encountering cerebral embolism and 5.4% reported encountering pulmonary embolism. However, among the respondents who continued antiplatelet drugs and those who continued anticoagulants, 26.3% and 27.2%, respectively, encountered an unexpected increase in intraoperative bleeding, and 10.3% and 8.7%, respectively, encountered postoperative spinal epidural hematoma requiring emergency surgery.

Conclusions: Our findings indicate that, in principle, >70% of JSSR members discontinue antithrombotic drugs before elective spine surgery. However, those with a discontinuation policy have encountered thrombotic complications, while those with a continuation policy have encountered hemorrhagic complications.

Keywords:

antiplatelet drugs, anticoagulants, elective spine surgery, perioperative complications, postoperative spinal epidural hematoma

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Introduction

In 2022, Japan had an aging rate of 29.1% and is categorized as a super-aged society. The extension of healthy life expectancy means that more elderly patients are undergoing spine surgery. Recently, there has been an increase in the number of patients requiring spine surgery while on antithrombotic drugs, such as antiplatelet drugs or anticoagulants, for comorbidities, such as cardiovascular disease and cerebrovascular disease. It has been reported that 22% of patients who receive percutaneous coronary intervention (PCI) also undergo noncardiac surgery within 3 years in Japan[1]. This figure is even higher in the US. In one study, 22.5% of patients who underwent coronary stent implantation underwent noncardiac surgery within 24 months, and their incidence of major adverse cardiac events (MACE) was 4.7%[2]. A history of stroke is associated with an increased risk of MACE, and patients undergoing elective noncardiac surgery with a history of stroke within the previous 3 months have an increased risk of mortality (odds ratio 3.07, 95% confidence interval 2.30-4.09)[3].

Most spine surgeons prefer to discontinue these drugs before elective spine surgery[4-6]. However, they face the dilemma of whether to discontinue or continue antithrombotic drugs. When patients stop taking these drugs before their surgery, there is an increased risk of thrombotic events, such as ischemic heart disease and stroke, which result in life-threatening complications. However, when patients undergo spine surgery while on antithrombotic medication, surgeons worry about perioperative hemorrhagic complications, such as unexpected massive bleeding requiring blood transfusion and postoperative spinal epidural hematoma (SEH), which can cause irreversible nerve damage and result in a poor postoperative outcome.

The purpose of this survey was to understand the current perioperative management of antithrombotic drugs in patients undergoing elective spine surgery in Japan.

Materials and Methods

Between April 2021 and May 2021, members of the Japanese Society for Spine Surgery and Related Research (JSSR) were sent an email from the office of the JSSR inviting them to complete a web-based questionnaire survey if they consented to participate in the research and providing a link to the URL for the questionnaire site. The questionnaire included items about the respondent's characteristics as a spine surgeon, their policy regarding the discontinuation or continuation of antithrombotic drugs before elective spine surgery, how they made a judgment regarding management of antithrombotic drugs, their experience of perioperative complications related to discontinuation or continuation of these drugs, and their impression of the relationship between antithrombotic drugs and postoperative SEH.

Results

The survey was completed by 1,181 spine surgeons, giving a response rate of 32.0%. Their characteristics are summarized in Table 1. The respondents were a mixture of less experienced and more experienced surgeons. The majority of respondents had 11-20 years of experience as surgeons; 75.1% were JSSR board-certified spine surgeons. The lifetime number of operations performed was <100 in 9.2% of respondents, 100-500 in 21.3%, 500-1,000 in 26.8%, and > 1,000 in 42.6%. The number of operations performed annually was <100 in 46.5% of respondents, 100-200 in 35.0%, 200-500 in 13.2%, and >500 in 5.3%.

We asked the surgeons about their policy regarding preoperative risk assessment related to antithrombotic drugs before elective spine surgery. The first question was, "Do you consult clinicians from other specialties when judging whether to discontinue or continue antithrombotic drugs before elective spine surgery?" The respondents were required to answer according to whether patients had cardiovascular disease, cerebrovascular disease, or peripheral artery disease (Table 2). For cases with cardiovascular disease, 77.1% of respondents reported always consulting the cardiologists, 1.7% did not, and 21.2% sought cardiology input depending on the case. Consultation with a cardiologist was less likely for cases with cerebrovascular disease ("yes," 75.1%; "no," 4.3%; "not always," 20.3%) and cases with peripheral artery disease ("yes," 68.5%; "no," 6.6%; "not always," 24.5%). The second question was, "Do you decide on the perioperative discontinuation of antithrombotic drugs according to your hospital's guidelines?" Seventy-two percent of respondents reported making their decision in accordance with their hospital's guideline for the management of antithrombotic drugs (Table 3).

Depending on their management policy for antithrombotic drugs according to each comorbidity, the respondents were divided into four groups: surgeons with a discontinuation policy (group A), surgeons with a continuation policy (group B), surgeons with a case-dependent policy (group C), and a "no response" group (group N) (Table 4, Fig. 1). Patients with coronary artery disease included those who were post-PCI and those who were post-coronary artery bypass grafting (CABG). The responses regarding the management of antiplatelet drugs were 72.8% in group A, 4.5% in group B, 22.3% in group C, and 0.4% in group N for PCI and 73.1%, 4.4%, 21.8%, and 0.7%, respectively, for CABG. The responses regarding the management of anticoagulant drugs in patients with paroxysmal atrial fibrillation were as follows: 81.0% in group A, 2.5% in group B, 16.1% in group C, and 0.3% in group N. The responses regarding the management of patients with chronic atrial fibrillation were very similar to those for patients with paroxysmal atrial fibrillation: 80.3% in group A, 2.5% in group B, 16.6% in group C, and 0.6% in group N. The responses regarding the management of antiplatelet drugs were 73.4% in group A, 4.1% in group B, 21.9% in group C, and 0.6% in group N for patients with cerebrovascular disease, and 73.2%, 5.0%, 21.4%, and 0.3%, respectively, for those with peripheral artery disease.

Among the respondents, 5.5% and 10.1% reported always switching antiplatelet and anticoagulant drugs, respectively, to intravenous heparin, whereas 21.3% and 8.2%, respectively, did not. Furthermore, 73% and 80% of respondents, respectively, reported sometimes switching antiplatelet and anticoagulant drugs to intravenous heparin, indicating that most respondents had a case-dependent policy regarding heparinization.

The respondents were allowed to give multiple answers regarding their personal experience of perioperative complications related to discontinuation or continuation of antithrombotic drugs (Table 5). Respondents had encountered ischemic heart disease (3.7%) and cerebral infarction (20.4%) after discontinuation of antiplatelet drugs and cerebral embolism (13.6%) and pulmonary embolism (5.4%) after discontinuation of anticoagulants; conversely, with continuation, they had encountered an unexpected increase in intraoperative bleeding (26.3% and 27.2%, respectively), an unexpected need for red blood cell transfusion (6.1% and 6.5%), and postoperative SEH requiring emergency evacuation (10.3% and 8.7%).

The final question concerned the occurrence of postopera-

Table 1. Respondents' Surgical Experience.

Experience as a surgeon (years)	Number (Percentage)
1–5	152 (12.9%)
6–10	178 (15.1%)
11–20	409 (34.6%)
21–30	317 (26.8%)
>31	125 (10.6%)
JSSR board-certified spine surgeon	
Yes	887 (75.1%)
No	294 (24.9%)
Total operations performed	
<100	109 (9.2%)
100–500	252 (21.3%)
500–1,000	317 (26.8%)
>1,000	503 (42.6%)
Annual number of operations	
<100	549 (46.5%)
100–200	413 (35.0%)
200–500	156 (13.2%)
>500	63 (5.3%)

JSSR, Japanese Society for Spine Surgery and Related Research

Table 2. Preoperative Risk Assessment: "Do You Consult Clinicians from Other Specialties When Judging Whether to Discontinue or Continue Antithrombotic Drugs before Elective Spine Surgery?".

	Yes	No	Not always	No answer
Cardiovascular disease	911 (77.1%)	20 (1.7%)	250 (21.2%)	0 (0%)
Cerebrovascular disease	887 (75.1%)	51 (4.3%)	240 (20.3%)	3 (0.3%)
Peripheral artery disease	809 (68.5%)	78 (6.6%)	289 (24.5%)	5 (0.4%)

The data are shown as the number and percentage.

tive SEH regardless of whether the patient was taking antithrombotic drugs. Eighty-three percent of respondents had encountered postoperative SEH requiring emergency evacuation. When asked "Do you think antithrombotic therapy is one of the risk factors for postoperative SEH?" the response was "yes" for antiplatelet drugs in 79.5% of respondents and for anticoagulants in 88.7%.

Discussion

The results of this web-based questionnaire show that the majority of surgeons in Japan discontinue antithrombotic drugs before elective spine surgery and that only a minority have a continuation policy. Similar questionnaire-based surveys have been performed in other countries. A survey of neurosurgical facilities in Germany found that 80.3% of respondents had a departmental policy of discontinuing low-dose aspirin for an average of 6.9 days before spinal surgery[5]. The investigators reported that 66.2% of respondents considered that patients taking low-dose aspirin had an increased risk of perioperative hemorrhagic complications, and 51.4% had personal experience of such problems. A study in Canada reported that 92% of spine surgeons discontinued low-dose aspirin 7 days before surgery[6].

However, there are many types of antithrombotic therapy, which have different mechanisms of pharmacological action and varying risks of hemorrhagic complications. Therefore, these drugs should be considered individually when considering whether or not they should be discontinued or continued before spine surgery.

Table 3. Preoperative Risk Assessment: "Do You Decide on Perioperative Discontinuation of Antithrombotic Drugs according to Your Hospital's Guideline".

Answer	Number (Percentage)
Yes	854 (72.3%)
No	327 (27.7%)

The data are shown as the number (percentage).

I: Preoperative antiplatelet therapy and spine surgery

Management of antiplatelet drugs, including low-dose aspirin, before elective spine surgery continues to be controversial. Some studies have shown an increased risk of hemorrhagic complications in patients who continue low-dose aspirin, and others have shown no increase in risk. These studies are discussed below.

1) Reports of increased hemorrhagic complications related to continuing low-dose aspirin

Several studies have demonstrated that continuation of low-dose aspirin for the primary and secondary prevention of cardiovascular, cerebrovascular, or peripheral artery disease increases the risk of perioperative hemorrhagic complications. Kang et al. evaluated the effect of discontinuing low-dose aspirin before lumbar spinal fusion surgery on perioperative blood loss and hemorrhagic complications[7]. They found that intraoperative blood loss was similar in patients who discontinued low-dose aspirin before surgery and controls who were not taking aspirin; however, postoperative blood drainage was significantly increased, and the blood transfusion requirement was significantly greater in the low-dose aspirin group despite stopping aspirin 7 days before surgery. Gerstein et al. concluded that the perioperative bleeding risk is minimal when continuing aspirin for many operative procedures, but that aspirin should be stopped in patients undergoing intracranial, middle eye, posterior eye, intramedullary spine, and possibly transurethral prostate surgery[8]. Park et al. compared the perioperative outcomes between patients who discontinued aspirin 3-7 or 7-10 days before one-level or two-level lumbar spinal fusion therapy with those in the control group who were not taking aspirin. They found that only the group in which aspirin was discontinued 3-7 days before surgery showed a higher total amount of postoperative blood drainage and a longer duration of catheter drainage, and that if aspirin was discontinued for >7 days before surgery, there was no difference in these parameters when compared with the control group[9]. Park et al. concluded that aspirin significantly increases the risk of bleeding in patients undergoing lumbar fusion at two or

Table 4. Perioperative Discontinuation or Continuation Policy for Antithrombotic Drugs before Elective Spine Surgery according to Type of Comorbidity.

	Discontinuation (A group)	Continuation (B group)	Case-dependent (C group)	No answer (N group)
Post-PCI	860 (72.8%)	53 (4.5%)	263 (22.3%)	5 (0.4%)
Post-CABG	863 (73.1%)	52 (4.4%)	258 (21.8%)	8 (0.7%)
PAF	957 (81.0%)	30 (2.5%)	190 (16.1%)	4 (0.3%)
CAF	948 (80.3%)	30 (2.5%)	196 (16.6%)	7 (0.6%)
CVD	867 (73.4%)	48 (4.1%)	259 (21.9%)	7 (0.6%)
PAD	865 (73.2%)	59 (5.0%)	253 (21.4%)	4 (0.3%)

The data are shown as the number (percentage). CABG, coronary artery bypass grafting; CAF, chronic atrial fibrillation; CVD, cerebrovascular disease; PAD, peripheral artery disease; PAF, paroxysmal atrial fibrillation; PCI, percutaneous coronary intervention

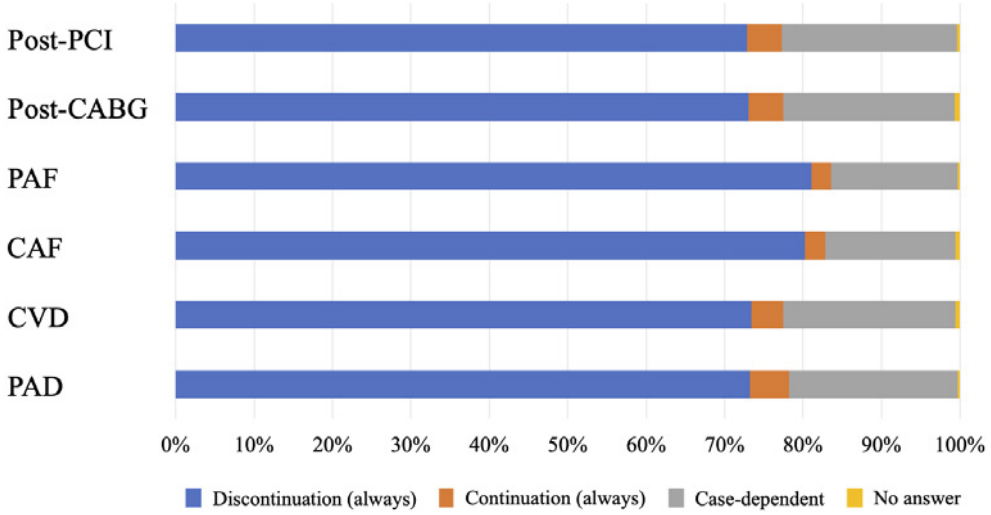

Figure 1. Analysis of perioperative discontinuation or continuation policies for antithrombotic drugs according to type of comorbidity showing that >70% of surgeons who are members of the Japanese Society for Spine and Related Research discontinue both antiplatelet and anticoagulant drugs before elective spine surgery. CABG, coronary artery bypass graft; CAF, chronic atrial fibrillation; CVD, cerebrovascular disease; PAD, peripheral artery disease; PAF, paroxysmal atrial fibrillation; PCI, percutaneous coronary intervention

Table 5. Experience of Perioperative Complications Related to Discontinuation or Continuation of Antithrombotic Drugs (Multiple Answers Allowed).

Discontinuation-related complications		
- Antiplatelet drugs		
Yes	Ischemic heart disease (acute myocardial infarction, angina pectoris)	44 (3.7%)
	Cerebral infarction	241 (20.4%)
	Other thrombotic complications	44 (3.7%)
No		888 (75.2%)
- Anticoagulants		
Yes	Cerebral embolism	161 (13.6%)
	Pulmonary embolism	64 (5.4%)
	Other embolism	44 (3.7%)
No		947 (80.2%)
Continuation-related complications		
- Antiplatelet drugs		
Yes	Unexpected increase in intraoperative bleeding	311 (26.3%)
	Unexpected red blood cell transfusion	72 (6.1%)
	Epidural hematoma requiring emergency evacuation	122 (10.3%)
No		797 (67.5%)
- Anticoagulants		
Yes	Unexpected increase in intraoperative bleeding	321 (27.2%)
	Unexpected red blood cell transfusion	77 (6.5%)
	Epidural hematoma requiring emergency evacuation	103 (8.7%)
No		798 (67.6%)

The data are shown as the number (percentage).

more levels and that this risk is present even in patients who discontinue aspirin 7 days before surgery[10]. They also demonstrated that nonsteroidal anti-inflammatory drugs increased surgical blood loss. Saitta et al. found that preoperative aspirin was associated with an increased risk of SEH even when appropriately discontinued in their retrospective cohort study[11]. They also suggested that surgeons should observe these patients more carefully after surgery and consider extending aspirin discontinuation to prevent the serious postoperative complication of SEH. Aono et al. investigated the incidence of postoperative SEH in 6,356 patients who underwent spinal decompression surgery during a study period of 19 years and found that 26 patients (0.41%)[12] required SEH evacuation. Antithrombotic therapy had been

stopped in all their patients in accordance with the protocol recommended by the drug manufacturers.

2) Studies reporting no increase in hemorrhagic complications related to continuing low-dose aspirin

In a randomized controlled trial that investigated the effectiveness of the perioperative continuation of aspirin in patients undergoing noncardiac surgery, there was a significant reduction in MACE within 30 days of surgery in patients who continued aspirin compared with patients who received a placebo, with no significant between-group difference in hemorrhagic complications[13]. The investigators reported that they had no cases of SEH; however, only a small number of patients in their study underwent orthopedic surgery. Based on multiple regression analysis, Nuttall et al. concluded that perioperative use of aspirin in patients undergoing multilevel spine surgery was not associated with an increased risk of bleeding or blood transfusion[14]. Referencing the findings of Nuttall et al., Burger et al. mentioned that although continuation of aspirin in patients undergoing multi-level spine surgery had a low risk of bleeding as a complication, continuation of aspirin was a risk factor for blood transfusion in those undergoing total hip arthroplasty[14,15]. A systematic review and meta-analysis of studies that had investigated the safety of continuing aspirin therapy during spinal surgery concluded that there was no evidence of an increased risk for bleeding, longer operation time, or increased risk of intraoperative blood transfusion[16]. Cueller et al. compared an aspirin continuation group with an aspirin discontinuation group and found no significant increase in the number of hemorrhagic complications, including postoperative SEH, in patients with cardiac stents undergoing spinal surgery[16]. Other reports support the safety of perioperative continuation of antiplatelet drugs in patients undergoing lumbar spinal surgery[17-19]. Shin et al. investigated the effects of antiplatelet drugs in patients undergoing spine surgery and concluded that aspirin did not increase the risk of postoperative SEH based on the evaluation of the thecal sac area on postoperative magnetic resonance images[20]. Another study found that perioperative continuation of antiplatelet drugs did not increase the incidence of hemorrhagic complications in patients undergoing minimally invasive lumbar spine surgery[21]. There has also been some relevant research in cervical spine surgery. Inoue et al. reported that low-dose aspirin therapy during the perioperative period did not increase perioperative bleeding or the risk of bleeding-related complications in patients who underwent cervical laminoplasty[22]. Before starting their study, they encountered cases of postoperative cerebral infarction when they discontinued low-dose aspirin before spine surgery.

II: Preoperative anticoagulation therapy and elective spine surgery

One review suggested that the management of oral anticoagulants, including warfarin, and direct oral anticoagulants, such as dabigatran, rivaroxaban, apixaban, and edoxaban, should be individualized for patients with a higher thromboembolic risk who are undergoing high-risk procedures, including intracranial, intraspinal, retroperitoneal, and intrathoracic surgeries[23]. Spine surgery is considered a high-risk procedure, so anticoagulants should be discontinued before surgery if possible.

III: Perioperative heparin bridging

Prophylactic heparin bridging therapy using unfractionated heparin or low-molecular-weight heparin is common but not recommended in all cases[23-26]. A review and meta-analysis of heparin bridging for patients receiving anticoagulant therapy found that although the bleeding rate is significantly increased, the data on the prevention of embolic events are limited[23]. However, when patients are on warfarin before a procedure, clinical judgment is needed regarding whether or not to use heparin bridging and should be based on the patient's risks of thrombosis and procedure-related bleeding[26]. Heparin bridging is necessary when antiplatelet therapy is discontinued in patients undergoing PCI with a first-generation drug-eluting stent, who have a high risk of stent thrombosis. Spine surgeons can assess the risk of procedure-related bleeding based on their experience and knowledge of the literature, but they alone cannot control a patient's risk of thrombosis. Therefore, a team-based approach involving attending physicians, anesthesiologists, and spine surgeons is important for the management of complicated cases.

IV: Postoperative SEH and antithrombotic drugs

A considerable proportion of respondents in our survey reported experiencing an unexpected increase in intraoperative bleeding and postoperative SEH requiring emergency evacuation. Most respondents considered the continuation of antithrombotic drugs to be one of the risk factors for postoperative SEH.

Carragee et al. reported a case of postoperative SEH related to clopidogrel use for protection against coronary stent thrombosis[27], while Yang et al. reported a case of spontaneous SEH during antithrombotic therapy for acute myocardial infarction[28]. There is also a case report of warfarin-related spontaneous SEH[29]. Although we should not think of postoperative SEH and spontaneous SEH as the same entity, we should be aware of the possibility of spontaneous SEH in patients taking antithrombotic drugs. In general, postoperative SEH occurs in 0.10%-0.24% of all patients who undergo spine surgery[30]. Postoperative SEH is multifactorial, and the effect of antiplatelet medication on SEH is still controversial. Finally, as mentioned in a systematic review[31], the rarity of postoperative SEH makes it difficult to reach conclusions regarding potentially predisposing risk factors.

Limitations

One of the limitations of this study is the low response rate of 32.0% to our web-based questionnaire. A meta-analysis of the rates of response to online surveys found the

average response rate to be 44.1%[32]. In retrospect, a more direct approach to JSSR members could have resulted in a higher response rate. However, the number of JSSR board-certified spine surgeons who agreed to participate in this research was 887 (75.1% of all respondents), who were 52.8% of all JSSR board-certified spine surgeons. Another limitation was that the study participants were not asked about restarting antithrombotic drugs after surgery. This is also an important issue that requires investigation in the future.

Conclusion

The results of our web-based questionnaire survey indicate that, in principle, >70% of JSSR members discontinue antithrombotic drugs before elective spine surgery. A considerable proportion have experienced thrombotic complications with discontinuation and hemorrhagic complications with continuation. In the current situation of an aging society and the development of new drugs, spine surgeons should keep updating their knowledge regarding drugs used for comorbidities, in particular their management. A case-by-case assessment of the risks of bleeding and thrombosis requires a team-based approach, and informed consent should be obtained from all patients undergoing spine surgery after thorough counseling about the potential risks and benefits of antithrombotic therapy.

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