

Safety of Continuous Low-Dose Aspirin Therapy for Cervical Laminoplasty

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Abstract:

Introduction: More spinal surgeries are being performed in patients taking low-dose aspirin for primary and secondary prevention of cardiovascular and cerebrovascular ischemic disease. However, there are no recommended guidelines for perioperative aspirin use in patients undergoing spinal surgery. This study evaluated the perioperative effect of continued low-dose aspirin on cervical laminoplasty.

Methods: This was a single-institute retrospective study of patients who underwent laminoplasty at the C2/3 to C7/T1 levels for cervical compression lesions. The comparison of 73 patients who continued to take aspirin at 100 mg/day during the perioperative period and 322 patients who took no antiplatelet or anticoagulant drugs examined their patient characteristics, perioperative parameters, and perioperative complications.

Results: A significantly higher proportion of patients with aspirin were men, and the mean age was significantly higher in patients with than without aspirin ($P=0.011$ and $P<0.001$, respectively). The preoperative hemoglobin level was significantly lower in patients with than without aspirin ($P=0.033$). The number of disk decompression levels, surgical time, intraoperative blood loss, and postoperative drainage volume were not significantly different between patients with and without aspirin. Reoperation for epidural hematoma formation was also not significantly different between patients with and without aspirin. Perioperative blood transfusions were performed in 1 of 73 patients with aspirin and 0 of 322 patients without aspirin, with no significant difference ($P=0.185$). No cardiovascular or cerebrovascular ischemic events occurred in either group.

Conclusions: Continuing low-dose aspirin therapy during a perioperative period for cervical laminoplasty did not increase perioperative bleeding or the risk of bleeding-related complications. Therefore, continuing low-dose aspirin may be acceptable for patients undergoing cervical laminoplasty to prevent increased risk of cardiovascular and cerebrovascular accidents due to aspirin withdrawal.

Keywords:

low-dose aspirin, laminoplasty, cervical spine, spine surgery, perioperative complication, epidural hematoma, perioperative bleeding, perioperative infusion

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Introduction

With the aging of society, increasing numbers of patients are taking low-dose aspirin for primary and secondary prevention of cardiovascular and cerebrovascular ischemic diseases¹⁻⁶. The number of spinal surgeries performed for patients taking low-dose aspirin is also increasing. There are no recommended guidelines for perioperative spinal surgery with aspirin, the most commonly used antiplatelet drug. Increased perioperative bleeding, increased blood transfusions,

and nerve damage due to postoperative spinal epidural hematomas associated with continued aspirin treatment are concerns. It is common to discontinue aspirin administration for some time before spinal surgery⁷⁻⁹. Each institution or physician decides to continue or discontinue low-dose aspirin for spinal surgery on an individual basis^{10,11}.

Concern has recently arisen regarding the risk of perioperative cardiovascular events associated with aspirin withdrawal¹². Historically, aspirin was discontinued at our hospital 7 days before surgery. However, cases of cerebral

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infarction after spinal surgery continued to occur for several years. Therefore, after consultation with a cardiologist, neurologist, and anesthesiologist to prevent perioperative myocardial infarction and cerebral infarction, spinal surgery without concern about massive bleeding has been performed with continuing aspirin therapy at our facility since 2005. In patients undergoing minimally invasive surgeries, we hoped that continuing aspirin would reduce the risk of cardiovascular and cerebrovascular thrombosis without increasing complications, including perioperative bleeding and epidural hematoma formation. The purpose of this study was to evaluate the safety of continuing low-dose aspirin treatment in patients undergoing cervical laminoplasty, a minimally invasive surgery.

Materials and Methods

The institutional review board of Kumamoto Chuo Hospital approved this study (Approval No. 202104-03). We used an opt-out approach instead of obtaining consent from individual patients because of the retrospective nature of this study.

This retrospective study, conducted at a single facility using electronic medical records, evaluated 704 patients. They underwent posterior decompression surgery without instrumentation for cervical lesions associated with degenerative spondylotic disease or ossification of the posterior longitudinal ligament (excluding idiopathic epidural hematomas, infection, tumors, and trauma) from January 2012 to November 2019. Among them, the decompression level was limited to lesions from C2/3 to C7/T1. Patients who underwent laminectomy alone, foraminotomy alone, or laminoplasty combined with foraminotomy and patients with a history of posterior cervical spine surgery were excluded; 613 patients underwent laminoplasty alone for the first time within the hospitalization period. Patients undergoing dialysis were also excluded, leaving 552 patients. Only patients taking low-dose aspirin (100 mg/day) were included; patients taking aspirin at other doses and patients taking antiplatelet or anticoagulant drugs other than aspirin were excluded, leaving 73 patients. A total of 326 patients were taking no antiplatelet or anticoagulant drugs. The excluded drugs were clopidogrel, cilostazol, ethyl eicosapentaenoate, prostaglandin E1, sarpogrelate, warfarin, dabigatran, apixaban, edoxaban, and rivaroxaban. We also excluded four patients without aspirin who developed intraoperative dural injury and postoperative cerebrospinal fluid leakage to eliminate the effects of surgical time, intraoperative bleeding, and postoperative drainage. Finally, the patients were divided into two groups: those taking low-dose aspirin (aspirin group, n=73) and those not taking aspirin (nonaspirin group, n=322) (Fig. 1). The two groups were compared and examined regarding their patient characteristics, perioperative parameters, and perioperative complications.

In most cases, we performed double open-door laminoplasty with hydroxyapatite lamina spacers; we performed

single open-door laminoplasty in only a few cases. Six surgeons were involved. In all cases, only one postoperative closed suction drainage tube was placed. If the drainage volume was ≤ 50 ml within 24 hours, the drainage tube was removed 2 days after surgery; otherwise, the tube was at the operator's discretion.

The examined patient characteristics were sex, age at surgery, body mass index (BMI), and medical history/comorbidities (hypertension, diabetes, angina, myocardial infarction, cerebral infarction, and history of coronary stenting or coronary artery bypass surgery). The perioperative parameters examined were the preoperative hemoglobin level, activated partial thromboplastin time (APTT), albumin level, estimated glomerular filtration rate (eGFR), number of disk decompression levels, surgical time, intraoperative bleeding volume, postoperative drainage volume, and length of hospital stay. Postoperative complications that were investigated were postoperative epidural hematomas requiring additional surgery, perioperative blood transfusions, postoperative infections requiring additional surgery, and other notable perioperative complications.

The statistical analysis was performed using SPSS version 27 (IBM Corp., Armonk, NY, USA). Continuous variables were compared using the Mann-Whitney U test, and categorical variables were compared using Pearson's chi-square test or Fisher's exact probability test. A P value of <0.05 was considered statistically significant.

Results

Patient characteristics

The male-to-female ratio was significantly higher in the aspirin group than in the nonaspirin group ($P=0.011$) (Table 1). Similarly, the average age was significantly higher in the aspirin group (77.3 [range, 57-94] years) than that in the nonaspirin group (69.8 [range, 36-92] years, $P<0.001$). The average BMI was not significantly different between the two groups (23.9 [range, 17.2-31.0] kg/m^2 vs. 24.6 [range, 14.4-39.0] kg/m^2 , respectively; $P=0.539$).

Comorbidities

The prevalence or history of hypertension, diabetes, angina, myocardial infarction, cerebral infarction, and coronary stenting or coronary artery bypass surgery were significantly higher in the aspirin group than in the nonaspirin group (Table 1).

Preoperative parameters

The preoperative hemoglobin level was significantly lower in the aspirin group (13.6 [range, 9.1-17.1] g/dL) than that in the nonaspirin group (14.0 [range, 9.3-19.0] g/dL, $P=0.033$) (Table 2). The preoperative APTT was not significantly different between the two groups (28.4 [range, 21.5-35.2] s vs. 27.9 [range, 18.6-58.6] s, respectively; $P=0.062$). The preoperative albumin level was significantly lower in

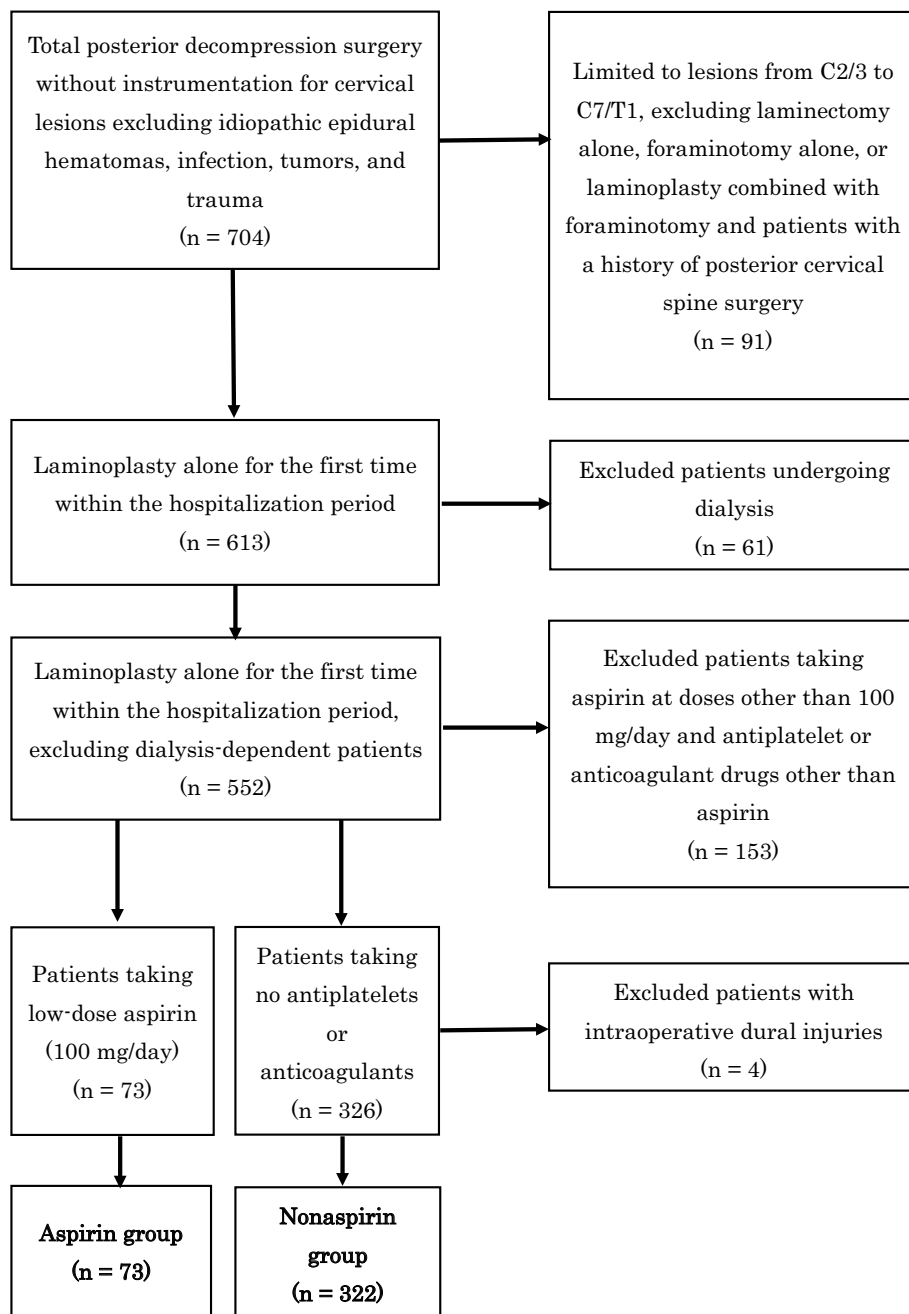


Figure 1. Patient selection process in this study.

the aspirin group (4.1 [range, 2.8-5.0] g/dL) than that in the nonaspirin group (4.3 [range, 2.5-5.4] g/dL, P=0.006). The preoperative eGFR was significantly lower in the aspirin group (63.7 [range, 122.9-28.0] mL/min/1.73 m²) than that in the nonaspirin group (70.6 [range, 140.3-16.6] mL/min/1.73 m², P=0.002).

Intraoperative parameters

The number of disk decompression levels, operative time, and amount of intraoperative blood loss were not significantly different between the two groups (4.3 [range, 2-6] vs. 4.3 [range, 2-6] levels, P=0.729; 104.4 [range, 51-227] vs. 106.0 [range, 49-229] min, P=0.935; and 49.4 [range, 3-275] vs. 47.3 [range, 0-560] mL, respectively; P=0.389).

Postoperative parameters

The postoperative drainage volume was not significantly different between the two groups (279.5 [range, 9-584] vs. 284.7 [range, 30-743] mL, respectively; P=0.847).

Other parameters

The average hospital stay was not significantly different between the two groups (19.3 [range, 7-37] vs. 19.0 [range, 9-49] days, respectively; P=0.157).

Perioperative complications

Reoperation for epidural hematomas was not significantly different between the two groups (0/73 [0.0%] vs. 3/322

Table 1. Characteristics of Patients Undergoing Cervical Laminoplasty.

	Aspirin (n=73)	Nonaspirin (n=322)	P
Sex, male:female	59:14	211:111	0.011*
Age, years	77.3 (57–94)	69.8 (36–92)	<0.001*
BMI, kg/m ²	23.9 (17.2–31.0)	24.6 (14.4–39.0)	0.539
Comorbidities			
Hypertension	49 (67.1%)	163 (50.6%)	0.011*
Diabetes	27 (37.0%)	76 (23.6%)	0.019*
Angina	23 (31.5%)	6 (1.9%)	<0.001*
Myocardial infarction	16 (21.9%)	3 (0.9%)	<0.001*
Cerebral infarction	16 (21.9%)	6 (1.9%)	<0.001*
Coronary stenting or coronary artery bypass surgery	24 (32.9%)	0 (0.0%)	<0.001*

Data are presented as n, mean (range), or n (%).

*Statistically significant difference

BMI, body mass index

Table 2. Perioperative Data from Patients Undergoing Cervical Laminoplasty.

	Aspirin (n=73)	Nonaspirin (n=322)	p
Preoperative parameters			
Hemoglobin, g/dl	13.6 (9.1–17.1)	14.0 (9.3–19.0)	0.033*
APTT, seconds	28.4 (21.5–35.2)	27.9 (18.6–58.6)	0.062
Albumin, g/dl	4.1 (2.8–5.0)	4.3 (2.5–5.4)	0.006*
eGFR, mL/min/1.73m ²	63.7 (28.0–122.9)	70.6 (16.6–140.3)	0.002*
Intraoperative parameters			
Number of decompressed intervertebral disc levels	4.3 (2–6)	4.3 (2–6)	0.729
Operative time, min	104.4 (51–227)	106.0 (49–229)	0.935
Intraoperative blood loss, ml	49.4 (3–275)	47.3 (0–560)	0.389
Postoperative parameters			
Postoperative drainage volume, ml	279.5 (9–584)	284.7 (30–743)	0.847
Others			
Hospital stay, days	19.3 (7–37)	19.0 (9–49)	0.157

Data are presented as the mean (range).

*Statistically significant

APTT, activated partial thromboplastin time. eGFR, estimated glomerular filtration rate.

Table 3. Perioperative Complications in Patients Undergoing Cervical Laminoplasty.

	Aspirin (n=73)	Nonaspirin (n=322)	P
Reoperation for epidural hematoma	0 (0.0%)	3 (0.9%)	0.541
Blood transfusion	1 (1.4%)	0 (0.0%)	0.185
Reoperation for surgical site infection	2 (2.7%)	1 (0.3%)	0.089
Pacemaker placement	1 (1.4%)	0 (0.0%)	0.185
C5 paresis	0 (0.0%)	2 (0.6%)	0.664
CO ₂ narcosis	0 (0.0%)	1 (0.3%)	0.815

Data are presented as n (%).

[0.9%], respectively; P=0.541) (Table 3). The preoperative postoperative epidural hematomas were 29.4, 31.3, and 33.5 APTT of the three patients who underwent reoperation for s, respectively. These values were above the mean APTT in

the group without aspirin, but they did not represent an extreme prolongation. Only one patient in the aspirin group underwent a blood transfusion, but there was no statistically significant difference between the two groups ($P=0.185$). Reoperation for surgical site infection was not significantly different between the two groups (2/73 [2.7%] vs. 1/322 [0.3%], respectively; $P=0.089$). No cardiovascular or cerebrovascular ischemic events occurred in either group. Still, one patient in the aspirin group underwent placement of a pacemaker after surgery because of persistent intraoperative bradycardia, which did not affect the patient's general condition. In addition, two patients in the nonaspirin group had C5 paresis. One patient in the nonaspirin group with obesity (BMI of 36.4 kg/m²) and preoperative sleep apnea syndrome developed carbon dioxide narcosis associated with worsening respiratory failure after surgery, but his condition improved with treatment.

Discussion

Summary of this study

This study demonstrated that continued low-dose aspirin therapy did not increase the amount of perioperative bleeding or the rate of reoperation for postoperative epidural hematomas and perioperative blood transfusion in cervical laminoplasty. This is the first study to investigate the effect of low-dose aspirin (100 mg/day) on the perioperative bleeding volume and perioperative complications associated with bleeding in cervical laminoplasty with the decompression range limited to C2/3 to C7/T1.

Conventional methods of aspirin withdrawal in patients undergoing general spinal surgery

Several studies have shown that aspirin may be a risk factor for epidural hematomas^{10,13,14}. Additionally, stopping aspirin about 7 days before surgery can normalize the bleeding tendency¹⁵. Therefore, despite the usefulness of aspirin in the prevention of cardiovascular and cerebrovascular thrombosis, spine surgeons discontinue aspirin ≥ 7 days before surgery to prevent increased perioperative bleeding and neurological damage due to postoperative epidural hematoma formation⁷⁻⁹.

Studies that advocate aspirin continuation in patients undergoing spine surgery

Park et al.¹⁶ evaluated patients who underwent two levels of decompression of the lumbar spine and posterolateral fusion. Three groups were compared: 38 patients who did not take aspirin, 38 patients who took aspirin and discontinued it 1 week before surgery, and 30 patients who continued aspirin during the perioperative period. Similar to the present study, the authors found no significant difference in the surgery time or perioperative bleeding volume among the three groups. No epidural hematomas or cardiovascular or cerebrovascular complications occurred. Cuellar et al.¹⁷ evalu-

ated the perioperative bleeding volume and perioperative complications in 100 patients who underwent placement of cardiovascular stents and continued aspirin before surgery and 100 patients who discontinued aspirin at least 5 days before surgery. They found no significant differences in the intraoperative bleeding volume, postoperative blood transfusion volume, or postoperative epidural hematoma incidence; however, they did not evaluate the postoperative bleeding volume¹⁸. In addition, the operation time was significantly shorter in the aspirin group whereas the proportions of cervical spine procedures and the lumbar fusion procedures with 3-4 fused segments were significantly higher in the control group. The two groups were not matched according to the surgical lesion or surgical invasion associated with the surgical procedure. Soleman et al.¹⁹ compared 40 patients in the aspirin continuation group with 62 patients in the aspirin discontinuation group at least 1 week before noninstrumented extradural lumbar spine surgery. There were no significant differences in the operation time, perioperative bleeding volume, average postoperative blood transfusion volume, or complication rate between the two groups. A systematic review and meta-analysis of these three studies showed that continuing aspirin did not increase the surgery time, perioperative bleeding, or complications, including epidural hematoma formation¹¹. These results are consistent with those of the present study. In these studies, the duration of surgery was about 1-2 times longer, intraoperative bleeding was about 3-14 times higher, and postoperative bleeding was more than 1/2 to 2 times higher. The degree of surgical invasion was equal to or greater than that of our series. The extent to which aspirin withdrawal causes perioperative coronary and cerebrovascular accidents was not clear in these studies. However, studies involving 5690 participants who underwent 5866 orthopedic surgeries of the spine (38.0%), hip (31.0%), and knee (31.0%) showed that the rate of perioperative continuation of aspirin in patients with coronary artery disease in recent cases significantly increased and that the incidence of postoperative myocardial infarction was significantly reduced²⁰. In the studies by Park et al.¹⁶ and Soleman et al.¹⁹, the aspirin group included more patients undergoing secondary prophylaxis for coronary artery disease. Cuellar et al.¹⁷ retrospectively enrolled patients in the aspirin withdrawal group and prospectively enrolled patients in the aspirin continuation group, suggesting the possibility of selection bias. The small number of cases in these studies may have also affected the results.

Studies that do not advocate aspirin continuation in patients undergoing spine surgery

Kang et al.⁷ compared perioperative bleeding and complications of lumbar fusion between patients who stopped taking aspirin 1 week before surgery and those who did not take aspirin. Although there was no difference in intraoperative bleeding or intraoperative blood transfusion between the two groups, the aspirin group had significantly higher postoperative bleeding and transfusion volumes. One patient re-

quired reoperation for an epidural hematoma. However, this patient had a significant intraoperative bleeding volume of 1500 mL, and postoperative coagulation abnormality associated with bleeding may occur¹⁷⁾. In addition, the authors noted that the patients in the aspirin group had more medical diseases that could have been associated with a bleeding tendency. Park et al.⁸⁾ compared perioperative bleeding in a 3 to 7 day preoperative aspirin discontinuation group, a 7 to 10 day preoperative aspirin discontinuation group, and a nonaspirin (control) group of patients undergoing one- or two-level lumbar interbody fusion. In contrast to the findings reported by Kang et al.⁷⁾, patients who discontinued aspirin 7-10 days before surgery showed no increase in drained blood. When aspirin was withdrawn 3-7 days before surgery, the amount of drained blood was higher in stand-alone and one-level fusion than in the control group; however, there was no difference between two-level fusion and the control group. In contrast, in two-level fusion, the postoperative bleeding volume was significantly higher in patients who discontinued aspirin 7-10 days before the operation than in the control group. In addition, three epidural hematomas requiring reoperation occurred in the two-level intervertebral fixation group, two hematomas occurred in the 7 to 10 day preoperative aspirin discontinuation group, and one hematoma occurred in the control group. The two papers recommended aspirin withdrawal at least 7 days before surgery, but as Cuellar et al.¹⁷⁾ pointed out, they included no patients who continued aspirin during the perioperative period. In a systematic review and meta-analysis of four studies, including that by Park et al.⁸⁾, aspirin did not increase the duration of surgery, intraoperative bleeding volume, or risk of blood transfusions, consistent with the present study²¹⁾.

Limitations of this study

This study has some limitations. The first is that it was a retrospective study. Additionally, it was impossible to divide the patients taking aspirin into a continuation group and a discontinuation group and directly compare and evaluate these two groups. Therefore, the risk of cardiovascular and cerebrovascular accidents could not be assessed when aspirin was withdrawn during the perioperative period of cervical laminoplasty. In addition, the effects of confounding factors associated with the indication for oral aspirin could not be ruled out. Aging is generally a risk factor for perioperative complications²²⁾, including postoperative spinal epidural hematoma²³⁾, mortality^{22,24)}, anemia, and chronic kidney disease which is an independent risk factor for in-hospital death after spinal surgery²⁵⁾. Considering the trend of a prolonged APTT in the aspirin group, we do not believe that the safety of perioperative administration is overestimated because these indices could have had a more unfavorable effect on the aspirin than nonaspirin group. Second, because perioperative complications occur relatively infrequently, the sample size in this study may be too small for statistical detection. Spinal epidural hematoma formation, a postoperative

complication of spinal surgery, is rare, and its cause is a complex effect of multiple factors^{13,14,23)}, making it difficult to assess the effects of aspirin in this study. However, although abnormal coagulation and anticoagulant therapy are generally considered risk factors for epidural hematoma formation^{13,23)}, antiplatelet drugs and anticoagulants have been distinguished in previous discussions despite their completely different mechanisms of action. Aspirin, an antiplatelet drug, does not induce a high international normalized ratio or prolonged APTT, which are risk factors for epidural hematoma formation²³⁾; therefore, these two drugs should be evaluated separately.

Recommendations from this study

The need for perioperative blood transfusion and reoperation for postoperative epidural hematomas are undesirable problems that spinal surgeons may encounter. Additionally, myocardial infarction or cerebral infarction during the perioperative period is a crucial problem that must be avoided, especially for patients of very advanced age with relatively vulnerable general conditions. Typically, continuing aspirin is reasonable when the risks of thrombotic events outweigh those of increased bleeding. Accordingly, continuing aspirin administration in perioperative period of cervical laminoplasty with a low risk of bleeding seems reasonable, particularly for patients preventing secondary thrombosis with aspirin, the withdrawal of which has a high risk of thrombosis.

Conflicts of Interest: The authors declare that there are no relevant conflicts of interest.

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Ethical Approval: The institutional review board and ethics committee of Kumamoto Chuo Hospital approved this retrospective study (Number: 202104-03).

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