

Effect of Antithrombotic Therapy on Secondary Bleeding After Proctological Surgery

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Abstract

Background: The purpose of this study was to identify the incidence and severity of secondary bleeding after proctological surgery for patients with or without antithrombotic therapy.

Methods: We retrospectively identified 113 patients who underwent proctological surgery in our hospital from March 2009 to February 2019. In general, antiplatelet drugs were continued and anticoagulant drugs were either substituted or withdrawn prior to the surgery. The severity of secondary bleeding was classified as mild, moderate, severe.

Results: Eighteen patients underwent antiplatelet therapy (A group) and 95 patients did not undergo antithrombotic therapy (N group). Secondary bleeding was observed in nine patients (8.0%) and patients in the A group exhibited significantly higher rate of secondary bleeding rate than patients in the N group (39% vs. 2.4%, $P < 0.01$). The median interval from surgery to the onset of secondary bleeding was 5 (range: 0-11 days). The severity of bleeding was the highest in patients administered direct oral anticoagulants (DOAC) and was the lowest in those administered aspirin. There was no mortality or cardiovascular event.

Conclusions: Antithrombotic therapy is associated with high risk of secondary bleeding after proctological surgery, particularly in patients who undergo anticoagulant therapy. Delaying of postoperative resumption of anticoagulants may be considered in balancing the individual risk of postoperative thromboembolic complications against the risk of secondary bleeding. Future prospective studies with larger number of patients are needed to determine the appropriate timing of resuming antithrombotic therapy.

Background

Surgery for patients taking the antithrombotic drugs for prevention and treatment to cardiovascular disease, including anticoagulant and antiplatelet drug, is increasing gradually because of aging society. Discontinuation of the antiplatelet drug in perioperative period could lead to a cardiovascular event in moderate to high risk patients at a high rate [1, 2, 3]. Nowadays, in patients with moderate to high risk for cardiovascular events, receiving antiplatelet therapy and requiring a noncardiac surgery, continuing antiplatelet drugs perioperatively is recommended [4]. Furthermore, anticoagulation bridging therapy is recommended in patients with high risk for thromboembolism, including those with mechanical heart valve, atrial fibrillation and venous thromboembolism, anticoagulation bridging therapy is recommended.

Several studies have evaluated the bleeding risk in patients who require noncardiac surgery with antithrombotic drugs [5, 6, 7]. Despite an increased risk of transfusion, continuing antithrombotic therapy during a noncardiac surgery is feasible. To date, there have been limited reports on the risk of secondary bleeding after proctological surgery in patients who are administered with antithrombotic drugs [8, 9, 10]. The purpose of this study was to identify the incidence and severity of secondary bleeding after proctological surgery in our hospital.

Methods

This was a retrospective observational study conducted in a single institution. A total of 113 consecutive patients who underwent proctological surgery from March 2009 to February 2019 were included in the study. Antithrombotic therapy consists of antiplatelet therapy and anticoagulant therapy. As a general rule in our hospital, we continued antiplatelet drugs for any proctological surgery. For patients receiving clopidogrel or cilostazol, we replaced their medications with aspirin 3 to 14 days prior to the surgery. If patients received doublet antiplatelet therapy, we replaced their medications with aspirin alone 7 to 14 days prior to the surgery. Patients on anticoagulant therapy were either bridged to low-molecular-weight heparin (LMWH), if they had high risk for thrombosis, or withdrawn before surgery. For example, warfarin therapy and direct oral anticoagulants (DOAC) were withdrawn 5 days and 1–2 days prior to the surgery, respectively. About 12–24 hours after the surgery, anticoagulant therapy was resumed if there were no signs of bleeding.

We compared short-term perioperative results (such as intra-operative bleeding, post-operative bleeding, and post-operative hospital stays) between patients who either (A group) or not received antithrombotic therapy (N group). According to Piot et al [8], the secondary bleeding was graded as minor if the patients were not readmitted (no hemodynamic disturbance and/or no serious underlying medical condition), moderate if the patients were readmitted (frequent heavy bleeding, severe associated pathology, hemodynamic variations, anxiety, and/or isolated patient) or severe if surgical hemostasis or blood transfusion was needed.

We used t-tests to compare the average values of continuous variables under normal distribution and Mann-Whitney U-tests to compare median values of continuous variables under non-normal distribution. Fisher's exact tests were used to compare the categorical variables between the groups. The threshold for significance was set at $P < 0.05$. All statistical analyses were conducted using EZR [11].

Results

Patients' demographic data are shown in Table 1, and the most frequent comorbidity was cardiovascular disease, which was observed in 39 (35%) patients. Table 2 shows perioperative data, including surgical procedures, rate of antithrombotic therapies, and complications. Eighteen (15.9%) patients received antithrombotic therapy (A group) for primary and secondary prophylaxes. Seventeen (15.0%) patients exhibited complications, including secondary bleeding events in nine (8.0%) patients. The severity of these bleeding complications was minor in five, moderate in three and severe in one patient. The secondary bleeding events were treated via ligation and excision in seven patients and simply via laying open in two patients. Table 3 shows comparison demographic and perioperative data between A group ($n = 18$) and N group ($n = 95$). Patients in the A group had a significantly higher age (68 ± 18 vs. 4 ± 17 years, $P < 0.01$) and higher secondary bleeding rate (39% vs. 2.4%, $P < 0.01$) than N group. Sex, body mass index, ASA-PS (American Society of Anesthesiologists Physical Status classification), operative time, intraoperative bleeding, and postoperative length of stay did not differ between A group and N group. The

median interval from completion of surgery to the onset of secondary bleeding was 5 days (range: 0–11 days). The antithrombotic therapies and secondary bleeding events are described in Table 4. Patients receiving anticoagulant therapy (such as taking warfarin and DOAC) were more likely to experience more severe secondary bleeding complications compared with those receiving antiplatelet therapy. There was no cardiovascular, pulmonary or cerebral events or mortality.

Table 1
Patients' demographic data.

Age (mean, standard deviation)	57 (± SD18)
Male/Female	85/28
BMI (median, range)	23.4 (15.8–63.7)
ASA-PS 1/2/3	27/58/28
Comorbidities	39 (35%)
□ Cardiovascular disease	21 (19%)
□ Endocrine and metabolism disease	14 (12%)
□ Inflammatory bowel disease	9 (8.0%)
□ Gastrointestinal disease	8 (7.1%)
□ Renal disease	7 (6.2%)
□ Hematological disease	5 (4.4%)
□ Infectious disease	5 (4.4%)
□ Psychiatry and neurology disease	4 (3.5%)
□ Respiratory disease	2 (1.8%)
□ Immunological disease	
Antithrombotic therapies	18(16%)
Reasons for antithrombotic therapies	7
□ Atrial fibrillation	3
□ Ischemic heart disease	3
□ Valve replacement	2
□ Brain stroke	1
□ Coronary artery bypass graft	1
□ Hypoplastic left heart syndrome	1
□ Hemodialysis	
BMI: Body mass index (kg/m ²), ASA-PS: American Society of Anesthesiologists Physical Status classification	

Table 2
 Perioperative data

Hemorrhoid/Fistula/Fissure	52/56/5
Surgical procedures	48
□Ligation and Excision	2
□Ligation	2
□PPH	32
□Lay open	18
□Seton	6
□Coring out	5
□Fissurectomy	
Antithrombotic therapies(rate)	18 (16%)
□Aspirin	5 (4.4%)
□Warfarin	10 (8.8%)
□DOAC	3 (2.7%)
Complications(rate)	17 (15%)
□Secondary bleeding	9 (8%)
□Infection	3 (2.7%)
□Recurrence	2 (1.8%)
□Others	3 (2.7%)
The interval days from surgery to secondary bleeding (median, range)	5(0–11)
Intervention for secondary bleeding	4
□Trans anal hemostasis	4
□Observation	1
□Intravenous drip of hemostyptic	
PPH: procedure for prolapse and hemorrhoids	
DOAC: direct oral anticoagulants	

Table 3
Comparison between A group and N group

	A group (n = 18)	N group (n = 85)	P value
Age (mean ± standard deviation)	68 ± 18	54 ± 17	< 0.01
Male/Female	14/4	71/24	1
BMI (median, range)	22.4 (15.8–30.7)	23.5 (16.1–63.7)	0.16
ASA-PS 1/2/3	0/10/8	27/38/20	0.07
Operative time (min) (median, range)	39 (22–98)	37 (9-140)	0.79
Intraoperative bleeding (mL) (median, range)	5 (5-106)	5 (5-150)	0.72
Postoperative length of stay (median, range)	5 (3–11)	4 (1–78)	0.63
*Secondary bleeding (rate)	7 (39%)	2 (2.4%)	< 0.01
Minor	4	1	
Moderate	2	1	
Severe	1		
BMI: Body mass index (kg/m ²)			
*Severity of secondary bleeding based upon Pigot et al ⁸⁾ classification			

Table 4
Antithrombotic therapies and secondary bleeding

*Severity of secondary bleeding	Aspirin (n = 5)	Warfarin and heparin-bridging (n = 10)	DOAC (n = 3)
Minor	2	1	1
Moderate		2	
Severe			1
Total	2	3	2
*Severity of secondary bleeding based upon Pigot et al ⁸⁾ classification			

Discussion

This study investigated the risk of secondary bleeding after proctological surgery in patients who received antithrombotic therapy. The results showed that patients with antithrombotic therapy exhibited higher risk of secondary bleeding than control group. According to previous studies, the frequency of secondary bleeding after hemorrhoid surgery is 0.6–2.4% [12, 13, 15] and it is likely to occur on 6-9th postoperative day [14, 15]. In our report, the incidence of secondary bleeding was slightly higher, because our hospital is one of the tertiary referral centers that treat high risk patients. As a result, 25% of the patients enrolled in this study were ASA-PS3 and about 35% of patients had cardiovascular disease.

A previous study showed that perioperative antiplatelet therapy for noncardiac surgery confers minimal bleeding risk with no thrombotic complications, which indicated that antiplatelet therapy was safe perioperatively [5]. This was in agreement with the results of the current study. Previously, there has been a study on the risk of secondary bleeding in patients receiving perioperative antithrombotic therapy during proctological surgery [8]. Multivariate analysis in that study revealed that administration of clopidogrel, discontinuing anticoagulant drugs, and bridging to LMWH were significantly high risk factors of secondary bleeding. Our study also showed that anticoagulant therapy, including warfarin, and DOAC, was associated with increased severity of secondary bleeding.

In this study, we showed that antithrombotic therapy during proctological surgery could lead to high risk of secondary bleeding. Hence, additional postoperative care is required for such cases. Since there was no cardiovascular, pulmonary, or cerebrovascular event and mortality during perioperative period, it was hypothesized that temporary modification or discontinuation of their medication could be done during proctological surgery for patients receiving antithrombotic therapy.

This study revealed that patients receiving perioperative antithrombotic therapy had high risk for secondary bleeding after proctological surgery and the severity of secondary bleeding was the highest in patients receiving DOAC and the lowest in those receiving aspirin. Since secondary bleeding caused by aspirin tend to be mild, aspirin could be administered during proctological surgery, while considering the risk of cardiovascular event caused by withdrawal. The medications of the patients receiving anticoagulant therapy should be tailored, while considering the risk of cardiovascular events, to minimize the severity of secondary bleeding. Based on the risk of cardiovascular events associated with mechanical heart valve, atrial fibrillation, and deep vein thrombosis, it is necessary to determine whether anticoagulant therapy can be discontinued temporarily or bridged to heparin before surgery. It has previously been recommended that anticoagulant therapy should be resumed after 12–24 hours postoperatively (evening of the day of surgery or the next morning after surgery) [4], however, in this study, the patients received warfarin. Generally, with warfarin therapy, the mean time attaining an $\text{INR} \geq 2.0$ is about 5 days, but same effect is achieved in a shorter time with DOAC. Our results that the median onset of secondary bleeding was 5 days after surgery indicated that resumption of DOAC could be delayed until the 5th postoperative day, which was more delayed than our current practice (after 12–24 hours after surgery). Although surgeons must have already acknowledged to pay attention to the patients

with antithrombotic therapy when they undergo proctological surgery, the actual data on postoperative outcome have been rarely available in the literature, in particular for those with DOAC. The incidence of postoperative bleeding and the timing of discontinuation and resumption of antithrombotic drugs remains to be investigated, in particular for patients with DOAC. Previous review articles recommended the discontinuation of antiplatelet or anticoagulant therapy about 5 to 7 days before and after any forms of surgery for hemorrhoids [16, 17]. Yano et al. [15] reported that 23 out of 1294 patients (1.7%) underwent second operation for postoperative bleeding after hemorrhoidectomy. In their study, 3.6% of the patients had previous use of anticoagulants and that did not correlate with the increased incidence of postoperative bleeding. They also described that anticoagulant therapy was routinely discontinued about 3 to 10 days before surgery and resumed 7 days after surgery [15].

There were several limitations of this study. First, this study was performed retrospectively at a single institute and the number of cases were small. Second, our study employed both antiplatelet and anticoagulant therapies, which could lead to varied results in the target population due to the different purposes of each type of antithrombotic therapy.

Conclusions

Antithrombotic therapy is associated with high risk of secondary bleeding after proctological surgery, particularly in patients with anticoagulant therapy. Delayed postoperative resumption of anticoagulants may be considered in balancing the individual risk of postoperative thromboembolic complications against the risk of secondary bleeding. Future prospective studies with larger number of patients are needed to determine the appropriate timing of resuming antithrombotic therapy.

Abbreviations

LMWH: Low-molecular-weight heparin; **DOAC:** Direct oral anticoagulants; **INR:** International normalized ratio; **BMI:** Body mass index; **ASA-PS:** American society of anesthesiologists-physical status classification; **PPH:** Procedure for prolapse and hemorrhoids

Declarations

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Bioethics Committee for Clinical Research, Saitama Medical Center, Jichi Medical University (Reference number S19-159), and it was performed in accordance with the Declaration of Helsinki. Because this was a retrospective observational study, written consent was not obtained from the patients in advance. Instead, the research information is disclosed to the patients through our hospital website in accordance with “opt-out method”.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIAL

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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AUTHORS' CONTRIBUTIONS

RM and ST (corresponding author) proposed study conception and design. RM, EM, NK, JT, ST and HI performed data collection and acquisition. RM and ST (corresponding author) interpreted the data. EM, NK, JT, ST, and HI edited the manuscript. YM and TR had a role in critical revision of the manuscript. All authors have read and approved the final version of the manuscript.

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