Original Article

Perioperative Antithrombotic Treatment in Proctological Surgery

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ABSTRACT

Background: This retrospective study attempted to identify the optimal perioperative antithrombotic treatment regimen for proctological surgery.

Methods: From April 2008 to August 2014, 529 patients (351 males and 178 females) underwent proctological surgery. Of these 529 patients, 73 (13.8%) received preoperative antithrombotic treatment. Perioperatively, antithrombotic treatment was unchanged for 26 patients, switched to heparin for 38 patients, and withdrawn for 9 patients.

Results: Postoperative hemorrhage occurred in 18 of the 529 patients (3.4%). No uncontrolled intraoperative bleeding was reported, and there were no intraoperative deaths. The incidence of postoperative hemorrhage was 1/26 (3.8%) in the antithrombotic drug continuation group, 14/38 (36.8%) in the heparin substitution group, 0/9 (0%) in the antithrombotic treatment discontinuation group, and 3/456 (0.7%) in the control group. The risk factors for hemorrhage were heparin substitution ($p < 0.001$; 95% confidence interval 14.557–166.588; odds ratio 49.241) and operative time ($p = 0.050$; 95% confidence interval 1.000–1.025; odds ratio 1.013).

Conclusions: The incidence of thromboembolism caused by preoperative discontinuation of antithrombotic treatment was very low; however, thromboembolism can result in serious complications. Heparin substitution was associated with the highest incidence of postoperative hemorrhage; thus, continuation of existing antithrombotic treatment appears to be a safer perioperative antithrombotic strategy for proctological surgery.

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KEYWORDS: hemorrhage, antithrombotic treatment, proctological surgery, heparin, warfarin

The incidence of hemorrhage after proctological surgery is about 5%.[1] Hemorrhage requires additional treatment and therefore decreases patient quality of life and increases medical costs. Because the incidence of cardiovascular disease has increased with the aging of the population, there is a greater likelihood that patients receiving antithrombotic treatment will undergo surgery. Antithrombotic treatment increases the risks of intra- and postoperative hemorrhage. However, if antithrombotic treatment is stopped before surgery, the risk of thromboembolism increases.

Guidelines for perioperative antithrombotic treatment

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in dermatological and endoscopic surgery have been published.[2–4] However, no definitive guidelines for perioperative antithrombotic treatment in proctological surgery are currently available. This retrospective study investigated perioperative antithrombotic treatment in proctological surgery.

Methods

From April 2008 to August 2014, a total of 529 patients (351 males and 178 females) underwent proctological surgery at our center. The mean patient age was 56 years (range 17–92 years). Of these 529 patients, 73 (13.8%) were receiving preoperative antithrombotic treatment; antithrombotic treatment was unchanged for 26 patients, switched to heparin for 38 patients, and withdrawn for 9 patients (Table 1, 2). Hemorrhage was defined as bleeding requiring treatment such as compression, suturing, or regulation of an antithrombotic. There were no guidelines available for perioperative antithrombotic therapy for proctological surgery when these procedures were performed. Therefore, the guidelines for perioperative antithrombotic therapy of the Japanese Circulation Society were used.[5] Heparin substitution or antithrombotic drug withdrawal were selected only after evaluating individual risk of thromboembolism. Patients at high risk for thromboembolism were assigned to heparin substitution (heparin substitution group). Antithrombotic drug treatment was discontinued for patients at low risk for thromboembolism (antithrombotic discontinuation group).

Table 1 Patient characteristics

Number of patients	529
Characteristic	
Sex	
Male	351
Female	178
Median age, years (range)	56 (17–92)
Disease	
Hemorrhoids	247
Fistula	93
Periproctal abscess	114
Rectal prolapse	44
Anal fissure	15
Anal polyp	8
Rectocele	4
Rectal tumor	4
Antithrombotic therapy	
Positive	73
Negative	456

In the heparin substitution group, the antithrombotic drug was changed to unfractionated heparin with a short half-life: 10000 to 25000 units of intravenous heparin were administered over a 24-hour period. The activated partial thromboplastin time (APTT) was then adjusted to 1.5 to 2.5 times the normal control value. Heparin treatment was stopped 6 hours before surgery and then immediately resumed after surgery. Warfarin therapy was also restarted on postoperative day 1. If the prothrombin time/International normalized ratio (PT/INR) was within therapeutic range, heparin was suspended. Aspirin, ticlopidine, and clopidogrel were stopped 7 to 14 days before surgery, and cilostazol was suspended 3 days before surgery. However, the incidence of hemorrhage was high when these antithrombotic therapies were continued in the perioperative period. Discontinuation of antithrombotic drug treat-

Table 2 Antithrombotic treatment, by group

Antithrombotic drug	Antithrombotic treatment continued	Heparin substitution	Antithrombotic treatment discontinued
Aspirin	4	0	5
Aspirin + clopidogrel	4	2	0
Aspirin + ticlopidine	1	1	0
Aspirin + cilostazol	1	0	2
Cilostazol	3	0	0
Ticlopidine	1	1	1
Warfarin	9	31	1
Warfarin + aspirin	1	1	0
Warfarin + aspirin + ethyl icosapentate	0	1	0
Dabigatran	1	1	0
Rivaroxaban	1	0	0
Total	26	38	9

ment increases the risk of thromboembolism. Consequently, we changed the antithrombotic therapy protocol, starting in October 2013. The modified anticoagulant therapy called for suspension of heparin substitution and converted the patient to antithrombotic continuation (antithrombotic continuation group). Patients who did not receive antithrombotic therapy were designated as the control group. Patients in the heparin substitution, antithrombotic therapy discontinuation, and control groups all underwent surgery performed under spinal anesthesia.

Postoperative hemorrhage was caused by bleeding from a wound or an excessive antithrombotic drug dose. To distinguish between these causes, a coagulation test was performed immediately after hemorrhage was identified. In patients with hemorrhagic complications and a PT/INR increase of 3.0 or more,[6] hemorrhage was presumed to have been caused by an excessive warfarin dose. An APTT twice that of normal controls indicated increased hemorrhagic risk from an excessive heparin dose.[7] The dose of the antithrombotic drug was reduced for patients with a suspected overdose. When the results of coagulation testing were normal, hemostasis treatment was continued. An absorbable hemostat was attached to the wound, to prevent postoperative bleeding.

This study was reviewed and approved on November 26, 2014 by the institutional ethics committee of Toho University Omori Medical Center (review no. 26-209).

Statistical analysis

The Statistical Package for the Social Sciences (SPSS), Version 19 (International Business Machines Corp. (IBM), Armonk, NY, USA) was used to analyze the data. The chi-square test was used to compare age, sex, antithrombotic treatment, and operative strategy. The *t* test was used to compare blood loss and operative time. Univariate logistic analysis was used to evaluate potential hemorrhagic risk factors, including age, sex, antithrombotic treatment, and operative strategy. Multivariate logistic regression analysis was used to assess variables that significantly differed in univariate analysis.

Results

Postoperative hemorrhage occurred in 18 of 529 patients (3.4%); postoperative hemorrhage was isolated in 17 patients and occurred 6 times in 1 patient (total 23 events). No uncontrolled intraoperative bleeding was reported, and there were no operative deaths. The mean interval from surgery to hemorrhage was 7 days (range 0–17 days). The incidence of postoperative hemorrhage was 1/26 (3.8%) in the antithrombotic drug continuation group, 14/38 (36.8%) in the heparin substitution group, 0/9 (0%) in the antithrombotic treatment discontinuation group, and 3/456 (0.7%) in the control group.

The pathogenesis of postoperative hemorrhage was classified as simple wound bleeding and bleeding caused by an excessively high antithrombotic drug dose. Wound bleeding caused 15 postoperative hemorrhage events (1 in the antithrombotic drug continuation group, 11 in the heparin substitution group, and 3 in the control group). Overdose of an antithrombotic drug caused 8 of the postoperative hemorrhage events (all in the heparin substitution group).

In 5 events, wound bleeding was treated conservatively by methods such as compression; 10 events required hemostasis treatment such as suturing (3 events were treated in the ward and 7 were treated in the operating room). In all 8 patients with hemorrhage caused by antithrombotic drug overdose, adjustment of the drug dose stopped the bleeding, and no additional treatment was required. There were no complications, such as thromboembolism, from heparin substitution or withdrawal of antithrombotic treatment.

Hemorrhagic risk factors identified in univariate logistic analysis were age, sex, lack of antithrombotic treatment, heparin substitution, and operative time (Table 3). Multivariate logistic regression analysis evaluated 5 risk profiles: the hemorrhagic risk factors identified were heparin substitution ($p < 0.001$; 95% confidence interval 14.557–166.588; odds ratio 49.241) and operative time ($p = 0.050$; 95% confidence interval 1.000–1.025; odds ratio 1.013) (Table 4).

Discussion

We studied perioperative antithrombotic treatment in proctological surgery and found that heparin substitution and operative time increased the incidence of postoperative hemorrhage. There were no serious complications associated with continuation of perioperative antithrombotic treatment.

Many previous studies have investigated antithrombotic treatment in dermatological surgery. Dixon et al examined perioperative antithrombotic treatment for 2394 patients with skin cancer (5950 surgical procedures)[2]; antithrombotic therapy was continued, and surgeries were performed under local anesthesia when the PTI/NR was

Table 3 Results of univariate logistic analysis

Variable	β	Wald statistic	Degrees of freedom	p value	Odds ratio	95% confidence interval	
						Lower limit	Upper limit
Age (years)	0.38	5.730	1	0.017 *	1.039	1.007	1.071
Sex (Male: 1, Female: 0)	2.126	4.220	1	0.04 *	8.383	1.103	63.738
Antithrombotic treatment							
None	−3.572	30.100	1	<0.001 **	0.028	0.008	0.101
Continuation	0.191	0.033	1	0.856	1.210	0.154	9.493
Heparin substitution	4.142	46.492	1	<0.001 **	62.920	19.131	206.941
Discontinuation	−17.822	<0.001	1	0.999	<0.001	<0.001	>999.999
Procedure							
Hemorrhoidopexy	0.533	0.254	1	0.614	1.705	0.021	13.569
Abscess	−18.057	<0.001	1	0.996	<0.001	<0.001	>999.999
Hemorrhoidectomy	0.367	0.551	1	0.458	1.443	0.548	3.800
Fistulectomy	0.676	1.540	1	0.215	1.966	0.676	5.721
Anterior levator plasty	−17.812	<0.001	1	0.999	<0.001	<0.001	>999.999
Rectal prolapse	−0.415	0.158	1	0.691	0.661	0.086	5.099
Fissurectomy	1.040	0.936	1	0.333	2.830	0.344	23.264
Sclerotherapy	−17.806	<0.001	1	1.000	<0.001	<0.001	>999.999
Tumor resection	−17.814	<0.001	1	0.999	<0.001	<0.001	>999.999
Operative bleeding (ml)	0.001	0.042	1	0.838	1.001	0.995	1.006
Operative time (min)	0.010	4.804	1	0.028 *	1.010	1.001	1.018

β: Partial regression coefficient
* p<0.05, ** p<0.001

Table 4 Results of multivariate logistic analysis

Variable	β	Wald statistic	Degrees of freedom	p value	Judgement	Odds ratio	95% confidence intervals	
							Lower limit	Upper limit
Sex (Male: 1, Female: 0)	1.896	2.760	1	0.097		6.658	0.711	62.335
Heparin substitution	3.897	39.278	1	<0.001	**	49.241	14.557	166.588
Operative time (min)	0.013	3.851	1	0.050	*	1.013	1.000	1.025
Constant	−7.553	25.569	1	<0.001				

β: Partial regression coefficient
* p<0.05, ** p<0.001

less than 3. The hemorrhagic risk factors identified were age 67 years or older and warfarin treatment; aspirin was not an independent risk factor for hemorrhage (Table 5).

Another study examined 2790 patients undergoing dermatological surgery with continued antithrombotic treatment.[8] Although 2.4% of the patients continued warfarin treatment, intraoperative hemorrhage was easily controlled, and there were no cases of postoperative hemorrhage. However, another report found that warfarin caused hemorrhagic complications in dermatological surgery and that the effect was dose-dependent[9]; hence, monitoring by means of coagulation testing should be used in order to prevent hemorrhage.

Pigot et al studied perioperative antithrombotic treatment in 2513 proctological surgical procedures and reported postoperative hemorrhage in 115 procedures

Table 5 Comparison of antithrombotic treatment selection in the present and past studies[1, 2]

	Treatment	Bleeding +	Bleeding −	Total	Rate of bleeding (%)
The present study					
Rate of antithrombotic treatment, 13.8%	Heparin substitution †	14	24	38	36.8
1 surgeon	Antithrombotic continuation	1	25	26	3.8
	Discontinuation	0	9	9	0
	Control	3	453	456	0.7
	Total	18	511	529	3.4
Pigot et al. (Proctology)					
Rate of antithrombotic treatment, 3%	Heparin substitution †	4	3	7	57.1
8 surgeons	Antithrombotic continuation † §	10	46	56	17.9
	No antithrombotic → Heparin	2	0	2	100
	Control	99	2,349	2,448	4
	Total	115	2,398	2,513	4.6
Dixon et al. (Dermatology)					
Rate of antithrombotic treatment, 17.2%	Warfarin †	6	61	67	9
1 surgeon	Aspirin	9	325	334	2.7
	Warfarin + Aspirin †	2	9	11	18.2
	Control	23	1,959	1,982	1.2
	Total	40	2354	2394	1.7

† Risk factor of bleeding

§ only clopidogrel

Bleeding + : perioperative hemorrhage occurred, Bleeding − : no hemorrhage.

(4.6%).[1)] The incidence of hemorrhage was higher in a heparin substitution group — 4 of 7 cases (57.1%) — as compared with only 10 of 56 cases (17.9%) in an antithrombotic drug continuation group. The incidence of postoperative hemorrhage was higher for patients who received heparin substitution and those receiving clopidogrel; however, aspirin was not a reported hemorrhagic risk factor. In the present study, heparin substitution was a risk factor for hemorrhage, but antiplatelet treatments, including clopidogrel, were not.

A previous study investigated postoperative bleeding after hemorrhoid surgery in 1294 patients, among whom antithrombotic treatment was discontinued in 47 patients (3.6%).[10)] Postoperative hemorrhage occurred in 23 patients (1.7%); only 1 patient (0.077%) receiving aspirin as an antithrombotic developed hemorrhage.[9)] There were no cases of thromboembolism resulting from discontinuation of an antithrombotic drug.[10)] The study emphasized prevention of postoperative hemorrhage rather than prevention of thromboembolism.

In a study of the incidences of complications and mortality associated with withdrawal of antithrombotic treatment before dermatological surgery,[11)] thrombotic complications due to discontinuation of antithrombotic treatment occurred in only 0.0078% of patients. However, these complications were severe and resulted in 3 deaths. The complications included stroke, cerebral embolism, myocardial infarction, transient ischemic attack, deep vein thrombosis, pulmonary thrombosis, and retinal artery obstruction resulting in blindness. They reported a relatively low estimated thrombotic risk of 1 event per 12816 operations, 1 in 6219 operations when warfarin was discontinued, and 1 in 21448 operations when aspirin was withheld.[10)] Thus, although continuation of antithrombotic treatment did not increase the incidence of serious hemorrhagic complications, the risk of a potentially fatal complication increased when antithrombotic treatment was discontinued.

The Japan Gastroenterological Endoscopy Society is currently developing guidelines regarding hemorrhage and is evaluating the risk of thromboembolism attributable to discontinuation of antithrombotic treatment.[4)] These guidelines will recommend procedures with low hemorrhagic risk and continuation of antithrombotic treatment. On the basis of past and present findings, we believe

that continuing perioperative antithrombotic treatment is the best practice for proctological surgery.

Conclusion

The incidence of thromboembolism caused by preoperative discontinuation of an antithrombotic treatment is very low; however, thromboembolism can result in serious complications. Therefore, it is necessary to continue antithrombotic treatment during the perioperative period of proctological surgery. Perioperative antithrombotic treatment can be continued or replaced by heparin. However, because heparin substitution was associated with the highest incidence of postoperative hemorrhage, continuing existing antithrombotic treatment appears to be the better perioperative period antithrombotic strategy for proctological surgery.

Conflicts of interest: The authors have no conflict of interest to disclose.

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