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Editorial Board Member of *World Journal of Clinical Cases*, Manabu Watanabe, MD, PhD, Full Professor, Division of Gastroenterology and Hepatology, Department of Internal medicine, Toho University Medical Center, Ohashi Hospital, Tokyo 153-8515, Japan

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EDITORS-IN-CHIEF
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Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
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Fax: +1-925-2238243
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Safety of laparoscopic surgery in digestive diseases with special reference to antithrombotic therapy: A systematic review of the literature

Takahisa Fujikawa, Kenji Ando

Takahisa Fujikawa, Department of Surgery, Kokura Memorial Hospital, Kitakyushu 802-8555, Fukuoka, Japan

Kenji Ando, Department of Cardiology, Kokura Memorial Hospital, Kitakyushu 802-8555, Fukuoka, Japan

ORCID number: Takahisa Fujikawa (0000-0002-4543-9282); Kenji Ando (0000-0003-0699-4248).

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Corresponding author to: Takahisa Fujikawa, MD, PhD, Chief Doctor, Surgeon, Department of Surgery, Kokura Memorial Hospital, 3-2-1 Asano, Kokurakita-ku, Kitakyushu 802-8555, Fukuoka, Japan. fujikawa-t@kokurakinen.or.jp
Telephone: +81-93-5112000
Fax: +81-93-5113240

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Abstract

AIM

To elucidate the effect of antithrombotic therapy (ATT) on bleeding and thromboembolic complications during or after laparoscopic digestive surgery.

METHODS

Published articles or internationally accepted abstracts between 2000 and 2017 were searched from PubMed, Cochrane Database, and Google Scholar, and studies involving laparoscopic digestive surgery and antiplatelet therapy (APT) and/or anticoagulation therapy (ACT) were included after careful review of each study. Data such as study design, type of surgical procedures, antithrombotic drugs used, and surgical outcome (both bleeding and thromboembolic complications) were extracted from each study.

RESULTS

Thirteen published articles and two internationally accepted abstracts were eligible for inclusion in the systematic review. Only one study concerning elective laparoscopic cholecystectomy in patients with peri-operative heparin bridging for ACT showed that the risk of postoperative bleeding was higher compared with those without ACT. The remaining 14 studies reported no significant differences in the incidence of bleeding complications between the ATT group and the group without ATT. The risk of thromboembolic events (TE) associated with laparoscopic digestive surgery in patients receiving ATT was not significantly higher than those with no ATT or interrupted APT.

CONCLUSION

Laparoscopic digestive surgery in ATT-burdened patients for prevention of bleeding and TE showed satisfactory results. The risk of hemorrhagic complication during or after these procedures in patients with continued APT or heparin bridging was not significantly higher than in patients with no ATT or interrupted APT.

Key words: Thromboembolic complication; Bleeding complication; Laparoscopic surgery; Anticoagulation therapy; Digestive surgery; Antithrombotic therapy; Antiplatelet therapy

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Core tip: In total, 15 published articles and abstracts concerning laparoscopic digestive surgery and antithrombotic therapy were systematically reviewed. These articles demonstrated that the risk of bleeding and thromboembolic complications during or after these procedures in patients with continued antiplatelets or heparin bridging was not significantly higher than in patients with no antithrombotics or interrupted antiplatelets.

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INTRODUCTION

Following cancer, heart disease and cerebrovascular disease are the major causes of death worldwide. With the arrival of an aging society in recent years, the number of patients with heart disease and/or cerebrovascular disease who require non-cardiac surgery is increasing. For the purpose of preventing thromboembolic events (TE), most of them receive antithrombotic therapy (ATT), including antiplatelet therapy (APT) and anticoagulation therapy (ACT). Perioperative management of these patients is challenging for surgeons, and they are often at high risk of bleeding and thromboembolic complications^[1-4].

Many digestive operations are currently performed laparoscopically. Several reports have shown advantages of laparoscopic digestive surgery, including early recovery of digestive function, reduction of body wall destruction, reduction of postoperative pain, less postoperative complications, and rapid return to daily life^[5-9]. During laparoscopic surgery, minimizing surgical blood loss to maintain a dry operative field is exclusively important. Improvement of several techniques and new surgical devices, such as ultrasonic coagulating

shears or saline-linked soft-coagulation system, led us to perform various types of advanced laparoscopic digestive operations including colorectal resection, esophagogastrectomy, and hepato-biliary-pancreas surgery. However, optimal management of patients receiving ATT during laparoscopic digestive surgery is still controversial.

The purpose of the current systematic review study is to elucidate the effect of ATT on bleeding and thromboembolic complications during or after laparoscopic digestive surgery.

MATERIALS AND METHODS

Articles written in English and published between 2000 and 2017 were collected from PubMed, Cochrane Database and Google Scholar. We also used PubMed and Google Scholar to search internationally accepted English abstracts. The following key words were used for the search: Clopidogrel, aspirin, antiplatelet, anticoagulant, warfarin, bleeding, hemorrhage, gastrointestinal, gastroenterological, digestive and laparoscopic surgery. Articles or abstracts were included when published in peer reviewed journals or when accepted at internationally renowned medical conferences. Types of eligible studies included randomized clinical trials, prospective or retrospective cohort studies, or case-control studies; guidelines, review articles, or case series/reports were not included.

After removing duplicates, articles were systematically excluded by careful review of each study. The quality of each study was assessed depending on study design, and eligible articles and abstracts were determined. Complete data were extracted from each study, which included study design, year of publication, sample size, type of surgical procedures, type of antithrombotic drugs, and surgical outcome (both bleeding and thromboembolic complications).

RESULTS

Characteristics of included studies

Research collection and screening was conducted from January 2018 to February 2018. In all, 13 articles and two abstracts were included^[10-24]. Among them, there were no randomized clinical trials or prospective cohort studies, and only retrospective cohort studies or case-control studies were seen. Among 15 studies, nine studies examined only APT use, two studies focused on ACT, and four studies investigated both. Concerning APT, patients who had continued preoperative APT were compared with those who did not receive APT. In patients with continued APT, only single antiplatelet agents, such as aspirin, were usually continued. One study focused on clopidogrel alone, and one study investigated aspirin alone. In studies regarding ACT, only warfarin was used, and most patients received heparin bridging perioperatively.

Only one retrospective cohort study used a large number of cases (over 1000 cases), but various types of laparoscopic surgery (mostly laparoscopic cholecystectomy) were included. This is the largest study to date, examining the effects of APT on outcome of abdominal laparoscopic operations. This study demonstrated that there was no significant difference in postoperative bleeding events between patients who continued APT and other patients.

We classified the type of surgery into two categories based on previous reports^[10]: Basic laparoscopic surgery (e.g., cholecystectomy, appendectomy, adhesiolysis, hernia repair) and advanced laparoscopic surgery (e.g., colorectal resection, gastrectomy, liver/pancreas resection). The results of basic surgery and advanced surgery are shown in Tables 1 and 2, respectively. Bleeding events included two categories: intraoperative bleeding complications (IBCs; increased surgical blood loss), and postoperative bleeding complications (PBCs; intraabdominal bleeding, gastroenterology bleeding, or abdominal wall hematoma).

Basic laparoscopic surgery

In basic laparoscopic surgeries, only two types of surgery (cholecystectomy and appendectomy) were included. Laparoscopic cholecystectomy was the most commonly reported overall, and a total of eight studies were included^[11-15,17,18,24]. Research on laparoscopic appendectomy included two case-control studies^[19,20].

For laparoscopic cholecystectomy, warfarin was described in three studies. With only one study, the risk of PBC in ACT patients was significantly higher than those without ACT^[11]. In the remaining two studies, the proportion of IBC or PBC did not increase, even with heparin bridging^[14,18]. In terms of APT, seven studies focusing on aspirin and/or thienopyridine were included^[12-14,17,18,24,25]. IBC was examined as an outcome in six of them, and PBC was analyzed in four studies. None of the studies demonstrated an increase in IBC or PBC when APT (mostly aspirin monotherapy) was continued preoperatively. In two laparoscopic appendectomy studies^[19,20], they were exclusively performed in an emergency setting. Both studies focused on preoperative APT continuation and showed that neither IBC nor PBC increased with continued APT.

These findings suggested that when basic laparoscopic digestive operations were performed, the risk of either IBC or PBC in patients undergoing preoperative continued monotherapy for APT or heparin bridging for ACT was not significantly higher than in those without ATT or interrupted APT.

Advanced laparoscopic surgery

Concerning advanced laparoscopic surgery, only limited numbers of studies were found in three types of surgery; one study on laparoscopic liver resection^[16], two studies on laparoscopic colorectal cancer resection^[12,21], and two studies regarding laparoscopic gastrectomy^[22,23].

Fujikawa *et al.*^[16] conducted a retrospective cohort study using liver resection cases (including laparoscopic and open surgery). The authors found that neither IBC nor PBC increased in the case of laparoscopic liver resection, even with aspirin monotherapy for APT and/or heparin bridging for ACT. In two studies of laparoscopic colorectal cancer resection, the effect of APT on IBC or PBC was assessed, and the authors found that APT continuation did not significantly affect hemorrhagic complications^[12,21].

Among two papers regarding laparoscopic gastrectomy, Takahashi *et al.*^[22] examined the difference in IBC and PBC between the ATT group and the group without ATT. The ATT group included preoperative APT continuation and heparin substitution for ACT, but there was no significant difference in IBC or PBC between the groups. Finally, Gerin *et al.*^[23] examined the difference in PBC during laparoscopic sleeve gastrectomy between the warfarin group and the group without warfarin. PBC occurred in 6.7% of patients who received ACT, whereas 3.3% of patients without ACT experienced PBC ($P = 0.60$).

Perioperative thromboembolic events and mortality

Among 15 included studies, the incidence of perioperative TE and the mortality rate was described in eight and 14 studies, respectively. In basic laparoscopic surgeries, the TE rate was 0%-2.2% in the continued APT group and 0%-0.2% in the control group. Six out of eight studies showed no mortality in the entire cohort. In the remaining two studies, there was no difference in mortality between the groups. In advanced laparoscopic surgery, the incidence of TE was identical between the groups, with only one expired case (1% of the ATT group). Overall, the risk of TE associated with laparoscopic digestive surgery for patients receiving ATT was not significantly higher than those without ATT or interrupted APT.

DISCUSSION

To the best of our knowledge, this is the first systematic review that assesses the effect of ATT on bleeding and thromboembolic complications during and after laparoscopic digestive surgery. The present review summarized results of various types of laparoscopic digestive surgery in patients receiving ATT for the prevention of thromboembolism. The risk of hemorrhagic or thromboembolic complications during or after these procedures in patients with continued APT or heparin bridging was not significantly higher than in patients with no ATT or interrupted APT. There are some promising results for both basic and laparoscopic surgery. However, in terms of advanced laparoscopic surgery, such as colorectal resection or liver resection, there is scarce evidence.

ATT includes two types of medications, classified as antiplatelets and anticoagulants. Antiplatelets

Table 1 Reported data concerning bleeding complications of "basic" abdominal surgery in patients with antithrombotic therapy (antiplatelet therapy and/or anticoagulation therapy)

First author of the reports	Year	Surgery type	Drug use and exposure	Bleeding events	TE, mortality
Laparoscopic surgery (overall) Fujikawa ^[10]	2013	Abdominal laparoscopic surgery (cholecystectomy (mostly), appendectomy, surgery for GI malignancy, liver resection, splenectomy <i>etc</i>)	Patients with continued use of ASA (<i>n</i> = 52) Patients with discontinuation of APT (<i>n</i> = 160) Patients not on APT (control, <i>n</i> = 863)	PBC 0% in continued ASA <i>vs</i> 2.5% in discontinuation <i>vs</i> 0.7% in control (<i>P</i> = 0.987)	TE 0% in continued ASA <i>vs</i> 0.6% in discontinued ASA <i>vs</i> 0.2% in control (<i>P</i> = 0.625) Only one mortality in continued ASA group (1.9%)
Laparoscopic cholecystectomy Ercan ^[11]	2010	Laparoscopic cholecystectomy (only elective)	Patients with ACT (w/ bridging, <i>n</i> = 44) Patients without ACT (control, <i>n</i> = 1377)	PBC 25% in ACT <i>vs</i> 1.5% in control (<i>P</i> < 0.001) One mortality due to severe bleeding	(not mentioned)
Ono ^[12]	2013	Laparoscopic cholecystectomy (<i>n</i> = 270) or Laparoscopic colorectal cancer resection (<i>n</i> = 218)	Patients with continued ASA (control, <i>n</i> = 436)	SBL 27 mL in continued ASA <i>vs</i> 17 mL in control (<i>P</i> = 0.430)	No mortality in both groups
Anderson ^[13]	2014	Laparoscopic cholecystectomy (elective and emergency)	Patients with continued clopidogrel (<i>n</i> = 36) Matched patients without clopidogrel (control, <i>n</i> = 36)	No difference in SBL (49 g <i>vs</i> 47 g, <i>P</i> = 0.85) PBC 0% in clopidogrel <i>vs</i> 2.8% in control (<i>P</i> = 0.31)	No TE in both groups No mortality in both groups
Noda ^[14]	2014	Early laparoscopic cholecystectomy for acute cholecystitis	Patients with continued use of ATT (<i>n</i> = 21) Patients without ATT (<i>n</i> = 162)	No conversion to open surgery No PBC in both groups	No mortality in both groups
Joseph ^[15]	2015	Emergency laparoscopic cholecystectomy	Patients with continued use of APT (<i>n</i> = 56), including those with preop Plt transfusion (<i>n</i> = 12) Patients without APT (control, <i>n</i> = 56) Patients with continued use of APT (<i>n</i> = 89)	SBL ≥ 100 mL 14.3% in continued ASA <i>vs</i> 9% in control (<i>P</i> = 0.50)	No difference in the rates of overall postop complications (8.9% <i>vs</i> 7.1%, <i>P</i> = 0.80)
Fujikawa ^[16]	2017	Emergency cholecystectomy including 106 laparoscopic surgery for acute cholecystitis	Patients without APT (control, <i>n</i> = 154) Patients with continued single APT (<i>n</i> = 49) Patients with discontinuation of APT (<i>n</i> = 106)	SBL ≥ 500 mL 12% in continued APT <i>vs</i> 5% in control (<i>P</i> = 0.240) PBC 7% in multiple APT <i>vs</i> 3% in single APT <i>vs</i> 0.6% in control (<i>P</i> = 0.027) SBL ≥ 200 mL 4.7% in continued APT <i>vs</i> 4.7% in discontinued APT <i>vs</i> 1.5% in control (<i>P</i> = 0.064) PBC 0% in continued APT <i>vs</i> 0.9% in discontinued APT <i>vs</i> 0.2% in control (<i>P</i> = 0.022)	No mortality in both groups TE 1.1% in continued APT <i>vs</i> 0% in control (<i>P</i> = 0.37) No mortality in both groups
Sakamoto ^[17]	2017	Laparoscopic cholecystectomy (only elective operation)	Patients with continued single APT (<i>n</i> = 49) Patients with discontinuation of APT (<i>n</i> = 106)	SBL ≥ 200 mL 4.7% in continued APT <i>vs</i> 4.7% in discontinued APT <i>vs</i> 1.5% in control (<i>P</i> = 0.064) PBC 0% in continued APT <i>vs</i> 0.9% in discontinued APT <i>vs</i> 0.2% in control (<i>P</i> = 0.022)	TE 0% in continued APT <i>vs</i> 0.9% in discontinued APT <i>vs</i> 0.2% in control (<i>P</i> = 0.296) No mortality in any group
Yun ^[18]	2017	Laparoscopic cholecystectomy (elective <i>vs</i> emergency) for acute cholecystitis	Patients not on APT (control, <i>n</i> = 653) Patients with continued use of ATT (almost APT, <i>n</i> = 22) Patients with discontinued ATT (almost APT, control, <i>n</i> = 45)	SBL ≥ 100mL 13.6% in continued ATT <i>vs</i> 22.2% in control (<i>P</i> = 0.613)	One case of TE (2.2%) in control Mortality 4.6% in continued ATT <i>vs</i> 2.2% in control (<i>P</i> > 0.999)
Laparoscopic appendectomy Chechik ^[19]	2011	Appendectomy including laparoscopic appendectomy (<i>n</i> = 78)	Patients with continued APT (<i>n</i> = 39) Patients without APT (control, <i>n</i> = 140)	No difference in SBL or PBC between the groups	No mortality in both groups
Pearcy ^[20]	2017	Laparoscopic appendectomy (urgent only)	Patients with continued APT (<i>n</i> = 287) Matched patients without APT (control, <i>n</i> = 287)	No difference in SBL (31 g <i>vs</i> 26 g) or blood transfusion rate (1% <i>vs</i> 0%) between the groups	Two cases of TE (MI) in continued APT (0.7%) No difference in the rates of mortality (1% <i>vs</i> 0%, <i>P</i> = 0.12)

ATT: Antithrombotic therapy; APT: Antiplatelet therapy; ACT: Anticoagulation therapy; TE: Thromboembolism; SBL: Surgical blood loss; PBC: Postoperative bleeding complications; ASA: Aspirin; GE: Gastroenterological; MI: Myocardial infarction.

Table 2 Reported data concerning bleeding complications of "advanced" abdominal surgery in patients with antithrombotic therapy (antiplatelet therapy and/or anticoagulation therapy)

First author of the reports	Year	Surgery type	Drug use and exposure	Bleeding events	TE, mortality
Laparoscopic liver resection Fujikawa ^[24]	2017	Laparoscopic liver resection <i>vs</i> open liver resection	Patients with ATT (<i>n</i> = 100) Patients without ATT (control, <i>n</i> = 158)	SBL ≥ 500 mL 23% in those with ATT <i>vs</i> 27% in control (<i>P</i> = 0.468) PBC 4.6% in those with ATT <i>vs</i> 4.3% in control	TE 1% in ATT <i>vs</i> 1.3% in control (<i>P</i> = 0.310) Mortality 1% in ATT <i>vs</i> 0% in control (<i>P</i> = 0.350)
Laparoscopic colorectal cancer resection Ono ^[22]	2013	Laparoscopic colorectal cancer resection (<i>n</i> = 218) or laparoscopic cholecystectomy (<i>n</i> = 270)	Patients with continued ASA (<i>n</i> = 52) Patients without ASA (control, <i>n</i> = 436)	SBL 27 mL in continued ASA <i>vs</i> 17 mL in control (<i>P</i> = 0.430)	No mortality in both groups
Shimoike ^[21]	2016	Colorectal cancer surgery including laparoscopic surgery (<i>n</i> = 191)	Patients with APT (<i>n</i> = 148) Patients without APT (control, <i>n</i> = 343)	PBC 0.7% in those with APT <i>vs</i> 0.9% in control (<i>P</i> = 1.000)	TE 0.7% in APT <i>vs</i> 0% in control (<i>P</i> = 0.301) No mortality in both groups
Laparoscopic gastrectomy Takahashi ^[22]	2017	Laparoscopic gastrectomy	Patients with ATT (continued in high risk, <i>n</i> = 12) Patients without ATT (<i>n</i> = 34)	No difference in SBL or PBC between the groups	No difference in overall complications between the groups
Gerin ^[21]	2015	Laparoscopic sleeve gastrectomy	Patients with ACT (<i>n</i> = 15) Matched patients without ACT (control, <i>n</i> = 30)	PBC 6.7% in ACT <i>vs</i> 3.3% in control (<i>P</i> = 0.60)	No mortality in both groups

ATT: Antithrombotic therapy; APT: Antiplatelet therapy; ACT: Anticoagulation therapy; TE: Thromboembolism; SBL: Surgical blood loss; PBC: Postoperative bleeding complications; ASA: Aspirin; HBP: Hepatobiliary and pancreas.

decrease platelet aggregation and prevent thrombus formation, and they are generally used for primary and secondary prevention of cardiovascular and cerebrovascular diseases, such as myocardial infarction or cerebral infarction. Antiplatelets include thienopyridine (*e.g.*, clopidogrel, ticlopidine, or prasugrel), type III phosphodiesterase inhibitor (*e.g.*, cilostazol), acetylsalicylic acid (aspirin), and other non-steroidal anti-inflammatory agents^[10,26]. On the other hand, anticoagulants interfere with the native clotting cascade and prevent blood clotting, and they are generally used for atrial fibrillation, deep vein thrombosis, cardiac endoprostheses, and acute coronary syndrome. These include vitamin K antagonists (*e.g.*, warfarin), heparin derivatives (*e.g.*, fondaparinux), direct thrombin inhibitors (*e.g.*, dabigatran), and factor Xa inhibitors (*e.g.*, rivaroxaban, apixaban, edoxaban)^[26,27]. The two latter types are now increasingly used and are referred to as direct-acting oral anticoagulants (DOACs) or non-vitamin K antagonist oral anticoagulants (NOACs). The types of antithrombotics, specific agents, and duration of action are summarized in Table 3.

So far, there has been scarce evidence concerning the definite protocols or guidelines for each specific gastrointestinal surgical procedure, including laparoscopic surgery. Thanks to the development of techniques and various energy devices, indication of laparoscopic digestive surgery is now expanded not only to basic procedures but also relatively advanced digestive operations^[6,9]. During laparoscopic surgery, minimizing surgical blood loss to maintain a dry operative field is required, and thus, this procedure results in less surgical blood loss and a lower incidence of postoperative complications^[16]. Although the optimal management of patients receiving ATT during laparoscopic digestive surgery is still controversial, rigorous antithrombotic management, such as continued aspirin monotherapy for APT or heparin bridging for ACT, is considered to be safe and feasible.

Using several recently updated guidelines concerning antithrombotics as references^[26-30], the recommended protocol of perioperative management for patients undergoing ATT in the case of elective open or laparoscopic digestive surgery is shown in Figure 1. The management generally consists of three approaches according to types of ATT; APT, warfarin, and DOACs. In patients with thromboembolic risks, aspirin monotherapy is continued in patients with APT, and warfarin is substituted by heparin bridging 3-5 d before surgery. In the case of DOACs, ATT is stopped 1-2 d before surgery (with some modification needed if decreased renal function exists); if the thromboembolic risk is very high, heparin bridging might be considered. Postoperatively, every antithrombotic agent is reinstituted as soon as possible (POD1-2).

Table 3 Types, specific agents, and acting duration of commonly used antithrombotic drugs

Class of agents	Type	Specific agents	Duration of action
Antiplatelets	Thienopyridines	Clopidogrel (Plavix), Ticlopidine (Panardine), Prasugrel (Effient)	5-7 d ¹
	Type III PDE inhibitor	Cilostazol (Pretal)	2 d
	Acetylsalicylic acid	Aspirin	7-10 d
	Other NSAIDs	Ibuprofen (Brufen, Advil), Loxoprofen (Loxonin), Diclofenac (Voltaren), <i>etc</i>	Varies
Anticoagulants	Vitamin K antagonist	Warfarin (Coumadin)	5 d
	Heparin derivatives	Fondaparinux (Arixtra) DOACs	1.5-2 d
	Direct thrombin inhibitor	Dabigatran (Pradaxa)	1-2 d
	Factor Xa inhibitors	Rivaroxaban (Xarelto), Apixaban (Eliquis), Edoxaban (Lixiana)	1-2 d

¹In ticlopidine, duration of action is 10-14 d. PDE: Phosphodiesterase; NSAID: Non-steroidal anti-inflammatory drug; DOAC: Direct-acting oral anticoagulant.

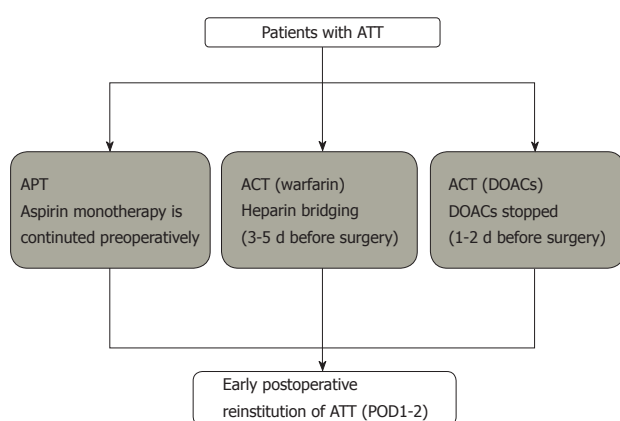


Figure 1 Recommended perioperative management protocol for patients undergoing antithrombotic therapy in the case of elective laparoscopic digestive surgery. The management generally consists of three ways according to the types of antithrombotic therapy (ATT): antiplatelet therapy (APT), warfarin, and Direct-acting oral anticoagulants (DOACs). In patients with thromboembolic risks, aspirin monotherapy is continued in patients with APT, and/or warfarin was substituted by heparin bridging 3-5 d before surgery. In the case of DOACs, ATT is stopped 1-2 d before surgery (with some modification needed if decreased renal function exists); if the thromboembolic risk is very high, heparin bridging might be considered. Postoperatively, every antithrombotic agent is reinstituted as soon as possible (POD1-2). ATT: Antithrombotic therapy; APT: Antiplatelet therapy; TE: Thromboembolism; ACT: Anticoagulation therapy; DOAC: Direct-acting oral anticoagulant.

Recent updated guidelines concerning antithrombotic management during non-cardiac surgery^[26,27,31-33] showed that the prevention of TE is more important than bleeding complications, as it might cause death or severe sequelae. Concerning implantation of a coronary stent, recent American College of Cardiology/American Heart Association (commonly known as ACC/AHA) and European Society of Cardiology (commonly known as ESC) guideline state that we should continue antiplatelet medications, at least aspirin monotherapy, in the perioperative period for patients with high risk of thromboembolism^[30], but most institutions practically choose to discontinue APT in the case of major digestive surgery with bleeding risks. Discontinuing aspirin or clopidogrel may lead to an increased risk of acute myocardial infarction,

cerebral infarction, and subsequent death^[34,35]. Although some studies, including the POISE-2 study, have reported that a modest increase in bleeding risk was observed in continued APT patients during non-cardiac surgery^[36,37], most studies have shown that there was no increase in significant bleeding events^[38,39]. Thus, sufficient consideration and emphasis should be placed on the prevention of thromboembolism caused by cessation of antithrombotic drugs, rather than the risk of perioperative bleeding.

Concerning patients with ACT, heparin bridging is a common management for warfarin^[40]. Recently, a large-scale randomized controlled trial (BRIDGE study) showed that heparin bridging was not recommended in the case of low bleeding risk surgery due to increased bleeding risks^[25]. However, this study included relatively small numbers of major digestive surgery, and it could not conclude that heparin bridging is unnecessary in major general or abdominal surgery. In the current review, only one study concerning warfarin use and laparoscopic cholecystectomy showed an elevated risk of postoperative bleeding when heparin bridging was used^[11]. The remaining studies demonstrated the safety of ACT bridging without an increase in severe bleeding complications. Especially in patients with high thromboembolic risks, heparin bridging might be considered to avoid critical thromboembolic complications.

In the present review, there was no report regarding patients who received DOACs during laparoscopic digestive surgery. Currently, DOACs are increasingly prescribed for the purpose of preventing arterial or venous thromboembolism. In large clinical trials, DOACs have been shown to have lower rates of intracranial hemorrhage compared to warfarin^[41-44]. Furthermore, in cases of intracranial bleeding, there are reports that hematoma sizes were small in patients receiving DOACs compared to those with warfarin administration^[45,46]. This difference is mainly due to the difference in mechanism of action in the blood clotting cascade. A sufficient understanding of these pharmacological characteristics, which is remarkably

different from warfarin, is of paramount importance for surgeons. A recently published review and an ongoing prospective study^[47,48] suggests safety and feasibility of perioperative management of DOACs during noncardiac surgery, which is rather simple compared with those of warfarin. Still, the detailed assessment of perioperative management protocol, such as the necessity of bridging anticoagulation, has not yet conducted and should be investigated further. In addition, these reports or reviews did not show results according to the procedure types. Safety of every surgical type, including laparoscopic digestive surgery, should be assessed in the future.

Summary and recommendations for future studies

Currently, there are only limited numbers of studies concerning the management of ATT-prescribed patients during laparoscopic digestive surgery. As the population ages and the morbidity of cardiovascular disease increases, this patient population is expanded further. Definite protocols or guidelines should be established using reliable studies with good design. In the future, a well-designed prospective randomized study or multicenter cohort study is mandatory to elucidate the safety and feasibility of laparoscopic digestive surgery.

In conclusion, laparoscopic digestive surgery in ATT-burdened patients for the prevention of bleeding and TE showed satisfactory results. The risk of hemorrhagic complication during or after these procedures in patients with continued APT or heparin bridging was not significantly higher than in patients with no ATT or interrupted APT.

ARTICLE HIGHLIGHTS

Research background

Recently, many digestive surgical procedures are being performed laparoscopically. However, the effect of antithrombotic therapy (ATT) on perioperative bleeding complications during laparoscopic surgery is still largely unclear.

Research motivation

The risk of bleeding complications in ATT is related to the perioperative use of antiplatelet therapy (APT) or anticoagulation therapy (ACT). To safely perform laparoscopic digestive surgery in patients with ATT, optimal perioperative management of antithrombotic drugs should be established.

Research objectives

The main objective of the present study is to elucidate the effect of ATT on bleeding and thromboembolic complications during or after laparoscopic digestive surgery.

Research methods

Published articles or internationally accepted abstracts between 2000 and 2017 were searched, and studies involving laparoscopic digestive surgery and ATT were included after careful review of each study. Data including study design, type of surgical procedures, type of antithrombotic drugs, and surgical outcome were analyzed.

Research results

In total, 15 studies were included. Only one study concerning laparoscopic cholecystectomy showed that patients with heparin bridging for ACT had

a higher risk of postoperative bleeding. The remaining 14 studies reported continued APT or that heparin bridging for ACT did not affect the incidence of bleeding complication. The risk of thromboembolic events after laparoscopic digestive surgery in patients receiving ATT was not significantly higher than those with no ATT or interrupted APT.

Research conclusions

The risk of hemorrhagic complication during or after these procedures in patients with continued APT or heparin bridging was not significantly higher than in patients with no ATT or interrupted APT.

Research perspectives

The definite protocol or guidelines should be established using reliable studies with good design. In the future, a well-designed prospective randomized study or multicenter cohort study is mandatory to elucidate the safety and feasibility of laparoscopic digestive surgery.

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