**Name of Journal:** *World Journal of Clinical Cases*

**Number ID**: 40089

**Manuscript Type:** SYSTEMATIC REVIEWS

**Safety of laparoscopic surgery in digestive diseases with special reference to antithrombotic therapy: A systematic review of the literature**

Fujikawa T *et al.* Laparoscopic digestive surgery and antithrombotic therapy

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).

**Author contributions:** Fujikawa T designed, performed research and analyzed data; Fujikawa T prepared the manuscript and Ando K reviewed it.

**Conflict-of-interest statement:** The authors report no relevant conflicts of interest.

**PRISMA Checklist:** The manuscript was prepared and revised according to the **PRISMA 2009 Checklist**.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

**Manuscript source:** Invited manuscript

**Correspondence 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](mailto:fujikawa-t@kokurakinen.or.jp)

**Telephone:** +81-93-5112000

**Fax:** +81-93-5113240

**Received:** May 31, 2018

**Peer-review started:** May 31, 2018

**First decision:** July 17, 2018

**Revised:** August 2, 2018

**Accepted:** October 17, 2018

**Article in press:**

**Published online:**

**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) (ATT) were included after careful reviewing of each study. Data such as design of the study, 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 perioperative 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 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: Laparoscopic surgery; Digestive surgery; Antithrombotic therapy; Antiplatelet therapy; Anticoagulation therapy; Bleeding complication; Thromboembolic complication**

**© The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** **Totally 15 published articles and abstracts concerning laparoscopic digestive surgery and antithrombotic therapy were systematically reviewed, and it is 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.**

Fujikawa T, Ando K. Safety of laparoscopic surgery in digestive diseases with special reference to antithrombotic therapy: A systematic review of the literature. *World J Clin Cases* 2018; In press

**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 are receiving 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 being 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 the peer review journal or when accepted at internationally renowned medical conferences. Types of the eligible study include 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 excluded systematically by careful reviewing 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 include design of the study, 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 were conducted from January 2018 to February 2018. In all, 13 articles and 2 abstracts were included[10–24]. Among them, there were no randomized clinical trial or prospective cohort study, and only retrospective cohort studies or case-control studies were seen. Among 15 studies, 9 studies examined only APT use, 2 studies focused on ACT, and 4 studies investigated both of them. 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 agent such as aspirin was usually continued. One study focused on clopidogrel only, and one study investigated only aspirin. In studies regarding ACT, only warfarin was used as ACT, and most patients received heparin bridging perioperatively.

Only one retrospective cohort study analyzed using the 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 the 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 were shown in Table 1 and Table 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 surgery, only two types of surgery (cholecystectomy and appendectomy) were included. Laparoscopic cholecystectomy was the most commonly reported overall, and a total of 8 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, 7 studies focusing on aspirin and/or thienopyridine were included[12–14,17,18,24,25]. IBC was examined as outcome in six of them and PBC was analyzed in four studies. All these studies showed that neither IBC nor PBC increased when APT (mostly aspirin monotherapy) was continued preoperatively. In 2 studies regarding laparoscopic appendectomy[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 3 types of surgery; one study on laparoscopic liver resection[16], 2 studies on laparoscopic colorectal cancer resection[12,21], and 2 studies regarding laparoscopic gastrectomy[22,23]. Fujikawa *et al*[16] conducted a retrospective cohort study using liver resection cases (including laparoscopic and open surgery). It revealed that IBC or PBC did not increase in 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, both studies assessed the effect of APT on IBC or PBC and showed 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 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 were described in 8 and 14 studies, respectively. In basic laparoscopic surgery, 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 2 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 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 so far.

ATT includes two types of medications, classified as antiplatelets and anticoagulants. Antiplatelets decrease aggregation of platelets and prevent thrombus formation, and 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 the blood clotting, and 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 called as direct-acting oral anticoagulants (DOACs) or non-vitamin K antagonist oral anticagulants (NOACs). The types of antithrombotics, specific agents, and duration of action are summarized in Table 3.

So far, there are scarce evidences concerning the definite protocols or guidelines for each specific gastroenterological surgical procedure, including laparoscopic surgery. Thanks to 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[6,8,9].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 the 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],recommended protocol of perioperative management for patients undergoing ATT in case of elective open or laparoscopic digestive surgery is currently used and shown in Figure 1. The management generally consists of 3 ways according to types of ATT, APT, warfarin, and DOACs. In patients with thromboembolic risks, aspirin monotherapy is continued in patients with APT, and warfarin was substituted by heparin bridging 3-5 d before surgery. In 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).

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 coronary stent, recent AHCC/AHA and ESC guideline said 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 case of major digestive surgery with bleeding risks. Discontinuing aspirin or clopidogrel may lead to increased risk of acute myocardial infarction, cerebral infarction, and following death[34,35]. Although some studies including 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 of other studies showed that there was no increase in the 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 the common management for warfarin[40].Recently, large-scale randomized controlled trial (BRIDGE study) showed that heparin bridging was not recommended in 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 is 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 the elevated risk of postoperative bleeding when heparin bridging was used[11]. The remaining studies demonstrated the safety of ACT bridging without increase of 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 a hematoma size was 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. Recently published review and 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 management of ATT-prescribed patients during laparoscopic digestive surgery. Since the population ages and the morbidity of cardiovascular disease increases, this patient population is expanded further. 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.

In 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.**

**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 reviewing of each study. Data including design of the study, type of surgical procedures, type of antithrombotic drugs, and surgical outcome were analyzed.

***Research results***

**Totally 15 studies were included. Only one study concerning laparoscopic cholecystectomy showed that patients with heparin bridging for ACT had higher risk of postoperative bleeding. The remaining 14 studies reported continued APT or heparin bridging for ACT did not affect the incidence of bleeding complication. T**he 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.

**REFERENCES**

1 **Thachil J**, Gatt A, Martlew V. Management of surgical patients receiving anticoagulation and antiplatelet agents. *Br J Surg* 2008; **95**: 1437-1448 [PMID: 18991253 DOI: 10.1002/bjs.6381]

2 **Kałuza GL**, Joseph J, Lee JR, Raizner ME, Raizner AE. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. *J Am Coll Cardiol* 2000; **35**: 1288-1294 [PMID: 10758971]

3 **Fujikawa T**, Tanaka A, Abe T, Yoshimoto Y, Tada S, Maekawa H. Effect of antiplatelet therapy on patients undergoing gastroenterological surgery: thromboembolic risks versus bleeding risks during its perioperative withdrawal. *World J Surg* 2015; **39**: 139-149 [PMID: 25201469 DOI: 10.1007/s00268-014-2760-3]

4 **Mita K**, Ito H, Murabayashi R, Sueyoshi K, Asakawa H, Nabetani M, Kamasako A, Koizumi K, Hayashi T. Postoperative bleeding complications after gastric cancer surgery in patients receiving anticoagulation and/or antiplatelet agents. *Ann Surg Oncol* 2012; **19**: 3745-3752 [PMID: 22805868 DOI: 10.1245/s10434-012-2500-6]

5 **Kiviluoto T,** Sirén J, Luukkonen P, Kivilaakso E. Randomised trial of laparoscopic versus open cholecystectomy for acute and gangrenous cholecystitis. *Lancet* 1998; **351**: 321-325 [PMID: 9652612 DOI: 10.1016/S0140-6736(97)08447-X]

6 **Guller U,** Jain N, Hervey S. Laparoscopic vs Open Colectomy. Outcomes Comparison Based on Large Nationwide Databases. *Arch Surg* 2003; 138: 1179 [PMID: 14609864 DOI: 10.1001/archsurg.138.11.1179]

7 **Kapischke M,** Caliebe A, Tepel J, Schulz T, Hedderich J. Open versus laparoscopic appendicectomy. *Surg Endosc* 2006; **20**: 1060-1068 [DOI: 10.1007/s00464-005-0016-x]

8 **Klarenbeek BR**, Veenhof AA, de Lange ES, Bemelman WA, Bergamaschi R, Heres P, Lacy AM, van den Broek WT, van der Peet DL, Cuesta MA. The Sigma-trial protocol: a prospective double-blind multi-centre comparison of laparoscopic versus open elective sigmoid resection in patients with symptomatic diverticulitis. *BMC Surg* 2007; **7**: 16 [PMID: 17683563 DOI: 10.1186/1471-2482-7-16]

9 **Nguyen KT**, Gamblin TC, Geller DA. World review of laparoscopic liver resection-2,804 patients. *Ann Surg* 2009; **250**: 831-841 [PMID: 19801936 DOI: 10.1097/SLA.0b013e3181b0c4df]

10 **Fujikawa T**, Tanaka A, Abe T, Yoshimoto Y, Tada S, Maekawa H, Shimoike N. Does antiplatelet therapy affect outcomes of patients receiving abdominal laparoscopic surgery? Lessons from more than 1,000 laparoscopic operations in a single tertiary referral hospital. *J Am Coll Surg* 2013; **217**: 1044-1053 [PMID: 24051069 DOI: 10.1016/j.jamcollsurg.2013.08.005]

11 **Ercan M**, Bostanci EB, Ozer I, Ulas M, Ozogul YB, Teke Z, Akoglu M. Postoperative hemorrhagic complications after elective laparoscopic cholecystectomy in patients receiving long-term anticoagulant therapy. *Langenbecks Arch Surg* 2010; **395**: 247-253 [PMID: 19294412 DOI: 10.1007/s00423-009-0483-y]

12 **Ono K**, Idani H, Hidaka H, Kusudo K, Koyama Y, Taguchi S. Effect of aspirin continuation on blood loss and postoperative morbidity in patients undergoing laparoscopic cholecystectomy or colorectal cancer resection. *Surg Laparosc Endosc Percutan Tech* 2013; **23**: 97-100 [PMID: 23386161 DOI: 10.1097/SLE.0b013e318278cdf8]

13 **Anderson K**, Jupiter DC, Abernathy SW, Frazee RC. Should clopidogrel be discontinued before laparoscopic cholecystectomy? *Am J Surg* 2014; **208**: 926-31; discussion 930-1 [PMID: 25435299 DOI: 10.1016/j.amjsurg.2014.08.001]

14 **Noda T**, Hatano H, Dono K, Shimizu J, Oshima K, Tanida T, Miyake M, Komori T, Kawanishi K, Morita S, Imamura H, Iwazawa T, Akagi K, Kitada M. Safety of early laparoscopic cholecystectomy for patients with acute cholecystitis undergoing antiplatelet or anticoagulation therapy: a single-institution experience. *Hepatogastroenterology* 2014; **61**: 1501-1506 [PMID: 25436333]

15 **Joseph B**, Rawashdeh B, Aziz H, Kulvatunyou N, Pandit V, Jehangir Q, O'Keeffe T, Tang A, Green DJ, Friese RS, Rhee P. An acute care surgery dilemma: emergent laparoscopic cholecystectomy in patients on aspirin therapy. *Am J Surg* 2015; **209**: 689-694 [PMID: 25064416 DOI: 10.1016/j.amjsurg.2014.04.014]

16 **Fujikawa T**, Kawamoto H, Kawamura Y, Emoto N, Sakamoto Y, Tanaka A. Impact of laparoscopic liver resection on bleeding complications in patients receiving antithrombotics. *World J Gastrointest Endosc* 2017; **9**: 396-404 [PMID: 28874960 DOI: 10.4253/wjge.v9.i8.396]

17 **Sakamoto Y,** Fujikawa T, Kawamoto H, Yoshimoto Y, Tanaka A. The safety and feasibility of elective laparoscopic cholecystectomy in patients with antiplatelet therapy: Lessons from more than 800 cases in a single tertiary referral hospital. In: World Congress of Surgery 2017 Abstract Book: International Society of Surgery ISS/SIC, 2017: PE413

18 **Yun JH**, Jung HI, Lee HU, Baek MJ, Bae SH. The efficacy of laparoscopic cholecystectomy without discontinuation in patients on antithrombotic therapy. *Ann Surg Treat Res* 2017; **92**: 143-148 [PMID: 28289668 DOI: 10.4174/astr.2017.92.3.143]

19 **Chechik O**, Inbar R, Danino B, Lador R, Greenberg R, Avital S. Anti-platelet therapy: no association with increased blood loss in patients undergoing open or laparoscopic appendectomy. *Isr Med Assoc J* 2011; **13**: 342-344 [PMID: 21809730]

20 **Pearcy C**, Almahmoud K, Jackson T, Hartline C, Cahill A, Spence L, Kim D, Olatubosun O, Todd SR, Campion EM, Burlew CC, Regner J, Frazee R, Michaels D, Dissanaike S, Stewart C, Foley N, Nelson P, Agrawal V, Truitt MS. Risky business? Investigating outcomes of patients undergoing urgent laparoscopic appendectomy on antithrombotic therapy. *Am J Surg* 2017; **214**: 1012-1015 [PMID: 28982518 DOI: 10.1016/j.amjsurg.2017.08.035]

21 **Shimoike N,** Shimoike N, Fujikawa T, Yoshimoto Y, Tanaka A. Does antiplatelet therapy affect short-term and long-term outcomes of patients undergoing surgery for colorectal cancer? - Surgical radicality versus perioperative antiplatelet-related morbidity risks. *J Gastroenterol Hepatol Res* 2016; 5: 1962-1969 [DOI: 10.17554/j.issn.2224-3992.2016.05.605]

22 **Takahashi K**, Ito H, Katsube T, Tsuboi A, Hashimoto M, Ota E, Mita K, Asakawa H, Hayashi T, Fujino K. Associations between antithrombotic therapy and the risk of perioperative complications among patients undergoing laparoscopic gastrectomy. *Surg Endosc* 2017; **31**: 567-572 [PMID: 27287908 DOI: 10.1007/s00464-016-4998-3]

23 **Gerin O**, Rebibo L, Dhahri A, Regimbeau JM. The Safety of Laparoscopic Sleeve Gastrectomy in Patients Receiving Chronic Anticoagulation Therapy: A Case-Matched Study. *Obes Surg* 2015; **25**: 1686-1692 [PMID: 25663098 DOI: 10.1007/s11695-015-1590-1]

24 **Fujikawa T,** Yoshimoto Y, Kawamura Y, Nishimura T, Kawamoto H, Yamamoto T, Emoto N, Sakamoto Y, Tanaka A. Impact of antiplatelet therapy on increased blood loss and bleeding complication in patients undergoing urgent cholecystectomy for acute cholecystitis. In: 12th Biennial E-AHPBA Congress 2017 Book of Abstracts: European-African Hepato Pancreato Biliary Association, 2017: P43.04

25 **Douketis JD**, Spyropoulos AC, Kaatz S, Becker RC, Caprini JA, Dunn AS, Garcia DA, Jacobson A, Jaffer AK, Kong DF, Schulman S, Turpie AG, Hasselblad V, Ortel TL; BRIDGE Investigators. Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation. *N Engl J Med* 2015; **373**: 823-833 [PMID: 26095867 DOI: 10.1056/NEJMoa1501035]

26 **ASGE Standards of Practice Committee.**, Acosta RD, Abraham NS, Chandrasekhara V, Chathadi KV, Early DS, Eloubeidi MA, Evans JA, Faulx AL, Fisher DA, Fonkalsrud L, Hwang JH, Khashab MA, Lightdale JR, Muthusamy VR, Pasha SF, Saltzman JR, Shaukat A, Shergill AK, Wang A, Cash BD, DeWitt JM. The management of antithrombotic agents for patients undergoing GI endoscopy. *Gastrointest Endosc* 2016; **83**: 3-16 [PMID: 26621548 DOI: 10.1016/j.gie.2015.09.035]

27 **Fujimoto K**, Fujishiro M, Kato M, Higuchi K, Iwakiri R, Sakamoto C, Uchiyama S, Kashiwagi A, Ogawa H, Murakami K, Mine T, Yoshino J, Kinoshita Y, Ichinose M, Matsui T; Japan Gastroenterological Endoscopy Society. Guidelines for gastroenterological endoscopy in patients undergoing antithrombotic treatment. *Dig Endosc* 2014; **26**: 1-14 [PMID: 24215155 DOI: 10.1111/den.12183]

28 **Douketis JD**, Spyropoulos AC, Spencer FA, Mayr M, Jaffer AK, Eckman MH, Dunn AS, Kunz R. Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; **141**: e326S-e350S [PMID: 22315266 DOI: 10.1378/chest.11-2298]

29 **Korte W**, Cattaneo M, Chassot PG, Eichinger S, von Heymann C, Hofmann N, Rickli H, Spannagl M, Ziegler B, Verheugt F, Huber K. Peri-operative management of antiplatelet therapy in patients with coronary artery disease: joint position paper by members of the working group on Perioperative Haemostasis of the Society on Thrombosis and Haemostasis Research (GTH), the working group on Perioperative Coagulation of the Austrian Society for Anesthesiology, Resuscitation and Intensive Care (ÖGARI) and the Working Group Thrombosis of the European Society for Cardiology (ESC). *Thromb Haemost* 2011; **105**: 743-749 [PMID: 21437351 DOI: 10.1160/TH10-04-0217]

30 **Levine GN**, Bates ER, Bittl JA, Brindis RG, Fihn SD, Fleisher LA, Granger CB, Lange RA, Mack MJ, Mauri L, Mehran R, Mukherjee D, Newby LK, O'Gara PT, Sabatine MS, Smith PK, Smith SC Jr. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease, 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction, 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes, and 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery. *Circulation* 2016; **134**: e123-e155 [PMID: 27026020 DOI: 10.1161/CIR.0000000000000404]

31 **Kushner FG**, Hand M, Smith SC Jr, King SB 3rd, Anderson JL, Antman EM, Bailey SR, Bates ER, Blankenship JC, Casey DE Jr, Green LA, Jacobs AK, Hochman JS, Krumholz HM, Morrison DA, Ornato JP, Pearle DL, Peterson ED, Sloan MA, Whitlow PL, Williams DO; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines. 2009 focused updates: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction (updating the 2004 guideline and 2007 focused update) and ACC/AHA/SCAI guidelines on percutaneous coronary intervention (updating the 2005 guideline and 2007 focused update): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Catheter Cardiovasc Interv* 2009; **74**: E25-E68 [PMID: 19924773 DOI: 10.1002/ccd.22351]

32 **Polkowski M**, Larghi A, Weynand B, Boustière C, Giovannini M, Pujol B, Dumonceau JM; European Society of Gastrointestinal Endoscopy (ESGE). Learning, techniques, and complications of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Guideline. *Endoscopy* 2012; **44**: 190-206 [PMID: 22180307 DOI: 10.1055/s-0031-1291543]

33 **Spyropoulos AC**, Douketis JD, Gerotziafas G, Kaatz S, Ortel TL, Schulman S; Subcommittee on Control of Anticoagulation of the SSC of the ISTH. Periprocedural antithrombotic and bridging therapy: recommendations for standardized reporting in patients with arterial indications for chronic oral anticoagulant therapy. *J Thromb Haemost* 2012; **10**: 692-694 [PMID: 22934291]

34 **Ho PM**, Peterson ED, Wang L, Magid DJ, Fihn SD, Larsen GC, Jesse RA, Rumsfeld JS. Incidence of death and acute myocardial infarction associated with stopping clopidogrel after acute coronary syndrome. *JAMA* 2008; **299**: 532-539 [PMID: 18252883 DOI: 10.1001/jama.299.5.532]

35 **Ferrari E**, Benhamou M, Cerboni P, Marcel B. Coronary syndromes following aspirin withdrawal: a special risk for late stent thrombosis. *J Am Coll Cardiol* 2005; **45**: 456-459 [PMID: 15680728 DOI: 10.1016/j.jacc.2004.11.041]

36 **Devereaux PJ**, Mrkobrada M, Sessler DI, Leslie K, Alonso-Coello P, Kurz A, Villar JC, Sigamani A, Biccard BM, Meyhoff CS, Parlow JL, Guyatt G, Robinson A, Garg AX, Rodseth RN, Botto F, Lurati Buse G, Xavier D, Chan MT, Tiboni M, Cook D, Kumar PA, Forget P, Malaga G, Fleischmann E, Amir M, Eikelboom J, Mizera R, Torres D, Wang CY, VanHelder T, Paniagua P, Berwanger O, Srinathan S, Graham M, Pasin L, Le Manach Y, Gao P, Pogue J, Whitlock R, Lamy A, Kearon C, Baigent C, Chow C, Pettit S, Chrolavicius S, Yusuf S; POISE-2 Investigators. Aspirin in patients undergoing noncardiac surgery. *N Engl J Med* 2014; **370**: 1494-1503 [PMID: 24679062 DOI: 10.1056/NEJMoa1401105]

37 Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. *Lancet* 2000; **355**: 1295-1302 [PMID: 10776741 DOI: 10.1016/S0140-6736(00)02110-3]

38 **Wolf AM**, Pucci MJ, Gabale SD, McIntyre CA, Irizarry AM, Kennedy EP, Rosato EL, Lavu H, Winter JM, Yeo CJ. Safety of perioperative aspirin therapy in pancreatic operations. *Surgery* 2014; **155**: 39-46 [PMID: 23890963 DOI: 10.1016/j.surg.2013.05.031]

39 **Fang X**, Baillargeon JG, Jupiter DC. Continued Antiplatelet Therapy and Risk of Bleeding in Gastrointestinal Procedures: A Systematic Review. *J Am Coll Surg* 2016; **222**: 890-905.e11 [PMID: 27016908 DOI: 10.1016/j.jamcollsurg.2016.01.053]

40 **Baron TH**, Kamath PS, McBane RD. Management of antithrombotic therapy in patients undergoing invasive procedures. *N Engl J Med* 2013; **368**: 2113-2124 [PMID: 23718166 DOI: 10.1056/NEJMra1206531]

41 **Connolly SJ**, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, Pogue J, Reilly PA, Themeles E, Varrone J, Wang S, Alings M, Xavier D, Zhu J, Diaz R, Lewis BS, Darius H, Diener HC, Joyner CD, Wallentin L; RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2009; **361**: 1139-1151 [PMID: 19717844 DOI: 10.1056/NEJMoa0905561]

42 **Patel MR**, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, Breithardt G, Halperin JL, Hankey GJ, Piccini JP, Becker RC, Nessel CC, Paolini JF, Berkowitz SD, Fox KA, Califf RM; ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med* 2011; **365**: 883-891 [PMID: 21830957 DOI: 10.1056/NEJMoa1009638]

43 **Granger CB**, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, Al-Khalidi HR, Ansell J, Atar D, Avezum A, Bahit MC, Diaz R, Easton JD, Ezekowitz JA, Flaker G, Garcia D, Geraldes M, Gersh BJ, Golitsyn S, Goto S, Hermosillo AG, Hohnloser SH, Horowitz J, Mohan P, Jansky P, Lewis BS, Lopez-Sendon JL, Pais P, Parkhomenko A, Verheugt FW, Zhu J, Wallentin L; ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2011; **365**: 981-992 [PMID: 21870978 DOI: 10.1056/NEJMoa1107039]

44 **Giugliano RP**, Ruff CT, Braunwald E, Murphy SA, Wiviott SD, Halperin JL, Waldo AL, Ezekowitz MD, Weitz JI, Špinar J, Ruzyllo W, Ruda M, Koretsune Y, Betcher J, Shi M, Grip LT, Patel SP, Patel I, Hanyok JJ, Mercuri M, Antman EM; ENGAGE AF-TIMI 48 Investigators. Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2013; **369**: 2093-2104 [PMID: 24251359 DOI: 10.1056/NEJMoa1310907]

45 **Komori M**, Yasaka M, Kokuba K, Matsuoka H, Fujimoto S, Yoshida M, Kameda K, Shono T, Nagata S, Ago T, Kitazono T, Okada Y. Intracranial hemorrhage during dabigatran treatment. *Circ J* 2014; **78**: 1335-1341 [PMID: 24662438]

46 **Hagii J**, Tomita H, Metoki N, Saito S, Shiroto H, Hitomi H, Kamada T, Seino S, Takahashi K, Baba Y, Sasaki S, Uchizawa T, Iwata M, Matsumoto S, Osanai T, Yasujima M, Okumura K. Characteristics of intracerebral hemorrhage during rivaroxaban treatment: comparison with those during warfarin. *Stroke* 2014; **45**: 2805-2807 [PMID: 25082810 DOI: 10.1161/STROKEAHA.114.006661]

47 **Verma A**, Ha ACT, Rutka JT, Verma S. What Surgeons Should Know About Non-Vitamin K Oral Anticoagulants: A Review. *JAMA Surg* 2018; **153**: 577-585 [PMID: 29710221 DOI: 10.1001/jamasurg.2018.0374]

48 **Douketis JD**, Spyropoulos AC, Anderson JM, Arnold DM, Bates SM, Blostein M, Carrier M, Caprini JA, Clark NP, Coppens M, Dentali F, Duncan J, Gross PL, Kassis J, Kowalski S, Lee AY, Le Gal G, Le Templier G, Li N, MacKay E, Shah V, Shivakumar S, Solymoss S, Spencer FA, Syed S, Tafur AJ, Vanassche T, Thiele T, Wu C, Yeo E, Schulman S. The Perioperative Anticoagulant Use for Surgery Evaluation (PAUSE) Study for Patients on a Direct Oral Anticoagulant Who Need an Elective Surgery or Procedure: Design and Rationale. *Thromb Haemost* 2017; **117**: 2415-2424 [PMID: 29212129 DOI: 10.1160/TH17-08-0553]

**P-Reviewer:** Huang LY **S-Editor:** Dou Y **L-Editor: E-Editor:**

**Specialty type:** Medicine, research and experimental

**Country of origin:** Japan

**Peer-review report classification**

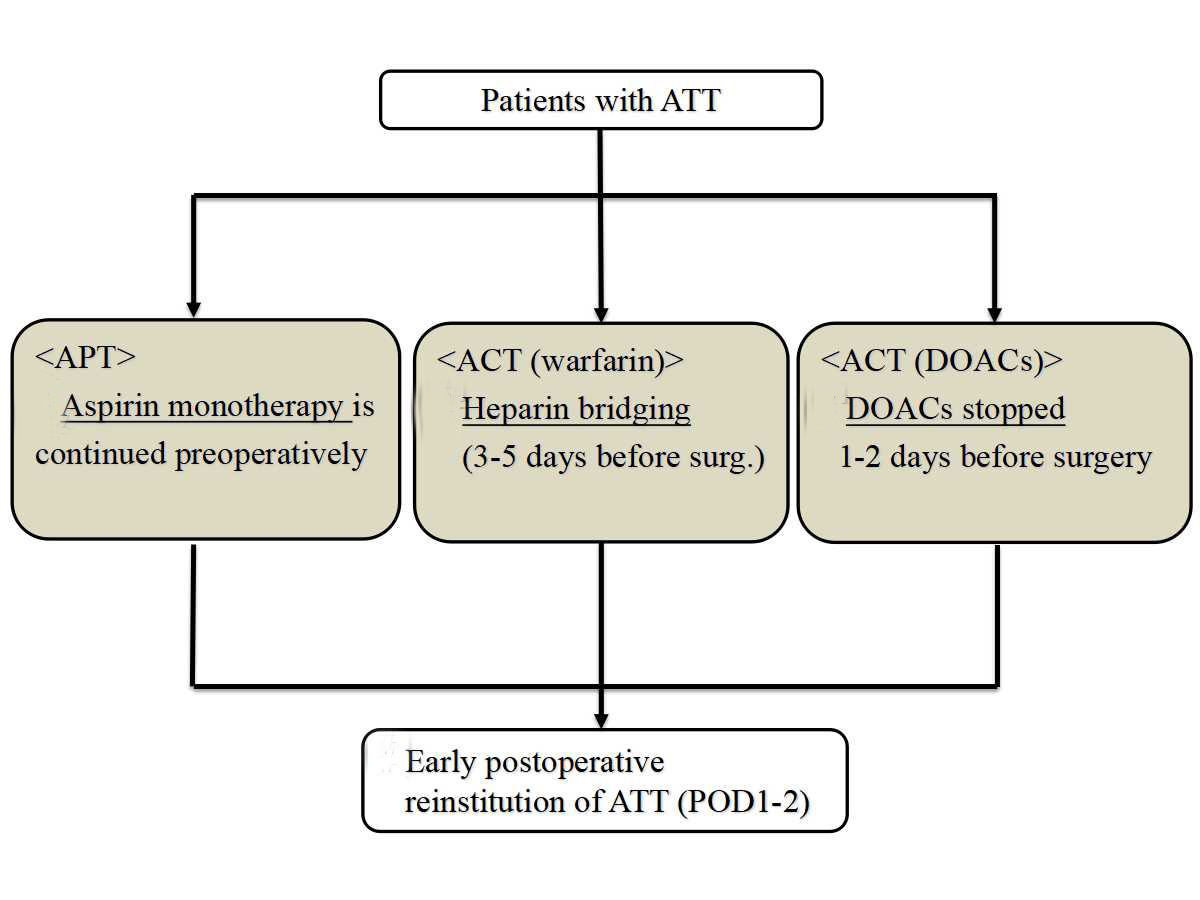
Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0



**Figure 1 Recommended perioperative management protocol for patients undergoing antithrombotic therapy in case of elective laparoscopic digestive surgery.** The management generally consists of 3 ways according to 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 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: Thromboemborism; ACT: Anticoagulation therapy; DOAC: Direct-acting oral anticoagulant.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **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** | **Yr** | **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 etc.) | | Patients with continued use of ASA (*n* = 52) Patients with discontinuation of APT (*n* = 160) Patients not on APT (control, *n* = 863) | PBC 0% in continued ASA *vs* 2.5% in discontinuation *vs* 0.7% in control (*P* = 0.987) | TE 0% in continued ASA *vs* 0.6% in discontinued ASA *vs* 0.2% in control (*P* = 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, *n* = 44) Patients without ACT (control, *n* = 1377) | | PBC 25% in ACT *vs* 1.5% in control (*P* < 0.001) One mortality due to severe bleeding | (not mentioned) |
| Ono[12] | 2013 | Laparoscopic cholecystectomy (*n* = 270) or Laparoscopic colorectal cancer resection (*n* = 218) | Patients with continued ASA (*n* = 52) Patients without ASA (control, *n* = 436) | | SBL 27mL in continued ASA *vs* 17mL in control (*P* = 0.430) | No mortality in both groups |
| Anderson[13] | 2014 | Laparoscopic cholecystectomy (elective and emergency) | Patients with continued clopidogrel (*n* = 36) Matched patients without clopidogrel (control, *n* = 36). | | No difference in SBL (49 g *vs* 47 g, *P* = 0.85) PBC 0% in clopidogrel *vs* 2.8% in control (*P* = 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 (*n* = 21) Patients without ATT (*n* = 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 (*n* = 56), including those with preop. Plt transfusion (*n* = 12) Patients without APT (control, *n* = 56) | | SBL ≥ 100mL 14.3% in continued ASA *vs* 9% in control (*P* = 0.50) | No difference in the rates of overall postop complications (8.9% *vs* 7.1%, *P* = 0.80) No mortality in both groups |
| Fujikawa[16] | 2017 | Emergency cholecystectomy including 106 laparoscopic sugery for acute cholecystitis | Patients with continued use of APT (*n* = 89) Patients without APT (control, *n* = 154) | | SBL ≥ 500mL 12% in continued APT *vs* 5% in control (*P* = 0.240) PBC 7% in multiple APT *vs* 3% in single APT *vs* 0.6% in control *(P* = 0.027) | TE 1.1% in continued APT *vs* 0% in control (*P* = 0.37) No mortality in both groups |
| Sakamoto[17] | 2017 | Laparoscopic cholecystectomy (only elective operation) | Patients with continued single APT (*n* = 49) Patients with discontinuation of APT (*n* = 106) Patients not on APT (control, *n* = 653) | | SBL ≥ 200mL 4.7% in continued APT *vs* 4.7% in discontinued APT *vs* 1.5% in control (*P* = 0.064) PBC 0% in continued APT *vs* 0.9% in discontinued APT *vs* 0.2% in control (*P* = 0.022) | TE 0% in continued APT *vs* 0.9% in discontinued APT *vs* 0.2% in control (*P* = 0.296) No mortality in any group |
| Yun[18] | 2017 | Laparoscopic cholecystectomy (elective *vs* emergency) for acute cholecystitis | Patients with continued use of ATT (almost APT, *n* = 22) Patients with discontinued ATT (almost APT, control, *n* = 45) | | SBL ≥ 100mL 13.6% in continued ATT *vs* 22.2% in control (*P* = 0.613) | One case of TE (2.2%) in control Mortality 4.6% in continued ATT *vs* 2.2% in control (*P* > 0.999) |
| Laparoscopic appendectomy | | | | | | |
| Chechik[19] | 2011 | Appendectomy including laparoscopic appendectomy (*n* = 78) | Patients with continued APT (*n* = 39) Patients without APT (control, *n* = 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 (*n* = 287) Matched patients without APT (control, *n* = 287) | | No difference in SBL (31g *vs* 26g) or blood transfusion rate (1% *vs* 0%) between the groups | Two cases of TE (MI) in continued APT (0.7%) No difference in the rates of mortality (1% *vs* 0%, *P* = 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.

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

|  |  |  |  |
| --- | --- | --- | --- |
| **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 d1 |
| Type III PDE inhibitor | Cilostazol (Pretal) | 2 d |
| Acetylsalicylic acid | Aspirin | 7-10 d |
| Other NSAIDs | Ibuprofen (Brufen, Advil), Loxoprofen (Loxonin), Diclofenac (Voltaren) *etc.* | Varies |
| Anticoagulants | | | |
|  | Vitamin K antagonist | Warfarin (Coumadin) | 5 d |
| Heparin derivatives | Fondaparinux (Arixtra) | 1.5-2 d |
| DOACs | | |
| 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.