Taking antithrombic therapy during emergency laparoscopic cholecystectomy for acute cholecystitis does not affect the postoperative outcomes: a propensity score matched study

Kentaro Oji1†, Yasunori Otowa1,2*,†, Yuta Yamazaki1, Keisuke Arai1, Yasuhiko Mii1, Keitaro Kakinoki1, Tetsu Nakamura1 and Daisuke Kuroda1

Abstract

Background: Continuing antithrombic therapy (ATT) during surgery increases the risk of bleeding. However, it is difficult to discontinue the ATT in emergency surgery. Therefore, safety of emergency laparoscopic cholecystectomy (LC) for acute cholecystitis (AC) is still unclear. We aimed to clarify the affect of ATT during emergency LC for AC.

Methods: Patients with AC were classified into ATT group (n = 30) and non-ATT group (n = 120). Postoperative outcomes were compared after propensity score matching (n = 22).

Results: Higher level of c-reactive protein level and shorter activated partial thromboplastin time (APTT) was observed in ATT group than in non-ATT group after matching. No significant difference was found between other patient characteristics and perioperative results. Blood loss over 100 mL was observed in 8 patients. Multivariate analysis showed that APTT was an independent risk factor for bleeding over 100 mL (P = 0.039), while ACT and APT was not.

Conclusions: Taking ATT does not affect the blood loss or complications during emergency LC for AC. Controlling intraoperative bleeding is essential for a safe postoperative outcome.

Keywords: Antithrombic therapy, Acute cholecystitis, Laparoscopic cholecystectomy

Background

Antithrombic therapy (ATT) is used to prevent primary and secondary thromboembolic complications after cardiovascular or cerebrovascular diseases and the use of ATT is more relevant in elder population [1, 2]. However, continuing ATT increases the risk of bleeding and discontinuing the ATT increases the risk of thrombosis during perioperation [3–6]. Several reports showed that it was safe to continue the ATT during perioperation in abdominal surgery [7–9]. But still, thromboembolic and bleeding risks should be considered whether to interrupt or continue the ATT in elected surgery. On the other hand, bleeding is more relevant in inflammatory phase and it is difficult to interrupt ATT in emergency surgery which increases the risk of bleeding [10].

*Correspondence: dregg338@hotmail.com
†Kentaro Oji and Yasunori Otowa contributed equally to this work
1 Department of Surgery, Kita-Harima Medical Center, 926-250 Ichiba-cho, Ono, Hyogo 675-1392, Japan
Full list of author information is available at the end of the article

© The Author(s) 2022. Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated in a credit line to the data.
Laparoscopic cholecystectomy (LC) is a standard treatment for cholecystitis and also for acute cholecystitis (AC). Previous studies showed that LC can be performed safely in patients with ATT in acute phase [11–14]. However, there was a significant difference in patient characteristics of those taking ATT and those without ATT or the age was relatively young. Generally, as the age raise, higher rate of comorbidity and uses of ATT is relevant [15]. Therefore, the safety of emergency LC for AC with ATT remains unclear. In this retrospective study, we aimed to clarify the affect of ATT during emergency LC for AC.

Materials and methods
We performed a retrospective review of all patients who underwent emergency LC for AC at our institution from October 2013 to October 2019. Patients treated with laparotomy, or who had gallbladder drainage before surgery were excluded from the study. Patients were classified into one of three severity grades by the 2018 Tokyo Guidelines (TG18) [16].

LC was performed with standard four-port technique. Extra port was added if necessary. Pneumoperitoneum pressures were maintained at 10 mmHg. Ultrasonic coagulating shears was mainly used around the Calot’s triangle to prevent bleeding from small vessels. Soft coagulation was used to stop the bleeding and keep the surgical field dry. Mechanical compression using hemostatic agent was performed when it was difficult to control the bleeding only by soft coagulation. Ultrasonic coagulating shears and soft coagulation was used in all cases. Postoperative complications were graded according to the Clavien–Dindo classification, and cases with a classification over grade II were defined as having a postoperative complication [17].

Statistical analysis
Statistical analysis was carried out using the EZR software which is a graphical user interface for R (R Foundation for Statistical Computing, Vienna, Austria, v. 4.0.3). The following covariates were included in the score matching: age, American Society of Anesthesiologists-Physical Status (ASA-PS), Charlson comorbidity Index (CCI), c-reactive protein (CRP), hemoglobin, TG18 grade, platelet, sex, and white blood cell. The relation between two variables was assessed using the Fisher exact test or Chi-squared test and Student’s T-test or Mann–Whitney U test. Variables with a P value < 0.1 in a univariate analysis were further evaluated in a multivariate analysis using the logistic regression model to assess the confounding variables. In all analyses, P < 0.05 was accepted as statistically significant.

Results
Two hundred one patients were diagnosed as AC and underwent surgery during the period. Fifty one patients were excluded: 50 patients due to gallbladder drainage before surgery and 1 patient due to laparotomy. One hundred fifty patients were analyzed. Patient characteristics are listed in Table 1. Thirty patients took ATT and 17 patients (56.7%) were over 75 years old. Seven patients (23.3%) had anticoagulation therapy (ACT) and 25 patients (83.3%) had antiplatelet therapy (APT). Five patients (16.7%) had multiple dosage of APT or combination of ACT and APT. Before matching, there were significant differences in patient characteristics between groups in ASA-PS, CCI, TG18 grade, and blood test results. There was a trend of elder patients and more male in ATT group than in non-ATT group. Significantly higher ASA-PS and CCI was observed in ages over 75 years old compared with age under 75 years old (P = 0.032 and P < 0.001, respectively). After matching, 22 patients had ATT. Among them, 9 patients (40.9%) were over 75 years old. Higher CRP level, longer prothrombin time-international normalized ratio (PT-INR), and shorter activated partial thromboplastin time (APTT) was observed in ATT group than in non-APT group (P = 0.002, P = 0.001, and P < 0.001, respectively). There was no difference in ASA-PS and CCI between ages over 75 years old and under.

The perioperative results are listed in Table 2. Before matching, one patient was converted to laparotomy in the non-ATT group. There was a trend of longer operation time and higher blood loss in ATT group compared with non-ATT group, although the difference was not significant. There was no difference in complications. After matching, there still was a trend of longer operation time and more blood loss in ATT group compared with non-ATT group, although the difference was not significant. There was no difference in complications and hospital stays.

We further analyzed what affected the blood loss over 100 mL. The difference in patient characteristics according to the blood loss is listed in Table 3. There was a trend of lower albumin level and longer PT-INR and APTT in patients with blood loss over 100 mL compared with blood loss under 100 mL. Multivariate analyze (Table 4) showed that APTT is an independent risk factors for bleeding over 100 mL (P = 0.039), while ACT and APT was not.

Discussion
Previous studies showed that emergency LC for AC can be safely perform with patients taking ATT [11–14]. However, there were significant differences in patient characteristics in these studies. Elder population is a
### Table 1 Patient characteristics

|                     | Before match | After match | P value | Before match | After match | P value |
|---------------------|--------------|-------------|---------|--------------|-------------|---------|
|                     | ATT (n = 30) | Non-ATT (n = 120) |         | ATT (n = 22) | Non-ATT (n = 22) |         |
| Age                 | 77 (44–90)   | 70 (25–100)  | 0.065   | 77 (59–90)   | 72 (51–92)   | 0.549   |
| Sex (Male/Female)   | 23/7         | 70/50       | 0.092   | 15/7         | 15/7        | 1.000   |
| BMI (kg/m²)         | 23.1 (3.9)   | 23.9 (3.8)  | 0.302   | 22.5 (3.4)   | 22.4 (3.1)  | 0.973   |
| ASA-PS (1,2/3,4)    | 16/14        | 105/15      | <0.001  | 14/8         | 17/5        | 0.510   |
| CCI                 | 1 (0–6)      | 0 (0–4)     | 0.001   | 1 (0–6)      | 1 (0–4)     | 0.714   |
| TG18 grade (1/2,3)  | 8/22         | 78/42       | <0.001  | 8/14         | 10/12       | 0.760   |
| WBC (10³/µL)        | 1.5 (0.5)    | 1.3 (0.5)   | 0.039   | 1.3 (0.5)    | 1.5 (0.4)   | 0.489   |
| Hb (g/dL)           | 12.7 (1.7)   | 13.6 (2.0)  | 0.028   | 12.7 (1.4)   | 12.7 (2.4)  | 0.970   |
| Plt (10³/µL)        | 21.0 (7.5)   | 23.2 (8.1)  | 0.180   | 21.5 (8.1)   | 23.1 (7.1)  | 0.489   |
| CRP (mg/dL)         | 14.8 (0.1–44.1) | 4.0 (0.0–18.4) | 0.004 | 15.8 (0.1–44.1) | 2.4 (0.0–30.9) | 0.022 |
| Alb (g/dL)          | 3.4 (0.7)    | 3.7 (0.7)   | 0.007   | 3.4 (0.7)    | 3.7 (0.8)   | 0.190   |
| Total bilirubin (mg/dL) | 1.2 (0.2–5.4) | 1.0 (0.2–16.8) | 0.195 | 1.1 (0.2–5.4) | 0.9 (0.4–10.3) | 0.597 |
| AST                 | 25 (14–513)  | 24 (11–1243) | 0.842   | 24 (14–201)  | 23 (11–390)  | 0.787   |
| ALT                 | 19 (6–515)   | 24 (6–866)  | 0.491   | 17 (6–114)   | 20 (6–866)  | 0.526   |
| ALP                 | 273 (155–1369) | 258 (115–1477) | 0.521 | 256 (155–627) | 270 (121–1477) | 0.771 |
| yGTP (IU/L)         | 50 (9–450)   | 40 (12–572) | 0.932   | 47 (9–128)   | 43 (14–572) | 0.488   |
| Cr                  | 0.8 (0.4–7.3) | 0.8 (0.3–7.1) | 0.116 | 0.8 (0.5–7.3) | 0.8 (0.5–7.1) | 0.953   |
| PT-INR              | 1.2 (1.0–2.0) | 1.1 (0.9–1.4) | <0.001 | 1.2 (1.0–1.6) | 1.0 (0.9–1.3) | 0.001   |
| APTT (s)            | 41.1 (26.6–76.1) | 33.5 (21.4–53.6) | <0.001 | 41.1 (26.6–76.1) | 33.5 (21.4–53.6) | <0.001 |
| ACT (%)             | 7 (23.3)     | 4 (18.2)    |         |             |             |         |
| APT (%)             | 25 (83.3)    | 18 (81.8)   |         |             |             |         |
| Multiple dosage (%) | 5 (16.7)     | 2 (9/1)     |         |             |             |         |
| Duration until operation from onset | 3 (1–10) | 2 (1–30) | 0.088 | 3 (1–10) | 3 (1–10) | 0.157 |

**Mean (SD) or median (range)**

ACT, anticoagulation therapy; APTT, activated partial thromboplastin time; ATT, antithrombic therapy; BMI, body mass index; ASA-PS, American Society of Anesthesiologists-Physical Status; CCI, Charlson Comorbidity Index; TG18, Tokyo guideline 2018; WBC, white blood cell; Hb, hemoglobin, Plt, platelet; CRP, c-reactive protein; Alb, albumin, γGTP, gamma glutamyl transpeptidase; PT-INR, prothrombin time-international normalized ratio

*a Multiple dosage of APT or combination of ACT and APT

### Table 2 Perioperative results

|                     | Before match | After match | P value | Before match | After match | P value |
|---------------------|--------------|-------------|---------|--------------|-------------|---------|
|                     | ATT (n = 30) | Non-ATT (n = 120) |         | ATT (n = 22) | Non-ATT (n = 22) |         |
| Open conversion (%) | 0            | 1 (0.8)     | 1.000   | 0            | 0           | 1.000   |
| Operative time (min)| 130 (79–260) | 119 (51–305) | 0.107   | 128 (79–260) | 116 (54–232) | 0.205   |
| Blood loss (mL)     | 17 (0–651)   | 10 (0–550)  | 0.179   | 13 (0–651)   | 10 (0–378)  | 0.179   |
| Blood loss > 100 mL (%) | 7 (23.3) | 21 (17.5) | 0.446 | 6 (27.3) | 2 (9.1) | 0.240 |
| All postoperative complications (%) | 4 (13.3) | 14 (11.7) | 0.759 | 3 (13.6) | 4 (18.2) | 1.000 |
| Bleeding (%)        | 0            | 0           | NA      | 0            | 0           | NA      |
| Abdominal abscess (%) | 1 (3.3)  | 2 (1.7)    | 0.491   | 1 (4.5)      | 1 (4.5)     | 1.000   |
| Bile leak (%)       | 0            | 4 (3.3)     | 0.584   | 0            | 0           | NA      |
| Respiratory (%)     | 1 (3.3)      | 2 (1.7)     | 0.491   | 1 (4.5)      | 0           | 1.000   |
| Others (%)          | 1 (3.3)      | 4 (3.3)     | 1.000   | 0            | 2 (9.1)     | 0.488   |
| Hospital stays (days) | 10.5 (5–42) | 7 (3–36)   | 0.002   | 11 (5–42)    | 7 (3–30)    | 0.409   |

**Mean (SD) or median (range)**

*a Some cases overlapped*
risk factor for bleeding when using ATT [18–21]. Also, liver disease, renal disease, and inflammation itself increases the bleeding risk [22–24]. From our study APTT was in independent risk factor for bleeding over 100 mL. PT and APTT are both valuable factors to measure the time it takes plasma to clot when various substances are added. When PT and APTT are both are prolonged, there is a problem in final common pathway of coagulation. This is observed in liver disease and disseminated intravascular coagulation. On the other hand, only APTT is prolonged when there is a problem in intrinsic pathway of coagulation. This is observed in several inherited bleeding disorders and due to several ACT such as heparin and direct oral anticoagulants. Therefore, patient characteristics need to be matched to exclude these affects. In this study, we showed that APTT affected the blood loss, while ACT and APT did not. Also, there was no significant difference in other postoperative complications between groups. These results suggest that ATT will not increase the risk of bleeding and emergency LC for AC is feasible and safe for patients taking ATT.

Prevention of bleeding by meticulous hemostasis during the laparoscopic surgery is a fundamental principle. Therefore, prompt management is required even when minor bleeding occurs. Recent improvement in surgical instruments have contributed to less bleeding. Argon beam coagulator, microwave coagulator, and ultrasonic coagulating shears have been developed and used to stop bleeding from the gallbladder bed during LC for AC [25]. Also, conjunction with mechanical compression using dry hemostatic agents help slower the bleeding. We believe that these new instruments have contributed to control the bleeding during surgery despite taking ATT in our study.

Multiple dosage of ATT is sometimes observed. Previous studies evaluated the risk of bleeding when taking multiple dosage of ATT; however, results differed between studies [26–30]. Xu et al. reported that age over 90 was a risk of higher bleeding when taking multiple dosage of ATT [28]. Kawamoto et al. reported that multiple dosage of ATT showed bleeding from the area of surgery and also gastrointestinal bleeding after surgery [2]. Multiple dosage was not a risk factor of bleeding from results of this study; however, we should still be aware of the risk of bleeding when elder is taking multiple dosage of ATT.

This study has several limitations. This is a retrospective study at a single institution, so the sample size, especially the number of patients taking ATT is small. Therefore, we could not completely match the patient characteristics and classify the ATT according to the types of antithrombotic agents that were administered. Also, not all cases with ATT had emergency LC, since TG18 also recommends biliary drainage as an alternate treatment for higher TG18 grade [31]. Therefore, the safety of emergency LC with those taking ATT with higher TG18 is still unclear. Further studies with a larger sample are necessary to clarify these limitations.

| Table 3 | Patient characteristics according to the blood loss |
|---------|---------------------------------------------------|
|          | Blood loss > 100 mL (n = 8)                        | Blood loss < 100 mL (n = 36) | P value |
| Age     | 79.6 (5.6)                                        | 72.7 (11.9)                   | 0.119   |
| Sex (Male/Female) | 6/2                 | 24/12                        | 1.000   |
| BMI (kg/m²) | 22.1 (3.8)                  | 22.5 (3.2)                   | 0.719   |
| ASA-PS (1,2/3,4) | 5/3                 | 26/10                        | 0.676   |
| CCI     | 1 (1–2)                                          | 1 (0–2)                      | 0.699   |
| TG18 grade (1/2,3) | 2/6                 | 16/20                        | 0.439   |
| WBC (10⁴/µL) | 1.5 (0.7)                    | 1.4 (0.4)                    | 0.496   |
| Hb (g/dL) | 11.9 (1.7)                                   | 12.9 (2.0)                   | 0.184   |
| Plt (10⁴/µL) | 20.3 (5.5)                   | 22.8 (7.9)                   | 0.416   |
| CRP (mg/dL) | 16.7 (6.3–27.6)            | 9.6 (0.0–44.1)               | 0.235   |
| Alb (g/dL) | 3.1 (0.5)                                   | 3.6 (0.7)                    | 0.089   |
| Total bilirubin (mg/dL) | 1.2 (0.6–5.4)              | 0.9 (0.2–10.3)               | 0.429   |
| AST     | 22 (14–62)                                      | 23 (11–390)                  | 0.626   |
| ALT     | 14 (7–47)                                       | 19 (6–866)                   | 0.201   |
| ALP     | 263 (202–627)                                   | 270 (121–1477)               | 0.629   |
| γGTP (IU/L) | 34 (9–87)                                | 46 (14–572)                  | 0.543   |
| Cr      | 0.8 (0.5–4.2)                                   | 0.9 (0.5–7.3)                | 0.692   |
| PT-INR  | 1.2 (1.1–1.2)                                   | 1.1 (1.0–1.2)                | 0.073   |
| APTT (s) | 42.0 (27.4–54.5)              | 34.2 (21.4–60.9)             | 0.055   |
| ACT (%) | 1 (12.5)                                        | 3 (8.3)                      | 0.566   |
| APT (%) | 5 (62.5)                                        | 13 (36.1)                    | 0.240   |
| Multiple dosage (%) | 0                   | 2 (5.6)                      | 1.000   |

Mean (SD) or median (range)

ACT, anticoagulation therapy; APTT, activated partial thromboplastin time; ATT, antithrombin therapy; BMI, body mass index; ASA-PS, American Society of Anesthesiologists-Physical Status; CCI, Charlson Comorbidity Index; TG18, Tokyo guideline 2018; WBC, white blood cell; Hb, hemoglobin, Plt, platelet; CRP, c-reactive protein; Alb, albumin, γGTP, gamma glutamyl transpeptidase; PT-INR, prothrombin time-international normalized ratio

| Table 4 | Multivariate analysis of preoperative risk factors for blood loss over 100 mL |
|---------|-----------------------------------------------|
|          | OR (95% CI)                                      | P value |
| Alb (3.5 ≤) | 0.207 (0.031–1.400)                              | 0.106   |
| PT-INR (1.5 ≤) | 0.000 (0.000–infinity)                           | 0.994   |
| APTT (40 ≤) | 7.380 (1.110–49.100)                             | 0.039   |

OR, odds ratio; CI, confidence interval; Alb, albumin; PT-INR, prothrombin time-international normalized ratio; APTT, activated partial thromboplastin time
Conclusion
Emergency ATT does not affect the blood loss or complications during emergency LC for AC. Controlling intraoperative bleeding is essential for a safe postoperative outcome.

Abbreviations
ATT: Antithrombotic therapy; LC: Laparoscopic cholecystectomy; AC: Acute cholecystitis; TG18: Tokyo guideline 2018; ASA-PS: American Society of Anesthesiologists-Physical Status; CCI: Charlson Comorbidity Index; CRP: C-reactive protein; ACT: Anticoagulation therapy; APT: Antiplatelet therapy; PT-INR: Prothrombin time-international normalized ratio; APTT: Activated partial thromboplastin time.

Acknowledgements
We have no acknowledgments.

Authors’ contributions
KO, YO, KA, YM, KK, and DK performed surgery and perioperative management on the patients. YO and KO conceived the study. KO and YY collected data. KO and YO performed the data analysis. YO and KO wrote the manuscript. TN and YY collected data. KO and YY contributed equally to this work. All authors read and approved the final manuscript.

Funding
There are no funding resources to be reported or declared.

Availability of data and materials
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The Ethics Committee of Kita-Harima Medical Center approved this retrospective study of clinical data, which was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all patients. The Ethics Committee of Kita-Harima Medical Center approved this retrospective study of clinical data, which was conducted in accordance with principles of the Declaration of Helsinki. Informed consent was obtained from all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
1Department of Surgery, Kita-Harima Medical Center, 926-250 Ichiba-cho, Ono, Hyogo 675-1392, Japan. 2Radiation Biology Branch, National Cancer Institute, 9000 Rockville Pike, Bethesda, Maryland 20892, USA.

Received: 27 September 2021 Accepted: 27 January 2022
Published online: 05 February 2022

References
1. Fujikawa T, Tanaka A, Abe T, Yoshimoto Y, Tada S, Maekawa H, et al. 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 Surgeons. 2013;217(6):1044–53.
2. Kawamoto Y, Fujikawa T, Sakamoto Y, Emoto N, Takahashi R, Kawamura Y, et al. Effect of antithrombolytic therapy on bleeding complications in patients receiving emergency cholecystectomy for acute cholecystitis. J Hepatobiliary Pancreat Sci. 2018;25(11):S18–26.
3. Torn M, Rosendaal FR. Oral anticoagulation in surgical procedures: risks and recommendations. Br J Haematol. 2003;123(4):676–82.
4. Spyropoulos AC, Douketis JD. How I treat anticoagulated patients undergoing an elective procedure or surgery. Blood. 2011;120(5):2954–62.
5. Devereaux PJ, Mirobrada M, Sessler DI, Leslie K, Alonso-Coello P, Kurz A, et al. Aspirin in patients undergoing noncardiac surgery. N Engl J Med. 2014;370(16):1494–503.
6. Ono K, Hidaka H, Sato M, Nakatsuka H. Preoperative continuation of aspirin administration in patients undergoing major abdominal malignancy surgery. J Anesth. 2019;33(1):90–5.
7. Yoshimoto Y, Fujikawa T, Tanaka A, Hayashi H, Shimoike N, Kawamoto H, et al. Optimal use of antithrombotic agents, especially aspirin, in the perioperative management of colorectal cancer patients undergoing laparoscopic colorectal resection. World J Surg Oncol. 2019;17:92.
8. Li J, Wang M, Cheng T. The safe and risk assessment of perioperative antiplatelet and anticoagulation therapy in inguinal hernia repair, a systematic review. Surg Endosc. 2019;33(10):3165–76.
9. Antolovic D, Rakow A, Conlin P, Ulrich A, Rahbari NN, Buchler MW, et al. A randomised controlled pilot trial to evaluate and optimise the use of anti-platelet agents in the perioperative management in patients undergoing general and abdominal surgery-the APAP trial (ISRCTN45810007). Langenbeck Arch Surg. 2012;397(2):297–306.
10. Cassahun WT, Wagner TC, Babel J, Mehndorff M. The effects of oral anti-coagulant exposure on the surgical outcomes of patients undergoing abdominal surgery for high-risk abdominal emergencies. J Gastrointest Surg. 2021.
11. Imamura H, Minami S, Isagawa Y, Morita M, Hirabaru M, Kawahara D, et al. The effect of antithrombolytic therapy in patients undergoing emergency laparoscopic cholecystectomy for acute cholecystitis—a single center experience. Asian J Endosc Surg. 2020;13(3):359–65.
12. Joseph B, Rawashdeh B, Aziz H, Kutuvanoyou N, Pandit V, Jehangir Q, et al. An acute care surgery dilemma: emergent laparoscopic cholecystectomy in patients on aspirin therapy. Am J Surg. 2015;209(4):689–94.
13. Noda T, Hatano H, Dono K, Shimizu J, Oshima K, Tanida T, et al. Safety of early laparoscopic cholecystectomy for patients with acute cholecystitis undergoing antiplatelet or anticoagulation therapy: a single-institution experience. Hepatogastroenterology. 2014;61(134):1501–6.
14. Vaccari S, Lauro A, Cervellera M, Bellini ML, Palazzini G, Girocchi R, et al. Effect of antithrombotic therapy on postoperative outcome of 338 consecutive emergency laparoscopic cholecystectomies for acute cholecystitis: two Italian center’s study. Updates Surg. 2021;73:1767–74.
15. Lu Q, Lu JW, Wu Z, Liu XM, Li JH, Dong J, et al. Perioperative outcome of elderly versus younger patients undergoing major hepatic or pancreatic surgery. Clin Interv Aging. 2018;13:347–51.
16. Yokoe M, Hata J, Takada T, Strauss SM, Asbruin HI, Wakabayashi G, et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholecystitis (with videos). J Hepatobiliary Pancreat Sci. 2018;25(1):41–54.
17. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results from a survey. Ann Surg. 2004;240(2):205–13.
18. Li LL, Geraghty OC, O’Corragain OA, Watthanasuntorn K, et al. Efficacy and safety of antiplatelet agents, especially aspirin, in elderly patients: practical recommendations. Clin Interv Aging. 2009;4:165–77.
19. Robert-Ebadi H, Le Gal G, Righini M. Use of anticoagulants in elderly patients: practical recommendations. Clin Interv Aging. 2009;4:165–77.
20. Benedetti G, Necca M, Agati L. Oral anticoagulants in patients undergoing non valvular atrial fibrillation: state of evidence. Minerva Cardioangiol. 2018;66(3):301–13.
21. Chokesuwattanaskul R, Thongprayoon C, Bathini T, Torres-Ortiz A, O’Corragain OA, Watthanasuntorn K, et al. Efficacy and safety of antiplatelet therapy in patients with non valvular atrial fibrillation: state of evidence. Minerva Cardioangiol. 2018;66(3):301–13.
22. Chokesuwattanaskul R, Thongprayoon C, Bathini T, Torres-Ortiz A, O’Corragain OA, Watthanasuntorn K, et al. Efficacy and safety of antiplatelet therapy in patients with non valvular atrial fibrillation: state of evidence. Minerva Cardioangiol. 2018;66(3):301–13.
23. Devereaux PJ, Mirobrada M, Sessler DI, Leslie K, Alonso-Coello P, Kurz A, et al. Aspirin in patients undergoing noncardiac surgery. N Engl J Med. 2014;370(16):1494–503.
24. Lin D, Wu S, Fan Y, Ke C. Comparison of laparoscopic cholecystectomy and delayed laparoscopic cholecystectomy in aged acute calculous cholecystitis: a cohort study. Surg Endosc. 2020;34(7):2994–3001.
25. Akahoshi K, Ochiai T, Takaoka A, Kitamura T, Ban D, Kudo A, et al. Emergency cholecystectomy for patients on antiplatelet therapy. Am Surg. 2017;83(5):486–90.
26. Cui RB, Ng KS, Young CJ. Complications arising from perioperative anticoagulant/antiplatelet therapy in major colorectal and abdominal wall surgery. Dis Colon Rectum. 2018;61(1):1306–15.
27. Vogt C, Allo G, Buerger M, Kasper P, Chon SH, Gillessen J, et al. Assessing guideline adherence in patients with non-variceal upper gastrointestinal bleeding receiving antiplatelet and anticoagulant therapy. Scand J Gastroenterol. 2019;54(11):1357–63.
28. Xu K, Chan NC. Bleeding in patients with atrial fibrillation treated with combined antiplatelet and anticoagulant therapy: time to turn the corner. Ann Transl Med. 2019;7(Suppl 6):S198.
29. Tinkham TT, Vazquez SR, Jones AE, Witt DM. Direct oral anticoagulant plus antiplatelet therapy: prescribing practices and bleeding outcomes. J Thromb Thrombolysis. 2020;49(3):492–6.
30. Yoshimoto M, Hioki M, Sadamori H, Monden K, Ohno S, Takakura N. Emergent cholecystectomy in patients on antithrombotic therapy. Sci Rep. 2020;10(1):10122.
31. Mayumi T, Okamoto K, Takada T, Strasberg SM, Solomkin JS, Schlissberg D, et al. Tokyo guidelines 2018: management bundles for acute cholangitis and cholecystitis. J Hepatobiliary Pancreat Sci. 2018;25(1):96–100.

**Publisher’s Note**
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.