

The effect of antithrombotic drug use on postoperative bleeding following laparoscopic appendectomy

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ABSTRACT

Introduction: Today, appendectomy is the most frequently performed emergency surgery in general surgery practice. While laparoscopic appendectomy is the gold standard, it is now performed more frequently under the use of antithrombotic drugs due to the increasing global quality of life. This study aimed to determine the incidence of postoperative bleeding and associated risk factors in patients receiving antithrombotic therapy who underwent laparoscopic appendectomy.

Materials and Methods: A total of 847 patients who underwent laparoscopic appendectomy with a diagnosis of acute appendicitis between January 2019 and August 2025 were retrospectively evaluated. Patients were divided into two groups based on antithrombotic drug use: The antithrombotic group (n=42) and the control group (n=805). The primary endpoint was postoperative bleeding, and secondary endpoints included operative time, length of hospital stay, transfusion requirement, and mortality.

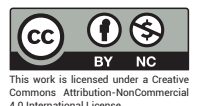
Results: The postoperative bleeding rate was 7.1% (n=3) in the antithrombotic group and 1.2% (n=10) in the control group (p=0.019). Multivariable analysis identified antithrombotic drug use (OR: 5.84, 95% CI: 1.52–22.45; p:0.010), age \geq 65 years (OR: 3.12, 95% CI: 1.08–9.02; p:0.036), and complicated appendicitis (OR: 2.67, 95% CI: 0.94–7.58; p:0.065) as independent risk factors. Transfusion requirement was significantly higher in the antithrombotic group (4.8% vs. 0.5%, p=0.023).

Conclusions: Antithrombotic drug use increases the risk of postoperative bleeding following laparoscopic appendectomy. However, this risk can be maintained at an acceptable level with careful patient selection and appropriate perioperative management. In emergency settings, proceeding with surgery without waiting for discontinuation of antithrombotic therapy may be a reasonable approach to prevent complications of appendicitis.

Keywords: Antithrombotic therapy, aspirin, laparoscopic appendectomy, postoperative bleeding, acute appendicitis



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Introduction

In recent years, antithrombotic drug use has been increasing worldwide in parallel with the rising prevalence of cardiovascular diseases and the aging population. In a study by Yoo et al.^[1] encompassing 51 countries, the rate of aspirin use for secondary prevention among individuals with a history of cardiovascular disease was reported as 40.3%, reaching up to 65% in high-income countries. This growing number of patients receiving antithrombotic therapy constitutes a significant patient population in surgical practice.

Anticoagulant and antithrombotic drugs have several implications in general surgical practice. These medications can increase intraoperative blood loss by affecting hemostatic mechanisms, prolong operative time, and contribute to the development of postoperative hematomas. According to the American College of Chest Physicians (ACCP) 2022 guidelines, approximately 15–20% of patients receiving antithrombotic therapy require surgical or invasive procedures annually.^[2] Studies in the literature have reported an increased incidence of bleeding complications in patients using these medications.^[3]

Among antithrombotic agents, aspirin (acetylsalicylic acid) is the most widely used. Aspirin has a broad spectrum of indications including primary and secondary cardiovascular prevention, cerebrovascular diseases, peripheral arterial disease, and coronary artery disease management. Aspirin inhibits platelet aggregation for 7–10 days through irreversible cyclooxygenase-1 (COX-1) inhibition. While this mechanism of action provides the antithrombotic efficacy of aspirin, it simultaneously increases the risk of bleeding.^[4]

Acute appendicitis is one of the most common causes of acute abdomen worldwide, with a lifetime risk ranging between 7–8%. According to the Global Burden of Disease Study 2021, the incidence of appendicitis is 214 per 100,000, corresponding to approximately 17 million new cases annually.^[5] In a systematic review by Ferris et al.^[6], the incidence of appendicitis in North America was reported as 100 per 100,000. Laparoscopic appendectomy is considered the gold standard in the treatment of acute appendicitis. Meta-analyses have demonstrated that the laparoscopic approach provides lower wound infection rates, shorter hospital stays, and earlier return to daily activities compared to open surgery.^[7,9]

Various studies exist in the literature regarding the effect of aspirin use on surgical outcomes. The POISE-2 trial

demonstrated that perioperative aspirin use in noncardiac surgery significantly increased the risk of major bleeding (HR: 1.23, 95% CI: 1.01–1.49).^[10] In a meta-analysis by Burger et al.^[11], perioperative continuation of aspirin was reported to increase the risk of bleeding by 50%. In a meta-analysis by Cai et al.^[12] focusing on laparoscopic cholecystectomy, bleeding outcomes in patients receiving antithrombotic therapy were evaluated, yielding conflicting results.

However, comprehensive studies evaluating the effects of antithrombotic drug use on postoperative bleeding in laparoscopic appendectomy, one of the most commonly performed emergency surgical procedures worldwide, remain limited. Although a multicenter retrospective study by Pearcy et al.^[13] reported that irreversible antithrombotic therapy did not adversely affect outcomes in emergency laparoscopic appendectomy, more data are needed in this area. This study aims to determine the incidence of postoperative bleeding and associated factors in patients receiving antithrombotic drugs who underwent laparoscopic appendectomy, thereby contributing to the development of perioperative patient management protocols.

Materials and Methods

Study Design and Patient Selection

This retrospective cohort study includes patients who underwent laparoscopic appendectomy with a diagnosis of acute appendicitis at our center between January 2019 and August 2025. The study was approved by our institutional review board (Ethics Committee No: 2025/437).

Patients aged 18 years and older who underwent laparoscopic appendectomy for acute appendicitis at our center were included. Exclusion criteria were as follows: Patients who underwent open appendectomy, patients converted from laparoscopic to open surgery, patients using anticoagulant drugs acting through different mechanisms, and patients who underwent additional surgical procedures concomitant with appendectomy.

Patients were divided into two groups based on antithrombotic drug use. Antithrombotic group: Patients who had been receiving antithrombotic drugs (aspirin, clopidogrel, ticagrelor, prasugrel, or their combinations) for at least 7 days prior to surgery. Control group: Patients not using any antithrombotic drugs.

Surgical Technique

All patients were operated under general anesthesia. A standard three-port technique was employed (umbilical 10 mm, suprapubic 5 mm, left lower quadrant 5 mm). Pneumoperitoneum was established at 14 mmHg pressure. The mesoappendix was dissected using LigaSure™. The appendiceal stump was secured with an endoloop or hemolock clip. In complicated cases, abdominal lavage and drain placement were performed as necessary.

Endpoints and Definitions

Primary endpoint: Clinically significant bleeding occurring within 30 postoperative days (hemoglobin decrease >2 g/dL, hematoma formation, or transfusion requirement). Secondary endpoints: Operative time, length of hospital stay, intensive care unit admission, 30-day mortality, and complications (surgical site infection, intraabdominal abscess, wound hematoma).

Complicated appendicitis was defined as the presence of gangrenous appendicitis, perforated appendicitis, or periappendicular abscess. The severity of postoperative bleeding was graded according to the Clavien-Dindo classification.

Statistical Analysis

All statistical analyses were performed using SPSS (Statistical Package for Social Sciences) for Windows version 25.0 software. Normality was assessed using the Kolmogorov–Smirnov test and graphical methods. Normally distributed data were expressed as mean ± standard deviation. Non-normally distributed variables were expressed

as median and minimum–maximum values. Categorical data were presented as frequency (n) and percentage (%). The chi-square test was used for comparison of categorical variables. For comparison of a categorical variable with a continuous variable, the independent samples t-test was used for normally distributed data and the Mann–Whitney U test for non-normally distributed data. Cox regression analysis was performed to evaluate factors influencing postoperative bleeding and the significance value of regression analysis as <1.00. All other statistical calculations were two-sided, and $p < 0.05$ was considered statistically significant at a 95% confidence interval.

Results

Patient Characteristics

A total of 912 patients were evaluated for laparoscopic appendectomy during the study period. After applying exclusion criteria, 847 patients were included in the study: 42 Patients in the antithrombotic group (5.0%) and 805 patients in the control group (95.0%). The majority of patients in the antithrombotic group were on low-dose aspirin (76.2%, $n=32$), followed by aspirin plus clopidogrel combination (14.3%, $n=6$) and clopidogrel alone (9.5%, $n=4$).

Mean age was significantly higher in the antithrombotic group (64.8 ± 10.6 vs. 37.4 ± 15.8 years, $p < 0.001$). Rates of cardiovascular disease (88.1% vs. 7.6%), hypertension (73.8% vs. 14.2%), and diabetes mellitus (45.2% vs. 8.9%) were significantly higher in the antithrombotic group ($p < 0.001$ for all). ASA scores were also higher in the antithrombotic group (Table 1).

Table 1. Demographic and clinical characteristics of the patients

Variable		Antithrombotic (n=42)	Control (n=805)	p
		n, (%)	n, (%)	p [†]
Gender	Male	27 (64.3)	458 (56.9)	0.342
ASA Score ≥III	≥III	21 (50.0)	89 (11.1)	<0.001
Cardiovascular disease	Yes	37 (88.1)	61 (7.6)	<0.001
Diabetes mellitus	Yes	19 (45.2)	72 (8.9)	<0.001
Complicated appendicitis	Yes	12 (28.6)	161 (20.0)	0.178
		Mean±SD	Mean±SD	p‡
BMI	(kg/m ²)	28.9±4.1	26.2±4.6	0.008
Age	(years)	64.8±10.6	37.4±15.8	<0.001

BMI: Body Mass Index; ASA: American Society of Anesthesiologists; SD: Standard Deviation, †:Chi-Square Test, ‡: Student T Test.

Mean operative time was significantly longer in the antithrombotic group (54.6±19.2 vs. 44.8±13.8 minutes, $p=0.002$). Length of hospital stay was also longer in the antithrombotic group (median 2 days vs. 1 day, $p=0.006$) (Table 2).

Postoperative Bleeding Analysis

Postoperative bleeding occurred in a total of 13 patients (1.5%). The bleeding rate was 7.1% ($n=3$) in the antithrombotic group and 1.2% ($n=10$) in the control group ($p=0.019$). Analysis of bleeding sources revealed that trocar site bleeding (38.5%) and mesoappendix bleeding (30.8%) were the most common.

Regarding the severity of bleeding, Clavien-Dindo Grade I bleeding was observed in 6 patients (46.2%), Grade II in 5 patients (38.5%), and Grade IIIa in 2 patients (15.4%). No Grade IIIb or higher bleeding was observed.

Risk Factor Analysis

Multivariable logistic regression analysis identified independent risk factors for postoperative bleeding (Table

3). Antithrombotic drug use (OR: 5.84, 95% CI: 1.52–22.45, $p=0.010$), age ≥ 65 years (OR: 3.12, 95% CI: 1.08–9.02, $p=0.036$), and complicated appendicitis (OR: 2.67, 95% CI: 0.94–7.58, $p=0.065$) were identified as potential risk factors (Table 3).

Discussion

In this study, the postoperative bleeding rate following laparoscopic appendectomy was demonstrated to be significantly higher in patients receiving antithrombotic drugs compared to the control group (7.1% vs. 1.2%, $p=0.019$). This finding is consistent with previous studies evaluating the effect of antithrombotic therapy on surgical outcomes. In the POISE-2 trial, perioperative aspirin use in noncardiac surgery was reported to increase the risk of major bleeding by 23%.^[10] A systematic review by Tang et al.^[3] also demonstrated that continuation of aspirin increased the risk of major bleeding (RR: 1.31, 95% CI: 1.15–1.50).

The 7.1% postoperative bleeding rate observed in our study is comparable to the rates reported in the multi-

Table 2. Perioperative and postoperative outcomes

Variable		Antithrombotic (n=42)	Control (n=805)	p
		n, (%)	n, (%)	p [†]
Postoperative bleeding	Yes	3 (7.1)	10 (1.2)	0.019
Transfusion requirement	Yes	2 (4.8)	4 (0.5)	0.023
30-day mortality	Yes	0 (0)	1 (0.1)	1.000
		Mean±SD	Mean±SD	p‡
Operative time	Minutes	54.6±19.2	44.8±13.8	0.002
		Median (IQR)	Median (IQR)	p*
Hospital stay	Days	2 (1–10)	1 (1–17)	0.006

SD: Standard Deviation, SD: Standard Deviation, †: Chi-Square Test, ‡: Student's T Test, *: Mann Whitney U Test.

Table 3. Multivariable logistic regression analysis for postoperative bleeding

Variable	Odds ratio	95% Confidence interval	p
Antithrombotic drug use	5.84	1.52–22.45	0.010
Age ≥ 65 years	3.12	1.08–9.02	0.036
Complicated appendicitis	2.67	0.94–7.58	0.065
Male sex	1.64	0.54–4.98	0.384
BMI ≥ 30 kg/m ²	1.38	0.42–4.52	0.594

BMI: Body Mass Index.

center study by Percy et al.^[13] However, that study concluded that antithrombotic therapy did not adversely affect outcomes of emergency laparoscopic appendectomy. This discrepancy may be attributable to differences in the definition of bleeding and patient populations. In our study, we evaluated clinically significant bleeding from a broader perspective.

In the multivariable analysis, in addition to antithrombotic drug use (OR: 5.84), age ≥ 65 years (OR: 3.12) was identified as an independent risk factor. Complicated appendicitis showed borderline significance (OR: 2.67, $p=0.065$). These findings underscore the need for more careful perioperative management in elderly patients. In a study by Thattamparambil et al.^[14] using ACS-NSQIP data, laparoscopic appendectomy was reported to be safe compared to open surgery in the setting of coagulopathy; however, special precautions were recommended for this patient population.^[14]

The ACCP 2022 guidelines recommend continuation of aspirin perioperatively in intermediate- to high-risk patients undergoing noncardiac surgery.^[2] However, these recommendations have been primarily developed for elective surgery and do not fully encompass emergency settings. In a recent review by Boschitz et al.^[15], it was emphasized that antithrombotic management in emergency surgery is particularly challenging and requires individualized approaches. A StatPearls review by Polania Gutierrez and Rocuts also indicated that anticoagulation management in emergency surgery requires different paradigms than those used in elective surgery.^[16]

The significantly longer operative time in the antithrombotic group in our study (54.6 vs. 44.8 minutes) may reflect the additional time required for intraoperative hemostasis control. This finding suggests that the surgical team adopted a more meticulous surgical approach in patients receiving antithrombotic therapy. Similarly, the higher transfusion requirement in the antithrombotic group (4.8% vs. 0.5%) indicates that bleeding control was more challenging in these patients.

An important finding of our study is that 30-day mortality rates did not differ statistically between the groups despite the increased bleeding risk. This result suggests that laparoscopic appendectomy has an acceptable safety profile in patients receiving antithrombotic therapy. In a meta-analysis by Li et al.^[7], laparoscopic appendectomy was shown to have lower complication rates compared to open surgery, and this advantage was maintained even in the presence of coagulopathy.

The importance of uninterrupted aspirin use for cardiovascular protection was highlighted in the meta-analysis by Burger et al.^[11] That study reported that perioperative discontinuation of aspirin significantly increased the risk of acute coronary syndrome. The Antithrombotic Trialists' Collaboration meta-analysis also clearly demonstrated the efficacy of aspirin in secondary prevention.^[17] Therefore, a careful balance between bleeding risk and thromboembolic risk must be established.

Our study has several limitations. First, due to the retrospective design, selection bias and confounding factors could not be fully controlled. Second, the single-center nature of the study limits the generalizability of the results. Third, the relatively small number of patients in the antithrombotic group ($n=42$) restricts the statistical power. Fourth, the higher age and comorbidity rates in the antithrombotic group complicate intergroup comparisons. The mean age in the antithrombotic group (64.8 ± 10.6 years) is approximately 27 years greater than in the control group (37.4 ± 15.8 years). Antithrombotic drugs are mostly used in older ages and it is an apparent limitation factor. Also limited number of the bleeding cases limits the evaluation. Finally, the possibility that some patients may have had their antithrombotic therapy discontinued prior to surgery cannot be excluded. Despite these limitations, our study is valuable in that it reflects the patient population encountered in daily clinical practice.

In the future, prospective, multicenter studies with larger sample sizes are needed on this topic. Furthermore, it is important to evaluate the effects of different antithrombotic agents (aspirin vs. P2Y12 inhibitors vs. combination therapy) on surgical outcomes separately. The development of risk scoring systems will enable the preoperative identification of high-risk patients and the implementation of individualized treatment approaches.

Conclusion

Antithrombotic drug use increases the risk of postoperative bleeding following laparoscopic appendectomy by approximately 6-fold. Age ≥ 65 years was also identified as an independent risk factor. However, this increased bleeding risk can be maintained at an acceptable level with careful perioperative management and close postoperative monitoring. The absence of a significant difference in mortality between the groups in our study suggests that laparoscopic appendectomy can be safely performed in this patient population. In emergency set-

tings, proceeding with surgery without waiting for discontinuation of antithrombotic therapy may be considered a reasonable approach to prevent complications of appendicitis. A multidisciplinary approach and individualized treatment strategies are recommended for this patient group.

Disclosures

Ethics Committee Approval: Ethical approval was obtained from the Ministry of Health Sancaktepe Dr. İlhan Varank Training and Research Hospital Ethical Committee (No:2025/437, Date 28/11/2025).

Peer-review: Externally peer-reviewed.

Conflicts of Interest: The authors declare no conflicts of interest.

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Data Availability Statement: The data that support the findings of this study are available from Ministry of Health Sancaktepe Dr. İlhan Varank Training and Research Hospital, but restrictions apply to the availability of these data, which were used under license for the current study and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of Ministry of Health Sancaktepe Dr. İlhan Varank Training and Research Hospital's administration.

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