

Is emergency gastrointestinal system tumor surgery safe under treatment of antitrombotics?

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ABSTRACT

BACKGROUND: The use of antitrombotic (antiaggregant and anticoagulant) drugs is increasing all over the world and in our country. About 12.6% of patients who underwent gastrointestinal tumor surgery receive antitrombotic therapy for various reasons, and in this study, we aimed to demonstrate the safe feasibility of elective or emergency gastrointestinal tumor surgery with the correct perioperative antitrombotic therapy management.

METHODS: The patients who were planned for gastrointestinal tumor surgery under antitrombotic treatment were analyzed in three groups as those whose pre-operative treatment management treatment was discontinued, those who underwent bridging treatment, and those whose treatment continued. Anti-embolic stockings or intermittent pneumatic compression devices were applied to all patients preoperatively and postoperatively as mechanical prophylaxis. Post-operative complications, especially post-operative bleeding and thrombosis, were evaluated using the Clavien–Dindo post-operative complication classification.

RESULTS: When patients who were under antithrombotic therapy, whose therapy was discontinued, and who underwent surgery under bridging therapy, no significant difference was found between the three groups in terms of bleeding complications.

CONCLUSION: In tertiary centers with high clinical experience, elective and emergency gastrointestinal system tumour surgery can be safely performed under antitrombotic therapy without increasing the thromboembolic risk.

Keywords: Antitrombotics; bleeding; bridging therapy; emergency surgery; gastrointestinal system tumour.

INTRODUCTION

While planning emergency and elective gastrointestinal tumour surgery, antitrombotic treatment management is important in terms of possible intraoperative and post-operative complications.^[1] The increase in screening programs, the widespread use of health services, and the COVID-19 disease, which is known to have increased thromboembolic complications recently, are some of the many reasons for the increased use of antitrombotic drugs.^[2]

Management of antitrombotic drugs before, during, and after surgery is a very difficult and important issue for patients. Pre-operative discontinuation of these pharmacological agents increases the risk of thromboembolism, while per-

forming surgery without interruption increases the risk of bleeding and re-surgical intervention during and after surgery.^[3] The management of antitrombotic drug use during surgical intervention should be applied by considering the profit and loss balance between the surgeon and the consultant physician, and making a decision on a patient basis. Caprini venous thromboembolism risk prediction index and bleeding risk prediction indexes such as hypertension, abnormal renal or liver function, stroke, bleeding, labile inrs, elderly, and drugs or alcohol (HASBLED), hepatic or renal disease, ethanol abuse, malignancy, older age, reduced platelet count, rebleeding risk, hypertension, anemia, genetic factors, excessive fall risk, and stroke (HEMORHAGES), ATRIA (Anemia, Severe renal disease, and Age, Prior bleeding, and Hypertension) can be used in the management of these treatments.^[4,5]

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Antitrombotic treatment of patients, who are in the first three months of the diagnosis of deep venous thrombosis (DVT), who have metal heart valv, and who are in the 1st year of coronary stent or by-pass surgery should be converted to bridging therapy. Perioperative antitrombotic treatment should be managed, using thromboembolism and bleeding risk prediction indexes. If there is no high risk of thromboembolism (according to Caprini and CHAD-VAS-C), Before an elective gastrointestinal surgery, discontinuation of antitrombotic drugs should be 7 days for acetylsalicylic acid (ASA), 5 days for Clopidogrel, 5 days for Coumadin (International normalized ratio [INR] <1.5), and 1–2 days for new oral anticoagulant (NOAC).^[1]

The aim of this study is to investigate complications such as bleeding and thrombosis in patients who underwent gastrointestinal tumor surgery under antitrombotic therapy and to determine the safety of surgery under antitrombotic therapy.

MATERIALS AND METHODS

Patients aged 18 years and older who underwent planned and emergency gastrointestinal system tumor surgery between January 2016 and December 2020 at İstanbul University, İstanbul Faculty of Medicine, General Surgery Clinic were retrospectively analyzed. Patients who did not receive any antitrombotic treatment, patients who underwent palliative endoscopic or surgical interventions, and patients who were not operated due to advanced stage or comorbidities were excluded from the study. Tumor surgery was performed in all cases according to oncological principles. Using the hospital data system and patient files, treatment modalities, demographic data, tumour stage, performed surgeries, urgency of the surgery, drugs used, blood products replaced during and after surgery, post-operative complications, and hospital the length of stay were evaluated.

Perioperative Management in Patients Receiving Antitrombotic Therapy in Our Hospital

Antiembolic stockings and/or low molecular weight heparin (LMWH) are applied to all patients for DVT prophylaxis. In the post-operative period when LMWH cannot be applied, intermittent pneumatic compression (IPC) is applied. Discontinuation of antitrombotic drugs is standardized with thromboembolism and bleeding risk prediction indexes as mentioned in introduction. Bridging therapy (treatment dose of LMWH) is performed in elective cases, and the timing, dose, and type of LMWH are determined by the surgeon and the consultant cardiologist or neurologist using the risk calculation systems Caprini, HASBLED, HEMORRHAGE, and CHAD-VAS-C. Pre-operative INR and activated partial thromboplastin time values of all patients are checked. Appropriate treatment is carried out in patients with prolonged INR. Pre-operative blood transfusion decision is made in consultation with the anesthesiologist. When enteral nutrition is started after the surgery, oral anticoagulant or antiaggregant

drugs are started. IPC treatment is continued in patients who cannot be mobilized early after surgery.

The patients were grouped as those whose treatment was completely discontinued in the pre-operative preparation, those who underwent bridging treatment, and those whose treatment was continued. The bleeding that developed in the cases, the decrease in hemoglobin and hematocrit values that caused deterioration in hemodynamics, and the need for blood replacement were determined. When assessing post-operative complications and mortality, events occurring during hospitalization or within 30 days of surgery were included in the analysis. Superficial and deep incisional infection, intra-abdominal sepsis, acute mechanical intestinal obstruction, stoma complications, acute renal failure, not weaning from mechanical ventilation for 48 h, hematoma found in the operating site, DVT, stroke, myocardial infarction, and intracranial hemorrhage were accepted as morbidity. Post-operative complications were categorized and evaluated using the Clavien–Dindo classification, and those with Grade II or higher were considered significant.

Statistical Analysis

The obtained qualitative data were compared using the Fisher test. Diagnostic values were calculated using probability tables. The results had a 95% confidence interval and were statistically significant with $p < 0.05$. Findings obtained in the study were calculated by entering IBM SPSS (SPSS Inc., ver. 21. Chicago, IL, USA).

RESULTS

Of the 932 patients who were operated on, 111 (12%) were receiving antitrombotic therapy. Of these, 83 (75%) were male and 28 (25%) were female. The mean age was 67 years. Tumours locations were 29 (26%) in stomach, 27 (24%) in right colon, 21 (19%) in sigmoid colon, 11 (9%) in pancreas, 10 (9%) in rectum, 10 (9%) in left colon, 1 (0.9%) in small intestine, and 1 (0.9%) in esophagus. One case was operated with the diagnosis of intra-abdominal mass (Table 1). Surgical approach was laparoscopic in 42 (38%) cases and open

Table 1. Surgery performed on patients using anticoagulant/antiaggregant drugs

Surgical procedure	Laparoscopic	Open
Gastrectomy	5	24
Right hemicolectomy	12	15
Left hemicolectomy	3	7
Anterior resection	13	8
Low anterior resection	8	0
Pankreatectomy	0	11
Eusophagectomy	1	0
Intraabdominal mass excision	0	1

surgery in 69 (62%) cases. In four cases, laparoscopic surgery was initiated and conversion was performed. These were included in the open group. Of these cases, 98 (88%) were operated on elective and 13 (12%) on emergency.

Of the cases, 70 (63%) ASA only, 14 (13%) dual antiaggregant (ASA and Clopidogrel) therapy, 9 (8%) NOAC, 8 (7%) warfarin, and 6 and 4 (4%) were using LMWH (5%) and Clopidogrel. The comorbidities of the patients antitrombotic therapy included atrial fibrillation, coronary artery disease (CAD), coronary artery bypass surgery, venous thrombosis, cerebrovascular accident, carotid stenosis, and other diseases (Table 2).

Surgery was performed without discontinuing antitrombotic therapy in 63 patients (57%), bridging therapy was applied

in 18 (16%) patients, and treatment was discontinued in 30 (27%) patients. One hundred and two patients (92%) needed intensive care after surgery. Post-operative complications were evaluated using the Clavien–Dindo classification. Of the 111 patients, 62 were Grade I, 30 Grade II, 10 Grade III, 1 Grade IV, and 8 Grade V.

Considering the bleeding findings, one bleeding was observed in the group that was operated under anticoagulant treatment and the drug was discontinued, and no bleeding was observed in the group that underwent bridging treatment. Post-operative ES and FFP replacement needs were the same in all three groups. Considering the morbidity rates, it was observed more in the group operated under anticoagulant therapy and treated with bridging therapy, although it was not

Table 2. Comorbidities of patients using antitrombotics

Medication indication	Total	Anticoagulant	Antiaggregant	Antiaggregant + Anticoagulant
Atrial fibrillation	19	13	4	2
Coronary artery disease	39	3	8	28
Coronary artery bypass surgery	20	2	12	4
Venous thromboembolism	6	5	1	0
Cerebrovascular accident	5	0	5	0
Pulmonary embolism	2	1	1	0
Carotid stenosis	3	1	2	0
Aortobifemoral bypass	1	0	1	0
Endovascular aortic aneurysm repair	1	0	1	0
Unclear	15	2	13	0

Table 3. Comparison of the groups whose anticoagulant treatment was discontinued, which were not discontinued, and whose bridging was performed

Features	On treatment (n=63)	Bridging treatment (n=18)	Treatment discontinued (n=30)	$\chi^2/K-W_{\chi^2}$	p
	n (%)	n (%)	n (%)		
Urgency situation				7.703 ^a	0.021 [*]
Urgent	12 (19)	0 (0)	1 (3.3)		
Elective	51 (81)	18 (100)	29 (96.7)		
Surgical procedure				2.511 ^a	0.285
Open	43 (68.3)	9 (50)	17 (56.7)		
Laparoscopic	20 (31.7)	9 (50)	13 (43.3)		
Morbidity	26 (41.3)	8 (44.4)	8 (26.7)	2.241 ^a	0.326
Bleeding	1 (1.6)	0 (0)	1 (3.3)	0.744 ^a	0.689
PRBC transfusion (U)	0.9±1.4	0.8±1.5	0.8±1.7	1.234 ^b	0.540
FFP transfusion (U)	0.30±1.2	0.33±0.6	0.23±0.7	2.643 ^b	0.267
Mortality	5 (7.9)	1 (5.6)	2 (6.7)	0.137 ^a	0.934
Hospitalization	15.2±11.6	13.7±5.9	12.8±8.4	2.116 ^b	0.347

PRBC: Packed red blood cells; FFP: Fresh frozen plasma.

statistically significant. However, none of these were associated with bleeding. The mean hospital stay was the same in all three groups (Table 3).

DISCUSSION

The aging of the population and the advancement of treatment for chronic medical problems has increased the medical complexity of surgical patients. Approximately 10% of surgical patients receive chronic antitrombotic therapy. Yamaji et al.^[6] showed that 20% of the 54,591 patients diagnosed with colorectal cancer were smokers, 5.5% used aspirin, 35% had hypertension, and 12.6% had CAD. This study shows us that the management of antitrombotic therapies plays a very important role in patients who are treated with the diagnosis of gastrointestinal system tumor, due to the increased co-incidence of concomitant atherosclerotic diseases.

In our study, the rate of patients who received antitrombotic therapy matches the literature. One hundred and eleven (11.9%) of 932 patients who antitrombotic therapy due to a previous thromboembolic event. Anticoagulant therapy is a therapy that poses a clinical challenge when it must be discontinued to allow surgical procedures.^[3,7]

The pre-operative management of the treatment in these patients depends on the indication for antitrombotic therapy, the time elapsed since the last thromboembolic event, and the extent of the surgery performed. Various protocols have been developed for patients using oral anticoagulants/antiaggregants.^[8-11] Minor surgical procedures with a low risk of bleeding can usually be performed, while the patient is on oral anticoagulant/antiaggregant therapy.^[12]

The so-called bridging anticoagulant therapy in patients undergoing major surgical procedures has not yet been properly investigated in well-designed clinical trials. Some authors recommend bridging anticoagulation therapy with LMWH for the majority of patients who need to discontinue Coumadin therapy.^[3,13] Other investigators argued that the risk of thromboembolism during discontinuation of Coumadin treatment was exaggerated and was higher than the risk of post-operative bleeding when compared with bridging therapy, except for high-risk patients who had recently experienced thromboembolic events.^[14]

Careful assessment of the risk of bleeding and thromboembolic complications in each patient in the post-operative period is critical to determine the optimal bridging protocol. In our study, the treatment management of the patients was chosen according to the preference of the responsible surgeon and consultant physicians. In the study of Devereaux et al.,^[15] patients who underwent non-cardiac surgery were examined as aspirin-using and placebo groups. Post-operative major bleeding was observed in 4.6% of patients using aspirin and 3.8% in the placebo group.

Bleeding was observed in only two patients in our study. The first was a case with splenic flexure tumor who received ASA treatment. The surgery was performed under ASA treatment after consulting with the cardiology preoperatively. The patient underwent subtotal colectomy with the open method. No bleeding was observed during the surgery and blood product replacement was not required. Gastrointestinal bleeding was observed in the patient in the post-operative period. It was treated conservatively without the need for re-operation. 6U ES and 4U FFP replacements were performed. The patient's hospitalization was prolonged due to wound infection and he was discharged on the 11th day. The other patient was a gastric tumor patient receiving ASA therapy. Preoperatively, the patient's ASA treatment was discontinued and he was prepared for surgery. The patient underwent total radical gastrectomy with an open method. No major bleeding was observed during the surgery and no need for blood product replacement. Intra-abdominal bleeding was observed in the post-operative period. The patient was re-operated due to bleeding and hemostasis was achieved. The patient underwent 7U ES and 3U FFP replacements. The patient was discharged on the 12th day.

In our study, the two bleeding patients were elective cases, there was no significant difference between elective and emergency cases on bleeding complication. In a retrospective study by Miura et al.,^[16] major intra-abdominal bleeding was observed in 15 of 708 pancreatobiliary surgery patients between 1981 and 2007 (2.1%).

In a study by Liu et al.,^[17] in which laparoscopic and open methods were compared in gastric cancer cases, major bleeding was observed in six of 214 patients in total (2.8%). In a study of 1,389 patients by Martínez-Serrano et al.,^[18] major bleedings from the anastomotic line were examined and bleeding was detected in seven patients (0.6%). When we look at the literature, we see that hematuria, melana, hematochezia, hemorrhagic drain fluid, decrease in Hb/Hct, deterioration of hemodynamic stability, and need for blood product replacement are accepted as bleeding findings in some studies.^[19]

In most of the patients included in our study, blood product replacement was performed with the aim of keeping the hemoglobin level above 10 g/dl due to cardiac problems. However, only a decrease in Hb/Hct that would impair hemodynamic stability was accepted as a sign of bleeding. Thanks to these replacements, we may have prevented subsequent bleeding that would impair hemodynamic stability.

Conclusions

We found that there was no clinically significant increase in bleeding after surgery performed under antitrombotic therapy and bridging therapy. Elective and emergency gastrointestinal system tumour surgery can be safely performed under antitrombotic therapy in tertiary centers with high

clinical experience. The results can be supported by prospective studies with larger sample sizes and comparing them with patients who did not receive antitrombotic therapy.

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ORİJİNAL ÇALIŞMA - ÖZ

Antitrombotik tedavi alan hastalarda, acil gastrointestinal sistem cerrahisi güvenli midir?

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AMAÇ: Antitrombotik (antiagregan ve antikoagulan) ilaç kullanımı tüm dünyada ve ülkemizde giderek artmaktadır. Gastrointestinal sistem tümör cerrahisi yapılan hastaların %12.6'sı çeşitli sebeplerden antitrombotik tedavi almakta olup, bu çalışmada, elektif veya acil gastrointestinal tümör cerrahisinin doğru antitrombotik tedavi yönetimi ile güvenli bir şekilde uygulanabilirliğini göstermeyi hedefledik.

GEREÇ VE YÖNTEM: Gastrointestinal tümör cerrahisi planlanan, antitrombotik tedavi alan hastaların ameliyat öncesi tedavi yönetimi tedavisi kesilenler, köprüleme tedavisi uygulananlar ve tedavisi devam edenler olarak üç grupta incelendi. Tüm hastalara anti-embolik çorap ya da intermitan pnömotik kompresyon cihazı mekanik profilaksi olarak ameliyat öncesi ve ameliyat sonrası olarak uygulandı. Clavien–Dindo postoperatif komplikasyon sınıflaması da kullanılarak başta ameliyat sonrası kanama ve tromboemboli olmak üzere ameliyat sonrası komplikasyonlar değerlendirildi.

BULGULAR: Antitrombotik tedavi alan, tedavisi kesilen ve köprüleme tedavisi altında cerrahi yapılan hastalar karşılaştırıldığında, kanama komplikasyonu açısından üç grup arasında anlamlı fark bulunmadı.

TARTIŞMA: Klinik deneyimin yüksek olduğu tersiyer merkezlerde tromboembolik riski artırmadan antitrombotik tedavi altında gastrointestinal sistem cerrahisi güvenli bir şekilde yapılabilir.

Anahtar sözcükler: Acil cerrahi; antitrombotikler; gastrointestinal sistem tümörü; kanama; köprüleme tedavisi.

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