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Research Article

Discontinuation of Antithrombotic Medications: Thrombosis or Bleeding in Patients Undergoing Thoracic Surgery

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Abstract

Background and Aim: Antithrombotic agents are often discontinued 5 to 10 days preoperatively in patients undergoing non-cardiac surgery to avoid perioperative bleeding, though discontinuation may also increase the risk for stent thrombosis, myocardial ischemia or infarction, and sudden death. In the present study we aimed to determine the incidence of thrombotic complications that may be associated with preoperative discontinuation of anticoagulants in patients undergoing thoracic surgery.

Materials and Methods: The study included 126 patients undergoing thoracic surgery. The patients were divided into two groups based on no medication and discontinuation of anticoagulant agents prior to surgery. Data were collected on demographic features, cardiac reserves, preoperative and postoperative hemograms and other laboratory tests, the frequency, duration and type of anticoagulants used, type of thoracic surgery, the amount of blood and blood products transfused, the need for re-exploration, length of hospital and ICU stay, complications, and mortality.

Results: There were no significant differences between groups in demographic characteristics, length of hospital and ICU stay, levels of Hb, Htc, and creatinine, the amount of perioperative fluid, platelet suspension, the use of ES, postoperative events (DVT, MI, and stroke), and the rates of severe arrhythmias, re-exploration, and mortality ($p>0.05$). Postoperative DVT and MI incidences were 2.9% in patients with discontinued antithrombotic agents. Patients who discontinued antithrombotic medication had a significantly higher preoperative INR value than no medication group ($p<0.05$).

Conclusion: We concluded that the discontinuation of antithrombotic agents may be related with serious thrombotic complications in patients undergoing thoracic surgery.

Keywords: Antithrombotic agent; Thoracic surgery; Complication; Outcome; Thrombosis

Introduction

Anti thrombotic therapy is frequently interrupted in the preoperative period in patients undergoing non-cardiac surgery which in turn increases the risk for stent thrombosis, myocardial ischemia or infarction or sudden death. On one hand, the interruption of antithrombotic agents prevents preoperative bleeding, but on the other hand, it may enhance the risk for cardiac complications. While the risk for surgical hemorrhage increases by 20% when aspirin or clopidogrel are solely taken, this risk rises up to 50% in case of dual therapy [1]. That is the reason why the use of anticoagulants is discontinued for 5 to 10 days prior to surgery, but in cases when there is an increased risk for stent thrombosis, anticoagulants may be continued. A meta-analysis evaluating the results of six studies demonstrated a 3-fold increase in the incidence of major cardiac complications in patients who discontinued aspirin [2]. The American College of Clinical Pharmacy (ACCP) recommends the acetylsalicylic acid to be continued in patients undergoing non-cardiac surgery around the time of surgery. The risk for thrombosis or bleeding should be assessed on an individual basis considering the severity and emergency of the surgery [3].

The management of anti platelet therapy is not adequately defined for patients undergoing major pulmonary resection [4]. The purpose of this retrospective study was to investigate the effects of the discontinuation of anti coagulant agents before the surgery on the postoperative outcomes of the patients undergoing thoracic surgery.

Materials and Methods

This study retrospectively analyzed the data of adult patients, who underwent thoracic surgery between January, 2014 and June, 2017. A comparison was made between the patients who never received anti coagulant agents and those who received anti coagulant but discontinued them in the preoperative period. The comparison revealed the relation between the rate of perioperative complications and mortality, blood and blood product transfusion. The data to be analyzed was obtained from the hospital's patient data recording system. If patients had more than one surgery, only the results of the first surgery were taken into consideration. The data on patients' demographics, cardiac reserves, pre operative and post operative blood parameters, the frequency and the duration of anti coagulant

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agent use, the type of administered anticoagulants, the amount of transfused blood products, resulting complications and mortality rates were recorded. Additionally, laboratory test results, the type of surgery, the length of ICU and hospital stay, and the causes of death were also recorded. Both open thoracic surgery cases and thoracoscopy cases were included in the study, and postoperative 30-day outcomes of patients were analyzed. The complications included postoperative Deep Vein Thrombosis (DVT), Myocardial Infarction (MI), stroke, arrhythmia, death and the incidence of re-exploration. Patients, who had emergency surgery; under 18 years; had a known bleeding disorder; and those with renal insufficiency, hepatic insufficiency, or congestive heart failure were excluded from the study.

Statistical Analysis

The SPSS 22.0 program was used for the analysis of the study data. The descriptive statistics employed in the study were mean, standard deviation, median, minimum, maximum, frequency, and ratio. The Kolmogorov-Smirnov test was used to measure the distribution of variables. The Mann-Whitney U test was used to analyze quantitative independent data while the Chi-square test was used to assess the qualitative independent data. In cases where the Chi-square conditions were not met, the Fisher test was used for the qualitative data. A value of $p<0.05$ was considered statistically significant.

Results

Data on a total of 126 patients were analyzed. Investigated operation types were VATS lobectomy (n=92), decortications (n=9), wedge resection (n=18), pneumolobectomy (n=4) and sleeve resection (n=3).

The groups receiving and not receiving antithrombotic agents did not significantly differ regarding the BMI, ASA distribution, duration of stay in the hospital, duration of stay in the ICU, preoperative and postoperative Hb, Htc, creatinine, postoperative INR, postoperative PLT level, perioperative fluid volume and urine output, intra operative TDP, administered PLT suspension, postoperative requirement for ES, TDP and PLT, and the rates of postoperative DVT, MI, stroke, severe arrhythmia, exitus, and re-exploration ($p>0.05$), (Table 1). In the group receiving antithrombotic agents, the patients were significantly older and their preoperative INR levels were significantly higher as compared to the groups not receiving antithrombotic ($p<0.05$).

Additionally, the duration of operation, the amount of perioperative bleeding and the rate of intra operative ES usage were significantly lower in the antithrombotic receiving group as compared to the group not receiving antithrombotic ($p<0.05$), (Table 1). The number of the patients using an antithrombotic agent in the preoperative period was 29 and they interrupted antithrombotic usage due to various reasons. All of these 29 patients, 26 patients were using only aspirin, 3 patients were receiving only dabigatran and 1 patient was receiving a dual therapy with clopidogrel and aspirin. All of the patients receiving clopidogrel and dabigatran underwent lobectomy, whereas the patients receiving aspiring therapy underwent all kinds of procedures. One patient (2.9%) developed MI and another one patient (2.9%) developed DVT in the postoperative period. Both complications appeared within the first 48 hours.

Discussion

In the present study, we compared the outcomes of the thrombotic surgery patients not receiving antithrombotic agents with those receiving antithrombotic but temporarily discontinued them before the procedure. The incidence of postoperative DVT and MI was found to be 2.9% in patients whose antithrombotic therapy was stopped prior to surgery.

Table 1: Comparison of demographic characteristics, length of hospital and ICU stay, laboratory findings, the amount of perioperative fluid and blood products, postoperative events with the rates of severe arrhythmias, re-exploration and mortality.

	No Antithrombotic agent		Antithrombotic agent discontinued		p
	Mean ± sd/n(%)	Median	Mean ± sd/n(%)	Median	
Age (years)	58.5 ± 13	61	63.7 ± 12.7	63	0.034[m]
BMI	3.3 ± 1.2	3	3.5 ± 1	3	0.608[m]
Gender	38 (41%)		16 (47%)		
	54 (59%)		18 (53%)		
ASA	2.9 ± 1.2	3	3.1 ± 1	3	0.144[m]
Duration of surgery (h)	4.3 ± 1.6	4	3.8 ± 1.3	4	0.065[m]
Duration of hospital stay (days)	8.4 ± 5.4	7	10.6 ± 13.9	7.5	0.98[m]
Duration of ICU stay (days)	0.5 ± 0.9	0	0.3 ± 0.5	0	0.486[m]
Preoperative Hb (g/dL)	12.8 ± 2	12.9	12.8 ± 1.6	12.7	0.854[m]
Postoperative Hb (g/dL)	11.2 ± 1.9	11.2	10.9 ± 1.5	11.1	0.632[m]
Preoperative Htc (%)	38 ± 5.9	38.4	38.6 ± 4.7	38	0.765[m]
Postoperative Htc (%)	33.5 ± 5.3	33.8	33.7 ± 4.4	33.7	0.746[m]
Preoperative INR	1 ± 0.5	1	1.1 ± 0.2	1.1	0.006[m]
Postoperative INR	1.1 ± 0.2	1.1	1.1 ± 0.4	1.1	0.17[m]
Preoperative Creatinin	1.1 ± 3.2	0.8	0.8 ± 0.2	0.8	0.366[m]
Postoperative Creatinin	0.8 ± 0.3	0.7	0.8 ± 0.3	0.8	0.066[m]
Preoperative Plt suspention	305.7 ± 107.3	287	329.2 ± 115.6	320	0.364[m]
Perioperative bleeding (mL)	521 ± 402	400	398 ± 363	360	0.5[m]
Perioperative crystalloid (mL)	1355 ± 508	1200	1222 ± 277	1200	0.593[m]
Perioperative urine output	378 ± 212	310	456 ± 296	375	0.211[m]
Intraoperative ES	11, 12.00%		10, 8.00%		0.15[X²]
Intra operative TDP	3, 3.30%		1, 2.90%		1[X²]
Intraoperative plt suspention	0, 0.00%		0, 0.00%		-
Postoperative ES	17, 18.50%		3, 8.80%		0.188
Postoperative TDP	0, 0.00%		1, 2.90%		0.27
Postoperative Plt suspention	0, 0.00%		0, 0.00%		-
Postoperative DVT	0, 0.00%		1, 2.90%		0.27[X²]
Postoperative MI	0, 0.00%		1, 2.90%		0.27[X²]
Postoperative Stroke	0, 0.00%		0, 0.00%		-
Postoperative arrhythmias	0, 0.00%		0, 0.00%		-
Exitus	0, 0.00%		0, 0.00%		-
Re-exploration	2, 2.20%		0, 0.00%		1[X²]

The number of the studies investigating the prevalence of Venous Thrombo Embolism (VTE) is limited [5]. In a review of 12 Randomized Clinical Trials (RCT) and 12 quasi-RCTs including a total of 6923 patients reported 15 symptomatic VTE cases among 2890 patients who underwent thoracic surgery [6]. The incidence of symptomatic VTE was reported to be 0.7%. Underlying diseases like cancer, comorbidities, and the type of the procedure (minimally invasive approaches or thoracotomy) impact the incidence. In our study, all the patients that discontinued the antithrombotic medication in the preoperative period were undergoing cancer surgery and they, therefore, were considered to be in the high-risk group. In a study investigating the outcomes of 6004 patients that underwent thoracic surgery under general anesthesia stated the prevalence of thromboembolic episodes as 0.18% [7].

The risk increases in the presence of one or more than one risk factors such as advanced age, high ASA classification, obesity and history of DVT. VTE is a major health problem especially among patients with cancer; therefore, patients undergoing thoracic surgery due to reasons other than cancer rare considered to have low risk for VTE [8,9]. Intermittent Pneumatic Compression (IPC) is recommended for these patients according to the European Society of Anesthesiology (ESA) guidelines on perioperative venous thromboembolism prophylaxis [10]. On the other hand, patients diagnosed with primary or metastatic cancer are considered to be in the high-risk group for VTE. For these patents, pharmacological prophylaxis is recommended to be applied in addition to IPC. In this way, it may be possible to prevent this complication, which is one of the major causes of death. In the present study, all the patients whose antithrombotic medication was stopped in the preoperative surgery were going to have surgery for cancer and they, therefore, were considered to be in the high-risk group. However, according to our study data, the incidence of both DVT and MI was 2.9% and higher than the general incidence of the complications.

DVT is one of the preventable major death causes and it affects approximately 0.1% of the population per year, men being more commonly affected than women. The overall average age- and sex-adjusted annual incidence of DVT is 48 per 100,000 [11]. While annual incidence rate per 1000 at age 65 to 69 years for DVT is 1.8, it increases up to 3.1 per 1000 at age 65 years to 69 years [12]. However, the patient developing postoperative DVT in our study was 44 years old and did not have any additional systemic disorder. He underwent decortications due to mesothelioma and the surgery lasted for 6 hours. The patient, who never received anticoagulant agents, stayed at the ICU for 1 day and at the hospital for 20 days after the operation.

The incidence of Post Operative Myocardial Infarction (POMI) after non cardiac surgery was reported to be 0.6% [13]. However, this rate increased to 2.9% in our study. The 54-year-old male patients that had POMI had been using ASA for two years due to medicated stent. He had VATS operation which lasted for 4.5 hours due to lung cancer. He underwent sleeve lobectomy and did not have major bleeding. He stayed at the hospital for 11 days in the postoperative period including 1-day follow-up at the intensive care unit in the early period.

According to the ESA guidelines on the management of severe perioperative bleeding, aspirin should not be discontinued unless the risk of bleeding in the perioperative period exceeds the thrombotic risk [14]. In this regard, it is recommended to continue aspirin therapy for low and moderate-risk surgeries but the decision should be made on patient-basis in case of high-risk surgeries. Also, the therapy should be started again as soon as possible in the postoperative period. It is stated in the same guidelines that the P2Y12 receptor inhibitors including clopidogrel, ticagrelor and prasugrel can be discontinued in the preoperative period only if the patients does have high risk for ischemic events. These patients must be given the first perioperative dose with in the 24 hours after the closure of the skin. In emergency or semi-urgent surgeries, the clopidogrel-aspirin or aspirin-prasugrel combinations should be continued if possible, if not, at least aspirin should be continued.

Limitations

One of the main limitations of this study is its retrospective design. Because retrospective studies have some disadvantages such as selection bias as the outcomes are already in hand at the data selection stage. In order to prevent such a bias, the researchers tried to be objective and transparent. Another limitation is the number of the patients analyzed within the study. This may be there as on for the thrombosis incidence to be higher in our study as compared to other relevant studies in the literature.

Conclusion

The results of this study demonstrate that discontinuation of antithrombotic agents in the preoperative period in patients who have cardiac risks and thus receive antithrombotic medication increases patients' predisposition to thrombotic events.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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