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CLINICAL STUDY

Does thromboprophylaxis cause bleeding after laparoscopic cholecystectomy?

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ABSTRACT
OBJECTIVES: This study reports the results of a single center experience on the use of pharmacological venous thromboembolism (VTE) prophylaxis in laparoscopic cholecystectomy patients.
BACKGROUND: The prevention of VTE is of crucial importance in surgical practice. However, the severity of thromboembolism risk and the necessity of thromboprophylaxis for laparoscopic cholecystectomy is still being debated.
METHODS: The data of the patients, who underwent laparoscopic cholecystectomy for symptomatic cholelitiasis in a single center between the years 2005 and 2015 were analysed retrospectively for incidents of symptomatic VTE and bleeding complications. Fisher Exact Test was used to compare the outcomes of the patients who did and did not receive thromboprophylaxis.
RESULTS: Of the 1485 patients who were included in the study, 307 (20.67 %) having a low VTE risk, did not receive any thromboprophylaxis; while 1178 (79.33 %) with a medium, high or a very high risk received VTE prophylaxis. A bleeding complication occurred in 14 (1.18 %) patients receiving prophylaxis and in 2 (0.65 %) patients not receiving prophylaxis (p = 0.548). No patients in this study experienced clinically symptomatic VTE.
CONCLUSIONS: The findings of this study indicate that the selective use of thromboprophylaxis does not significantly increase the risk of bleeding after laparoscopic cholecystectomy and probably decreases the incidence of symptomatic thrombotic complications *(Ref. 18)*. Text in PDF *www.elis.sk.*
KEY WORDS: laparoscopic cholecystectomy, bleeding, venous thromboemboly, prophylaxis, low molecular weight heparin.

Introduction

Deep venous thrombosis (DVT) and pulmonary thromboembolism (PTE) are the manifestations of venous thromboembolism (VTE) (1), which is a frequent complication of surgical procedures (2). Since PTE is the most common cause of preventable deaths in hospitalized surgical patients (2), the prevention of VTE is of crucial importance. It is now widely accepted that surgical patients in moderate to high risk of VTE must be given some sort of thromboprophylaxis (3). For laparoscopic cholecystectomy, however, there has been considerable debate on the severity of risk of thromboembolism and hence the necessity of thromboprophylaxis for this surgical procedure (4–8). Although there is an advantage of laparoscopic cholecystectomy over an open procedure due to reduced surgical trauma; the pneumoperitoneum and reverse Trendelenburg position during the procedure may theoretically lead to venous stasis in legs (5), which may be speculated to increase the risk for thromboembolic complications. On the other hand, a meta-analysis of 153,832 patients (9) and recent large scale clinical studies revealed rather low rates of complications related to venous thromboembolism after laparoscopic cholecystectomy (4, 10). One of these studies reported an increased risk of bleeding complications in patients receiving thromboprophylaxis, further questioning the routine use of antithrombotic medication in patients undergoing laparoscopic cholecystectomy (10). This, points out the need for defining effective and safe regiments of VTE prophylaxis in these patients.

The present study reports the retrospective results of a single center experience on the use of pharmacological VTE prophylaxis in patients undergoing laparoscopic cholecystectomy and associated bleeding complications.

Material and methods

Study population

The third training and working group of the General Surgery Department of Ankara Atatürk Training and Research Hospital

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has a database in which every cholecystectomy performed by the surgeons in this group is recorded. This trial analyses the data of the patients, who have signed an informed consent for their personal data to be used in retrospective studies and who underwent a laparoscopic cholecystectomy by this group between June 2005 and December 2015. Declaration of Helsinki principles were followed in this study. The data of the patients with the diagnosis of acute cholecystitis, or whose operation lasted for more than 90 minutes or the patients, who underwent an additional surgical procedure during the same operation were not included in this study. The exclusion criteria also involved the presence of preoperative hemodynamic instability and the existence of comorbidities with a potential to increase the risk of bleeding, such as diabetes mellitus, hypertension and congestive heart failure.

Outcome criteria and definitions

The VTE risk of every patient was calculated using the Caprini Score (11) and prophylaxis was planned accordingly.

The patients with a low VTE risk did not receive any prophylaxis, while the moderate risk group had two doses of enoxaparin (Clexane®, Sanofi Winthrop Industrie, Maisons-Alfort, France), at the 6th and 30th postoperative hours. The patients with a high VTE risk (Caprini Score = 3–4) received the first dose of enoxaparin sodium 12 hours before the operation, and had a daily dose of the same medication for one week starting at the 6th postoperative hour. Finally, the patients with a very high risk of VTE (Caprini score ≥ 5) received mechanical prophylaxis (compression stockings) in addition to enoxaparin sodium treatment, which started 12 hours before the operation and extended to a month according to the clinical situation of the patient.

In the patients, who were using acetylsalicylic acid and warfarin, the medication was ceased after a bridging therapy with enoxaparin sodium so that the previous medication was totally ceased at least 5 days prior to the operation.

Intraoperative and postoperative bleeding complications were accepted as the outcome measures.

Bleeding due to any operative technical errors – i.e. injury to the vascular structures or the liver- were excluded. Patients with unexpected bleeding, which could not be stopped by ordinary measures such as: diathermy or clipping, or required intraoperative blood transfusions or conversion to open cholecystectomy, were accepted to have a bleeding complication. Also, patients with bleeding that necessitated more than one day of postoperative hospital stay, postoperative blood transfusions, or a re-laparoscopy or a re-laparotomy were acknowledged to have a bleeding complication.

Patient records were searched for any incidents of VTE or PTE in the first postoperative month.

Statistical analysis

Fisher Exact Test was used to compare the groups of patients, who received thromboprophylaxis for 1 day, 1 week or 1 month with those patients, who did not receive any prophylaxis for bleeding complications. A p value less than 0.05 was accepted to be statistically significant. SPSS 15.0 (SPSS Inc., Chicago, USA) program was used for statistical calculations.

Results

Totally, 1590 patients, who underwent laparoscopic cholecystectomy, were matching the study criteria. One hundred and five of these patients, who were converted to open surgery due to various reasons, were excluded from the study. The reason for conversion was not a bleeding complication in any of the patients except in nine patients, who had bleeding due to iatrogenic injury to the cystic artery.

Of the 1485 patients, who were included in the study, 1112 (median age 48 (min = 20, max = 78)) were female and 373 (median age 52 (min = 22, max = 75)) were male. The indication for cholecystectomy was symptomatic cholelithiasis in all the patients.

The patients with a low VTE risk according to the Caprini score (n = 307, 20.67 %) did not receive any thromboprophylaxis. Medium risk patients (n = 541, 36.43 %) and patients having a high or a very high risk (n = 637, 42.90 %) received LMWH for VTE prophylaxis.

In the preoperative period, 107 patients (7.21 %) were using acetylsalicylic acid and 16 (1.08 %) were using warfarin. None of these patients experienced a bleeding complication after laparoscopic cholecystectomy.

A bleeding complication occurred in 14 (1.18 %) of the patients receiving thromboembolic prophylaxis and in 2 (0.65 %) patients not receiving VTE prophylaxis. An abdominal drain had been placed in all these patients and all the patients with a bleeding complication stayed at least one extra day in the hospital due to bleeding. None of them received postoperative transfusions or required a re-laparotomy or re-laparoscopy.

There was no significant difference between the 1178 patients (79.33 %), who received antithrombotic medication and 307 patients (20.67 %), who did not receive any sort of VTE prophylaxis regarding bleeding complications (p = 0.548).

None of the patients in this study had clinically symptomatic VTE (deep venous thrombosis or PTE) during the hospital stay or within the first 30 postoperative days.

Discussion

The correct application of thromboembolic prophylaxis reduces the rates of VTE and PTE (3). However, the concern for the increased bleeding risk causes surgeons to hesitate in administering these medications, especially in patients undergoing certain operations such as laparoscopic cholecystectomy. Unfortunately, there are few studies in literature regarding the outcomes of VTE prophylaxis in laparoscopic cholecystectomy and even fewer studies on the bleeding risk after this operation associated with the administration of antithrombotic medication. Also, the wide variety in the methods used and in the duration of prophylaxis in these studies makes it challenging to extract clear conclusions regarding the efficacy of thromboprophylaxis administration or the risk of bleeding related to prophylaxis.

Some of these reports in literature demonstrated no impact of pharmacological prophylaxis on VTE risk after laparoscopic cholecystectomy (10, 12, 13) and the study by Persson et al (10)

even showed an increased risk of bleeding complications caused by medical prophylaxis in patients undergoing this procedure.

The present study demonstrated no significant increase in bleeding risk in the patients, who received antithrombotic prophylaxis when compared with the group which received no such medication. The study that showed an increase in the risk of bleeding with the implementation of VTE prophylaxis was a multicenter, retrospective study, in which there was lacking data on the various doses and types of antithrombotic medication administered to the patients in various surgery clinics (10). The authors reported a wide variety in implementations of VTE prophylaxis amongst the centers, whose data was included (10). They also did not mention, which selection criteria were used for defining the patients that the medication was administered, most probably because there were no such uniform criteria among the centers, from which the data were acquired (10). Although it is difficult to speculate on the reasons of the differences between the results of the two studies, one explanation may be the difference in the implementation of thromboprophylaxis. Despite having a smaller number of patients, the present study has the advantage of analysing the data of a single center, which has a uniform VTE prophylaxis regimen. All the patients, who received prophylaxis were administered the same LMWH agent, which was preferred for the advantages of LMWH over unfractionated heparin such as not requiring any monitoring, a longer plasma half-life, a significantly higher bioavailability and a more predictable anticoagulant response (14). Also the dosage and duration of the therapy given to every single patient were strictly controlled according to the VTE risk calculated by the Caprini score. This selective application and the uniformity of antithrombotic medication may have contributed to the results obtained from this study.

Another important finding of this study is that there was no clinically apparent VTE in any of the two groups, although a higher incidence of thromboembolic complications would be expected in higher risk patients. When it is considered that more than half of all the patients in this study had either a high or a very high risk of VTE, it may be speculated that prophylaxis with LMWH must have decreased the incidence of thromboembolic complications. This high proportion of patients with a Caprini score ≥ 3 in this patient series can be explained by the status of the hospital that the study was carried out, as a reference hospital that receives many patients with co-morbidities.

Although the most frequent reason for conversion was stated to be intraoperative bleeding complications in some studies (15, 16), the most common cause for conversion in the present study was the difficulty of dissection of the abdominal adhesions (74.2 %). Only 9 patients underwent a conversion cholecystectomy due to intraoperative bleeding. However, all these bleeding complications occurred as a result of technical errors such as injury to the cystic artery or the displacement of an arterial clip.

It has been reported that in patients receiving long-term anticoagulation therapy, there was an increased incidence of bleeding from the liver bed after laparoscopic cholecystectomy even if the therapy was ceased preoperatively and the international normalized ratio returned to normal values before the operation (17). In the present study, no such observation was made since none of the patients under long term anticoagulation experienced a bleeding complication.

A limitation of this retrospective study is that, the patients enrolled were not subjected to routine radiologic or laboratory examinations for the diagnosis of VTE. Consequently, it is possible that cases of VTE may have been overlooked in this series. Even if this is the case, however, these cases can be accepted to be asymptomatic and the significance of such cases of VTE can be debated, since the majority of calf vein and small non-occlusive proximal vein thrombi are reported to be insignificant (18).

In conclusion, the findings of this study indicate that the selective use of VTE prophylaxis in the form of LMWH does not significantly increase the risk of bleeding after laparoscopic cholecystectomy and probably decreases the incidence of symptomatic thrombotic complications.

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