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Comparison of bleeding risks related to venous thromboembolism prophylaxis in laparoscopic vs open colorectal cancer surgery: a multicenter study in Japanese patients

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Abstract

BACKGROUND: Venous thromboembolism is the most common preventable cause of hospital death. The objective of this study was to clarify risk factors for postoperative bleeding related to thromboprophylaxis after laparoscopic colorectal cancer surgery.

METHODS: The study was conducted at 23 Japanese institutions and included patients with colorectal cancer who underwent laparoscopic or open surgery followed by fondaparinux treatment. We performed a retrospective analysis from a prospectively maintained database. We used multivariate analyses to evaluate clinical risk factors for prophylaxis-related bleeding events.

RESULTS: After multivariate analysis, male gender, intraoperative blood loss of less than 25 mL, and a preoperative platelet count below $15 \times 10^4/\mu L$ were found to be independent risk factors in the laparoscopic surgery group. Only the preoperative platelet count was an independent risk factor in the open surgery group.

CONCLUSIONS: Different prophylactic treatments for postoperative venous thromboembolism may be necessary in laparoscopic vs open surgery for colorectal cancer.

Venous thromboembolism (VTE) is the most common preventable cause of hospital death in surgical patients in the United States. In a Japanese study, VTE occurred in 24.3% of patients that received abdominal surgery, including cases with symptomatic pulmonary embolism. Thus, active VTE prophylaxis is important after abdominal surgery.[1] Postoperative bleeding is a concern in patients receiving pharmacologic prophylaxis for VTE. Bleeding is easily detectable but can cause serious complications. In the 9th edition of the American College of Chest Physicians (ACCP) guidelines,[2] relevant information about baseline risks, risk factors, and risk stratification are discussed for thrombosis as well as postoperative bleeding. Thromboprophylaxis-related postoperative bleeding should be considered when selecting a prophylactic method. Several researchers[3–5] have identified risk factors for postoperative bleeding related to thromboprophylaxis in gastrointestinal surgeries. Although the bleeding risk factors in gastric cancer surgery,[3] pancreatic surgery,[4] and hepatic surgery[5] were reported, little is known about bleeding risk factors and pharmaceutical prophylaxis for colorectal cancer surgery. There have been no reports about postoperative bleeding related to prophylaxis after laparoscopic colorectal cancer surgery compared with an open procedure, despite the fact that bleeding complications may depend on the surgical procedure. Indeed, several randomized trials[6,7] reported that there is less intraoperative bleeding in laparoscopic colorectal surgery vs an open procedure. To clarify the risk factors for postoperative bleeding events, we analyzed the data from a multicenter prospective study[8] to evaluate the safety of fondaparinux (FPX) for the prevention of VTE in Japanese patients.

Methods

Study population

Between February 2009 and December 2010, 665 patients with colorectal cancer from 23 institutions were screened for a study evaluating the safety of FPX. The study protocol excluded patients that used drugs with antiplatelet activity, such as aspirin or ketorolac tromethamine. Of these patients, 619 (93.1%) met the inclusion criteria, received at least one dose of FPX, and were included in the present analyses. Reasons for exclusion from the study were reported previously.[8] The baseline clinical characteristics of the 619 patients are presented in Table 1. Patients underwent either open surgery (n = 200) or laparoscopic surgery (n = 419; Table 1); analyses of the latter group included 27 (6.4%) conversions to open surgery. The study was approved by the institutional review board of each institution.

VTE prophylaxis

Administration of FPX was started 24 hours after surgery, once hemostasis was established, according to the Japanese regimen for VTE prevention. FPX (2.5 or 1.5 mg) was administered once daily for 4 to 8 days; the Japanese insurance system does not allow preoperative or intraoperative use of FPX. Mechanical VTE prophylactic treatments, such as intermittent pneumatic compression, elastic stockings, and elastic bandages, were not prohibited by the protocol and their use and duration were left to the discretion of the investigators or the institutions. An FPX dose of 1.5 mg was administered when creatinine clearance was less than 50 mL/min, body weight was less than 40 kg, or when the patient was aged $\geq$ 80 years old.

Assessment and outcome definitions

Patients who met the inclusion criteria and received at least one dose of FPX were analyzed. Bleeding was classified as major if the event met at least one of the following definitions: fatal bleeding, retroperitoneal or intracranial bleeding, bleeding of critical organs (intraocular, adrenal, endocardial, or spinal bleeding), surgical site bleeding that required surgical intervention, or clinically overt bleeding (when hemoglobin level decreased by at least 2 g/dL or requiring a transfusion of $\geq$800 mL red blood cells or whole blood). Minor bleeding was clearly defined as bleeding that did not meet any of the major bleeding criteria. In the laparoscopic surgery group,