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Risk modification for postoperative pulmonary embolism: Timing of postoperative prophylaxis☆

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ABSTRACT

Introduction: Risk factors for postoperative pulmonary embolism can often not be modified and are patient related. The purpose of this case control study was to identify possible modifiable risk factors for postoperative pulmonary embolism.
Materials and methods: We undertook a case control study among 210,269 patients who underwent noncardiac surgery from 2000 to 2009 at the Erasmus Medical Center. Case subjects were all 199 (0.09%) patients who experienced a pulmonary embolism within 30 days after surgery. From the remaining patients, 1 control was selected for each case and was stratified according to calendar year. For cases and controls, information was obtained regarding risk factors and the type and dose of thromboprophylaxis as well as the time of postoperative initiation.
Results: Overweight, surgery for malignancy, a history of cerebrovascular disease and a history of thromboemblic diseases, intraoperative blood transfusions and delayed use of thromboprophylaxis were more common in cases than in controls. After correction delayed use of thromboprophylaxis was associated with a 4 fold increased risk (OR 4.1; 95% CI: 2.1 – 7.7) for postoperative pulmonary embolism.
Conclusion: Delayed timing of postoperative thromboprophylaxis is an important modifiable risk factor for postoperative pulmonary embolism after noncardiac surgery. This study emphasises the importance of on time administration of thromboprophylaxis.

Introduction

Surgical patients are at increased risk of developing postoperative venous thromboembolic complications (VTE) which include deep vein thrombosis (DVT) and pulmonary embolism (PE). In the absence of prophylactic treatment, the incidence of postoperative VTE varies between 10% to nearly 80% [1,2]. Pulmonary embolism is a devastating complication with mortality rates between 0.2% and 7.5% [1,3]. A variety of prophylactic strategies via physical and pharmalogical means have shown to be effective in preventing postoperative VTE in different surgical populations. The efficacy of thromboprophylaxis with low-molecular weight heparin (LMWH) administered during the in-hospital period is well documented, but the optimal dose, timing of initiation and duration of thromboprophylaxis after surgery still remains controversial. Concern among surgeons about the risks of bleeding may result in delayed and suboptimal use of thromboprophylaxis. The current study aimed to examine the association between risk factors and postoperative pulmonary embolism in a large cohort of patients undergoing noncardiac surgery (Fig. 1).

Materials and methods

The study was approved by the Medical Ethics Committee of the Erasmus Medical Center. Since the data were recorded retrospectively and without any specific intervention, the Medical Ethics Committee agreed to waive informed consent. We performed a case control study using a cohort of 210,269 adult patients, 19 years of age and older, who underwent a noncardiac surgical procedure between January 1 2000, and January 1 2009 at the Erasmus Medical Center, Rotterdam, the Netherlands.

Patient selection

Both cases and controls were identified using a computerized hospital information system which contained data on demographic and

Abbreviations: (VTE), Venous thromboembolism; (DVT), deep vein thrombosis; (PE), pulmonary embolism; (LMWH), low-molecular weight heparin; (CT), computed tomography; (BMI), Body Mass Index.

☆ All authors have had full access to the data and contributed to drafting of the paper.

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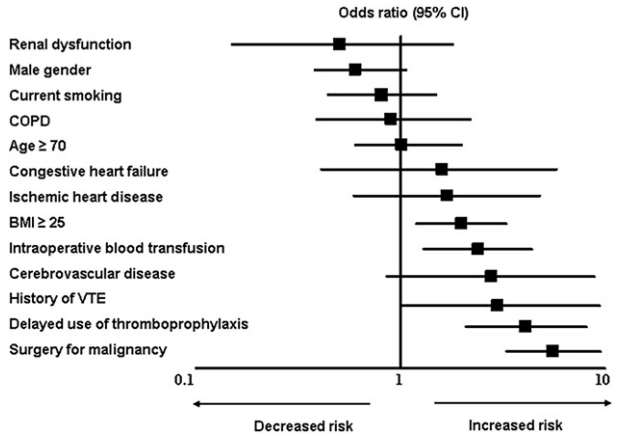

Fig. 1. Odds ratios for pulmonary embolism.

clinical characteristics, as well as the clinical course in hospital of all patients, who were admitted for noncardiac surgery (n = 210,269). Using key words 'pulmonary embolism', 'PE' or 'pulmonary infarct', all cases of perioperative pulmonary embolism were ascertained from discharge abstracts. The case definition included only incident cases and those confirmed by computed tomography (CT) or a high probability on ventilation and perfusion lung scanning or by autopsy. Patients readmitted to our hospital, as well as in hospital patients with a pulmonary embolism occurring more than 30 days following surgery were excluded from the current study.

Using this approach, we identified 343 (0.16%) patients with postoperative pulmonary embolism. We excluded 144 patients because the embolic event occurred following cardiac surgery (n = 2) or because patients did not underwent a surgical procedure (n = 142). This left 199 patients for initial analysis. In 183 patients (92%) pulmonary embolism was confirmed by CT scan, in 12 patients (6%) by high probability on ventilation and perfusion lung scanning and in 4 patients (2%) by autopsy.

For each case one control patient was selected from the total surgical population of 210,269 patients. Cases and controls were matched according to calendar year of surgery using the computerized hospital information system. Type of surgery was classified, according to the classification recommended by the American Heart Association/American College of Cardiology[4].

Definitions

To study the relationship of postoperative pulmonary embolism and various risk factors medication use, patient medical records, nursing reports, surgical reports, anesthetic reports and discharge letters were analyzed to obtain the following information on cases and controls: type of surgery, length of surgery, intraoperative- and postoperative blood transfusions, year of surgery, age, sex, Body Mass Index (BMI), presence of coronary heart disease, previous DVT or PE, heart failure, peripheral arterial disease, cerebrovascular disease, chronic obstructive pulmonary disease, diabetes, renal insufficiency, electrocardiographic abnormalities and smoking. Coronary heart disease was defined as a history of angina pectoris, myocardial infarction, coronary artery bypass grafting or percutaneous coronary intervention. Preoperative medication use was noted and included statins, beta-blockers, steroids, oral anticoagulants, heparin/LMWH and aspirin. The type and dose of thromboprophylaxis was noted as well as the time of postoperative initiation. The timing of postoperative thromboprophylaxis was at the discretion of the surgeon. Delayed use of thromboprophylaxis was defined as thromboprophylaxis starting more than 24 hours after surgery. As per hospital protocol nadroparin 2850 IE or dalteparin 2500 IE subcutaneous once daily is the standard for postoperative thromboprophylaxis in low risk patients. Patients with an increased risk of VTE are prescribed 5700 IE of nadroparin or 5000 IE of dalteparin once daily. In addition to pharmacological prevention, non-pharmacological methods (stockings and pneumatic compression) are used in patients with an active malignancy and in long lasting procedures (>6 hours). Ambulatory surgery patients did not receive thromboprophylaxis, unless indicated by the surgeon.

Statistical Analysis

The baseline characteristics between cases and controls were compared using a chi-square test for categorical variables and t-test for continuous variables. Logistic regression analyses were applied to evaluate the relation between clinically important characteristics (age > 70, bmi ≥ 25, gender, surgery for malignancy, length of surgery, history of VTE, history of cardiovascular or cerebrovascular disease, chronic obstructive pulmonary disease, renal dysfunction, intraoperative blood transfusion and delayed use of thromboprophylaxis) and postoperative pulmonary embolism.

Results

Baseline clinical characteristics of cases and controls are presented in Table 1. Increased age, increased BMI, history of cerebrovascular disease, history of VTE, surgery for malignancy and blood transfusions intraoperatively were more common in cases than in controls. The median length of surgery was significantly longer in cases (200 minutes) compared to control patients (138 minutes; P<0.01). This was consistent among the different types of surgical procedures. The median day on which pulmonary embolisms occurred was the seventh postoperative day, interquartile range (IQR) 4–15. From the 199 patients with postoperative pulmonary embolism 67 patients (34%) underwent abdominal surgery and 32 patients (16%) underwent neurosurgical procedures. Nine patients (5%) with postoperative pulmonary embolism died, while no deaths were reported in control patients. Massive pulmonary embolism was the cause of death in 6 patients, 2 patients died because of cardiovascular failure and 1 patient suffered postoperative stroke. Intraoperative bloodtransfusions were needed in 29% of the cases versus 15% of the control patients (p = 0.001). No pulmonary embolism was recorded in ambulatory surgical patients (Table 3).

Thromboprophylaxis

Dalteparin was used most often as thromboprophylaxis (50% of the cases and 46% of the control patients). The dose of thromboprophylaxis used was not different between cases and controls, except for nadroparin. The median dose of nadroparin used in cases was 5700 IE while the median dose in control patients was 2850 IE of nadroparin (p = 0.02). Delayed use (more than 24 hours after surgery) of thromboprophylaxis was more common in cases than in controls (57 cases [29%] and 20 controls [10%]; p<0.001). Delayed use was most often seen after abdominal surgery (31%) and neurosurgical procedures (18%). In patients who received thromboprophylaxis > 24 hours after surgery, thromboprophylaxis was given on the fourth postoperative day (IQR 2–6). There was no relation between intraoperative bloodtransfusions and delayed use of thromboprophylaxis (Table 2). Also no relationship was observed between the initiation of thromboprophylaxis less than 24 hours after surgery and the need for postoperative bloodtransfusions. After multivariable correction the following risk factors for postoperative pulmonary embolism were identified: BMI ≥ 25 (OR 1.8; 95% CI: 1.0 - 2.8), surgery for malignancy (OR 4.4; 95% CI: 2.6 - 4.7), length of surgery (OR 1.003; 95% CI: 1.001 – 1.004), a history of VTE (OR 4.0; 95% CI: 1.2 - 12.7) and the use of intraoperative blood transfusion (OR 2.7; 95% CI: 1.6 - 5.3). Delayed