A study of pulmonary embolism after abdominal surgery in patients undergoing prophylaxis

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INTRODUCTION

Pulmonary embolism (PE) is a life-threatening condition or complication and might be one of the worst nightmares for most surgeons. PE is a partial obstruction of the pulmonary arterial tree. The embolus that causes the obstruction usually travels through the venous system from a distant site. PE causes symptoms such as dyspnea, chest pain or collapse. Moreover, the clinical severity of PE can vary, ranging from asymptomatic cases to sudden death. Despite advances in diagnosis and treatment, PE remains a significant cause of morbidity and mortality and is still one of the most common preventable causes of death.
Risk factors for deep vein thrombosis (DVT) and PE are prior medical history of DVT or PE, recent surgery, general anesthesia lasting longer than 30 min, pregnancy, prolonged immobilization, age > 40 years, obesity or underlying malignancy[3,4]. Moreover, gynecologic surgery, major trauma and indwelling venous catheters are risk factors for DVT at any location. Otherwise, venous thrombosis commonly involves lower limbs, affecting most frequently calf veins, which are involved in virtually 100% of symptomatic, spontaneous lower extremity DVT. Although DVT usually starts in calf veins, it is propagated above the knee in 87% of symptomatic patients before the diagnosis has been made. However, more than 35% of patients who die from PE may have isolated calf vein thrombosis[5].

MATERIALS AND METHODS

Subjects
We identified 54,690 patients who had surgery between January, 1985 and December, 2003. The study included 39,526 patients who underwent colorectal abdominal surgery. Of them, 15,622 were cancer cases. Among colorectal cancer patients who underwent surgery from January, 1985 and December, 1990, we included 4,304 patients who underwent colorectal surgery. 39,263 patients who received prophylaxis, 37 (0.09%) were not receive prophylaxis developed a PE. Among the 39,263 patients who had received prophylaxis, 37 (0.09%) developed a PE in the postoperative period. Of the 39,263 patients who received prophylaxis, 37 (0.09%) developed a PE in the postoperative period.

Retrospective analysis
The database of the Institute for Digestive Disease, Clinical Center of Serbia was reviewed to identify patients who had undergone surgery from January, 1985 to December, 1990. Age, final pathologic diagnosis at autopsy, surgical procedures and venous thromboembolism prophylaxis modalities were recorded.

In a first retrospective evaluation, out of the 15,427 patients who had undergone surgery between 1985 and 1990, we included 41 cases (20 men, 21 women) of PE confirmed at autopsy. These patients had not received any prophylaxis prior to elective surgery, as prophylaxis was not performed on a regular basis during that period in our country. The PE patients had undergone the following surgical procedures: total gastrectomy, 5 (13.5%); ulcer suture, 2 (5.4%); cholecystectomy, 4 (10.8%); gastrostomy, 2 (5.4%); ileal resection, 1 (2.7%); appendectomy, 1 (2.7%); hernioplasty, 1 (2.7%); abscess drainage, 1 (2.7%); laparotomic exploration with biopsy of the tumor, 2 (5.4%); total colectomy, 2 (5.4%); right hemicolecotomy, 3 (8.1%); left hemicolecotomy, 3 (8.1%); Dixon-type resection, 2 (5.4%); Hartman-type resection, 2 (5.4%); Belsey-type resection, 1 (2.7%) and double colostomy, 1 (2.7%) (Table 1).

Statistical analysis
Results were presented as mean ± SD or as stated. Distribution data were compared by χ² analysis or Kruskal-Wallis test, if data were not normally distributed. In addition, logistic regression tests were conducted. All statistical analyses were performed with the SPSS 10.0 for Windows package (SPSS Inc., Chicago, IL). Values at the P = 0.05 level were considered statistically significant.

RESULTS
No significant difference as to the gender distribution existed between the two groups (χ² test, P > 0.05). No significant difference in the mean age was found between patient groups (Kruskal-Wallis test, P > 0.05). However, a higher incidence of thromboembolism (43.9% and 46.34%) was found in older patients (60-69 year range) in both groups of patients.

Forty-one patients out of 15,427 (0.27%) who did not receive prophylaxis developed a PE. Among the 39,263 patients who received prophylaxis, 37 (0.09%) developed a PE in the postoperative period.

Among the 15,427 cases evaluated retrospectively, we identified 4,304 patients who underwent colorectal abdominal surgery. Of them, 15,622 were cancer cases. Among colorectal cancer patients who underwent major abdominal surgery, 0.64% (10/1,562) developed PE postoperatively, while the incidence of PE in all remaining patients was 0.11% (17/13,865) (P < 0.05, OR = 5.577, 95% CI, 2.526-12.311).

Among the 39,263 patients who had received prophylaxis before major surgery, 37 (0.09%) were diagnosed as having postoperative PE. Of the 39,263 major cases evaluated prospectively, we identified 11,735 patients who underwent colorectal abdominal surgery.
Of them, 4316 were cancer cases. Among colorectal cancer patients who underwent major abdominal surgery, 0.25% (11/4316) developed PE postoperatively, while the incidence of PE in all remaining patients was 0.05% (17/34947) (P < 0.05, OR = 5.250, 95% CI, 2.457-11.216).

The incidence of PE after colorectal cancer surgery among patients who had received prophylaxis was significantly lower compared to that observed in subjects with colorectal surgery due to carcinoma who had not received any prophylaxis, i.e. 0.26% (11/4316) vs 0.64% (10/1562) (P < 0.05, OR = 2.522; 95% CI, 1.069-5.949). Moreover, incidence of PE after major abdominal surgery of patients who had received prophylaxis was significantly lower compared to that seen in subjects with the same diagnoses who had not received any prophylaxis (P < 0.001, OR = 2.825; 95% CI, 1.811-4.408).

**DISCUSSION**

PE is third most common cause of death in the US, with at least 650000 cases occurring annually. Furthermore, PE represents the first or second most common cause of unexpected death in most age groups. The highest incidence of recognized PE occurs in hospitalized patients. Autopsy results are showing that up to 60% of patients who die at a hospital have PE, and that diagnosis is missed in about 70% of cases. The annual incidence of known DVT and PE in the Western world is 1.0 and 0.5 per 1000, respectively. There are 65000 cases each year among hospital patients in England and Wales. The prevalence of unsuspected PE diagnosed at autopsy is 3%-8%, and has been unchanged for 3 decades.

PE is common during all trimesters of pregnancy and puerperium, and incidence of PE is increasing with oral contraceptive or hormone replacement therapy. However, sex alone is not an independent risk factor.

Although the frequency of PE increases with age, this is not independent risk factor. Nevertheless, the accumulation of different risk factors, such as underlying illnesses and decreased mobility, increases the frequency of PE in older patients. Unfortunately, diagnosis of PE is often missed, especially in older patients. PE is diagnosed in 30% of all patients who die with massive PE, but only in 10% of those who are 70 years of age or older. Thus, PE still remains the most commonly missed diagnosis in the elderly institutionalized patients.

In our study, we found a higher incidence of PE in older patients (> 60 years of age) in both groups (43.9% and 46.34%).

Surgical patients have long been recognized to be at special risk for DVT and PE, but these problems are not confined to surgical patients. Surgeons should always suspect PE in case of a sudden circulatory collapse occurring within one to two weeks after surgery.

The risk of postoperative venous thromboembolism is reported to be twice as high in patients with cancer compared of those without cancer undergoing comparable surgery. This risk is also higher in patients undergoing surgery for colorectal cancer as compared to those having abdominal surgery without malignancy. Thromboembolic complications are responsible for about half of deaths following elective colorectal surgery. The highest rate (1.8%) of fatal PE was reported in patients following colorectal surgery, with a 3.3-fold increase compared to the overall rate observed among surgical patients, according to a retrospective 10-year review from Switzerland. In this study, the increased risk of PE can be explained by a number of factors, such as malignancy-related hypercoagulable
state, postoperative infectious complications, prolonged surgery, pelvic dissection et al.\textsuperscript{[13]}

Overall, the incidence of PE after general surgery observed in Japan was 0.33%. Fatal PE was reported in 0.08% of the surgical population and the mortality rate of patients with PE was 31%. In addition, the incidence of PE after cancer surgery ranged from 0.57% after colon malignancy to 3.85% after pancreatic cancer surgery, and was significantly higher than in non-cancerous conditions (0.20%)\textsuperscript{[14]}. An increased risk of PE after colorectal surgery has also been shown by Lee et al.\textsuperscript{[15]} in a study on Chinese patients who underwent colorectal surgery without DVT prophylaxis. The authors demonstrated the occurrence of asymptomatic calf vein thrombosis in 41.7% of patients using serial Duplex ultrasound studies\textsuperscript{[16]}. In our experience, the incidence of PE after colorectal cancer surgery was significantly higher compared with other surgical procedures. However, the incidence of PE after colorectal cancer surgery of patients who received prophylaxis was significantly lower compared to that seen among subjects with colorectal surgery due to carcinoma without prophylaxis.

In the study by Shukla et al.\textsuperscript{[11]}, 99 patients with colorectal cancer selected for surgery were included. Fifty-one patients were randomized to receive LMWH while 48 patients did not receive any prophylaxis. At the end of the study, neither DVT nor PE cases were observed\textsuperscript{[17]}. Anticoagulant prophylaxis is effective in preventing PE in hospitalized patients, since it reduces mortality after surgery. Prophylaxis with LMWH leads to effective reductions in the incidence of DVT after abdominal surgery in patients at risk for thromboembolic complications.

Initial treatment with LMWH following oral anticoagulant therapy with INR ranging from 2 to 3 was associated with an incidence of major bleeding of 3% at 3 mo while the mortality rate was 0.3%\textsuperscript{[18]}. However, Diener et al.\textsuperscript{[19]} showed that there may be a dose-dependent risk of bleeding with LMWH therapy.\textsuperscript{[19]}

Low dose of LMWH was arbitrarily defined as a fixed dose of less than 6000 IU daily, whereas any higher dose of LMWH was considered as LMWH high dose. Concerning weight-adjusted doses of LMWH, 86 IU/kg per day was considered as LMWH low dose, while 86 IU/kg twice a day was considered as LMWH high dose.

In our study, patients who received prophylaxis with low dose LMWH after major abdominal surgery did not have any side effects (such as bleeding). Moreover, incidence of PE was significantly lower compared to subjects with the same conditions who did not receive prophylaxis.

The incidence of PE was four to six times lower in patients who had mechanical prophylaxis, although the difference was not significant. Preoperative prophylaxis for DVT is important, but further research is needed to estimate its effects and benefits\textsuperscript{[20]}. In our study, older age (> 60 years) was identified to be a risk factor for PE. Prophylaxis with LMWH is highly recommended for patients with colorectal cancer before major surgery. As the mortality from PE depends on correct and timely diagnosis, it is of the utmost importance for clinicians to consider this possibility and perform proper diagnostic tests, especially in patients with colorectal cancer.

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