

Clinical Science

Postoperative early thromboembolism as a prognostic indicator in patients with curatively resected pancreatic cancer



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Abstract

BACKGROUND: Information regarding postoperative thromboembolism in curatively resected pancreatic cancer is limited. This study aimed to assess the incidence and significance of postoperative thromboembolism.

METHODS: We retrospectively reviewed the medical records of 121 curatively resected pancreatic cancer patients. Early and late thromboembolisms were defined as events that occurred within 1 year and after 1 year, respectively.

RESULTS: Twenty-two patients (18%) experienced thromboembolism. Seven thromboembolic events occurred within 1 month (7, 6%), and the incidence rate decreased over time. Ten (63%) of the 16 patients with early thromboembolism experienced thromboembolism before or at the same time as recurrence; however, 5 (83%) of the 6 patients with late thromboembolism experienced recurrence before thromboembolism ($P = .005$). A significant difference in recurrence-free survival ($P = .016$) and borderline difference in overall survival ($P = .050$) were observed between patients with early thromboembolism and others.

CONCLUSIONS: Thromboembolic events after curative surgery are prevalent in pancreatic cancer, especially within 1 month. Thromboembolic events within 1 year of surgery should be cautiously monitored.

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Thrombus formation is the most clinically significant process arising from hemostasis, which maintains the integrity of a circulatory system after vascular damage.¹ Thrombus formation is normally controlled by regulatory mechanisms; however, thrombosis that occludes noninjured vessels can occur in various pathological situations. Among these, thromboembolism has been observed frequently in patients with malignancies because of the hypercoagulable

state triggered by cancer itself.^{1,2} Several pathological mechanisms are associated with malignancy, including Virchow's triad, high tissue factor expression, mutant coagulation factors, and various clinical factors such as advanced age, immobility, ethnicity, and chemotherapy.³ In addition, the clinical significance of thromboembolism as an indicator of poor prognosis has been reported consistently by many studies.^{4,5}

Among various malignancies, pancreatic cancer is particularly notorious for high incidence rates of thromboembolism, which have been reported to range from 17% to 57%.⁶⁻⁹ However, most studies primarily assessed patients with advanced stage disease, and few studies have investigated patients who underwent curative surgery.^{10,11} Moreover, little is known about long-term outcomes after surgery in patients with pancreatic cancers because these studies focused on the perioperative period only.

On the basis of this background, in this study we aimed to assess the incidence of postoperative thromboembolism in pancreatic cancer patients who underwent curative surgery and to determine its clinical significance.

Patients and Methods

Patients

Data on patients who underwent curative resection, including pancreaticoduodenectomy, distal pancreatectomy, and subtotal or total pancreatectomy for pancreatic cancer, were retrospectively collected between May 2003 and March 2013 at Seoul National University Bundang Hospital. Patients with different types of cancer other than pancreatic adenocarcinoma or metastatic lesion and those who did not achieve R0 resection were excluded. Thirteen patients were excluded from the analysis for the following reasons because it was too small a number to be analyzed and prosthetic grafts might affect the postoperative thrombosis although it is biocompatible: 1 patient died within 30 days after undergoing surgery, 8 patients received neoadjuvant therapy, 7 patients underwent vascular graft insertion during surgery, and 1 patient underwent pancreatectomy more than twice. The remaining 121 patients were included. In this study, the patients were treated with intermittent pneumatic compression after surgery until they could ambulate. However, other routine perioperative thromboprophylactic treatment was not used in this study because of bleeding risk. Clinicopathological parameters including patient age, sex, type of surgery, tumor size, lymph node status, differentiation of the tumor, and angiolymphatic/venous/perineural invasion in resected pancreas were investigated. Tumor stages were classified according to the American Joint Committee on Cancer Staging Manual, 7th edition.¹² Tumor grade was categorized as well, moderately, or poorly differentiated or undifferentiated. The study was approved by the institutional review board of Seoul National University Bundang Hospital.

Thromboembolism and tumor recurrence

Thromboembolism was identified by computerized tomography (CT) examination as part of regular postoperative follow-up with an interval of every 2 to 3 months for 6 months, 3 to 6 months for 2 years, and 6 to 12 months after 2 years after surgery. Doppler or CT angiography was used in select patients who complained of symptoms suggestive of thromboembolism. Two types of thromboembolism were defined according to anatomical location: those occurring in the venous system or pulmonary artery and those in the arterial system except the pulmonary artery. Additionally, early and late postoperative thromboembolism was defined as an event that occurred within 1 year and after 1 year, respectively.

Tumor recurrence was defined on the basis of newly detected pathological lesions that were confirmed pathologically with tissue or demonstrated progression on serial imaging examinations including CT, magnetic resonance imaging, or positron emission tomography and computerized tomography. Serial imaging examinations were performed with postoperative follow-up.

Statistics

All statistical analyses were performed using SPSS version 21 (IBM Corporation, Armonk, NY). Pearson's chi-square test or Fisher's exact test was used to determine differences between categorical groups. Continuous variables were compared with the Mann-Whitney *U* test. The association between time from operation to thromboembolism and recurrence-free survival (RFS) was investigated by linear regression analysis. Overall survival (OS) and RFS were compared by log-rank tests. To identify significant clinicopathological variables associated with OS and RFS, Cox regression analysis was used. Clinicopathological variables with a 2 sided *P* value less than .10 in univariate Cox proportional hazards regression analysis were chosen for multivariate Cox proportional hazards regression analysis with stepwise selection. A 2-sided *P* value less than .05 was considered statistically significant.

Results

Baseline characteristics

Baseline characteristics are presented in [Table 1](#). A total of 121 patients were included in this study, of whom 22 patients experienced thromboembolism. Sixty-eight patients (56%) were male, and patients' median age was 65 years (range 40 to 81 years). Median body mass index was 23.1 kg/m², and accompanying comorbidities considered potential risk factors of thromboembolism as follows: diabetes (48, 39%), hypertension (54, 44%), cerebrovascular disease (5, 4%), coronary artery disease (3, 2%), and other cancer (11, 9%). Thirty-five patients were smokers, and 35

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