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Predictive Markers for Occurrence of Surgical Site Infection after Pancreaticoduodenectomy

Research Article

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Abstract

Objective: Surgical site infection (SSI) is a well-known potential complication following pancreaticoduodenectomy (PD). SSI leads to increased medical costs and a longer hospital stay. Several risk factors for developing SSI have been reported. In the present study, we analyzed preoperative and intraoperative predictive markers for SSI after PD.

Materials and Methods: One hundred consecutive patients who underwent PD in our department from January 2006 to December 2018 were retrospectively analyzed. The patients' preoperative age, body mass index (BMI), history of smoking, alcohol use, and American Society of Anesthesiologists physical status classification were recorded. The Glasgow prognostic score, prognostic nutritional index, and geriatric nutritional risk index were calculated from routine preoperative blood samples. We also evaluated the operation time, blood loss, and blood transfusion as intraoperative markers. All patients were followed up for the occurrence of postoperative complications, including SSI.

Results: SSI was detected in 47 of 100 patients (47%), and 3 patients died of SSI after PD. Thus, the SSI-related operative mortality rate was 3%. According to the univariate risk analysis and multivariable logistic regression analysis, we found that only intraoperative blood transfusion was a risk factor for occurrence of SSI after PD (a high BMI was a risk factor only in the multivariate analysis).

Conclusions: We must pay special attention to the occurrence of SSI after PD for patients who undergo an intraoperative blood transfusion and the correlation between intraoperative blood transfusion and low postoperative immunity should be analyzed.

Keywords

Blood transfusion; Immunosuppression; Pancreaticoduodenectomy; Surgical site infection

Abbreviations

ALB: albumin, BMI: body mass index, CRP: C-reactive protein, GNRI: geriatric nutritional risk index, GPS: Glasgow prognostic score, PD: pancreaticoduodenectomy, PNI: prognostic nutritional index , SSI: Surgical site infection, TLC: total lym

Introduction

PD is the standard treatment method for patients with periampullary or gastrointestinal malignancies. However, a major problem after PD is the frequent occurrence of SSI, including postoperative pancreatic fistula, intra-abdominal abscess, or severe wound infection. SSI is a well-known factor that leads to increased medical costs and a prolonged hospital stay. Moreover, SSI after PD is associated with a high perioperative mortality rate. Kimura et al [1]. reported that the 30-day postoperative and in-hospital mortality rates after PD were 1.2% and 2.8%, respectively. Shidara et al [2]. reported that in in-hospital mortality was 2.0 %, and 30-day mortality was 1.0 % in Japanese University Hospital. And they identified high-risk surgery was one of the independent preoperative risk factors for in-hospital mortality. PD and esophagectomy are well known as high-risk surgeries for occurrence of SSI. Because, it takes long operation time and much operative blood loss to perform these operations.

The correlation between various preoperative and intraoperative markers and the occurrence of SSI after PD has been discussed. Poruk et al. [3] indicated that in their multivariate analysis, preoperative bile stent/drain placement and neoadjuvant chemotherapy were independent predictors of SSI after PD. Recent reports have also shown that malnourishment and a high inflammatory status negatively affect normal immune function and often result in poor wound healing, placing the patients at risk for SSI and poor postoperative outcomes [4,5]. Thus, we focused on patients' preoperative C-reactive protein (CRP), serum albumin (ALB), and peripheral blood total lymphocyte count (TLC). Using these parameters, we calculated the Glasgow prognostic score (GPS), prognostic nutritional index (PNI), and geriatric nutritional risk index (GNRI) as markers of inflammation, nourishment, and immunity [6-8].

To reduce the medical costs and duration of hospitalization, preoperative and intraoperative identification of patients with a high risk of SSI after PD is very important. Patients with a high risk of SSI require special attention. In the present study, we retrospectively evaluated these preoperative and intraoperative high risk markers for SSI after PD.

Materials and methods

Patients

We retrospectively analyzed 100 consecutive patients who underwent PD for malignant or benign tumors in the periampullary region or at the pancreas head or gastro-intestinal tumors that had invaded the pancreas head or duodenum from 2006 to 2018. No patients received chemotherapy or radiation therapy before the operation. The patients were followed at Tottori Prefectural Central Hospital. All of our patients were Japanese, and all of them lived in the San-in district of Japan. But, we did not check their occupations and their educational degree. All patients provided informed consent for medical treatment and use of clinical data from their medical records. This study was reviewed and approved by the ethics review board of Tottori Prefectural Central Hospital (approval number: 2019-60).

Parameters

Blood samples were routinely taken from each patient before the operation. The CRP concentration, ALB concentration, and TLC were recorded. The patients' preoperative and intraoperative parameters, including, age, body mass index (BMI), history of smoking, alcohol use, American Society of Anesthesiologists (ASA) physical status classification, intraoperative blood loss, operation time, and intraoperative blood transfusion were also collected from the individual medical records. The GPS consisted of the combination of the CRP and ALB measurements. Patients with CRP concentration of < 1.0 mg/dL and ALB concentration of > 3.5 g/dL had a GPS of 0 and were classified as the low GPS group. Patients with either one of these abnormal factors (GPS = 1) or both abnormal factors (GPS = 2) were classified as the high GPS group [9]. The PNI was estimated by the following formula: 10 × serum ALB concentration (g/dL) + 0.005 × TLC (cells/mm3) in the peripheral blood [9]. According to a previous report, a PNI of < 40 was classified as a low PNI [6]. The GNRI was calculated from the serum ALB concentration and body weight using the following formula: GNRI = (1.489 × ALB (g/L)) + (41.7 × (body weight/ideal body weight)). The body weight/ideal body weight value was set to 1 when the patient's body weight exceeded the ideal body weight [8]. The ideal body weight was defined as a BMI of 22 kg/m2. Additionally, a GNRI of <94 was defined as a low GNRI [11].

Surgical procedure

All patients underwent open laparotomy. Reconstruction after PD was performed by Child's method. Pancreaticojejunostomy was performed and an internal short stent was placed across the pancreaticojejunostomy site, but no stent was placed following choledochojejunostomy.

Postoperative complications

According to the Centers for Disease Control and Prevention guidelines [12], diagnosis of an SSI requires that one of the following criteria be met: (1) superficial infection (infection at the incisional site), (2) deep infection (infection in the incisional muscle), and (3) organ or space infection within 30 days after surgery. Patients with an SSI must have clear evidence of infection, positive culture results of surgical sites or drainage fluid from the abdominal cavity, or positive blood culture results with high fever. In the present study, the surgical wound was examined by a physician and a nurse at least once a day and by the SSI surveillance team of our institution once a week. The diagnosis of SSI was made after discussions with surgeons, nurses, and members of the SSI surveillance team. Additionally, the severity of postoperative complications including SSI was graded according to the Clavien-Dindo classification [13]. Clavien Dindo grade > III complications were considered major complications.

Statistical analysis

Differences between two normally distributed parameters were compared using the χ2 test and Fisher's exact probability test. The Mann–Whitney U test was used to compare differences between two parameters with non-normal distributions. Potential risk factors for SSI were evaluated using univariate and multivariate analyses. Independent risk factors for SSI were identified by multivariate analysis using logistic regression. All data were analyzed by StatView software (Abacus Concepts, Inc., Berkeley, CA, USA). A P value of < 0.05 was considered statistically significant.

Results

Patient characteristics

The patients' characteristics are shown in (Table 1). The mean preoperative CRP concentration was 0.85 mg/dL (range: 0.01 – 13.69 mg/dL), the mean preoperative ALB concentration was 3.6 g/dL (range: 2.2 – 4.9 g/dL), and the mean preoperative TLC was 1755 cells/mm3 (range: 650 – 3720 cells/mm3). Clavien-Dindo grade > III SSIs were detected in 47 of 100 patients. We found four types of SSIs after PD (Table 2). Most of the Clavien-Dindo grade > III SSIs were postoperative pancreatic fistulas caused by leakage at the pancreaticojejunostomy site (68.1%). Three patients died of an SSI at 23 (postoperative pancreatic fistula), 27 (intra-abdominal abscess), and 48 (intra-abdominal abscess) days after PD. Thus, the SSI-related operative mortality rate was 3%. The mean postoperative hospital stay of 47 patients with SSIs (57.4 days) was significantly longer than that of 53 patients without SSIs (26.6 days, P < 0.001).

Table 1: Patients' background data.

Gender (male/female)	67/33
Mean age (years, SD)	72.9 (9.1)
Mean BMI (SD)	22.1 (3.2)
Both consumption of tobacco and alcohol (yes, %)	46 (46)
ASA classification (1/2/3)	5/78/17
Pathological diagnosis Pancreatic cancer Bile duct cancer Duodenal cancer Other malignancies Benign tumors	 34 31 13 11 11
Preoperative biliary drainage (yes, %)	51 (51)
GPS (0/1/2)	59/26/15
Mean preoperative PNI (SD)	44.4 (7.6)
Mean preoperative GNRI (SD)	95.2 (10.6)
Mean time of operation (min, SD)	370.4 (109.1)
Mean intraoperative blood loss (mL, SD)	988.1 (870.7)
Blood transfusion (yes, %)	32 (32)
Occurrence of SSI (yes, %)	47 (47)
Death related with SSI (%)	3 (3)
Mean postoperative hospital stays (days, SD)	41.1 (33.4)

ASA: American Society of Anesthesiologists, BMI: body mass index, GNRI: geriatric nutritional risk index, GPS: Glasgow prognostic score, PNI: prognostic nutritional index, SD: standard deviation, SSI: surgical site infection

Table 2: Types of surgical site infections.

Total	47
Leakage at pancreaticojejunostomy	32 (68.1%)
Intra-abdominal abscess	11 (23.4%)
Leakage at choledochojejunostomy	3 (6.4%)
Surface	1 (2.1%)

Univariate risk analysis for SSI after PD

The sample size of each type of SSI was small, so, we did not analyzed factors thought to influence the occurrence of SSI after PD individually, we analyzedthe factors about the whole SSIs.

The patients were divided into two groups according to their median age, BMI, intraoperative blood loss, and operation time. The patients' clinical and demographic data are summarized in (Table 3). No statistically significant difference was found in age, BMI, smoking alcohol use, ASA classification, preoperative biliary drainage, preoperative GPS, PNI, GNRI, intraoperative blood loss, or operation time. The univariate analysis showed that only intraoperative blood transfusion was a risk factor for SSI after PD.

Table 3: Univariate analysis for occurrence of SSI.

	Occurrence of SSI	P
Age ≥ 74 (N = 51) < 74 (N = 49)	28 (54.9%) 19 (38.8%)	0.106
BMI ≥ 21.9 (N = 51) < 21.9 (N = 49)	28 (54.9%) 19 (38.8%)	0.106
Both consumption of tobacco and alcohol Yes (N = 46) No (N = 54)	21 (45.7%) 26 (48.1%)	0.803
ASA classification 1 and 2 (N = 83) 3 (N = 17)	40 (48.2%) 7 (41.2%)	0.6
Preoperative biliary drainage Yes (N = 51) No (N = 49)	26 (51%) 21 (42.9%)	0.416
GPS 0 (N = 59) 1 or 2 (N = 41)	24 (40.7%) 23 (56.1%)	0.129
PNI ≤ 40 (N = 29) > 40 (N = 71)	16 (55.2%) 31 (43.7%)	0.295
GNRI < 94 (N = 46) ≥ 94 (N = 54)	24 (51.1%) 23 (48.9%)	0.339
Intraoperative blood loss ≥ 825 mL (N = 50) < 825 mL (N = 50)	24 (48%) 23 (46%)	0.841
Blood transfusion Yes (N = 32) No (N = 68)	21 (65.6%) 26 (38.2%)	0.011
Time of operation ≥ 351 min (N = 50) < 351 min (N = 50)	26 (52%) 21 (42%)	0.316

ASA: American Society of Anesthesiologists, BMI: body mass index, GNRI: geriatric nutritional risk index, GPS: Glasgow prognostic score, PNI: prognostic nutritional index, SD: standard deviation, SSI: surgical site infectio

Multivariable logistic regression analysis

The multivariate logistic regression analysis revealed that intraoperative blood transfusion (P = 0.02) and a high BMI (P = 0.037) were independent predictors of SSI (Table 4).

Discussions

To ensure appropriate management of SSI after PD, it is very important to estimate high risk factors for SSI. In general, risk factors for postsurgical wound complications following abdominal procedures include the ASA score, obesity, diabetes, age, operation time, estimated blood loss, and poor nutrition [14,15]. In this study, we found that obesity and intraoperative blood transfusion were important risk factors for SSI after PD. Angiolini et al. [16] and Chang et al. [17] reported that a high-BMI was an independent risk factor for SSI after PD by their

Table 4: Multivariate analysis by logistic regression.

	Odds ratio	95% confidence interval	*P*
Age ≥ 74 vs. < 74	1.81	0.73 – 4.48	0.198
BMI ≥ 21.9 vs. < 21.9	3.38	1.08 – 10.64	0.037
Both consumption of tobacco and alcohol Yes vs. No	1.47	0.57 – 3.8	0.427
ASA classification 3 vs. 1 and 2	0.43	0.12 – 1.5	0.184
Preoperative biliary drainage Yes vs. No	1.22	0.48 – 3.09	0.672
GPS 3 vs. 1 or 2	0.81	0.2 – 3.3	0.767
PNI ≤ 40 vs. > 40	0.91	0.18 – 4.65	0.91
GNRI < 94 vs. ≥ 94	2.71	0.72 – 10.2	0.141
Intraoperative blood loss ≥ 825 mL vs. < 825 mL	3.59	0.13 – 1.19	0.1
Blood transfusion Yes vs. No	4.14	1.25 – 13.75	0.02
Time of operation ≥ 351 min vs. < 351 min	1.95	0.72 – 5.31	0.19

ASA: American Society of Anesthesiologists, BMI: body mass index, GNRI: geriatric nutritional risk index, GPS: Glasgow prognostic score, PNI: prognostic nutritional index, SD: standard deviation

multivariate analysis. Patients with obesity seem to require a long operation time and have high amounts of intraoperative blood loss. In the present study, however, we found no significant correlation between the patients' BMI and operation time (ρ = 0.127, P = 0.206) or between the patients' BMI and intraoperative blood loss (ρ = 0.067, P = 0.506) by Spearman's rank correlation coefficient (data not shown). Balentine et al. [18] concluded that in pancreatic surgery, intra-abdominal-fat was a better predictor than the BMI for determining the risk of complications after surgery. To identify the correlation between intra-abdominal-fat and the occurrence of SSI, further research is needed in patients undergoing pancreatic surgery.

We also found a strong positive correlation between intraoperative blood transfusion and the occurrence of SSI after PD. Preoperative-, intraoperative-, and postoperative blood transfusion is reportedly as the major risk factor for SSI in various surgeries [19-21]. The intraoperative blood transfusion may be resulted by various disadvantage status of the patients. Truly, the mean operation time among 32 patients with intraoperative blood transfusion

(421.3 minutes) was longer than that among 68 patients without intraoperative blood transfusion (345.6 minutes, P = 0.001), additionally, the mean intraoperative blood loss volume of 32 patients with intraoperative blood transfusion (1524.4 mL) was greater than that of 68 patients without intraoperative blood transfusion (696 mL, P < 0.001) in the present study. Recent studies have shown a strong correlation between depressed preoperative immunity and the occurrence of postoperative complications, such as SSI [22–24]. And, Mauser et al [25] reported that postoperative low CD4 count in peripheral blood of patients was important marker for occurrence of anastomotic leakage in damage control surgery.

Blood transfusion inhibited IL-2 production, decrease interferon gamma, suppress natural killer cell function, release immunosuppressive prostaglandins, decrease monocyte activity, and increase of regulatory T cells (suppressor T cells) [26,27]. Also, blood transfusion increased in IL-6, vascular endothelial growth factor, and hepatocyte growth factor, which play fundamental roles in tumor growth, malignant transformation, invasion of tumor cells, and a poor prognosis [28]. Overexpression of immunosuppressive cytokines caused by blood transfusion may play an important role for occurrence of postoperative complications. But, the correlation between postoperative low immunity caused by intraoperative blood transfusion and occurrence of SSI should be analyzed more extensively in the future.

Conclusions

Because SSIs are associated with a prolonged hospital stay, they may lead to higher medical costs. Surgeons need to pay special attention to the patients with low postoperative immunity to prevent SSI.

Contributors list and Conflicts of Interest

The authors declare that we have no commercial associations that might create a conflict of interest in connection with submitted manuscript and we have no funding about this manuscript.

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