Original Article

Pancreatoduodenectomy within 2 weeks after endoscopic retrograde cholangio-pancreatography increases the risk of organ/space surgical site infections: a 5-year retrospective cohort study in a high-volume centre

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Background: Organ/space surgical site infections (OSSI) after pancreaticoduodenectomy (PD) are not rare events. The role of diagnosis and treatment for pancreatic and biliary diseases with an endoscopic retrograde cholangio-pancreatography (ERCP) procedure is currently controversial. However, the ERCP procedure might play a role in surgical outcomes after PD.

Methods: We conducted a retrospective cohort study for patients who underwent PD in the First Affiliated Hospital with the Nanjing Medical University from 1st September 2012 to 31st January 2018. The relationship between ERCP exposure and OSSI after PD was analyzed by univariate and forward stepwise multivariate logistic regression model.

Results: Of the 1,365 patients who underwent PD, 136 developed OSSI (10.0%). We found that ERCP exposure before PD (EEBPD) was significantly associated with an increased incidence rate of post-operative pancreas fistula (POPF) [24.2% (23/95) *vs.* 14.9% (189/1,270), risk ratio (RR) =1.63, 95% confidence interval (CI), 1.11–2.38, P=0.015]. Hypertension, a higher level of preoperative low-density lipoprotein (LDL) and creatinine (Cr) were associated with elevated risks of post-operative OSSI [adjusted odds ratio (Adj-OR) (95% CI) were 1.59 (1.09–2.32), 1.70 (1.16–2.51), 1.99 (1.36–2.92)], whereas a preoperatively higher level of aspartate aminotransferase (AST) would decrease the risk [Adj-OR (95% CI), 0.62 (0.42–0.91)]. Remarkably, EEBPD would significantly increase and more than double the OSSI risk [Adj-OR (95% CI), 2.56 (1.46–4.47)] especially if it was within 14 days before surgery (Spearman =–0.698, P<0.001).

Conclusions: ERCP, as an independent risk factor, significantly increased the risk of post-operative OSSI after PD if it is performed within 14 days prior to surgery. Our findings would assist clinical decision-making, and improve OSSI control and prevention.

Keywords: Endoscopic retrograde cholangio-pancreatography (ERCP); pancreaticoduodenectomy (PD); organ/space surgical site infections (OSSI); logistic regression

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Introduction

The CDC healthcare-associated infection (HAI) prevalence survey found that there were an estimated 157,500 surgical site infections (SSIs) [e.g., superficial incisional, deep incisional and organ/space surgical site infections (OSSI)] associated with inpatient surgeries in 2011 (1), and surgical-site infection was the leading cause of infection in hospitals (pooled cumulative incidence 5.6 per 100 surgical procedures), strikingly higher than the proportions recorded in developed countries (2). OSSI after surgery, are among the most common complications after bile duct, liver or pancreatic surgery [e.g., pancreaticoduodenectomy (PD)], and are associated with a prolonged length of stay in hospital and increased cost of treatment, imposing a significant economic burden on health care (3) and increasing the levels of hospital readmission (4). The occurrence of OSSI was adversely associated with long-term survival (5). PD is a standard of care for patients with malignant or benign disease of the pancreatic head or periampullary region (6,7). PD is one of the most difficult techniques for gastroenterological surgeons, with long operation times, complicated gastrointestinal reconstruction procedures, and high morbidity rates (8). Postoperative SSI is more common after PD secondary to the extensive physiologic alterations (fluid shifts, blood loss, and systemic vasodilation) and multiple enteric anastomoses associated with the procedure. Even at high-volume tertiary referral centres, the incidence of post-PD wound infection is estimated to be approximately 10% to 17% (9-11).

An endoscopic retrograde cholangio-pancreatography (ERCP) procedure was sometimes applied to help identify the pancreaticobiliary limb or aiding in the visualisation of pancreatic and/or biliary anastomoses in patients with a PD resection (12). In patients awaiting PD, preoperative biliary drainage with ERCP was occasionally used to reduce bilirubin. However, the role of ERCP is being challenged as it is thought to increase infection and morbidity (13-15). The aim of this cohort study was to investigate the risks of preoperative ERCP procedure and OSSI for patients following PD.

We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/gs-20-826).

Methods

Study design and setting

This retrospective analysis of anonymous data was approved by the Institutional Review Board of the First Affiliated Hospital of Nanjing Medical University (2018-SR-295). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). And written informed consent was obtained from all the study participants. We conducted an observational cohort study for patients who underwent PD in the First Affiliated Hospital of Nanjing Medical University from 1st September 2012 to 31st January 2018 and 1,365 patients were included. We installed the software of Healthcare associated infection Surveillance Platform (HSP) in 2012 which linked to a clinical database to extract the patients' data of inspection, diagnosis and treatment, and early warning of HAI. All the patients' data were extracted from the HSP and each OSSI was judged by infection control personnel (ICP) and the patient's attending doctor.

Definitions

OSSI were defined according to the National Healthcare Safety Network (NHSN). OSSI had to meet the following criteria: (I) date of event occurred within 30–90 days after the NHSN operative procedure (where day 1= the procedure date); (II) involves any part of the body deeper than the fascial/muscle layers that are opened or manipulated during the operative procedure; (III) the patient has at least one of the following: (i) purulent drainage from a drain that is placed into the organ/space [for example, closed suction drainage system, open drain, T-tube drain, computed tomography (CT)-guided drainage]. (ii) Organism(s) identified from fluid or tissue in the organ/space by a culture- or non-culture-based microbiologic testing method, which is performed for purposes of clinical diagnosis or treatment [for example, not active surveillance culture/testing (ASC/AST)]. (iii) An abscess or other evidence of infection involving the organ/space that is detected as the result of a gross anatomical or histopathologic examination, or imaging test evidence suggestive of infection; and (IV) meets at least one criterion for a specific organ/space infection site (these criteria are found in the Surveillance Definitions for Specific Types of Infections chapter) (CDC NHSN, https://www.cdc.gov/HAI/ssi/ssi.html, Accessed 10/6/2018).

ERCP exposure was defined as the patients undergoing ERCP procedure within 3 months before PD.

Pancreatic fistulas (PFs) were defined and classified consistent with ISGPS criteria (16) Extracted data included patient demographics (age, gender, smoking status, alcohol abuse), comorbidities (hypertension, diabetes, coronary heart disease, obstructive jaundice), preoperative laboratory tests [total protein (TP), albumin (ALB), low-density lipoprotein (LDL), high-density lipoprotein (HDL), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), creatinine (Cr), creatine kinase (CK), urea, fasting blood-glucose (Glu), total bilirubin (TB)], ERCP exposure before PD (EEBPD), duration of ERCP and PD, blood transfusion and length of hospitalisation (LOH). Superficial and deep SSIs were not included in the analysis because they have different risk profiles and should be analyzed separately.

Statistical analysis

Data are presented as median [interquartile range (IQR)] or number (percentage). Instead of excluding cases with some missing data, multiple imputations were carried out. Each missing piece of data was imputed five times with the 'predictive mean matching' (PMM) method containing all of the predictor variables and the median one of these five values were imputed as missing data. Imputing a missing value could make the best use of the entire medical records (17). Categorical variables were compared using the Pearson's chi-square test or Fisher's exact test. Nonparametric continuous variables were analyzed using the Mann-Whitney U test. Univariate and forward stepwise multivariate logistic analyses were performed to analyse the independent risk factors (18). For the subgroup analyses, we performed 1:4 propensity score matching (PSM) using the nearest neighbor matching on 95 EEBPD case and 1,270 no-EEBPD patients to optimize balance of baseline characteristics for assessing the independent effect of EEBPD. The primary matching criteria included hypertation, TP, Cr, ALB, LDL, HDL, CK, ALP, Glu, whose distribution was statistically different between the EEBPD and no-EEBPD groups. Propensity scores were calculated using the logistic regression model. After 1:4 PSM, the analysis included 95 EEBPD case and 380 no-EEBPD patients and the variables were not significantly different between these two groups. The imputation of missing values was made using the '*mice*' package (19), and the nomogram was developed and validated using the '*rms*' package. The PSM was performed by '*MatchIt*' package. The decision-making tree was analysed and drew using the '*rpart*' and '*rpart.plot*' packages. The above statistical analyses were performed using Stata SE, version 11.0 (StataCorp., USA) or/and R software, version 3.5.1 (https://www.r-project.org/). All statistics were two-tailed, and statistical significance was accepted at the P<0.05 level.

Results

A total of 1,365 patients, who underwent PD from 1st September 2012 to 31st January 2018 in the First Affiliated Hospital with Nanjing Medical University, were identified in this cohort study. An additional figure showed this in more detail (see Figure S1). Within this total, there were 95 patients with ERCP exposure (7.0%) and 1,270 patients without ERCP exposure (93.0%). Patients' age, gender, history of smoking, alcohol abuse, hypertension, diabetes mellitus, coronary heart disease, obstructive jaundice and blood transfusion were similar between the two groups (*Table 1*). Perioperative ALB was discrepant between the two groups as well and ERCP exposure patients had higher ALB [median (IQR): 39.4 (36.2–42.8) *vs.* 36.5 (34.1–40.1) g/L, respectively; P<0.001]. The distribution of HDL, CK and Glu was also significantly discrepant in the ERCP and non-ERCP exposure group. We found that the patients under EEBPD

Table 1 Baseline characteristics and outcomes of the study population

Number of participants	ERCP exposure (n=95)	Non-ERCP exposure (n=1,270)	P value
Age, median [IQR], years	63 [55–69]	62 [52–68]	0.196
Male, n (%)	59 (61.1)	771 (60.7)	0.788
Smoking status (ever), n (%)	18 (18.9)	180 (14.2)	0.202
Alcohol abuse (ever), n (%)	14 (14.7)	154 (12.1)	0.455
Preoperative, median (IQR)			
TP, g/L	66.0 (61.5–70.6)	65.2 (58.6–68.9)	0.032
ALB, g/L	39.4 (36.2–42.8)	36.5 (34.1–40.1)	<0.001
LDL, mmol/L	3.37 (2.65–4.30)	3.11 (2.46–4.08)	0.086
HDL, mmol/L	0.97 (0.74–1.25)	0.83 (0.66–1.03)	0.001
ALT, U/L	68.4 (20.4–214.0)	62.4 (25.6–128.8)	0.601
AST, U/L	51.7 (23.5–140.3)	49.0 (29.5–103.6)	0.848
ALP, U/L	252.6 (95.6–519.9)	248.0 (151.1–444.9)	0.226
Cr, μmol/L	61.2 (52.2–71.2)	60.7 (50.2–74.4)	0.617
CK U/L	55.0 (38.7–76.0)	37.0 (27.0–50.0)	<0.001
Urea mmol/L	4.68 (3.74–5.85)	4.71 (3.88–6.30)	0.319
Glu mmol/L	5.87 (5.17–7.05)	5.42 (4.82–6.85)	0.004
TB, μmol/L	30.8 (11.9–168.1)	29.9 (14.4–115.0)	0.945
Comorbidities, n (%)			
Hypertension	27 (28.4)	386 (30.4)	0.686
Diabetes mellitus	14 (14.7)	203 (16.0)	0.748
Coronary heart disease	0 (0.0)	95 (7.5)	0.258
Obstructive jaundice	35 (36.8)	514 (40.5)	0.486
Cholangitis	13 (13.7)	181 (14.3)	0.879
Outcomes			
POPF (B or C), n (%)	23 (24.2)	189 (14.9)	0.015
LOH, median (IQR), day	25.0 (18.0–31.5)	19.0 (16.0–26.0)	<0.001

ERCP, endoscopic retrograde cholangio-pancreatography; IQR, interquartile range; TP, total protein; ALB, albumin; LDL, low-density lipoprotein; HDL, high-density lipoprotein; ALT, alanine transaminase; AST, alanine aminotransferase; ALP, alkaline phosphatase; Cr, creatinine; CK, creatine kinase; Glu, fasting blood-glucose; TB, total bilirubin; POPF, post-operative pancreas fistula; LOH, length of hospitalisation.

were significantly associated with an increased incidence rate of post-operative pancreas fistula (POPF) [23/95 (24.2%) *vs.* 189/1,270 (14.9%), P=0.015] and the LOH [25.0 (18.0–31.5) *vs.* 19.0 (16.0–26.0), P<0.001]. For all of these 95 patients with ERCP exposure, 61 (64.2%) patients were taken for preoperative diagnosis, 22 (23.2%) patients were taken for biliary drainage, 5 (5.3%) patients were taken for stent placement and 7 (7.4%) patients were taken for other causes.

Risk factors of OSSI

The overall incidence rate of OSSI was 10.0% (136/1,365). We found that the incidence rate of OSSI in the ERCP exposure group was significantly increased compared to that in the non-ERCP exposure group (20.0% *vs.* 9.21%, 19/95 *vs.* 117/1,270, P<0.002). Logistic regression analysis identified a history of EEBPD and hypertension were significantly associated with increased risk of post-operative OSSI [adjusted odds ratio (Adj-OR) (95% CI), 2.56 (1.46–4.47) and 1.59 (1.09–2.32), respectively], and higher levels of preoperative LDL and Cr were significantly associated with higher risk of OSSI [Adj-OR (95% CI), 1.70 (1.16–2.51) and 1.99 (1.36–2.92), respectively]. However, we found that a higher level of preoperative ALP would significantly decrease the OSSI risk [Adj-OR (95% CI), 0.62 (0.42–0.91)] (*Table 2*). The nomogram for the prediction

Table 2 Risk factors for OSSI in this cohort study

Variables	No. (n=1,365)	Univariate logistic regression		Multivariate logistic regression	
		OR (95% CI)	P	Adj-OR (95% CI)	P
Age, years					
≤63	713	1.00 (Ref.)			
>63	652	1.10 (0.77–1.58)	0.589		
Gender					
Male	830	1.00 (Ref.)			
Female	535	0.81 (0.56–1.18)	0.283		
EEBPD					
No	1,270	1.00 (Ref.)		1.00 (Ref.)	
Yes	95	2.37 (1.37–4.10)	0.002	2.56 (1.46–4.47)	0.001
Smoking status					
No	1,167	1.00 (Ref.)			
Yes	198	1.28 (0.79–2.06)	0.317		
Alcohol abuse					
No	1,197	1.00 (Ref.)			
Yes	168	1.06 (0.62–1.81)	0.834		
TP, g/L					
≤65.8	681	1.00 (Ref.)			
>65.8	684	0.76 (0.53–1.09)	0.137		
ALB, g/L					
≤39.3	687	1.00 (Ref.)			
>39.3	678	0.77 (0.54–1.11)	0.167		
LDL, mmol/L					
≤3.36	685	1.00 (Ref.)		1.00 (Ref.)	
>3.36	680	1.37 (0.95–1.96)	0.091	1.70 (1.16–2.51)	0.007
HDL, mmol/L					
≤0.95	684	1.00 (Ref.)			
>0.95	681	0.72 (0.50–1.03)	0.072		

Table 2 (*continued*)

Table 2 (*continued*)

Variables	No. (n=1,365)	Univariate logistic regression		Multivariate logistic regression	
		OR (95% CI)	P	Adj-OR (95% CI)	P
ALT, U/L					
≤68.1	683	1.00 (Ref.)			
>68.1	682	0.91 (0.63–1.30)	0.589		
AST, U/L					
≤51.6	683	1.00 (Ref.)			
>51.6	682	0.82 (0.57–1.17)	0.276		
ALP, U/L					
≤252.1	683	1.00 (Ref.)		1.00 (Ref.)	
>252.1	682	0.69 (0.48–0.99)	0.044	0.62 (0.42–0.91)	0.014
Cr, μmol/L					
≤61.2	677	1.00 (Ref.)		1.00 (Ref.)	
>61.2	688	1.96 (1.35–2.85)	<0.001	1.99 (1.36–2.92)	<0.001
CK					
≤52.5	677	1.00 (Ref.)			
>52.5	688	1.32 (0.92–1.89)	0.137		
Urea					
≤4.68	589	1.00 (Ref.)			
>4.68	676	1.53 (1.07–2.21)	0.021		
Glu					
≤5.83	684	1.00 (Ref.)			
>5.83	681	0.97 (0.68–1.39)	0.876		
TB, μmol/L					
≤30.8	685	1.00 (Ref.)			
>30.8	680	1.01 (0.70–1.44)	0.965		
Hypertension					
No	953	1.00 (Ref.)		1.00 (Ref.)	
Yes	412	1.57 (1.08–2.27)	0.017	1.59 (1.09–2.32)	0.015
Diabetes					
No	1,148				
Yes	217	1.57 (1.01–2.43)	0.046		
Coronary heart disease					
No	1,336	1.00 (Ref.)			
Yes	29	1.98 (0.74–5.28)	0.171		

Table 2 (*continued*)

Table 2 (*continued*)

Variables	No. (n=1,365)	Univariate logistic regression		Multivariate logistic regression	
		OR (95% CI)	P	Adj-OR (95% CI)	P
Obstructive jaundice					
No	816	1.00 (Ref.)			
Yes	549	0.81 (0.55–1.17)	0.256		
Cholangitis					
No	1,171	1.00 (Ref.)			
Yes	194	1.16 (0.71–1.90)	0.557		

OSSI, organ/space surgical site infections; OR, odds ratio; Adj-OR, adjusted OR; CI, confidence interval; EEBPD, ERCP exposure before PD; ERCP, endoscopic retrograde cholangio-pancreatography; PD, pancreaticoduodenectomy; TP, total protein; ALB, albumin; LDL, low-density lipoprotein; HDL, high-density lipoprotein; ALT, alanine transaminase; AST, alanine aminotransferase; ALP, alkaline phosphatase; Cr, creatinine; CK, creatine kinase; Glu, fasting blood-glucose; TB, total bilirubin.

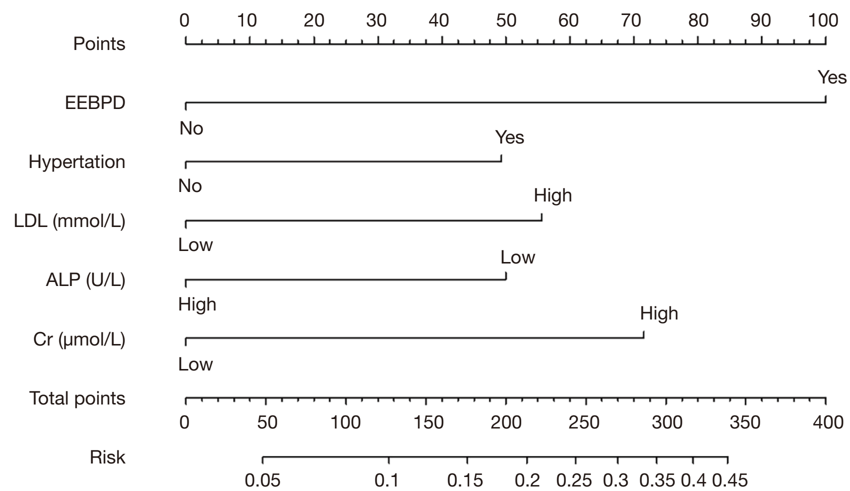

Figure 1 Nomogram for the risk prediction of OSSI. To use the nomogram, for an individual patient, the value is loaded on each variable axis (the 2nd–6th lines), and a line is drawn upward to determine the number of points received for each variable value (the 1st line). The sum of these numbers is located on the total points axis (the 6th line), and a line is drawn downward to the risk axes (the 8th line) to determine the risk of OSSI. OSSI, organ/space surgical site infections; EEBPD, ERCP exposure before PD; ERCP, endoscopic retrograde cholangio-pancreatography; PD, pancreaticoduodenectomy; LDL, low-density lipoprotein; ALP, alkaline phosphatase; Cr, creatinine.

of postoperative OSSI integrating all these independent predictors is presented in *Figure 1*.

ERCP functional analysis and clinical decision

Among 1,365 patients, 95 received ERCP before PD. 57.9% (55/95) ERCP procedure was conducted in our hospital. In our current cohort, we found that the OSSI rate was negatively correlated with the interval days between ERCP and surgery (Spearman r=–0.698, P<0.001). With further analysis, we found that 14 days between ERCP and PD might be the appropriate interval time for a lower OSSI rate with 25% reduction (*Figure 2*).

Subgroup analyses of patients after propensity score-matching

After propensity score-matching for hypertation, TP, Cr,

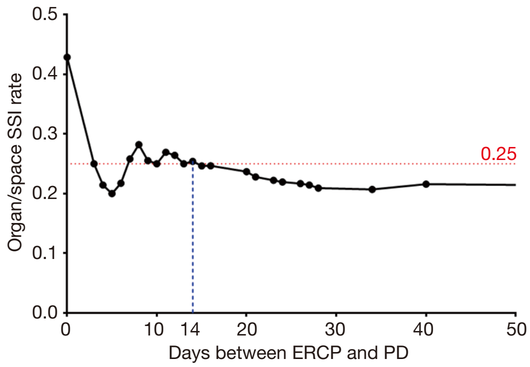

Figure 2 Appropriate time of ERCP for post-PD OSSI rate. The dotted red line presented the infection rate of 25% and the dotted blue line presented the inflection day for infection rate. ERCP, endoscopic retrograde cholangio-pancreatography; PD, pancreaticoduodenectomy; OSSI, organ/space surgical site infections.

ALB, LDL, HDL, CK, ALP, Glu, there was no significant differences in these nine variables between patients with or without EEBPD (*Table 3*). Patients with EEBPD exhibited an increased the risk of SSI [OR, 2.29; 95% CI, 1.23 to 4.28, P=0.009] compared with those not receiving EEBPD after adjusted hypertation, Cr, LDL and ALP.

Microbiology analysis of OSSI

Among 144 isolations, the predominant microorganisms cultured from OSSI after PD were *E. coli* (34 episodes, 23.61%, 34/144), *K. pneumoniae* (30 episodes, 20.83%, 30/144) and *E. faecium* (19 episodes, 13.19%, 19/144) (*Figure 3*). An additional table showed this in more detail (see Table S1).

Discussion

PD is one of the most stressful types of surgery for gastroenterological surgeons. The development of OSSI is a common complication after PD with the incidence of wound infection as high as 10% to 17% (3,9-11,20) and the incidence of OSSI was 48% in Japan in 2012 (21). The postoperative OSSI for these patients poses a significant clinical1and economic burden in the field of surgery (22), often leading to extended length of stay, readmissions, and attendant increased costs (23). Therefore, reducing the incidence of OSSI is important; however, we know little about the risk factors for PD-related OSSI. For these reasons, we analyzed the incidence of OSSI following PD and tried to find a method to reduce the incidence of OSSI.

In this large volume teaching hospital, we performed a retrospective cohort study between 1st September 2012 and 31st January 2018 and the overall OSSI incidence rate was 10.0% for the patients undergoing PD. Sugiura and the group revealed several risk factors such as length of operation >480 min, main pancreatic duct (MPD) ≤3 mm, body mass index (BMI) >23.5 kg/m^2, semi-closed drain and PF, that were associated with OSSI. The presence of a PF was the strongest risk factor for OSSI (21). Patients who develop a POPF have a higher risk of dying after surgery, and need to stay longer in the hospital (7). A PF after PD always occurs due to autolysis caused by activated trypsin, resulting in tissue damage around the pancreatic ductal anastomosis (23). A study from Scheufele found that the postoperative wound infections would be increased after preoperative biliary drainage (24) and there were fundamental differences in the biliary microbiome of patients with periampullary cancer who undergo preoperative biliary drainage and those who do not (25). In our study, we analyzed the risk factors associated with OSSI before PD. The EEBPD was the strongest risk factor for developing an OSSI (Adj-OR =2.56). The incidence of OSSI in patients with ERCP exposure was 20%, which was over one time higher than that observed in patients without (9%). Barreto *et al.* also found that preoperative ERCP and stenting may result in a significantly higher risk of SSIs while they were unable to document an association between the development of POPF and SSIs (P=0.308) (26). Besides, many studies had reported that preoperative biliary drainage is associated with positive intraoperative bile cultures (27-30), and accessing the biliary tract from the digestive tract is known to increase the risk of postoperative infectious complications (31-33). Results from Wu *et al.* Showed that ERBD was associated with an increased risk of intra-abdominal abscess (IAA) in patients undergoing PD (34). It's similar to SSI that Endoscopy, angiography, and/or exploratory laparotomy was associated with grade B or C hemorrhage (23 of 54, 42.6%) in post-PD patients (35). ERCP is a procedure that enables the physician to examine the pancreatic and bile ducts and it needs a small opening in the duodenum (ampulla) and a small plastic tube (cannula) is then passed through the endoscope and into this opening. The small opening might be the reason for increased risk. Interestingly, we also found that the risk of ERCP operation within 14 days of PD is associated with a higher risk of OSSI, which strongly suggested that this

Table 3 Subgroup analyses of patients after propensity score-matching

Parameters	No-EEBPD	EEBPD	χ^2	P	Multivariate logistic regression*	
					OR (95% CI)	P
SSI			6.770	0.009		
No	344	77				
Yes	36	18				
Hypertation			0.627	0.428	1.09 (0.57–2.07)	0.804
No	287	68				
Yes	93	27				
LDL			0.135	0.713	2.38 (1.18–4.81)	0.016
Low	180	47				
High	200	48				
HDL			0.760	0.383		
Low	189	52				
High	121	43				
ALP			0.305	0.581	0.95 (0.50–1.83)	0.890
Low	208	49				
High	172	46				
Cr			0.239	0.625	1.61 (0.85–3.05)	0.143
Low	258	62				
High	122	33				
TP			0.096	0.757		
Low	278	68				
High	102	27				
ALB			0.100	0.752		
Low	282	72				
High	98	23				
CK			0.109	0.741		
Low	233	60				
High	147	35				
Glu			0.019	0.89		
Low	211	52				
High	169	43				
EEBPD			–	–	2.29 (1.23–4.28)	0.009
No	380	0				
Yes	0	95				

*, multivariate logistic regression analyses for PD-patients with or without OSSI after propensity score-matching. EEBPD, ERCP exposure before PD; ERCP, endoscopic retrograde cholangio-pancreatography; PD, pancreaticoduodenectomy; OR, odds ratio; CI, confidence interval; SSI, surgical site infection; LDL, low-density lipoprotein; HDL, high-density lipoprotein; ALP, alkaline phosphatase; Cr, creatinine; TP, total protein; ALB, albumin; CK, creatine kinase; Glu, fasting blood-glucose.

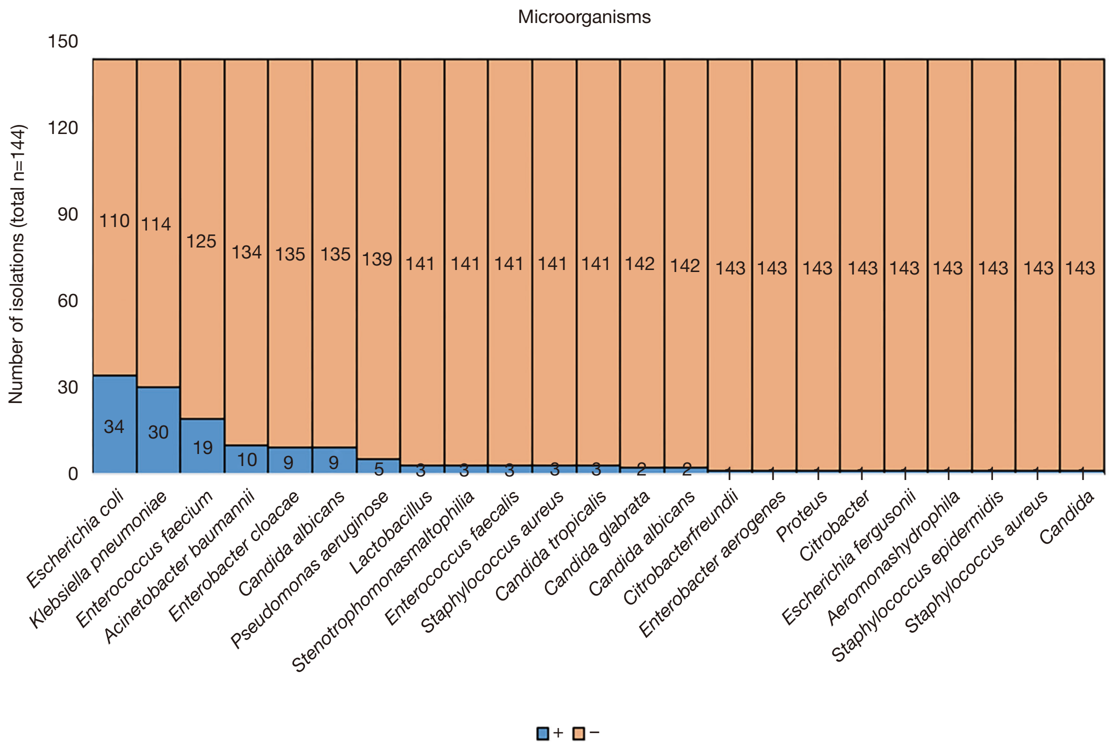

Figure 3 Microbiology analysis of OSSI. Each column represents a microorganism and the row represents the numbers of patients; orange represented uninfected and blue represented infected. OSSI, organ/space surgical site infections.

elective PD time should be delayed for at least 14 days without any contraindications.

When analyzing OSSI culture microorganisms, among 144 isolations, gram-negative bacteria were identified in most cases and the predominant microorganisms cultured from post-PD OSSI were *E. coli*, *Kpneumoniae* and *E. faecium*. The most frequently isolated bacteria were *Enterococcus species* (51%), *Klebsiella species* (28%), and *Escherichia coli* (27%) (34). The change of the bacterial spectrum could be the selection of microorganisms through the use of antibiotics (36,37), which could result in different microbiology profiles of the cultured bacteria.

We found that preoperative higher level of LDL and Cr was significantly with higher risk of OSSI while higher level of ALP would significantly decrease the OSSI risk. Our finding suggested that biomarkers in concentration could be predictors for SSIs. Delgado-Rodríguez *et al.* found that serum HDL-C and total cholesterol seem to be associated with the risk of nosocomial infection in surgical patients (38). Meanwhile, Mahdi *et al.* revealed that serum Cr concentration ≥2 mg/dL was significantly associated with SSI among those who underwent laparoscopic hysterectomy (39). Watanabe *et al.* consider that chronic kidney disease (serum Cr concentration >1.2 mg/dL) correlated with a higher risk of incisional SSI. Kidney disease may be a potential risk factor for abdominal infection (40). Based on these risk factors, we developed the nomogram to display the results and the decision-making tree to assist clinicians in decision-making.

Although the results were promising, this study had some shortcomings. Firstly, preoperative jaundice reduction was not performed routinely in our hospital, which resulted in a smaller proportion of preoperative ERCP. The total number of cases with preoperative ERCP was only 95, which might introduce some bias. In addition, this study was a retrospective study and several factors such as duct diameter and BMI were not available. All these results and more factors need to be validated by prospective studies.

Conclusions

Our analysis of data from a cohort study over 5 years identified that EEBPD would significantly increase risks of OSSI for patients following PD, especially within 2 weeks.

We propose that the patients undergoing ERCP who are preparing for PD should be delayed for at least 2 weeks. Otherwise, a non-invasive procedure for diagnosis should be selected, such as CT or magnetic resonance cholangiopancreatography (MRCP). Hypertension, preoperative higher LDL and Cr would significantly increase OSSI risks while a preoperatively higher level of ALP was significantly associated with lower risks of OSSI. Based on our reported data, the predictive function of nomogram could be referred to lower the risks of OSSI for the patients following PD.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/gs-20-826

Data Sharing Statement: Available at https://dx.doi.org/10.21037/gs-20-826

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/gs-20-826). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of (as revised in 2013). This study had been approved by the Ethical Review Committee of the First Affiliated Hospital of Nanjing Medical University (2018-SR-295) and informed consent was taken from all individual participants.

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Supplementary

Table S1 One hundred and forty-four isolated microorganisms among 136 OSSI patients

Microorganisms	Isolations (n=144)
Gram-negative bacilli	100
Escherichia coli	34
Klebsiella pneumoniae	30
Acinetobacter baumannii	10
Enterobacter cloacae	9
Pseudomonas aeruginosa	5
Lactobacillus	3
Stenotrophomonasmaltophilia	3
Citrobacterfreundii	1
Enterobacter aerogenes	1
Proteus	1
Citrobacter	1
Escherichia fergusonii	1
Aeromonashydrophila	1
Gram-positive cocci	27
Enterococcus faecium	19
Enterococcus faecalis	3
Staphylococcus aureus	3
Staphylococcus epidermidis	1
Staphylococcus aureus	1
Fungi	17
Candida albicans	9
Candida tropicalis	3
Candida glabrata	2
Candida albicans	2
Candida	1

OSSI, organ/space surgical site infections.

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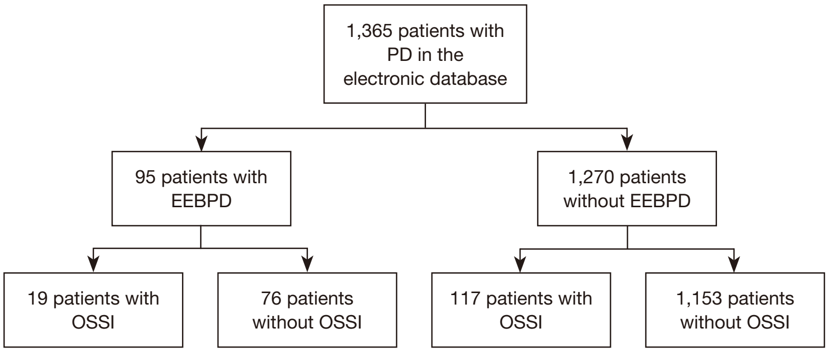

Figure S1 Study flowchart. PD, pancreaticoduodenectomy; EEBPD, ERCP exposure before PD; ERCP, endoscopic retrograde cholangiopancreatography; OSSI, organ/space surgical site infections.

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