ORIGINAL ARTICLE

Can Prophylactic Drains After Pancreaticoduodenectomy Be A Risk Factor for Organ/Space Surgical Site Infection?

Takashi Orii, Yukihiko Karasawa, Hiroe Kitahara, Masaki Yoshimura

Department of Surgery, Showa Inan General Hospital, Akaho 3230, Komagane, Nagano 399-4117, Japan

ABSTRACT

Introduction Although some authors have reported that retrograde infection by longterm placement of prophylactic drain may be the main cause of organ/space surgical site infection after pancreaticoduodenectomy. **Materials and Methods** The study included 93 patients who underwent pancreaticoduodenectomy. We assessed the risk factors for organ/space surgical site infection and examined the microorganisms detected at organ/space surgical site infection to determine the origin of microorganisms. **Results** Of the 93 patients, 29 were included in the organ/space surgical site infection+ group. The risk factors for organ/space surgical site infection on univariate analysis were blood transfusion (OR, 2.70; p <0.05), the amount of peritoneal lavage <5,000 mL (OR, 3.08; p<0.05), open type of prophylactic drain (OR, 2.92; p<0.05), and the incidence of pancreatic fistula (OR, 7.54, p<0.001). The microorganisms, detected in cultured specimen from prophylactic drain at organ/space surgical site infection, belonged to intestinal flora in 22 out of 29 patients (75.9%), and 30 of all 48 detected microorganisms (62.5%) were occupied by those of intestinal flora. **Conclusion** We confirmed that pancreatic fistula was the most significant risk factor. Based on the microorganisms identified, retrograde infection via drain placement could not be confirmed; therefore, the time of the drain removal should be carefully considered.

INTRODUCTION

Surgical site infection (SSI) after abdominal gastrointestinal surgery extends hospital stay and increases medical costs. Additionally, it has a negative impact on not only patients but also hospital management [1, 2, 3]. Therefore, techniques should be identified to avoid and appropriately treat SSI.

Many studies have reported that a prophylactic drain is not required for gastrointestinal surgery [4, 5], and one study concluded that the drain was needed only at esophagectomy and total gastrectomy [6]. However, other studies have advocated the requirement of a prophylactic drain in cases of pancreatic resection, including pancreaticoduodenectomy (PD) [7, 8, 9]. Several studies have reported that long-term dwelling of the drain can cause pancreatic fistulas and increase the incidence of organ/space SSIs (o/s-SSIs) [10, 11]. Because clinicians often have the impression that complications such as o/s-SSI and pancreatic fistulas would be more serious without a drain than complications with a drain [7], these beliefs may contradict the findings of many previous studies.

The present study analyzed the risk factors for o/s-SSI after PD and examined the relationship between prophylactic drain placement and the occurrence of o/s-SSI according to the classification of microorganisms detected in samples cultured from the drain at the time of o/s SSI.

METHODS

A total of 97 consecutive patients who underwent PD were considered for inclusion in this retrospective study. However, four patients were excluded because of lack of data. Therefore, 93 patients were finally enrolled between 2001 and 2014. These patients were divided into either the o/s-SSI-positive (o/s-SSI+) group, which had a positive bacterial culture of the drainage fluid, or the o/s-SSI-negative group (o/s-SSI−), which had a negative bacterial culture of the fluid. The risk factors for o/s-SSI were examined by comparing the following variables between the two groups: age; sex; body mass index (BMI); indication for operation; laboratory data at first visit, including total bilirubin level, albumin level, hemoglobin A1c (HbA1c) level, white blood cell (WBC) count, and C-reactive protein (CRP) level; preoperative biliary stent placement; American Society of Anesthesiologists physical status (ASA-PS) classification; operation time; operative blood loss; blood transfusion; quantity of peritoneal lavage during operation; type of prophylactic drain used (open or closed); duration of prophylactic drain placement; duration of prophylactic antibiotic administration; and pancreatic fistula development.

Additionally, by differentiating the bacteria detected in the drainage fluid and by identifying the relationship between the bacteria from the drainage fluid at the time of o/s-SSI and the bacteria from bile samples obtained pre- or intra-operatively, we determined whether the causative bacteria of o/s-SSI were present in the abdominal cavity or outside the body.

The preoperative biliary stents were selected from the following: endoscopic biliary stent, endoscopic nasobiliary drainage tube, and self-expandable metallic stent, according to the preference of the endoscopic physician and the quality of the existing cholangitis.

Prophylactic peritoneal drains were placed in all patients. The types of prophylactic drains were "open" and "closed." The former was used from 2001 to 2007, and the latter was used thereafter. The closed drain was maintained with vacuum at low pressure. o/s-SSI was suspected by the property of the drain fluid and diagnosed from results of the bacterial culture of the fluid.

The severity of the pancreatic fistulas was classified according to International Study Group on Pancreatic Fistula definitions [12].

Data are expressed as means ± standard deviation (SD). Patient characteristics and perioperative and postoperative variables were compared between the o/s-SSI+ and o/s-SSI− groups using the χ^2 and Fisher exact tests. Variables with p-values<0.05 were incorporated into a logistic regression model in order to determine the independent risk factors for o/s-SSI. The independent risk factors were expressed as odds ratios (ORs) and 95% confidence intervals (CIs). All statistical analyses were performed using JMP, version 12 (SAS Institute, Cary, NC, USA). P-values <0.05 were considered statistically significant.

RESULTS

The mean age of the patients was 72.6±9.3 years (range, 52–92 years). Of the 93 patients, 58 were male and 35 were female. The indications for operation were pancreas head tumors in 44 patients (pancreatic head cancer in 36, intraductal papillary mucinous neoplasm in seven, and serous cystadenoma in one), bile duct tumors in 34 patients (bile duct cancer in 33, and gall bladder cancer in one), tumors of the papilla of Vater in seven patients (cancer in five and adenoma in two), duodenal tumors in five patients (cancer in three, gastrointestinal stromal tumor in one, and lymphoma of mucosa-associated lymphoid tissue in one), and others in two patients (fibrosing cholangitis in one and gastric cancer recurrence in one).

Comparison of Perioperative Variables between the o/s-SSI+ and o/s-SSI− Groups

Of the 93 patients, 29 and 64 were included in the o/s-SSI+ and o/s-SSI− groups, respectively. The comparison of variables between the o/s-SSI+ and the o/s-SSI− groups are presented in **Table 1**. Age and sex did not differ significantly between the groups. However, BMI was significantly higher in the o/s-SSI+ group than in the o/s-SSI− group (23.1±3.6 kg/m² *vs.* 20.7±2.9 kg/m², p<0.01). The number of patients with pancreas head tumors was higher in the o/s-SSI− group than in the o/s-SSI+; however, the difference was not statistically significant. The total bilirubin, albumin, and HbA1c levels did not differ significantly between the two groups. The WBC counts (7981±3775/mL *vs.* 6120±2198/mL, p<0.05) and CRP levels (5.5±8.7 mg/dL *vs.* 2.0±3.0 mg/dL p<0.05) were significantly higher in the o/s-SSI+ group than those in the o/s-SSI− group. The incidence of preoperative biliary stent placement and ASA-PS classifications did not differ significantly between the two groups. Among operative variables, blood loss was significantly higher in the o/s-SSI+ group than that in the o/s-SSI− group (1389±843 mL *vs.* 980±467 mL, p<0.05), and blood transfusions were performed more frequently in the o/s-SSI+ group than in the o/s-SSI− group (17/29 *vs.* 22/64, p<0.05); however, operative time and volume of peritoneal lavage did not differ significantly between the two groups. The open drain induced o/s-SSI significantly more frequently than the closed drain (18/41 *vs.* 11/52, p<0.05). The duration of prophylactic antibiotic administration was significantly longer in the o/s-SSI+ group than in the o/s-SSI− group (12.3±13.3 days *vs.* 4.8±2.4 days, p<0.0001). The duration of drain placement was significantly longer in the o/s-SSI+ group than in the o/s-SSI− group (36.3±26.5 days *vs.* 11.5±6.2 days, p <0.000000001). All grades of pancreatic fistulas occurred in 54 of 93 patients, and they were significantly more common in the o/s-SSI+ group than in the o/s-SSI− group (25 of 29 patients *vs.* 29 of 64 patients, p <0.001). High-grade (grades B and C) pancreatic fistulas were not observed in the o/s-SSI− group (13 of 29 patients *vs.* 0 of 64 patients, p <0.0000001).

Risk Factors for o/s-SSI

The risk factors for o/s-SSI in univariate analysis are presented in **Table 2**. The risk factors included blood transfusion (OR, 2.70; p<0.05), peritoneal lavage volume<5,000 mL (OR, 3.08; p<0.05), open type of prophylactic drain (OR, 2.92; p<0.05), and the incidence of pancreatic fistula (OR, 7.54, p<0.001).

Multivariate logistic regression analysis did not reveal an independent risk factor among the risk factors for o/s-SSI.

Microorganisms Related to o/s-SSI

Twenty-nine of the 93 patients were diagnosed with o/s-SSI. **Table 3** shows the microorganisms detected in cultured fluid from the prophylactic drain when o/s-SSI was clinically suspected. The microorganisms belonging to intestinal flora were isolated from the drained fluid sampled from 22 out of the 29 patients (75.9%). The postoperative period, when microorganisms were detected in the drained fluid, was 9.4±4.5 days (2 – 22 days, median 9 days). There was not a significant difference in this period between patients with open drains (8.4±5.1 days,

Table 1. Patient characteristics and perioperative variables of all patients.

Organ/space Surgical site infection		+	-	p value
Age		73.1±10.2	72.0±8.9	0.4239
Sex	Male	20	38	0.3765
	Female	9	26	
BMI		23.1±3.6	20.7±2.9	<0.01
Indication for surgery	Pancreas head tumor	9	36	0.2141
	Bile duct tumor	16	18	
	Tumor of papilla Vater	2	5	
	Duodenal tumor	2	3	
	Others	1	1	
Laboratory data	Total bilirubin [mg/dL]	5.8±6.0	7.7±6.4	0.2542
	Albumin [g/dL]	4.0±0.6	3.8±0.5	0.2087
	Hemoglobin A1c [%]	6.0±2.0	6.1±2.0	0.7423
	White blood cell [/µL]	7981±3775	6120±2198	<0.05
	C reactive protein [mg/dL]	5.5±8.7	2.0±3.0	<0.05
Preop biliary stent	+/-	23/6	42/22	0.7498
ASA-PS	1/2/3	1/26/2	4/52/8	0.3526
Operative variables				
	Time [minutes]	563±126	515±108	0.0615
	Blood loss [mL]	1389±843	980±467	<0.05
	Blood transfusion			
	+/-	17/12	22/42	<0.05
	[units]	5.1±3.4	4.4±1.3	0.3454
	Peritoneal lavage [mL]	3669±2294	6143±1618	0.3072
	Drain			
	Open	18	23	<0.05
	Closed	11	41	
Postoperative variables				
	Duration of antibiotics [days]	12.3±13.3	4.8±2.4	<0.0001
	Duration of drainage [says]	36.3±26.5	11.5±6.2	<0.000000001
	Pancreatic fistula			
	+/-	25/4	29/35	<0.001
	Grade B*/non & A	13/16	0/64	<0.0000001

BMI body mass index; Preop preoperative

* Grade C was not experienced in this series.

Table 2. Risk factors for organ/space surgical site infection on univariate analyses.

		Odds ratio	95% CI	p value
Age [years]	≥75	1.49	0.61 – 3.59	0.3781
Sex	Male	1.52	0.60 – 3.86	0.3765
BMI	≥21	2.1	0.86 – 5.16	0.1017
Total bilirubin [mg/dl]	≥2.0	2.86	0.56 – 14.57	0.1904
Albumin [g/dl]	<4.0	0.69	0.25 – 1.94	0.486
Hemoglobin A1c [%]	≥6.0	0.75	0.25 – 2.23	0.6016
White blood cell [/ml]	≥6,000	1.91	0.68 – 5.35	0.2147
C reactive protein [mg/dl]	≥1.0	1.88	0.66 – 5.35	0.2372
Preoperative biliary drainage	Yes	2.01	0.71 – 5.66	0.1826
Operative time [minutes]	≥480	1.8	0.69 – 4.67	0.2265
Blood loss [ml]	≥1,000	2.24	0.91 – 5.51	0.3346
Blood transfusion	Yes	2.7	1.10 – 6.66	<0.05
Peritoneal lavage [ml]	<5,000	3.08	1.19 – 7.98	<0.05
Type of prophylactic drain	Open	2.92	1.18 – 7.23	<0.05
Type of prophylactic antibiotics	3rd generation	2.65	0.68 – 10.36	0.1521
Pancreatic fistula	Yes	7.54	2.35 – 24.17	<0.001

BMI body mass index; CI confidence intervals

Table 3. Microorganisms detected in specimens from organ/space surgical site infections.

Patient No.	Detected microorganisms			Contained intestinal flora	Type of drain	Postoperative day microorganisms detected
1	*Enterococcus faecalis**	*Candida albicans*	*Candida glabrata*	Yes	Closed	16
2	*Enterococcus faecium**			Yes	Open	7
3	*Enterobacter cloacae**	*Pseudomonas aeruginosa*		Yes	Open	7
4	*Citrobacter freundii**			Yes	Closed	8
5	*Pseudomonas aeruginosa*			No	Open	9
6	*S. maltophilia*			No	Open	11
7	*Enterococcus faecium**	*Acinetobacter baumannii*		Yes	Open	6
8	*Streptococcus viridans*	*GPR*		No	Closed	13
9	*S. maltophilia*			No	Closed	14
10	*MRSA*			No	Closed	12
11	*MRSA*			No	Open	22
12	*Enterococcus faecium**			Yes	Open	6
13	*Escherichia coli**	*Klebsiella pneumoniae**	*Klebsiella oxytoca**	Yes	Open	9
14	*Enterococcus faecium**			Yes	Closed	9
15	*Enterococcus faecalis**	*Anaerobic GNC**	*Pseudomonas aeruginosa*	Yes	Closed	12
16	*Klebsiella oxytoca**			Yes	Open	14
17	*Enterococcus faecium**	*Enterobacter cloacae**	*Citrobacter freundii**	Yes	Open	2
18	*Enterococcus faecalis**	*Pseudomonas aeruginosa*	*MRSA* *S. haemolyticus*	Yes	Open	5
19	*Enterococcus faecium**			Yes	Open	2
20	*Enterococcus faecalis**	*S. maltophilia*		Yes	Closed	11
21	*Enterococcus faecium**	*Klebsiella pneumoniae**		Yes	Open	6
22	*Enterobacter cloacae**			Yes	Closed	7
23	*Enterococcus faecalis**	*Escherichia coli**	*Klebsiella oxytoca**	Yes	Open	6
24	*MRSA*			No	Open	16
25	*Enterococcus faecalis**			Yes	Closed	13
26	*Enterococcus faecium**			Yes	Open	10
27	*Enterococcus faecalis**			Yes	Open	11
28	*Enterobacter cloacae**			Yes	Open	3
29	*Enterococcus faecalis**			Yes	Closed	7

GNC gram-negative coccus; GPR gram-positive rod; MRSA methicillin-resistant *Streptococcus aureus*; *S. maltophilia stenotrophomonas maltophilia*; *S. haemolyticus streptococcus haemolyticus*

Asterisk (*) indicates the microorganism belonging to the intestinal flora.

2 – 22 days, median 7 days) and those with closed drains (11.1±3.0 days, 7 – 16 days, median 12 days) (p = 0.1300).

The 48 detected microorganisms included 30 (62.5%) typically observed in intestinal flora, 7 (14.6%) from environmental flora, 7 (14.6%) from skin flora, 1 (2.1%) from oral flora, 2 (4.3%) from fungi, and 1 (2.1%) from unclassified gram-positive rod. Bacteria of intestinal flora were the most common cause of o/s-SSI **(Table 4)**.

When classified by the type of drain, intestinal flora were identified in samples from 21 patients (67.7%), environmental flora in four patients (12.9%), and skin flora in six patients (19.4%) with open drains, while intestinal flora were identified in samples from nine patients (52.3%), environmental flora in three patients (17.6%), skin flora in two patients (11.8%), fungus in two patients (11.8%), and unclassified gram-positive rod in one patient (5.9%) with closed drains. These results indicated that there was not a significant difference between the two types of prophylactic drain.

Microorganisms were identified in preoperatively sampled bile or intra-operatively collected biliary stent from 15 of 29 patients with o/s-SSI. In 11 of the 15 patients (73.3%), these microorganisms were the same kind as those detected at the site of the o/s-SSI. Pre- and intraoperative samples from the remaining 14 patients were free from biliary microorganisms; in 10 of these patients (71.4%), the microorganisms detected in the o/s-SSI samples belonged to intestinal bacterial flora (p = 0.1729).

DISCUSSION

SSI is the most common type of nosocomial infection, which is defined as an operation-related infection that occurs at or near the incision site within 30 days, according to the criteria from the United States Centers for Disease Control and Prevention (CDC) [13].

The reported incidence rates of o/s-SSI after colorectal surgery, and hepatectomy are 2.8–10% [5, 14, 15] and

4.0–8.6% [16, 17]. In comparison, the reported incidence rates of o/s-SSI after PD are 47.8% (195 of 408 cases) [9] and 45.0% (27 of 60 cases) [18]. In the present study, the incidence of o/s-SSI after PD was 31.2% (29 of 93 cases), which was much higher than that after any other type of abdominal operation.

The relationship between prophylactic abdominal drains and o/s-SSI has become the subject of debate. Kato *et al*. reported that intra-abdominal abscesses after PD were found in the open-drain group only [19], and Sugiura *et al*. showed in multivariate analysis that the use of semi-closed drain system was significantly associated with o/s-SSI [9]. Also in our series, open drains were picked up as a risk factor for o/s-SSI. The superiority of closed-type drains has been confirmed for the suppression of o/s-SSI.

Only one paper was found, which concluded that perioperative transfusions were associated with increased risk factors of surgical site infections in newborns [20]. Also in our analyses, intraoperative blood transfusion was one of the risk factors of o/s-SSI. Because the necessity of blood transfusion depends on the condition of the patients, our efforts not to transfuse are limited.

There have been several reports of pancreatic fistulas as a risk factor for o/s-SSI after PD. Sugiura *et al*. emphasized that the presence of pancreatic fistulas was the strongest risk factor for o/s-SSI [9], and Nanashima *et al*. reported the results of multivariate analysis indicating that only postoperative pancreatic fistulas were significantly associated with SSIs [21]. Because there is a report that infection control could effectively prevent pancreatic fistulas [22], it is clear that there may be a close relationship between pancreatic fistulas and o/s-SSI.

To our knowledge, no reports have concluded that prophylactic drain placement after PD is meaningless for the prevention of o/s-SSI. Many authors [23, 24, 25] concluded that prophylactic drainage after pancreatic resection did not decrease the frequency and severity of postoperative complication; however, they did not always deny drain placement. Wang *et al*. [23] concluded that the necessity of drain placement was controversial, and Dou *et al*. [8] stated in their systematic review and meta-analysis that, although prophylactic drain placement did not have a beneficial effect on the clinical outcome, it did not significantly increase the risk of abdominal abscess formation and that the elimination of prophylactic abdominal drainage after PD led to a significantly increased mortality rate (OR, 2.39; p = 0.01). Based on the literature, it is impossible to deny the requirement of prophylactic drain placement after PD.

Kawai *et al*. reported that drain removal on postoperative day 4 was an independent factor in reducing the incidence of intra-abdominal infection [10]. Bassi *et al*. also reported that a prolonged period of drain insertion was associated with a higher rate of postoperative complication, and that, in patients at low risk of pancreatic fistula, drains could be safely removed on post-operative day three [11].

Thus, although the propriety of prophylactic drain placement is controversial, there appears to be a consensus that o/s-SSI may be less of a concern if the drain were to

Table 4. Classification of microorganisms detected in specimen at organ/space surgical site infection.

Cultured Microorganisms		Positive Titer of Cultured Microorganisms									Total	Total in Group	% in total
Intestinal flora	*Enterococcus faecium*	2	3	4	3	2	2	3	2	1	9	30	62.5
	Enterococcus faecalis	1	3	1	2	2	2	1			7		
	Enterobacter cloacae	4	2	1	3						4		
	Klebsiella oxytoca	1	2	2							3		
	Klebsiella pneumonia	3	2								2		
	Escherichia coli	2	2								2		
	Citrobacter freundii	3	4								2		
	Anaerobic GNC	1									1		
Environmental flora	*Pseudomonas aeruginosa*	4	2	3	3						4	7	14.6
	Stenotrophomonas maltophilia	4	3	1							3		
Skin bacterial flora	MRSA	3	3	3	3						4	7	14.6
	Streptococcus haemolyticus	3									1		
	Acinetobacter baumannii	2	4								2		
Oral bacterial flora	*Streptococcus viridans*	2									1	1	2.1
Fungus	*Candida albicans*	1									1	2	4.3
	Candida glabrata	1									1		
Others	GPR	2									1	1	2.1

GNC gram-negative coccus; GPR gram-positive rod; MRSA methicillin-resistant Staphylococcus aureus

Table 5. Transmission of detected microorganisms from pre- or intraoperatively to postoperatively in o/s-SSI.

Patient No.	Microorganisms detected pre- or intraoperatively						Transmission	Microorganisms detected postoperatively in o/s-SSI			
1	*K. oxytoca*	*C. freundii*	***C. glabrata***	***C. albicans***	*E. cloacae*	***E. faecalis***	Yes	***E. faecalis***	***C. albicans***	***C. glabrata***	
2	***E. faecium***						Yes	***E. faecium***			
3								*E. cloacae*	*P. aeruginosa*		
4	***C. freundii***						Yes	***C. freundii***			
5								*P. aeruginosa*			
6								*S. maltophilia*			
7								*A. baumannii*	*E. faecium*		
8								GPR	*S. viridans*		
9	*K. oxytoca*	*E. faecalis*					No	*S. maltophilia*			
10	*E. casseliflavus*	*E. faecalis*					No	MRSA			
11								MRSA			
12								*E. faecium*	*A. baumannii*		
13								*K. pneumoniae*	*E. coli*	*K. oxytoca*	
14	*E. aerogenes*	*A. hydrophilia*					No	*E. faecium*			
15	*E. coli*	***P. aeruginosa***	*C. glabrata*	*K. oxytoca*	***E. faecium***		Yes	***P. aeruginosa***	Anaerobic GNC	***E. faecium***	
16	***K. oxytoca***						Yes	***K. oxytoca***			
17								*E. cloacae*	*E. faecalis*	*C. freundii*	
18								*E. faecalis*	*P. aeruginosa*	MRSA	*S. haemolyticus*
19	*E. faecalis*	***E. faecium***					Yes	***E. faecium***			
20								*E. faecalis*	*S. maltophilia*		
21								*K. pneumoniae*	*E. faecium*		
22	***K. cloacae***						Yes	***E. cloacae***			
23	***E. coli***	*E. avium*	***K. oxytoca***				Yes	***E. coli***	***K. oxytoca***	*E. faecalis*	
24	*S. mitis*						No	MRSA			
25								*E. faecalis*			
26								*E. faecium*			
27	***E. faecalis***						Yes	***E. faecalis***			
28	***E. cloacae***						Yes	***E. cloacae***			
29	*E. coli*	***E. faecalis***					Yes	***E. faecalis***			

A. baumannii acinetobacter baumannii; A. hydrophilia aeromonas hydrophilia; C. albicans candida albicans; C. freundii citrobacter freundii; C. glabrata candida glabrata; E. aerogenes enterobacter aerogenes; E. avium enterococcus avium; E. casseliflavus enterococcus casseliflavus; E. cloacae enterobacter cloacae; E. coli escherichia coli; E. faecalis enterococcus faecalis; E. faecium enterococcus faecium; GNC gram-negative coccus; GPR gram-positive rod; K. oxytoca Klebsiella oxytoca; K. pneumoniae klebsiella pneumoniae; MRSA methicillin-resistant Staphylococcus aureus; P. aeruginosa pseudomonas aeruginosa; S. haemolyticus streptococcus haemolyticus; S. maltophilia stenotrophomonas maltophilia; S. mitis streptococcus mitis; S. viridans streptococcus viridans
The bacteria supposed to be transmitted are indicated in bald letters.

be removed within term three to four days. However, this consensus is inconsistent with the actual clinical course after PD.

Sugiura *et al.* concluded that bacterial contamination during PD had an adverse impact on the development of o/s-SSI [26]. Horzog *et al.* also concluded that SSI was often caused by the same microorganisms that were present in intraoperative bile duct cultures [27]. In addition, we showed intraoperative peritoneal lavage volumes <5000 mL to be a significant risk factor by univariate analysis for the occurrence of o/s-SSI; furthermore, the use of the antibiotics effective against the bacteria detected in the perioperative bile samples inhibit the occurrence

of postoperative peritoneal infections [28, 29, 30]. Thus, microorganisms derived from the bile may contaminate the abdominal cavity intra-operatively, and induce o/s-SSI.

In our analyses, intestinal bacterial flora was detected in 75.9% patients with o/s-SSI **(Table 3)**, and comprised 62.5% of all detected bacteria in patients with o/s-SSI **(Table 4)**. Herzog *et al*. [27] and Sugiura *et al*. [9] also reported gut-derived microorganisms to be the predominant bacterial species in SSI foci. Because biliary bacteria are gut-derived and bile contamination may be the main cause of o/s-SSIs and intestinal bacteria were identified in o/s-SSI in patients with both open and closed drains, there is no contradiction in the

conclusion that the origin of most o/s-SSI after PD was the intra-peritoneal space or organs and that retrograde infection through prophylactic drains is not the main cause of o/s-SSI **(Table 5)**.

CONCLUSION

The results of the current study confirm that pancreatic fistulae are the most significant risk factor of o/s-SSI after PD; in addition, based on our analysis of the microorganisms detected in patients with o/s-SSI, the main causative microorganisms of o/s-SSI originate in the peritoneal space or organs. Several authors have recommended early removal of prophylactic drain in order to prevent retrograde infection through the drain, which could make o/s-SSI worse; therefore, it is necessary to analyze and investigate the various aspects related to drain management after PD.

Conflict of Interest

The authors have no financial conflicts of interest concerning the manuscript to disclose.

References

1. Berenguer CM, Ochsner MG Jr, Lord SA, Senkowski CK. Improving surgical site infections: using national surgical quality improvement program data to institute surgical care improvement project protocols in improving surgical outcomes. J Am Coll Surg 2010; 210:737-741. [PMID: 20421041]

2. Mahmoud NN, Turpin RS, Yang G, Saunders WB. Impact of surgical site infections on length of stay and cost in selected colorectal procedures. Surg Infect 2009; 10:539-544. [PMID: 19708769]

3. Urban JA. Cost analysis of surgical site infections. Surg Infect 2006; 7 Suppl 1:S19-22. [PMID: 16834543]

4. Liu HP, Zhang YC, Zhang YL, Yin LN, Wang J. Drain versus no-drain after gastrectomy for patients with advanced gastric cancer: systematic review and meta-analysis. Dig Surg 2011; 28:178-189. [PMID: 21540606]

5. Tang R, Chen HH, Wang YL, Changchien CR, Chen JS, Hsu KC, et al. Risk factor for surgical site infection after elective resection of the colon and rectum: a single-center prospective study of 2,809 consecutive patients. Ann Surg 2001; 234:181-189. [PMID: 11505063]

6. Petrowsky H, Demartines N, Rousson V, Clavien PA. Evidence-based value of prophylactic drainage in gastrointestinal surgery. Ann Surg 2004; 240:1074-1085. [PMID: 15570212]

7. Van Buren G 2nd, Bloomston M, Hughes SJ, Winter J, Behrman SW, Zyromski NJ, et al. A randomized prospective multicenter trial of pancreaticoduodenectomy with and without routine intraperitoneal drainage. Ann Surg 2014; 259:605-612. [PMID: 24374513]

8. Dou CW, Liu ZK, Jia YL, Zheng X, Tu KS, Yao YM, et al. Systemic review and meta-analysis of prophylactic abdominal drainage after pancreatic resection. World J Gasrtoeterol 2015;21: 5719-5734. [PMID: 25987799]

9. Sugiura T, Uesaka K, Ohmagari N, Kanemoto H, Mizuno T. Risk factor of surgical site infection after pancreaticoduodenectomy. World J Surg 2012; 36:2888-2894. [PMID: 22907393]

10. Kawai M, Tani M, Terasawa H, Ina S, Hirono S, Nishioka R, et al. Early removal of prophylactic drains reduced the risk of intra-abdominal infections in patients with pancreatic head resection. Ann Surg 2006; 244: 1-7. [PMID: 16794381]

11. Bassi C, Molinari E, Malleo G, Crippa S, Butturini G, Salvia R, et al. Early versus late drain removal after standard pancreatic resections: results of a prospective randomized trial. Ann Surg 2010; 252:207-214. [PMID: 20622661]

12. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, et al. International Study Group on Pancreatic Fistula Definition. Postoperative pancreatic fistula: an international study group (ISDPF) definition. Surgery 2005; 138:8-13. [PMID: 16003309]

13. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Infect Control Hosp Epidemiol 1992; 13:606-608. [PMID: 1334988]

14. Biondo S, Kreisler E, Fraccalvieri D, Basany EE, Codina-Cazador A, Ortiz H. Risk factors for surgical site infection after elective resection for rectal cancer. A multivariate analysis on 2131 patients. Colorectal Dis 2012; 14:e95-e102. [PMID: 21883813]

15. Ho VP, Barie PS, Stein SL, Trencheva K, Milsom JW, Lee SW, et al. Antibiotic regimen and the timing of prophylaxis are important for reducing surgical site infection after elective abdominal colorectal surgery. Surg Infect (Larchmt) 2011; 12:255-260. [PMID: 21790479]

16. Kokudo T, Uldry E, Demartines N, Halkic N. Risk factors for incisional and organ space surgical site infections after liver resection are different. World J Surg 2015; 39:1185-1192. [PMID: 25561190]

17. Sadamori H, Yagi T, Shinoura S, Umeda Y, Yoshida R, Satoh D, et al. Risk factors for major morbidity after liver resection for hepatocellular carcinoma. Br J Surg 2013; 100:122-129. [PMID: 23175234]

18. Kimura F, Shimizu H, Yoshidome H, Ohtsuka M, Kato A, Yoshitomi H, et al. Increased plasma levels of IL-6 and IL-8 are associated with surgical site infection after pancreaticoduodenectomy. Pancreas 2006; 32:178-185. [PMID: 16552338]

19. Kato D, Sasaki T, Yamashita K, Shinya S, Nakashima R, Yamashita Y, et al. Drain selection reduces pancreatic fistulae risk: a propensity-score matched study. Hepatogastroenterology 2015; 62:485-492. [PMID: 25916087]

20. Fawley J, Chelius TH, Anderson Y, Cassidy LD, Arca MJ. Relationship between perioperative blood transfusion and surgical site infections in the newborn population: An ACS-NSQIP-Pediatrics analysis. J Pediatr Surg 2016; 51:1397-1404. [PMID: 27325358]

21. Nanashima A, Abo T, Arai J, Oyama S, Mochinaga K, Matsumoto H. Clinicopathological parameters associated with surgical site infection in patients who underwent pancreatic resection. Hepatogastroenterology 2014; 61:1739-1743. [PMID: 25436372]

22. Kobayasi S, Gotohda N, Kato Y, Takahashi S, Konishi M, Kinoshita T. Infection control for prevention of pancreatic fistula after pancreaticoduodenectomy. Hepatogastroenterology 2013; 60:876-882. [PMID: 23732781]

23. Wang Q, Jiang YJ, Li J, Yang F, Di Y, Yao L, et al. Is routine drainage necessary after pancreaticoduodenectomy? World J Gastroenterol 2014; 20:8110-8118. [PMCID: PMC4081682]

24. Adham M, Chopin-Laly X, Lepilliez V, Gincul R, Valette PJ, Ponchon T. Pancreatic resection: drain or no drain? Surgery 2013; 154:1069-1077. [PMID: 23876363]

25. Kaminsky PM, Mezhir JJ. Intraperitoneal drainage after pancreatic resection: a review of the evidence. J Surf Res 2013; 184: 925-930. [PMID: 23866787]

26. Sugiura T, Mizuno T, Okamura Y, Ito T, Yamamoto Y, Kawamura I, et al. Impact of bacterial contamination of the abdominal cavity during pancreaticoduodenectomy on surgical-site infection. Br J Surg 2015; 102:1561-1566. [PMID: 26206386]

27. Herzog T, Belyaev O, Akkuzu R, Hölling J, Uhl W, Chromik AM. The impact of bile duct cultures on surgical site infection in pancreatic surgery. Surg Infect 2015; 16:443-449. [PMID: 26110464]

28. Sudo T, Murakami Y, Uemura K, Hashimoto Y, Kondo N, Nakagawa N, et al. Perioperative antibiotics covering bile contamination prevent abdominal infectious complications after pancreaticoduodenectomy in patients with preoperative biliary drainage. World J Surg 2014; 38:2952-2959. [PMID: 25022981]

29. Augenstein VA, Reuter NP, Bower MR, McMasters KM, Scoggins CR, Martin RC. Bile cultures: a guide to infectious complications after pancreaticoduodenectomy. J Surg Oncol 2010; 102:478-481. [PMID: 20872951]

30. Kondo K, Chijiiwa K, Ohuchida J, Kai M, Fujii Y, Otani K, et al. Selection of prophylactic antibiotics according to the microorganisms isolated from surgical site infection (SSIs) in a previous series of surgeries reduces SSI incidence after pancreaticoduodenectomy. J Hepatobiliary Pancreat Sci 2013; 20:286-293. [PMID: 22481442]