Langenbeck's Archives of Surgery (2023) 408:333
https://doi.org/10.1007/s00423-023-03080-3

RESEARCH

Failure of peritoneal lavage to prevent operative site infection and peritoneal tumor recurrence in pancreatic surgery

Mai Ishihara[1] · Akihiro Nakamura[1] · Yuki Takahashi[1] · Yuzo Minegishi[1] · Kenichi Matsuo[1] · Kuniya Tanaka[1]

Received: 6 March 2023 / Accepted: 18 August 2023 / Published online: 25 August 2023

Abstract

Background Although intraoperative peritoneal lavage often is performed routinely with the aim of reducing peritoneal contamination, evidence of lavage benefit in elective pancreatic surgery is limited.

Methods We retrospectively classified patients who had undergone pancreatic surgery to groups given or not given peritoneal lavage, then comparing clinical results. This saline lavage was performed at the end of the operation. The primary endpoint was rate of surgical site infection. Frequency of peritoneal recurrence also was evaluated.

Results Among all 104 patients in the study, incidence of infectious complications in the lavage group ($n = 65$) was significantly higher than in the non-lavage group ($n = 39$; 35% vs. 15%, $P = 0.041$), while incidences of postoperative complications overall and surgical site infection did not differ between lavage (80% and 26%) and non-lavage groups (67% and 10%, $P = 0.162$ and 0.076, respectively). Among 63 patients undergoing pancratoduodenectomy, frequencies of positive bacterial cultures of drainage fluids on postoperative days 1 and 3 were greater in the non-lavage group ($P < 0.001$ and $P = 0.012$), but surgical site infection was significantly more frequent in the lavage group ($P = 0.043$). Among patients with pancreatic and biliary cancers, lavage did not affect frequency of peritoneal recurrence.

Conclusion Intraoperative lavage did not prevent surgical site infection or peritoneal recurrence of pancreatobiliary cancer.

Keywords Peritoneal lavage · Surgical site infection · Pancreas · Cancer recurrence

Abbreviations

BMI	Body mass index
CI	Confidence interval
CT	Computed tomography
CTx	Chemotherapy
DP	Distal pancreatectomy
Hb	Hemoglobin
ISGPF	International Study Group on Pancreatic Fistula Definition
PD	Pancreatoduodenectomy
PNI	Prognostic nutritional index
POD	Postoperative day
POPF	Postoperative pancreatic fistula
PV	Portal vein
R	Resection
RAMPS	Radical antegrade modular pancreato-splenectomy
RFS	Recurrence-free survival
SMA	Superior mesenteric artery
SMV	Superior mesenteric vein
SSI	Surgical site infections
TP	Total pancreatectomy

Introduction

With refinement of surgical technique, operative equipment, and perioperative management, operative mortality of pancreatic surgery has decreased to less than 3% of patients undergoing pancreatoduodenectomy (PD) [1–3] and about 1% for both distal [4] and total pancreatectomy [5]. However, pancreatic surgery still carries substantial risk of postoperative complications, ranging from 40 to 70% [6–8]. Complications include pancreatic fistula, biliary fistula, and delayed gastric emptying. Among these, septic complications have occurrence rates around 35% [9]. Wound infections and intraabdominal abscesses arising in proximity to

✉ Kuniya Tanaka
u1792ts235@med.showa-u.ac.jp

[1] General and Gastroenterological Surgery, Showa University Fujigaoka Hospital, 1-30 Fujigaoka, Aoba-ku, Yokohama, Kanagawa 227-8501, Japan

intraoperative manipulations, collectively considered surgical site infections (SSI), represent the most common septic complication following pancreatic surgery [9]. As overall incidence of SSI after pancreatic surgery is reported to be about 25% [10], control of infectious complications, especially SSI, is particularly important for further increasing safety of these procedures.

Intraoperative peritoneal lavage is performed routinely at the end of the operation, with the aim of reducing peritoneal contamination. According to a previous report [11], 97% of surgeons practiced intraoperative peritoneal lavage, while 34% included lavage even in macroscopically clean cases; about 36% performed lavage during intraabdominal cancer surgery. Several studies have concluded that intraoperative peritoneal lavage decreased postoperative infectious morbidity and mortality [12, 13]. Nonetheless, widespread acceptance of this treatment may owe more to historic practice than to rigorous evaluation, so debate continues as to whether lavage should be performed.

So far, only scarce data are available concerning occurrence of surgical site infections (SSI) after pancreatic procedures that included intraoperative peritoneal lavage. We therefore retrospectively investigated efficacy of intraoperative peritoneal lavage in reducing postoperative infectious complications of pancreatic surgery. We also evaluated frequency of peritoneal recurrence after pancreatectomy for malignant diseases.

Patients and methods

Patients who underwent pancreatic surgery at Showa University Fujigaoka Hospital, Yokohama, Japan during the years 2019 to 2021 were enrolled retrospectively, numbering 104. Among them, PD was performed in 62, distal pancreatectomy (DP) in 37, and total pancreatectomy (TP) in 5. Peritoneal lavage was performed routinely at the end of the operation for patients undergoing pancreatic surgery before November 2020, but not for patients undergoing such surgery during or after November 2020. Accordingly, peritoneal lavage was performed for 65 patients and not performed for 39.

Study intervention

All patients in this study underwent open pancreatic surgery; none underwent a laparoscopic operation. Preoperative biliary drainage was performed using an endoscopic nasal approach when serum concentrations of total bilirubin exceeded 5 mg/dL and intrahepatic bile ducts appeared dilated in images.

All PD patients underwent subtotal stomach-preserving pancreatoduodenectomy including duct-to-mucosa, end-to-side pancreatojejunostomy. An internal or external pancreatojejunal stent was placed to assure flow of pancreatic juice to the jejunum. Internal stents typically passed spontaneously within 1 to 2 months after surgery, while external stents were clamped at about 2 weeks and removed 2 months after surgery. Internal or external stents were selected case-by-case according to the surgeon's preference. After pancreatic reconstruction, end-to-side hepatojejunostomy and end-to-side gastrojejunostomy were performed with an antecolic Billroth type II reconstruction. For total pancreatectomy, end-to-side hepaticojejunostomy and gastrojejunostomy with Billroth type II reconstruction were performed, including reduction of the size of the remnant stomach when findings indicating congestion were apparent from intraoperative indocyanine green fluorescence imaging [14]. Regional lymphadenectomy was routinely performed. Dissection of the nerve plexus surrounding the superior mesenteric artery (SMA) was avoided in most patients in order to prevent severe postoperative diarrhea. Even when tumor invasion of the SMA nerve plexus was suspected, only the right side of this SMA nerve plexus was dissected. Partial resection of the superior mesenteric vein (SMV) or portal vein (PV) was carried out if the surgeon observed tumor invasion of the vein. Venous continuity was restored by end-to-end anastomosis or interposition of a venous graft.

Radical antegrade modular pancreato-splenectomy (RAMPS) [15] was carried out for patients undergoing DP. In brief, these operations proceeded from the pancreatic head toward the tail, with early division of the pancreas. Splenectomy was performed as the final stage of the procedure, except in 2 patients undergoing spleen-preserving DP.

During PD, 2 closed suction drains (J-Vac drain, Johnson & Johnson, Somerville, NJ, USA) were placed near the hepatojejunostomy and pancreatojejunostomy in both lavage and non-lavage groups. Two closed-suction drains also were placed near the cut end of the pancreas and the left subphrenic space during DP. Closed-suction drains were placed near the hepatojejunostomy and left subphrenic space during TP. The drains were brought out through a separate stab wound in the anterior abdominal wall and connected to a closed collection system. Patient warming devices were used during the operation. In both groups, wound washout was performed using 2 L of warm sterile saline after fascial closure but before skin closure.

After removal of the resected specimen and confirmation of hemostasis, the lavage group underwent irrigation with sterile saline at approximately 37 °C, directed particularly at the dissected area. The 2 L saline volume was based upon previous reports in which lavage generally used at least 1 L, continuing until the fluid was clear [11].

Postoperative management

All patients routinely received a prophylactic antibiotic (cefmetazole sodium; Alfresa Pharma Co., Osaka, Japan). On the day of operation, 1 g was administered intravenously 30 min before surgery, 1 g every 3 h during surgery, and 1 g 2 h after completion of surgery. Following the day of operation, 2 g was given daily (1 g every 12 h) until postoperative day (POD) 4. This dosage protocol was generally the same for patients with preoperative biliary drainage.

Drainage fluid was cultured on POD 1 and POD 3. The abdominal drainage tube usually was removed 4 postoperative days after disappearance of abnormal fluid collections from the dissected area according to computed tomography (CT) which routinely was performed on POD 4, provided that the amylase concentration in drainage fluids was less than 3 times the serum concentration. Delays in tube removal were allowed if intraabdominal infection or pancreatic fistula developed. Patients were discharged when all of the following predetermined criteria were met: absence of signs of systemic infection such as fever, toleration of meals without nausea or vomiting, normalization of all hematologic and biochemical test results, and adequate pain control with oral analgesia.

Study endpoints

Primary outcome measures for this study were rates of postoperative complications and infectious complications, especially SSI, at the time of a follow-up assessment 4 weeks after surgery. Success was defined as absence of signs or symptoms of complications including infection and lack of need for further antimicrobial therapy or surgery. All inpatient morbidity was recorded prospectively as a component of routine patient care. Assessment of complications followed a recently published standardized complication assessment system (Dindo-Clavien classification) [16]. Complications were defined as any deviations from an uneventful postoperative course. Failure to prevent infection was determined on the basis of criteria for SSI developed by the Centers for Disease Control [17]. SSI was defined as incisional infection (either superficial or deep) or infection in an organ or space. Superficial incisional infection involved skin and subcutaneous tissue, while deep incisional infection involved deeper soft tissue related to the incision. Organ or space infection involved any organ or space other than the incised layers of body wall that were opened or manipulated during the initial surgical procedure. Incisional infection was defined by clinically apparent cellulitis, induration, or purulent discharge from the closure site. Organ or space infection was defined by radiologic evidence of a fluid collection necessitating drainage or need for antibiotic therapy when drainage was difficult to establish. Remote infection was defined as a condition where bacteria were detected in sputum, blood, or urine, in association with signs of inflammation such as leukocytosis and fever. Postoperative pancreatic fistula (POPF) was defined as drainage fluid with an amylase concentration 3 times that in serum. Such fistulas were graded according to standards of the International Study Group on Pancreatic Fistula Definition (ISGPF) [18]. When amylase concentrations in drainage fluid remained high at POD 4 (typically more than 1000 IU/L) and the white blood cell count or serum C-reactive protein was persistently high, we initiated saline irrigation in the area of the pancreatojejunostomy, collecting the fluid via the drains inserted intraoperatively, aiming to reduce amylase in the drainage fluid. New drains were substituted during this process as appropriate. These patients were considered to have grade B postoperative pancreatic fistula (POPF). Biliary fistula was defined as presence of bile in drainage fluid that remained detectable at POD 4. Following surgery for malignant disease, we additionally evaluated frequency of peritoneal recurrence. To detect disease recurrence, serum tumor markers such as carcinoembryonic antigen, carbohydrate antigen (CA) 19-9, Duke pancreatic monoclonal antigen (DU-PAN)-2, and S-pancreas-1 antigen (SPan)-1 were evaluated monthly; CT was performed every 4 months.

Other data recorded

Vital signs were recorded daily while the patient was hospitalized and at the 4-week follow-up assessment. Nutritional status was evaluated using a prognostic nutritional index (PNI) derived from the peripheral blood lymphocyte count and the serum albumin concentration according to the formula: lymphocyte count (/mm^2) × 0.005 + serum albumin (g/dL) × 10 [19]. Drainage fluid specimens for bacteriologic culture were obtained from all patients early in the morning on postoperative days 1 and 3. Amylase concentrations in drainage fluids were assessed on each postoperative day until removal of drainage tubes. Investigators performed detailed wound assessments at least daily for up to 7 days during hospitalization, at discharge, and at the 4-week follow-up visit.

Statistical analysis

Continuous variables were expressed as the median with range or the mean ± standard deviation and compared using the Mann-Whitney *U* test. Categorical variables, expressed as numbers followed by percentages in parentheses, were analyzed with Fisher's exact test. Univariate and multivariate analyses were performed using a Cox proportional hazard model. Cumulative recurrence-free survival (RFS) was

calculated using the Kaplan–Meier method, and differences between curves were evaluated using the log-rank test. A difference was considered significant when the 2-sided *P* value was below 0.05. All statistical analyses were carried out using SPSS statistical software (version 23; IBC SPSS, Chicago, IL, USA).

Ethical approval and consent to participate

The study protocol was approved by the Institutional Ethical Committee (IRB) at Showa University, Japan (IRB approval of protocol number, 22-183-A). All patients included in this study provided informed consent for use of anonymous data through an opt-out methodology.

Results

Background characteristics of all patients (Table 1)

Among all 104 patients, the lavage group ($n = 65$) and the non-lavage group ($n = 39$) were comparable with regard to age, sex, body mass index (BMI), and specific diagnoses of pancreatic and biliary disease. Prevalence of diabetes mellitus as a co-morbidity before surgery, indicated by preoperative hemoglobin A1c (HbA1c) concentration, also was comparable between groups. Although preoperative chemotherapy tended to be performed more frequently in the non-lavage group, nutritional status determined according to the PNI was somewhat better in the non-lavage than in the lavage group. Operative procedures, duration of operation, intraoperative blood loss, administration of blood transfusions, and numbers of lymph nodes dissected were similar between groups. Fifteen patients (14.4%) underwent resection of the superior mesenteric vein (SMV) or the portal vein (PV), and 2 (1.9%) underwent arterial resection. Frequencies of resection of the SMV, PV, and hepatic artery were similar between groups. Attainment of R0 resection also was similar between groups.

Postoperative course of all patients (Table 2)

One patient in the lavage group died of respiratory failure from aspiration pneumonia within 90 days of pancreatoduodenectomy. In the lavage group, 52 patients (80%) experienced some grade of postoperative complications, as did 26 patients (67%) in the non-lavage group ($P = 0.162$). Incidences of postoperative complications among lavage patients were grade I in 6 (9%), grade II in 22 (34%), grade IIIa in 19 (29%), grade IIIb in 3 (5%), grade IV in 1 (2%), and grade V in 1 (2%). In the non-lavage group, respective incidences were 1 (3%), 7 (18%), 16 (41%), 1 (3%), 1 (3%), and 0 ($P = 0.354$). Two patients in the lavage group (3.1%) experienced bleeding from the spleen caused by laceration of its capsule during abdominal lavage following completion of pancreatic surgical procedures; splenectomy was required. (This direct complication of lavage is not listed in the table.) Twenty-three patients in the lavage group (35%) had 25 infectious complications, including either superficial or deep incisional infection in 7, organ or space infection in 10, and remote infection in 8. In the non-lavage group, 6 patients (15%) had 7 infectious complications including incisional infection in 2, organ or space infection in 2, and remote infection in 3. Contrary to our expectation, incidence of infectious complications was significantly higher in the lavage group than in the non-lavage group ($P = 0.041$), and SSI was more likely in the lavage than the non-lavage groups ($P = 0.076$). Pancreatic fistula developed in 29 patients (29/61 or 48%) in the lavage group and 22 (22/38 or 58%) in the non-lavage group, showing no significant difference between groups in fistula frequency or grade. Length of hospital stay was similar between groups.

When the risk factors for SSI listed in Table 1 were subjected to multivariate analysis (with median value used as the cut-off point for continuous variables), absence of lavage fell short of selection as a factor reducing SSI (odds ratio, 0.300; 95% confidence interval or CI, 0.077 to 1.172; $P = 0.083$; Table 3).

Tumor recurrences in patients with pancreatic and biliary cancer (Table 4)

The 39 patients with pancreatic and biliary cancer in the lavage group had a median follow-up period of 668 days (range, 48–1235) while the 27 in the non-lavage group were followed up for a median of 196 days (60–418, $P < 0.001$). Twenty patients in the lavage group and 7 in the non-lavage group had recurrences of disease ($P = 0.046$). Recurrences numbered 3 among 12 biliary cancers in the lavage group vs. 5 among 12 in the non-lavage group, $P = 0.667$, and 17 among 27 pancreatic cancers in the lavage group vs. 2 among 15 in the non-lavage group, $P = 0.003$. Cumulative RFS did not differ between groups (1-year RFS, 55.3% in the lavage group vs. 55.5% in the non-lavage group; $P = 0.811$). Since follow-up periods differed between groups, the difference in recurrence rates was not clinically meaningful. However, no differences between groups were evident in initial recurrence sites ($P = 0.603$). In particular, peritoneal dissemination was detected in 3 lavage patients (8%) and in 1 non-lavage patient (4%, $P = 0.639$).

Background characteristics of patients undergoing PD (Table 5)

Among 63 patients with PD, the lavage group ($n = 39$) and the non-lavage group ($n = 24$) were comparable with regard to age, sex, PNI, BMI, HbA1c, and specific

Table 1 Background characteristics of all patients, by group

	Lavage group (n=65)	Non-lavage group (n = 39)	P value
Age	72 (40-90)	73 (47-87)	0.609
Sex			
Male	33 (51%)	24 (62%)	0.315
Female	32 (49%)	15 (38%)	
PNI	47.1 (31.7-63.3)	49.4 (37.7-58.6)	0.054
BMI	22.22 (16.4-30.88)	22.3 (16.8-29.3)	0.822
HbA1c	6.2 (4.7-10.8)	5.85 (4.9-13.2)	0.267
Disease			
Malignant (n = 66)			
Pancreatic cancer	26 (40%)	15 (38%)	0.091
Stage 0	1	0	
IA	2	0	
IIA	7	4	
IIB	15	11	
IV	1	0	
Bile duct cancer	12 (18%)	12 (31%)	
Stage 0	3	0	
IA	0	5	
IB	1	0	
IIA	3	0	
IIB	5	1	
IIIA	0	1	
IIIB	0	5	
Pancreatic and bile duct cancer	1 (2%)	0	
Non-malignant (n = 38)			
IPMN	9 (14%)	8 (21%)	
pNEN	11 (17%)	0	
Others	6 (9%)	4 (10%)	
Preoperative chemotherapy			
Performed	3/39 (8%)	6/27 (22%)	0.144
Operative procedures			
PD	39 (60%)	24 (62%)	0.707
DP	22 (34%)	14 (36%)	
TP	4 (6%)	1 (3%)	
Duration of operation, min	610 (188-821)	607 (356-819)	0.867
Blood loss, mL	410 (10-2495)	380 (50-1175)	0.895
Blood transfusion			
Performed	2 (3%)	0	0.527
Number of lymph nodes dissected	30 (4-76)	26 (5-58)	0.377
SMV or PV resection			
Performed	9 (14%)	5 (13%)	> 0.999
Arterial resection			
Performed	1 (2%)	1 (3%)	> 0.999
R0 resection	61 (94%)	36 (92%)	> 0.999

PNI, prognostic nutritional index; *BMI*, body mass index; *IPMN*, intraductal papillary mucinous neoplasm; *pNEN*, pancreatic neuroendocrine neoplasm; *PD*, pancreatoduodenectomy; *DP*, distal pancreatectomy; *TP*, total pancreatectomy; *SMV*, superior mesenteric vein; *PV*, portal vein

diagnoses of disease. Preoperative chemotherapy was given to relatively more non-lavage patients. Duration of operation; intraoperative blood loss; administration of blood transfusions; numbers of lymph nodes dissected; resections including SMV, PV, or hepatic artery; and R0 resections were similar between groups.

Table 2 Postoperative course of all patients, by group

	Lavage group ($n = 65$)	Non-lavage group ($n = 39$)	P value
Mortality	1 (2%)	0	> 0.999
Morbidity	52 (80%)	26 (67%)	0.162
Clavien-Dindo class			
I	6 (9%)	1 (3%)	0.354
II	22 (34%)	7 (18%)	
IIIa	19 (29%)	16 (41%)	
IIIb	3 (5%)	1 (3%)	
IV	1 (2%)	1 (3%)	
V	1 (2%)	0	
Infectious complication			
Present	23 (35%)	6 (15%)	0.041
Surgical site infection			
Present	17 (26%)	4 (10%)	0.076
Superficial or deep incisional	7	2	
Organ or space	10	2	
Remote infection			
Present	8 (12%)	3 (8%)	0.530
Pancreatic fistula grade[#]			
Present	29 (48%)	22 (58%)	0.409
None	32	16	
BL (biochemically evident)	12	6	
B (intervention required	17	16	
C (severe sequelae)	0	0	
NA	3	1	
Length of stay, days	29 (11 - 103)	31 (14-67)	0.579

NA, not applicable due to total pancreatectomy

[#]Excluding total pancreatectomy

Postoperative course of patients undergoing PD (Table 6)

Among PD patients in the lavage group, 30 (77%) experienced some grade of postoperative complication, as did 20 patients (83%) in the non-lavage group ($P = 0.750$). Incidence of postoperative complications was grade I in 1 lavage patient (3%), grade II in 12 (31%), grade IIIa in 15 (38%), grade IIIb in 0, grade IV in 1 (3%), and grade V in 1 (3%). In the non-lavage group, these frequencies were grade I in 1 (4%), grade II in 5 (21%), grade IIIa in 12 (50%), grade IIIb in 1 (4%), grade IV in 1 (4%), and grade V in 0 ($P = 0.646$).

Table 3 Multivariate analysis of risk factors for SSI

Variables		Odds ratio (95% CI)	P value
Abdominal lavage	Non-lavage	0.300 (0.770-1.172)	0.083
Age	>74 years	1.081 (0.320-3.647)	0.901
Sex	Male	1.608 (0.433-5.968)	0.478
PNI	>47.8	0.790 (0.232-2.698)	0.707
BMI	>22.3 kg/m^2	0.708 (0.206-2.436)	0.584
HbA1c	>6.0%	1.662 (0.511-5.409)	0.399
Disease	Malignant	3.226 (0.342-30.459)	0.307
Pre-CTx	Performed	1.796x10^{-6}	0.973
Blood transfusion	Performed	5.590x10^{-7}	0.991
R status	R1	0.352 (0.330-3.782)	0.389

SSI, surgical site infection; *CI*, confidence interval; *PNI*, prognostic nutritional index; *BMI*, body mass index; *Pre-CTx*, preoperative chemotherapy; *R*, resection

Table 4 Tumor recurrences in patients with pancreatic and biliary cancer, by group

		Lavage group ($n = 39$)	Non-lavage group ($n = 27$)	P value
Recurrence	Present	20 (51%)	7 (26%)	0.046
Initial recurrence site (s)				
	Liver	10	4	0.603
	Lung	3	2	
	Lymph nodes	6	2	
	Local	6	0	
	Peritoneum	3	1	

Table 5 Background characteristics of patients undergoing PD, by group

	Lavage group (n = 39)	Non-lavage group (n = 24)	P value
Age	74 (46-90)	73.5 (62-87)	0.697
Sex			
Male	19 (49%)	17 (71%)	0.117
Female	20 (51%)	7 (29%)	
PNI	47.1 (31.7-57.3)	48.7 (37.7-58.6)	0.179
BMI	22.22 (16.9-30.88)	21.9 (17.0-26.2)	0.966
HbA1c	6.1 (4.7-8.4)	5.85 (4.9-13.2)	0.633
Diseases			
Malignant (n = 50)			
Pancreatic cancer	17 (44%)	9 (38%)	0.340
Stage 0	1	0	
IA	2	0	
IIA	1	2	
IIB	13	7	
Bile duct cancer	12 (31%)	12 (50%)	
Stage 0	3	0	
IA	0	5	
IB	1	0	
IIA	3	0	
IIB	5	1	
IIIA	0	1	
IIIB	0	5	
Non-malignant (n = 13)			
IPMN	8 (21%)	3 (13%)	
pNEN	2 (5%)	0	
Preoperative chemotherapy			
Performed	1/29 (3%)	4/21 (19%)	0.148
Preoperative biliary drainage			
Performed	16 (41%)	14 (58%)	0.205
Duration of operation, min	655 (435-800)	649 (504-819)	0.893
Blood loss, mL	464 (150-2495)	573 (200-1175)	0.739
Blood transfusion			
Performed	2 (5%)	0	0.521
Number of lymph nodes dissected	33 (12-57)	31 (13-58)	0.470
SMV or PV resection			
Performed	9 (23%)	5 (21%)	> 0.999
Arterial resection			
Performed	1 (3%)	1 (4%)	> 0.999
R0 resection	37 (95%)	22 (92%)	0.632

PNI, prognostic nutritional index; *BMI*, body mass index; *IPMN*, intraductal papillary mucinous neoplasm; *pNEN*, pancreatic neuroendocrine neoplasm; *PD*, pancreatoduodenectomy; *DP*, distal pancreatectomy; *TP*, total pancreatectomy; *SMV*, superior mesenteric vein; *PV*, portal vein; *R*, resection

Eighteen patients in the lavage group (46%) had 21 infectious complications including incisional infection in 7, organ or space infection in 8, and remote infection in 6. In the non-lavage group, 5 patients (21%) had 6 infectious complications including incisional infection in 2, organ or space infection in 1, and remote infection in 3. Incidence of SSI was significantly higher in the lavage group than in the non-lavage group (P = 0.043).

When the risk factors for SSI listed in Table 5 were subjected to multivariate analysis with the median value representing the cut-off for continuous variables, absence of lavage was selected as an independent factor reducing SSI (odds ratio, 0.1010; 95% CI, 0.015 to 0.680; P = 0.019; Table 7).

Table 6 Postoperative course of patients undergoing PD, by group

	Lavage group ($n = 39$)	Non-lavage group ($n = 24$)	P value
Mortality	1 (3%)	0	> 0.999
Morbidity	30 (77%)	20 (83%)	0.750
Clavien-Dindo class			
I	1 (3%)	1 (4%)	0.646
II	12 (31%)	5 (21%)	
IIIa	15 (38%)	12 (50%)	
IIIb	0	1 (4%)	
IV	1 (3%)	1 (4%)	
V	1 (3%)	0	
Infectious complication			
Present	18 (46%)	5 (21%)	0.060
Surgical site infection			
Present	15 (38%)	3 (13%)	0.043
Superficial or deep incisional	7	2	
Organ or space	8	1	
Remote infection			
Present	6 (15%)	3 (13%)	> 0.999
Pancreatic fistula grade			
Present	16 (41%)	14 (58%)	0.205
None	23	10	
BL (biochemically evident)	6	2	
B (intervention required)	10	12	
C (severe sequelae)	0	0	
Length of stay, days	35 (15-88)	38.5 (17-67)	0.994

PD, pancreatoduodenectomy

Table 7 Multivariate analysis of risk factors for SSI in patients undergoing PD

Variables		Odds ratio (95% CI)	P value
Abdominal lavage	Non-lavage	0.101 (0.015-0.680)	0.019
Age	>75 years	1.349 (0.270-6.731)	0.715
Sex	Male	2.020 (0.372-10.960)	0.415
PNI	>47.5	1.127 (0.245-5.179)	0.878
BMI	>22.0 kg/m^2	1.039 (0.200-5.400)	0.964
HbA1c	>6.0%	2.115 (0.460-9.720)	0.336
Disease	Malignant	0.099 (0.003-3.371)	0.199
Pre-CTx	Performed	1.069x10^{-5}	0.982
Biliary drainage	Performed	3.711 (0.690-19.947)	0.127
Blood transfusion	Performed	1.918x10^{-6}	0.991
R status	R1	0.895 (0.056-14.184)	0.937

CI, confidence interval; *PNI*, prognostic nutritional index; *BMI*, body mass index; *Pre-CTx*, prehepatectomy chemotherapy; *R*, resection

Table 8 Tumor recurrences in patients undergoing PD, by group

		Lavage group ($n = 29$)	Non-lavage group ($n = 21$)	P value
Recurrence	Present	15 (51%)	7 (26%)	0.254
Initial recurrence site (s)				
	Liver	9	4	0.621
	Lung	2	2	
	Lymph nodes	6	2	
	Local	4	0	
	Peritoneum	2	1	

PD, pancreatoduodenectomy

Tumor recurrence in patients undergoing PD (Table 8)

Fifteen patients in the lavage group and seven in the non-lavage group had recurrences of disease ($P = 0.254$). Among 12 biliary cancer patients in the lavage group, 3 had recurrence; among 12 in the non-lavage group, 5 had recurrence ($P = 0.667$). Among 17 pancreatic cancer patients in the lavage group, 12 had recurrence compared with 2 among 9 in the non-lavage group ($P = 0.038$). Cumulative RFS did not differ between groups (1-year RFS was 57.1% in the lavage

group vs. 52.5% in the non-lavage group, $P = 0.718$). No differences in site of initial recurrence were evident between lavage and non-lavage groups ($P = 0.621$). Peritoneal dissemination occurred in 2 patients (7%) in the lavage group and 1 patient (5%) in the non-lavage group ($P > 0.999$).

Bacteriologic findings (Table 9)

Cultures of drainage fluid on POD 1 were positive in 15.4% of lavage patients (6 patients among 39), as were cultures from 10.3% of drains (8 drains among 78), compared with 37.5% of patients (9 patients among 24) and 35.4% of drains (17 drains among 48) in the non-lavage group ($P = 0.068$ and $P < 0.001$, respectively). On POD 3, however, 30.8% of patients (12 patients among 39) and 17.9% of drains (14 drains among 78) cultured in the lavage group were positive, while 45.8% of patients (11 patients among 24) and 39.6% of drains (19 drains among 48) cultured in the non-lavage group were positive ($P = 0.285$ and $P = 0.012$, respectively). Species of bacteria isolated from drainage fluid did not differ notably between POD 1 and 3 in the non-lavage group, but greater numbers of species were detected on POD 3 than on POD 1 in the lavage group.

Among patients with postoperative SSI, *Enterococcus faecalis*, *Enterococcus faecium*, *Candida albicans*, *Enterobacter cloacae*, and *Enterobacter aerogenes*, among others, were frequently isolated from the focus of infection. No difference in bacterial species was evident between groups.

Discussion

Considering all patients with pancreatic resections, incidence of all infections was significantly higher in the lavage group, and incidence of SSI also was higher in the lavage group, nearly affecting statistical significance. Focusing on patients who underwent PD, SSI also were more frequent in the lavage group than the non-lavage group. Further, according to multivariate analysis, absence of lavage was selected as an independent factor reducing SSI in the PD cohort, though not in the larger cohort including all patients.

Considering all patients, preoperative chemotherapy was more common but preoperative nutritional status was better in the non-lavage group, so favorable nutritional status may have reduced frequency of infectious complications. However, in the subgroup undergoing PD, background characteristics including preoperative nutritional status differed less between lavage and non-lavage patients. As PD typically involves multiple intestinal anastomoses such as pancreatojejunostomy, hepatojejunostomy, and gastrojejunostomy,

Table 9 Bacterial culture results in patients undergoing PD

Bacterial culture results	Lavage ($n = 39$)	Non-lavage ($n = 24$)	P value
POD 1			
Positive culture			
Lavage/non-lavage patients	15.4% (6/39)	37.5% (9/24)	0.068
Lavage/non-lavage culture specimens	10.3% (8/78)	35.4% (17/48)	< 0.001
Bacteria			
Enterococcus faecalis	7	13	
Enterococcus faecium	1	2	
Enterobacter cloacae	-	2	
Citrobacter freundii	-	2	
POD 3			
Positive culture			
Lavage/non-lavage patients	30.8% (12/39)	45.8% (11/24)	0.285
Lavage/non-lavage culture specimens	17.9% (14/78)	39.6% (19/48)	0.012
Bacteria			
Staphylococcus epidermidis	4	-	
Enterococcus faecalis	4	15	
Enterococcus faecium	4	2	
Coryneform bacteria	1	-	
Pseudomonas aeruginosa	1	-	
Enterobacter cloacae	-	4	
Citrobacter freundii	-	1	
Candida albicans	1	-	

PD, pancreatoduodenectomy; *POD*, postoperative day

intraoperative lavage might be considered more important for avoiding bacterial contamination. Instead, surgical site infection was significantly less frequent in the non-lavage group among our patients undergoing PD.

Intraoperative peritoneal lavage may have several actions. Sterile saline and water can accomplish mechanical cleansing to wash away bacteria, debris, and body fluids such as blood or bile. Lysis of tumor and bacterial cells also might result, depending upon differences between cell and lavage fluid tonicity. Lavage can disperse or remove not only bacteria but also contaminants favoring bacterial proliferation such as blood, as well as proinflammatory cytokines that may exacerbate local inflammation [20, 21]. However, lavage can interfere with peritoneal defense mechanisms [22] and mesothelial healing [23]; peritoneal mesothelium tends to slough after even brief exposure to air, saline, or other fluids [24–26]. Lavage also might displace important antiinfectious mediators such as opsonic proteins, complement, proteases, and immunoglobulins [27, 28], and could even accelerate entry of bacteria and endotoxin into the systemic circulation via diaphragmatic lymphatic stomata [22, 29].

Among patients who underwent PD, frequency of positive bacterial cultures from drainage fluid was greater in the non-lavage group than in the lavage group on both POD 1 and POD 3. In spite of this, postoperative SSI were more frequent in the lavage group than in the non-lavage group. Further, in the lavage group, various bacterial species were newly detected in POD 3 drainage fluid cultures that had not been detected on POD 1. Further, 6 lavage-group patients had positive drainage fluid cultures on POD 1, while 12 lavage-group patients had positive cultures on POD 3. Such increases were much less frequent among non-lavage patients (from 9 patients on POD 1 to 11 on POD 3). This suggests that intraoperative lavage might interfere with intraabdominal antiinfectious mechanisms. In a previous non-randomized study of patients undergoing elective colorectal surgery who underwent intraoperative peritoneal lavage with 5 L of normal saline, swab specimens from various sites within the abdomen showed greatly decreased bacterial counts; nonetheless, the lavage group had higher rates of postoperative wound infection (47%), intraabdominal abscess (26%), and septicemia (13%) than did the non-lavage group (rates of 37%, 8%, and 3%, respectively) [30]. This previous result is essentially in agreement with our own. Little species difference was evident among our bacterial isolates from surgical sites between lavage and non-lavage groups, but the number of patients was limited.

Among lavage group patients undergoing PD, bleeding from the spleen during lavage occurred in 2; repeated instillation and aspiration of saline within the abdomen was complicated by laceration of the spleen, possibly favored by disruption of adipose tissue related to the spleen.

Some reports have noted increased incidence of SSI in patients after bile duct drainage [31–33]. In our study, SSI was more likely to occur in patients who had insertion of a biliary drainage tube before PD (11/30 or 36.7%) than in patients without preoperative biliary drainage (7/33 or 21.2%). However, statistical significance was not attained ($P = 0.264$; data not shown). Frequency of preoperative biliary drainage did not differ significantly between our lavage and non-lavage patients undergoing PD.

From an oncologic perspective, tumor recurrence in the entire cohort was more frequent in the lavage group, but the follow-up period was longer in the lavage group than the non-lavage group. On the other hand, cumulative RFS and frequency of peritoneal dissemination did not differ between our lavage and non-lavage groups, either among all patients or among patients undergoing PD. Recently, preoperative lavage cytologic examination has been advocated as a way to predict disease malignancy [34]. Although intraoperative lavage at completion of surgery might appear attractive as a way to remove or lyse tumor cells in the peritoneal cavity, our study did not support its value in preventing peritoneal recurrence of disease. Some studies have suggested that peritoneal lavage could reduce incidence of peritoneal recurrence [35, 36]. However, the main end-point of those studies was oncologic effect, and extensive washing with 10 L of saline [35.36] or distilled water [36] was performed for more than 15 min; their objectives and details of lavage differed somewhat from those in the present study, which included patients with a variety of tumor stages and perioperative treatment such as preoperative chemotherapy. Although oncologic conclusions are difficult to draw, our findings suggest that routine peritoneal lavage using a fluid volume of 1 to 2 L at the end of surgery ordinarily should not be performed.

As the present study is retrospective, the results could have been influenced by various factors including preoperative biliary drainage and perioperative antibiotic therapy. A prospective evaluation of intraoperative lavage during pancreatic surgery involving a greater number of patients would be desirable for verifying and refining the present results. We do not believe that inapparent differences in patient management or other factors between operations preceding and following the end of October 2020 have influenced our results, but a prospective study could fully eliminate this possibility. Nonetheless, based on the results of this study, we now believe that intraoperative lavage has limited and variable ability to prevent surgical site infection and peritoneal disease recurrence, and should not be routinely performed unless a prospective study with greater power demonstrates a positive clinical impact.

Authors' contributions Study conception and design, Dr. Tanaka; acquisition of data, Drs. Ishihara, Takahashi, Minegishi, and Nakamura; analysis and interpretation of data, Drs. Ishihara, Takahashi, and Nakamura; drafting the article, Drs. Ishihara and Tanaka; revising the article, Drs. Matsuo and Tanaka; final approval, Dr. Tanaka.

Declarations

Conflict of interest The authors declare no competing interests.

References

1. Büchler MW, Wagner M, Schmied BM, Uhl W, Friess H, Z'graggen K (2003) Changes in morbidity after pancreatic resection: toward the end of completion pancreatectomy. Arch Surg 138:1310–1315
2. Kimura W, Miyata H, Gotoh M, Hirai I, Kenjo A, Kitagawa Y, Shimada M, Baba H, Tomita N, Nakagoe T, Sugihara K, Mori M (2014) A pancreaticoduodenectomy risk model derived from 8575 cases from a national single-race population (Japanese) using a web-based data entry system: the 30-day and in-hospital mortality rates for pancreaticoduodenectomy. Ann Surg 259:773–780
3. Cameron JL, He J (2015) Two thousand consecutive pancreaticoduodenectomies. J Am Coll Surg 220:530–536
4. Riviere D, Gurusamy KS, Kooby DA, Vollmer CM, Besselink MG, Davidson BR, van Laarhoven CJ (2016) Laparoscopic versus open distal pancreatectomy for pancreatic cancer. Cochrane Database Syst Rev 4:CD011391
5. Scholten L, Stoop TF, Del Chiaro M, Busch OR, van Eijck C, Molenaar IQ, de Vries JH, Besselink MG, Dutch Pancreatic Cancer Group (2019) Systematic review of functional outcome and quality of life after total pancreatectomy. Br J Surg 106:1735–1746
6. Winter JM, Cameron JL, Campbell KA, Arnold MA, Chang DC, Coleman J, Hodgin MB, Sauter PK, Hruban RH, Riall TS, Schulick RD, Choti MA, Lillemoe KD, Yeo CJ (2006) 1423 pancreaticoduodenectomies for pancreatic cancer: a single-institution experience. J Gastrointest Surg 10:1199–1210
7. Vin Y, Sima CS, Getrajdman GI, Brown KT, Covey A, Brennan MF, Allen PJ (2008) Management and outcomes of postpancreatectomy fistula, leak, and abscess: results of 908 patients resected at a single institution between 2000 and 2005. J Am Coll Surg 207:490–498
8. Simons JP, Shah SA, Ng SC, Whalen GF, Tseng JF (2009) National complication rates after pancreatectomy: beyond mere mortality. J Gastrointest Surg 13:1798–1805
9. Okano K, Hirao T, UnnoM FT, Yoshitomi H, Suzuki S, Satoi S, Takahashi S, Kainuma O, Suzuki Y (2015) Postoperative infectious complications after pancreatic resection. Br J Surg 102:1551–1560
10. Joliat GR, Sauvain MO, Petermann D, Halkic N, Demartines N, Schäfe M (2018) Surgical site infections after pancreatic surgery in the era of enhanced recovery protocols. Medicine 97(31):e11728
11. Whiteside OJH, Tytherleigh MG, Thrush S, Farouk R, Galland RG (2005) Intra-operative peritoneal lavage — who does it and why? Ann R Coll Surg Engl 87:255–258
12. Burnett WE, Brown GR Jr, Rosemond GP, Caswell HT, Buchor RB, Tyson RR (1957) The treatment of peritonitis using peritoneal lavage. Ann Surg 145:675–682
13. Schein M, Gecelter G, Freinkel W, Gerding H, Becker PJ (1990) Peritoneal lavage in abdominal sepsis A controlled clinical study. Arch Surg 125:1132–1135
14. Morimoto M, Taniguchi K, Yamamoto O, Naka T, Sugitani A, Fujiwara Y (2021) Evaluation of blood supply with indocyanine green fluorescence in resection for concurrent gastric and pancreatic cancer: a case report. Yonago Acta Med 64:133–136
15. Strasberg SM, Drebin JA, Linehan D (2003) Radical antegrade modular pancreatosplenectomy. Surgery 133:521–527
16. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240:205–213
17. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR (1999) Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 20:250–280
18. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, Allen P, Andersson R, Asbun HJ, Besselink MG, Conlon K, Del Chiaro M, Falconi M, Fernandez-Cruz L, Fernandez-Del Castillo C, Fingerhut A, Friess H, Gouma DJ, Hackert T et al (2017) The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. Surgery 161:584–591
19. Onodera T, Goseki N, Kosaki G (1984) Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. Nippon Geka Gakkai Zasshi 85:1001–1005 (In Japanese with English abstract)
20. Hall JC, Heel KA, Papadamitriou J, Platell C (1998) The pathobiology of peritonitis. Gastroenterology 114:185–196
21. Adam U, Ledwon D, Hopt UT (1997) Programmed lavage as a basic principle in therapy of diffuse peritonitis. Langenbecks Arch Chir 382:S18–S21
22. Platell C, Papadimitriou JM, Hall JC (2000) The influence of lavage on peritonitis. J Am Coll Surg 191:672–680
23. Tolhurst Cleaver CL, Hopkins AD, Kee Kwong KC, Raftery AT (1974) The effect of postoperative peritoneal lavage on survival, peritoneal wound healing and adhesion formation following fecal peritonitis: an experimental study in the rat. Br J Surg 61:601–604
24. Whitaker D, Papadimitriou JM, Walters MN (1982) The mesothelium and its reactions: a review. Crit Rev Toxicol 10:81–144
25. Yaacobi Y, Goldberg EP, Habal MB (1991) Effect of Ringer's lactate irrigation on the formation of postoperative abdominal adhesions. J Invest Surg 4:31–36
26. Breborowicz A, Rodela H, Oreopoulos DG (1992) Toxicity of osmotic solutes on human mesothelial cells in vitro. Kidney Int 41:1280–1285
27. Maddaus MA, Ahrenholz D, Simmons RL (1988) The biology of peritonitis and implications for treatment. Surg Clin North Am 68:431–443
28. Lamperi S, Carozzi S (1988) Immunologic patterns in CAPD patients with peritonitis. Clin Nephrol 30:S41–S44
29. Dunn DL, Barke RA, Ahrenholz DH, Humphrey EW, Simmons RL (1984) The adjuvant effect of peritoneal fluid in experimental peritonitis Mechanism and clinical implications. Ann Surg 199:37–43
30. Minervini S, Bentley S, Youngs D, Alexander-Williams J, Burdon DW, Keighley MR (1980) Prophylactic saline peritoneal lavage in elective colorectal operations. Dis Colon Rectum 23:392–394
31. van der Gaag NA, Rauws EA, van Eijck CH, Bruno MJ, van der Harst E, Kubben FJ, Gerritsen JJ, Greve JW, Gerhards MF, de Hingh IH, Klinkenbijl JH, Nio CY, de Castro SM, Busch OR, van Gulik TM, Bossuyt PM, Gouma DJ (2010) Preoperative biliary drainage for cancer of the head of the pancreas. N Engl J Med 362:129–137
32. Morris-Stiff G, Tamijmarane A, Tan YM, Shapey I, Bhati C, Mayer AD, Buckels JA, Bramhall SR, Mirza DF (2011) Preoperative stenting is associated with a higher prevalence of postoperative complications following pancreatoduodenectomy. Int J Surg 9:145–149

33. Cortes A, Sauvanet A, Bert F, Janny S, Sockeel P, Kianmanesh R, Ponsot P, Ruszniewski P, Belghiti J (2006) Effect of bile contamination on immediate outcomes after pancreaticoduodenectomy for tumor. J Am Coll Surg 202:93–99
34. Tsuchida H, Fujii T, Mizuma M, Satoi S, Igarashi H, Eguchi H, Kuroki T, Shimizu Y, Tani M, Tanno S, Tsuji Y, Hirooka Y, Masamune A, Mizumoto K, Itoi T, Egawa S, Kodama Y, Hamada S, Unno M et al (2019) Prognostic importance of peritoneal washing cytology in patients with otherwise resectable pancreatic ductal adenocarcinoma who underwent pancreatectomy: a nationwide, cancer registry-based study from the Japan Pancreas Society. Surgery 166:997–1003
35. Yamamoto K, Shimada S, Hirota M, Yagi Y, Matsuda M, Baba H (2005) EIPL (extensive intraoperative peritoneal lavage) therapy significantly reduces peritoneal recurrence after pancreatectomy in patients with pancreatic cancer. Int J Oncol 27:1321–1328
36. Saif A, Teke M, Ryan C, Papai E, Nevler A, Hernandez JM, Lavu H (2022) The WASH (Water or Saline at High Volumes) Trial: a randomized trial to assess the survival impact of extensive peritoneal lavage using distilled water or saline at high volumes after pancreatic resection for pancreatic ductal adenocarcinoma. Ann Surg Oncol 29:5372–5374