

Surgical site infections after pancreatic surgery in the era of enhanced recovery protocols

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Abstract

Few data exist on risk factors (RF) for surgical site infections (SSI) among patients treated in an enhanced recovery after surgery (ERAS) pathway. This study aimed to assess RF for SSI after pancreas surgery in a non-ERAS group and an ERAS cohort.

An exploratory retrospective analysis of all pancreas surgeries prospectively collected (01/2000–12/2015) was performed. RF for SSI were calculated using uni- and multivariable binary logistic regressions in non-ERAS and ERAS patients.

Pancreas surgery was performed in 549 patients. Among them, 144 presented a SSI (26%). In the non-ERAS group (n=377), SSI incidence was 27% (99/377), and RF for SSI were male gender and preoperative biliary stenting. Since 2012, 172 consecutive patients were managed within an ERAS pathway. Forty-five patients (26%) had SSI. On multivariable analysis no RF for SSI in the ERAS cohort was found. In the ERAS group, patients with a pathway compliance $\leq 70\%$ had higher occurrence of SSI (30/45 = 67% vs. 7/127 = 6%, $p < 0.001$) and patients with and without SSI had similar median overall compliances (77%, IQR 71–80 vs. 80%, IQR 73–83, $p = 0.097$).

In the non-ERAS cohort, male gender and preoperative biliary stenting were RF for SSI, whereas in the ERAS group no RF for SSI was found. In an ERAS pathway, having an overall compliance $>70\%$ might diminish the SSI rate.

Abbreviations: ASA = American Society of Anesthesiologists, CDC = Centers for Disease Control and Prevention, DGE = delayed gastric emptying, ECOG = Eastern Cooperative Oncology Group, ERAS = enhanced recovery after surgery, ICU = intensive care unit, ISGPS = International Study Group for Pancreas Surgery, LoS = length of stay, NRS = nutritional risk screening, POPF = postoperative pancreatic fistula, SSI = surgical site infections.

Keywords: enhanced recovery after surgery, intra-abdominal infection, pancreas surgery, pancreatectomy, risk factor, wound infection

1. Introduction

Pancreas surgery induces a substantial number of postoperative complications, ranging from 40% to 70%.^[1–3] In particular, septic complications are common (around 35%).^[4] Different risk factors for septic complications after pancreas surgery are known, such as age >70 years, prolonged operative time, intraoperative blood transfusion, total parenteral nutrition, bile contamination, high body-mass index, and open surgery.^[4–6]

Wound infections and intra-abdominal abscesses subsumed as surgical site infections (SSI) represent the most common septic

complication after pancreas surgery.^[4] Malnutrition, small main pancreatic duct, biliary stenting, or operative time have been found to increase the risk for SSI after pancreatectomy.^[7–9]

Recently, enhanced recovery after surgery (ERAS) protocols have been implemented in pancreas surgery with favorable results.^[10,11] This new perioperative management reduces the surgical stress response by maintaining the physiological homeostasis and diminishes in certain reports postoperative complications.^[12] So far, only scarce data exist concerning the occurrence of SSI after pancreas surgery in patients treated within ERAS protocols.

The aim of this study was to define risk factors for SSI after pancreas surgery in patients treated within an ERAS pathway and in patients with non-ERAS management.

2. Methods

2.1. Patients and data collection

All consecutive patients who underwent surgery of the pancreas at the Department of visceral surgery (Lausanne University Hospital CHUV, Lausanne, Switzerland) were included. An exploratory retrospective analysis was performed. Patients' data were collected from our prospectively maintained institutional database from January 2000 to December 2015. All types of pancreas operations for various etiologies were included.

Complications occurring during hospitalization or within the first 30 postoperative days were graded according to the Clavien classification.^[13] Minor complications were defined as grade I to II, whereas major complications as grade III to IV.^[13] Grade V defined the mortality rate.^[13] Definitions from the International

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Study Group for Pancreas Surgery (ISGPS) were used for postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE), and hemorrhage.^[14–16] SSI was defined according to the Centers for Disease Control and Prevention (CDC).^[17] Superficial (skin and subcutaneous) and deep (fascia and muscle layer) incisional SSI was defined as an infection occurring within 30 days after surgery or during hospitalization with at least one of the following: purulent drainage from the incision, wound dehiscence, and fever or local pain, wound abscess seen on anatomical, histological, or imaging.^[17] Organ/space SSI was defined as infection occurring within 30 days after surgery or during hospitalization and involving a body part deeper than the fascial/muscle layer that was opened or manipulated during the surgical procedure with at least one of the following: purulent drainage from a drain located in an organ/space, microbiological identification of organisms, abscess involving the organ/space seen on anatomical, histological or imaging.^[17] Non-pancreatic fistulas (biliary and enteric postoperative fistulas) were classified into organ/space SSI.

The preoperative general state of a patient was measured according to the American Society of Anesthesiologists (ASA) score^[18] and the Eastern Cooperative Oncology Group (ECOG) performance status.^[19] Length of stay (LoS) was calculated from operation day until discharge day or patient's in-hospital death. Active smoking was defined preoperatively by direct question to the patients.

2.2. ERAS group

ERAS was implemented in October 2012 for all pancreas patients without exclusion.^[10] The institutional ERAS protocol is based on the guidelines of the ERAS Society.^[11] In particular, for patients with tumors of the pancreatic head and preoperative jaundice, biliary stenting was performed only if the serum bilirubin concentration was $>250 \mu\text{mol/L}$, in case of cholangitis, delayed surgery and/or if a neoadjuvant treatment was intended. Early postoperative mobilization (out of bed on operation day, walking on postoperative day 1) and oral intake (from postoperative day 1) were encouraged. In the ERAS group, the P-POSSUM score^[20] was calculated and the Nutritional Risk Screening (NRS)^[21] was used to establish the nutritional state of patients preoperatively. The mean general ERAS compliance was defined as the mean of the sum of all fulfilled ERAS items divided by all ERAS items per patient. In the ERAS cohort, comparison of SSI incidences was performed in patients with median overall compliance $\leq 70\%$ and $>70\%$ (threshold based on our previous report of compliance in ERAS pancreas).^[10] Uni- and multivariable analyses of risk factors for SSI were performed including the same variables as in the non-ERAS group. Potential risk factors in both groups included patient demographics, patient characteristics, intraoperative details, intensive care unit (ICU) stay, malignant etiology, and POPF based on previous literature and possible association with SSI.

2.3. Statistical analysis

For continuous variables, a Mann-Whitney *U* test or student *t* test was used depending on the normality of the distribution and homogeneity of the variances. Uni- and multivariable analyses were performed using binary logistic regressions. Multivariable analysis was performed on items that showed a $P < .1$ in univariable binary logistic regression analysis. All statistical analyses were performed using GraphPad Prism 5.0 (GraphPad

Software Inc., San Diego, CA) for Mac OS X and SPSS 22 for Mac OS X (IBM, Armonk, NY). This study was approved by the local ethics committee and respects the Declaration of Helsinki.

3. Results

3.1. Included patients

There were 549 patients who underwent pancreatic surgery during the study period. Among these patients, 144 (26%) presented a SSI. Incisional SSI (wound infections) were observed in 70 patients and organ/space SSI (intra-abdominal abscess) in 50 patients. Twenty-four patients had a concomitant incisional and organ/space SSI.

Among the 549 patients, 172 followed an ERAS pathway, and 377 had standard pre-ERAS care (non-ERAS group). Characteristics of the patients are presented in Table 1. There were more men in the non-ERAS group compared to the ERAS group (60% vs 48%, $P = 0.012$). Active smokers, diabetic patients, and ECOG status ≥ 2 were also more frequent in the non-ERAS group. Otherwise, all other parameters were similar between both groups.

3.2. Perioperative outcomes (ERAS vs non-ERAS)

The perioperative outcomes of ERAS and non-ERAS patients are summarized in Table 2. There were more laparotomies (95% vs 85%, $P < .001$) in the non-ERAS group, and more patients in the non-ERAS group needed a stay in the ICU (36% vs 19%, $P < .001$). Postoperative complications and LoS were similar between the 2 groups. Of note, postoperative pulmonary and cardiac complications were similar in the non-ERAS and ERAS groups, respectively (60/377 vs 24/172, $p = 0.554$ and 21/377 vs 11/172, $P = .702$). In the non-ERAS group, 99 patients (27%) had a SSI (50 incisional SSI, 30 organ/space SSI, and 19 both incisional and organ/space SSI). In the ERAS group, 45 patients (26%) presented a SSI (20 incisional SSI, 20 organ/space SSI, and 5 both incisional and organ/space SSI). In the entire cohort, the only independent risk factor for SSI was preoperative biliary

Table 1
Preoperative characteristics of included patients.

	ERAS patients n = 172	Non-ERAS patients n = 377	<i>P</i> [†]
Age, y [*]	67 (57–74)	65 (54–74)	.301 [‡]
Men	83 (48%)	226 (60%)	.012
BMI, kg/m ² *	24 (22–27)	24 (21–27)	.474
Active smokers	54 (31%)	160 (42%)	.014
Preoperative jaundice	60 (35%)	158 (42%)	.076
Preoperative biliary stenting	53 (31%)	138 (37%)	.209
ECOG status ≥ 2	6 (4%)	37 (10%)	.009
ASA score			.184
1/2	9 (5%)/111 (65%)	26 (7%)/244 (65%)	
3/4	52 (30%)/0	99 (26%)/8 (2%)	
Diabetes	20 (12%)	75 (20%)	.021
Hypertension	51 (30%)	129 (34%)	.327
Hypercholesterolemia	26 (15%)	65 (17%)	.621
Neoadjuvant treatment	7 (4%)	5 (1%)	.060

Values are numbers plus percentages in parentheses unless indicated otherwise.

* Values are medians (interquartile range).

[†] χ^2 test, except.

[‡] Mann-Whitney *U* test. Significant *P*-values appear in bold.

ASA = American Society of Anesthesiologists, BMI = body mass index, ECOG = Eastern Cooperative Oncology Group, ERAS = enhanced recovery after surgery.

Table 2
Intraoperative and postoperative outcomes of included patients.

	ERAS patients n = 172	Non-ERAS patients n = 377	P [‡]
Laparotomy/laparoscopy	147 (85%)/25 (15%)	358 (95%)/19 (5%)	<.001
Whipple/DP/others	116 (67%)/ 38 (22%)/18 (11%)	254 (67%)/ 80 (21%)/43 (12%)	.934
Operative time, min [*]	304 (255–353)	315 (240–394)	.201 [§]
Pancreatic anastomosis [†]	118 (69%)	261 (69%)	.921
Vascular resection	26 (15%)	57 (15%)	1
Blood loss, mL [*]	400 (200–713)	400 (200–875)	.262 [§]
Intensive care unit stay	33 (19%)	134 (36%)	<.001
Diagnosis			.155
Malignant	115 (67%)	227 (60%)	
Benign	57 (33%)	150 (40%)	
Length of stay, d [*]	14 (10–24)	16 (11–26)	.197 [§]
Surgical site infections	45 (26%)	99 (27%)	1
Morbidity rate	113 (66%)	227 (60%)	.256
Clavien I–II	44 (26%)	114 (30%)	
Clavien III–IV	69 (40%)	113 (30%)	
Mortality (Clavien V)	5 (3%)	15 (4%)	.630
Reoperation	30 (17%)	63 (17%)	.832

Values are numbers plus percentages in parentheses unless indicated otherwise.
^{*} Values are median (interquartile range). DP; others included total pancreatectomy, central pancreatectomy, Beger operation, or enucleation.
[†] Pancreaticogastric or pancreaticojejunal anastomosis after Whipple and Beger operations.
^{*} χ^2 test except.
[§] Mann–Whitney *U* test. Significant *P*-values appear in bold.
 DP = distal pancreatectomy, ERAS = enhanced recovery after surgery.

stenting (multivariate analysis, hazard ratio, HR: 1.9 [1.4–2.3], *P* = .031).

3.3. Complications and length of stay associated with SSI

The overall morbidity rate, that is, minor and major complications, was 66% for the entire cohort (ERAS and

Table 3
Postoperative complications in the entire cohort (ERAS and non-ERAS) among patients with and without SSI.

	Patients without SSI n = 405	Patients with SSI n = 144	P [*]
Complication rate	216 (53%)	144 (100%)	NA
Minor complication	105 (26%)	54 (38%)	.007
Major complication	94 (23%)	87 (60%)	<.001
Mortality	17 (4%)	3 (2%)	.308
Reoperation	46 (11%)	47 (33%)	<.001
POPF	63 (16%)	46 (32%)	<.001
Grade A	29 (8%)	25 (17%)	
Grade B	21 (5%)	16 (12%)	
Grade C	13 (3%)	5 (3%)	
DGE	71 (18%)	48 (33%)	<.001
Grade A	29 (7%)	12 (8%)	
Grade B	24 (6%)	14 (10%)	
Grade C	18 (5%)	22 (15%)	
Hemorrhage	63 (16%)	50 (35%)	<.001
Grade A	30 (7%)	22 (15%)	
Grade B	25 (6%)	25 (17%)	
Grade C	5 (3%)	3 (3%)	

Values are numbers plus percentages in parentheses unless indicated otherwise.
^{*} χ^2 test. Significant *P*-values appear in bold.
 DGE = delayed gastric emptying, ERAS = enhanced recovery after surgery, NA = not applicable, POPF = postoperative pancreatic fistula, SSI = surgical site infections.

Table 4
Postoperative complications in the non-ERAS cohort (n = 377) among patients with and without SSI.

	Patients without SSI n = 278	Patients with SSI n = 99	P [*]
Complication rate	143 (51%)	99 (100%)	NA
Minor complication	70 (25%)	42 (42%)	.001
Major complication	58 (21%)	43 (43%)	.001
Mortality	15 (5%)	14 (14%)	.005
Reoperation	30 (11%)	33 (33%)	<.001
POPF	40 (14%)	29 (29%)	<.001
Grade A	8 (3%)	15 (15%)	
Grade B	20 (7%)	9 (9%)	
Grade C	12 (4%)	5 (5%)	
DGE	47 (17%)	26 (26%)	.043
Grade A	14 (5%)	6 (6%)	
Grade B	24 (9%)	11 (11%)	
Grade C	9 (3%)	9 (9%)	
Hemorrhage	45 (16%)	39 (39%)	<.001
Grade A	24 (9%)	2 (2%)	
Grade B	4 (1%)	18 (18%)	
Grade C	17 (6%)	19 (19%)	

Values are numbers plus percentages in parentheses unless indicated otherwise. POPF, postoperative pancreatic fistula.
^{*} χ^2 test. Significant *P*-values appear in bold.
 DGE = delayed gastric emptying, ERAS = enhanced recovery after surgery, NA = not applicable, POPF = postoperative pancreatic fistula, SSI = surgical site infections

non-ERAS). The mortality rate (grade V) was 3.6%. There were more minor and major complications in the SSI group compared to the group without SSI (38% vs 26%, *P* = .007 and 60% vs 23%, *P* < .001), whereas the mortality rate was similar in both groups. The SSI group had higher rates of reoperations, POPF, DGE, and hemorrhages. Table 3 summarizes the postoperative complications in patients with and without SSI. Median LoS was longer in case of SSI (25 vs 13 days, *P* < .001).

In the non-ERAS cohort (n = 377), postoperative complications in patients with and without SSI are shown in Table 4. SSI was associated with higher minor and major complications, mortality, reoperations, POPF, DGE, and hemorrhages.

In the ERAS cohort (n = 172), postoperative complications in patients with and without SSI are summarized in Table 5. SSI patients had more major complications, reoperations, POPF, DGE, and hemorrhages.

3.4. Uni- and multivariable analyses of risk factors for SSI in the non-ERAS group

In the non-ERAS group, male gender and preoperative biliary stenting were significant risk factors for SSI on multivariable analysis. Results of the uni- and multivariable analyses are shown in Table 6.

3.5. Uni- and multivariable analyses of risk factors for SSI in the ERAS group

Two elements were significant on univariable analysis: preoperative biliary stenting and pancreatic anastomosis (pancreaticogastric or pancreaticojejunal anastomoses). On multivariable analysis, no element was significant for risk factor for SSI. The detailed results are summarized in Table 7.

Table 5

Postoperative complications in the ERAS cohort (n=172) among patients with and without SSI.

	Patients without SSI n=127	Patients with SSI n=45	P*
Complication rate	77 (61%)	45 (100%)	NA
Minor complication	35 (28%)	11 (24%)	.804
Major complication	40 (31%)	31 (69%)	<.001
Mortality	2 (2%)	3 (7%)	.064
Reoperation	16 (13%)	19 (42%)	<.001
POPF	27 (21%)	22 (49%)	<.001
Grade A	17 (14%)	12 (27%)	
Grade B	6 (4%)	5 (11%)	
Grade C	4 (3%)	5 (11%)	
DGE	28 (22%)	26 (58%)	<.001
Grade A	17 (14%)	7 (16%)	
Grade B	3 (2%)	4 (9%)	
Grade C	8 (6%)	15 (33%)	
Hemorrhage	22 (17%)	14 (31%)	.028
Grade A	9 (7%)	3 (7%)	
Grade B	8 (6%)	7 (16%)	
Grade C	5 (4%)	4 (9%)	

Values are numbers plus percentages in parentheses unless indicated otherwise.
 * χ^2 test. Significant P-values appear in bold.
 DGE=delayed gastric emptying, ERAS= enhanced recovery after surgery, NA=not applicable, POPF=postoperative pancreatic fistula, SSI = surgical site infections

3.6. Compliance and SSI in the ERAS group

Median overall compliance to the ERAS protocol was 80% (interquartile range, IQR: 73–83) in the ERAS group. In addition, median overall compliances to the ERAS pathway were similar between patients with SSI and without SSI (77%, IQR: 71–80 vs 80%, IQR: 73–83, *P*=.097). A compliance to the ERAS

Table 6

Uni- and multivariable binary logistic regressions for risk factor for surgical site infection after pancreatectomy in the non-ERAS cohort (n=377).

	Univariable HR	P [†]	Multivariable HR	P [†]
Age, >70 y	1.2 (0.7–1.9)	.553		
Gender (men)	1.8 (1.1–3.0)	.014	2.2 (1.1–4.5)	0.035
BMI, >25 kg/m ²	0.8 (0.5–1.3)	.311		
Active smokers	1.0 (0.6–1.6)	.879		
Preoperative jaundice	0.7 (0.5–1.2)	.201		
Preoperative biliary stenting	1.9 (1.2–3.0)	.009	2.5 (1.2–5.4)	0.018
ECOG status ≥2	2.0 (0.9–4.5)	.107		
ASA score >2	1.0 (0.6–1.7)	.940		
Diabetes	0.9 (0.5–1.6)	.819		
Hypertension	0.8 (0.5–1.3)	.303		
Hypercholesterolemia	1.1 (0.6–2.1)	.680		
Laparotomy	6.8 (0.9–51.6)	.065	2.5 (0.2–26.2)	0.443
Operative time, >300 min	2.2 (1.2–4.0)	.011	1.4 (0.6–3.4)	0.437
Pancreatic anastomosis*	2.0 (1.2–3.6)	.013	0.9 (0.3–2.4)	0.849
Vascular resection	2.0 (1.1–3.6)	.021	1.3 (0.6–2.9)	0.533
Blood loss, >500 mL	1.8 (1.1–2.9)	.028	1.4 (0.7–2.9)	0.371
Intensive care unit stay	0.7 (0.4–1.1)	.119		
POPF	1.5 (0.8–3.2)	.184		
Malignancy	0.9 (0.6–1.4)	.636		

Values are hazard ratios plus 95% confidence intervals in parentheses.
 * Pancreaticogastric or pancreaticojejunal anastomosis after Whipple and Beger operations.
 † Binary logistic regression. Significant P-values appear in bold.
 ASA=American Society of Anesthesiologists, BMI=body-mass index, ECOG=Eastern Cooperative Oncology Group, HR=hazard ratio, POPF=postoperative pancreatic fistula.

Table 7

Uni- and multivariable binary logistic regressions for risk factor for surgical site infection in the ERAS cohort (n=172).

	Univariable HR	P [†]	Multivariable HR	P [†]
Age, >70 y	1.1 (0.5–2.3)	.840		
Gender (men)	0.7 (0.4–1.5)	.380		
BMI, >25 kg/m ²	0.7 (0.3–1.4)	.294		
Active smokers	2.2 (1.0–5.1)	.057	1.1 (0.4–3.2)	.884
Preoperative jaundice	2.1 (1.0–4.5)	.053	1.3 (0.4–4.5)	.650
Preoperative biliary stenting	2.2 (1.0–4.7)	.041	1.8 (0.5–5.8)	.360
ECOG status ≥2	4.3 (0.7–27.7)	.115		
ASA score >2	0.5 (0.2–1.1)	.075	0.8 (0.3–2.0)	.627
Diabetes	0.6 (0.2–1.5)	.270		
Hypertension	0.7 (0.3–1.6)	.448		
Hypercholesterolemia	0.9 (0.4–2.4)	.883		
Laparotomy	4.7 (0.6–37)	.141		
Operative time, >300 min	0.6 (0.3–1.2)	.143		
Pancreatic anastomosis*	17.9 (2.4–134.8)	.005	1.6 (0.5–3.4)	.124
Vascular resection	1.2 (0.4–3.1)	.753		
Blood loss, >500 mL	0.6 (0.3–1.4)	.272		
Intensive care unit stay	0.8 (0.3–1.8)	.516		
POPF	2.1 (0.6–4.2)	.216		
Malignancy	0.9 (0.4–2.0)	.833		

Values are hazard ratios plus 95% confidence intervals in parentheses.
 * Pancreaticogastric or pancreaticojejunal anastomosis after Whipple and Beger operations.
 † Binary logistic regression. Significant P-values appear in bold.
 ASA=American Society of Anesthesiologists, BMI=body-mass index, ECOG=Eastern Cooperative Oncology Group, HR=hazard ratio, POPF=postoperative pancreatic fistula.

protocol <70% in the ERAS group was associated with higher occurrence of SSI (30/45 = 67% vs 7/127 = 6%, *P* < .001).

3.7. Immunonutrition and postoperative oral supplement nutrition

In the ERAS group, 101 out of 172 patients (59%) received preoperative immunonutrition. On postoperative day (POD) 1, 62/172 patients (36%) had oral supplement nutrition. On POD 2 and POD 3, 58/172 patients (34%) and 69/172 patients (40%) received oral supplement nutrition, respectively.

4. Discussion

In this series, the overall incidence of SSI following pancreatic surgery was 26%, and of note, there was no difference between non-ERAS (27%) and ERAS patients (26%). Preoperative biliary stenting and male gender were significant risk factors for SSI in the non-ERAS group, whereas in the ERAS group no significant risk factor was found on multivariable analysis. A lower ERAS pathway compliance rate was found to be associated with a higher SSI rate.

Both, preoperative biliary obstruction and its endoscopic treatment by stent insertion carry an increased infectious risk.^[7,22,23] It has been shown that endoscopic biliary interventions increase the risk for postoperative complications, in particular cholangitis and POPF.^[24,25] Therefore, preoperative biliary stenting should only be performed in selected patients, such as jaundiced patients necessitating neoadjuvant chemotherapy or when biliary sepsis precludes the operation.^[7] The ERAS guidelines for pancreaticoduodenectomy recommend a preoperative biliary drainage only in patients with serum bilirubin concentrations >250 μmol/L.^[11] Gavazzi et al^[7] suggested that in preoperatively stented patients antibiotic prophylaxis before incision with anti-enterococcal activity should be used, whereas

Sudo et al.^[26] recommended to perform bile cultures to adjust the antibiotic prophylaxis according to the culture results in patients who had preoperative biliary drainage. Male gender has also been described as a risk factor for infectious complications after pancreaticoduodenectomy by Okano et al.^[4] The exact mechanism is not known but men might react differently to the stress induced by surgery. Surgical stress response is indeed influenced by a quantity of variables. The operative duration, a tumoral inflammatory state with the presence of inflammatory cytokines, as well as the nutritional status, and the use of laparoscopy play a role.^[27]

This study also showed that the risk factors for SSI after pancreas surgery were different in the ERAS and non-ERAS groups. Comparing the same items in the ERAS and non-ERAS cohorts on uni- and multivariable analyses, all studied elements were not significant risk factors for SSI in the ERAS group. The clinical impact of this finding might be that ERAS put all patients (even patients with previously known risk factors such as male gender and preoperative biliary stenting) at the same risk for SSI. This could be explained by the fact that ERAS diminishes the surgical stress response and improves the recovery by maintaining the physiological homeostasis.^[28] Early mobilization and nutrition can also play a role in this change. It is also important to mention that demographic characteristics and comorbidities of the patients, such as gender, smoking, diabetes, and performance status were not evenly distributed in both groups. This temporal evolution could also be an explanation for the changes found in risk factors for SSI. Moreover, the smaller number of patients in the ERAS group might also have played a role in the results.

The nutritional status is a well-known risk factor for wound problems in surgery in general.^[22] Regarding pancreas surgery, Kanda et al.^[29] showed that the nutritional status was associated with survival and postoperative complications. In the ERAS group, the nutritional status was not associated with SSI. In the present ERAS cohort, patients with cancer and malnourished patients (NRS >3) received preoperative supplemental nutrition for 7 days, which could explain the fact that the nutritional status was not correlated with SSI.

A high level of compliance to the ERAS pathway was associated with less SSI than a low compliance level. Moreover, median overall compliances were similar between the SSI group and the group without SSI, suggesting that occurrence of SSI does not impair the ERAS compliance. This highlights the importance of applying all ERAS items, and that it is not a single element that is more important than another, but really the powerful association of all of them. A low compliance to ERAS pathways has already been shown to be related to higher postoperative complication rates, especially in colorectal surgery,^[30,31] but also in pancreatic surgery.^[28] Based on this finding, it is therefore important to try to achieve the best possible compliance for every single patient in order to improve the postoperative outcomes. In addition, the fact that ERAS and non-ERAS patients had in this cohort similar postoperative complications and LoS can be partly explained by a decline in compliance to the ERAS pathway in 2015 (data not shown). This decrease in compliance can be an explanation for the absence of complication and LoS difference compared to the recent published literature on ERAS in pancreas surgery.

LoS was prolonged for patients with SSI compared to patients without SSI. As SSI is one of the most common complications after pancreas surgery,^[4] it impacts considerably on hospital costs.^[32] Prevention of SSI should therefore be undertaken to improve patient recovery and to reduce hospital stay and its related additional costs.^[32]

This study has several limitations that need to be mentioned. This was a retrospective study inducing possible collection biases. Moreover, this study covered a 15-year period where treatment trends have changed. Of note, patients operated between 2000 and 2009 had similar pre-, intra-, and postoperative data as patients operated between 2010 and 2015. Risk factors in the ERAS group could also have been influenced by a temporal trend, and not only by implementation of an ERAS pathway. The number of patients in the ERAS group (twice less as the pre-ERAS cohort) could also have influenced the risk factor analysis, considering the number of variables included in the multivariable analysis. Finally, nutritional status (NRS) was not available for the non-ERAS group precluding a comparison between non-ERAS and ERAS patients. Despite these limitations, this article is original as it is one of the first studies assessing risk factors for SSI within an ERAS protocol for pancreas surgery.

In conclusion, preoperative biliary stenting and male gender were the most relevant risk factors to develop SSI after pancreas surgery in a non-ERAS cohort. In the ERAS group, no significant perioperative risk factors for SSI were found. Moreover, in the present cohort of ERAS patients, obtaining a high overall ERAS pathway compliance rate was associated with a lower SSI rate.

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Author contributions

GRJ contributed in the design of the study, acquisition and analysis of the data, draft of the manuscript, final approval of the article version to be published, and agreement to be accountable for all aspects of the work. MOS, DP, NH, ND, and MS contributed in the analysis of the data, critical revision of the manuscript, final approval of the article version to be published, and agreement to be accountable for all aspects of the work.

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