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Preoperative Bacterobilia Is an Independent Risk Factor of SSIs after Partial PD

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Keywords
Bacterobilia · Pancreaticoduodenectomy · Postoperative pancreatic fistula · Surgical site infection

Abstract
Introduction: The impact of bacterobilia on postoperative surgical and infectious complications after partial pancreaticoduodenectomy (PD) is still a matter of debate. ***Methods:*** All patients undergoing PD with and without a preoperative biliary drainage (PBD) with complete information regarding microbial bile colonization were included. Logistic regression was applied to assess the influence of bacterobilia on postoperative outcome. ***Results:*** One hundred seventy patients were retrospectively analysed. Clinically relevant postoperative complications (Clavien-Dindo ≥ III) occurred in 40 (23.5%) patients, clinically relevant postoperative pancreatic fistulas in 29 (17.1%) patients, and surgical site infections (SSIs) in 16 (9.4%) patients. Thirty-seven of 39 (94.9%) patients with PBD and 33 of 131 (25.2%) patients without PBD had positive bile cultures ($p < 0.001$). A polymicrobial bile colonization was reported in 9 of 33 (27.3%) patients without PBD and 27 of 37 (73%) patients with PBD ($p < 0.001$). Resistance to ampicillin-sulbactam was shown in 26 of 37 (70.3%) patients with PBD and 12 of 33 (36.4%) patients without PBD ($p = 0.001$). PBD (OR 0.015, 95% CI 0.003–0.07, $p < 0.001$) and male sex (OR 3.286, 95% CI 1.441–7.492, $p = 0.005$) were independent predictors of bacterobilia in the multivariable analysis. Bacterobilia was the only independent predictor of SSIs in the multivariable analysis (OR 0.143, 95% CI 0.038–0.535, $p = 0.004$). ***Conclusions:*** Patients with a PBD show significantly higher rates of bacterobilia, polymicrobial bile colonization, and resistance to ampicillin-sulbactam. Bacterobilia is an independent predictor of SSI after PD.

Introduction

Patients with pancreatic head cancer commonly present with obstructive jaundice at the time of diagnosis. Although the routine placement of a preoperative biliary drainage (PBD) is frequently used in most patients during the past decade, its role is still a matter of debate. PBD is usually performed with endoscopic retrograde cholangiopancreatography-guided stent placement or less commonly by percutaneous transhepatic biliary drainage. In 2017, a meta-analysis [1] assessing the routine use of PBD

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showed that PBD was significantly associated with increased overall complications and wound infections with no beneficial effect on postoperative outcome [1]. Similarly, a more recent network meta-analysis [2] also concluded that in patients with resectable pancreatic cancer, routine PBD may not be the best management prior to surgery. However, a recent large retrospective series of 1,500 consecutive patients assessing the impact of a PBD on postoperative outcome after pancreaticoduodenectomy (PD) concluded that PBD does not increase major complications and mortality rates after PD but is associated with a higher rate of surgical site infection (SSI) [3]. Moreover, biliary infection (bacterobilia) related to PBD has been shown to be associated with postoperative infectious complications [4–9]. A recent systematic review with meta-analysis [10] assessing the impact of bacterobilia on morbidity after PD concluded that bacterobilia was detected in almost every second patient undergoing PD and was associated with an increased rate of SSI, whereas overall postoperative morbidity, including postoperative pancreatic fistula (POPF), as well as mortality were not significantly influenced [10]. The aim of the present retrospective study was to examine the microbial colonization of the bile of patients with and without PBD as well as to assess the impact of bacterobilia on postoperative surgical and infectious complications after PD.

Material and Methods

Data Collection

Data from all consecutive patients who underwent an elective partial PD between January 2009 and March 2019 at University Hospital Marburg were obtained from a prospectively maintained database and retrospectively analysed. Clinical data included age, sex, BMI, the American Society of Anaesthesiologists (ASA) status, PBD, which was routinely performed endoscopically, and underlying pathology. Only patients with existing samples from intraoperative bile cultures were included in the study. Microbiological data were obtained by conventional standard culture. The bile fluid was taken intraoperatively directly after dissection of the common bile duct. No intraoperative Gram staining was performed. Microbiological test results were reported according to the type of bacterium, including the sensitivity and resistance pattern of the cultured microorganisms.

All procedures were done by laparotomy. All patients received a single-shot intravenous antibiotic, usually ampicillin/sulbactam prior to laparotomy and once again 3–4 h after skin incision. Somatostatin analogues were also routinely used perioperatively. A pylorus-preserving PD with reconstruction through a pancreatogastrostomy [11, 12] was the procedure of choice, when feasible. Otherwise, a standard Whipple procedure was performed. Intraoperative swabs were obtained from the bile duct after transection.

Postoperative outcomes including clinically relevant complications, POPF, SSIs, postoperative mortality, and length of hospital stay were assessed. Postoperative complications were classified according to the Clavien-Dindo classification system [13]. POPF was classified according to the most recent definition provided by the International Study Group of Pancreatic Surgery (ISGPS) [14]; delayed gastric emptying (DGE) and postpancreatectomy haemorrhage (PPH) were defined according to the proposed definitions of the ISGPS [15, 16]. Non-surgical, for example, infectious complications included urinary tract infection, pneumonia, bacteremia, sepsis [17], and SSIs, defined according to the Centers for Disease Control and Prevention (CDC) classification [18]. The length of hospital stay was defined as the number of days from surgery to the date of discharge. Postoperative mortality included deaths occurring prior to hospital discharge or within 30 days of surgery. The results of the present study have been reported in line with the STROBE guidelines [19].

Statistical Analysis

Continuous variables are expressed as medians with interquartile ranges (IQR), and categorical variables are presented as proportions. Quantitative variables were compared using the student's *t* test or Mann-Whitney *U* test and qualitative variables using the χ^2 test or Fisher's exact test as appropriate. Factors that were significantly associated on univariate analysis were included in a multivariable binary logistic regression model. All reported probability values (*p* values) are based on two-sided tests, and the level of statistical significance was set at $p < 0.05$. Analyses were performed using SPSS 23.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, version 23.0., IBM Corp., Armonk, NY, USA).

Results

Baseline Characteristics and Perioperative Outcomes

One hundred seventy of 192 consecutive patients who underwent an elective PD had complete information regarding microbiological analysis of intraoperative bile swabs, and thus represent the analysed study population. Eighty-eight (51.8%) patients were male, the median age at surgery was 69 (IQR, 58.8–75) years, and the median patient BMI was 24.6 (IQR, 22.8–27.5) kg/m^2. Four of 170 (2.4%) patients were classified as ASA I, 90 of 170 (52.9%) patients were classified as ASA II, 75 (44.1%) as ASA III, and 1 (0.6%) patient as ASA IV, respectively. Median serum albumin was 3.6 g/dL (IQR, 3.0–4.0), and hypoalbuminemia (serum albumin <3.5 g/dL) was preoperatively diagnosed in 69 of 170 (40.6%) patients. PBD was performed in 36 of 170 (21.2%) patients; 32 of the 36 (88.9%) patients received plastic stents, and the remaining 4 (11.1%) patients received fully covered metal stents. Three (1.8%) of 170 patients underwent PTBD. The median delay from endoscopic intervention to surgical resection was 17 (IQR, 12.25–25) days. The general and

perioperative characteristics of the study population are summarized in Table 1.

Median operative time was 353 (IQR, 310.5–403.5) min, median estimated blood loss was 300 (IQR, 200–400) mL, and intraoperative blood transfusion was necessary in 11 of 170 (6.5%) patients. Pylorus-preserving PD was performed in 148 (87.1%) patients and a standard Whipple procedure in the remaining 22 (12.9%) patients. A vascular resection, for example, portal vein or superior mesenteric vein resection, was performed in 16 (9.4%) patients. A soft pancreatic gland texture was reported in 40 (23.5%) patients, the median estimated pancreatic duct diameter was 4 (IQR, 2–6) mm. The most frequent underlying pathology was pancreatic ductal adenocarcinoma in 90 (52.9%) patients, followed by ampullary carcinoma in 20 (11.8%) patients and distal bile duct carcinoma in 13 (7.6%) patients. Fifteen of the 20 patients with ampullary carcinoma had positive bile cultures, 8 of those had PBD, and 7 patients received no PBD. Other pathologies included pancreatic neuroendocrine neoplasia and intraductal papillary mucinous neoplasia in 11 (6.5%) patients each, chronic pancreatitis in 6 (3.5%) patients, duodenal carcinoma in 3 (1.8%) patients, and various pathologies in the remaining 16 (9.4%) patients. The median tumor size was 2.6 (IQR, 2.3–3.5) cm, and the median number of resected lymph nodes was 20 (IQR, 16–26, Table 1). In patients with malignant disease, an R0 resection was reported in 113 of 126 (89.7%) patients.

Clinically relevant postoperative complications (Clavien-Dindo ≥ III) occurred in 40 (23.5%) patients that were classified grade IIIa in 15 (8.8%) patients, grade IIIb in 18 (8.8%) patients, grade IVa in 3 (1.8%) patients, grade IVb in 1 (0.6%) patients, and grade V in 6 (3.5%) patients, respectively. A clinically relevant POPF was reported in 29 (17.1%) patients, including 20 (11.8%) patients with grade B and 9 (5.3%) patients with grade C POPF. SSIs were reported in 16 of 170 (9.4%) patients, all of which were classified as superficial incisional SSIs according to the CDC criteria [18]. Relevant DGE grades B and C were reported in 33 (19.4%) and 21 (12.4%) patients, respectively. A clinically relevant PPH (grade B/C) was reported in 20 (11.8%) patients. The median length of hospital stay was 14 (IQR, 12–20) days.

Microbiological Analysis

Microorganisms could be cultured from bile samples of 70 from 170 (41.2%) patients. Thirty-seven of 39 (94.9%) patients with PBD had positive bile cultures. In contrast, only 33 of 131 (25.2%) patients without PBD had positive bile samples ($p < 0.001$). Moreover, polymi-

Table 1. General and perioperative patients' characteristics

Variable	Median (IQR) or *n* (%)
Gender (male)	88 (51.8%)
Age, years	69 (58.8–75)
BMI, kg/m^2	24.6 (22.8–27.5)
ASA	
ASA I	4 (2.4%)
ASA II	90 (52.9%)
ASA III	75 (44.1%)
ASA IV	1 (0.6%)
Preoperative biliary stenting	39 (23%)
via ERC	36 (21.2%)
via PTBD	3 (1.8%)
Operative time, min	353 (310.5–403.5)
Estimated blood loss, mL	300 (200–400)
Pat. with intraoperative blood transfusion	11 (6.5%)
Surgical procedure performed	
PPPD	148 (87.1%)
Kausch-Whipple resection	22 (12.9%)
Vascular resection	16 (9.4%)
Soft pancreatic texture	40 (23.5%)
Estimated pancreatic duct diameter, mm	4 (2–6)
Entity	
PDAC	90 (52.9%)
Ampullary carcinoma	20 (11.8%)
Distal bile duct carcinoma	13 (7.6%)
IPMN	11 (6.5%)
pNEN	11 (6.5%)
Chronic pancreatitis	6 (3.5%)
Duodenal carcinoma	3 (1.8%)
Other	16 (9.4%)
R0 resection*	113/126 (89.7%)
Lymph nodes resected	20 (16–26)
Tumor size, cm	2.6 (2.3–3.5)
Clinically relevant POPF (all)	29 (17.1%)
Grade B	20 (11.8%)
Grade C	9 (5.3%)
Clavien-Dindo complications ≥ III (all)	40 (23.5%)
IIIa	15 (8.8%)
IIIb	18 (8.8%)
IVa	3 (1.8%)
IVb	1 (0.6%)
V	6 (3.5%)
DGE grade B	33 (19.4%)
DGE grade C	21 (12.4%)
PPH (grade B/C)	20 (11.8%)
SSI	16 (9.4%)
LOS, days	14 (12–20)

ASA, American Society of Anesthesiologists; ERCP, endoscopic retrograde cholangiopancreatography; PTBD, percutaneous transhepatic biliary drainage; PPPD, pylorus-preserving pancreaticoduodenectomy; PDAC, pancreatic ductal adenocarcinoma; IPMN, intraductal papillary mucinous neoplasia; pNEN, pancreatic neuroendocrine neoplasia; POPF, postoperative pancreatic fistula; DGE, delayed gastric emptying; PPH, post-pancreatectomy haemorrhage; SSI, surgical site infection; LOS, length of hospital stay; IQR; interquartile range. * R0 resection rate reported in patients with PDAC, ampullary, distal bile duct and duodenal carcinoma, values are median unless indicated otherwise.

Table 2. Microorganisms isolated in the bile of patients with and without PBD

No PBD		PBD	
species (n = 48)	n (%)	species (n = 84)	n (%)
Enterococcus sp.	9 (18.8)	*Candida* sp.	16 (19)
E. coli	8 (16.7)	*Enterococcus* sp.	11 (13.1)
Enterobacter sp.	6 (12.5)	*Enterobacter* sp.	9 (10.7)
Streptococcus sp.	6 (12.5)	*Enterococcus faecium*	9 (10.7)
Other	6 (12.5)	*E. coli*	8 (9.5)
Klebsiella sp.	5 (10.4)	*Klebsiella* sp.	8 (9.5)
Staphylococcus sp.	4 (8.3)	*Streptococcus* sp.	7 (8.3)
Citrobacter sp.	3 (6.3)	*Enterococcus faecalis*	4 (4.8)
Enterococcus faecalis	1 (2.1)	*Staphylococcus* sp.	4 (4.8)
		Pseudomonas sp.	4 (4.8)
		Citrobacter sp.	3 (3.6)
		Other	1 (1.2)

PBD, preoperative biliary drainage; *E. coli*, *Escherichia coli*; sp., species.

Table 3. Predictors of bacterobilia in the univariate and multivariable analysis

Variable	Univariate analysis			Multivariable analysis		
	OR	95% CI	p value	OR	95% CI	p value
Age, years						
≤69	1					
>69	1.154	0.626–2.129	0.65			
Sex						
Female	1					
Male	2.386	1.272–4.476	**0.007**	3.286	1.441–7.492	**0.005**
ASA						
≤II	1					
>II	1.304	0.706–2.411	0.40			
BMI, kg/m^2						
≤24.6	1					
>24.6	1.427	0.773–2.635	0.26			
PBD						
Yes	1					
No	0.018	0.004–0.080	**<0.001**	0.015	0.003–0.07	**<0.001**
Serum albumin, g/dL						
≤3.6	1					
>3.6	0.556	0.300–1.031	0.06			
Operative time, min						
≤353	1					
>353	1.339	0.726–2.471	0.35			
Estimated blood loss, mL						
≤300	1					
>300	1.200	0.631–2.283	0.58			

Values are median unless indicated otherwise. ASA, American Society of Anesthesiologists; PBD, preoperative biliary drainage; OR, odds ratio; 95% CI, 95% confidence interval.

Table 4. Predictors of SSIs in the univariate and multivariable analysis

Variable	Univariate analysis			Multivariable analysis		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Age, years						
≤69	1					
>69	1.547	0.548–4.367	0.41			
Sex						
Female	1					
Male	1.252	0.444–3.535	0.67			
ASA						
≤II	1					
>II	3.108	1.029–9.386	**0.04**	2.528	0.783–8.162	0.12
BMI, kg/m^2						
≤24.6	1					
>24.6	3.609	1.114–11.695	**0.03**	2.672	0.774–9.220	0.12
PBD						
Yes	1					
No	2.094	0.454–9.660	0.34			
Serum albumin, g/dL						
≤3.6	1					
>3.6	0.758	0.268–2.138	0.6			
Bile culture						
Positive	1					
Negative	0.131	0.036–0.479	**0.002**	0.143	0.038–0.535	**0.004**
Operative time, min						
≤353	1					
>353	2.319	0.769–6.994	0.14			
Estimated blood loss, mL						
≤300	1					
>300	2.528	0.690–9.256	0.16			

Values are median unless indicated otherwise. ASA, American Society of Anesthesiologists; PBD, preoperative biliary drainage; OR, odds ratio; 95% CI, 95% confidence interval.

crobial bile colonization was only reported in 9 of the 33 (27.3%) patients without PBD, whereas in 27 of the 37 (73%) patients with PBD, more than one species was isolated ($p < 0.001$). Resistance to ampicillin-sulbactam was seen in 26 of 37 (70.3%) patients with PBD versus 12 of 33 (36.4%) patients without PBD ($p = 0.001$). In patients without PBD, a total of 48 organisms comprising 13 different species were isolated (see also Table 2). The most commonly isolated organisms included *Enterococcus* sp. in 9 (18.8%), *Escherichia coli* in 8 (16.7%), *Enterobacter* sp. in 6 (12.5%), and *Streptococus* sp. in 6 (12.5%) bile cultures. In patients with PBD, a total of 84 microorganisms comprising 12 species were isolated. The most frequently isolated microorganisms in patients with PBD were *Candida* sp. in 16 (19%), *Enterococcus* sp. in 11 (13.1%), *Enterobacter* sp. in 9 (10.7%), *Enterococcus faecium* in 9 (10.7%), *Klebsiella* sp. in 8 (9.5%), and *E. coli* in 8 (9.5%) bile cultures. It is of note that *E. faecium*, *Pseudomonas*, and *Candida* sp. were only reported in bile samples from patients with PBD, as shown in Table 2.

Predictors of Bacterobilia and Impact of Bacterobilia on Postoperative Outcomes

Male sex (OR 2.386, 95% CI 1.272–4.476, $p = 0.007$) and PBD (OR 0.018, 95% CI 0.004–0.080, $p < 0.001$) were identified as significant predictors of bacterobilia in the univariate analysis. PBD (OR 0.015, 95% CI 0.003–0.07, $p < 0.001$) and male sex (OR 3.286, 95% CI 1.441–7.492, $p = 0.005$) remained independent predictors of bacterobilia in the multivariable analysis (Table 3).

On univariate analysis, preoperative bacterobilia was neither associated with overall clinically relevant (Clavien-Dindo ≥ III) postoperative complications (OR 0.931, 95% CI 0.454–1.909, $p = 0.85$) nor with clinically relevant

Table 5. Subgroup analysis of baseline characteristics and postoperative outcomes in patients with and without PBD

Variable*	No PBD (n = 131)	PBD (n = 39)	p value
Age, years	68 (57–65)	70 (61–77)	0.11
Sex (male)	66 (50.4%)	22 (56.4%)	0.51
BMI	24.6 (23–27.4)	24.3 (22.4–27.8)	0.67
ASA > II	57 (43.5%)	19 (48.8%)	0.39
Preoperative diabetes present	29 (22.1%)	8 (20.5%)	0.83
Clavien-Dindo ≥ III	33 (25.2%)	7 (17.9%)	0.35
Clinically relevant POPF	25 (19.1%)	4 (10.3%)	0.20
DGE (grade B/C)	43 (32.8%)	11 (28.2%)	0.94
PPH (grade B/C)	17 (13%)	3 (7.7%)	0.37
Postoperative LOS	15 (12–20)	14 (11–18)	0.50
SSIs	14 (10.7%)	2 (5.1%)	0.26

PBD, preoperative biliary drainage; ASA, American Society of Anesthesiologists; POPF, postoperative pancreatic fistula; DGE, delayed gastric emptying; PPH, post-pancreatectomy haemorrhage; LOS, length of hospital stay; SSIs, surgical site infections.
* Median (interquartile range) or n (%).

POPF (OR 1.694, 95% CI 0.721–3.982, p = 0.23). Bacterobilia was, however, a significant predictor of SSI in the univariate analysis (OR 0.131, 95% CI 0.036–0.479, p = 0.002). BMI > 24.6 kg/m^2 (OR 3.609, 95% CI 1.114–11.695, p = 0.03) and ASA ≥ II (OR 3.108, 95% CI 1.029–9.386, p = 0.04) were also identified as significant predictors of SSI in the univariate analysis (Table 4), but only bacterobilia remained an independent predictor of SSI in the multivariable analysis (OR 0.143, 95% CI 0.038–0.535, p = 0.004), as shown in Table 4.

We further assessed the potential impact of bacterobilia on infectious complications other than SSIs. Among 170 patients, 9 (5.3%) patients had pulmonary infection/pneumonia, 16 (9.4%) had bacteraemia, 25 (14.7%) patients urinary tract infections, 11 (6.5%) patients had sepsis, 3 (1.8%) patients developed postoperative cholangitis, and 9 of 170 (5.3%) patients had central venous catheter-related infection. On univariate analysis, bacterobilia was not significantly associated with infectious complications other than SSI (OR 0.963, 95% CI 0.477–1.942, p = 0.92).

Subgroup Analysis of Patients with and without PBD

Thirty-nine (22.9%) of 170 patients received PBD. The baseline characteristics of the 2 subgroups (patients with and without PBD) are shown in Table 5. No significant differences were found regarding age (median 70 vs. 68 years, p = 0.11), male sex (56.4 vs. 50.4%, p = 0.51), median BMI (24.3 vs. 24.6, p = 0.67), ASA > II (48.8 vs. 43.5%, p = 0.39), and diagnosis of a preoperative diabetes (20.5 vs. 22.1%, p = 0.83) in patients with (n = 39) and without (n = 131) PBD, as shown in Table 5. When comparing the postoperative outcomes in both groups, no significant differences were found regarding clinically relevant postoperative complications (17.9 vs. 25.2%, p = 0.35), relevant POPF (10.3 vs. 19.1%, p = 0.20), DGE grade B/C (28.2 vs. 32.8%, p = 0.94), PPH grade B/C (7.7 vs. 13%, p = 0.37), length of hospital stay after resection (14 vs. 15 days, p = 0.50), and SSIs (10.7 vs. 5.1%, p = 0.26), as shown in Table 5.

Discussion

The present study aimed to assess the impact of preoperative bacterobilia on postoperative outcomes after PD and to examine the biliary microbiome in patients with and without PBD in order to identify potentially significant differences in the microbial colonization in each group. Patients receiving PBD had significantly higher rates of bacterobilia (94.9 vs. 25.2%) than those without PBD, results which are in line with those of previous studies and meta-analyses [7, 10, 20–22]. The 25.2% rate of bacterobilia reported in the present study is in line with the results of previous studies, which reported rates between 18.6 and 31% in patients without PBD [5, 7, 21]. Bacterobilia in patients without PBD is possibly explained by the fact that malignant biliary obstruction leads to biliary stasis and consecutive colonization of the initially sterile bile duct. Moreover, the present study showed that microbial colonization of the bile duct in patients with and without PBD is substantially different, as PBD is significantly associated with polymicrobial bacterobilia (73 vs. 27.3%), whereas in most patients without PBD, only one species was isolated. Resistance to ampicillin-sulbactam, which is the standard antibiotic prophylaxis prior to PD in our clinic, was also significantly higher in patients with PBD than those without (70.3 vs. 26.4%). Scheufele et al. [7] also showed that the biliary microbiota of patients with and without PBD were different and that PBD was associated with a more antibiotic-resistant bacterium in the bile, which may require changing the type of perioperative antibiotics used for prophylaxis or treatment of infections [7]. The most commonly isolated microorganisms in the present study were *Enterococcus* sp., *E. coli*, and *Enterobacter* sp., results in line with those of previous studies [4, 8, 10, 20, 21, 23–25]. Although few retrospective studies

suggest that postoperative antimicrobial therapy decreases infectious complications following PD in patients at risk for bile contamination, a routine antibiotics treatment cannot be recommended based on the current evidence. Interestingly, *Candida* sp. were only isolated in bile samples from patients with PBD, as in 2 previous studies [7, 20]. The presence of *Candida* sp. in the bile of patients with PBD and its clinical implications require further investigation before any recommendations regarding a routine, antifungal prophylaxis can be made.

The present study also examined the impact of preoperative bacterobilia on postoperative outcomes after PD, including both surgical and infectious complications. In accordance with the results of a recent meta-analysis [10], in the present study, preoperative bacterobilia was not significantly associated with the occurrence of clinically relevant postoperative complications (Clavien-Dindo ≥ III). In addition, clinically relevant POPF was also not significantly influenced by the presence of bacterobilia. The impact of bacterobilia on the occurrence of POPF is still a matter of debate. Only recently, Heckler et al. [26] showed that colonization of bile ducts in previously stented patients is associated with the prevalence of major surgical complications such as POPF C, as POPF type C occurred more frequently in *E. coli*-colonized patients. Ohgi et al. [4] also concluded that bacterobilia was found to be a risk factor for grade B/C POPFs, and bacteria from the infected bile may be the source of the grade B/C POPFs. Contrary to those studies though, Müssle et al. [10] concluded in their meta-analysis that bacterobilia is not associated with POPF, results which are in line with those of the present study. However, in the present study, preoperative bacterobilia was an independent predictor of SSI in the multivariable analysis. This result is in line with that in a recent meta-analysis [10], including 28 studies with 8.523 patients.

Since we included both patients with and without PBD, we performed a subgroup analysis to examine whether PBD was associated with adverse clinical outcomes after PD. No differences were found in patients with and without PBD with regard to the occurrence of clinically relevant (Clavien-Dindo ≥ III) complications, relevant POPF (grade B/C), DGE (grade B/C), PPH (grade B/C), and length of hospital stay postoperatively. Similarly, DePastena et al. [3] in one of the largest retrospective series published to date including 1,500 patients, 714 of whom received biliary stenting prior to operation, reported similar rates of major postoperative complications in both groups [3]. Gavazzi et al. [20] in a retrospective cohort of 180 patients, both stented and non-stented, also found no differences regarding the overall incidence of postoperative surgical complications.

The retrospective characteristic of the present study should be acknowledged as its main limitation. Moreover, as in most retrospective studies, selection bias may have existed regarding the indications for PBD. Also, some variables regarding PBD, such as PBD-associated complications, were not completely available for analysis. Moreover, due to the restrictions in the information provided by the prospectively maintained database, some low-grade complications (Clavien-Dindo < III) may have been missed.

Conclusions

In conclusion, preoperative bacterobilia is an independent risk factor of SSI after PD, whereas clinically relevant postoperative complications including POPF are not significantly influenced by positive bile cultures. Patients with PBD show significantly higher rates of polymicrobial bile colonization with resistance to ampicillin-sulbactam as well as fungal bile colonization, compared to patients without PBD.

Statement of Ethics

According to the Institutional Review Board of University Hospital Marburg, an IRB approval was not mandatory for conducting the present retrospective analysis.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

I.M. and D. B.: conception and design of the study, and analysis and interpretation of data. I.M., D.B., M.L., E.M., and V.K.: drafting and revision of the article. All authors: final approval of the version to be published.

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