

Effect of preoperative biliary drainage on intraoperative biliary cultures and surgical outcomes after pancreatic resection

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Background: Prolonged obstructive jaundice (OJ), associated with resectable pancreatic pathology, has many deleterious effects that are potentially rectifiable by preoperative biliary drainage (POBD) at the cost of increased postoperative infective complications. The aim of this study is to assess the impact of POBD on intraoperative biliary cultures (IBCs) and surgical outcomes in patients undergoing pancreatic resection.

Methods: Data from patients at Groote Schuur Hospital, Cape Town, between October 2008 and May 2019 were analysed. Demographic, clinical, and outcome variables were evaluated, including perioperative morbidity, mortality, and 5-year survival.

Results: Among 128 patients, 69.5% underwent POBD. The overall perioperative mortality in this study was 8.8%. The POBD group had a significantly lower perioperative mortality rate compared to the non-drainage group (5.6% vs. 25.6%). POBD patients had a higher incidence of surgical site infections (55.1% vs. 23.1%), polymicrobial growth from IBCs and were more likely to culture resistant organisms. Five-year survival was similar in the two groups.

Conclusion: POBD was associated with a high incidence of resistant organisms on the IBCs, a high incidence of surgical site infections and a high correlation between cultures from the surgical site infection and the IBCs.

Keywords: pancreaticoduodenectomy, preoperative biliary drainage, surgical site infection, complications, pancreatic cancer, obstructive jaundice

Introduction

Obstructive jaundice (OJ) is a common presenting symptom in patients with periampullary tumours who may need surgical resection, which is the only curative-intended treatment for patients with periampullary cancers.^{1,2} Unrelieved and prolonged OJ is associated with malnutrition, coagulopathy, impaired immune and renal function and poor wound healing.³ Infective complications occur in up to 38% of patients after pancreaticoduodenectomy and are associated with increased length of hospital stay, increased cost of treatment, need for additional invasive procedures, post-pancreatectomy bleeding, delay in commencing adjuvant chemotherapy and diminished disease-free survival.⁴ Endoscopic or percutaneous preoperative biliary drainage (POBD) will correct the physiological abnormalities associated with OJ.⁵ Endoscopic stenting with placement of self-expanding metal stents (SEMS) is favoured.^{6,7} Routine POBD, however is associated with an increase in postoperative infective complications and has generally been reserved for patients with cholangitis, malnutrition, very high bilirubin levels and those requiring neo-adjuvant therapy.⁸⁻¹²

Perioperative antimicrobial therapy has been shown to reduce surgical site infections. Evidence suggests that

patients who undergo POBD biliary drainage may benefit from more prolonged antimicrobial therapy.¹³ Antibiotics used for prophylaxis should be tailored to the antibiotic sensitivities of the most prevalent organisms cultured in bile of patients following POBD at the specific institution.

The aim of this study was to evaluate the effect of POBD on the intraoperative biliary cultures (IBCs) of patients undergoing pancreaticoduodenectomy (PD) and to assess a possible correlation between IBCs, postoperative infective complications and mortality.

Patients and methods

Patients who underwent a PD or total pancreatectomy at Groote Schuur Hospital, Cape Town, between 1 October 2008 and 31 May 2019 and were followed up for at least five years were identified from a Human Research Ethics Committee approved registry (HREC R016/2016). Only patients with malignant pathology who had IBCs performed during the pancreatic resection were included in the study. Perioperative variables analysed included demographic data, preoperative blood tests, operation performed, details of POBD, prophylactic antibiotic use, morbidity and management of complications, length of ICU and hospital

stay, tumour stage and mortality (perioperative and 5-year overall survival).

Perioperative morbidity and mortality were defined as complications or death occurring within 30 days of surgery or during the index hospital admission. Postoperative bleeding, pancreatic leaks and delayed gastric emptying were defined and graded according to the International Study Group of Pancreatic Surgery definitions.¹⁴ Sites of infection and surgical site infections were classified according to the Centre for Disease Control and Prevention guideline for the prevention of surgical site infection¹⁵ and the severity of postoperative complications were graded according to the Clavien-Dindo classification.¹⁶

Intraoperative biliary cultures (IBCs) in patients who underwent POBD were compared to those without drainage. Sub-analyses were performed in patients with positive and negative IBCs in the two groups comparing length of ICU and hospital stay, tumour stage, and morbidity and mortality. In patients with infective complications, postoperatively acquired microbiological specimens were compared to IBCs. In addition, prophylactic antibiotics use was evaluated.

Statistical analysis was performed using IBM SPSS Statistics version 29.0 software. Demographic and clinical characteristics were described as frequencies and percentages or as a median and range. Survival data were analysed using the Kaplan-Meier method. Differences between the POBD and non-drained groups were evaluated using the Fisher exact test for categorical data and the t-test for continuous

data. The statistical significance level was set at 0.05 and all *p*-values were two sided.

Ethical approval for the study was obtained from the University of Cape Town Human Research Ethics Committee (HREC 065/2021).

Results

One hundred and twenty-eight patients met the inclusion criteria of whom 89 (69.5%) had POBD (Figure 1). Seventy-three (82.0%) patients in the POBD group had endoscopically placed biliary stents, 12 (13.5%) had percutaneously placed stents and four (4.5%) had combined endoscopic and percutaneous procedures.

The POBD and non-drainage groups had similar demographic and preoperative blood results with the only significant difference being a higher preoperative total bilirubin in the POBD group (Table I). Sixty-six patients (51.6%) had pancreatic ductal adenocarcinoma (PDAC), 35 (27.3%) ampullary adenocarcinoma and 21(16.4%) distal cholangiocarcinoma. A higher proportion of patients in the POBD group had PDAC (66.7% vs 45%) although this result was not significant (Table I).

One hundred and twenty-one patients (94.5%) had a pylorus preserving pancreaticoduodenectomy, three (2.3%) a classic pancreaticoduodenectomy and four (3.1%) a total pancreaticoduodenectomy. Eighty-one (63.3%) patients had T3 tumours, 35 (27.3%) had T2 tumours, nine (7.0%) had

Table I: Patient demographics, laboratory results, surgical treatment and tumour stage in relation to biliary drainage

Variable	POBD <i>n</i> = 89		No POBD <i>n</i> = 39		<i>p</i> -value
	<i>n</i>	%	<i>n</i>	%	
Gender					
Male	49	55	19	48.7	0.57
Female	40	45	20	51.3	
Type of tumour					
Pancreatic ductal adenocarcinoma	40	45	26	66.7	0.34
Ampullary carcinoma	28	31.5	7	17.9	0.14
Cholangiocarcinoma	18	20.2	3	7.7	0.12
Neuroendocrine tumour	2	2.2	0	0	1.00
Melanoma	1	1.1	0	0	1.00
Type of surgery					
Pylorus preserving PD*	83	93.3	38	97.4	0.67
Classic PD*	2	2.2	1	2.6	
Total PD*	4	4.5	0	0	0.31
Cancer T stage					
T1	5	5.6	4	10.3	0.45
T2	26	29.2	9	23.1	0.52
T3	55	61.8	26	66.7	0.69
T4	3	3.4	0	0	0.55
	Median	Range	Median	Range	
Age median (range)	59	35–76	60	36–77	0.67
Biochemistry at presentation					
Total bilirubin (umol/l)	235	7–723	137	3–454	0.01
Albumin (g/l)	35	15–51	38	24–52	0.89
Creatinine(umol/l)	59	12–147	69	27–118	0.78
Haemoglobin (g/dl)	11.8	7.8–16.9	12.7	8.7–15.4	0.66
White cell count (10 ⁹ /l)	8.5	4.6–37.4	8.6	3.6–17.3	0.800

*PD – Pancreaticoduodenectomy, # POBD – Preoperative biliary drainage

Table II: Postoperative complications in relation to biliary drainage

Clavien-Dindo classification	POBD# n = 89		No POBD# n = 39		p-value
	n	%	n	%	
1	10	11.2	2	5	0.34
2	29	32.6	7	17.9	0.13
3	7	7.9	4	10.3	0.73
4	8	9.0	1	2.6	0.27
5	0	0	1	2.6	0.3
6	5	5.6	10	25.6	< 0.01
Surgical complications					
Surgical site infection	49	55.1	9	23.1	< 0.01
Superficial	38	47	5	12.8	< 0.01
Deep	11	12.4	4	10.3	1
Pancreatic fistula	22	24.7	7	17.9	0.49
Biliary fistula	2	2.2	2	5.1	0.58
Other fistula	3	3.4	2	5.1	0.64
Bleeding (extra-luminal)	7	7.9	1	2.6	0.43
Bleeding (intra-luminal)	3	3.4	0	0	0.55
Delayed gastric emptying	5	5.6	0	0	0.32
Other	8	9.0	5	12.8	0.53
Non-surgical complications					
	Median	Range	Median	Range	
Time of in hospital deaths* (days)	17	7–36	5	3–9	

POBD – Preoperative Biliary Drainage, *Calculated from day of surgery

Table III: Organisms cultured from intraoperative biliary specimens in relation to biliary drainage

Intraoperative culture	Total	POBD# n = 89		No POBD# n = 39		p-value
		n	%	n	%	
Enterobacter cloacae	22	18	20.2	4	10.6	0.21
Escherichia coli	21	20	22.4	1	2.6	< 0.01
Klebsiella pneumonia	19	16	17.9	3	7.7	0.18
Enterococcus faecalis	12	9	10.1	3	7.7	1.00
Klebsiella oxytoca	10	8	8.9	2	5.1	0.72
Candida sp	9	9	10.1	0	0	0.06
Serratia marascens	4	3	3.3	1	2.6	1.00
Citrobacter braaki	3	2	2.3	1	2.6	1.00
Citrobacter freundii	3	3	3.4	0	0	0.55
Enterobacter aerogens	3	2	2.3	1	2.6	1.00
Morganella morganii morganii	3	3	3.4	0	0	0.55
Proteus mirabilis	3	2	2.3	1	2.6	1.00
Pseudomonas aeruginosa	3	3	3.4	0	0	0.55
Aeromonas sp	2	2	2.3	0	0	1.00
Corynebacterium sp	2	1	1.1	1	2.6	0.55
Enterococcus hiare	2	1	1.1	1	2.6	0.55
Raoltella ornitholytica	2	2	2.3	0	0	1.00
Raoltella planticola	2	2	2.3	0	0	1.00
Serratia liqefascens	1	1	1.1	0	0	1.00
Acinetobacter baumannii complex	1	1	1.1	0	0	1.00
Enterobacter asburiae	1	1	1.1	0	0	1.00
Proteus vulgaris	1	1	1.1	0	0	1.00
Pseudomonas putida	1	1	1.1	0	0	1.00
Staphylococcus haemolyticus	1	1	1.1	0	0	1.00
Streptococcus anginosus	1	0	0	1 (2.6)	2.6	0.30

POBD – Preoperative biliary drainage

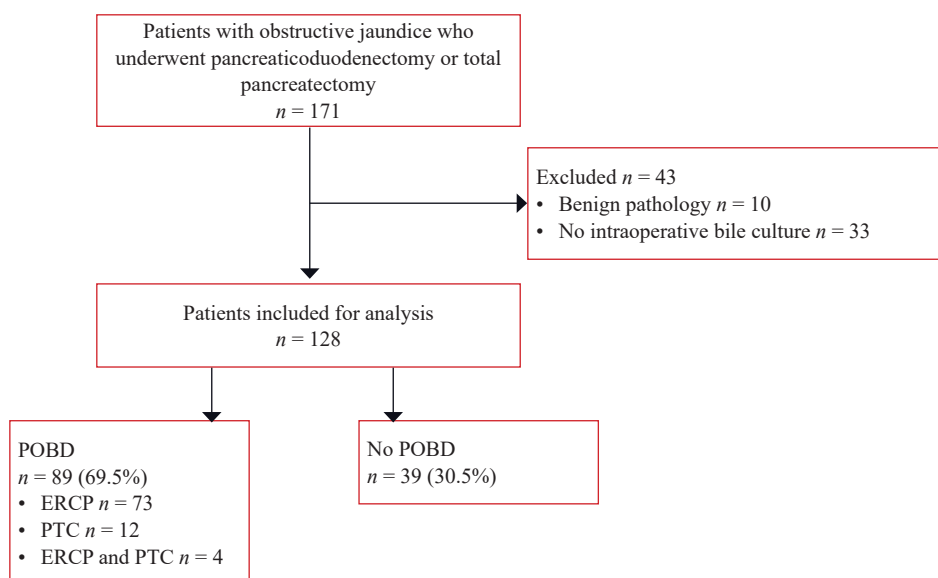


Figure 1: Details of patients included in the study

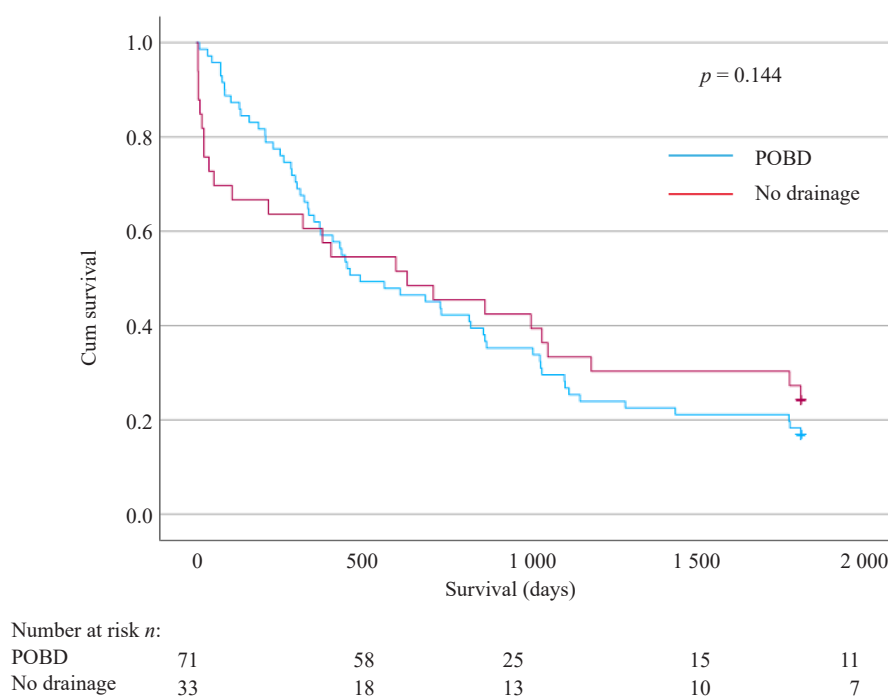


Figure 2: Overall survival

T1 tumours and three (2.3%) had T4 tumours. Prophylactic antibiotic use varied with no standardised policy for patients undergoing pancreatic surgery (Table I).

The overall perioperative mortality rate in this study was 8.8%. The perioperative mortality rate in the non-drainage group was significantly higher than the POBD group (25.6% versus 5.6%). The deaths in the non-drainage group occurred earlier than the deaths in the POBD group (median 5 vs. 17 days post-surgery) and were more frequently related to non-surgical complications (Table II). One hundred and four (81.3%) patients were followed up until death or at least five years. The overall 5-year survival was 19.2% with no difference between the two groups (Figure 2).

The culture results in patients who underwent POBD were compared to those who did not have drainage. The upfront surgical group were significantly more likely to have no

growth on the IBC compared to the POBD group (38.5% vs 6.7%). Patients in the POBD were more likely to grow multiple organisms. The most common bacteria cultured from IBC were *Enterobacter cloacae*, *Klebsiella pneumonia*, *Escherichia coli* and *Enterococcus faecalis* (Table III). *Escherichia coli* was significantly more common in the POBD drainage group (22.47% vs 2.56%). *Candida spp* were cultured in 9 (10.11%) patients in the POBD drainage group and none of the non-drainage group. The organisms cultured in the POBD were more likely to be resistant to commonly used antibiotics (Supplementary Tables I and II).

Surgical site infections occurred in 58 (45.3%) patients and pancreatic fistula in 29 (22.7%) of patients and were significantly more likely to occur in the POBD group (Table II). Fifteen (11.7%) patients with surgical site infections required percutaneous drainage of intra-abdominal

collections. Post-pancreatectomy bleeding occurred in 11 (8.5%) patients of whom seven required angiography with stenting or coiling of the bleeding vessel (Table II).

Forty-five (50.6%) patients in the POBD group had at least one positive postoperative culture versus 21 (53.8%) in the non-drainage group. These cultures were significantly more likely to correlate with the IBC in the POBD group (40.0% vs 19.0%).

Discussion

Preoperative biliary drainage is known to result in colonisation of the biliary tract and has been shown in several meta-analyses to be associated with an increased incidence of surgical site infections.^{4,17,18} These findings were confirmed in this study, with the non-drainage group significantly more likely to have no growth on the IBC compared to the POBD group. Patients undergoing POBD were also more likely to culture resistant organisms and have polymicrobial growth from the IBC. *Candida* were also more commonly cultured in the POBD group. The IBCs in our cohort were similar to studies from other parts of the world (Tables III and IV).¹⁹⁻²²

Prolonged systemic perioperative antimicrobial therapy compared to perioperative prophylactic antimicrobial therapy only at the time surgery has been shown to decrease the incidence of deep surgical site infections.^{13,23,24} In this study patients in the POBD group were more likely to develop surgical site infections and have a correlation between IBCs and postoperative cultures. As POBD results in biliary contamination with organisms that are often resistant to conventional prophylactic antibiotics, antimicrobial therapy should be guided by local hospital surveillance data based on routine IBCs during pancreatic resections.²⁵⁻³⁰ The IBCs in this study support the use of piperacillin and tazobactam, ceftriaxone, ciprofloxacin, bactrim (sulfamethoxazole and trimethoprim), aminoglycosides and carbapenems. A high proportion of the cultured organisms were resistant to co-amoxiclav and cefuroxime.

The overall perioperative mortality rate in this study was 8.8% which is comparable to other studies.³¹ Unexpectedly there was a significantly higher perioperative mortality in the non-drainage group (25.6% versus 5.6%) in contrast to most other studies. These findings support routine POBD in our patient population. Many of the patients in this study were from low socio-economic backgrounds with extensive comorbidities and very high bilirubin levels (> 250 µmol/l) at presentation. This cohort of patients may benefit more from POBD and prehabilitation than patients from better resourced environments with fewer comorbidities and lower bilirubin levels at presentation.³²⁻³⁴ The perioperative deaths in the non-drainage group occurred earlier and were mostly due to multiple organ failure. The deaths in the POBD drainage occurred later and were frequently associated with surgical site infections, pancreatic fistulas and post-pancreatectomy bleeding. Despite the significant differences in perioperative deaths there was no significant difference in the 5-year survival between the two groups.

Although neo-adjuvant chemotherapy (NAC) has primarily been used in patients with borderline resectable PDAC, there is an increasing trend towards offering neo-adjuvant chemotherapy to patients with upfront resectable PDAC to allow improved assessment of tumour biology and prehabilitation prior to surgery.³⁵⁻³⁸ This has resulted in more

patients requiring POBD. This trend may be associated with an increase in surgical site infections.

Limitations of this study include the variable use of prophylactic antibiotics and the lack of a defined antibiotic policy making assessment of prophylactic antibiotic use difficult. The study was also conducted in a single centre necessitating a long study period to include an adequate number of patients. IBCs were not performed routinely in all patients during the study period with 33 (19.3%) patients being excluded because they did not have an IBC.

In conclusion, this is one of a few studies from sub-Saharan Africa assessing the effect of POBD on IBCs and surgical outcomes after pancreatic resection. POBD was associated with a high incidence of resistant organisms on the IBCs, a high incidence of surgical site infections and a high correlation between cultures from the surgical site infection and the IBCs. This supports prolonged antibiotic therapy after pancreatic surgery guided by local hospital surveillance data based on routine IBCs during pancreatic resections.

Conflict of interest

The authors declare no conflict of interest.

Funding source

None.

Ethical approval

Ethical approval for the study was obtained from the University of Cape Town Human Research Ethics committee (HREC 065/2021).

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