

ORIGINAL ARTICLE

Preoperative surveillance rectal swab is associated with an increased risk of infectious complications in pancreaticoduodenectomy and directs antimicrobial prophylaxis: an antibiotic stewardship strategy?

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Abstract

Background: Despite improvements in the perioperative care, the morbidity rate after pancreaticoduodenectomy (PD) is still higher than 50%. The aim of this study was twofold: first, to assess the correlation between preoperative rectal swab (RS) and intraoperative bile cultures; to examine the impact of RS isolates on postoperative course after PD.

Methods: An observational study was conducted analyzing all consecutive PD performed from January 2015 to July 2016. Based on the positivity/negativity of preoperative RS for multi-drug resistant bacteria, two groups of patients were identified (RS+ vs. RS-) and then compared.

Results: Three hundred thirty-eight patients were considered for the analysis. RS culture showed a perfect correlation (species and phenotypic antibiotic susceptibility pattern) with bile culture in 157 patients (86.7%). Fifty patients (14.8%) had a RS+. Preoperative biliary drain (PBD) was the single independent preoperative risk factor associated to RS+ ($p = 0.021$, OR = 2.6, 95% CI = 1.5–11.7). Infective complications (IC) and mortality were independently correlated to RS+ ($p = 0.013$, OR = 2.9, 95% CI = 1.3–6.7; $p = 0.009$ OR = 3.4, 95% CI = 1.8–14.9, respectively).

Conclusions: Preoperative surveillance RS-culture's positivity correlates to biliary colonization that occurs after PBD. IC and mortality after PD are associated with RS+. Preoperative RS can direct antibiotic prophylaxis to reduce morbidity and mortality after PD.

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Introduction

In the last decades, continuous progress has been made in peri- and post-operative management of patients submitted to pancreatic resection. Despite these improvements, the post-operative morbidity rate after pancreaticoduodenectomy (PD) remains high, ranging from 30 to 50% even in high volume centers.^{1,2} Particularly, infectious complications (IC) are the primary cause of postoperative morbidity, occurring in nearly

one-third of PDs and almost one-quarter of distal pancreatectomies.^{3–5}

Several studies show an association among preoperative biliary drain (PBD), contaminated bile and IC in patients undergoing PD.^{6–8} The correlation between the microorganisms isolated from the intraoperative bile samples and the surgical site infections (SSI) culture has been also demonstrated.⁶ The most common micro-organisms detected in bile cultures are *Enterococcus* spp., *Enterobacteriaceae*, in particular *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae* and non-fermenter *Pseudomonas aeruginosa*.^{9–12}

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Recently, the emergence of multidrug-resistant (MDR) bacteria became a challenge due to the additional increase in morbidity/mortality rates and treatment costs.¹³ Extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae* and carbapenemase-producing *Enterobacteriaceae* (CPE) have rapidly disseminated during the last two decades, evolving in a global epidemic.^{14,15} Since the first description in the 90s, the infections sustained by ESBL *Enterobacteriaceae* increased tenfold in the last years¹⁶ and, recently, the epidemiological panorama has get worse with the rapid dissemination of CPE, in particular *K. pneumoniae*.³⁶

The spread of these resistant microorganisms explains the increase in morbidity and mortality when the antibiotic resistance comes to the fore.¹⁷ Indeed the antibiotic equipment against CPE is quite poor, leading to persistent infections, which increase length of stay, supplementary treatments and costs.¹³ Furthermore, it has been demonstrated that the antibiotic prophylaxis (AP) used for PD is usually inefficient, especially against the MDR bacteria present in the contaminated bile.^{18,19} Many centers have proposed surveillance protocols to early recognize an enteric colonization by Gram-positive and Gram-negative MDR and to introduce a proper infection control program. For example, the institution of contact-isolation of colonized patient limits the spread of these bacteria, especially in an epidemic setting.²⁰ In this scenario, the rectal swab (RS) seems to be the cheapest, simple and reliable test for routine detection of MDR as enteric colonizers.²¹

The aim of the present study was twofold: to assess the correlation between preoperative RS and intraoperative bile cultures and to examine the impact of our institutional surveillance program of infections, based on RS, on postoperative course after PD.

Methods

The study was conducted, after the Institutional Review Board approval, according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.²²

Study design

An observational study was conducted querying our Institutional electronic prospectively maintained database for all consecutive PD performed from January 2015 to July 2016. Data extracted were retrospectively analyzed. Demographic and clinical details included age, gender, ASA score, Body Mass Index, diabetes mellitus, Charlson Age-related Comorbidity Score Index,²³ jaundice and PBD. Based on the positivity/negativity of preoperative surveillance RS for multi-drug resistant bacteria, the population was divided into two groups subsequently compared (RS+ vs. RS-).

Microbiological method

RS was streaked on selective media ChromoID® ESBL (bioMérieux, Lyon, France) plus an ertapenem disk (10 µg) and

MacConkey agar plus a meropenem disk (10 µg) were used to detect ESBL producing Enterobacteria, CPE and *P. aeruginosa*. CNA agar plus 6 mg/ml of vancomycin was used to detect Vancomycin Resistant Enterococci (VRE). The strains were identified using Maldi-tof technology with VITEK MS® (bioMérieux, Lyon, France). Carbapenemase production was confirmed with CarbaNP rapid test²⁴ while ESBL production was confirmed with ESBL NDP rapid test.²⁵ The antimicrobial susceptibility testing was performed by VITEK-2® automated system (bioMérieux, Lyon, France). Results were interpreted according to the latest EUCAST guidelines.²⁶ Glycopeptides resistance for enterococci was confirmed by Etest (bioMérieux, Lyon, France).

Operative procedure and definitions

All patients scheduled for PD were enrolled in the surveillance program. RS were collected at the preoperative testing, typically two to three weeks before surgery. The Institutional surgical technique of PD used in the series has already been described.²⁷ PD was usually carried out with pylorus preservation and standard lymph node dissection, according to ISGPS definition.²⁸ A vascular resection was performed when portal vein or superior mesenteric vein were involved. Management of the pancreatic stump consisted in a single-layer end to side pancreaticojejunostomy or a single-layer pancreaticogastrostomy fashioned through an anterior gastrotomy (with or without duct-to-mucosa anastomosis and with or without Wirsung duct external stenting).^{29,30} Two drains were positioned according to the intraoperative Fistula Risk Score.³¹ All patients with PBD and patients with preoperative positive RS underwent to intraoperative bile sampling. All patients of the cohorts received an AP, if a PBD was present the AP was adapted accordingly. The standard AP consisted of ampicillin/sulbactam (2 g + 1 g i.v. before skin incision, then 1 g + 0.5 g every 3 h until the end of surgery). Whereas, the patients carrying a PBD received an additional short-term antibiotic course, consisting of the administration of 2 g + 1 g i.v of ampicillin/sulbactam three times daily until the third postoperative day.

The results of RS were recorded. Major and minor postoperative complications were registered and classified according to Clavien–Dindo classification of surgical complications.³² IC included surgical site infections (SSI), clinical sepsis, pneumonia, urinary tract and blood stream infections. The presence of bacteria or fungi in a sample was considered expressive of IC if associated to a septic syndrome (as defined by ACCP/SCCM 2001 International sepsis definitions criteria³⁰), to an imaging (CT or MRI) suggestive of infected abdominal collections and to a significant biomarkers modification (i.e.: high-levels of C-reactive protein, procalcitonin, white blood cells count), in order to consider real infections and not just colonization. The severity of septic episodes was classified according to the ACCP/SCCM 2001 Consensus Conference updated definitions as well.³³ Clinically relevant pancreatic fistula (CR-POPF) was defined

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