

ORIGINAL ARTICLE

# Early biliary complications following pancreaticoduodenectomy: prevalence and risk factors

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## Abstract

**Background:** Early biliary complications (EBC) following pancreaticoduodenectomy (PD) are poorly known. This study aimed to assess incidence, predictive factors, and treatment of EBC including bilio-enteric stricture, transient jaundice, biliary leak, and cholangitis.

**Method:** From 2007 to 2011, 352 patients underwent PD. Statistical analysis including logistic regression was performed to determine EBC predictive factors.

**Results:** 49 patients (14%) developed 51 EBC, including 7(2%) bilio-enteric strictures, 15(4%) transient jaundices, 9(3%) biliary leaks, and 20(6%) cholangitis with no mortality and a 18% reoperation rate. In multivariate analysis, male gender, benign disease, malignancy with preoperative chemoradiation, and common bile duct (CBD) diameter  $\leq 5$  mm were predictive of EBC. Of the 7 strictures, all were associated with CBD  $\leq 5$  mm and 5(71%) required reoperation. Transient jaundice resolved spontaneously in all 15 cases. Among 8 patients with serum bilirubin level  $>50$   $\mu\text{mol/L}$  (3 mg/dL) at POD3, 7(88%) developed bilio-enteric stricture. Biliary leak resolved spontaneously in 5(56%); otherwise, it required reoperation. Cholangitis recurred after antibiotics discontinuation in 5(25%).

**Conclusions:** EBC following PD do not increase mortality. EBC are more frequent with male gender, benign disease, malignancy with preoperative chemoradiation, and CBD  $\leq 5$  mm. Transient jaundice or cholangitis has a favorable outcome, whereas bilio-enteric stricture or biliary leak can require reintervention.

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## Introduction

In high-volume centers, pancreaticoduodenectomy (PD) is presently associated with a mortality rate below 5%, but peri-operative morbidity remains significant, occurring in 40–50% of patients.<sup>1,2</sup> The most frequent complications following PD are pancreatic fistula, delayed gastric emptying, and hemorrhage, justifying the recent publications of their own grading system.<sup>3–5</sup> Incidence, risk factors, and management of these complications

have been extensively studied, including through prospective randomized trials.<sup>6–9</sup> On the other hand, less frequent post-operative early complications such as ischemic complications,<sup>10</sup> infectious complications,<sup>11</sup> gastrojejunostomy fistula,<sup>12</sup> chylous leak,<sup>13</sup> or biliary complications<sup>14,15</sup> have been poorly investigated, and their management remain challenging. Particularly, early biliary complications (EBC) following PD are only reported as biliary leak or stenosis.<sup>14,15</sup> However, EBC consist of a wider spectrum also including cholangitis and transient jaundice, which have not been extensively characterized. The aim of the present study was to describe incidence, predictive factors, and management of the spectrum of EBC following PD.

This study was presented at the 11th World IHPBA Congress, 22–27 March 2014, Seoul.

## Methods

### Data acquisition

From January 2007 to December 2011, 352 patients underwent PD in the department of Hepato-Biliary and Pancreatic Surgery, Beaujon Hospital. Demographic, radiologic, postoperative course, and pathologic data were obtained from a prospective database with additional retrospective medical record review. All clinical, biochemical, and radiologic data were prospectively collected. The database was analyzed in regards to prevalence and risk factors of postoperative biliary complications.

All procedures were performed through laparotomy by three experienced surgeons (AS, SD, BA). PD were performed as previously described.<sup>10</sup> Pancreatico-enteric continuity was restored by pancreaticogastrostomy or pancreaticojejunostomy according to the surgeon's preference. In patients who had pancreaticogastrostomy, hepaticojejunostomy was performed on the first jejunal loop 60 cm upstream of the gastrojejunostomy. In patients who had pancreaticojejunostomy, hepaticojejunostomy was performed 40–50 cm downstream of the pancreatic anastomosis. Hepaticojejunostomy was routinely performed on the upper part of the common bile duct (CBD) in case of malignancy and on the CBD divided at the upper edge of the pancreas in case of benign disease. In the latter setting, low CBD division was chosen to obtain a larger diameter, and care was taken to avoid CBD devascularization caused by extensive dissection in the hepatic pedicle. Anastomosis modalities were driven by technical considerations. Briefly, interrupted sutures were preferentially used for the small CBD diameter ( $\leq 5$  mm), a running suture was used for the large CBD diameter ( $> 1$  cm), and a mixed technique (i.e., posterior running suture and interrupted anterior suture) was used otherwise. In case of a small CBD diameter, an enlargement plasty by either anterior ductal wall incision or side-to-side ductoplasty using a cystic duct was performed. Sutures were always performed with 5/0 or 6/0 monofilament synthetic absorbable sutures. No biliary stenting was used. A retrocolic gastrojejunostomy was performed 40–50 cm below the hepaticojejunostomy. A routine bile sampling was routinely performed at the beginning of PD for microbiological examination, including bacterial susceptibility to antibiotics. According to our institutional protocol, all patients with preoperative biliary stenting or ampulloma received a routine 5-days postoperative antimicrobial therapy, as previously reported.<sup>2,11</sup> At the end of the procedure, a multichannel, open silicone drain was placed close to both pancreatic and biliary anastomoses and externalized through a separate right flank incision.

### Postoperative management and complications

Octreotide (Sandostatin<sup>®</sup>, 100  $\mu$ g subcutaneously 3 times per day, Novartis, Rueil Malmaison, France) was given to patients with a soft pancreas and started intraoperatively. Postoperatively, biological assessment including amylase level in the drain fluid was routinely done on days 3, 5, 7, and 10. The bilirubin level in

the drain fluid was only assessed in case of clinical suspicion of biliary leak.

The drain was removed incrementally over a course of days from postoperative day 5. Postoperative mortality included all deaths that occurred before postoperative day (POD) 90. Morbidity included all complications following surgery until discharge and/or readmission and was graded according to the Clavien-Dindo classification.<sup>16</sup> Major postoperative complication was defined as a Clavien-Dindo grade  $\geq 3$ . Postoperative pancreatic fistula (POPF), hemorrhage, and delayed gastric emptying were defined according to the International Study Group of Pancreatic Surgery (ISGPS).<sup>3,5</sup>

Early biliary complications (EBC) (occurring within 90 postoperative days) were defined and treated as follows:

- 1 *Bilio-enteric stricture* was defined by a new onset of jaundice increasing continuously and related to obstruction confirmed by biliary dilatation on postoperative imaging (ultrasonography or CT). Strictures were managed by interventional radiology (percutaneous transhepatic balloon dilatation and stenting of the anastomosis) or reoperation, according to surgeon's preference.
- 2 *Transient jaundice* was defined by a temporary increase of serum bilirubin level 2 times above the upper limit of the normal range (i.e., above 35  $\mu$ mol/L, 2 mg/dL). Imaging was usually performed to exclude intra-hepatic biliary dilatation. Apart from monitoring liver function tests, no specific treatment was given.
- 3 *Biliary leak* was defined by a bilious aspect of the drainage fluid confirmed biologically in patients without concomitant pancreatic fistula or bile duct ischemic complications.<sup>10</sup> Particularly, to avoid inclusion of patients with biliary fistula secondary to POPF, we excluded from the diagnosis of biliary leak every patient with amylase assay in the drainage fluid greater than three times the upper normal value at diagnosis of biliary leak. No fistulography was used. Biliary leak were managed by drainage until resolution or reoperation (revision of the bile duct anastomosis  $\pm$  T tube) in case of sepsis or high output persistent fistula.
- 4 *Cholangitis* was defined by the association of clinical signs of infection (fever and chills), an increase in serum inflammatory markers, and abnormal liver functions tests improving over time under antibiotic therapy.

### Statistical analysis

Values are expressed as median (interquartile range, IQR), mean (standard deviation, SD), or number of patients and percentage, as appropriate. Univariate analysis was performed to test the association between the patients' characteristics and EBC occurrence using the Chi-squared test or Fisher's exact test when appropriate. Multivariate analysis was then performed to determine the main independent risk factors for EBC. All independent variables for which the p-value was  $\leq 0.20$  at the univariate

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