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Original Research

Substantial atherosclerotic celiac axis stenosis is a new risk factor for biliary fistula after pancreaticoduodenectomy

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A R T I C L E I N F O

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A B S T R A C T

Background: Biliary fistula (BF) is a major surgical complication that can develop after pancreaticoduodenectomy (PD) whose risk factors remain unclear. Substantial atherosclerotic celiac axis stenosis (SACAS) has not been reported to be one of them.

Methods: Data from 507 patients undergoing PD between Jan 1, 2013 and Dec 31, 2015 were retrospectively collected. Clinical data from patients with SACAS were studied, and the independent risk factors for BF underwent multivariate logistic regression analysis, including SACAS.

Results: BF occurred in 22 (4.3%) patients, and the incidence of BF was significantly higher in patients with SACAS than in those without it (27.0% vs 2.6%, $P < .001$). In the univariate analysis, BF was significantly related to SACAS, older age, a higher ASA score, history of coronary disease, greater blood loss and RBC transfusion during surgery, smaller CBD diameter and higher POD 1 BUN level. The multivariate analysis showed that only SACAS (OR 8.91, 95% CI 2.36–33.69, $P = .001$), older age (OR 1.08, 95% CI 1.01–1.15, $P = .028$) and smaller preoperative CBD (OR 0.79, 95% CI 0.69–0.92, $P = .002$) were independent risk factors for postoperative BF.

Conclusion: Older age and a smaller preoperative CBD diameter are independent risk factors for BF after PD, which is consistent with the literature. In addition, SACAS is a new independent risk factor for BF. For patients with SACAS, postoperative drainage should be carefully managed to precisely observe the potential for BF.

1. Introduction

Pancreaticoduodenectomy (PD) remains the standard procedure for patients with pancreatic head and periampullary neoplasms and also in managing some benign diseases [1,2]. Biliary fistula (BF) is one of the postoperative surgical complications after PD which occurs in 1%–8% of patients [3–8]. Although BF is a less frequent complication of PD procedure than postoperative pancreatic fistula (POPF), post-pancreatectomy hemorrhage (PPH) and delayed gastric emptying (DGE), it is the second most common leakage complication behind POPF, and severe BF can be life threatening [9]. Compared with hundreds of studies focused on POPF published in the last 30 years, BF has been rather under-reported in the pancreatic literature [10], hence the potential risk factors for BF have only been occasionally studied and remain unclear.

Celiac axis stenosis (CAS) is not a finding hardly to be seen in patients undergoing PD which is mainly caused by median arcuate ligament syndrome (MALS) or by atherosclerosis [11–13]. In the circumstances, celiac axis (CA) receives blood supply from superior mesenteric artery (SMA) via the gastroduodenal artery (GDA) and the pancreaticoduodenal arcades [14]. As PD involves resection of this blood supply communication, patients with CAS may suffer from CBD ischemia after the surgery which can potentially lead to biliary anastomotic failure, namely postoperative BF. If caused by MALS, CAS can be resolved by median arcuate ligament division [15,16], but for patients with CAS caused by atherosclerosis, the revascularization of celiac axis can only be achieved, theoretically, by a relatively aggressive manner like preoperative endovascular stenting or simultaneous aortohepatic bypass during PD procedure.

This study aims to use a retrospective database to evaluate the influence of substantial atherosclerotic celiac axis stenosis (SACAS) detected on preoperative CT scan, if not treated, on incidence of postoperative BF, on condition that CAS caused by MALS is surgically resolved.

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2. Method

2.1. Patients' eligibility criteria

Data from 520 consecutive patients undergoing PD procedure between Jan 1, 2013 and Dec 31, 2015 at our institute were retrospectively collected. All patients underwent either classical Whipple procedure or pylorus-preserving pancreaticoduodenectomy (PPPD), by either laparotomy or robotic surgery. Exclusion criteria were: adolescent below 18 years old, pre-existing distal pancreatectomy, insufficient pancreatic tissue for pancreaticojejunostomy, resection and reconstruction of hepatic artery, additional organ resection (kidney, colon) and associated surgical procedure (coronary artery bypass graft). A portal vein (PV)/superior mesenteric vein (SMV) resection was allowed. 508 patients were finally included in this study.

Data collection included patient demographics (gender, age, BMI, ASA score, comorbidity, smoke and alcohol habit), preoperative biliary drainage, operational details (surgery type, veinal resection, operative time, blood loss, intraoperative transfusion), common bile duct (CBD) diameter, preoperative and postoperative day 1 (POD 1) laboratory data, pathological analysis, postoperative surgical complications (mortality, reintervention, BF, POPF, PPH, drainage for abscess, DGE, severe wound infection, ileus, portal thrombosis etc.) and postoperative hospital stay.

2.2. Detection of atherosclerotic celiac axis stenosis and surgical procedure

Patients' preoperative abdominal CTA or injected CT scan were carefully studied to identify the hepatic arterial variation, which was divided into 6 types: CHA arising from CA with LHA arising from CA (Type I, standard); CHA arising from CA with LHA arising from LGA (Type II); CHA arising from SMA (Type III); RHA arising from SMA with LHA/CHA arising from CA (Type IV); RHA arising from SMA with LHA arising from LGA (Type V); Coeliacomesenteric trunk (Type VI).

The diameter stenosis [17] of celiac axis on CT scan was used as the index of atherosclerotic celiac axis stenosis severity. For patients with left and right hepatic arteries both arising from CA (Type I, Type II or Type VI), the atherosclerotic CA stenosis was used to reflect the potential postoperative CBD ischemia. In few patients with hepatic arteries both arising from SMA (Type III), however, we used the atherosclerotic SMA stenosis instead. And in patients with left hepatic artery (LHA) arising from CA and right hepatic artery (RHA) from SMA (Type IV or Type V), the potential postoperative CBD ischemia was considered unpredictable if either CA or SMA stenosis was detected.

PD were performed according to standard procedure. For all patients, before ligating GDA, bulldog clamps were applied to eliminate potential CAS by detecting hepatic arterial pulsation. If not detected, the MALS was routinely suspected, and the median arcuate ligament was divided by median or lateral process [15,16]. No aggressive practice like endovascular stenting or aortohepatic bypass was conducted in patients included in this study. All patients underwent routine digestive reconstruction by pancreaticojejunostomy, biliojejunostomy and gastrojejunostomy successively, with surgical drainage applied for the first two anastomotic sites.

2.3. Definition of outcomes

BF was defined as clinical observation of bilious abdominal drainage beyond 7 days, that was, from POD 8, no matter whether it was associated with POPF (dignosed by amylase level in the drainage) or not. Other diagnostic criteria included necessitation of CT-guided abdominal drainage after removal of drains which turned out to be bilious and reintervention confirming BF. In case of uncertainty for patients with hyperbilirubinemia and that drainage fluid remained bilious, BF was confirmed if bilirubin concentration in drains was more than 3 times higher than serum total bilirubin level.

Substantial atherosclerotic celiac axis stenosis (SACAS) was defined as a diameter stenosis of celiac axis $\geq 50\%$. ROC curve based on atherosclerotic celiac axis stenosis severity was used to evaluate its predictive value for postoperative BF. 508 patients were then divided into those with SACAS and those without. Patients of the 2 groups were compared in terms of demographics, operational details, perioperative data and postoperative surgical complications.

Finally, the risk factors for BF were analyzed. Potential risk factors included in univariate analysis were SACAS, MAL division, and other factors reported in literature [8,10,18–20]: gender, age, BMI, ASA score, diabetes mellitus (DM) and hypertension (HTN) history, smoke and alcohol intake, preoperative biliary drainage, nutrition status, bilirubin level, surgical technique, operative time, intraoperative blood loss, red blood cell (RBC) transfusion, CBD diameter, malignant diseases, POD 1 albumin and prealbumin level, reintervention, associated grade B or C POPF and DSA procedure for hemorrhage. Coronary disease history and POD 1 blood urea nitrogen (BUN) level were also included because they were significantly related to patients with SACAS.

2.4. Statistical analysis

Statistical analysis was performed by SPSS 22.0. Data were presented as prevalence (percentage) for discrete variables, mean ± SD for normal distribution continuous variables, median (range) for non-normal distribution continuous variables and OR (95% CI) for risk factors. The Chi-square test or fisher exact test was used for discrete data, and *t*-test or Mann-Whitney *U* test for continuous data. Variables with $P < .05$ in univariate analysis or for specific reasons were entered into multivariate logistic regression model to determine independent risk factors for BF. A two sided *P* value $< .05$ was considered to be statistically significant.

3. Results

3.1. Patients' clinical data

A total of 508 patients were included in the study (315 male and 193 female, from 19 to 88 years old), of whom 405 underwent laparotomy and 103 underwent robotic surgery. PD were mostly conducted for pancreatic head cancers and periampullary carcinomas.

Patients' hepatic variation is shown in Table 1. The majority of patients' left and right hepatic arterial blood flow originated from CA (Type I, Type II or Type VI arterial variation, n = 483, 95.1%). There existed 400 patients without atherosclerotic CA stenosis, 47 patients with mild stenosis (1%–49% of diameter stenosis) and 36 patients with substantial stenosis (50%–99% of diameter stenosis). For 6 patients (1.2%) with Type III arterial variation, the atherosclerotic CA stenosis was replaced by SMA stenosis to reflect postoperative CBD ischemia. For the rest 19 patients (3.7%) with Type IV or Type V arterial variation, 18 of them was considered to have no CBD ischemia because

Table 1
Patients' hepatic arterial variation according to blood supply.

Type of variation	Number (%)
CHA arising from CA	480 (94.5)
With LHA arising from CA (Type I, Standard)	433 (85.2)
With LHA arising from LGA (Type II)	47 (9.3)
CHA arising from SMA (Type III)	6 (1.2)
RHA arising from SMA	19 (3.7)
With LHA/CHA arising from CA (Type IV)	18(3.5)
With LHA arising from LGA (Type V)	1 (0.2)
Coeliacomesenteric trunk (Type VI)	3 (0.6)
Total	508 (100)

CA, celiac axis; SMA, superier mesenteric artery; CHA, common hepatic artery; LGA, left gastric artery; LHA, left hepatic artery; RHA, right hepatic artery.