



Original article

Influence of bile duct obstruction on the results of Frey's procedure for chronic pancreatitis

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ARTICLE INFO

Article history:

Received 4 May 2013

Received in revised form

19 October 2013

Accepted 21 October 2013

Keywords:

Chronic pancreatitis

Frey's procedure

Biliary obstruction

Pain

Diabetes

ABSTRACT

Objectives: To evaluate the influence of a biliary obstruction (BO) requiring biliary bypass on both short and long-term outcomes of patients undergoing Frey's procedure for chronic pancreatitis (CP).

Methods: From 1999 to 2010, 33 consecutive patients underwent Frey's procedure for CP in two centers. Seventeen (54%) patients underwent biliary bypass to treat an associated BO. Characteristics and outcomes of these patients were compared to those of 16 others without BO.

Results: Patients with BO had more severe disease including lower BMI and larger pancreatic head (4 cm vs. 6 cm, $p = 0.021$). The operative mortality was nil. Patients with BO experienced more overall post-operative complications (71% vs. 31%, $p = 0.024$) but similar major complication rates (18% vs. 6%, $p = 0.316$) compared to those without BO. After a median follow-up of 51 (1–96) months, 91% of the patients experienced either partial or complete relief of their symptoms and 36% exhibited deterioration of their endocrine function. Multivariate analysis revealed preoperative BO to be associated with long-term impairment of endocrine function (OR: 43.249; 95% CI 2.221–84.277; $p = 0.013$).

Conclusion: In patients undergoing Frey's procedure for CP, associated BO can be safely managed using biliary bypass. However, the severity of CP in these patients is responsible for a higher risk of long-term endocrine insufficiency.

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1. Introduction

The management of patients suffering from chronic pancreatitis (CP) remains a major therapeutic challenge. Pain represents the over-riding symptom and is the main indication for surgical therapy [1]. In patients with pain or complications of CP with dilated main pancreatic duct or markedly enlarged fibrotic pancreatic head, Frey's procedure [2,3] has been reported to provide excellent results [4–7], preserving both endocrine and exocrine functions as well as improving quality of life. In case of associated obstruction of the common bile duct (CBD) resulting from pancreatic head enlargement and peri-biliary inflammation, biliary bypass is usually associated with pancreatic ductal decompression. The preoperative characteristics of these patients as well as the operative and long-term influence of associated biliary bypass in this setting remain poorly studied. The aim of this bicentric study was to compare preoperative characteristics and post-operative outcomes

of patients with CP undergoing Frey's procedure and associated biliary bypass for biliary obstruction (BO) to those of patients without biliary stenosis.

2. Patient and methods

2.1. Patient selection

From January 2004 to March 2012, 33 patients underwent Frey's procedure for CP at Saint Antoine Hospital ($n = 20$) and CHU Amiens-Picardie ($n = 13$). Preoperative, operative, postoperative characteristics and long-term results of the 17 (51.5%) patients with BO requiring biliary bypass were compared to those of the other 16 without BO. Patients were identified from two prospectively maintained institutional databases and additional information was obtained by reviewing medical records and contacting patients.

2.2. Diagnosis of chronic pancreatitis and biliary obstruction

Diagnosis of CP was based on clinical history, physical examination, ultrasonography (US), CT-scan, magnetic resonance imaging

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(MRI). Diagnosis of CP was considered in the presence of one or more of the following three criteria: (i) at least moderate duct anomalies, according to the Cambridge classification [8], (ii) the presence of pancreatic calcifications or (iii) extensive fibrosis in pancreatic preoperative biopsies [9]. Postoperative histological examination confirmed CP in all cases. The pancreatic head was considered as enlarged when its maximal diameter exceeded 3.5 cm. The pancreatic duct was considered as dilated when its maximal diameter exceeded 5 mm. The retained criterion for BO requiring biliary bypass was the association of a documented cholestasis (serum conjugated bilirubin >30 $\mu\text{mol/l}$ or alkaline phosphatase (ALP), >3 -fold normal values) and CBD dilatation (>8 mm) as detected on preoperative imaging and confirmed by routine intraoperative cholangiography.

2.3. Surgical procedure

The technique originally described by Frey et al. [2,3,10] was used at both medical centers with modifications or associated procedures taking into account the operative findings. Pancreatography by direct puncture of the main pancreatic duct (MPD) was not routinely performed. Conversely, intraoperative cholangiography was always performed and systematically associated with cholecystectomy. In patients with evidence of BO, a biliary bypass was performed using either hepatico-duodenostomy (HD) or a Roux-en-Y hepatico-jejunostomy (HJ). The type of bilioenteric anastomosis was decided according to the intraoperative findings and the surgeon's preference. No patient underwent marsupialization of the common bile duct into the cephalic resection cavity. In case of symptomatic duodenal compression as demonstrated by either gastroscopy or CT scan on preoperative work-up, a side-to-side gastro-enterostomy was performed.

2.4. Parameters definition

Pain assessment included both frequency of pain bouts using a 3-point pain score and class of analgesics as well as their frequency of use. The pain score was defined as follows: 0: no pain, 1: one to five pain attacks per month, 2: one to six pain attacks per week and 3: one or more pain attacks per day. Analgesic requirements were scored as major (Class 3 morphinomimetic used continuously), moderate (Class 3 morphinomimetic intermittently or Class 2 non-morphinomimetic continuously) and minimal (Class 2 non-morphinomimetic intermittently or Class 1 continuously or intermittently).

Endocrine pancreatic function was assessed according to the existence of glucose intolerance or established diabetes mellitus as defined by the WHO classification [11]. Glucose intolerance was considered in the presence of fasting glucose >1.1 g/l but <1.26 g/l. Diabetes mellitus was defined by a fasting blood glucose >1.26 g/l or a random blood glucose >2 g/l.

Exocrine pancreatic function was defined as the presence of clinical steatorrhea and/or the need for oral pancreatic enzyme supplementation. Measurements of other parameters of exocrine function such as fecal elastase were not routinely performed.

Postoperative complications were stratified according to the "Clavien-Dindo" classification [12]. Major complications (Clavien III–IV) and operative mortality (Clavien V) were defined as occurring within 90 days after surgery or at any time during postoperative hospitalization. Specific complications following pancreatic surgery were defined as follows: (a) post-operative fistula was classified according to the ISGPF [13] and stratified into Grades A, B and C; (b) bile leakage was defined as bilirubin concentration in the drain fluid at least 3-fold serum bilirubin concentration after postoperative day 3 or requiring radiological or

operative procedures to treat biliary collections or peritonitis [14] (c). Delayed gastric emptying and post pancreatectomy hemorrhage were assessed using the ISGPS definitions [15,16].

2.5. Follow-up

After surgery, patients were followed-up at the outpatient clinic, with clinical and laboratory examinations at one and three months and every year thereafter. Clinical examination focused on weight measurement and recent occurrence of jaundice or occult fever in order to detect episodes of cholangitis. Pain was assessed using the above-mentioned pain score. Complete pain relief was considered only in patients with a pain score of 0 at the last follow-up. Endocrine function was assessed by measuring glycosylated hemoglobin (HbA1c), insulin requirements or changes in the type of antidiabetic medications.

2.6. Statistical analysis

Patient baseline characteristics are expressed as median and range for continuous data, or percentages, for categorical data. Preoperative, operative and postoperative characteristics as well as long-term outcomes of patients were compared according to the existence of a preoperative biliary obstruction. Fisher's exact test was used to compare differences in categorical variables, and the Mann Whitney test was used for continuous variables. Risk factors for both incomplete pain relief and late endocrine insufficiency achieving statistical significance at a 0.1 level in univariate analysis were included in multivariable analysis. A backward variable procedure was used to identify independent predictive factors. All tests were 2-sided. A p -value ≤ 0.05 was considered statistically significant. Statistical analyses were performed using SPSS[®] version 18.0 for Windows software (SPSS, Chicago, Illinois, USA).

3. Results

3.1. Preoperative characteristics (Table 1)

The study population of 33 patients included 27 (82%) men. Median age was 48 years (31–74 years). CP was related to chronic alcohol consumption in 26 (79%) cases. In these patients, median consumption was 115 g/day (38–700) and 16 (61.5%) patients had ceased alcohol consumption for more than 6 months prior to surgery with a median duration of abstinence of 24 months (6–240 months). Twenty-six (79%) patients were smokers.

Sixteen patients (48%) presented with endocrine insufficiency including glucose intolerance in 2 (6%) patients and diabetes mellitus in 14 (32%) patients. Nine (27%) patients presented with overt exocrine pancreatic insufficiency. Median duration of symptoms before surgery was 5 years (0–15 years). Overall, 32 (97%) patients presented with episodes of pain including 24 (73%) with a pain score of 3. Thirteen (39%) patients required daily use of Class 3 analgesics.

Seventeen patients (51%) patients presented with evidence of BO including 5 (15%) with preoperative jaundice. Patients with BO had longer duration of their symptoms although the difference was not significantly different (6 years vs. 3 years, $p = 0.291$), had significantly lower BMI, (18 vs. 21 kg/m^2 , $p = 0.021$), were significantly more likely to have an alcohol related CP (94% vs. 62.5%, $p = 0.026$), and displayed larger pancreatic head diameter (6 cm vs. 4 cm, $p = 0.021$).

Thirty-two (97%) patients had pancreatic calcifications mostly localized in the pancreatic head (94%). Fourteen (42%) patients had at least one pseudocyst and two patients (6%) had symptomatic duodenal compression.

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