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Risk factors of exocrine and endocrine pancreatic insufficiency after pancreatic resection: A multi-center prospective study

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KEYWORDS

Exocrine pancreatic function; Endocrine pancreatic function; Pancreatic resection **Summary** Management of functional consequences after pancreatic resection has become a new therapeutic challenge. The goal of our study is to evaluate the risk factors for exocrine (ExoPI) and endocrine (EndoPI) pancreatic insufficiency after pancreatic surgery and to establish a predictive model for their onset.

Patients and methods: Between January 1, 2014 and June 19, 2015, 91 consecutive patients undergoing pancreatoduodenectomy (PD) or left pancreatectomy (LP) (72% and 28%, respectively) were followed prospectively. ExoPI was defined as fecal elastase content < 200μ g per gram of feces while EndoPI was defined as fasting glucose > 126 mg/dL or aggravation of preexisting diabetes. The volume of residual pancreas was measured according to the same principles as liver volumetry.

Results: The ExoPI and EndoPI rates at 6 months were 75.9% and 30.8%, respectively. The rate of ExoPI after PD was statistically significantly higher than after LP (98% vs. 21%; P < 0.001), while the rate of EndoPI was lower after PD vs. LP, but this difference did not reach statistical significance (28% vs. 38.5%; P = 0.412). There was no statistically significant difference in ExoPI found between pancreatico-gastrostomy (PG) and pancreatico-jejunostomy (PJ) (100% vs. 98%; P = 1.000). Remnant pancreatic volume less than 39.5% was predictive of ExoPI.

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Conclusion: ExoPI occurs quasi-systematically after PD irrespective of the reconstruction scheme. The rate of EndoPI did not differ between PD and LP. © 2017 Published by Elsevier Masson SAS.

Abbreviations

- ExoPI exocrine pancreatic insufficiency EndoPI endocrine pancreatic insufficiency **IPMN** intraductal papillary mucinous neoplasm AFC Association française de chirurgie, French Association of Surgery PD pancreatoduodenectomy LP left pancreatectomy PJ pancreatico-jejunostomy PG pancreatico-gastrostomy SIRIC Site de Recherche Intégrée en Cancérologie, Integrated Cancerologic Research Site CEA carcinoembryonic antigen CA 19.9 carbohydrate antigen 19.9 glycosylated hemoglobin HbA1c FG fasting glucose MPD main pancreatic duct СТ computerized tomodensitometry BMI body mass index
- PPI proton pump inhibitor

Introduction

The physiognomy of pancreatic surgery has changed in the last 30 years. Effectively, the 2010 French Surgical Association (AFC) report (1480 pancreatic resections) found not only a statistically significant decrease in postoperative mortality over time (9% vs. 3%), but, also, a statistically significant increase in long-term survival (median survival: 27 vs. 11 months) for patients undergoing pancreatic resection [1,2], as compared to the results of the 1991 French Surgical Association report [3,4]. The extremely poor prognosis of pancreatic adenocarcinoma and the necessity to develop new therapeutic strategies have driven the functional consequences of pancreatic resection into the background. Nonetheless, the increased expectation of survival, the substantial impact on the quality of life of exocrine pancreatic insufficiency (ExoPI) and endocrine pancreatic insufficiency (EndoPI) after pancreatic resection for benign or malignant lesions imply that the functional consequences of this surgery should be an integral part of discussion. The quality of studies reporting the incidence of ExoPI (ranging from 33 to 100%) is limited by the retrospective, heterogeneous nature of the small populations studied, as well as the variability of the biological measurements and definition of ExoPI (steatorrhea, number of pancreatic extract pills taken, C13 triglyceride breath test, test of fecal concentration of elastase) [5-11]. Likewise, the incidence of post-pancreatectomy EndoPI varies from 0 to 50%, with once again, variable results for the same reasons as the studies on ExoPI [6,8,9,11-18]. The goal of our study is to evaluate the risk factors for ExoPI and EndoPI with standardized biological measurements in a multi-center prospective series coming from expert centers in France.

Patients and methods

Between January 1, 2014 and June 19, 2015, the metabolic profiles of 91 patients who had undergone pancreatic resection [pancreatoduodenectomy (PD) or left pancreatectomy (LP)] were analyzed. This was a prospective multi-center study of patients originating from four expert centers. The study was approved by the scientific committee of the French Integrated Research on Cancer Organization (SIRIC).

Patients with chronic pancreatitis, any history of surgery that could alter intestinal absorption (gastrointestinal resection), postoperative death or who had undergone total pancreatectomy were not included.

Preoperative clinical data (weight, height, diarrhea, antecedent diabetes, preoperative malnutrition) and surgical data [type of operation, type of anastomosis, parenchymal consistency of the pancreatic remnant, pancreatic thickness, size of the main pancreatic duct (MPD)], and intubation or not of the MPD were collected prospectively. Pancreatic consistency was evaluated by the surgeon intraoperatively as "hard", "soft" or "friable". Preoperative biological data [complete blood cell counts, carbohydrate antigen 19-9 (CA 19.9), carcinoembryonic antigen (CEA), albuminemia, glycohemoglobin (HbA1c), fasting glucose (FG)] were collected. For LP, the pancreas was divided flush with the superior mesenteric vein.

Contrast-enhanced abdomino-pelvic CT scan (GE Discovery CT750 HD and SIEMENS Somatom Definition) with 1 mm slices was performed one month before operation according to the pancreatic study protocol [plain scout abdominal film, then abdominal (35 s), abdomen and pelvis CT scan (70 s) with intravenous injection of 350 mg iodine/mL], in order to analyze the tumor type, size (mm) and resectability. The thickness of the pancreas (mm), the diameter of the MPD (mm) and the volume of the pancreas (in cm³) were also evaluated. The thickness of the pancreas and the diameter of the MPD were measured on preoperative imaging at the level of the superior mesenteric vein. The thickness of the pancreas was then calculated subtracting the diameter of the MPD.

Initial pancreatic volumetry was calculated by transfer of images to the (Advantage workstation 4.6, GE Healthcare) software and outlined by hand for 1 mm slices. Each pancreatic section was traced, excluding the dilated MPD and biliary tract. The initial pancreatic volume was calculated in each sectional image and the total pancreatic volume was obtained by summing the product of pancreas area (cm²) of each image.

Postoperative complications were evaluated by the Dindo-Clavien classification [19]. Postoperative clinical and laboratory follow-up was performed every six months including body mass index (BMI), evaluation of malnutrition, calculation of intake of pancreatic extract, complete blood counts, and measurement of CA 19-9, CEA, albuminemia, HbA1c, FG and fecal elastase.

Exocrine and endocrine function was evaluated six months after pancreatic resection. ExoPI was measured by the fecal elastase concentration [Elisa (ScheBo $^{\circ}$ Pancreas

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2

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