The American Journal of Surgery (2015) 210, 783-789

The American Journal of Surgery®

Clinical Science

Metabolic consequences of the occlusion of the main pancreatic duct with acrylic glue after pancreaticoduodenectomy

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KEYWORDS:
Pancreaticoduodenectomy;
Pancreaticojejunostomy;
Pancreatic duct occlusion;
Metabolic evaluation;
Insulin secretion

Abstract

BACKGROUND: Pancreaticoduodenectomy represents the major treatment for pancreatic and periampullary neoplasms. Complications related to pancreaticojejunostomy are still the leading cause of morbidity and mortality. A solution proposed by some surgeons is the occlusion of main pancreatic duct by acrylic glue, avoiding pancreaticojejunostomy. Nevertheless, the consequences of this procedure on glucose metabolism are not well-defined.

METHODS: We retrospectively analyzed a cohort of 50 patients who underwent pancreaticoduodenectomy and had metabolic assessments available. The metabolic evaluation included the following: body composition and clinical evaluation, an oral glucose tolerance test, and an hyperinsulinemic euglycemic clamp procedure.

RESULTS: Twenty-three patients underwent pancreatic duct occlusion and were compared with 27 patients, well-matched controls, who underwent pancreaticojejunostomy. Pancreatic duct occlusion leads to a greater impairment in insulin secretion compared with classic pancreaticojeunostomy.

CONCLUSION: Pancreatic duct occlusion is associated with a greater reduction in insulin secretion but does not lead to meaningful differences in the management of patients with diabetes.

This study was supported by grants to A.G. from the Università Cattolica del Sacro Cuore (Fondi Ateneo Linea D.3.2 Sindrome Metabolica), the Italian Ministry of Education, University and Research (PRIN 2010JS3PMZ_011), and Fondazione Don Gnocchi (00018.5). T.M. is the recipient of the Albert Reynolds Travel Fellowship by European Association for the Study of Diabetes and Fellowship Prize by the Società Italiana di Diabetologia. G.P.S. is the recipient of fellowship from Laboratori Guidotti.

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Manuscript received November 19, 2014; revised manuscript December 27, 2014

Whipple's procedure represents the standard treatment of the tumors of the head of the pancreas and other periampullary neoplasms (cancers of the ampulla, distal common bile duct, or duodenum). Despite notable improvements in mortality, currently reported with an incidence of less than 5%,[1,2] morbidity remains a significant problem, being reported in up to 50% of cases.[3] Complications related to pancreatic anastomosis are still the leading cause of morbidity and mortality associated

0002-9610/$ - see front matter © 2015 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.amjsurg.2014.12.052

with this procedure, and pancreatic postoperative fistula (POPF) is the most dreaded complication and the major potential cause of mortality.[4] A number of alternative techniques have been developed over the years in an attempt to reduce the incidence of POPF, including end-to-end or end-to-side pancreaticojejunostomy (PJ), duct-to-mucosal anastomosis, pancreaticogastrostomy, wider distance between PJ and hepaticojejunostomy, and administration of somatostatin or analogs.[4] Nevertheless, to date, there is no consensus on the best technique for pancreatic anastomosis, and the issue seems to be far from being resolved.[4] A solution adopted by different groups is to avoid the anastomosis and to perform a pancreatic duct occlusion (PDO) with different types of glue. This procedure has led to a marked reduction in mortality in some experiences,[5–7] but has been criticized for favoring the occurrence of postoperative complications and even for resulting in a major impairment of endocrine function of the pancreas.[4,8] Contrasting findings have been published on the effects of PDO on endocrine function and the risk of developing postoperative diabetes in humans,[6] and whether the Wirsung occlusion has a negative effect on endocrine function is still a matter of debate.

Therefore, in this study, we aimed to determine the endocrine effects of these procedures on endocrine function and to define the metabolic outcomes in nondiabetic patients. To pursue this aim, we retrospectively analyzed metabolic changes in insulin secretion and glucose metabolism in a cohort of patients who underwent PDO or classic PJ after pancreaticoduodenectomy, and who had undergone thorough metabolic assessments.

Patients and Methods

Patients and study design

Fifty patients (27 women and 23 men; mean age 63 ± 13 years, body mass index 24.9 ± 1.6 kg/m^2) who underwent pancreaticoduodenectomy for periampullary neoplasms and had metabolic assessments available were considered for the present analysis. Indications for surgery were only periampullary neoplasms: Vater's ampulla (27 cases), distal common bile duct (21 cases), and cancer of the duodenum (2 cases). Patients with pancreatic cancer were excluded from the study. We specifically selected patients with pancreatic texture presumptively "soft" and not dilated main pancreatic duct. Pancreatic texture and duct size were evaluated with preoperative magnetic resonance imaging by an experienced radiologist. As previously described,[9] pancreatic fat infiltration was quantified, and pancreata displaying elevated degrees of intralobular, interlobular, and total fat were considered as having soft pancreatic texture.[10]

All patients had normal cardiopulmonary and kidney function and no family history of diabetes. Patients with preoperative diabetes, as assessed by a 2-hour 75 g oral glucose tolerance test (OGTT) and measurement of glycated hemoglobin (HbA1c) according to the American Diabetes Association criteria,[11] were excluded from the present analysis. Pancreatitis, as determined by altered serum lipase and amylase levels before surgery and/or magnetic resonance imaging morphologic criteria, was considered as an exclusion criterion. In addition, patients who had severe obesity (body mass index $>$ 40), uncontrolled hypertension, and/or hypercholesterolemia were excluded. The study protocol was approved by the local Ethics Committee. All participants provided written informed consent.

Surgical procedures

All patients underwent standard pylorus-preserving pancreaticoduodenectomy.[12] The pancreatic resection margin was the pancreatic neck, in correspondence with portal vein and the amount of the pancreatic head resection was similar in all patients. At the beginning of reconstruction time, in some patients the pancreatic stump was treated by injection in the main pancreatic duct of 3 or 4 mL of acrylic glue (Glubran 2; GEM Srl, Viareggio, Italy) and it was left "free" within the abdominal cavity. Subsequently, a hepaticojejunostomy and a duodenojejunostomy were performed on the same loop, whereas other patients were treated according to the Child[13] classic procedure, including end-to-side PJ with "stump invagination technique,"[14] hepaticojejunostomy, and then duodenojejunostomy on the same loop. All the anastomoses were performed using long-term absorbable sutures. During operation, the surgeons performed PDO or PJ according to their personal evaluation of local conditions. Postoperative morbidity and mortality were recorded. Complications such as POPF, delayed gastric emptying, and postoperative hemorrhage were defined according to the International Study Group of Pancreatic Fistula criteria.[15–17] Postoperative hospital stay was also recorded. All patients undergoing PDO received pancreas enzyme replacement after surgery (80,000 UI pancrelipase per day).

Metabolic evaluation

The metabolic evaluation was performed 1 week before surgery and 40 ± 10 days after surgery. One year after surgery, patients underwent an additional clinical evaluation and HbA1c measurement. The metabolic evaluation was performed at the Division of Endocrinology and Metabolic Diseases of the Catholic University of the Sacred Heart on 3 consecutive days.

Day 1: body composition and clinical evaluation. Patients underwent clinical evaluation and anthropometric assessments according to standard procedures. All patients had blood samples drawn for serum lipid assays (total cholesterol, high-density lipoprotein and low-density lipoprotein cholesterol) and HbA1c in the morning after an overnight (8 hours) fast. All the procedures were performed with the subjects in a supine position throughout the experiments.