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Diabetes after pancreaticoduodenectomy: can we predict it?

Anand Narayan Singh, MS, MCh,[a,*] *Sujoy Pal, MS, MCh,*[a] *Ragini Kilambi, MS, MCh,*[a] *Kumble Seetharama Madhusudhan, MD,*[b] *Nihar Ranjan Dash, MS,*[a] *Nikhil Tandon, MD, DM,*[c] *and Peush Sahni, MS, PhD*[a]

[a] *Department of Gastrointestinal Surgery and Liver Transplantation, All India Institute of Medical Sciences, New Delhi, India*

[b] *Department of Radiodiagnosis, All India Institute of Medical Sciences, New Delhi, India*

[c] *Department of Endocrinology, Metabolism and Diabetes, All India Institute of Medical Sciences, New Delhi, India*

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ABSTRACT

Background: There is limited literature about the perioperative factors which can predict endocrine insufficiency after pancreaticoduodenectomy (PD). The primary aim was to correlate percentage pancreatic remnant volume (%RV) after PD in nondiabetic patients with the development of new-onset impaired glucose tolerance/diabetes mellitus (IGT/DM). The secondary aim was to identify the risk factors for new-onset IGT/DM.

Methods: In this prospective study, all consecutive patients with resectable periampullary carcinoma and without IGT/DM were evaluated with fasting and postprandial plasma glucose, HbA1c, insulin, and C-peptide levels preoperatively and at 3 mo postoperatively. After that, all patients were followed up with fasting and postprandial plasma glucose level assessed at 3-mo intervals for 24 mo or till death, whichever occurred earlier. The %RV was determined from computed tomography measurements preoperatively.

Results: Of the 50 patients, 11 (22%) patients developed IGT/DM after median follow-up of 32 mo. The patients' with/without IGT/DM were similar in demographic/perioperative variables. The %RV was found to be an independent factor associated with new-onset IGT/DM. A %RV of <48.8% was found to be a predictor of new-onset IGT/DM (sensitivity, 89.7%; specificity, 73.6%). Plasma sugar and glycosylated hemoglobin levels were significantly higher postoperatively after PD than the preoperative levels. Insulin and C-peptide levels were significantly lower after PD, irrespective of new-onset IGT/DM.

Conclusions: The incidence of IGT/DM after PD was 22%, and %RV < 48.8% was found to be a significant risk factor for new-onset IGT/DM. (CTRI/2013/12/004233).

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* *Corresponding author.* Assistant Professor, Department of Gastrointestinal Surgery and Liver Transplantation, All India Institute of Medical Sciences, 1005, Teaching Block, New Delhi 110029. Tel.: +919891140200; fax: +911126593461.

E-mail address: anandnsingh@gmail.com (A.N. Singh).

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Introduction

An improvement in the postoperative outcomes of pancreaticoduodenectomy (PD), lower mortality as well as a larger number of procedures being done for benign/low-grade malignant tumors, has led to an increased interest in the long-term results of PD.[1] Impaired glucose tolerance/diabetes mellitus (IGT/DM) is an important long-term complication with reported prevalence rates of 4.8%-60%.[2-4] This wide range is attributable to the heterogeneous patient population and variable pancreatic remnant volume. The old dogma that resection of up to 80% of pancreatic parenchyma is tolerated without the development of diabetes has now been challenged.[5,6] Animal and human metabolic studies after a partial pancreatectomy have suggested that 50% pancreatectomy results in impaired fasting glucose and glucose intolerance in short term[7] and diabetes in some patients over a few years.[8,9] Interestingly, PD results in removal of 30%-70% of pancreatic parenchymal tissue.[7] Hence, all patients undergoing PD are not at equal risk for development of new-onset IGT/DM. Few studies have investigated the reduction in volume of pancreatic parenchyma after PD as a risk factor for the development of diabetes. Sakata *et al.*[10] assessed computed tomography (CT) volumetry of the pancreas and endocrine parameters and found that thickness of the pancreatic parenchyma correlated with the postoperative glycemic state. They found CT to be a useful tool to evaluate pancreatic endocrine function. Another study[11] investigated the functional consequences of distal pancreatectomy in patients and found that the preoperative functional reserve of the endocrine pancreas and reduction in the volume of pancreatic parenchyma were important factors in postoperative glycemic control. No study has assessed the association of reduction in volume of pancreatic parenchyma after PD with the endocrine insufficiency. We aimed to quantify the volume of remnant pancreas after PD and to assess its relationship with new-onset IGT/DM.

Methods

Study design and oversight

This prospective, observational study was done at a tertiary care center from June 2013 to June 2015. Approval was obtained from the institutional ethics committee (Ref. No. IESC/T-253-15.06.2013), and the trial was registered with clinical trials registry (CTRI/2013/12/004233).

Patients

All consecutive patients with resectable periampullary mass who required PD and gave consent were included in the study. Patients with preexisting diabetes, underlying pancreatic carcinoma, or associated acute or chronic pancreatitis were excluded. Other exclusion criteria were poor performance status (Eastern Cooperative Oncology Group score 3 or 4), etiology other than adenocarcinoma, and age >70 y.

Procedures and quality control

All patients were evaluated preoperatively for preexisting diabetes by testing their fasting and postprandial glucose and glycosylated hemoglobin (HbA1c) levels. Diabetes and IGT were defined using WHO criteria.[12] Patients who had IGT or DM were excluded from the study. Pancreatic volumetry was done by two authors (A.N.S. and R.K.) under the supervision of an experienced consultant radiologist (K.S.M.). The technique of pancreatic transection was standardized and practiced uniformly by all the operating surgeons.[13] An hepaticojejunostomy stent was placed routinely in all the patients according to our technique described previously.[13] All the patients were followed up at 3-month intervals with the same laboratory tests, and any abnormal value was reconfirmed by testing after 2 wk. All patients were followed up for a minimum of 24 mo or till death, whichever was earlier.

Outcome measures

The primary aim was to correlate the percentage pancreatic remnant volume (%RV) of pancreatic parenchyma after PD in nondiabetic patients with the development of new-onset IGT/DM. The secondary aim was to identify the risk factors for the new-onset IGT/DM.

Data collection

Demographic, clinical, biochemical, and radiological investigations were recorded in a prestructured pro forma manner within the 4 wk preceding the surgery. A family history of type 2 diabetes in first-degree relatives was also obtained. Nutritional status and pancreatic endocrine functions were assessed based on measurement of body mass index (BMI), serum albumin, and plasma glucose. The %RV was determined using preoperative abdominal multidetector computed tomography (MDCT) measurements as described later. Intraoperatively, the diameter of the pancreatic duct, pancreatic texture, type of pancreaticojejunostomy (PJ), and whether the anastomosis was stented were recorded. The occurrence of postoperative complications such as pancreatic fistula, delayed gastric emptying, postpancreatectomy hemorrhage, bile leak, surgical site infections, reexplorations, hospital stay, 30- and 90-d mortality, and readmissions was recorded and graded according to standard definitions (described in the online-only data). Patency of the PJ was assessed with ultrasonography/CT during follow-up.

Assessment of preoperative and postoperative glycemic status

Plasma glucose, serum insulin, and C-peptide levels were assessed at fasting and 30 and 120 min after 75-g glucose intake, preoperatively and 3 mo postoperatively. HbA1c level was also assessed preoperatively and at 3 mo postoperatively. Thereafter, each patient was followed up with fasting and postprandial glucose level assessed at every 3 mo for a minimum of 24 mo postoperatively or till death, whichever was earlier.