Clinical Science

Significance of preoperative radiographic pancreatic density in predicting pancreatic fistula after surgery for pancreatic neuroendocrine tumors

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Abstract

   BACKGROUND: Postoperative pancreatic fistula remains the most severe and worrisome complication after surgery. Predictive preoperative assessment remains challenging. The authors examine the role of pancreatic computed tomography density in predicting postoperative pancreatic fistula after surgery for pancreatic neuroendocrine tumors.

   METHODS: A single institutional retrospective review of pancreatic surgery for neuroendocrine tumors between 1998 and 2010 was conducted. Preoperative contrast-enhanced computed tomography scans were reviewed, with mean region of interest measurements of pancreatic parenchymal density obtained from 10-mm thick axial computed tomography images.

   RESULTS: A total of 119 patients were identified: 59 with enucleations and 60 with resections. Decreased preoperative pancreatic density was significantly associated with an increased grade of postoperative pancreatic fistula ($P < .01$). Subgroup analyses revealed that decreased gland density was associated with increased grade of postoperative pancreatic fistula in the resection ($P < .01$) but not in the enucleation group ($P = .34$).

CONCLUSIONS: A significant association between postoperative pancreatic fistula grade and preoperative pancreatic computed tomography density is observed in patients undergoing resection for pancreatic neuroendocrine tumors.
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Pancreatic fistula remains a significant complication after surgery, and predictive preoperative assessment remains challenging.[1] Pancreatic fistula occurrence after tumor resection adds significant morbidity to a patient's postoperative course and can be life-threatening. Patients who experience a pancreatic leak are at greatly increased risk of other morbidities, including sepsis, biliary strictures, and mortality.[2]

Although fistulas have an overall mortality of 5% to 8%, and can generally be managed conservatively with prolonged nil per os (npo) status and parenteral nutrition, mortality for patients with a high-grade fistula can be as high as 28% to 40%.[3,4] Patients with higher grade fistulas will require procedural interventions varying from percutaneous drain placement to reoperation.

Many factors have been implicated in a higher incidence of postoperative pancreatic fistula, including pancreatic neuroendocrine tumors, hereditary syndromes, elevated body mass index, and a soft pancreas.[5–9] A consensus definition of fistula grades developed by the New International Study Group for Pancreatic Surgery has allowed for objective analysis and comparison of patient outcomes across institutions.[10] It has been independently validated and found consistently to correlate with clinical outcomes.[11]

Use of imaging to predict fistula rate has been examined in patients undergoing pancreaticoduodenectomy for pancreatic adenocarcinoma. Studies of preoperative computed tomography scans determined that visceral fat area was more accurate than body mass index in predicting pancreatic fistula.[12,13] Pancreatic density and fistula rate or severity has not been evaluated in patients with neuroendocrine tumors, nor for other resection options such as distal pancreatectomy or enucleation. Herein, the authors aim to examine the role of pancreatic computed tomography density in predicting postoperative pancreatic fistula after surgery for pancreatic neuroendocrine tumors.

Methods

After approval by the Office of Human Subject Research at the National Institutes of Health, a retrospective review was conducted on all patients who underwent resection or enucleation for pancreatic neuroendocrine tumors from March 1998 to April 2010. All participants provided informed written consent and were enrolled on protocols at the National Cancer Institute. Patient variables including age, gender, body mass index, hereditary syndrome type, tumor characteristics, and preoperative serum albumin level were reviewed. Body mass index classification (kg/m^2) was noted as normal $\leq$ 24.9, overweight 25 to 29.9, and obese $\geq$ 30.0.

Operative reports were reviewed for surgical approach and type of resection. After resection or enucleation, closed-suction drains were placed at the surgical bed. Perioperative octreotide as prophylaxis was not used in this series. Drains were removed once patients were tolerating a regular diet and maintaining a normal drain amylase level with output of less than 100 mL/day.

Drain amylase levels were obtained for all patients postoperatively. From strict International Study Group for Pancreatic Surgery criteria, postoperative pancreatic fistula were categorized as follows: grade A, asymptomatic and clinically silent fistula, only demonstrated by drain amylase level greater than 3 times the normal serum level; grade B, a fistula requiring a postoperative drain for greater than 21 days, nonoperative intervention such as total parenteral nutrition, octreotide, percutaneous drainage, or readmission within 30 days of hospitalization; and grade C, a severe fistula requiring surgical intervention, intensive care unit care greater than 48 hour, or death within 30 days of operation. Clinically significant postoperative pancreatic fistula was defined as any grade B fistula requiring an intervention and all grade C fistulas. Intervention was defined as requiring an intra-abdominal drain placement or a reoperation. Additional drains were placed when clinically indicated due to fever, leukocytosis, or increased pain necessitating a computed tomography scan showing an inadequately drained collection. Patient records were reviewed to determine the length of stay, clinical course, and complications.

Preoperative contrast-enhanced triple phase computed tomography scans were reviewed. Mean region of interest measurements of pancreatic parenchymal density in Hounsfield units were obtained every 10 mm in axial computed tomography images acquired during the portal venous phase. Measurements were determined by blind evaluators and verified independently by a radiologist who was also blind to the clinical course of the subjects. The pancreas density was determined by calculating the mean of the region of interest measurements for each pancreas (Fig. 1).

Continuous parameters were compared between patients with and without clinically significant postoperative pancreatic fistula using an exact Wilcoxon rank sum test. The significance of the trends in continuous parameters across ordered categorical parameters such as increasing fistula grade were determined by a Jonckheere–Terpstra test for trend. All P values are 2 tailed and presented without any adjustment for multiple comparisons. P value less than .05 is considered statistically significant.