Annals of Surgical Oncology, **9**(8):799–806
DOI: 10.1245/ASO.2002.03.072

Clinical Utility of Positron Emission Tomography in the Diagnosis and Management of Periampullary Neoplasms

Matthew F. Kalady, MD, Bryan M. Clary, MD, Lisa A. Clark, MD, Marcia Gottfried, MD, Eric M. Rohren, MD, R. Edward Coleman, MD, Theodore N. Pappas, MD, and Douglas S. Tyler, MD

Background: This study examined the effect that 18-fluorodeoxyglucose positron emission tomography (^{18}FDG-PET) imaging had on the clinical management of patients with suspected periampullary malignancy.

Methods: Fifty-four patients with suspected pancreatic neoplasms underwent both whole-body ^{18}FDG-PET and abdominal computed tomography (CT). Malignant or benign disease was confirmed pathologically in 47 patients.

Results: Of the 41 patients with malignancy, ^{18}FDG-PET failed to identify the primary tumor in 5 patients. ^{18}FDG-PET demonstrated increased uptake suggesting primary malignancy in 37 patients. Malignant pathology was confirmed in 36 cases. ^{18}FDG-PET identified malignant locoregional lymph node metastases in six of ten patients. All nodes identified before surgery by ^{18}FDG-PET were also seen on preoperative CT. Six patients who were thought to have resectable disease by CT were found to have distant metastasis at laparotomy. ^{18}FDG-PET did not detect metastasis in any of these cases. Before surgery, ^{18}FDG-PET identified distant metastases that were not detected by CT in one patient.

Conclusions: Despite high sensitivity and specificity in diagnosing periampullary malignancy, ^{18}FDG-PET did not change clinical management in the vast majority of patients previously evaluated by CT. In addition, ^{18}FDG-PET missed >10% of periampullary malignancies and did not provide the anatomical detail necessary to define unresectabilty.

Key Words: Pancreatic cancer—Positron emission tomography—Computed tomography—Diagnostic imaging—Periampullary cancer.

It is often difficult to diagnose and differentiate periampullary masses. Neoplasms located near the ampulla of Vater may originate from the pancreas, ampulla, common bile duct, or duodenum. Pancreatic cancer represents approximately 85% of periampullary masses,[1] and as the fifth leading cause of cancer-related mortality, it is responsible for more than 28,000 deaths annually.[2] Overall prognosis is poor, and <4% of patients are alive 5 years after diagnosis.[2,3] Early diagnosis and surgical resection provide the best chance for favorable outcomes, but 5-year survival is still only 15% to 20%.[4,5]

A variety of diagnostic imaging modalities have been used to evaluate suspected periampullary malignancy, including computed tomography (CT), transabdominal ultrasonography (US), endoscopic retrograde cholangiography, endoscopic US, and magnetic resonance imaging. Although these imaging techniques are often helpful, they do not always provide a definitive diagnosis or detect malignancy at an early stage, when surgical intervention is most effective. If a mass is diagnosed as malignant, the surgeon relies on imaging to provide information regarding the resectability of the disease. In general, contiguous tumor spread causing vascular encasement, regional nodal disease, or distant metastases renders a tumor unresectable. Unfortunately, approximately 20% of cases that are preoperatively presumed

Received March 15, 2002; accepted May 24, 2002.

From the Departments of Surgery (MFK, BMC, LAC, TNP, DST), Pathology (MG), and Radiology (EMR, EC), Duke University Medical Center, Durham, North Carolina.

Presented at the 55th Annual Cancer Symposium of the Society of Surgical Oncology, Denver, Colorado, March 14–17, 2002.

Address correspondence and reprint requests to: Douglas S. Tyler, MD, Duke University Medical Center, Box 3118, Durham, NC 27710; Fax: 919-681-8701; E-mail: tyler002@acpub.duke.edu.

resectable by imaging are determined inoperable at the time of celiotomy.[6,7] Improved diagnostic modalities are needed. 18-Fluorodeoxyglucose positron emission tomography (^{18}FDG-PET) has emerged with the proposed potential to distinguish between benign and malignant conditions, as well as detect deposits of metastatic disease.[8–10]

^{18}FDG-PET is a noninvasive imaging technique dependent on the relative hypermetabolism of malignant cells compared with normal cells. FDG, a glucose analog, is transported into cells via the same pathway as glucose and is converted to FDG-6-phosphate. This metabolite cannot be processed by the cell and thus accumulates in those cells with high glucose uptake, such as cancer cells. Most solid tumors, including pancreatic adenocarcinoma, have demonstrated increased glucose uptake.[11,12] Thus, unlike its conventional imaging counterparts CT or US, which rely on anatomical or architectural changes to detect malignancy, ^{18}FDG-PET uses functional biological characteristics of cancer cells.

^{18}FDG-PET has been proposed as an effective technique for diagnosis and staging of pancreatic adenocarcinoma.[13–15] However, the added benefit of ^{18}FDG-PET compared with information obtained by conventional imaging, such as CT, remains controversial, and the exact role of ^{18}FDG-PET in periampullary malignancy remains undefined. The goal of this study was to delineate the clinical utility of ^{18}FDG-PET in the diagnosis and management of periampullary masses. Specifically, we evaluated the ability of ^{18}FDG-PET to differentiate benign from malignant periampullary disease and its ability to define local resectability and identify extraperiampullary metastasis.

METHODS

Patient Population

Patients with suspected primary pancreatic cancer by clinical history between December 1994 and July 2001 were identified at a single tertiary care center. Fifty-four patients who were evaluated by both abdominal CT and ^{18}FDG-PET were included in this study. During the time of this study, strict indications for ^{18}FDG-PET were not defined, and this test was ordered at the discretion of individual surgeons, gastroenterologists, and medical oncologists. Patient demographics and clinical information were retrospectively reviewed.

Positron Emission Tomography

The protocol for pancreatic ^{18}FDG-PET study at our institution has been previously described.[16] Before evaluation by ^{18}FDG-PET, patients fasted for 4 hours to avoid potentially confounding hyperglycemia. Patients with a history of diabetes mellitus were evaluated for serum glucose levels, and the test was postponed if glucose levels were >200 mg/dl. ^{18}FDG-PET was performed in the two-dimensional mode on an Advance scanner (General Electric Medical Systems, Milwaukee, WI), which produces 35 image planes spaced every 4.2 mm, with an axial field of view of 15.2 cm. The intrinsic in-plane full width at half maximum is 5 mm. A minimum of two bed positions was acquired.

Transmission scanning with a orbiting germanium-68 pin source was performed on all patients either immediately before or after image acquisition. Before 1999, axial emission and transmission images of the abdomen and pelvis were obtained for 10 minutes each per bed position beginning 60 minutes after intravenous injection of 10 mCi of ^{18}FDG. Beginning in 1999, because of the use of iterative reconstructions and a segmented attenuation correction algorithm, the time for emission scan acquisition was 4 minutes per bed position, and the time for transmission scan was 3 minutes per bed position. The images were reviewed in axial, coronal, and sagittal formats.

Pancreatic activity was assessed by experienced nuclear medicine radiologists and was determined to be positive or negative by visual inspection. ^{18}FDG-PET with activity greater than background was determined as a positive test. Conversely, a test with activity less than or equal to background was considered negative. The background activity was defined as activity in the paraspinal muscles. A subset of patients (n = 18) were retrospectively analyzed to quantify uptake within lesions by using the mean activity within a 1-cm circular region of interest (ROI) placed within an area of maximum activity. After correction for radioactive decay, the ROI was semiquantitatively analyzed by computing a standardized uptake value (SUV) with the following formula:

$$\text{SUV} = \text{mean ROI activity (mCi/mL)} / \text{injected dose (mCi)/bodyweight (g)}$$

The mean ROI activity was corrected for decay. ROI and SUV were determined without knowledge of clinical history or final pathologic diagnosis.

Computed Tomography

Abdominal CT was performed at our institution for 43 patients by use of a dual-phase pancreatic protocol. After intravenous administration of 175 mL of iopamidol (Isovue 300, Bracco Diagnostics, Princeton, NJ), scans during the arterial phase were acquired 20 to 40 seconds

TABLE 1. *Final diagnoses of patients with suspected periampullary malignancy*

Diagnosis	n (%)
Malignancy	41 (75.9)
Adenocarcinoma	33 (61)
Neuroendocrine tumor	4 (7.4)
Ampullary carcinoma	1 (1.9)
Mucinous cystic neoplasm	1 (1.9)
Metastatic renal cell carcinoma	1 (1.9)
Unspecified malignancy	1 (1.9)
Benign	13 (24.1)
Chronic pancreatitis	8 (14.8)
Benign cyst	2 (3.7)
Obstructive cholelithiasis	1 (1.9)
Small-bowel adhesions	1 (1.9)
Inflammatory bowel disease	1 (1.9)

after injection, and scans during the venous phase were obtained 70 to 100 seconds after injection of contrast material. Images were obtained at 3-mm collimation through the pancreas during the arterial phase and at 5-mm collimation during the venous phase. Contrast-enhanced CT was performed on 11 patients at other institutions with various scanning protocols at increments of 5 to 10 mm through the pancreas. CT findings were interpreted by an abdominal radiologist as positive, negative, or suggestive of neoplasm. On all CT scans, local nodes >6 mm were noted in the gastrohepatic, portal, para-aortic, or paracaval region.

Statistical Analysis

The SUVs for benign and malignant lesions were statistically analyzed for differences by using the two-tailed Student's *t*-test at a 95% confidence interval.

RESULTS

Final Diagnosis

Pathologic diagnosis was confirmed by percutaneous or endoscopic biopsy, or by histopathology in 47 patients. The remaining seven patients had benign disease on the basis of clinical follow-up of at least 12 months. A diagnosis of malignancy was established in 41 patients by cytology, surgery, or both. Thirty-three patients had pancreatic adenocarcinoma, and four had neuroendocrine tumors. One patient each had the following diseases: ampullary adenocarcinoma, pancreatic mucinous cystic neoplasm, metastatic renal cell carcinoma, and unspecified periampullary malignancy. Benign disease was confirmed by cytology, surgery, or clinical follow-up in 13 patients. Chronic pancreatitis was the most common benign condition (n = 8), followed by benign cyst (n = 2), obstructive cholelithiasis, small-bowel adhesions, and inflammatory bowel disease. Table 1 summarizes the final diagnoses for patients included in this study.

^{18}FDG-PET and Diagnosis of Primary Disease

Thirty-seven patients had increased activity in the area of the pancreas on ^{18}FDG-PET. Of these patients, malignancy was confirmed pathologically in 36, and 1 was found to have chronic pancreatitis by histology after surgical resection (Fig. 1), yielding a false-positive rate of 5%. Seventeen patients had no evidence of increased uptake on PET, suggesting benign disease. Among this group of patients, five were pathologically confirmed to have malignancy (false-negative result). Four patients had pancreatic adenocarcinoma, and one had a neuroendocrine tumor. Figure 2 presents the ^{18}FDG-PET and histopathology of a patient with pancreatic adenocarcinoma that was not detected by ^{18}FDG-PET. The overall sensitivity and specificity for ^{18}FDG-PET to detect primary pancreatic malignancy by visual inspection interpretation were 88% and 86%, respectively. The positive predictive value was 95%, and the negative predictive value was 71% (Table 2).

The mean SUVs for a subset of patients with benign disease (n = 6) and malignancy (n = 13) were .64 (range, 0–3.2) and 5.5 (range, 0–10.5). This difference was significant at a 95% confidence interval (P = .03). The individual SUV for each patient in the subset is shown in Fig. 3.

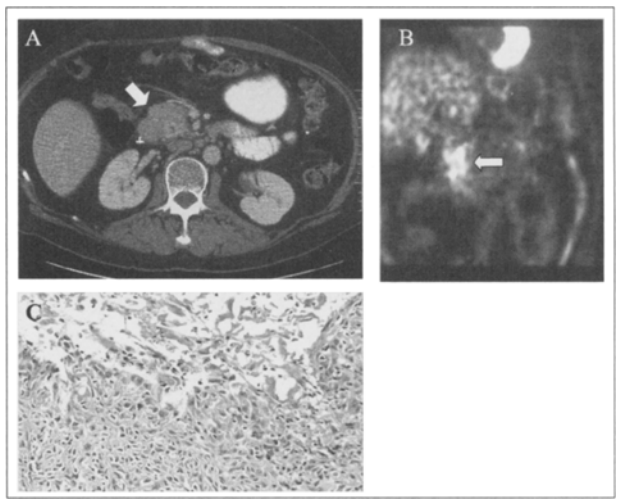

FIG. 1. A 55-year-old man with recurrent bouts of pancreatitis. (**A**) Abdominal computed tomography with intravenous contrast demonstrated a mass in the head of the pancreas (arrow) suggestive of malignancy. (**B**) On 18-fluorodeoxyglucose positron emission tomography, there was hypermetabolic activity in the region of the head of the pancreas (arrow) suggestive of malignancy. The patient underwent exploratory laparotomy and pancreatic biopsy. (**C**) Hematoxylin and eosin (10×) revealed chronic inflammation and fibrosis consistent with chronic pancreatitis.

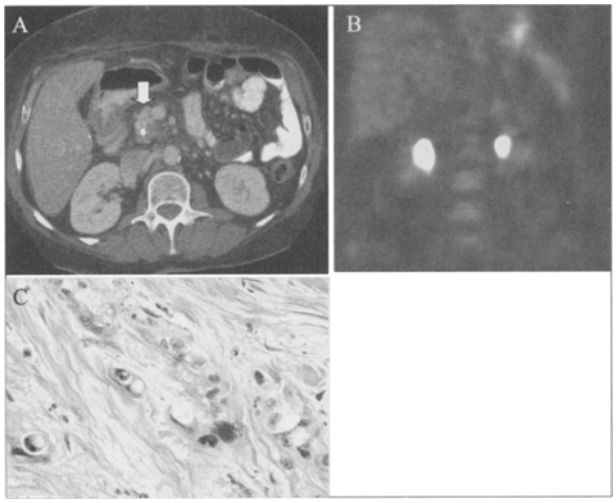

FIG. 2. A 56-year-old woman with painless jaundice and weight loss. (**A**) Abdominal computed tomography detected pancreatic head fullness (arrow) with a distal common bile duct stricture, but no definite mass. (**B**) 18-Fluorodeoxyglucose positron emission tomography showed no abnormal areas of increased uptake. (**C**) Hematoxylin and eosin stain (40×) of the pancreaticoduodenectomy specimen revealed well-differentiated pancreatic adenocarcinoma.

Seven patients who did not have a defined mass on abdominal CT were suspected of periampullary disease by clinical history and examination. All seven patients were evaluated by ^{18}FDG-PET and underwent exploratory laparotomy. Three patients had malignancy (two patients with adenocarcinoma and one patient with a neuroendocrine tumor), two patients had chronic pancreatitis, one patient had chronic obstructive cholelithiasis, and one patient had severe adhesive disease. The preoperative ^{18}FDG-PET was positive in only one of the three patients with malignancy. None of the four patients with benign disease had increased uptake on ^{18}FDG-PET before surgery.

^{18}FDG-PET and Evaluation of Extraperiampullary Disease

Determining Local Extension of Malignancy

Of the 41 patients with pathologically proven malignancy, 7 patients were considered to have unresectable disease secondary to local extension of disease with vascular encasement. This information was determined by preoperative abdominal CT in four cases and at celiotomy in three patients. ^{18}FDG-PET did not predict vascular involvement in any of these cases.

Determining Metastases to Regional Lymph Nodes

Peripancreatic lymph node metastases were confirmed pathologically in six patients. ^{18}FDG-PET identified positive nodes in three of these patients. Of the nodes in the three patients that were not detected by ^{18}FDG-PET, two were diagnosed with the pancreaticoduodenectomy specimen, and one was biopsied at exploratory laparotomy.

Analyzed from a different approach, six patients had increased activity on ^{18}FDG-PET in areas that were interpreted as disease spread to local lymph nodes. Of these six patients, three patients had biopsy-proven distant metastasis at laparotomy, and nodes were not sampled. Nodal metastasis was confirmed pathologically in the other three patients.

Thirteen patients had lymph nodes resected or biopsied that did not contain malignancy. ^{18}FDG-PET did not show increased uptake to suggest nodal involvement in any of these patients. Because not all nodes that were considered positive were assessed pathologically, the exact sensitivity and specificity for detecting nodal metastasis are not known.

Determining Distant Metastases

Increased tracer uptake on ^{18}FDG-PET was interpreted as distant metastasis in 17 patients. Metastasis was pathologically confirmed in nine patients and not assessed in seven patients. There was one false-positive interpretation in which ^{18}FDG-PET suggested a hepatic metastasis in a patient with ampullary carcinoma. This lesion was biopsied at pancreaticoduodenectomy and determined to be a benign biliary cyst with surrounding fibrotic changes.

Twelve patients had pathologic diagnoses of metastatic disease. ^{18}FDG-PET detected 9 of the 12 distant metastases. ^{18}FDG-PET failed to identify liver metastases in two patients and carcinomatosis in one patient. Because not all potentially positive distant metastatic sites were assessed pathologically, the exact sensitivity and specificity for detecting nodal metastasis are not known.

Clinical Utility of ^{18}FDG-PET

The performance of ^{18}FDG-PET in assessing the primary tumor and extra-ampullary disease was compared with that of abdominal CT to determine its clinical utility compared with conventional imaging techniques.

TABLE 2. *Efficacy of ^{18}FDG-PET and CT in diagnosing primary periampullary malignancy*

Test	Sensitivity	Specificity	PPV	NPV
^{18}FDG-PET	88%	86%	95%	71%
CT	90%	62%	88%	67%

^{18}FDG-PET, 18-fluorodeoxyglucose positron emission tomography; CT, computed tomography; PPV, positive predictive value; NPV, negative predictive value.

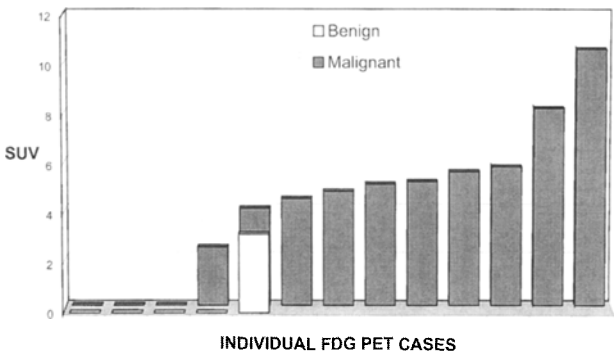

FIG. 3. Standard uptake value (SUV) for a subset of patients with benign (n = 5, white bars) and malignant (n = 13, gray bars) disease. FDG PET, 18-fluorodeoxyglucose positron emission tomography.

Change in Management Based on Diagnosis of Primary Disease

The patient population evaluated by ^{18}FDG-PET also underwent abdominal CT. Preoperative CT identified 37 of 41 patients with confirmed malignancy. The four patients who were misdiagnosed by CT underwent resection on the basis of clinical suspicion for malignancy. Three of these four patients had pancreatic adenocarcinoma, and one patient had a neuroendocrine tumor. ^{18}FDG-PET demonstrated increased uptake in the pancreatic head in only one of three patients with adenocarcinoma and did not identify the neuroendocrine tumor. Although ^{18}FDG-PET correctly diagnosed one additional patient with cancer, the surgical management was not changed.

Five patients were incorrectly presumed to have malignancy by CT (false-positive). Four of these patients had chronic pancreatitis, and one had inflammatory bowel disease. There was increased activity on ^{18}FDG-PET in one case of chronic pancreatitis. Therefore, following the ^{18}FDG-PET results may have spared four patients an unnecessary operation. However, if surgical intervention had been avoided on the basis of ^{18}FDG-PET findings alone, three cancers would have been missed. The overall performance of ^{18}FDG-PET and CT in detecting primary periampullary malignancy is given in Table 2.

Change in Management Based on Local Extension of Tumor, Regional Nodal Involvement, and Distant Metastasis

Seven patients had unresectable malignancy because of vascular encasement by local tumor extension. ^{18}FDG-PET did not provide any additional information to determine local resectability. Whereas ^{18}FDG-PET lacked the anatomical detail to define vascular involvement, CT determined preoperative unresectability in four of these cases and thus avoided an unnecessary laparotomy. Two patients who were preoperatively deemed unresectable secondary to vascular encasement also had liver metastasis detected by CT and ^{18}FDG-PET. Thus, these patients would have avoided laparotomy by other criteria.

Nineteen patients had histopathologic assessment of regional lymph nodes. Thirteen patients had no evidence of metastatic disease, and six patients had malignancy in at least one lymph node. Three of the patients with nodal disease had suspected disease by CT evaluation, and three had disease detected as part of the resected specimen. ^{18}FDG-PET did not detect any of the nodes missed by CT, and it identified only two of the three detected by CT. The lymph nodes that were detected by CT, but not identified by PET (Fig. 4), measured 1.0 to 1.5 cm. ^{18}FDG-PET did not identify any nodal disease that was not detected by CT.

On the basis of preoperative CT evaluation, 12 patients were considered unresectable secondary to distant metastatic disease, all of which were detected by cytology or histopathology. One additional patient had bony metastases confirmed by magnetic resonance imaging. ^{18}FDG-PET identified another patient with liver and chest wall metastases that were not detected by CT. In this case, an unnecessary laparotomy was avoided on the basis of the results of ^{18}FDG-PET.

Six patients who were considered resectable by preoperative CT evaluation were found to have biopsy-proven distant metastases at exploratory laparotomy. Four patients had hepatic metastases measuring 1.0 to 2.1 cm, one patient had peritoneal studding, and one

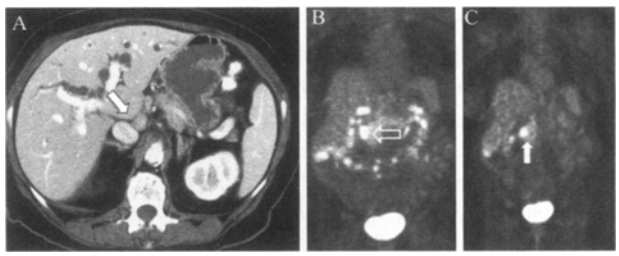

FIG. 4. A 67-year-old woman with new-onset abdominal pain and jaundice. (**A**) Contrast-enhanced abdominal computed tomography demonstrated a pancreatic head mass (not shown) and peripancreatic lymphadenopathy (arrow). (**B**) Coronal 18-fluorodeoxyglucose positron emission tomography images demonstrate hypermetabolism in the pancreatic head (open arrow) and normal uptake within the gastrointestinal tract. (**C**) There is persistent enhancement in the region of the pancreatic head (arrow), but this area could not be delineated to discern nodal involvement. The periduodenal node contained metastatic moderately differentiated pancreatic carcinoma.

patient had carcinomatosis. ^{18}FDG-PET did not detect any of these lesions.

DISCUSSION

Early and accurate preoperative diagnosis for pancreatic cancer remains challenging. Despite technological advances in imaging and surgery, survival outcomes have not dramatically improved in the last 30 years. Therefore, new approaches to early diagnosis and intervention are greatly needed. However, performing redundant preoperative diagnostic tests introduces further patient risk, cost, and delay of definitive treatment. Thus, new technology must be evaluated and applied in the appropriate clinical situations. This study evaluated the effect of ^{18}FDG-PET scanning on the initial evaluation and clinical management of patients with suspected periampullary cancer.

In our opinion, the ideal diagnostic test for evaluation of a periampullary mass would include the following: the ability to detect and define the anatomical location of the mass, the ability to distinguish benign from malignant disease, and the ability to determine resectability of malignant disease. Unfortunately, no diagnostic test is 100% sensitive or specific for these goals, and new diagnostic modalities are welcomed. When evaluating a new test, it must be determined whether the information gained will change the natural history of the disease or improve clinical outcomes compared with current standards. In our study, ^{18}FDG-PET did not meet these criteria for pancreatic cancer.

Overall, the sensitivity and specificity of ^{18}FDG-PET in our study were 88% and 86%, respectively. These results correlate with those of many others in the literature, which report sensitivities of 85% to 96% and specificities of 66% to 100%.[15–22] Although it is useful to know the sensitivity and specificity of ^{18}FDG-PET in detecting pancreatic cancer, the true utility remains in the ability to change patient management. Preoperative imaging for pancreatic masses affects management by making a diagnosis or, in cases of malignancy, determining tumor resectability. Despite high sensitivity, specificity, and positive predictive values, ^{18}FDG-PET may serve as a complementary test but cannot replace current imaging modalities. ^{18}FDG-PET relies on the increased uptake of glucose by malignant cells, but it cannot define precise anatomical location. Areas of increased uptake must be correlated with anatomical abnormalities seen by CT or US. Thus, the sensitivity and specificity of PET relies on conventional imaging and cannot replace it.

Increased areas of hypermetabolism on ^{18}FDG-PET may be semiquantitatively analyzed by determining the SUV of a particular lesion. In general, malignant lesions have higher values than benign lesions.[17] The exact value that determines the boundary between benign and malignant conditions is debated. Depending on what value is used, the sensitivity and specificity vary.[22] For example, decreasing the value used to define malignancy will identify more cases and increase sensitivity but lower specificity. Delbeke et al.[22] determined a cutoff SUV of 2 to be the optimal value. At our institution, we have experienced that visual inspection provides better diagnostic accuracy, and we do not routinely measure SUVs. Although the general trend holds, there tends to be considerable overlap between values for benign and malignant conditions.[18]

In our study, ^{18}FDG-PET faltered in its ability to accurately exclude malignancy, missing four cases of adenocarcinoma and one neuroendocrine malignancy. In all of these cases, suspicion of cancer by history and other imaging prompted surgical intervention. One possible explanation for the high false-negative rate is that the accuracy of ^{18}FDG-PET is greatly affected by serum glucose levels. The labeled glucose analog ^{18}FDG competes for entry into hypermetabolic cells with normal circulating glucose. Thus, hyperglycemia leads to a higher rate of false-negative results and a lower sensitivity.[23,24] During the early part of our study, the relationship of hyperglycemia to ^{18}FDG-PET sensitivity was not appreciated, and patients were not routinely tested for hyperglycemia before imaging. This could possibly account for two false-negative results in the initial years of our study. One other false-negative result in our study was in detecting a neuroendocrine tumor. ^{18}FDG-PET is known to have difficulty in detecting neuroendocrine tumors, with a sensitivity of only approximately 50%.[25,26]

In terms of false-positive results, CT had a lower specificity for pancreatic cancer than PET in our study and in others.[14,15,27] Fibrotic changes associated with chronic pancreatitis often appear as a mass on CT scan, and differentiation from cancer is difficult. It is well documented that inflammatory cells may also preferentially take up glucose[28] and cause a false-positive reading on ^{18}FDG-PET.[29] The one false-positive result in our study was in a patient with chronic pancreatitis who underwent resection. Other series report false-positive results in chronic pancreatitis and other inflammatory conditions.[18,21,22,30] Although ^{18}FDG-PET has improved the ability to differentiate chronic pancreatitis from cancer, it still lacks the specificity to direct surgical management.

The other aspect of surgical management of suspected pancreatic cancer is determining disease resectability.

Unfortunately, a considerable number of patients who are deemed resectable by conventional imaging techniques are found to have inoperable disease at laparotomy. CT has been shown to be the most accurate study to predict unresectability on the basis of its anatomical delineation around the pancreas and its ability to detect vascular involvement. However, CT inaccurately predicts resectability in approximately 20% of cases.[7,31,32] PET lacks the anatomical detail to define direct tumor extension, local lymph node enlargement, and vascular involvement. Several authors have reported ^{18}FDG-PET to accurately detect small-volume disease in lymph nodes.[18,21,22,31] In our experience, ^{18}FDG-PET did not improve over CT in detecting involved lymph nodes, although we can comment only on the six patients for whom we had histological confirmation of malignancy. In terms of distant metastases, PET has been reported to detect small foci not seen by CT in the liver,[10,14] lungs,[14] and peritoneum.[31] In our series, ^{18}FDG-PET diagnosed only one patient with newly found metastasis. Thus, ^{18}FDG-PET may avoid an unnecessary laparotomy in a small percentage of patients.

Our data do not support the routine use of ^{18}FDG-PET in evaluating periampullary masses and reiterate the conclusions of other recent articles. Kasperk et al.[21] prospectively evaluated 103 patients with suspected pancreatic disease by ^{18}FDG-PET, as well as CT, US, and endoscopic retrograde cholangiography. All patients underwent surgery and histopathologic analysis, and the results were compared with diagnosis by preoperative imaging. On review of their data, the authors reported that results from ^{18}FDG-PET would not have changed their surgical strategy for a single patient. Similarly, Sendler et al.[30] analyzed 42 patients with a periampullary mass who underwent ^{18}FDG-PET before surgery. They report an overall accuracy of detecting malignancy to be 69%, with a high rate of false-negative results in stage I cancers. These results preclude the use of ^{18}FDG-PET to exclude pancreatic malignancy.

Conversely, other groups have published results in opposition to our findings.[15,22] Rose et al.[15] reported a large series on the use of ^{18}FDG-PET to evaluate pancreatic malignancy. In their study, the authors retrospectively reviewed 65 patients with suspected or proven malignancy and reported that the use of ^{18}FDG-PET would have potentially altered management in 28 cases (43%). The majority of these cases (n = 18) involved an equivocal result on CT that was diagnosed as malignancy on ^{18}FDG-PET. Stating that ^{18}FDG-PET changed management in these cases assumes that surgical exploration and possible resection would not have been performed without the support of the ^{18}FDG-PET scan. Similarly, for five cases in which CT provided a false-positive result for pancreatic cancer, ^{18}FDG-PET interpreted three of those cases as true negatives. With a CT sensitivity of 75% and a PET specificity of 85%, a positive result on CT discordant with a negative PET scan would still warrant exploration or aggressive attempts at tissue diagnosis, in our opinion. Thus, the actual effect of ^{18}FDG-PET on clinical management would be significantly less in practice than that reported statistically.

This study focused on the effect of ^{18}FDG-PET during the initial evaluation of periampullary tumors. We did not evaluate the use of ^{18}FDG-PET for other instances, such as monitoring disease recurrence. In contrast to colorectal cancer metastatic to the liver, in which early detection by PET provides a chance for intervention and improved survival,[10,33] detection of pancreatic cancer recurrence—by ^{18}FDG-PET or other means—does not provide an opportunity to make a meaningful therapeutic intervention. In the absence of effective therapies or experimental protocols for recurrent disease, we do not recommend the use of ^{18}FDG-PET to detect recurrent disease.

In addition, this study did not focus on the use of ^{18}FDG-PET to monitor pancreatic cancer response to preoperative neoadjuvant therapy. One study reports that ^{18}FDG-PET is an accurate means to detect tumor response to neoadjuvant therapy.[15] Our institution uses neoadjuvant chemotherapy for pancreatic cancer,[34] and ^{18}FDG-PET may be useful in these situations. Further large prospective studies may delineate this role.

^{18}FDG-PET has been shown to be particularly useful in the evaluation of pancreatic cystic neoplasms.[35] Sperti et al.[35] evaluated 56 patients who had suspected pancreatic cystic tumors with ^{18}FDG-PET and found a sensitivity and specificity of 94% and 97%, respectively. There were only two cystic masses in our study population, both of which were accurately diagnosed by ^{18}FDG-PET. One patient had a benign cystic neoplasm, confirmed histologically, that did not display activity on ^{18}FDG-PET. The other patient had a mucinous cystic neoplasm without histological evidence of invasion. This tumor was detected on CT and also demonstrated increased uptake on ^{18}FDG-PET. On the basis of histopathology, we classified this patient as having carcinoma in situ and thus considered the ^{18}FDG-PET to be a true-positive result.

The exact role of ^{18}FDG-PET in evaluating periampullary disease continues to evolve. Perhaps future prospective trials evaluating its use in a subset of patients in whom current diagnostic techniques perform poorly will elucidate its use. Examples of such patients are those with common bile duct or pancreatic duct strictures with-

out a detectable mass on CT or those patients who have atypical or suspicious fine-needle biopsy results. At the current time, despite its high sensitivity, specificity, and positive predictive values similar to those obtained by abdominal CT, ^{18}FDG-PET does not provide additional surgically significant information, and we do not recommend its routine use.

REFERENCES

1. Yeo CJ, Cameron JL. The pancreas. In: Sabiston DC, ed. *Textbook of Surgery: The Biological Basis of Modern Surgical Practice.* Philadelphia: WB Saunders, 1997:1152–86.
2. Greenlee R, Murray T, Bolden S, Wingo P. Cancer statistics, 2000. *CA Cancer J Clin* 2000;50:7–33.
3. National Cancer Institute. *SEER Cancer Statistics Review 1973–1990.* Bethesda, MD: National Institutes of Health, 1993.
4. Sohn TA, Yeo CJ, Cameron JL, et al. Resected adenocarcinoma of the pancreas—616 patients: results, outcomes, and prognostic indicators. *J Gastrointest Surg* 2000;4:567–79.
5. Yeo CJ, Cameron JL, Sohn TA, et al. Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. *Ann Surg* 1997;226:248–57; discussion, 257–60.
6. Reddy KR, Levi J, Livingstone A, et al. Experience with staging laparoscopy in pancreatic malignancy. *Gastrointest Endosc 1999*; 49:498–503.
7. Warshaw AL, Gu ZY, Wittenberg J, Waltman AC. Preoperative staging and assessment of resectability of pancreatic cancer. *Arch Surg* 1990;125:230–3.
8. Berberat P, Friess H, Kashiwagi M, Beger HG, Buchler MW. Diagnosis and staging of pancreatic cancer by positron emission tomography. *World J Surg* 1999;23:882–7.
9. van Heertum RL, Fawwaz RA. The role of nuclear medicine in the evaluation of pancreatic disease. *Surg Clin North Am* 2001;81: 345–58.
10. Frohlich A, Diederichs CG, Staib L, Vogel J, Beger HG, Reske SN. Detection of liver metastases from pancreatic cancer using FDG PET. *J Nucl Med* 1999;40:250–5.
11. Higashi T, Tamaki N, Honda T, et al. Expression of glucose transporters in human pancreatic tumors compared with increased FDG accumulation in PET study. *J Nucl Med* 1997;38:1337–44.
12. Reske SN, Grillenberger KG, Glatting G, et al. Overexpression of glucose transporter 1 and increased FDG uptake in pancreatic carcinoma. *J Nucl Med* 1997;38:1344–8.
13. Jadvar H, Fischman AJ. Evaluation of pancreatic carcinoma with FDG PET. *Abdom Imaging* 2001;26:254–9.
14. Mertz HR, Sechopoulos P, Delbeke D, Leach SD. EUS, PET, and CT scanning for evaluation of pancreatic adenocarcinoma. *Gastrointest Endosc* 2000;52:367–71.
15. Rose DM, Delbeke D, Beauchamp RD, et al. ^{18}Fluorodeoxyglucose-positron emission tomography in the management of patients with suspected pancreatic cancer. *Ann Surg* 1999;229:729–37.
16. Keogan MT, Tyler D, Clark L, et al. Diagnosis of pancreatic carcinoma: role of FDG PET. *AJR Am J Roentgenol* 1998;171: 1565–70.
17. Imdahl A, Nitzsche E, Krautmann F, et al. Evaluation of positron emission tomography with 2-[^{18}F]fluoro-2-deoxy-D-glucose for the differentiation of chronic pancreatitis and pancreatic cancer. *Br J Surg* 1999;86:194–9.
18. Zimny M, Buell U. ^{18}FDG-positron emission tomography in pancreatic cancer. *Ann Oncol* 1999;10:28–32.
19. Inokuma T, Tamaki N, Torizuka T, et al. Evaluation of pancreatic tumors with positron emission tomography and F-18 fluorodeoxyglucose: comparison with CT and US. *Radiology* 1995;195:345–52.
20. Friess H, Langhans J, Ebert M, et al. Diagnosis of pancreatic cancer by 2[^{18}F]-fluoro-2-deoxy-D-glucose positron emission tomography. *Gut* 1995;36:771–7.
21. Kasperk RK, Riesener KP, Wilms K, Schumpelick V. Limited value of positron emission tomography in treatment of pancreatic cancer: surgeon's view. *World J Surg* 2001;25:1134–9.
22. Delbeke D, Rose DM, Chapman WC, et al. Optimal interpretation of FDG PET in the diagnosis, staging and management of pancreatic carcinoma. *J Nucl Med* 1999;40:1784–91.
23. Diederichs CG, Staib L, Glatting G, Beger HG, Reske SN. FDG PET: elevated plasma glucose reduces both uptake and detection rate of pancreatic malignancies. *J Nucl Med* 1998;39:1030–3.
24. Lindholm P, Minn H, Leskinen-Kallio S. Influence of blood glucose concentration on FDG uptake in cancer: a PET study. *J Nucl Med* 1993;34:1–6.
25. Nakamoto Y, Higashi T, Sakahara H, et al. Evaluation of pancreatic islet cell tumors by fluorine-18 fluorodeoxyglucose positron emission tomography: comparison with other modalities. *Clin Nucl Med* 2000;25:115–9.
26. Adams S, Baum R, Rink T, Schumm-Drager PM, Usadel KH, Hor G. Limited value of fluorine-18 fluorodeoxyglucose positron emission tomography for the imaging of neuroendocrine tumours. *Eur J Nucl Med* 1998;25:79–83.
27. Diederichs CG, Staib L, Vogel J, et al. Values and limitations of ^{18}F-fluorodeoxyglucose-positron-emission tomography with preoperative evaluation of patients with pancreatic masses. *Pancreas* 2000;20:109–16.
28. Kubato R, Yamada Y, Torizuka T. Intratumoral distribution of fluorine-18-fluorodeoxyglucose in vivo: high accumulation in macrophages and granulation tissues studied by microradiography. *J Nucl Med* 1992;33:1972–80.
29. Shreve P. Focal fluorine-18 fluorodeoxyglucose accumulation in inflammatory pancreatic disease. *Eur J Nucl Med* 1998;25:259–64.
30. Sendler A, Avril N, Helmberger H, et al. Preoperative evaluation of pancreatic masses with positron emission tomography using ^{18}F-fluorodeoxyglucose: diagnostic limitations. *World J Surg* 2000;24:1121–9.
31. Schwarz M, Pauls S, Sokiranski R, et al. Is a preoperative multidiagnostic approach to predict surgical resectability of periampullary tumors still effective? *Am J Surg* 2001;182:243–9.
32. Hommeyer SC, Freeny PC, Crabo LG. Carcinoma of the head of the pancreas: evaluation of the pancreaticoduodenal veins with dynamic CT-potential of improved accuracy in staging. *Radiology* 1995;196:233–8.
33. Ruers T, Langenhoof B, Neeleman N, et al. Value of positron emission tomography with [F-18] fluorodeoxyglucose in patients with colorectal liver metastases: a prospective study. *J Clin Oncol* 2002:20:388–95.
34. White R, Hurwitz H, Lee C, et al. Neoadjuvant chemoradiation for localized adenocarcinoma of the pancreas. *Ann Surg Oncol* 2001; 8:758–65.
35. Sperti C, Pasquali C, Chierichetti F, Liessi G, Ferlin G, Pedrazzoli S. Value of 18-fluorodeoxyglucose positron emission tomography in the management of patients with cystic tumors of the pancreas. *Ann Surg* 2001;234:675–80.