Optimal Interpretation of FDG PET in the Diagnosis, Staging and Management of Pancreatic Carcinoma

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This study had two purposes: to optimize the semiquantitative interpretation of ^{18}F-fluorodeoxyglucose (FDG) PET scans in the diagnosis of pancreatic carcinoma by analyzing different cutoff levels for the standardized uptake value (SUV), with and without correction for serum glucose level (SUV_{gluc}); and to evaluate the usefulness of FDG PET when used in addition to CT for the staging and management of patients with pancreatic cancer. **Methods:** Sixty-five patients who presented with suspected pancreatic carcinoma underwent whole-body FDG PET in addition to CT imaging. The PET images were analyzed visually and semiquantitatively using the SUV and SUV_{gluc}. The final diagnosis was obtained by pathologic (n = 56) or clinical and radiologic follow-up (n = 9). The performance of CT and PET at different cutoff levels of SUV was determined, and the impact of FDG PET in addition to CT on patient management was reviewed retrospectively. **Results:** Fifty-two patients had proven pancreatic carcinoma, whereas 13 had benign lesions, including chronic pancreatitis (n = 10), benign biliary stricture (n = 1), pancreatic complex cyst (n = 1) and no pancreatic pathology (n = 1). Areas under receiver operating characteristic curves were not significantly different for SUV and SUV_{gluc}. Using a cutoff level of 3.0 for the SUV, FDG PET had higher sensitivity and specificity than CT in correctly diagnosing pancreatic carcinoma (92% and 85% versus 65% and 61%). There were 2 false-positive PET (chronic pancreatitis, also false-positive with CT) and 4 false-negative PET (all with true-positive CT, abnormal but nondiagnostic) examinations. There were 5 false-positive CT (4 chronic pancreatitis and 1 pancreatic cyst) and 18 false-negative CT (all with true-positive FDG PET scans) examinations. FDG PET clarified indeterminate hepatic lesions or identified additional distant metastases (or both) in 7 patients compared with CT. Overall, FDG PET altered the management of 28 of 65 patients (43%). **Conclusion:** FDG PET is more accurate than CT in the detection of primary tumors and in the clarification and identification of hepatic and distant metastases. The optimal cutoff value of FDG uptake to differentiate benign from malignant pancreatic lesions was 2.0. Correction for serum glucose did not significantly improve the accuracy of FDG PET. Although FDG PET cannot replace CT in defining local tumor extension, the application of FDG PET in addition to CT alters the management in up to 43% of patients with suspected pancreatic cancer.

Key Words: pancreas; neoplasms; PET; fluorodeoxyglucose

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Pancreatic ductal adenocarcinoma is the fourth leading cause of cancer death in the United States and is increasing in incidence. Only 3% of newly diagnosed patients will survive 5 y. Pancreaticoduodenectomy improves 5-y survival to >20%, with a 2%–3% mortality in patients carefully selected for the procedure (*1*).

Diagnosis, clinical staging and treatment of pancreatic carcinoma remain difficult. Suspicions of pancreatic cancer are often raised by sonography or CT findings, including the presence of a low-attenuation pancreatic mass and dilatation of the pancreatic duct or biliary tree (to both). CT is the most common diagnostic imaging modality used in the preoperative diagnosis of pancreatic cancer. This technique can also assess vascular involvement and invasion of adjacent organs (*2–4*). Unfortunately, interpretation of CT is sometimes difficult in mass-forming pancreatitis or in questionable findings, such as enlargement of the pancreatic head without definite signs of malignancy. Other anatomic imaging modalities, including sonography, endoscopic retrograde cholangiopancreatography (ERCP) and MRI have similar limitations. Endoscopic sonography allows detailed images of the head and body of the pancreas and permits biopsy (*5*). However, it does not allow evaluation of the entire body to detect unsuspected metastases. Although CT-guided fine-needle biopsy may provide a tissue diagnosis, this technique may suffer from significant sampling error and cause complications, including necrotizing pancreatitis (*6*).

In this setting, functional imaging may provide a more accurate means of delineating benign versus malignant pancreatic disease. The glucose analog ^{18}F-fluorodeoxyglucose (FDG) is a radiopharmaceutical that allows direct evaluation of glucose metabolism with PET. Most malignan-

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cies, including pancreatic carcinoma, show increased glucose utilization as a result of an increased number of glucose transporter proteins and increased hexokinase and phosphofructokinase activities (*7–9*). Published evidence suggests that the overexpression of glucose transporters by malignant pancreatic cells contributes to the increased uptake of FDG by these neoplasms (*10,11*). A potential role for FDG PET in imaging pancreatic carcinoma has been reported (*12–18*). FDG PET imaging usually is interpreted semiquantitatively using the standarized uptake value (SUV), which estimates fractional FDG uptake by tumor. The increased rate of glucose intolerance exhibited by patients with pancreatic pathology represents a potential limitation of this modality in the diagnosis of pancreatic cancer because elevated serum glucose levels decrease FDG uptake by competitive inhibition. This has led some investigators to suggest that the SUV be corrected according to serum glucose level (*19–21*).

The purposes of the current study were twofold: first, to optimize the semiquantitative interpretation of FDG PET scans in the diagnosis of pancreatic carcinoma by analyzing different cutoff levels for the SUV, with and without correction for serum glucose level (SUV_{gluc}); and second, to evaluate the usefulness of FDG PET when used in addition to CT for the staging and management of patients with pancreatic cancer.

MATERIALS AND METHODS

Patient Population

Sixty-five consecutive patients (33 men, 32 women; age range 36–80 y, mean age 60 ± 20 y) with suspected pancreatic carcinoma who underwent both FDG PET and CT were included in the study. In all cases, PET imaging was performed within a 1-mo interval of CT.

The final diagnosis was obtained by pathology in 56 patients. Tissue was obtained during surgical exploration in 33 patients (including 5 patients with benign disease), by CT or endoscopic sonographically guided fine-needle biopsy in 20 patients (positive for malignancy) and by cytologic brushings obtained during ERCP in 3 patients (positive for malignancy). In 9 patients, the diagnosis was established with clinical and radiologic follow-up. Two of these patients were diagnosed by CT with unresectable disease and died within a few weeks of imaging studies. Seven patients had no definite evidence of malignancy. These patients have remained clinically stable, with no evidence of malignant disease over a 6-mo follow-up period.

CT

For scans performed in our institution, helical CT scans of the abdomen were obtained with 5-mm collimation and a table speed of 5 mm/s (pitch 1 or 2) after oral contrast administration and 30 s after intravenous contrast administration (150 mL at 3 mL/s) and then again during the portal phase to examine the liver. The images were reconstructed with 5-mm thicknesses. The CT scans were interpreted with the clinical information available by two radiologists who were experts in body imaging but unaware of the PET scan findings. CT scans showing a discrete low-attenuation mass in the pancreas were considered positive for pancreatic carcinoma. CT scans showing diffuse enlargement of the pancreatic head or uncinate process (but no discrete low-attenuation mass) in the setting of distant metastases were also considered positive for pancreatic carcinoma. Enlargement of the pancreatic head without definite signs of malignancy was classified as benign. Hypoattenuating masses with calcifications and pseudocysts without additional findings were considered typical for chronic pancreatitis and classified as benign.

Twenty-two patients presented with CT of the abdomen performed at outside institutions. These studies were not repeated. Three of these CT examinations were performed with the same technique used in this study. Although the CT technique may have varied for the other 19 patients, CT imaging in these patients was not repeated because intravenous contrast was identified in the superior mesenteric vein, and pancreatic parenchymal enhancement was present.

PET

FDG PET was performed with an ECAT 933/08/16 tomograph (Siemens, Iselin, NJ), which has eight ring detectors that simultaneously collect images in 15 planes, each 8-mm thick. The axial field of view of this system is 12.8 cm. The reconstructed resolution is 6.5 × 6.5 × 8.0 mm (full width at half maximum) when measured with a line source in nonscattering media and data were reconstructed with a ramp filter (*22*). Patients were required to fast for at least 4 h before PET scanning. The patients were scanned with as many sequential images as necessary to include the entire thorax, abdomen and pelvis. Transmission images were obtained for 10 min per bed position to correct for photon attenuation using a ^{68}Ge ring source. After the intravenous administration of 370 MBq (10 mCi) FDG, emission images were acquired for 15 min per bed position. The uptake period between FDG injection and the beginning of the emission scanning was approximately 60 min. Patients were moved for the uptake phase, and accurate repositioning of the patient between transmission and emission scanning was performed using laser marks. The arms were elevated and not in the field of view. The images were reconstructed with a filtered backprojection using a Hamming filter with a cutoff frequency of 0.5.

Both attenuation-corrected and non–attenuation-corrected images were interpreted visually by two expert nuclear medicine physicians. Clinical information was used in addition to CT scans for localization of the pancreatic head to differentiate between abnormal uptake in the head of the pancreas and physiologic uptake in an adjacent loop of bowel. Visual analysis was performed using background liver uptake as a reference (uptake greater than liver background corresponding to the head of the pancreas on CT was considered malignant). The attenuation-corrected images were analyzed semiquantitatively, using the SUVs by the physician who performed the visual interpretation. Although visual analysis is often satisfactory for clinical interpretation, semiquantitative analysis can be helpful when the size of the lesion is known. In this study, it was also performed to compare the effect of correcting the uptake for serum glucose levels using receiver operating characteristic (ROC) analysis. For the semiquantitative analysis, regions of interest (ROI) measuring 1.0 ± 0.5 cm^2 were drawn over the areas of maximum activity in each lesion. The SUV was calculated as:

SUV = (activity in ROI in μCi/mL)/(injected dose in mCi/weight in kg).

The analysis was also performed with the SUV corrected for the serum glucose level:

$SUV_{[gluc]}$ = SUV × serum glucose level/100.

The serum glucose level was measured just before the administration of FDG to each patient. The SUV was not corrected for partial-volume effect in small lesions.

Parallel analyses were performed using cutoff values of ≥2.0 and ≥3.0, respectively. PET images were considered positive when a focus of increased uptake was identified in the region of the pancreas, with an SUV greater or equal to these values. Patient 12 had a serum glucose level of 176 mg/100 mL and was the first patient with an elevated serum glucose level and a false-negative PET scan. All subsequent patients with a serum glucose level of >150 mg/100 mL on the day of study received regular insulin intravenously by boluses of 2–10 U every 15 min up to 15 U or until the serum glucose level dropped below 150 mg/100 mL. In these 6 patients, among whom were 3 known diabetics, the serum glucose level fell below 150 mg/100 mL and was >70 mg/100 mL at the end of the PET study. The serum glucose level used to calculate the SUV_{gluc} was the level obtained just before FDG injection.

Statistical Analysis

Results were expressed as mean ± SD, and comparison was performed using the Mann-Whitney test for two samples. The comparison between SUVs and SUV_{gluc} was completed using the ROC analysis, and the area under the curve was calculated. All tests were two-sided, and differences were considered statistically significant when $P < 0.05$.

RESULTS

The prevalence of pancreatic carcinoma was 80% in our series of patients, which is in the same range (59%–100%) as published series (*12–18*).

The dimensions of the malignant pancreatic lesions were measurable in 49 of 52 patients. Tumor sizes were assessed from surgical specimens when available (n = 16) and otherwise by CT (n = 22). Size as measured by endoscopic sonography was used only for patients who had no surgery and in whom lesions were not well defined on CT (n = 11). The sizes ranged from 0.5 to 5 cm (14 lesions ≤ 2 cm, 15 lesions were 2–4 cm and 20 lesions ≥ 4 cm).

The serum glucose levels from these 65 patients ranged from 49 to 176 mg/100 mL (94 ± 26 mg/100 mL [mean ± SD]) at the time of FDG injection. Eleven patients were treated for diabetes (8 with pancreatic carcinoma, 3 with benign lesions). Ten patients had serum glucose levels of >120 mg/100 mL (8 with pancreatic carcinoma, 2 with pancreatitis), but only 3 of these had known diabetes mellitus. Figure 1 shows the ROC curves of FDG PET using the SUV and the SUV_{gluc}. The area under the curve was slightly higher for SUV_{gluc} (area = 0.9812) compared with the uncorrected SUV (area = 0.9238), but the difference was not statistically significant. Therefore, SUV without correction for serum glucose level was used in the analysis.

The distribution of SUV in benign and malignant pancreatic lesions is shown in Figure 2. The SUV was 5.1 ± 2.6 (mean ± SD) for the malignant lesions and 0.85 ± 1.7 for the benign lesions. This difference was statistically significant ($P < 0.0001$). The SUV for malignant lesions ranged from 2.2 to 15. Normal pancreas and most benign lesions (n = 10) had low levels of FDG uptake. Only 3 of 10 patients with chronic pancreatitis had FDG uptake, with SUVs of 2.4, 3.0 and 4.9. In the population of patients in this study, a value of 2.0 for the cutoff level of SUV was equivalent to the visual analysis. Increasing the value of the cutoff level to diagnose a malignant lesion will decrease the number of false-positive but will increase the number of false-negative studies. Values between 2.5 and 3.5 have been shown to be optimal for differentiating benign from malig-

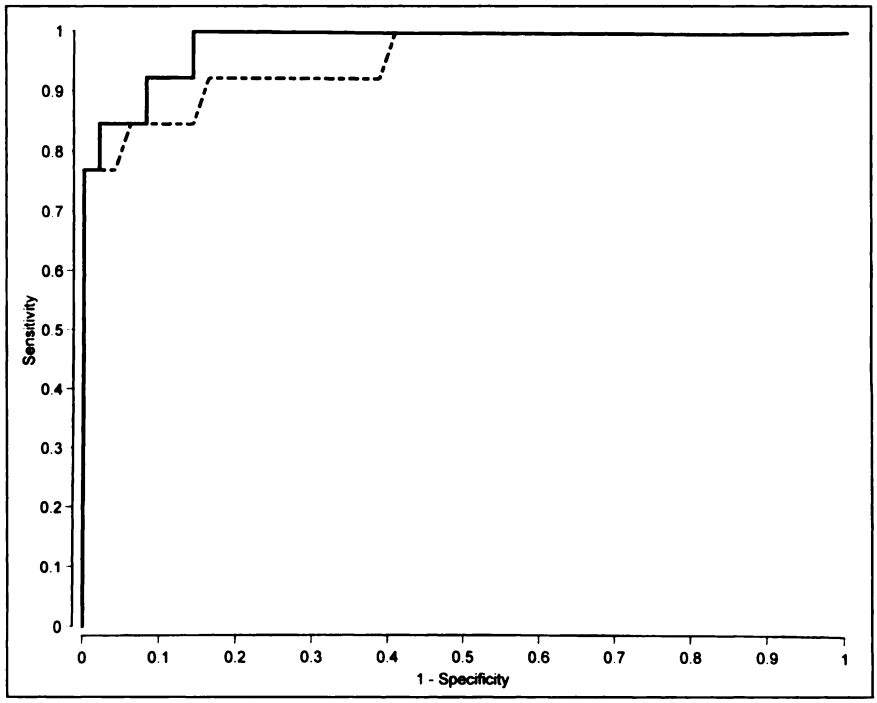

FIGURE 1. ROC curve for FDG PET using SUV (dashed line) and SUV_{gluc} (solid line) for semiquantitative evaluation of FDG uptake. Areas under curves are not statistically different.

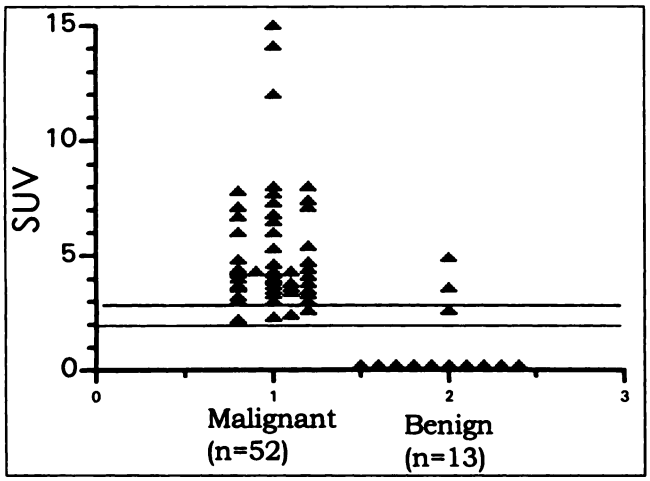

FIGURE 2. Distribution of standardized uptake values (SUVs) for benign and malignant pancreatic lesions. Horizontal lines represent cutoff levels of SUVs of 2.0 and 3.0, respectively.

nant lesions in other organs (*23,24*). In this study, we analyzed the effects of using a cutoff level of 2.0 versus 3.0 on the sensitivity, specificity, accuracy and predictive values of FDG PET.

The sensitivity, specificity, accuracy and predictive values of CT and of FDG PET used in addition to CT are listed in Table 1, with cutoff SUVs of 2.0 and 3.0, respectively. CT diagnosed pancreatic carcinoma correctly in 34 of 52 patients and diagnosed benign lesions correctly in 8 of 13 patients. Of the 5 false-positive and 18 false-negative CT examinations, all were true-positive on FDG PET imaging. The false-positive CT studies showed mass-forming pancreatitis and a complex cyst. Among the false-negative CT examinations, 12 patients had malignant lesions ≤ 2 cm. An example of a patient with a pancreatic carcinoma that was false-negative on CT but correctly diagnosed on FDG PET is shown in Figure 3.

When a cutoff level of 2.0 for the SUV was used to define a positive FDG PET scan, there were no false-negative but three false-positive FDG PET scans in patients with chronic pancreatitis.

Using a cutoff level of 3.0 for the SUV, FDG PET

TABLE 1
FDG PET and CT in the Detection of Pancreatic Carcinoma Using SUV Cutoff Levels of 2.0 and 3.0

Modality	TP	FN	TN	FP	SEN (%)	SPE (%)	NPV (%)	PPV (%)	ACC (%)
CT	34	18	8	5	65	61	31	87	65
FDG PET									
Cutoff level of SUV 2.0	52	0	10	3	100	77	100	94	95
Cutoff level of SUV 3.0	48	4	11	2	92	85	73	96	91

FDG = ^{18}F-fluorodeoxyglucose; SUV = standardized uptake value; TP = true-positive; FN = false-negative; TN = true-negative; FP = false-positive; SEN = sensitivity; SPE = specificity; NPV = negative predictive value; PPV = positive predictive value; ACC = accuracy.

Lesions of all sizes in 65 patients were included.

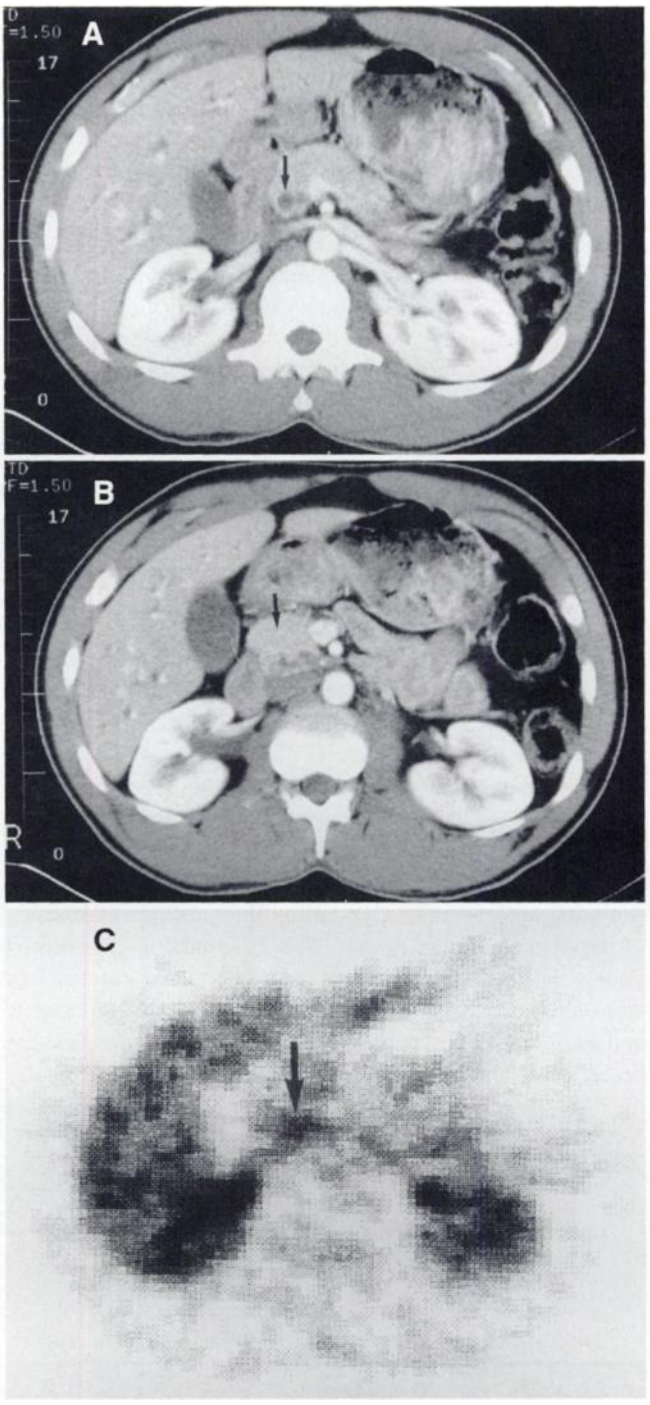

FIGURE 3. Axial CT (A and B) and PET (C) images of 37-y-old man who presented with biliary obstruction. CT of abdomen shows dilatation of intrahepatic biliary system and of common bile duct (A, arrow). No definite mass is seen in pancreatic head (B, arrow). PET scan reveals focus of FDG uptake (C, arrow, SUV = 3.0) corresponding to pancreatic head on CT image, which led to pancreaticoduodenectomy. Pathologic examination of specimen revealed 0.5-cm pancreatic carcinoma in pancreatic head.

identified 48 of 52 patients with pancreatic carcinoma and 11 of 13 patients with benign lesions. There were 2 false-positives identified with PET, showing focal FDG uptake in chronic pancreatitis (SUVs = 3.0 and 4.9). There were 4 false-negative PET scans in patients with poor FDG uptake in pancreatic carcinomas (SUVs = 2.2, 2.2, 2.4 and 2.6). Among these patients with 4 false-negative PET scans, 1 had insulin-dependent diabetes mellitus and a serum glucose level of 111 mg/100 mL, and another had a serum glucose level of 176 mg/100 mL without known diabetes.

Four patients who received insulin had true-positive PET scans, 1 a true-negative PET scan and 1 a false-negative PET scan.

Using a cutoff level of 3.0 instead of 2.0 for the SUV decreased the sensitivity of PET from 100% to 92%, the negative predictive value from 100% to 73% and the accuracy from 95% to 91%. However, the specificity was increased from 77% to 85% and the positive predictive value from 94% to 96%.

Table 2 shows the tumor stage of 49 of 52 patients with pancreatic carcinoma and lists the results of staging according to the modality used. Three patients with limited disease by imaging criteria refused surgery and therefore could not be staged definitively. Stage II disease is characterized by extrapancreatic extension, stage III by lymph node involvement and stage IV by distant metastases. Extrapancreatic extension was diagnosed on CT in 7 patients who had no surgery and by surgical exploration in 3 patients. FDG PET provided no information regarding the presence or absence of extrapancreatic extension. Both CT and PET performed poorly in detecting lymph node involvement. Metastases were diagnosed both on CT and PET in 10 of 21 patients, and PET revealed hepatic metastases not seen or equivocal on CT or distant metastases (or both) unsuspected clinically in 7 additional patients. In these 7 patients, the distant metastases were confirmed by biopsy or another imaging modality. Liver metastases equivocal on CT were all confirmed by biopsy or surgery. Figures 4 and 5 show examples of such patients. In 4 patients, neither CT nor PET imaging showed evidence of metastases, and surgical exploration showed carcinomatosis in 3 patients and a small liver metastasis in 1 patient.

TABLE 2
Staging According to Modality Used in Patients with Pancreatic Carcinoma

Stage	CT	PET	Surgery only	Total*
I	6	6	—	6
II (extrapancreatic extension)	7†	0	3	10
III (N1)	1	2	10	12
IV (M1)	10	17‡	4	21
Total	24	25	—	49§

*Total = total number of patients with disease in each stage.

†CT showed vascular invasion in 7/49 (14%) patients, not seen on PET.

‡PET showed metastases in 7/49 patients (14%), not seen or indeterminate on CT. In 2 of these patients, CT showed unresectable vascular invasion. Therefore, use of PET avoided unnecessary surgery in 5 patients.

§Three patients refused therapy and could not be staged accurately.

PET facilitated surgical planning in 20 of 65 (30%) patients by identifying a focus of tumor in the pancreas in 18 patients who had negative or indeterminate CT results and by clarifying the benign nature of CT-indeterminate liver lesions (<1 cm) in 2 patients. PET helped avoid unnecessary surgery in 8 of 65 (13%) patients by identifying unsuspected liver or distant metastases (or both) in 5 patients with otherwise resectable disease and by clarifying the benign nature of pancreatic lesions seen on CT in 3 patients (pancreatitis and benign complex cyst).

DISCUSSION

The preoperative differentiation between malignant and benign lesions in patients with suspected pancreatic carcinoma remains a diagnostic challenge. The traditional imaging modality used to evaluate these lesions is CT, which is relatively insensitive in detecting pancreatic cancers < 2 cm in size. In contrast to the inherent limitations of this anatomic imaging modality, functional imaging using FDG PET appears to represent a significant advance in the detection and staging of pancreatic malignancy.

This study shows that metabolic-based imaging with FDG PET is extremely useful in the detection of pancreatic carcinoma. We found that the sensitivity (92%), specificity (85%) and accuracy (91%) of FDG PET in this setting are in the same range as those reported by other investigators, who reported sensitivities of 85%–100%, specificities of 67%–99% and accuracies of 85%–93% (*12–18*). As in these studies, we found that the performance of FDG PET is superior to that of CT, with accuracies of 91% and 65%, respectively (*12–14*). However, the sensitivity and specificity of CT in our study may be low because of the criteria used. Equivocal findings on CT, such as an enlarged pancreatic head without definite lesion and without additional evidence of malignancy, were classified as benign, whereas such findings may have been classified as malignant in other studies, such as that of Diehl et al. (*3*). Three patients were classified as false-negative on CT because the only anomaly was mild nonspecific enlargement of the head of the pancreas. Had they been classified as true-positive, the sensitivity, positive predictive value and accuracy of CT would have improved from 65% to 71%, 87% to 94% and 65% to 69%, respectively, values that are still below those of the FDG PET performance.

One limitation of the current study involves the nonuniformity of technique used in the 22 CT studies performed at outside institutions. The overall accuracy of CT in this study was 65%. For the 22 scans performed at outside institutions, this accuracy dropped to 50% compared with 72% for the 43

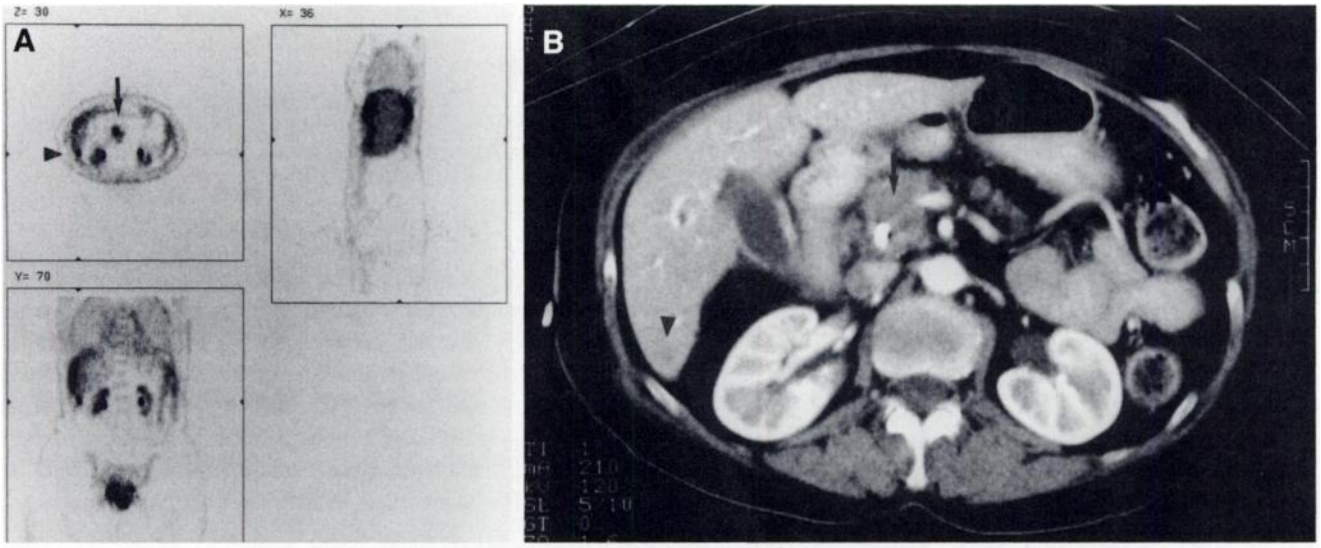

FIGURE 4. (A) PET images without attenuation correction of 59-y-old woman with biliary obstruction and lesion in head of pancreas on CT (not shown). PET images (transverse, top left; coronal, bottom; sagittal, right) show uptake in pancreatic head as expected (arrow) but also show focus of increased FDG uptake in liver consistent with small metastasis (arrowhead). (B) Thin-cut repeat CT scan shows equivocal lesion in that location (arrowhead). Lesion was explored, and small metastasis was proven by pathology.

patients scanned according to the protocol at this institution. However, even when the analysis is limited to those patients undergoing helical CT in this institution, the 91% accuracy rate observed for FDG PET proves superior. There is a statistically significant difference between these two groups ($P = 0.017$), and the power of this test is about 80%, with a type 1 error of 5%.

Some benign inflammatory lesions, including chronic active pancreatitis with abscess formation, can accumulate FDG and result in false-positive interpretations on PET images (*25–29*). Other lesions that have been reported with false-positive images are serous cystadenoma and retroperitoneal fibrosis (*13–15*). In addition, small lesions that suffer from partial volume averaging can lead to false-negative interpretation (i.e., small ampullary carcinomas) (*30*).

In evaluating patients with pancreatic pathology, glucose intolerance represents another important factor that may influence the accuracy of FDG PET. FDG competes with glucose for cellular transport, and high serum glucose levels competitively inhibit FDG uptake by malignant cells (*19–*

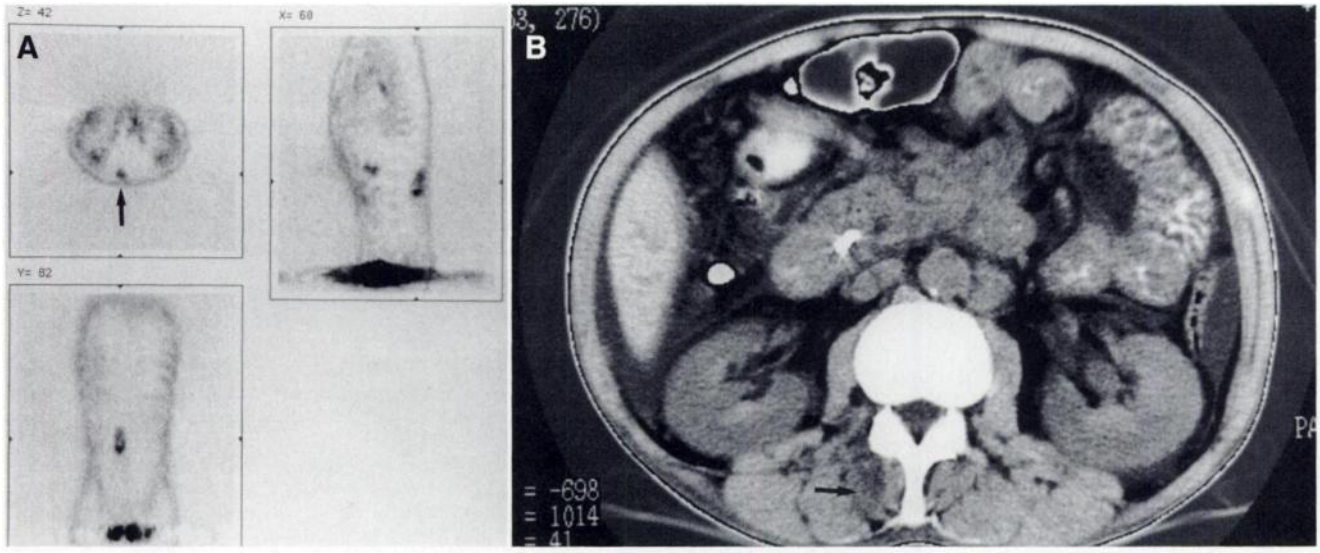

FIGURE 5. PET images without attenuation correction (A) and CT scan (B) of 50-y-old man, known alcohol and drug abuser, who presented with right upper quadrant pain and worsening back pain. PET images (transverse, top left; coronal, bottom; sagittal; right) show uptake in pancreas consistent with malignant lesion (not shown) but also show focus of increased FDG uptake in right paravertebral muscle (arrow). When first interpreted, CT scans showed enlargement of pancreas, intrahepatic biliary tree dilatation and dilatation of common bile duct. Only retrospective examination of CT scan revealed necrotic lesion in that location (arrow). Percutaneous biopsy revealed metastasis.

21). Studies have shown a lower sensitivity in hyperglycemic compared with euglycemic patients (*13,17*). For example, in a study of 106 patients with a prevalence of disease of 70%, Zimny et al. (*17*) found that FDG PET had a sensitivity of 98%, specificity of 84% and accuracy of 93% in a subgroup of euglycemic patients compared with 63%, 86% and 68%, respectively, in a subgroup of hyperglycemic patients. However, this was not confirmed in the study by Friess et al. (*16*). False-negative studies for the evaluation of pancreatic cancer have been reported previously in patients with insulin-dependent diabetes mellitus. In the current study, the presence of elevated serum glucose levels or diabetes mellitus (or both) may have contributed to false-negative interpretation, especially when a cutoff SUV level of 3.0 was used. However, we found that correction of the SUV for serum glucose levels did not significantly improve the accuracy of FDG PET in the diagnosis of pancreatic carcinoma, confirming data from another study (*31*). In this regard, the rigorous attempts to normalize serum glucose levels before PET imaging may have had some impact on our rate of false-negative scans.

SUV results might have been better if the values had been corrected for partial volume. Among the 14 patients with tumors $\leq$ 2 cm, 7 had tumors of 2 cm, 4 had tumors $\geq$ 1.5 cm and three had tumors $<$ 1.5 cm. All of these patients had SUVs $\geq$ 3.0. Correction for partial volume would not have influenced the data in this study.

FDG imaging allows evaluation of the entire body without additional radiation to the patient, allowing identification of distant metastases. CT of these regions may be performed subsequently to provide anatomic correlation and guide tumor-directed therapy. In this study, PET was especially helpful in clarifying the nature of CT-indeterminate liver lesions and in identifying unsuspected distant metastases.

FDG PET significantly influenced surgical strategy in up to 43% of patients by clarifying the benign nature of a pancreatic or hepatic lesion seen on CT, by revealing metastases that were unsuspected clinically in apparently resectable patients (n = 5) or by identifying primary tumors not identified by CT (n = 18). A similar impact has been reported on the surgical management of colorectal carcinoma by this group (*23,32*) and by other investigators (*33–38*).

It is well known that functional imaging does not have the same resolution and landmarks as anatomic imaging. PET cannot evaluate local extension of the tumor and the relationship of the tumor with surrounding vessels. Therefore, functional imaging is always additional and complementary to anatomic imaging in patients considered for surgery. In addition, FDG uptake normally present in the gastrointestinal tract can sometimes be difficult to differentiate from an adjacent pancreatic lesion. Careful correlation between PET and anatomic imaging is necessary to verify that an area of increased uptake corresponds anatomically to the pancreas.

CONCLUSION

The optimal cutoff level of SUV to differentiate benign from malignant pancreatic lesions was 2.0. PET successfully detected primary pancreatic tumors not detected by CT in 18 of 65 (28%) patients. PET cannot assess extrapancreatic extension and cannot replace CT in the preoperative evaluation of patients with suspected pancreatic carcinoma. Both PET and CT were poor predictors of regional nodal involvement. Whole-body PET allowed detection of unsuspected distant metastases and helped clarify the nature of equivocal lesions on CT. Overall, the use of FDG PET in addition to CT altered the surgical management in up to 43% of the patients by identifying or clarifying the malignant or benign nature of the pancreatic lesion in 30% and by identifying unsuspected distant metastases or by clarifying the benign nature of CT-indeterminate lesions in 13% of the patients.

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REFERENCES

1. Gold EB, Goldin SB. Epidemiology of and risk factors for pancreatic cancer. *Surg Oncol Clin North Am.* 1998;7:67–91.
2. Campbell JP, Wilson SR. Pancreatic neoplasms: how useful is evaluation with US? *Radiology.* 1988;167:341–344.
3. Diehl SJ, Lehman KJ, Sadick M, Lachman R, Georgi, M. Pancreatic cancer: value of dual-phase helical CT in assessing resectability. *Radiology.* 1998;206:373–378.
4. Lu DSK, Reber HA, Krasny RM, Sayre J. Local staging of pancreatic cancer: criteria for unresectability of major vessels as revealed by pancreatic-phase, thin-section helical CT. *AJR.* 1997;168:1439–1444.
5. Wanebo HJ, Vezeridis MP. Pancreatic carcinoma in perspective: a continuing challenge. *Cancer.* 1996;78:580–591.
6. Brandt KR, Charbrideau JW, Stephens DH, Welch TJ, Goellner JR. CT and US guided biopsy of the pancreas. *Radiology.* 1993;187:99–104.
7. Hoh CK, Schiepers C, Seltzer MA, et al. PET in oncology: will it replace the other modalities? *Semin Nucl Med.* 1997;27:94–106.
8. Flier JS, Mueckler MM, Usher P, Lodish HF. Elevated levels of glucose transport and transporter messenger RNA are induced by ras or src oncogenes. *Science.* 1987;235:1492–1495.
9. Monakhov NK, Neistadt EL, Shavlovskil MM, et al. Physiochemical properties and isoenzyme composition of hexokinase from normal and malignant human tissues. *J Natl Cancer Inst.* 1978;61:27–34.
10. Higashi T, Tamaki N, Honda T, et al. Expression of glucose transporters in human pancreatic tumors compared with increased F-18 FDG accumulation in PET study. *J Nucl Med.* 1997;38:1337–1344.
11. Reske S, Grillenberger KG, Glatting G, et al. Overexpression of glucose transporter 1 and increased F-18 FDG uptake in pancreatic carcinoma. *J Nucl Med.* 1997;38:1344–1348.
12. Bares R, Klever P, Hauptmann S, et al. F-18 fluorodeoxyglucose PET in vivo evaluation of pancreatic glucose metabolism for detection of pancreatic cancer. *Radiology.* 1994;192:79–86.
13. Stollfuss JC, Glatting G, Friess H, Kocher F, Beger HG, Reske SN. F-(fluorine-18) fluoro-2-deoxy-d-glucose PET in detection of pancreatic cancer: value of quantitative image interpretation. *Radiology.* 1995;195:339–344.
14. 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;195:345–352.
15. Ho CL, Dehdashti F, Griffeth LK, et al. F-18 FDG-PET evaluation of indeterminate pancreatic masses. *J Comput Assist Tomogr.* 1996;20:363–369.

16. 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;36:771–777.
17. Zimny M, Bares R, Fass J, et al. Fluorine-18 fluorodeoxyglucose positron emission tomography in the differential diagnosis of pancreatic carcinoma: a report of 106 cases. *Eur J Nucl Med.* 1997;24:678–682.
18. Minn H, Zasadny KR, Quint LE, Wahl RL. Lung cancer: reproducibility of quantitative measurements for evaluating 2-[F-18]-fluoro-2-deoxy-D-glucose uptake at PET. *Radiology.* 1995;196:167–173.
19. Wahl RL, Henry CA, Ethrer SP. Serum glucose: effects on tumor and normal tissue accumulation of 2-[F-18]-fluoro-2-deoxy-D-glucose in rodents with mammary carcinoma. *Radiology.* 1992;183:643–647.
20. Lindholm P, Minn H, Leskinen-Kallio S, et al. Influence of blood glucose concentration on FDG uptake in cancer: a PET study. *J Nucl Med.* 1993;34:1–6.
21. Langen KJ, Braun U, Kops ER, et al. The influence of serum glucose levels on fluorine-18-fluorodeoxyglucose uptake in bronchial carcinomas. *J Nucl Med.* 1993;34:355–359.
22. Delbeke D, Patton JA, Martin WH, Sandler MP. FDG PET and dual-head gamma camera positron coincidence detection imaging of suspected malignancies and brain disorders. *J Nucl Med.* 1999;40:110–117.
23. Delbeke D, Vitola J, Sandler MP, et al. Staging recurrent metastatic colorectal carcinoma with PET. *J Nucl Med.* 1997;38:1196–1201.
24. Lowe VL, Fletcher JW, Gobar L, et al. Prospective investigation of PET in lung nodules (PIOPLIN). *J Clin Oncol.* 1998;16:1075–1084.
25. Kubota R, Yamada S, Kubota K, Ishiwata K, Tamahashi N, Ido T. Intratumoral distribution of fluorine-18-fluorodeoxyglucose in vivo: high accumulation in macrophages and granulocytes studied by microautoradiography. *J Nucl Med.* 1992;33:1972–1980.
26. Tahara T, Ichita Y, Kuwabara T, et al. High [^{18}F]-fluorodeoxyglucose uptake in abdominal abscesses: a PET study. *J Comput Assist Tomogr.* 1989;13:829–831.
27. Guhlmann A, Brecht-Krauss D, Suger G, et al. Chronic osteomyelitis: detection with F-18 FDG-PET and correlation with histopathological findings. *Radiology.* 1998;206;749–754.
28. Strauss LG. Fluorine-18 deoxyglucose and false-positive results: a major problem in the diagnostics of oncological patients. *Eur J Nucl Med.* 1996;23:1409–1415.
29. Zimny M, Buell U, Diedrichs CG, Reske SN. False-positive FDG-PET in patients with pancreatic masses: an issue of proper patient selection? *Eur J Nucl Med.* 1998;25:1352.
30. Hoffman EJ, Huang SC, Phelps ME. Quantitation in positron emission computed tomography: effect of object size. *J Comput Assist Tomogr.* 1979;3:299–308.
31. 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;39:1030–1033.
32. Vitola JV, Delbeke D, Sandler MP, et al. Positron emission tomography to stage metastatic colorectal carcinoma to the liver: comparison with computed tomography (CT) and CT portography. *Am J Surg.* 1996;171:21–26.
33. Flanagan FN, Dehdashti F, Ogunbiyi OA, et al. The role of F-18 FDG-PET in advanced primary and recurrent colorectal cancer [abstract]. *J Nucl Med.* 1996;37:132P.
34. Valk PE, Abella-Columna E, Haseman MK, et al. Whole-body PET imaging with [^{18}F]fluorodeoxyglucose in management of recurrent colorectal cancer. *Arch Surg.* 1999;134:503–511.
35. Scott AM, Akhurst T, Berlangieri SU, et al. Comparison of F-18 fluorodeoxyglucose (FDG) positron emission tomography (PET) with computed tomography in the detection of recurrent colorectal carcinoma [abstract]. *J Nucl Med.* 1996;37:132P.
36. Beets G, Pennincks F, Schiepers C, et al. Clinical value of whole-body positron emission tomography with [^{18}F]fluorodeoxyglucose in recurrent colorectal carcinoma. *Br J Surg.* 1994;81:1666–1670.
37. Schiepers C, Pennincks F, De Vadder N, et al. Contribution of PET in the diagnosis of recurrent colorectal cancer: comparison with conventional imaging. *Eur J Surg Oncol.* 1995;21:517–522.
38. Lai DT, Fulham M, Stephens MS, et al. The role of whole-body positron emission tomography with [^{18}F]fluorodeoxyglucose in identifying operable colorectal cancer. *Arch Surg.* 1996;131:703–707.