PANCREAS, BILIARY TRACT, AND LIVER

18-Fluorodeoxyglucose Positron Emission Tomography Does Not Aid in Diagnosis of Pancreatic Ductal Adenocarcinoma

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BACKGROUND & AIMS: **There are no accurate and reliable tools for diagnosis of early stage pancreatic ductal adenocarcinoma (PDA) or small metastatic lesions. It is also a challenge to differentiate PDA from focal mass-forming pancreatitis (FMP). There is controversy regarding the efficacy of 18-fluorodeoxyglucose positron-emission tomography (FDG-PET) in the diagnosis of PDA. We investigated whether FDG-PET provides information that, combined with data from other imaging techniques, can aid in decision making for patients with suspected PDA.**

METHODS: **We performed a retrospective analysis of data collected from 232 consecutive patients with suspected PDA at Kobe University Hospital from January 2006 through June 2012. All patients underwent a diagnostic imaging protocol that included multidetector row computed tomography, superparamagnetic iron oxide–enhanced magnetic resonance imaging, and FDG-PET. Based on endoscopic ultrasonography, fine-needle aspiration biopsy, or endoscopic retrograde cholangiopancreatography analyses, 218 patients had PDA (89 underwent resection and 129 did not) and 14 patients had FMP (8 had focal mass-forming chronic pancreatitis and 6 had focal mass-forming autoimmune pancreatitis).**

RESULTS: **FDG-PET detected 50% of stages 0 and I, 91.9% of stage II, 100% of stage III, and 96.8% of stage IV tumors. Detection was affected significantly by tumor size ($P = .024$) and T stage ($P = .023$) in resected tumors. Multidetector row computed tomography detected significantly more liver metastases than FDG-PET. Few para-aortic lymph node or peritoneal metastases were detected by FDG-PET. FDG-PET correctly identified 11 of the 14 patients with FMP (5 of 8 with focal mass-forming chronic pancreatitis and 6 of 6 with focal mass-forming autoimmune pancreatitis).**

CONCLUSIONS: **FDG-PET is not effective in detecting early stage PDA and small metastases, or in differentiating PDA from FMP. Combining FDG-PET with current diagnostic techniques for PDA did not provide any decisive information, therefore it should not be included in this analysis.**

Keywords: Pancreatic Cancer; Identification; Early Detection; Metastasis.

Pancreatic ductal adenocarcinoma (PDA) is one of the leading causes of cancer death in Japan and Western countries. Prognosis remains extremely dismal with a 5-year survival rate still less than 5%. Surgery is the only therapeutic option to achieve long-term survival. Despite progress in diagnostic technology, the majority of patients with PDA developed advanced disease at the time of diagnosis and fewer than 20% of patients are eligible for curative surgical resection.[1–3]

A suspicion of PDA is often raised by ultrasonography (US) or computed tomography (CT) findings, as represented by the presence of a low-attenuation pancreatic solid mass, and dilatation of the pancreatic duct and/or biliary tree. Thin-slice (0.5–3 mm), contrast-enhanced, dual-phased, multidetector row computed tomography (MDCT) is essential for the diagnosis and staging of PDA.[3–5] MDCT provides greater anatomic detail

Abbreviations used in this paper: AIP, autoimmune pancreatitis; CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasonography; FDG-PET, 18-fluorodeoxyglucose positron emission tomography; FMAIP, focal mass-forming autoimmune pancreatitis; FMCP, focal mass-forming chronic pancreatitis; FMP, focal mass-forming pancreatitis; FNA, fine-needle aspiration; MDCT, multidetector row computed tomography; MRI, magnetic resonance imaging; PDA, pancreatic ductal adenocarcinoma; SPIO-MRI, superparamagnetic iron oxide-enhanced magnetic resonance imaging; SUV, standardized uptake values; UICC, International Union Against Cancer; US, ultrasonography.

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1542-3565/$36.00
http://dx.doi.org/10.1016/j.cgh.2012.12.033

with relationships between a suspected pancreatic mass and adjacent structures that are crucial to determine surgical resectability. The diagnostic performance of magnetic resonance imaging (MRI) including MR cholangiopancreatography remains similar to that of CT. Endoscopic ultrasonography (EUS) offers cytologic or histologic diagnosis with fine-needle aspiration (FNA) biopsy. Endoscopic retrograde cholangiopancreatography (ERCP) allows visualization of the ductal structures and/or tissue sampling for diagnosis. ERCP also can be used to place stents for biliary decompression.

Although EUS is superior to MDCT in overall tumor detection and in the detection of small PDA,[6] the combined diagnostic approach is still limited for the diagnosis of small tumors (<2 cm) and early stage PDA. Detection rates of metastatic lesions in the liver, peritoneum, and lymph node are even worse when they are less than 1 cm.[3–5,7,8] Early detection of small PDA is essential to allow the performance of potentially curative resection. Some studies have reported that preoperatively undetected metastases are found during laparotomy in up to 30% of patients with PDA.[9–11] Furthermore, differentiating between PDA and focal mass-forming pancreatitis (FMP) is still a major clinical problem.[12,13] Thus, sensitive and specific imaging modalities should be explored to select the most appropriate candidates for surgical resection.

18-Fluorodeoxyglucose positron emission tomography (FDG-PET) has been shown to detect solid lesions owing to focal uptake of FDG-labeled glucose in malignant tumor cell populations. The usefulness of FDG-PET in the diagnosis of PDA with a high sensitivity ranging from 80% to 100% has been reported many times since the 1990s.[14–22] Several studies have shown FDG-PET to be more accurate than conventional imaging modalities in the preoperative work-up for suspected PDA.[14–17] In contrast, however, subsequent studies highlighted some diagnostic limitations of FDG-PET as a stand-alone modality.[18–22] In particular, few studies have reported the efficacy and utility of FDG-PET for lesions that were not diagnosed using conventional techniques in patients with suspected PDA.

Thus, we investigated whether FDG-PET could provide decisive information on lesions not diagnosed with the current techniques in patients with suspected PDA. The present study focused on the following issues: diagnosis of small tumors and early stage PDA, detection of small metastatic lesions, and differentiating PDA from FMP.

Methods

Patients

We retrospectively reviewed a consecutive series of 232 patients referred to the Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Kobe University Hospital, from January 2006 to June 2012 for suspected primary PDA without distant metastasis at the time of referral. The majority of patients had solid hypoechoic pancreatic lesions detectable by US and/or solid low-density lesions detectable by CT at the referral centers. Other pancreatic neoplasms, including intraductal papillary-mucinous neoplasm, neuroendocrine neoplasm, and other cystic neoplasms were excluded from this study. Chronic pancreatitis and autoimmune pancreatitis (AIP), in which lesions were diffuse in the pancreas without focal masses or typically were diagnosed by conventional imaging modalities, also were excluded. All patients were re-evaluated by FDG-PET in addition to our preoperative PDA diagnostic protocol at our institution. The work-up was completed within 1 month of the time of the referral and surgical exploration was performed within 1 month after the work-up. The protocol included MDCT, MRI, MR cholangiopancreatography, and EUS. Superparamagnetic iron oxide–enhanced MRI (SPIO-MRI) and chest CT were performed for the detection of liver and lung metastases, respectively. ERCP was performed when the patients required pancreatography or cytology for diagnosis or insertion of a stent for biliary decompression. In principle, EUS-FNA, or cytology of pancreatic juice or bile on ERCP, was performed to obtain histologic diagnosis. Inoperable patients who had suspected PDA by imaging modalities without tissue diagnosis underwent chemotherapy. Patients who had suspected FMA without surgery were followed up carefully as an outpatient. Those patients were examined with carbohydrate antigen 19-9[23] every month and CT or MRI every 3 months to confirm their diagnosis.

Staging was performed according to the TMN staging system of the International Union Against Cancer (UICC).[24] Tumor sizes were measured on surgical specimens histologically.

Multidetector Row Computed Tomography Imaging Protocol

CT examination was performed using a 64-detector row CT system (Aquilion 64; Toshiba Medical Systems, Ohtawara, Japan) with the following parameters: 64 × 0.5-mm detector collimation, reconstructed to transverse slices with a thickness of 5 mm, 0.5 s/gantry rotation, 120 kVp, and 0.94 beam pitch. Each subject was first examined using unenhanced CT, followed by the injection of iodinated contrast medium (Iomeron 350; Eisai Co, Ltd, Tokyo, Japan) with a power injector (Dual Shot GX; Nemoto Kyorindo, Tokyo, Japan) at 600 mg iodine per kg body weight. Because duration was fixed at 25 seconds, the injection rate depended on the patient's body weight. A bolus tracking program was used to optimize the scanning delay for dual-arterial dynamic scans. Portal- and delayed-phase images also were obtained 70 and 150 seconds after injection. Late arterial- and portal-phase images also were reconstructed to coronal slices with a thickness of 5 mm.

Superparamagnetic Iron Oxide–Enhanced Magnetic Resonance Imaging Protocol

The SPIO-MRI examination was performed with a superconducting imager operating at 1.5 Tesla (Achieva; Philips Medical Systems, Best, The Netherlands) and using a 4-element phase-array body coil. The precontrast imaging protocol included balanced fast field-echo images, dual-echo T1-weighted gradient-echo, breath-hold fast spin-echo T2-weighted, spin-echo–echo planar imaging diffusion-weighted images, and breath-hold long echo time gradient-echo images. SPIO (Resovist; FUJIFILM RI Parma, Co, Tokyo, Japan) was administered at a dose of 0.016 mL/kg body weight by means of the power injector at a rate of 1 mL/s, followed by a 20-mL saline push. Five minutes after injection, T1-weighted gradient-echo images were repeated. Fifteen minutes after injection, breath-hold T2-weighted fast spin-echo and breath-hold long echo time gradient-echo images were repeated as postcontrast images. For evaluation of primary pancreatic lesions, transverse multisection images were obtained with a section thickness of 5 mm and a 1-mm intersection gap to cover the entire pancreas. For evaluation of metastatic lesions, transverse multisection images

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