ORIGINAL ARTICLE

The clinical usefulness of 18F-fluorodeoxyglucose positron emission tomography–computed tomography (PET–CT) in follow-up of curatively resected pancreatic cancer patients

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Abstract

Background: Computed tomography and serum tumor markers have limited value in detecting recurrence after curative surgery of pancreatic cancer. This study evaluated the clinical utility of 18F-fluorodeoxyglucose positron emission tomography–computed tomography (PET–CT) in diagnosing recurrence.

Methods: One hundred ten patients underwent curative resection of pancreatic cancer were enrolled. The diagnostic value of abdominal computed tomography (CT), PET–CT and serum carbohydrate antigen (CA) 19-9 concentration were compared. The prognostic value of SUVmax on PET–CT was evaluated.

Results: PET–CT showed relatively higher sensitivity (84.5% vs. 75.0%) and accuracy (84.5% vs. 74.5%) than CT, whereas PET–CT plus CT showed greater sensitivity (97.6%) and accuracy (90.0%) than either alone. In detecting distant recurrences, PET–CT showed higher sensitivity (83.1% vs. 67.7%) than CT. Nineteen patients showed recurrences only on PET–CT, with eleven having invisible or suspected benign lesions on CT, and eight had recurrences in areas not covered by CT. SUVmax over 3.3 was predictive of poor survival after recurrence.

Conclusions: PET–CT in combination with CT improves the detection of recurrence. PET–CT was especially advantageous in detecting recurrences in areas not covered by CT. If active post-operative surveillance after curative resection of pancreatic cancer is deemed beneficial, then it should include PET–CT combined with CT.

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Introduction

Pancreatic cancer is a malignancy with a poor prognosis. Patients with pancreatic cancer have an estimated 5-year survival rate of 5%.[1,2] Complete surgical resection combined with adjuvant chemotherapy is the only potential curative treatment for pancreatic cancer. Unfortunately, only 15–20% of patients presenting with pancreatic cancer are eligible for such an approach[2,3] and five year survival rates of patients who undergo curative resections with adjuvant chemotherapy are only 15–25%.[1,4–8]

Most recurrences after attempted curative resection of pancreatic cancer occur within two years.[9,10] Surveillance after surgery usually includes physical examination, measurements of serum tumor markers such as CA19-9 and radiological imaging modalities such as ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI). Guidelines of the National Comprehensive Cancer Network (NCCN) recommend

regular surveillance, including history taking, physical examination, serum CA19-9 levels and CT scans, every 3–6 months for the first two years after curative resection.[11] These recommendations, however, were based on low-level evidence, and only a few small studies have evaluated the optimal methods of detecting recurrence.[12] In addition, it is not clear early detection translates into better quality of life or increase in survival.

Previously 18F-fluorodeoxyglucose positron emission tomography/computed tomography (PET–CT) has been reported to be helpful in detecting and staging pancreatic cancers,[13–16] as well as early and distant recurrences,[12,16–18] although this remains controversial. PET–CT combination with abdominal CT was reported to have limited clinical utility because additional metastases were rarely found in other study.[19]

The maximal standardized uptake value (SUVmax) is a quantitative marker of the uptake of 18F-fluorodeoxyglucose by the tumor and may be associated with prognosis in pancreatic cancer patients.[20,21] Less is known, however, about the prognostic value of SUVmax in recurrent pancreatic cancer.

This study was designed to compare the clinical usefulness of PET–CT with that of abdominal CT in follow-up of patients who underwent curative resection of pancreatic cancer and to explore the diagnostic potential of SUVmax as a prognostic biomarker in recurrent pancreatic cancer.

Methods

Patients

One hundred ten patients who underwent curative resection for pancreatic cancer and were followed-up at least once by PET–CT at Seoul National University Hospital between May 2004 and June 2012 were analyzed. The patients who had both abdominal CT and PET–CT performed within one month were enrolled. Clinicopathologic features, including serum tumor marker concentrations, abdominal CT and PET–CT results, pathologic results, recurrences and survival outcomes, were reviewed retrospectively.

Follow-up after resection included serum CA19-9 measurements and abdominal CT at 3, 6, and 12 months and every 6 months thereafter. Most patients also underwent PET–CT once yearly, as well as when other follow-up tests suggested tumor recurrence.

Abdominal CT images were obtained from lower lung to pelvis during the arterial and portal venous phases using a multidetector-row CT scanner (Mx 8000, Philips Healthcare; LightSpeed Ultra, GE Healthcare; Sensation 16, Siemens Healthcare) following administration of 90 mL of nonionic contrast material at a rate of 3.0–4.0 mL/s. The slice thickness was 3–5 mm.

PET–CT was performed using a Philips Gemini Dual (Best, The Netherlands) or Siemens Biograph TruePoint (Germany) system. After fasting for at least 8 h, patients were administered 5.18 MBq/kg (0.14 mCi/kg) of fluorodeoxyglucose (FDG). One hour later, whole body PET scan was performed from the skull base to the mid-thigh.

Recurrence

Recurrences were classified as pathologically or clinically confirmed. Clinically confirmed recurrences were defined as recurrences suspected on abdominal CT and/or PET–CT and/or elevation of serum CA19-9, which were confirmed as recurrence on subsequent follow-up. For example, a patient with suspected recurrent lesion on abdominal CT at 6 months after operation, showed more progressive lesion on abdominal CT and elevated serum CA19-9 level at 9 months after operation and thereafter. This patient was regarded as clinically confirmed recurrence at 6 months and the results of PET–CT and serum CA19-9 at 6 months post-operatively were assessed as a false negative result. On the contrary, another patient with suspected recurrent lesion on abdominal CT at 6 months post-operatively, showed similar lesion on abdominal CT and negative results on PET–CT and serum CA19-9 level at 9 months after operation and thereafter. This patient was regarded as clinically no recurrence and the result of abdominal CT at 6 months was assessed as a false positive result. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of each tests were assessed based on the recurrence definition of this study and diagnostic values of abdominal CT, PET–CT and serum CA19-9 level performed at the same period of time (within 1 month) were compared.

Survival outcome after recurrence

Survival outcome after recurrence detection was assessed to evaluated prognostic value of SUVmax. On the basis of the date when recurrence was detected first, survival duration after recurrence was calculated.

Statistical analysis

Statistical analyses were performed using SPSS version 21.0 (SPSS Inc., Chicago, USA). The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of abdominal CT, PET–CT, serum CA19-9 and their combinations were calculated and compared using McNemar's test and Fisher's exact test. Receiver operating characteristics (ROC) curve analysis was used to determine the optimal SUVmax cutoff value for 24-month survival after recurrence. Cumulative survival rates were estimated using the Kaplan–Meier method. P-values ≤ 0.05 were considered statistically significant.

Results

The clinicopathological findings of the 110 patients who underwent curative resection for primary pancreatic cancer are shown in Table 1.

The overall recurrence rate was 76.4% (84/110). Recurrences were pathologically confirmed in 31 patients (36.9%) and clinically confirmed in 53 (63.1%). Of the patients with recurrence,