LETTER

Accuracy of Multi-Detector Computed Tomography, Fluorodeoxyglucose Positron Emission Tomography-CT, and CA 19-9 Levels in Detecting Recurrent Pancreatic Adenocarcinoma

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ABSTRACT

Context We compared the accuracy of fluorodeoxyglucose positron emission tomography-CT (FDG-PET-CT), multi-detector computed tomography (MDCT) and CA 19-9 levels in detecting pancreatic cancer recurrence in patients with resected CA 19-9 positive pancreatic adenocarcinomas. **Methods** We retrospectively evaluated 122 patients with pancreatic adenocarcinomas who underwent surgical resection of the tumor between January 2002 and December 2011. Twenty-five patients had MDCT, FDG-PET-CT and CA 19-9 levels performed no less than six weeks post-operation and within 8 weeks of each other for detection of tumor recurrence. Of these, 20 patients had high pre-operative CA 19-9 levels that dropped to a normal level postoperatively which will be the focus of this study. The sensitivity, specificity, positive and negative predictive value (PPV, NPV), and accuracy of MDCT, FDG-PET-CT, and CA 19-9 in detecting recurrence were compared. **Results** Operations performed included pyloric sparing pancreaticoduodenectomy (n=9), pancreaticoduodenectomy (n=7), distal pancreatectomy (n=3) and total pancreatectomy (n=1). Three patients had no recurrence, but local recurrence and distant metastasis were seen in 8 (40%) and 12 (60%) patients, respectively. In our study, sensitivity, specificity, PPV, NPV and diagnostic effectiveness (accuracy) were: 82%, 100%, 100%, 50%, 85% for MDCT; 82%, 100%, 100%, 50%, 85% for FDG-PET-CT and 94%, 100%, 100%, 75%, 95% for CA 19-9. The difference in recurrence detection accuracy of the tests was not statistically significant. A combination of CA 19-9 with MDCT or FDG-PET-CT was 100% accurate in detecting cancer recurrence in our patients. **Conclusion** Our data suggests that CA 19-9 levels can be used reliably to detect recurrent pancreatic adenocarcinomas in patients with CA 19-9-positive primary tumors. Combination of CA 19-9 with MDCT or FDG-PET-CT is potentially the most accurate approach in detecting pancreatic cancer recurrence.

Sir,

With the highest mortality among all cancers, pancreatic cancer diagnosis, staging, and restaging are still challenging for radiologists, medical and surgical oncologists. In patients with localized disease, a complete surgical resection is the only curative treatment and the 5-year overall survival can occasionally be as high as 25% [1].

While the majority of the previous studies have focused on finding the optimal combination of imaging and/or tumor markers that can accurately differentiate benign from malignant pancreatic pathologies and diagnose cancer in its early stage, the optimal imaging and tumor marker tests for accurate and early detection of pancreatic cancer recurrence have not been well explored. The emergence of new imaging modalities in the past decade, including the clinical introduction of the fluorodeoxyglucose positron emission tomography-computed tomography (FDG-PET-CT) and development of the new generation of multi-detector computed tomography (MDCT) scanners, have all taken these challenges to a new level.

The recent introduction of chemotherapeutic medications with a high response rate and an improved survival even in the pancreatic metastatic cancer (multicenter phase I study on gemcitabine and S-1 regimen) [2] have been promising and has

made the argue for clinical importance of early pancreatic cancer recurrence detection much stronger. In this study we compared the accuracy of FDG-PET-CT, MDCT, and CA 19-9 levels in detecting pancreatic cancer recurrence in patients with resected CA 19-9 positive pancreatic adeno-carcinomas.

In a retrospective institutional review board approved chart review, we studied a cohort of 395 patients who underwent FDG-PET-CT study for the evaluation of a suspected pancreatic lesion between January 2002 and December 2011. During this period, 122 patients with pancreatic adeno-carcinomas underwent surgical resection of the tumor. Twenty-five patients had MDCT, FDG-PET-CT and CA 19-9 levels performed no less than six weeks post-operation and within eight weeks of each other for the detection of tumor recurrence. Of these, 20 patients (8 males and 12 females; mean age 64±10 years, range: 50-81 years) had high preoperative CA 19-9 levels (reference range: 0-35 U/mL) that dropped to a normal level postoperatively, which will be the focus of this study.

All CT scans were obtained using 16 and 64 MDCT units. MDCT exams evaluated include: pre-contrast protocol only (n=2), pre- and post-contrast exams (n=13), or post-contrast exams only (n=5).

MDCT scans were evaluated for recurrence by a single radiologist blinded to the final diagnosis. This evaluation was based on the presence of lymph nodes equal to, or greater than, 1 cm, presence of a residual pancreatic mass, pancreatic ductal dilation, peripancreatic fat stranding, and presence of peripancreatic soft tissue mass in the MDCT imaging. All patients underwent PET/CT imaging per standard protocol followed at our imaging center. The fasting blood sugar level was confirmed to be less than 200 mg/dL on the day of the scan.

A single nuclear-radiologist blinded to the diagnosis also evaluated the FDG-PET-CT results. FDG-PET-CT images were evaluated for recurrence based on visual evaluation for abnormal focal intense FDG accumulation, and the maximum and average standardized uptake value (SUV_{max} and average SUV) of these abnormal foci was also obtained.

Patients were followed indefinitely. The sensitivity, specificity, positive (PPV) and negative (NPV) predictive values, and accuracy of MDCT, FDG-PET-CT, and CA 19-9 in detecting recurrence were compared. Descriptive statistics were used to summarize the data. The Fisher's exact test was used for comparison between the diagnostic modalities. A P value less than 0.05 was considered significant. All analysis was performed using the SAS system 9.2 (SAS Institute, Inc., Cary, NC, USA).

Stage of the tumors at the time of surgery (based on American Joint Committee on Cancer TNM Staging Manual, 7th edition, 2010) were: IB (n=1, 5%), IIA (n=8, 40%), IIB (n=9, 45%), III (n=1, 5%) and IV (n=1, 5%). Fifty percent of the patients (n=10) had lymph node involvement at the time of surgery. Pancreatic tumor stage T1 was present in 5% (n=1), T2 in 5% (n=1), T3 in 85% (n=17) and T4 in 5% (n=1) of the patients. Operations performed included pyloric sparing pancreaticoduodenectomy (n=9, 45%), pancreaticoduodenectomy (n=7, 35%), distal pancreatectomy (n=3, 15%) and total pancreatectomy (n=1, 5%). Three patients had no recurrence, but local recurrence and distant metastasis were seen in 8 (40%) and 12 (60%) patients, respectively (i.e., 3 patients had both local recurrence and distant metastasis). Site of distant metastasis included liver (n=4), lung (n=1), peritoneal (n=1), and lymph node (n=6). In 13 patients, MDCT scan included both pre- and post-contrast phases (in nine patients the results were true positive, in two patients it was true negative and in two patient it was false negative). In two patients MDCT included the pre-contrast stage only (one case was a true positive result and the other one was a false negative result) and in five patients the MDCT scan only included post-contrast stage (in four patients the MDCT results were true positive, in one case it was a true negative).

Accuracy, cost and potential risks are the main factors to be considered when assessing the suitability of a tumor surveillance test. The current global cost of FDG-PET-CT, chest-abdomen-pelvis MDCT and CA 19-9 are 3,525 US$, 810 US$ and 265 US$, respectively. In our center, Medicare reimbursement of the FDG-PET-CT, chest-abdomen-pelvis MDCT and CA 19-9 test are currently 1,198 US$, 406 US$ and 29 US$, respectively. In our study, sensitivity, specificity, PPV, and NPV were: 82%, 100%, 100%, 50%, for MDCT; 82%, 100%, 100%, 50% for FDG-PET-CT; and 94%, 100%, 100%, 75% for CA 19-9. The effectiveness (i.e., the proportion of correctly classified subjects [3]), considered as global measure of diagnostic accuracy, was 85%, 85%, and 95% for FDG-PET-CT, MDCT and CA 19-9, respectively. Therefore, in our study the difference in accuracy of the tests to detect the pancreatic cancer recurrence was not statistically significant (FDG-PET-CT *vs.* MDCT: P=1.000; FDG-PET-CT or MDCT *vs.* CA 19-9: P=0.605). While MDCT and FDG-PET-CT cost considerably more, CA 19-9 offered a comparable accuracy in the detection of pancreatic cancer recurrence. A combination of CA 19-9 with MDCT or FDG-PET-CT was 100% accurate in detecting cancer recurrence in our patients.

Our study results are consistent with the previous published studies in the literature [4, 5] in showing high and comparable accuracy rates for FDG-PET-

CT and MDCT in the detection of pancreatic cancer recurrence following surgery. However, in this paper we have gone one step further and compared the accuracy of the mentioned imaging modalities (MDCT and FDG-PET-CT) with the tumor marker level of CA 19-9 in the detection of pancreatic adenocarcinoma recurrence in a selected group of patients. Based on our results, we suggest that in selected groups of patients with known CA 19-9 producing pancreatic adenocarcinoma (patients with high preoperative CA 19-9 levels that drops to a normal level postoperatively), regular CA 19-9 level blood tests can be considered as a safe and reliable screening test during the post operative cancer surveillance. The clinical significance of any raise of the CA 19-9 levels can be further investigated by the available imaging modalities, which include MDCT and/or FDG-PET-CT scans. Our data suggests that the CA 19-9 level is highly sensitive and can be used reliably to detect recurrent pancreatic adenocarcinomas in patients with CA 19-9 producing primary tumors. The combination of CA 19-9 with MDCT or FDG-PET-CT is potentially the most accurate approach in detecting pancreatic cancer recurrence. Considering the lower cost of the MDCT compared with the FDG-PET-CT, the combination of CA 19-9 with MDCT is highly accurate and cost effective. Our data supports that incorporating tumor marker CA 19-9 with radiologic imaging enhances accuracy of surveillance.

References

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