Differentiation of pancreatic ductal adenocarcinoma from other neoplastic solid pancreatic lesions: a tertiary oncology center experience

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Background: Pancreatic ductal adenocarcinoma (PDAC), pancreatic neuroendocrine tumors (pNET), and metastatic lesions (pMET) are the most common neoplastic solid pancreatic lesions (SPLs). Early diagnosis enables prompt treatment.

Objective: To identify factors differentiating PDAC from non-PDAC lesions and assess the accuracy of EUS-guided FNA.

Design and Setting: Retrospective tertiary center.

Patients and Intervention: Consecutive patients referred for EUS evaluation of SPLs from 2004 to 2011.

Main Outcome Measurements: Pretest (preceding EUS-guided FNA [EUS-FNA]) predictors of PDAC among neoplastic SPLs and accuracy of EUS-FNA.

Results: A total of 1333 EUS scans with 1108 EUS-FNAs were performed for pancreatic lesions. Of the 672 patients with neoplastic SPLs, 528 had PDAC and 144 non-PDAC. The sensitivity, specificity, positive predictive value, and accuracy of EUS-FNA for the diagnosis of PDAC were 97.3%, 99.3%, 99.8%, and 97.8%, respectively. Years of EUS experience significantly correlated with fewer needle passes ($R_s = -0.18$, $P < .001$). Controlling for all potential confounders, multivariable regression analysis demonstrated that patients with PDAC compared with pNETs and pMETs were older (odds ratio [OR] 4.42; 95% confidence interval [CI], 2.1-9.5; $P < .001$), had weight loss (OR 3.0; 95% CI, 1.6-5.4; $P < .001$), hyperbilirubinemia (OR 3.7; 95% CI, 1.8-7.5; $P < .001$), elevated CA19-9 (OR 6.9; 95% CI, 2.4-20.3; $P < .01$), evidence of arterial invasion (OR 6.5; 95% CI, 2.7-15.4; $P < .001$), and PD dilation (OR 3.3; 95% CI, 1.8-5.9; $P < .001$).

Limitations: Retrospective design, single center.

Conclusions: When evaluating neoplastic SPLs, demographic, clinical, laboratory, and imaging characteristics can reliably discern and suggest PDAC. In addition, EUS-FNA is exceedingly sensitive and specific for PDAC. (Gastrointest Endosc 2015;81:370-9.)

Abbreviations: CI, confidence interval; EUS-FNA, EUS-guided FNA; MDCT, multirow detector CT; MRI, magnetic resonance imaging; NPV, negative predictive value; OR, odds ratio; PD, pancreatic duct; PDAC, pancreatic ductal adenocarcinoma; pMET, metastatic lesion to the pancreas; pNET, pancreatic neuroendocrine tumor; PPV, positive predictive value; SPL, solid pancreatic lesion.

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Pancreatic ductal adenocarcinoma (PDAC) is an aggressive cancer of the pancreas with a 5-year survival rate of less than 5%.[1] This high mortality rate is due to the fact that more than 80% of patients have locally advanced or metastatic disease at the time of diagnosis.[2] On the other hand, patients with early or localized lesions have 5-year survival rates of 25% to 30% after surgical resection.[3,4] Unfortunately, at the time of surgical exploration, 25% of the patients are found to be unresectable.[5] This suggests that early and accurate diagnosis before the development of metastatic disease will improve survival.

Among neoplastic solid pancreatic lesions (SPLs), PDAC accounts for approximately 90%, whereas other tumors such as pancreatic neuroendocrine tumors (pNETs) and metastatic lesions to the pancreas (pMETs), referred to collectively as nonpancreatic ductal adenocarcinomas (non-PDAC), account for the remaining 10% to 15%.[6,7]

There are multiple imaging techniques for evaluating SPLs. In the past decade, EUS-guided-FNA (EUS-FNA) has emerged as the most sensitive modality for detection and diagnosis of pancreatic masses.[8] Multiple retrospective and prospective studies evaluating EUS-FNA of solid pancreatic lesions have been published with a range of diagnostic accuracy between 62% and 96% showing variability in sensitivity and specificity. However, for an EUS-FNA diagnosis of pancreatic cancer, 2 recent large meta-analyses comprising of more than 30 studies have both demonstrated pooled sensitivity and specificity of 91% and 94%, respectively.[9,10]

Among neoplastic SPLs, it is important to distinguish PDAC from non-PDAC lesions. Most pNETs are slowly progressive and require a different therapeutic approach from that for PDACs. Metastatic lesions to the pancreas could be either from a primary cancer in another organ system or as a part of a systemic disease. The role of conventional EUS and other imaging methods in the differential diagnosis of neoplastic SPLs can be challenging.[11] There is a paucity of medical literature on pretest differentiation of neoplastic SPLs, especially PDAC from non-PDAC lesions.[7]

The primary aim of this study was to identify pretest (preceding FNA during EUS) factors differentiating PDAC from non-PDAC neoplastic SPLs based on risk factors, demographic features, clinical presentation, EUS characteristics, and survival curves. The secondary objectives include evaluation of EUS-FNA for diagnosis of PDACs and analysis of the effect of operator characteristics on the yield of FNA.

METHODS

Patients

This is a retrospective analysis of all patients who underwent EUS-FNA for a suspected SPL between January 2004 and December 2011 (excluding an additional year of follow-up) at the University of Texas MD Anderson Cancer Center. Institutional review board approval was obtained before data collection. Patients were referred to the oncology center for further evaluation of suspected or diagnosed pancreatic masses based on previous imaging studies inclusive of multidetector row CT (MDCT) scan, magnetic resonance imaging (MRI), and/or EUS examination. The study cohort was thus limited to patients with neoplastic solid or mixed solid/cystic neoplastic pancreatic mass lesions. Further restrictions of the study population limited the patient database to those who underwent EUS-guided FNA (EUS-FNA).

Procedure

Although most EUS examinations were performed with intravenous propofol-based sedation under the direction of an anesthesiologist, elective intubation to protect the airway in a few high-risk patients was at the discretion of the supervising anesthesiologist. EGD was performed before EUS for all patients. A curvilinear echoendoscope (Olympus GF-UC140P-AL5; Olympus America, Center Valley, Pa) with ProSound Alpha 5 or Alpha 10 (Aloka, Wallingford, Conn) was used to evaluate and perform EUS and FNA of SPLs. The choice of the needle used and the number of needle passes was at the discretion of the endosonographer. The obtained FNA sample was expressed onto glass slides, and both air-dried and Papanicolaou-fixed smears were prepared. An attending cytopathologist provided immediate assessment of the cytological features on direct smear (air-dried and Papanicolaou-stained slides) while the patient was kept under sedation. The procedure was terminated when an adequate specimen was obtained.

Variables

Patient demographic information included age, sex, race, history of smoking and alcohol consumption, presenting symptoms, and history of diabetes. Findings on EUS included location, number and size of the lesions, lesion characteristics, evidence of dilation of the pancreatic duct (PD) or common bile duct, evidence of vascular invasion, presence of suspicious lymph nodes (malignant appearing), type of FNA needle used, and number of passes for each type of FNA needle.

If there was no documentation of dilation of PD and/or common bile duct (on CT, EUS, or both), it was considered as a negative finding. The absence of documentation of suspicious lymph nodes or evidence of vascular invasion in the EUS report was considered missing data because EUS-based accurate staging of pancreatic cancer was not universally followed. The surgical and medical oncologists used a dedicated pancreatic protocol MDCT scan (or MRI when intravenous contrast was contraindicated) as a prerequisite staging test of choice (including evaluating resectability).

Diagnosis of a pancreatic malignancy required the cytological confirmation of neoplasia after EUS-FNA and at least 1 of the following criteria: (1) surgical pathology confirming a malignant lesion, (2) patient had a metastatic lesion on imaging study, (3) patient died within 1 year after diagnosis, (4) CT or MRI evidence of arterial/venous invasion, (5) diagnostic