Diagnostic accuracy of quantitative EUS elastography for discriminating malignant from benign solid pancreatic masses: a prospective, single-center study

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Background: Recent data suggest that quantitative EUS elastography, a novel technique that allows real-time quantification of tissue stiffness, can accurately differentiate malignant from benign solid pancreatic masses.

Objective: To externally validate the diagnostic utility of this technique in an independent cohort.

Design and Setting: Prospective, single-center study.

Patients, Interventions, and Methods: A total of 104 patients with evidence of a solid pancreatic mass on cross-sectional imaging and/or endosonography underwent 111 quantitative EUS elastography procedures. Multiple elastographic measurements of the mass lesion and soft-tissue reference areas were undertaken, and the corresponding strain ratios (SRs) were calculated. The final diagnosis was based on pancreatic cytology or histology.

Main Outcome Measurements: The area under the receiver-operating characteristic curve, sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of quantitative EUS elastography for discriminating malignant from benign pancreatic masses.

Results: The final diagnoses were primary pancreatic carcinoma (71.2%), neuroendocrine tumor (10.6%), metastatic cancer (1.9%), and pancreatitis (16.3%). Malignant masses had a higher SR ($P = .01$) and lower mass elasticity ($P = .003$) than inflammatory ones. The areas under the receiver-operating characteristic curve for the detection of pancreatic malignancy of both SR and mass elasticity (0.69 and 0.72, respectively) were less favorable than reported recently. At the cut points providing the highest accuracy in this cohort (4.65 for SR and 0.27% for mass elasticity), quantitative EUS elastography had a sensitivity of 100.0% and 95.7%, specificity of 16.7% and 22.2%, positive predictive value of 86.1% and 86.4%, negative predictive value of 100.0% and 50.0%, and overall accuracy of 86.5% and 83.8%, respectively.

Limitations: Relatively small number of patients with benign disease.

Conclusion: In the largest single-center study to date, the diagnostic utility of quantitative EUS elastography for discriminating pancreatic masses was modest, suggesting that it may only supplement rather than supplant the role of pancreatic tissue sampling in the future. (Gastrointest Endosc 2012;76:953-61.)

Abbreviations: EUS-FNA, EUS-guided FNA; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver-operating characteristic; SR, strain ratio.

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Pancreatic cancer is a major public health problem in the industrialized world, currently ranking as the fourth and fifth most common cause of cancer-related mortality in the United States and United Kingdom, respectively.[1,2] Most patients are managed with chemotherapy, and as many as 20% undergo surgical resection.[3] Tissue acquisition is currently considered a prerequisite for chemotherapy and desirable for those requiring surgery to exclude benign mimics of the disease.[4]

EUS has become an indispensable tool in the investigation and management of pancreatic cancer. In addition to being the most sensitive imaging modality for detecting small-volume disease, EUS enhances disease staging, informs decision-making about operability, and, crucially, provides tissue diagnosis by means of FNA or biopsy, yielding further diagnostic and staging information.[5,6]

However, the differential diagnosis of solid pancreatic masses remains a challenge; EUS–guided FNA (EUS-FNA) may be time-consuming and technically demanding, is associated with low, but not insignificant, morbidity,[7] and has a limited sensitivity for malignancy with false-negative results in 15% to 17% of patients,[8,9] particularly those with concurrent chronic pancreatitis who comprise 20% to 35% of patients undergoing EUS-FNA.[5,10-13]

Given these shortcomings, novel imaging technologies such as EUS elastography, have recently been explored. Elastography is a technique with applications in the fields of optics, US, and magnetic resonance imaging that allows assessment of the elasticity or firmness of a given tissue relative to that of adjacent normal tissue by measuring the strain or displacement generated in response to compression or vibration. The magnitude of the strain generated by a given tissue is thought to be inversely proportional to the risk of malignancy. At minimal additional cost and no attendant morbidity or mortality, real-time elastography images can be rapidly obtained with a conventional echoendoscope attached to an US workstation running the appropriate software. The elastography image is displayed as a color map depicting the distribution of tissue elasticity within a given preselected region of interest superimposed over the conventional B-mode image in which hard tissue is depicted in blue, soft tissue in red, and tissue in the intermediate elasticity range falling somewhere in the green-yellow spectrum. Visual interpretation of the elastography images is inherently subjective and thus quantitative, more objective methods of reporting the results have been developed. The simplest of these methods utilizes the ratio of the elasticity of a given mass to that of a selected reference region within adjacent soft tissue, the so-called strain ratio (SR).

The utility of quantitative EUS elastography in the differential diagnosis of pancreatic masses has been assessed in a number of recent studies,[14-24] the most impressive results having been found in a single-endosonographer study of 86 patients reporting a sensitivity of 100%, specificity of 92.9%, positive predictive value (PPV) of 96.7%, negative predictive value (NPV) of 100%, overall accuracy of 97.7%, and area under the receiver-operating characteristic (ROC) curve for the detection of malignancy of 0.98.[17] The objective of this study was to undertake a prospective external validation of the diagnostic utility of this technology using the same protocol in a large independent cohort of patients with solid pancreatic masses.

Take-home Message

- In the largest single-center study reported to date, EUS elastography was found to be less accurate for differentiating pancreatic masses than recently reported, suggesting that it may only complement rather than substitute the role of pancreatic cytology in the future.

PATIENTS AND METHODS

The Freeman Hospital serves as a tertiary referral center of hepatobiliary and pancreatic surgery for the North East region of England with a population of approximately 3.5 million, undertaking approximately 750 pancreaticobiliary EUS procedures per year. EUS, EUS-FNA, and qualitative tissue elastography are standard procedures in clinical practice and are used routinely at our center for the assessment of pancreatic masses. In accordance with the UK National Research Ethics Service guidelines, formal ethical review was not required. Confirmation of this was obtained from the North East Research Ethics Committee.

A total of 104 patients with solid pancreatic masses were enrolled between August 2010 and October 2011. Before enrollment in the study, all participants had undergone cross-sectional imaging (by means of computed tomography with or without magnetic resonance imaging), which in the vast majority identified a pancreatic mass, with the remaining patients having clinical and laboratory evidence of underlying insulinoma. For logistic reasons, not all patients were consecutively enrolled in this study. Patients with cholangiocarcinoma or masses with a predominant cystic component were excluded.

All EUS procedures were undertaken, after obtaining informed patient consent, by 2 experienced endosonographers (K.W.O and M.K.N) who were not blinded to the results of previous investigations using the Hitachi EUB-7500 or Preirus US workstations (Hitachi Medical Systems Europe, Zug, Switzerland) and Pentax linear echoendoscopes (Pentax Europe GmbH, Hamburg,