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Differentiation of pancreatic ductal adenocarcinoma from inflammatory mass: added value of magnetic resonance elastography

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AIM: To examine whether incorporating magnetic resonance elastography (MRE) with contrast-enhanced computed tomography (CE-CT) or dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) can provide a benefit in differentiating pancreatic ductal adenocarcinoma (PDAC) from inflammatory mass (IM).

MATERIALS AND METHODS: Thirty patients with IM and 56 patients with PDAC confirmed by histopathology were identified retrospectively via a prospectively maintained database. All patients underwent CE-CT or DCE-MRI together with dual-frequency MRE at 40 and 60 Hz. A five-point scale for likelihood of pancreatic malignancy was used by two experienced radiologists in consensus. Diagnostic accuracy of CE-CT/DCE-MRI, MRE, and their combination (modeled by logistic regression analysis) was estimated using receiver operating characteristic (ROC) analysis with a leave-one-out cross validation.

RESULTS: Accuracies for determination of PDAC by 60-Hz MRE, 40-Hz MRE, CE-CT/DCE-MRI, and the combination of CE-CT or DCE-MRI and 60- and 40-Hz MRE, were 70.2%, 77.4%, 83.3%, 75%, and 92.9%, respectively. CE-CT or DCE-MRI combined with 40-Hz MRE significantly improved diagnostic performance versus CE-CT or DCE-MRI alone (area under the ROC curve [AUC]: 0.937 versus 0.783, $p<0.01$) by increasing specificity (96.9% versus 62.1%, $p=0.002$) without a significant loss of sensitivity (90.9% versus 94.6%, $p=0.727$), while combined CE-CT or DCE-MRI with 60-Hz MRE did not significantly change diagnostic performance versus CE-CT/DCE-MRI alone (AUC: 0.760 versus 0.783, $p=0.697$).

CONCLUSION: Combined assessment by 40-Hz MRE with CE-CT/DCE-MRI may help to differentiate PDAC from IM in a relatively non-invasive fashion.

Introduction

Pancreatic cancer has a poor prognosis, and is the fifth leading cause of cancer deaths worldwide for both genders, correspondingly pancreatic ductal adenocarcinoma (PDAC) accounts for 85–95% of all pancreatic cancers.[1,2] Although mortality rates for some cancers have been decreasing over

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the past decade, the mortality rate of pancreatic cancer has remained unchanged,[2] and the overall 5-year survival rate of pancreatic cancer, all stages, remains at approximately 5%.[3] At present, surgery is the major treatment of choice, and complete (R0) resection is the primary goal to improve outcomes in patients with pancreatic cancer. Diagnostic imaging performs well in detection and locoregional staging of pancreatic cancer in its classic form,[4] but other solid pancreatic masses continue to present a diagnostic challenge to both clinicians and radiologists,[5,6] and pseudotumoural inflammatory pancreatitis, including mass-forming focal pancreatitis and autoimmune pancreatitis, is the final diagnosis in 5–10% of putative cancer surgeries.[1,7–11]

The recent National Comprehensive Cancer Network (NCCN) Clinical Practice Guideline[2] has approved high-quality, multiphase imaging techniques including contrast-enhanced (CE) computed tomography (CT) or dynamic contrast-enhanced (DCE) magnetic resonance imaging (MRI) as suitable techniques for detection, differentiation, and staging of pancreatic malignancy; however, morphological features alone are rarely sufficient for distinguishing between pancreatic malignancy and inflammatory masses (IMs), especially as the preferred site of IMs is the pancreatic head, and this location is associated with biliary or pancreatic duct deformities that can mimic a carcinoma. The potential shortfalls of conventional CE imaging techniques that show only morphological and enhancing features can be overcome by adding MR elastography (MRE) to the routine imaging protocol. MRE is a state-of-the-art technique that quantitatively assesses *in vivo* tissue stiffness (shear modulus) by imaging the propagating shear waves in the tissues.[15] Stiffness values are now well known to be strongly associated with the amount and extent of fibrosis, which is characteristically distinct in pancreatic malignancy versus IM.[12] The typical histopathological feature of pancreatic malignancy is complete disappearance of normal pancreatic parenchyma secondary to carcinogenesis and desmoplasia (abundant fibrotic stroma). In contrast, in IM, the pancreatic parenchyma is not totally replaced by fibrosis. Acinar cells are preserved and there is usually a loose interstitial fibrosis. Several recent studies have reported attempts to measure pancreatic stiffness with an echo-planar imaging (EPI) pulse sequence using 40- and 60-Hz vibrations,[13–15] and a preliminary study has shown that MRE-determined stiffness values are significantly higher in pancreatic malignancy versus IM, and that this characteristic is useful for differentiation between the two.[11]

Hence, it was hypothesised that incorporation of MRE into a standard CT or MRI protocol might provide added diagnostic value for differentiation of pancreatic malignancy and IM, and the purpose of the present study was to determine whether incorporating 40-Hz and 60-Hz MRE with conventional CE imaging techniques could provide this benefit.

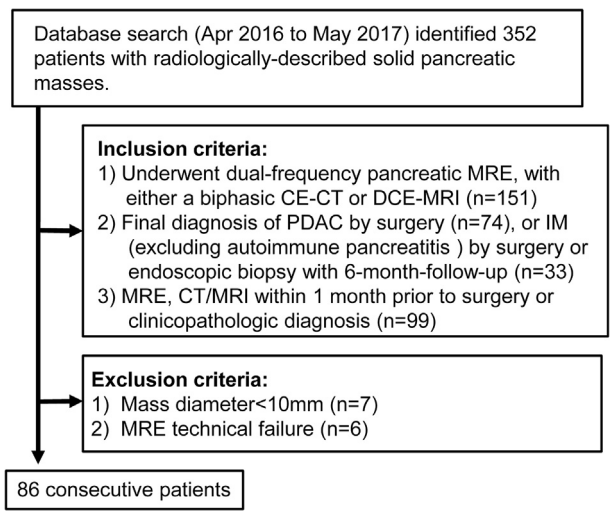

Figure 1 Patient selection flowchart. MRE, magnetic resonance elastography; PDAC, pancreatic ductal adenocarcinoma; IM, inflammatory mass.

Materials and methods

Study population

This retrospective study was approved by the Institutional Review Board and the requirement for informed consent was waived. The institutional radiological imaging database was searched between Apr 2016 and May 2017 for cases that met the following inclusion criteria (Fig 1): (1) the patient underwent dual-frequency pancreatic MRE (40 and 60 Hz) combined with either standard biphasic pancreatic CE-CT or DCE-MRI, in addition to (2) surgical resection of PDAC or surgical resection or endoscopic ultrasound (EUS)-guided biopsy for IM (excluding autoimmune pancreatitis) with histologically confirmed pancreatitis and no evidence of malignancy, and (3) MRE and CT/MRI studies were performed within 1 month (mean, 9 days; range, 1–30 days) prior to surgical cancer diagnosis or biopsy-confirmed diagnosis of pancreatitis. Among 99 patients who met these criteria, six were excluded because of invalid stiffness measurements or small lesions (<10 mm diameter, n=7).[11] Therefore, a total of 86 patients were included in the final analysis, 30 with confirmed IM (excluding autoimmune pancreatitis) and 56 with confirmed PDAC. The diagnosis of IM was established after surgical resection in 16 patients and by EUS-guided biopsy together with at least 6 months of follow-up in 14. All PDACs were diagnosed by histopathological examination after surgical resection. Clinical data including patient characteristics, laboratory values, and tumour grade according to the three-tier grading scheme, were reviewed and recorded.

Image acquisition

The MRI examinations were performed on a Signa HDX 3 T MRI system (GE Healthcare, Milwaukee, WI, USA) equipped with an eight-channel phased-array body coil. All patients fasted for at least 8 h prior to MRI examination. MRE was performed before injection of contrast medium. A soft

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