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Multiphase evaluation of contrast-enhanced endoscopic ultrasonography in the diagnosis of pancreatic solid lesions

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ABSTRACT

Background/Objectives: Time-intensity curve (TIC) under contrast-enhanced EUS (CE-EUS) allows continuous and quantitative evaluation of targeted area in the pancreas. However, TIC is not always available and the procedure is complicated. We aimed to propose a simplified method by evaluating multiple phases of CE-EUS in the diagnosis of pancreatic solid lesions.
Methods: We retrospectively reviewed 210 patients with pancreatic solid lesions including 142 with pancreatic ductal cancer (PDAC), 31 with pancreatic neuroendocrine neoplasm, 13 with solid pseudopapillary neoplasm and 24 with mass-forming pancreatitis who underwent CE-EUS and achieved final diagnoses. The CE-EUS images were continuously recorded for 60 s, and each image at 20, 40 and 60 s was used for the evaluation. The images were classified into three patterns as hypoechoic, hyperechoic and isoechoic vascular patterns compared with the surrounding pancreas, and the relevance between the multiphase evaluation of CE-EUS and each disease group was investigated.
Results: In PDAC group, majority of the lesions showed hypovascular pattern at 20 or 40 s after injection of contrast medium following early enhancement. The sensitivity, specificity and accuracy of PDAC pattern in the differentiation of PDAC from other lesions was 83.1%, 86.8% and 84.3%, respectively. On histopathological analysis, significant differences were seen in histologic types, infiltration (INF), and neural invasion (ne) between those who showed PDAC pattern and those who didn't.
Conclusions: Multiphase evaluation of CE-EUS is convenient and useful method for the differentiation of pancreatic solid lesions which can be alternatively used for TIC.
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Introduction

Endoscopic ultrasonography (EUS) is a modality which is widely used for a detailed evaluation of pancreas with its high resolution compared to other modalities. In recent years, electronic EUS has made it possible to use new diagnostic imaging techniques such as harmonic imaging and color Doppler mode. In addition, a contrast medium for ultrasonography has made the evaluation of hemodynamics possible, and we have previously reported the usefulness of contrast-enhanced EUS (CE-EUS) to diagnose pancreatic diseases [1–8]. Using Sonazoid™ (Daiichi-Sankyo, Tokyo, Japan), the second-generation contrast medium, real-time vascular images can be acquired for a prolonged time under a low sound pressure [6]. We reported the usefulness of CE-EUS preparing time-intensity curve (TIC) for the differential diagnosis of pancreatic diseases including pancreatic ductal cancer and mass-forming pancreatitis [6]. Time-intensity curve allows continuous and quantitative evaluation of enhancement pattern in the targeted area, however, TIC is only available in specific devices and the process is somewhat complicated. Thus, here we propose a simplified method evaluating multiple phases of CE-EUS in the diagnosis of pancreatic solid lesions, not relying on the devices to be used.

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Methods

Patients

We retrospectively reviewed 210 patients with pancreatic solid lesions who underwent CE-EUS using Sonazoid™ and achieved final diagnoses between January 2006 and December 2016. A total of 127 men and 83 women with a mean age of 62.7 ± 13.8 (range, 28–86) were included in the study. Final diagnoses of 210 patients were as follows; 142 patients with pancreatic ductal adenocarcinoma (PDAC), 31 patients with pancreatic neuroendocrine neoplasm (PNEN), 13 patients with solid pseudopapillary neoplasm (SPN) and 24 patients with mass-forming pancreatitis (MFP). Pathological evidences of PDAC, PNEN and SPN were all obtained by surgery. Twenty-four patients with MFP underwent EUS-guided fine needle aspiration and 20 out of 24 MFPs were diagnosed with focal-type autoimmune pancreatitis according to the International Consensus Diagnostic Criteria [9], and all MFPs were followed up for more than one year to exclude malignancy (Fig. 1). This study was performed with the approval of the ethics committee of Nagoya University Graduate School of Medicine.

EUS and CE-EUS settings

All EUS procedures were performed by three endoscopists who had experience on more than 5000 cases, and the one who was blinded to the final diagnoses conducted this study. Endoscopic ultrasonography was performed in the left lateral position under midazoram-induced sedation with heart rate monitoring. The electronic radial scanning mode was used in all cases. The endoscope and ultrasound observation system used were EG-3670URK (Pentax Co., Ltd, Tokyo, Japan) with Hi Vision Ascendus or Hi Vision 900 (Hitachi-Aloka Medical, Ltd, Tokyo, Japan), GF-UE260-AL5 (Olympus Co., Ltd, Tokyo, Japan) with Prosound α-10 (Hitachi-Aloka Medical, Ltd, Tokyo, Japan), or EG-580UR (Fujifilm Co., Ltd, Tokyo, Japan) with Sonart SU-1 (Fujifilm Co., Ltd, Tokyo, Japan). On CE-EUS, EG3670URK with Hi Vision Ascendus or Hi Vision 900 used the wide-band pulse inversion method, and the mechanical index was automatically set at 0.16 to 0.23 in accordance with the focus point. GF-UE260-AL5 with Prosound α-10 used the extended pure harmonic detection method, and the mechanical index was set at 0.25. EG-580UR with Sonart SU-1 used pulse inversion method, and the mechanical index was automatically set between 0.2 and 0.4. A single focus was set on the distal side of the targeted lesion. The selection of scope and system was left to the discretion of the endoscopist, but there was a tendency of EG-3670URK in combination with Hi Vision 900 and GF-UE260-AL5 being used more often between 2006 and 2011, EG-3670URK in combination with Hi Vision Ascendus from 2011, and EG-580UR from 2014, depending on the release times of each scope or system.

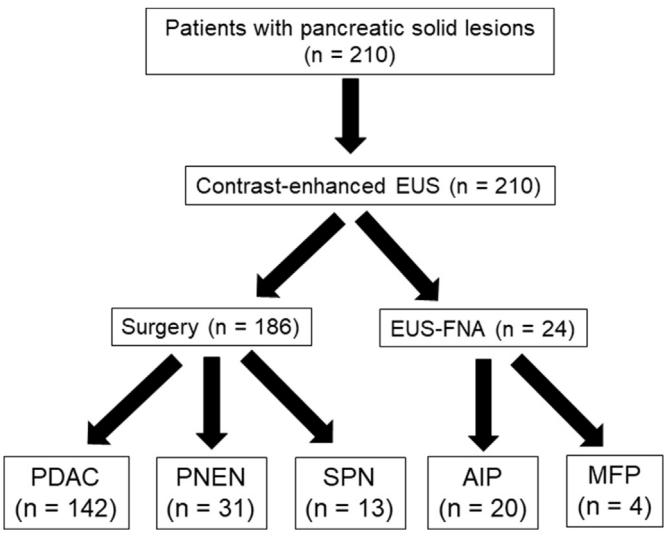

Fig. 1. Flow diagram of the study. EUS: Endoscopic ultrasonography, EUS-FNA: EUS-guided fine needle aspiration, PDAC: Pancreatic ductal adenocarcinoma, PNEN: Pancreatic neuroendocrine neoplasm, SPN: Solid pseudopapillary neoplasm, AIP: Autoimmune pancreatitis, MFP: Mass-forming pancreatitis.

Multiphase evaluation of CE-EUS

The contrast medium was administered intravenously. One vial of Sonazoid™ (16 μl as perfluorobutane) (Daiichi-Sankyo, Tokyo, Japan) was suspended with 2 ml of water for injection, and the suspension was administered by bolus injection at 0.015 ml/kg. After Sonazoid™ injection, the CE-EUS images were recorded as a movie for 60 s continuously, and the stored data was used for analysis. Each image at 20, 40 and 60 s was used for the evaluation. The images were classified into three patterns as hypoechoic (−), hyperechoic (+) and isoechoic (0) vascular patterns compared with the surrounding pancreatic parenchyma (Fig. 2). All data were reviewed by two readers (T. I. and Y. H.) without the information of US, CT, MRCP or final results in a blinded fashion. The interobserver variability of CE-EUS vascular patterns was assessed by calculating the κ-coefficient after the two blinded readers had made their individual independent reading. The two readers reassessed the images of that yielded discrepant findings together to reach an agreement. The pancreatic solid lesions were divided into three groups (PDAC, PNEN + SPN and MFP), and the relevance between the multiphase evaluation of CE-EUS and each group was investigated. Pancreatic neuroendocrine neoplasms and SPNs were dealt in the same group as they show similar radiological and pathological findings and are not easy to differentiate preoperatively.

Time-intensity curve

In 73 out of 210 cases (30 with PDAC, 16 with PNEN and 27 with MFP), TIC was created after the EUS procedure, which was used for our previous study [6]. A round region of interest (ROI) with maximum possible size was set in the center of the lesion while reproducing the digital data stored on a hard disk, and TIC was constructed using software built in the observation system. Echo intensity (EI) reduction rate from the peak contrast at 1 min after injection of contrast agents was evaluated, which was significantly different between PDAC and other lesions in our previous study [6], and the TIC findings and the results of our new methods were compared.

Histopathological findings and CE-EUS

The characteristics of histopathological findings in the resected specimen of PDAC were compared between those who showed a PDAC pattern and those who showed other patterns on CE-EUS. Histopathological diagnosis was performed according to the General Rules for the Study of Pancreatic Cancer (The 7th Edition, Japan Pancreas Society), and differentiation, histologic type, interstitial change, infiltration (INF), venous invasion (v), lymphatic invasion (ly) and neural invasion (ne) were evaluated, respectively.

Statistics

Statistical analysis was performed using the software SPSS Statistics 17.0 (SPSS, Inc, Chicago, Ill). The χ 2 test and Fisher's exact

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