Qualitative and Quantitative Analyses of Perfusion Imaging with Contrast-enhanced EUS

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Introduction

EUS is superior to other imaging techniques, including conventional transabdominal ultrasound, computed tomography (CT), and magnetic resonance imaging, in terms of the reliability and efficiency with which it detects and stages various benign and malignant conditions in the pancreatobiliary system. However, the ability of conventional fundamental B-mode EUS to characterize the lesions is limited. Recent developments that aim to overcome this limitation of conventional EUS have led to the evolution of contrast-enhancement technique. Contrast-enhanced harmonic EUS technique provides detailed information on the structure of the tissue and thus greatly improve the diagnostic capabilities of conventional EUS. Images obtained by contrast-enhanced harmonic EUS are analyzed by qualitative and quantitative methods. Qualitative analysis using the classification of pancreatic lesions based on their enhancement patterns on contrast-enhanced EUS is a convenient way to characterize conventional EUS-depicted lesions. In contrast, quantitative analysis using time-intensity curves (TICs) can characterize pancreatobiliary tumors with various parameters avoiding subjective assessment.

Qualitative analysis

1. Pancreatic solid masses

On contrast-enhanced EUS, solid pancreatic lesions can be characterized on the basis of their enhancement patterns relative to their surrounding tissue. There are three main enhancement patterns, namely, hypo-, iso- or hyper-enhancement.\(^1\)\(^-\)\(^4\) Contrast-enhanced harmonic EUS depicts pancreatic ductal carcinomas as nodules with hypo-enhancement that mostly have irregular vessels.\(^1\)\(^-\)\(^4\) By contrast, most pancreatitis-associated masses exhibit iso-enhancement while most neuroendocrine tumors display hyper-enhancement.\(^1\)\(^-\)\(^4\) A recently published meta-analysis showed that hypo-enhancement in contrast-enhanced harmonic EUS diagnoses pancreatic adenocarcinomas with a pooled diagnostic sensitivity and specificity of 94% and 89%, respectively.\(^5\) Moreover, contrast-enhanced harmonic EUS detects pancreatic adenocarcinomas (defined as hypo-enhanced lesions) with better sensitivity and specificity (96% and 64%, respectively) than conventional fundamental B-mode EUS where pancreatic adenocarcinomas are defined as hypoechoic lesions (sensitivity and specificity of 86% and 18%, respectively).\(^1\) Contrast-enhanced harmonic EUS also improves the depiction of the outline
of ductal carcinomas whose conventional EUS findings are uncertain.\textsuperscript{1,2,4} Compared to contrast-enhanced CT, contrast-enhanced harmonic EUS differentiates ductal carcinomas from other masses with comparable sensitivity and specificity. However, contrast-enhanced harmonic EUS (91% sensitivity and 94% specificity) is superior to contrast-enhanced CT (71% sensitivity and 92% specificity) in diagnosing small (\(\leq 2\) cm) ductal carcinomas.\textsuperscript{2} In particular, contrast-enhanced harmonic EUS is useful for characterizing small neoplasms that contrast-enhanced CT cannot identify.\textsuperscript{2}

2. Pancreatic cystic lesions

Conventional EUS occasionally misdiagnoses the mucus clots in these tumors as a mural nodule, which can lead to unnecessary surgical resection. This problem is avoided by using contrast-enhanced harmonic EUS to determine whether the mural nodule or mucous clot exhibits vascularity. In contrast-enhanced EUS, the mural nodules exhibit enhancement suggestive of positive vascularity while the mucous clots do not. This approach is supported by the recent study by Yamashita \textit{et al.}, which showed that contrast-enhanced EUS distinguishes the mural nodules from mucous clots in intraductal papillary mucinous neoplasms with an excellent sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy (100%, 80%, 92%, 100% and 94%, respectively).\textsuperscript{6} Furthermore, relative to conventional EUS, contrast-enhanced EUS improves the diagnosis of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms by more accurately identifying mural nodules.\textsuperscript{7} Also, when the presence of a mural nodule was considered indicative of a malignant cyst, contrast-enhanced EUS was significantly more accurate than conventional EUS (sensitivity, 97% vs 97%; specificity, 75% vs 40%; accuracy, 84% vs 64%, \(p = 0.0001\)).\textsuperscript{7}

Quantitative analysis

1. Pancreatic solid masses

The classification of pancreatic lesions based on their enhancement patterns on contrast-enhanced EUS is a convenient way to characterize conventional EUS-depicted lesions. However, the classification system depends on subjective assessment, which means that different readers can differ in their interpretations. This problem may be overcome by using time-intensity curves (TICs) to quantitatively analyze contrast-enhanced EUS images. Several TIC variables are useful for the differential diagnosis of pancreatic masses. In particular, a low ratio of the uptake inside the mass relative to the uptake of the surrounding parenchyma,\textsuperscript{8} a low median intensity,\textsuperscript{9} a low maximum intensity,\textsuperscript{10} a long time to peak uptake,\textsuperscript{10} a high area under the curve,\textsuperscript{10} and a high echo intensity reduction rate\textsuperscript{11} have been found to be predictive of ductal adenocarcinomas. Recently, Săftoiu \textit{et al.} performed a prospective multicenter trial to assess the ability with which quantitative contrast-enhanced EUS can differentially diagnose focal pancreatic masses. This study showed that the TIC variables accurately differentiated CP from pancreatic carcinoma and could be used in an automated computer-aided diagnostic system with good diagnostic results.\textsuperscript{12}

2. Pancreatic cystic lesions

The time intensity curve (TIC) of contrast-enhanced harmonic EUS can be applied to preoperative diagnosis of the pathological grade of intraductal papillary mucinous neoplasms (IPMNs). The echo intensity change,
echo intensity reduction rate, and nodule/pancreatic parenchyma contrast ratio were significantly higher in the malignant group than in the benign group, suggesting quantitative analysis using TIC of contrast-enhanced harmonic EUS is potentially useful for differentiating between malignant and benign IPMNs.\textsuperscript{13}

**Conclusions**

Contrast-enhanced harmonic EUS characterizes pancreatic solid masses using qualitative analysis with enhancement patterns as well as quantitative analysis using parameters of TIC. It can be also applied to differentiating mucous clots from mural nodules using qualitative analysis and diagnosing the pathological grade of IPMNs.

**References**