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Endoscopic ultrasound-guided tissue acquisition of pancreatic masses

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ABSTRACT

Endoscopic ultrasound (EUS) has assumed an increasing role in the management of pancreaticobiliary disease over the past 2 decades but its impact is particularly evident in the management of pancreatic masses. EUS helps improve patients' outcomes by enhancing tumor detection and staging while providing safe and reliable tissue diagnosis. This review provides an evidence-based approach to the use of EUS for the diagnosis of pancreatic cancer, its staging, and for the determination of resectability compared to other imaging modalities. We will focus on techniques specific to obtaining tissue from solid pancreatic masses and will review best practices in EUS-guided tissue acquisition.

1. Introduction

Advancements in radiologic and endoscopic ultrasound (EUS) imaging have improved our ability to detect and stage pancreatic masses allowing for more selective surgical intervention for patients with "resectable disease." Owing to the low sensitivity of cross-sectional imaging to detect small tumors in the pancreas, endoscopic diagnosis by using EUS has become a mainstay for the assessment of pancreatic masses. EUS also provides a reliable method for tissue sampling hence securing a histopathologic diagnosis [1-3]. This review will focus on the role of EUS in the evaluation of pancreatic masses compared to other imaging modalities, and highlights the best practices to improve tissue yield from EUS-guided tissue acquisition (EUS-TA).

2. Pancreatic cancer

2.1. Background and epidemiology

Pancreatic cancer is the fourth leading cause of cancer-related mortality in the United States. Over 45,000 patients are diagnosed each year in the United States, and the majority of these patients succumb to their disease [4]. Eighty percentage of patients are diagnosed with advanced, unresectable disease. According to the latest statistics, only 7% of patients survive 5 years after diagnosis [4]. While the 5-year survival rate improves to 25% in patients presenting with stage 1 or localized disease, only 9% of patients are identified at this early stage. The majority of patients (53%) presents with distant, metastatic disease, and have a 5-year survival of 2%. Identification of risk factors and establishing earlier detection methods are therefore of paramount importance [5].

2.2. Cross-sectional imaging

2.2.1. Computed tomography

Computed tomography (CT) is the most widely used imaging modality for the assessment of suspected pancreatic ductal adenocarcinoma (PDAC). CT imaging has significantly improved with the introduction of multiple-detector CT (MDCT), which allows high-resolution and multiplanar image reconstruction. CT is reported to have a sensitivity of 89%-97% for PDAC, though it is less effective in diagnosing small ($<$ 2 cm) lesions with a sensitivity of 65%-75% [6]. In this respect, EUS is superior in tumor detection. Comparative studies between EUS and MDCT for pancreatic tumors have demonstrated the superiority of EUS for tumor detection compared to multirow CT. Agarwal et al [7] reported an EUS sensitivity of 100% for the diagnosis of cancer compared to 86% for MDCT. Similarly, DeWitt et al [8] reported that the sensitivity of EUS (98%) was statistically superior to MDCT (86%) in a cohort of 80 patients with pancreatic cancer.

2.2.2. Magnetic resonance imaging

Contrast-enhanced magnetic resonance imaging (MRI) has a sensitivity and accuracy at least similar to that of MDCT for diagnosis and staging of pancreatic cancer, but it is costlier and less readily available than MDCT. MRI, however, may more reliably detect smaller, non–contour-deforming tumors compared with CT [9]. MRI also more accurately detects and characterizes smaller hepatic metastases [10]. A recent study concluded that MRI was

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superior to CT for tumor detection but performed similarly for the evaluation of resectability [11]. In a study that compared the diagnostic performance (detection, local staging) of multiphasic 64-detector CT with gadobenate dimeglumine-enhanced 3.0-T MRI in patients suspected of having pancreatic cancer, both CT and MRI were found to be equally suited for detecting and staging pancreatic cancer [12]. Therefore, the choice of imaging modality for detection and staging of pancreatic cancer depends on test availability and local expertise.

2.2.3. Positron emission tomography and integrated PET/CT

The role of functional imaging especially positron emission tomography with 2-deoxy-2-[fluorine-18]fluoro-D-glucose integrated with CT (FDG-PET/CT) is still uncertain in the staging of pancreas cancer. The NCCN guidelines list the possible performance of PET/CT for the detection of regional lymph nodes and extrapancreatic metastases, although it has not been incorporated in routine practice [13]. The sensitivity and specificity of FDG-PET/CT in the diagnosis and evaluation of pancreas cancer ranges from 71%-100% and 64%-95%, respectively, significantly higher than those of CT alone [14,15]. The sensitivity of PET/contrast-enhanced CT in detecting local recurrence, abdominal lymph node metastasis, and peritoneal dissemination are 83%, 88%, and 83%, respectively [16]. A meta-analysis of 51 studies involving 3857 patients compared the diagnostic performance of ^{18}FDG PET alone, ^{18}FDG PET/CT, and EUS for diagnosing pancreatic cancer [17]. The study concluded that the pooled sensitivity for combined PET/CT (90.1%) was significantly higher than PET (88%) and EUS (81%). However, the pooled specificity estimate for EUS (93.2%) was significantly higher than PET (83%) and PET/CT (80%).

2.3. Staging of pancreatic adenocarcinoma

Staging of pancreatic cancer is performed according to the American Joint Committee for Cancer (AJCC) Staging TNM classification, which describes the tumor extension (T), lymph node (N), and distant metastases (M) of tumors, respectively [18]. The accuracy of EUS for T staging of pancreatic tumors ranges from 62%-94% [19-21]; while its accuracy for N staging ranges from 41%-86% [5].

Para-aortic lymph nodes (PALNs) are considered nonregional lymph nodes for both pancreatic head and body or tail cancers, thus meticulous survey of this region is critical during staging of all pancreatic tumors [22]. Kurita et al [23] conducted a prospective, nonrandomized single-center trial, of 208 patients with pancreatobiliary cancers without apparent distant metastases except for PALNs. PET/CT and EUS-guided fine-needle aspiration (EUS-FNA) were performed sequentially as a single combined procedure to evaluate PALN metastasis. EUS-FNA had higher sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for the diagnosis of PALNs metastasis than PET/CT. The differences for the sensitivity and accuracy were significant ($P < 0.001$). An EUS survey of mediastinal stations for metastatic adenopathy is also warranted since these are also considered nonregional lymph nodes.

For detection of nonnodal metastatic cancer, CT and MRI are superior to EUS due to both anatomical considerations of the upper gastrointestinal tract and the limited range of EUS imaging. However, EUS still has an important role in the evaluation of hepatic metastasis in the left or caudate lobe (Figure 1) and malignant ascites, some of which can be missed on cross-sectional imaging and both of which can be accessible by EUS-FNA. Identification of liver metastases or malignant ascites by EUS-FNA may preclude surgical resection and is associated with poor survival following diagnosis [24].

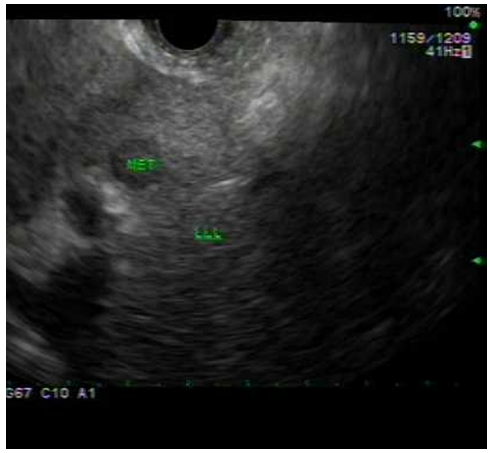

Fig. 1. A linear EUS image of a small liver lesion not visualized on CT scan in a patient undergoing staging and FNA of a pancreatic body mass. Cytology from the lesion confirmed metastatic pancreatic adenocarcinoma. (Color version of figure is available online.)

2.4. Assessment of vascular invasion

The overall accuracy of EUS for vascular invasion ranges from 68%-93% [19,25-27]. The overall accuracy of CT is reportedly equivalent [19,26] or inferior [25] to EUS. The overall accuracy of MRI is reportedly equivalent [19] or superior [26] to EUS.

The overall sensitivity and specificity of EUS for malignant vascular invasion range from 42%-91% and 89%-100%, respectively [19,25-27]. The sensitivity of EUS for tumor invasion of the PV or porto-splenic confluence is 60%-100% [28,29] with most studies demonstrating sensitivities over 80%. The sensitivity of EUS for PV invasion (Figure 2) is consistently superior to that of CT [28,30,31]. For the superior mesenteric vein, superior mesenteric artery (Video 1), and celiac artery, the sensitivity of EUS is 17%-83% [27], 17% [32], and about 50% [28], respectively. The sensitivity of CT for staging of the superior mesenteric artery [31,32] and celiac artery [28] appears to be better than EUS. Until further conclusive data becomes available, assessment of tumor resectability should be done by both EUS and CT (or MRI) rather than by EUS alone.

2.5. Resectability of pancreatic tumors

In a pooled analysis of 9 studies involving 377 patients, the sensitivity and specificity of EUS for resectability of pancreatic cancer was 69% and 82%, respectively [8,19,25-27,33-36]. The

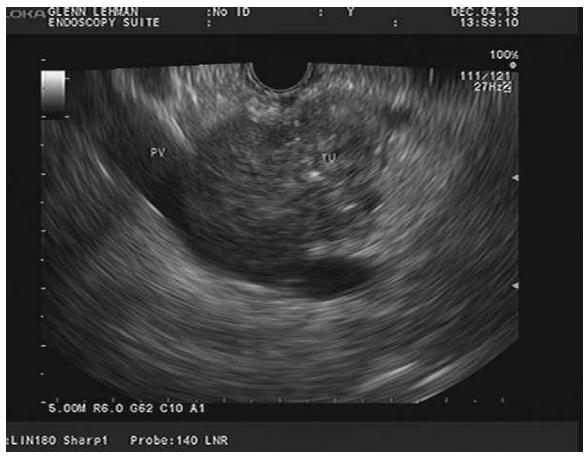

Fig. 2. A linear EUS image of a pancreatic head mass invading the portovenous confluence. This patient underwent neoadjuvant therapy to downstage the tumor followed by pancreaticoduodenectomy with venous reconstruction.