—Commentary—

The borderline resectable/locally advanced pancreatic ductal adenocarcinoma: EUS oriented

Sevastița Iordache, Dana-Maria Albulescu[1], Adrian Săftoiu
Departments of Gastroenterology and [1]Imaging, Research Center in Gastroenterology and Hepatology, University of Medicine and Pharmacy Craiova, Craiova, Romania

INTRODUCTION

Staging pancreatic cancer is mandatory for clinical practice. Endoscopic ultrasound (EUS) is a valuable technique with high accuracy in local invasion assessment. EUS can be considered as one stop shop for pancreatic diseases offering valuable information concerning diagnosis, staging, and therapy decisions. For an accurate staging of pancreatic cancer, clinicians have important imaging tools in clinical practice: computed tomography (CT) scan, magnetic resonance imaging (MRI), EUS as well as diagnostic laparoscopy. The aim of accurate staging is to establish the optimal therapy in these patients. Although surgery is the only curative option in resectable tumors, in clinical practice, it is often difficult to obtain an accurate staging due to inherent limitations of imaging procedures.

T STAGING

Some patients with pancreatic cancer are classified as borderline, with locally advanced disease. In this set of patients, imaging methods such as EUS seem to represent an accurate method for selecting patients undergoing curative surgery. The assessment of pancreatic cancer resectability is based mainly on the extent of the peripancreatic vasculature involvement with tumor mass.[1] According to the American Joint Committee on Cancer,[2] a pancreatic tumor is considered to be surgically resectable (curative) in a few situations: no involvement of the superior mesenteric vein (SMV) or SMV-portal vein (PV) confluence (defined as occlusion or encasement); no direct extension to the superior mesenteric artery (SMA); no direct extension to the inferior vena cava (IVC), aorta, or celiac trunk; no extensive peripancreatic or celiac lymph nodes involvement; no distant metastases (liver, peritoneal, *etc.*). There are some situations when the primary tumor is considered borderline resectable: SMV/PV impingement/short-segment SMV occlusion; SMA abutment; encasement of the gastroduodenal artery up to its origin at the hepatic artery (HA); limited IVC involvement; and colon or mesocolon invasion.

There is variability in the definition of the tumor-vascular relationships. Thus, MD Anderson Cancer Centre classified locally advanced borderline pancreatic cancers (LAPC) in three types: Type A (local

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Address for correspondence
Dr. Adrian Săftoiu, Department of Gastroenterology, University of Medicine and Pharmacy Craiova, Petru Rares Street No. 2-4, Craiova, Romania. E-mail: adrian.saftoiu@umfcv.ro
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tumor-artery abutment), Type B (questionable distant metastasis), and Type C (patients with altered performance status).[3] A multidisciplinary approach is highly recommended in the treatment of patients with LAPC.[4,5]

CT and MRI had similar sensitivities and specificities for both diagnosis and vascular involvement in patients with pancreatic cancer.[6] Multislice CT (MSCT) seems to have a very good sensitivity in detecting resectable pancreatic tumors reaching 100% in some studies.[7,8] However, CT staging was not predictive of resectability and pathological response in treated patients with neoadjuvant chemotherapy.[9] Resectability based on dual-source CT angiography showed higher sensitivity, specificity, and diagnostic accuracy than that obtained from MSCT angiography scanning.[1]

According to a recent meta-analysis, EUS is a reliable and accurate diagnostic tool for the TN staging and evaluation of vascular invasion in pancreatic cancer [Figure 1a-d]. Thus, sensitivity of EUS for vascular involvement is 87% with a very good specificity reaching 90%. The sensitivity of EUS for T1–T2 stages is 76% but is significant higher in patients with T3–T4 stages, reaching 90%. Accuracy of EUS in the nodal staging is lower, the sensitivity being 62% with a specificity of 74%.[10] EUS is a reliable method for selection of patients with borderline resectable pancreatic cancer due to its high sensitivity and specificity for staging T3–T4 tumors.

The main limitation of CT is the lack of sensitivity for early pancreatic lesions. EUS provides an excellent complement to CT for both diagnosis and staging of pancreatic cancer and allows easy access for needle aspiration and tissue diagnosis.[11] Although EUS is generally considered superior to CT for the diagnosis and local staging of pancreatic cancer, it is however limited by availability and inability to assess for distant metastases.[12] Thus, EUS is considered to be superior for the detection of clinically suspected lesions, especially if the results of other cross-sectional imaging modalities are equivocal. The major advantage of EUS is the high negative predictive value that approaches 100%, indicating that the absence of a focal mass reliably excludes pancreatic cancer.[13]

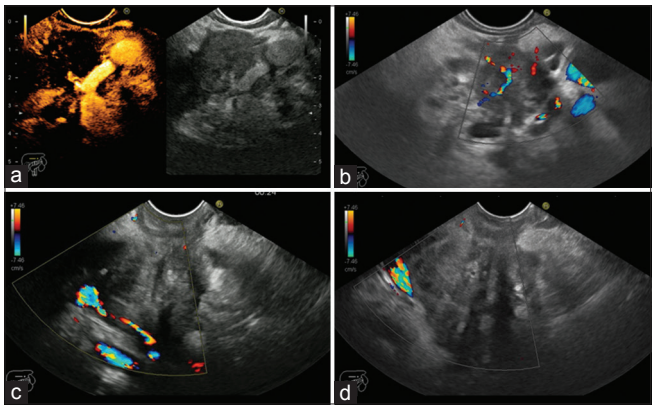

Figure 1. Vascular involvement in locally advanced pancreatic cancer. (a) Splenic artery encasement – contrast enhancement endoscopic ultrasound; (b) Hepatic artery encasement – color Doppler endoscopic ultrasound; (c) Celiac trunk invasion – color Doppler endoscopic ultrasound; (d) Portal vein invasion – color Doppler endoscopic ultrasound

In a study published in 2011, authors compared the tumor size measured by CT ± EUS before surgery and after surgery on resected specimen. 84% of patients had a primary tumor 7 mm larger on pathology than CT. EUS was somewhat more accurate, with pathologic tumor size being a median of only 5 mm larger compared with EUS size.[14] Nevertheless, a cost-minimization analysis strengthened the sequential strategy, MSCT followed by EUS, in potentially resectable cancers;[15] if both methods confirm resectability, there is general agreement between experts that the patient can proceed to surgery.[16]

Newly developed EUS techniques such as contrast enhancement combined with three-dimensional (3D) acquisitions could conduct to a better accuracy of the method for assessment of vascular involvement.[17] The technique has some disadvantages: it is time-consuming and the examiner should be experienced in EUS and novel techniques. The newest refinements such as contrast-enhanced EUS, EUS elastography, and tridimensional EUS slowly become important tools for staging pancreatic tumors.[13] Anyway, new CT-based techniques also improved the T staging. Thus, a peripancreatic 3D vascular reconstruction can reveal the vascular anatomy, variations of peripancreatic vascular, and tumor-induced vascular changes.[18]

N STAGING

EUS is useful as a complementary method to MSCT for N staging in pancreatic cancer. Peripancreatic and distant lymph nodes (mediastinal) can be evaluated by EUS [Figure 2]. Moreover, fine-needle aspiration (FNA) comes to improve the accuracy of the method, representing a major advantage as compared to (positron emission tomography [PET]) CT or MRI. Sensitivity and specificity of EUS are only 62% and 74%, respectively.[10]

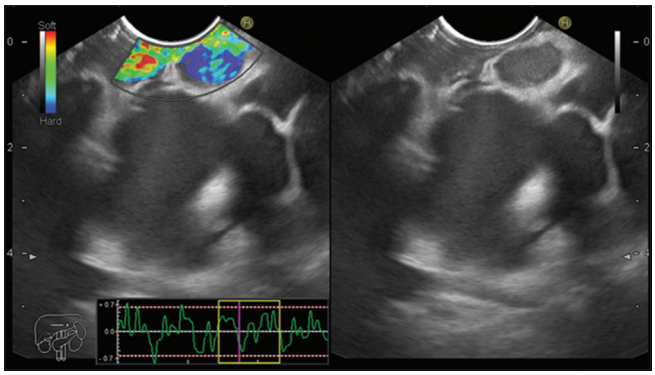

Figure 2. Mediastinal lymph node in a patient with pancreatic cancer - hard appearance in real-time elastography-endoscopic ultrasound

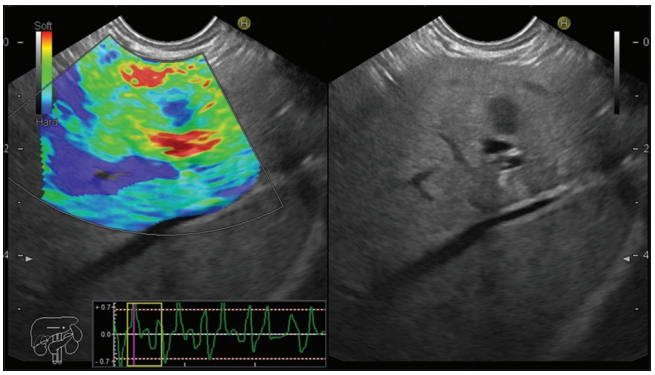

Figure 3. Metastasis in the left lobe of the liver, hard-blue appearance in real-time-endoscopic ultrasound

Contrast-enhanced EUS (CE-EUS) and real-time elastography (EUS) show potential to improve the accuracy of EUS for the differential diagnosis of benign and malignant lymph nodes.[19] Computer-enhanced dynamic analysis based on hue histograms of the EUS elastography movies represents a promising method that might allow the differential diagnosis of benign and malignant lymph nodes[20,21] [Figure 2]. Coagulation necrosis has also been described in malignant lymph nodes. EUS features for coagulation necrosis as marker for malignant invasion have a sensitivity of 54% but a very good specificity of 91%.[22]

M STAGING

EUS can be useful for M staging if the distant metastases are located nearby the digestive tract. Thus, left lobe liver metastases can be evaluated and EUS-FNA is possible in this situation [Figure 3]. Distant lymph nodes (mediastinal) can be also assessed and punctured.

EUS has the ability to detect much smaller volumes of ascites than traditional CT or MRI, and EUS-guided FNA might be a useful modality for the standard metastatic workup of any newly diagnosed or suspected malignancy.[23] Patients with pancreatic cancer may also develop remote malignant thrombi (RMT), defined as a malignant intravascular thrombus noncontiguous to the primary tumor. Intravascular FNA is a potential safe procedure to detect radiographically occult RMT, which has impact on staging and resectability.[24] European Society of Gastrointestinal Endoscopy consequently suggests performing EUS-guided sampling from distant lymph nodes, left liver lobe metastases, and ascites in patients with digestive cancers.[25]

CONCLUSION

EUS is a complementary method to CT/MRI for TNM staging of pancreatic cancer having the advantage of tissue sampling by EUS-guided FNA. The newly developed techniques (3D, contrast enhancement, or elastography) conduct to a better and accurate diagnostic and staging.

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