Endoscopic Ultrasound in the Diagnosis and Staging of Pancreatic Cancer

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Drs. Levy and Wiersema have provided an authoritative review of the role of endoscopic ultrasonography in the diagnosis and staging of pancreatic cancer. As outlined in their article, endoscopic ultrasound has emerged as an important tool in the diagnostic evaluation of many patients with suspected pancreatic neoplasms. We concur that endoscopic ultrasound is part of the standard preoperative evaluation of patients with biochemically confirmed insulinoma and gastrinoma syndromes and of at-risk patients with multiple endocrine neoplasia type 1. Endoscopic ultrasound and endoscopic ultrasound-guided fine-needle aspiration (FNA) can also accurately determine the etiology of a cystic pancreatic neoplasm by differentiating between mucinous, serous, and inflammatory (pseudocyst) lesions.

A major incentive for the continued development of endoscopic ultrasound technology, however, is the care of patients with presumed pancreatic and periampullary adenocarcinoma. In such patients, Levy and Wiersema correctly point out that the primary limitation of diagnostic endoscopic ultrasound is a relatively low negative predictive value. Further understanding of the limitations of endoscopic ultrasound for accurate staging of pancreatic neoplasms requires an appreciation of the three-dimensional anatomy of the proximal gastrointestinal tract and pancreas and knowledge of the criteria utilized by surgeons to assess resectability.

Assessment of Resectability: Essential Anatomic Distinctions

In the absence of radiographically visible metastatic disease, the primary goal of pretreatment staging studies is accurate definition of the relationship between the pancreatic neoplasm and adjacent vascular structures, including the celiac axis (and the common hepatic artery), superior mesenteric artery, superior mesenteric vein, and portal vein. A tumor that extends to, or involves, arterial structures such as the celiac axis or superior mesenteric artery is uniformly considered unresectable. However, a tumor with isolated involvement of the superior mesenteric vein or superior mesenteric vein/portal vein confluence is not necessarily considered unresectable. Indeed, some regional centers for pancreatic surgery perform segmental venous resection and reconstruction for management of tumors with isolated venous involvement in the absence of concurrent arterial extension.[1-3]

This anatomic distinction is important because it shifts the focus of endoscopic ultrasound from tumor-venous assessment, where endoscopic ultrasound is relatively sensitive, to the definition of tumor-arterial (celiac axis and superior mesenteric artery) relationships, where the sensitivity of endoscopic ultrasound may be lower. While characterization of the relationships of the pancreatic tumor to the superior mesenteric vein and portal vein is important, these relationships are not considered essential determinants of resectability by experienced pancreatic surgeons.[1-3]

Figure 1 illustrates these anatomic distinctions. It includes three computed tomography (CT) scans that demonstrate the spectrum of potential tumor-vessel relationships. In panel A, a low-density tumor mass is visualized within the pancreatic head with a clearly definable tissue plane between the medial edge of the tumor and both the superior mesenteric vein and superior mesenteric artery.
In contrast, panel B demonstrates a lesion that extends to or involves the superior mesenteric vein without involvement of the superior mesenteric artery (located slightly posterior and medial to the superior mesenteric vein). Levy and Wiersema’s opinion notwithstanding, such a lesion is indeed resectable at a treatment center with surgeons experienced in vascular resection and reconstruction at the time of pancreaticoduodenectomy. Panel C depicts a locally advanced tumor that involves both the superior mesenteric artery and superior mesenteric vein; this tumor is unresectable. Most regional centers are currently utilizing contrast-enhanced multidetector helical CT to accurately define these critical tumor-vessel relationships. In centers where vascular resection and reconstruction are performed routinely, endoscopic ultrasound may provide minimal staging benefit over high-quality helical CT. However, if high-quality CT is unavailable, or there is no capacity for vascular resection and reconstruction at the time of pancreaticoduodenectomy, endoscopic ultrasound may be of value in identifying patients with CT-occult vascular involvement. Such patients can then be referred to a regional center with experience in vascular resection and reconstruction during pancreaticoduodenectomy.

In contrast to the experience of Levy and Wiersema, data from our institution suggest that isolated involvement of the superior mesenteric vein is more common. In a series of 300 consecutive patients undergoing pancreaticoduodenectomy at our institution, 89 (30%) required some form of vascular resection and reconstruction.[4] Importantly, segmental vascular resection and reconstruction did not increase pancreaticoduodenectomy-associated morbidity or mortality rates.[3] Furthermore, patients who require vascular resection at the time of pancreaticoduodenectomy have a complete resection rate (R0 rate) and long-term survival rate comparable to patients who do not have venous involvement.[3]

**Proper Role of Endoscopy in the Diagnostic Schema**

We would agree that in the absence of a plan for preoperative chemotherapy or chemoradiation, radiographically resectable pancreatic neoplasms do not require preoperative tissue diagnosis. Thus, the routine use of endoscopic ultrasound FNA for resectable tumors may not seem justified. However, physicians at regional referral centers or tertiary care cancer centers do not perform most pancreatic resections.

Indeed, a review of over 7,000 patients undergoing pancreaticoduodenectomy nationwide revealed that more than 50% of patients had their surgery at a hospital performing fewer than two such procedures per year, where the operative mortality rate ranged from 12% to 16%.[5] Since the majority of patients undergo pancreaticoduodenectomy with this high risk for death, many physicians, including some surgeons, are not willing to proceed with pancreaticoduodenectomy in the absence of a tissue diagnosis of malignancy.

Despite improvements in radiographic imaging, such diagnostic uncertainty often results in therapeutic indecision. Therapeutic indecision often leads to exploratory surgery, at which time surgeons frequently attempt intraoperative biopsy (leading to unnecessary complications) or incorrectly judge a primary pancreatic tumor to be resectable or unresectable. In contrast to the diagnostic and staging evaluation of other solid tumors, in which the diagnostic phase is distinct from the treatment phase, diagnosis and treatment are often a continuum with pancreatic and periampullary malignancies. Patients undergo a rapid transition from excellent health to painless jaundice to the operating room; their first chance to seek a second opinion or explore available options for protocol-based therapy is after already having undergone an unsuccessful attempt at surgical resection or when recovering from complications secondary to an ill-advised intraoperative pancreatic biopsy.

The advent of endoscopic ultrasound-guided FNA (combined with high-quality CT and endobiliary stent placement) allows pancreatic cancer to be treated like other solid tumors: The diagnostic phase is separate from the treatment phase. Patients with suspected pancreatic or periampullary cancer can be accurately staged with contemporary CT, biliary obstruction can be relieved with endobiliary decompression, and the diagnosis can be established endoscopically with endoscopic ultrasound FNA. Patients can then be counseled as to available treatment options and the established short- and long-term benefits of referral to a regional center with expertise in pancreatic surgery.[6-7]

Thus, we believe that endoscopic ultrasound for the purpose of FNA biopsy will become a routine part of the staging evaluation of patients with periampullary or pancreatic malignancies, and represents a major innovation in the care of these patients.

**Figure 2** outlines a series of clinical situations that can occur after initial staging of a suspected pancreatic neoplasm and that illustrate the potential role for endoscopic ultrasound. Endoscopic ultrasound may be helpful for assessment of patients with suspected venous involvement in centers...
that do not practice vascular resection and reconstruction. Endoscopic ultrasound FNA is the biopsy technique of choice for establishing a tissue diagnosis of malignancy in patients with locally advanced (unresectable) disease and in patients with potentially resectable disease before protocol-based therapy.

**Conclusions**

As implied by Levy and Wiersema, the optimal evaluation of patients with pancreatic or periampullary neoplasms requires the close interaction of a multidisciplinary team, including a gastroenterologist, pancreatic surgeon, and practitioners in medical oncology and radiation oncology. Such collaboration is essential to accurately stage and properly treat these patients.

**References:**


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