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Knowing Your Boundaries: A Review of the Definitions and Imaging Features of Borderline Resectable Pancreatic Carcinoma

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Introduction

Pancreatic adenocarcinoma is the fourth leading cause of cancer death in the United States and has the lowest survival rate of any solid malignancy.[1] Additionally, it is one of the few cancers with an increasing incidence over the past decade.[2] Owing to the tumor's insidious onset and aggressive biology, tumors often present at an advanced stage. Margin-negative tumor resection is the only curative technique, but only 15%-20% of patients have potentially resectable disease at the time of presentation.[3] Although surgical techniques and chemotherapeutic options have become more advanced, the mortality rate has actually slightly increased between 1996 and 2011.[1]

Imaging is the primary means for staging pancreatic cancer and therefore carries substantial implications for appropriate patient management. Most commonly, the staging of pancreatic carcinoma follows American Joint Committee on Cancer guidelines. In the absence of metastatic disease, tumors are classified into resectable, borderline resectable, and unresectable locally advanced disease for the purposes of clinical management.[4,5] Unfortunately, multiple classification definitions have been proposed, making standardization difficult.

In this article, we will discuss different imaging strategies used to assess pancreatic adenocarcinoma and review the current, most common definitions of borderline resectable pancreatic carcinoma, including recent updates. We will review and demonstrate the imaging features of borderline resectable tumors. Examples will illustrate how using different definitions can cause the same tumor to be classified differently, as either resectable, borderline resectable, or locally advanced.

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Imaging Evaluation

The goals of imaging in pancreatic adenocarcinoma include assessment for metastatic disease, evaluation of the mass and its relationship to adjacent vasculature and other structures, and identification of any aberrant vascular anatomy. High-quality cross-sectional imaging and interpretation by experienced radiologists are paramount for proper staging.[6] Without clear, understandable radiological reports, there may be confusion as to the pertinent findings on imaging. A recent consensus statement by the Society of Abdominal Radiologists and the American Pancreatic Association has proposed a standardized nomenclature and reporting template to improve completeness and avoid confusion.[7]

Computed tomography (CT) is the most widely available and best-validated imaging modality for staging of pancreatic carcinoma. Multidetector pancreatic protocol CT is essential for proper tumor evaluation, allowing for thin-section imaging (3 mm or less slice thickness) and subsequent multiplanar and 3-dimensional reconstructions. Rapid image acquisition allows for multiphase protocols optimized for tumor detection, vascular assessment, and metastatic disease evaluation. Imaging is generally performed in the arterial or pancreatic parenchymal phase, as well as the portal venous (hepatic) phase.[8] Pancreatic phase imaging is performed during maximum contrast enhancement of the pancreatic parenchyma to allow optimal differentiation between normal pancreatic tissue and tumor, with adequate opacification of the adjacent vasculature as well.[9] (Fig. 1) Portal venous phase imaging allows evaluation for hepatic metastases that are hypodense relative to the maximally enhancing hepatic parenchyma (Fig. 2).

Magnetic resonance imaging (MRI) is considered equal in sensitivity and specificity to CT for tumor evaluation,[10-12] but has not been as widely used because of the cost, availability, and difficulty in interpretation. Evaluation of metastatic disease is well documented by MRI that is able to characterize small hepatic lesions better than CT.[13,14] MRI also may be particularly useful in detecting tumors that are isoattenuating on CT[15] and in patients with contraindications to iodinated contrast administration (Fig. 3).

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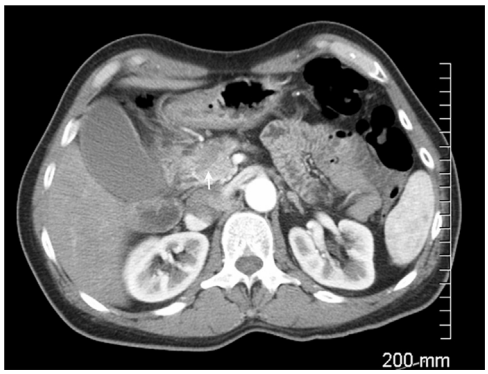

Figure 1 Multidetector pancreatic parenchymal phase CT demonstrates a hypoenhancing tumor (arrow).

Abdominal ultrasound is frequently the initial examination in a patient with jaundice and is sensitive for detection of biliary ductal dilation. Poor evaluation of the pancreas due to patient body habitus and overlying bowel gas limits its use for tumor assessment and staging.[16] positron emission tomography / computed tomography (PET/CT) has been shown to be a useful adjunct to conventional imaging in initial tumor evaluation,[17] but the limited CT images are routinely performed without intravenous contrast, which is not adequate for evaluation of local vascular involvement.[18] Endoscopic ultrasound is indicated when a tumor is suspected but not identified on CT, and gives high-resolution images of the pancreas and surrounding structures as well as allowing for biopsy of suspected lesions. Its invasiveness and limited ability to evaluate for distant metastases limit its use for staging.[14]

Definitions: Resectable, Borderline Resectable, and Locally Advanced

Pancreatic adenocarcinoma is considered resectable when it does not contact major surrounding vessels (preserved fat plane between tumor and vessel wall) and has no evidence of distant metastatic disease (Fig. 4).[19] Some classification systems consider limited tumor contact with adjacent venous structures to be resectable as well.[20] Tumors with distant metastases or adenopathy outside of the surgical field are considered unresectable (Fig. 5). Locally advanced tumors are also considered unresectable because of the involvement of adjacent vasculature, though the specific definition depends on the classification system used.

Borderline resectable tumors are defined as those which are technically resectable, but with a high incidence of micrometastatic disease and margin-positive resection. Patients currently undergo neoadjuvant therapy (chemotherapy or radiation or both) with subsequent restaging and then undergo surgery if no disease progression is found or if there is downstaging of the tumor. Borderline resectable pancreatic adenocarcinoma has been an evolving concept based on clinical observations over the past few decades.[21] In the 1990s, multiple articles demonstrated the feasibility of venous resection with pancreaticoduodenectomy, with these patients having equivalent survival to those undergoing standard pancreaticoduodenectomy.[22-24] During the same time period, several additional articles demonstrated the efficacy of neoadjuvant chemoradiation for patients with resectable tumors.[25-27] In 2001, the term marginally resectable was first used in the context of using neoadjuvant chemoradiation to potentially downstage tumors and improve resectability.[28]

The imaging evaluation and definition of resectable and unresectable tumors also have evolved since the 1990s. Ishikawaet al[29] first described in 1992 that patients with semicircular or less tumor involvement of the portal vein and superior mesenteric vein (based on conventional angiography) had significantly better outcomes than those with greater than semicircular involvement. In 1997, Lu et al[30] was the first to describe staging of pancreatic cancer with thin-section CT, and also found that tumors involving less than half the vessel circumference were more likely to be resectable at surgery. These articles were the basis for the current imaging definitions of borderline resectable disease.

Although several groups have proposed guidelines to define borderline resectable tumors, there is no universally accepted definition. The National Comprehensive Cancer Network (NCCN) was the first to publish CT findings of borderline resectable pancreatic cancer in 2004. The MD Anderson Cancer Center published a modified definition for borderline resectable tumors in 2005.[31] In 2009, the Americas

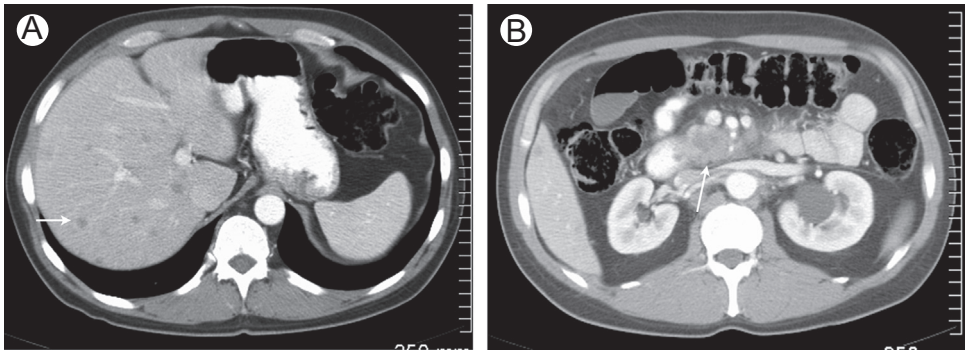

Figure 2 Multiple hypodense metastatic foci (arrow, A) on a portal venous phase CT in a patient with a pancreatic uncinate process mass (arrow, B).