

The borderline resectable and locally advanced pancreatic ductal adenocarcinoma: Definition

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INTRODUCTION

Pancreatic ductal adenocarcinoma (PDAC) is the fourth most common cause of cancer death in the United States with around 50,000 incident cases and 40,000 deaths in 2015.^[1] Despite the tremendous recent advances in diagnostic and therapeutic interventions, the 5-year survival rate remains dismal at approximately 5%. At initial presentation, the majority of patients (50%–55%) have metastatic disease while only 20% have resectable disease.^[2,3] The remaining 25%–30% of patients present with either borderline resectable (BR) or locally advanced (LA) disease.^[2,4] In both BR-PDAC and LA-PDAC, the tumor is localized to the pancreas but adheres to or invades adjacent vascular structures, including the celiac axis (CA) vessels, superior mesenteric artery (SMA), superior mesenteric vein (SMV), and portal vein (PV). Patients with BR-PDAC and LA-PDAC represent a unique subset of patients with PDAC who are not candidates for primary surgical resection. Identification of such patients requires a team of experts in the fields of gastroenterology/endosonography and radiology (computed tomography, magnetic resonance imaging). This

identification is vital for the planning of a potentially curative multimodality treatment that relies on chemotherapy, radiotherapy (RT), and surgery. The objective of treatment for BR-PDAC is to achieve tumor downstaging to facilitate margin-negative (R0) resection, while that for LA-PDAC is local disease control with improvement of survival.

BR-PDAC

Over the past decade, the concept of “BR” PDAC has emerged to describe a distinct spectrum of patients ranging from “resectable” to LA disease, for whom a microscopically margin-positive (R1) resection is considered relatively more likely, primarily due to the relationship between the primary pancreatic tumor and the surrounding blood vessels. Unfortunately, both anatomic and imaging criteria to define “borderline resectability” are not yet universally agreed upon, with several classification systems proposed in the literature and considerable variability among medical institutions. Thus, as a result of: the lack of consensus regarding the definition, the relatively small numbers of patients in this category, and the paucity

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of dedicated clinical trials; accurate evidence-based diagnostic categorization and treatment selection for this subgroup of patients remains a major challenge.

Hence, although there is no consensus regarding the definition, BR-PDAC is often defined as a tumor confined to the pancreatic bed with limited involvement of the adjacent vascular structures where vascular reconstruction options are feasible.^[4] However, there is not yet a universally accepted definition in the oncology community regarding the extent of vascular involvement that would be amenable to reconstruction.^[5,6] More specifically, according to the Society of Surgical Oncology/American Hepato-Pancreato-Biliary Association/Society for Surgery of the Alimentary Tract consensus definition, which had been incorporated into the National Comprehensive Cancer Network (NCCN) guidelines, BR tumors have: (a) no distant metastases; (b) venous involvement of the SMV/PV with or without impingement and narrowing of the lumen; (c) short segment venous occlusion but with suitable vessel proximal and distal to occlusion, allowing for safe resection and reconstruction; (d) gastroduodenal artery (GDA) encasement up to the hepatic artery (HA) with either short segment encasement or direct abutment of HA, without extension to the CA; and (e) tumor abutment of the SMA not to exceed 180° of the circumference.^[5-8] To complicate matters further, there is even internal conflict within the individual consensus statements. For example, it is noted in the 2016 NCCN guidelines that there is disagreement among various panelists regarding the second celiac criterion (>180° contact without involvement of the aorta and with intact and uninvolved GDA), which some would deem unresectable.^[7,9]

A growing body of evidence suggests that the BR group may particularly benefit from neoadjuvant therapy to increase the likelihood of a margin-negative (R0) resection. Recent data have revealed that PDAC patients with involvement of the adjacent mesenteric vessels who were undergoing R0 resections had the same survival outcomes as those who underwent resection for primarily resectable PDAC.^[10,11] The main challenge in the surgical management of BR-PDAC is the high rate of positive margins at the reconstructed vessel segments, leading to high risk of local and systemic recurrence.^[12] Selection of patients who will benefit from neoadjuvant therapy or upfront surgical resection is a particularly challenging task that is highly dependent on the expertise of the multidisciplinary team members.

LA-PDAC

On the other hand, LA-PDAC is often defined as the involvement of the CA or the encasement of >180° of the SMA (T4) and/or involvement of SMV/PV with no reconstruction options, irrespective of nodal involvement, provided that no distant metastasis exists outside the pancreatic bed.^[13] Historically, BR-PDAC has been included in trials that involved LA-PDAC patients.

The median overall survival ranges from 5.5 to 22 months (LA-PDAC around 16 months, whereas BR-PDAC rarely reaches 2 years).^[3,13-17] Optimal treatment for BR-PDAC is still controversial with regard to the type, dose, and regimen of chemotherapy, use of RT, RT field and dose, and sequence of the multimodality treatment approach. The chance of surgical resection in patients with LA-PDAC is <5%. LA-PDAC is often treated with combination chemotherapy or combined chemoradiation therapy. These approaches have not shown any improvement in survival.^[16,17]

CONCLUSIONS

It is very important to recognize and closely follow the evolving imaging criteria for defining BR and LA disease given their profound implications for treatment strategy, follow-up recommendations, and overall prognosis.

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