Diagnosis and Management of Borderline Resectable Pancreatic Adenocarcinoma

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KEYWORDS

• Borderline resectable • Pancreatic cancer • Pancreatoduodenectomy
• Neoadjuvant therapy • Chemotherapy • Chemoradiation

KEY POINTS

- Pancreatic cancers with borderline resectable anatomy are those at high risk for a microscopically positive (R1) resection when surgery is used as primary therapy.
- Local tumor anatomy is best assessed radiographically with high-quality computed tomography using a pancreatic protocol.
- Patients with clinical findings suggestive of metastatic disease or at high risk for pancreatic surgery also may be considered borderline resectable on the basis of nonanatomic parameters.
- Patients with borderline resectable pancreatic cancer should be treated with neoadjuvant therapy before planned surgical resection.
- Response to neoadjuvant therapy for pancreatic cancer is difficult to assess radiographically or serologically.
- Laparotomy with intent to resect the primary tumor should be performed for all patients with borderline resectable disease who have no evidence of disease progression and who have a performance status and comorbidity profile appropriate for major surgery after receipt of neoadjuvant therapy.

INTRODUCTION

A margin-negative resection of the primary tumor with a complete regional lymphadenectomy represents a necessary condition for cure of pancreatic ductal adenocarcinoma (PDAC).[1,2] The staging designation "borderline resectable" has been

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historically used to characterize local tumor anatomy that confers high risk for a microscopically positive surgical resection and/or early treatment failure after an initial surgical approach. For this reason, borderline resectable disease has been considered an intermediate stage of disease on a spectrum of resectability delimited by "resectable" and "unresectable" PDAC.

Many definitions and criteria for this disease stage exist, however, and all have been used heterogeneously in the literature. Interpretation of existing data regarding diagnosis, treatment, and outcomes for patients with borderline resectable cancer is therefore difficult. Furthermore, no data from prospective trials have been generated to guide the evaluation, diagnosis, or management of patients with this stage of disease, so essentially all decision-making is directed by low-level data or consensus.[3–8]

Herein we describe current thinking regarding the classification, definition, diagnosis, and management of patients with borderline resectable PDAC and discuss ongoing controversies relevant to this disease stage.

DEFINITIONS

Anatomic Staging (Borderline Resectable Pancreatic Ductal Adenocarcinoma Type A)

It has long been recognized that the prognosis of patients who undergo surgical resection for PDAC is highly dependent on the histopathologic status of the surgical margins. Indeed, complete excision of the primary tumor to microscopically negative margins (R0 resection) is associated with the best postoperative outcome. In contrast, patients who undergo total gross excision but have histologically positive margins (R1 resection) have a shorter duration of overall survival in most series.[9–12] Moreover, patients with gross residual disease (R2) after surgery have a prognosis similar to that of patients who do not undergo resection and are treated with palliative intent.[1,2] For these reasons, the likelihood of attaining negative surgical margins is a critical consideration when determining whether or not a patient is a potential candidate for pancreatectomy.[13] A precise assessment of resectability represents the most critical component of the pretreatment workup (**Table 1**).[14]

As it was first described in the 1990s,[15–17] borderline resectability was an anatomic designation that was used to describe tumors that appeared to involve the superior mesenteric vein (SMV) and/or portal vein (PV), hepatic artery, superior mesenteric artery (SMA), or adjacent organs on cross-sectional imaging, because resection of cancers involving these peripancreatic structures was typically complicated by high rates of positive margins, postoperative complications, disease recurrence, and early

Table 1
Intergroup criteria for the clinical staging of localized PDAC

Vessel	Potentially Resectable	Borderline Resectable	Locally Advanced
SMV-PV	TVI <180	TVI ≥180 and/or reconstructible occlusion[a]	Unreconstructable occlusion
SMA	No TVI	TVI <180	TVI ≥180
CHA	No TVI	Reconstructible[a], short-segment TVI of any degree	Unreconstructable TVI
Celiac trunk	No TVI	TVI <180	TVI ≥180

Abbreviations: CHA, common hepatic artery; PDAC, pancreatic ductal adenocarcinoma; SMA, superior mesenteric artery; SMV-PV, superior mesenteric or portal vein; TVI; tumor-vessel interface.

[a] Normal vein or artery proximal and distal to the site of suggested tumor-vessel involvement suitable for vascular reconstruction.