Advances in Surgery 50 (2016) 115–128

ADVANCES IN SURGERY

Treatment of Locally Advanced Pancreatic Ductal Adenocarcinoma

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Keywords

• Neoadjuvant Therapy • Pancreatic cancer • Pancreatic ductal adenocarcinoma

Key points

- Pancreatic cancer is increasingly common, and up to 40% of cases are locally advanced at the time of presentation.
- The incorporation of neoadjuvant chemotherapy and more aggressive surgical resections have provided incremental improvement in survival, but overall prognosis for most patients remains poor.
- Ongoing study of multimodality therapy and prognostic markers are needed to more accurately and appropriately tailor treatment for individual patients.

INTRODUCTION

Pancreatic ductal adenocarcinoma (PDAC) is increasingly common and the fourth leading cause of cancer mortality in the United States, with overall 5-year survival of less than 4% [1]. Surgical resection remains the only potential for cure. Unfortunately, less than 20% of patients present with resectable disease and 45% present with overtly metastatic disease [2]. Increasing attention has been placed on the remaining 40% of patients with locally advanced PDAC (LA-PDAC). Although the overall prognosis for pancreatic cancer remains quite poor, increased use of more effective multimodality therapy has allowed for significantly improved survival for even the most challenging cases of LA-PDAC [3]. With this review, the authors aim to summarize recent

The authors have nothing to disclose.

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0065-3411/16/$ – see front matter
http://dx.doi.org/10.1016/j.yasu.2016.03.010

advances in the management and treatment of patients with LA-PDAC as well as to highlight some promising new directions moving forward.

SIGNIFICANCE OF RESECTABILITY

For patients with LA-PDAC, surgical consideration rests on the ability to obtain negative resection margins. A recent analysis compared survival between wide R0 resections, R0 resections with tumor within 1 mm of margin, and R1 resections. Median survival for patients with wide R0 resections was significantly greater than those with margins of less than 1 mm or R1 resections (35 vs 16 vs 14 months, respectively; $P<.001$) [4]. Yet preoperative determination of resectability has been challenging; therefore, multiple definitions of LA-PDAC or borderline resectable PDAC have been established. Early radiologic definitions deemed tumors locally advanced if tumors abutted the celiac trunk or superior mesenteric artery or involved the portal vein or superior mesenteric vein (SMV) [5]. Because of the heterogeneity of definitions, the University of Texas MD Anderson Cancer Center, Americas Hepato-Pancreato-Biliary Association/Society of Surgical Oncology/Society for Surgery of the Alimentary Tract, and the National Comprehensive Cancer Network have modified these definitions based on vascular involvement [6–9]. At the authors' center, they consider locally advanced tumors as cancers with (1) no distant metastasis, (2) absence of blood flow through the SMV and/or portal vein lumen or venous involvement not amenable to reconstruction, (3) involvement of the common hepatic artery or superior mesenteric artery over greater than 180° of the vessel circumference, (4) any celiac abutment, or (5) aortic or inferior vena cava invasion or encasement. The utility of these traditional definitions is under ongoing evaluation as we determine the accuracy of radiographic imaging following neoadjuvant therapy (discussed later). Examples of computed tomography (CT) images before and after neoadjuvant therapy are seen in Fig. 1. The challenges of identifying truly

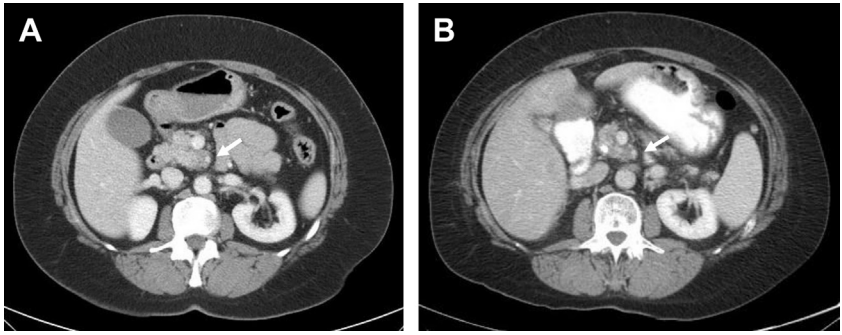

Fig. 1. CT scan of patients with pancreatic adenocarcinoma (*A*) before and (*B*) after neoadjuvant chemotherapy ± chemoradiation. The white arrows are pointing to the superior mesenteric arty.