Management of Locally Advanced Pancreatic Cancer

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KEYWORDS

• Stage 3 pancreatic cancer • Locally advanced pancreatic cancer • Treatment
• Algorithm

KEY POINTS

- The optimal management of these patients is evolving quickly with the advent of newer chemotherapeutics, radiation, and nonthermal ablation modalities.
- For patients with locally advanced pancreatic cancer (stage III), the addition of irreversible electroporation to conventional chemotherapy and radiation therapy results in substantially prolonged survival compared with historical controls.
- The CORRECT and ACCURATE diagnosis for locally advanced pancreatic cancer must be based on high-quality, thin cut (<2mm) cross-sectional imaging, which demonstrates tumor abutment into the celiac/superior mesenteric arteries (>180 degrees) and/or encasement of the superior mesenteric/portal venous system that is not reconstructable.

INTRODUCTION

Pancreatic ductal adenocarcinoma is one of the most aggressive cancers and is the fourth most frequent tumor-related cause of death in the Western world.[1] Locally advanced disease is difficult to control, and limited improvement in outcomes has been achieved in the last 30 years despite the advances in diagnostic modalities and therapeutic options. For all stages combined, the 1-year survival rate is 20%, and the overall 5-year survival rate has remained dismally poor at 5%.[2] Complete surgical resection remains the only potentially curative treatment of pancreatic cancer. Advanced T stage of pancreatic adenocarcinoma is defined according to the involvement of the superior mesenteric artery (SMA), the celiac axis, long-segment portal vein occlusion, or their combination on cross-sectional imaging.[3,4]

Surgical resection offers the only chance of long-term disease control for nonmetastatic exocrine pancreatic cancer. However, only 15% to 20% of patients have potentially resectable disease at diagnosis; approximately 40% have distant metastases, and another 30% to 40% have locally advanced unresectable tumors. Typically,

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patients with locally advanced unresectable pancreatic cancer have tumor invasion into adjacent critical structures, particularly the celiac artery and SMA. Pancreatic tumors become symptomatic at a very advanced stage; therefore, a small percentage (15%–20%) of patients may undergo therapeutic resection. In the remaining patients, there might be either advanced locoregional disease without distant metastases (expected survival of 6–12 months) or locoregional disease with distant metastases (expected survival of 3–6 months).[5]

Chemoradiation therapy (CRT) provides short-term disease control. Most chemotherapeutic regimens do not prolong survival greatly, and only recently did gemcitabine-associated CRT seem to offer a modest survival benefit of 3 months.[6,7] FOLFIRINOX (5-fluorouracil [5FU], leucovorin, irinotecan, and oxaliplatin) recently showed better response and survival rates in stage 3 and 4 patients; however, long-term results from ongoing trials for stage 3 alone are not yet available.[8] The usefulness of radiation therapy (RT) was also assessed; however, the results were not significant.[7,9]

Considering the limited duration of effect of CRT, there is a clear need for an adjunctive or consolidative local treatment to provide greater durable local control to provide pain relief and possibly improve overall survival in patients with locally advanced pancreatic cancer (LAPC). Image-guided ablation techniques, such as radiofrequency ablation, microwave ablation, high-intensity focused ultrasonography, and irreversible electroporation (IRE), have been proposed as new treatment options in such cases.

CRITERIA FOR UNRESECTABILITY

An assessment of resectability should be made based on a thin cut (0.5–1 mm), triple-phase contrast-enhanced computed tomography (CT) scan and/or dynamic MRI. These minimal quality standards must be met to accurately and definitively stage patients at initial diagnosis. A detailed discussion of CT and magnetic resonance assessment of resectability is found elsewhere in this issue.

The accuracy of a single-phase diagnostic CT scan at thicker cuts (ie, 5 or 7 mm) is only 40% to 50% for assessing the presence of metastatic disease to the liver or peritoneum and even less accurate for assessing abutment and/or encasement of the portal venous and arterial structures.[10,11] Regardless of when a suboptimal referral CT scan was performed, it should be repeated for accurate initial staging. A diagnostic laparoscopy is also commonly performed to evaluate for subradiologic occult peritoneal or liver metastases. This procedure should be performed before any local nonsystemic therapy is being considered or if there are equivocal findings on CT or MRI. This procedure is critical because even these subtle changes seen on CT can have significant overall survival effects (**Table 1**).

Proper determination of the disease extent on imaging studies at the time of staging is one of the most important steps in optimal patient management. Given the variability in expertise and definition of disease extent among different practitioners, as well as a frequent lack of reporting of pertinent imaging findings, adoption of a standardized template for radiology reporting, using universally accepted and agreed-on terminology for solid pancreatic neoplasms, is needed. A recent consensus statement describing the standardization reporting template was developed under the joint sponsorship of the Society of Abdominal Radiologists and the American Pancreatic Association.[12] This standardized template is discussed in detail elsewhere in this issue. Adoption of this standardized reporting template can improve the decision-making process for the management of patients with pancreatic ductal adenocarcinoma by providing a complete and accurate assessment of disease staging to optimize treatment recommendations. A standardized imaging template can also