



Contents lists available at ScienceDirect

Curr Probl Cancer

journal homepage: www.elsevier.com/locate/cpcancer

Locally advanced pancreatic cancer: An emerging entity

Grainne M. O'Kane, MB, BCH, BAO, MRCPI, MD*,
Jennifer J. Knox, MD, MSc, FRCPC

Princess Margaret Cancer Centre, Toronto, Canada

ARTICLE INFO

Keywords:

Pancreatic ductal adenocarcinoma
locally advanced
chemotherapy
radiation
irreversible electroporation
radiofrequency ablation

ABSTRACT

Pancreatic adenocarcinoma (PDAC) remains a highly fatal disease that is increasing in incidence. PDAC can be classified according to resectability status with 3 nonmetastatic groups defined: resectable, borderline resectable, and locally advanced PDAC (LAPC). Delineating these subtypes is important with the optimal treatment approach dictated by high-quality CT imaging and multidisciplinary team discussion. Patients with LAPC are thought unresectable and are therefore rarely cured. In these patients, chemotherapy remains the mainstay of treatment. Aggressive approaches in this cohort are increasingly employed. Local therapies after induction chemotherapy including standard fractionation radiation, stereotactic body radiotherapy (SBRT), and irreversible electroporation (IRE) are being investigated in an attempt to improve long-term control. In some cases, responses to neoadjuvant therapy may facilitate surgical resection. Biomarkers that can select patients most likely to benefit from these options are urgently needed. This review aims to highlight the emerging treatment of patients with LAPC and to discuss current trials.

© 2017 Elsevier Inc. All rights reserved.

Introduction

Pancreatic ductal adenocarcinoma (PDAC) is a highly lethal malignancy with 5-year survival rates remaining under 6% for the past 3 decades.¹ Annual incidence and mortality rates are similar, and

*Correspondence to: Dr. Grainne M O'Kane, Princess Margaret Cancer Centre, 700 University Avenue, Toronto, Canada M5S 1Z5.

E-mail address: grainne.okane@uhn.ca (G.M. O'Kane).

PDAC is expected to become the second leading cause of cancer-related mortality by 2020, underscoring the need for research investment.² Early detection is an important determinant of patient outcomes, however, remains challenging with little success in attempted screening programs.³ The surgical classification of PDAC have been refined over a number of years in the past, as a result of improved imaging techniques that can delineate the intimate tumor-vessel interface more clearly. Four categories are now recognised: resectable, borderline resectable (BR), locally advanced unresectable (LAPC), and metastatic PDAC.⁴

Surgery offers the only possibility of cure with approximately 10%-15% presenting with resectable disease. In these patients, negative margin surgery followed by adjuvant chemotherapy has resulted in 5-year survival rates of 20%.⁵ More recent combination chemotherapy regimens are estimated to improve this to 29%.⁶ Almost one-third of cases have locoregional tumor with extension to surrounding vasculature or structures but absent distant spread.⁷ This group includes BR and LAPC cases. In BR tumors, extended surgeries and neoadjuvant approaches to facilitate R0 resection offer a median survival of approximately 18 months. The overall survival in patients with LAPC, however, are between 9 and 13 months, similar to results from combination chemotherapy regimens in the metastatic setting.⁸⁻¹⁰

This review aims to highlight the subtype “locally advanced pancreatic cancer (LAPC)” and to appraise the biological characteristics and optimal management of this emerging entity.

Anatomy and staging

Integral to the staging and management of PDAC is high-quality imaging to ascertain resectability. A dedicated computed tomography (CT) with pancreatic protocol using a multidetector scanner is preferred. Magnetic resonance imaging (MRI) with contrast can also be considered as an alternative.⁴ CT has been shown to predict resectability in 70%-85% of cases and should be performed within 4 weeks of surgery.¹¹ Discussion at multidisciplinary team meetings in high-volume centres is imperative and has been shown to change treatment pathways in up to 25% of cases.¹² Tumors that do not involve surrounding vasculature are thought resectable upfront, and patients with metastatic disease are generally treated with systemic therapy. Given the complexity of adjacent anatomical structures, the continuum between borderline resectable (BR) and locally advanced tumors (implying unresectability) is intricate and may be difficult to dichotomize. The most important underlying distinction in these groups is the attainability of an R0 resection. Slight variations in definitions from large institutional groups do exist particularly in relation to celiac artery and superior mesenteric vein (SMV)-portal vein (PV).¹³ These are highlighted in [Table 1](#). According to NCCN guidelines, patients with LAPC have greater than 180° tumor contact with either the superior mesenteric artery (SMA), celiac artery, or have involvement of the first jejunal branch of the SMA or aorta. Tumor involvement or occlusion of the SMV or PV, which precludes reconstruction of vessels, also renders patients unresectable. For all major groups, abutment of the SMA or abutment or short encasement of the common hepatic artery (CHA) can be defined as borderline. Although the TNM classification is used for prognostication in PDAC, consensus on resectability is the most critical staging piece.

Other radiological modalities used to complement CT/MRI staging include endoscopic ultrasound. This is the preferred modality for obtaining a tissue diagnosis but may also visualize small tumors and nodal extent; EUS is not, however, a staging requirement.¹⁴ The role of positron-emission tomography (PET)-CT in pancreatic cancer diagnostics and as a biomarker of response to treatment is currently not known. PET-CT cannot replace contrast-enhanced CT for detailed staging but has been shown to have a higher sensitivity in the detection of metastatic disease.¹⁵

Borderline resectable pancreatic cancer

The term locally advanced disease has in the past included BR cases given the tumor association with adjacent vascular structures and a lack of consensus on definitions. Although this review focuses on LAPC, which implies both the absence of metastases disease and nonresectable disease,

Download English Version:

<https://daneshyari.com/en/article/8733851>

Download Persian Version:

<https://daneshyari.com/article/8733851>

[Daneshyari.com](https://daneshyari.com)