

Editorial

Does Size Matter Most? Reassessing Clinical Staging for Pancreatic Cancer

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Cancer staging is an ever-evolving entity. Most would agree that staging systems are generally accurate and never perfect but, nonetheless, an integral tool in treatment planning, communication, research, and education. Although current American Joint Committee on Cancer (AJCC) staging systems fulfill these missions adequately for most solid tumors, in this issue of *Annals of Surgical Oncology*, Morganti et al.¹ question the utility of staging for pancreatic cancer. It is certainly true that AJCC staging is rarely referred to during treatment planning for pancreatic cancer patients. Clinically, patients are generally classified as potentially resectable, unresectable because of locally advanced disease, and incurable because of the presence of metastatic disease. These clinical strata and the AJCC stages they encompass successfully segregate patients by their median survival and have formed the basis for clinical trial design. As is all too familiar to the readership, with current available therapies nearly all patients with pancreatic cancer are incurable at diagnosis because of the presence of metastatic disease, whether it is immediately visible or occult. Although we strive to cure, even for resectable patients, prolongation of survival with acceptable quality of life is what we can realistically achieve for most patients. Because of the morbidity of pancreatic surgery, numerous studies have been performed to determine whether clinical factors can identify patients who, even in the face of radiographically resectable disease, are unquestionably incurable and therefore should not be considered

for operation. Although various authors have reported that CA19-9 levels of > 750 or 1000 U/ml are associated with an ultimately fatal outcome, the ability to prognosticate length of life after resection is more difficult.² This, coupled with the lack of alternative treatments, makes it difficult for the surgeon to counsel against operation on the basis of a single clinical factor. Apart from the question of operability, then, what information should we seek from the diagnostic imaging tests we obtain in newly diagnosed pancreatic cancer patients?

In their current article, Morganti et al.¹ analyze the accuracy of clinical staging by using endoscopic retrograde cholangiopancreatography (ERCP), computed tomography (CT), and transabdominal ultrasound imaging in predicting pathologic stage. In addition, they assessed the prognostic effect of clinical staging to identify patients who may benefit from diagnostic laparoscopy and laparotomy and those in whom surgery may not be at all beneficial. The authors analyzed the results of ERCP, CT scan, and transabdominal ultrasound from 54 patients and compared its accuracy in predicting the AJCC pathologic stage documented by surgical staging. The authors then assessed the prognostic effect of clinical staging and pathologic factors on survival. An immediate issue worthy of comment is the choice of diagnostic imaging modalities used in the study. ERCP and transabdominal ultrasound are rarely used to stage patients with pancreatic cancer because they do not add any useful data over and above CT staging.³ Helical thin-section scan remains the workhorse of pancreatic imaging because it provides accurate representation of the relationship of primary pancreatic tumors to the surrounding vasculature, as well as sensitive detection of hepatic metastases and nodal disease >1 cm.⁴ When adjunctive staging

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modalities are required for local staging, endoscopic ultrasound has proven to be highly accurate and has the advantage of allowing for biopsy of both the primary tumor and regional nodes.⁵ Positron emission tomography scanning remains investigational but is of great interest for its ability to detect otherwise occult metastatic disease.⁶ In this series, all patients underwent laparotomy; however, only 31 patients underwent resection. Six patients were found to have metastatic disease, and 17 patients were found to have locally advanced unresectable disease. It is not explicitly stated in the article but must be assumed that all patients in the study were believed to have potentially resectable disease after the preoperative imaging. Assuming so, this represents an extremely high rate of nontherapeutic laparotomy; particularly concerning is the presence of undetected vascular involvement in nearly one third of the patients. Abundant literature has documented the ability of thin-cut helical CT scan to accurately evaluate the relationship of pancreatic tumors to the superior mesenteric portal vein, superior mesenteric artery, and celiac axis branches.⁵ Unfortunately, the authors do not comment on this issue.

From their analysis, the authors found that clinical staging was accurate in its representation of T stage and that the presence of a clinical stage T4 tumor or a tumor >3 cm was associated with a median survival of 8 months, versus 25 months for patients with clinical stage T1 to T3 and tumors <3 cm. The article describes the poor survival of patients with T4 tumors and tumors >3 cm but does not detail how many patients in these two groups underwent resection. The authors do report that more patients in the T4/T >3 cm group were found to have metastatic disease at laparotomy; however, the margin status of the resected patients is not provided, nor are data on how many patients in each group received adjuvant therapy. Although it is not surprising that patients with larger tumors would have a worse prognosis, the absence of critical data on margins and adjuvant treatment, as well as the small sample size, makes it impossible to calculate the true hazard ratio associated with T4 status and tumor size. The main conclusion that can be drawn from the article, then, is that larger tumors (>3 cm) and T4 tumors were

associated with a worse outcome. For the practicing surgeon, this finding can be added to those from other studies that strongly suggest the use of diagnostic laparoscopy in patients with large tumors that otherwise appear resectable by CT criteria.⁷ Such patients will likely have a higher incidence of harboring visible metastatic disease at laparoscopy and could therefore be spared the morbidity of a nontherapeutic laparotomy.

Apart from identifying patients who should undergo laparoscopic evaluation, the accuracy of clinical staging has relevance for studies of neoadjuvant therapy. In neoadjuvant trials, an understanding of pretreatment prognostic factors is critical to accurately assessing treatment efficacy. For a multiarm study, balancing these factors between treatment arms will be required to eliminate bias. To date, no randomized studies using a neoadjuvant approach have been conducted in pancreatic cancer. As Morganti et al. have suggested, when such studies are planned, it will be critical to understand the prognostic weight of clinical staging data so that appropriate stratification of patients can be assured.

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