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Trends in utilization of neoadjuvant therapy and short-term outcomes in resected pancreatic cancer

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Abstract

BACKGROUND: Surgical resection and chemotherapy offer the only chance of long-term survival for pancreatic cancer. Neoadjuvant therapy (NAT) is increasingly used to optimize outcomes. Trends in NAT utilization and short-term outcomes in resected pancreatic cancer were evaluated.

METHODS: The National Cancer Database (2003 to 2011) was analyzed for pancreatic cancer patients who underwent surgery ± NAT, evaluating utilization, 30- and 90-day mortality, hospital readmissions, and length of stay (LOS).

RESULTS: About 16,007 underwent initial surgery and 1,736 received NAT. Over the past decade, initial surgery and multimodality NAT have steadily decreased, whereas the use of neoadjuvant radiation has remained low and the use of neoadjuvant chemotherapy (neoCT) has steadily increased. Thirty- and 90-day mortality rates and hospital readmissions were significantly higher for NAT vs initial surgery on univariate analysis. There was no significant difference in LOS or readmission rate. On multivariate analysis, neoCT had no significant impact on odds of mortality at 30 and 90 days (hazard ratio = .68, $P = .285$, hazard ratio = 1.32, $P = .161$, respectively). Advanced age, greater comorbidities, greater clinical stage disease, and resection with pancreaticoduodenectomy or total pancreatectomy negatively impacted 30- and 90-day mortality.

CONCLUSION: The use of neoCT has increased over the past decade and does not appear to adversely affect short-term outcomes, including 30- and 90-day mortality, LOS, and readmission rates.

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The authors declare no conflicts of interest.

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Pancreatic cancer is the 10th most common cancer in the United States, but the 4th leading cause of cancer-related death.[1] Despite improvements in other cancer outcomes, pancreatic cancer has exhibited both an increasing incidence and death rate with minimal improvement in survival despite best available therapies.[1] With a sobering overall 5-year survival of 7%, pancreatic cancer remains one of the deadliest malignancies.[1] Upon initial diagnosis, only 10% to 20% of patients present with resectable disease.[2] Even for those eligible for surgical resection, 5-year survival remains under 20%[3–8] and only 15% of these patients experience long-term survival.[9]

With 85% of patients experiencing disease recurrence despite best surgical and medical therapy,[9] and 70% to 85% of patients with evidence of systemic recurrence on autopsy,[10] there is good reason to consider pancreatic cancer as a systemic disease in most patients.[11] Clinical trials such as the European Study Group for Pancreatic Cancer and Charite Onkologie trial demonstrated improved survival with adjuvant chemotherapy compared with surgery alone,[12–14] and adjuvant chemotherapy is now recommended in the National Comprehensive Cancer Network guidelines for resected pancreatic cancers.[15]

Neoadjuvant therapy (NAT) offers several theoretical advantages including the potential to down-stage disease, optimizes margin-negative resections, and allows for better patient selection by providing an opportunity to observe the biologic behavior of the cancer. There have been several reports of increased resectability with NAT due to disease regression from therapy,[16–20] improved median survival,[21–23] and no association with increased postoperative complications.[24–26] The guidelines currently recommend the use of NAT for patients with borderline resectable disease and allow for the consideration of NAT within the context of a clinical trial for resectable disease.[25,27] For all these reasons, administration of NAT appears to be a growing strategy in anatomically resectable or potentially resectable pancreatic cancer.[28]

Despite the survival benefit reported in clinical trials, national practice patterns of NAT in the management of pancreatic cancer, particularly as relates to each type of modality, remain relatively unknown. The objective of this study was to analyze trends in the United States with respect to NAT utilization; in addition, because of the possibility of debilitation from the NAT itself, short-term outcomes in patients receiving NAT and surgical resection to patients undergoing surgery as first therapy for clinical stage I to III pancreatic cancer were compared.

Methods

Data

This study was a retrospective cohort study using data from the National Cancer Database (NCDB), a clinical oncology database, sourced from hospital registry data collected from over 1,500 commission on cancer-accredited facilities. The NCDB captures approximately 80% of cancer cases in the United States from 2003 to 2011.

Patient selection

The study population included patients in the NCDB diagnosed with clinical stages I to III pancreatic adenocarcinoma and carcinoma of the pancreas, who underwent surgical resection, with or without NAT. Of the 17,743 patients diagnosed with stage I to III pancreatic cancer, 16,007 underwent initial surgical resection and 1,736 underwent NAT followed by surgical resection. Patients with clinical stage IV disease or unknown stage were excluded. Clinical stage is a coded variable within the NCDB which is determined per individual cancer institute; it is typically based on cross-sectional imaging, with or without further adjunct tests such as endoscopic ultrasound. Histologies included carcinoma, adenocarcinoma, and subtypes within these histologic groups. Patients who did not undergo surgical resection, underwent an unknown surgical procedure, or who underwent local excision of tumor were excluded. NAT was defined as first course therapy received $\leq$200 days before surgery. This time frame was chosen to capture most patients who underwent NAT, inclusive of those who may also have experienced delays in undergoing surgery. The patients were divided into 2 groups: those who underwent initial surgical resection (n = 16,007) and those who received NAT followed by surgical resection (n = 1,736). NAT was then further stratified as neoadjuvant chemotherapy (neoCT, n = 375), neoadjuvant radiation (neoRT, n = 148), and multimodality therapy (receipt of both neoCT and neoRT, n = 1,213).

Outcomes and covariates

The primary outcomes assessed were trends in utilization, length of hospital stay, 30-day hospital readmission rate, and 30- and 90-day mortality from date of surgery. Univariate analyses controlled for demographic data including age, sex, race, insurance type (private, Medicare, Medicaid, and other government programs, unknown, not insured), median income, and the Charlson-Deyo Comorbidity Index, an index of 15 comorbidities including myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, mild liver disease, diabetes, diabetes with chronic complications, hemiplegia or paraplegia, renal disease, moderate or severe liver disease, and AIDS.[29,30]

Treatment facilities were stratified by facility type (community, comprehensive community, academic or research institution, and other) and geographic region (Northeast, South, Midwest, and West). Disease was characterized by the American Joint Committee on Cancer clinical stage, surgery type (distal pancreatic resection,