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Greater lymph node retrieval and lymph node ratio impacts survival in resected pancreatic cancer

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ABSTRACT

Background: Surgical resection is the mainstay of pancreatic cancer treatment; however, the ideal lymphadenectomy remains unsettled. This study sought to determine whether number of examined lymph nodes (eLNs) and lymph node ratio (LNR) impact survival.

Methods: The U.S. National Cancer Data Base (2003-2011) was reviewed for patients who underwent initial resection for clinical stage I and II pancreatic adenocarcinoma. Univariate and multivariate survival analyses were performed.

Results: Of 14,007 patients, 15.6% had 0-6 eLN, 27.1% 7-12, 13.4% 13-15, and 38.6% > 15 eLN. Median eLN was 11 for pancreaticoduodenectomy, and 14 for distal, total pancreatectomy, or other procedure. ELN >15 was associated with significantly improved survival in both node negative and positive disease ($P < 0.001$, both). In multivariable analysis, 7-12, 13-15, and >15 eLN had improved survival relative to 0-6 eLN (HR 0.87, $P < 0.001$, HR 0.89, $P = 0.002$, HR 0.82, $P < 0.001$, respectively). A total of 34.5% of patients had an LNR of 0, 31.5% ≤ 0.2, 20.3% 0.2-0.4, 11.7% 0.4-0.8, and 2.0% had an LNR >0.8. Patients with LNR 0 had improved survival in T1-T3 disease ($P < 0.01$). In multivariable analysis, higher LNR was negatively associated with survival (LNR 0-0.2: HR 1.44, $P < 0.001$, LNR 0.2-0.4: HR 1.82, $P < 0.001$, LNR 0.4-0.8: 2.03, $P < 0.001$, LNR >0.8, $P < 0.001$). Even with suboptimal eLN (eLN ≤6 or ≤12), higher LNR remained an independent predictor of mortality.

Disclaimer: The National Cancer Data Base (NCDB) is a joint project of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society. The CoC's NCDB and the hospitals participating in the CoC NCDB are the source of the deidentified data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

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Conclusions: Greater lymph node retrieval in stage I & II pancreatic adenocarcinoma may have prognostic value, even in node-negative disease. Lymph node ratio is inversely related to survival and may be useful with suboptimal eLN.

Introduction

Surgical resection with adjuvant therapy offers the only potentially curative treatment for pancreatic adenocarcinoma. As such, extent of resection, particularly in regard to lymphadenectomy, remains an important topic of debate. A standard lymphadenectomy entails the removal of lymph nodes at the pancreas, duodenum, the right side of the hepatoduodenal ligament and SMA, and the anterior and posterior pancreaticoduodenal lymph nodes.[1] An extended lymphadenectomy involves further resection of the soft tissue of the retroperitoneum from the hilum of the right kidney to the left lateral border of the aorta on the right, and the portal vein to the origin of the inferior mesenteric artery on the left, in addition to the standard lymphadenectomy.[1] While this remains routine practice in Japan, several prospective randomized controlled trials demonstrating no improvement in survival have prompted the standard lymphadenectomy to be the standard of care in the United States.[2-5] Current National Comprehensive Cancer Network guidelines recommend standard lymphadenectomy including all the regional lymph nodes.[6] Based on retrospective reviews suggesting improved prognosis with greater number of examined lymph nodes, some groups have advocated a minimum number of lymph nodes examined of 11-17.[7-9] However, the ideal number of retrieved lymph nodes remains unsettled. Lymph node ratio (LNR), defined as the ratio of number of positive lymph nodes to the total number of examined lymph nodes, has also been reported as a prognostic indicator in resected pancreatic disease.[10,11] Interestingly, the American Joint Committee on Cancer staging system classifies lymph node involvement on a binary basis, as either N1: regional lymph node involvement, or N0: no regional lymph node involvement, with no mention of number of lymph nodes examined, number of positive lymph nodes, or LNR.[12]

The objective of this study was to determine whether number of examined lymph nodes (eLNs), a proxy for lymphadenectomy, and LNR are associated with survival in patients with stage I or II pancreatic carcinoma or adenocarcinoma.

Methods

Data

This study was a retrospective cohort study using data from the National Cancer Data Base (NCDB), a clinical oncology database, sourced from hospital registry data collected from over 1500 Commission on Cancer accredited facilities in the United States. The NCDB captures approximately 80% of the cancer cases in the United States from 2003 to 2011.[13] The NCDB contains readily available deidentified data, and therefore this study was not subject to institutional review board approval or oversight.

Patient selection

This study population included patients diagnosed with clinical stages I-II pancreatic adenocarcinoma and carcinoma in the NCDB between 2003 and 2011, who underwent surgical resection (n = 15,093). Patients who received neoadjuvant therapy (n = 1050) were excluded. Clinical stage is coded in the NCDB according to standard practice at each individual institution. Histologies included in this analysis were adenocarcinoma identified using the third edition of the International Classification of Diseases for Oncology primary site codes: C250-C254, C257-C259 and histology codes: 8050/3 8140/3, 8144/3, 8148/3, 8160/3, 8230/3, 8255/3, 2890/3, 8310/3, 8323/3, 8342/3, 8346/3, 8380/3, 8430/3, 8460/3, 8461/3, 8480/3, 8481/3, 8500/3, 8503/3, 8504/3, 8507/3, 8510/3, 8521/3, 8523/3, 8550/3, 8560/3, 8562/3, 8570/3, 8574/3, 8576/3. Patients who underwent local excision of tumor were excluded (n = 36), to best capture those patients undergoing formal pancreatic resection.[14]

Outcomes and covariates

The primary outcome assessed was survival from date of diagnosis. We controlled for other patient and disease characteristics, including age, sex, race/ethnicity, insurance type (private, Medicare, Medicaid, and other government programs, unknown, not insured), median income, and the Charlson/Deyo comorbidity index (CCI). The CCI is a weighted index of 15 comorbidities including myocardial

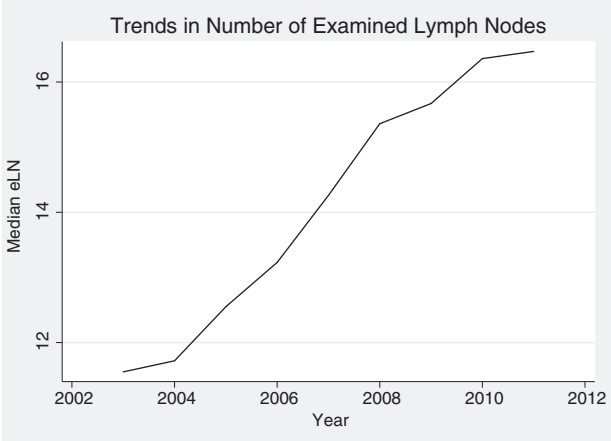

Fig. 1 – Trends in number of examined lymph nodes.