Increased pancreatic cancer survival with greater lymph node retrieval in the National Cancer Data Base

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ABSTRACT

Background: We evaluated the role of lymph node (LN) retrieval in pancreatic adenocarcinoma (PA) patients undergoing pancreaticoduodenectomy (PD).
Methods: We utilized the National Cancer Data Base; Cox regression models and logistic regression models were used for statistical evaluation.
Results: We evaluated 26,792 patients with PA who underwent PD. The mean LN retrieved in LN(−) patients was 10.8 vs 14.4 for LN(+) patients (P < 0.0001). Greater LN retrieval is an independent predictor of a negative microscopic margin and decreased length of stay. The median survival of LN(−) patients exceeded that of LN(+) patients (24.5 vs 15.1 months, P < 0.0001). Increasing LN retrieval is a significant predictor of survival in all patients, and in LN(−) patients. The relationship of increased LN retrieval and enhanced survival is a nearly linear trend.
Conclusions: Rather than demonstrating an inflection point that defines the extent of adequate lymphadenectomy, this dataset demonstrates an incremental relationship between LN retrieval and survival.
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1. Introduction

The implementation of multimodality therapy has refined the role of lymphadenectomy in gastrointestinal malignancies. Historically, the value of lymphadenectomy for gastrointestinal malignancies stems from its ability to provide prognostic information, and potentially as a form of regional nodal control. More recently, lymphadenectomy parameters have been utilized as surrogates for the quality of the oncologic resection and of its subsequent pathologic evaluation. Various consensus statements and guidelines have attempted to define the minimum number of lymph nodes which defines an adequate lymphadenectomy for colorectal, gastric, and esophageal adenocarcinoma.[1–5] Failure to meet these minimum lymph node thresholds has been proposed as a proxy for the quality of cancer care.[6]

The majority of the data relating to the appropriate extent of lymphadenectomy for pancreatic head adenocarcinoma resection relates to the performance of standard versus extended lymphadenectomy. Compared to standard lymphadenectomy, extended lymphadenectomy at the time of pancreaticoduodenectomy (PD) failed to improve long-term survival in 4 randomized controlled trials.[7–13] The anatomic boundaries for "standard" lymphadenectomy has been defined by the International Study Group on Pancreatic Surgery.[14] Utilizing retrospective databases for pancreatic cancer patients, investigators have proposed the minimum number of lymph nodes required for an adequate lymphadenectomy to be between eleven to sixteen lymph nodes after PD.[15–20] These studies have not considered the effect of the extent of standard lymphadenectomy on inpatient length of stay and on hospital readmission following discharge.

The purpose of this study is to investigate the relationship of short and long-term outcomes of PD with respect to the number of lymph nodes (LN) examined in the surgical specimen. The National Cancer Data Base (NCDB) is sourced from hospital registry data that are collected from Commission on Cancer (CoC) facilities accredited by the American College of Surgeons. These data represent

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approximately 70% of the newly diagnosed cancer cases nationwide in over 1500 CoC facilities.[21]

2. Material & methods

2.1. Patient selection

Patients with primary adenocarcinoma were identified from the NCDB data set from 1998 to 2011. Patients with non-adenocarcinoma pancreatic tumors were excluded, as were those whose adenocarcinoma tumors were recorded as being metastatic to the pancreas. Patients with less than 90 days of follow up available were eliminated. Pancreaticoduodenectomy (PD) patients were identified using the following RX_SUMM_SURG_PRIM_SITE values: "Whipple, NOS", "pylorus sparing Whipple (without partial gastrectomy)" and "standard Whipple (with partial gastrectomy)". Patients undergoing distal pancreatectomy, extended pancreatectomy, total pancreatectomy, or other unspecified pancreatic resections were excluded.

2.2. Statistical analysis

Patient characteristics and clinical measures for health status and treatments were summarized using descriptive statistics, such as means, standard deviations, frequencies, and percentages. Logistic regression models were used to assess bivariate and multivariate predictors of mortality, lymph node status, margin status, and readmission status. Linear regression models were used to assess bivariate and multivariate predictors of length of stay. Cox regression models were used to assess bivariate and multivariate predictors of time to death. The Kaplan-Meier method was used to generate survival curves and the log-rank test was used to compare survival curves. Correlation analysis was used to assess the relationship between the number of lymph nodes examined and the median survival time. Variable selection for multivariable analysis was based on the use of the stepwise procedure, which assumed a significance level of 0.05 for entry of a variable into the model and 0.0001 for a variable to remain in the model, and also on the clinical relevance of the variable to the specific outcome. Statistical tests were two-sided. Data analyses were performed using SAS, version

Table 1
Patient and tumor characteristics.

Characteristics	All (N = 26,792) n (%)	Node Positive (n = 16,697) n (%)	Node Negative (n = 10,095) n (%)
Demographics			
Age, mean (SD)	65.9 (10.8)	65.6 (10.7)	66.4 (32.2)
Gender			
Male	13,583 (50.7)	8549 (51.2)	5034 (49.9)
Female	13,209 (49.3)	8148 (48.8)	5061 (50.1)
Race			
White	23,261 (86.8)	14,565 (87.2)	8696 (86.1)
Black	2443 (9.1)	1494 (9)	949 (9.4)
Others	1088 (4.1)	638 (3.8)	450 (4.5)
Health Status and Treatments			
Grade			
Undifferentiated	290 (1.2)	184 (1.2)	106 (1.2)
Well Differentiated	2670 (10.9)	1344 (8.5)	1326 (15.3)
Moderately Differentiated	12,518 (51)	8058 (50.7)	4460 (51.5)
Poorly Differentiated	9083 (37)	6316 (39.7)	2767 (32)
AJCC Stage			
0	519 (2)	3 (0.02)	516 (5.3)
I	3752 (14.5)	120 (0.7)	3632 (37.4)
II	16,224 (62.6)	11,256 (69.6)	4968 (51.1)
III	4190 (16.2)	3942 (24.4)	248 (2.6)
IV	1214 (4.7)	859 (5.3)	355 (3.7)
Nodes Examined			
0—4	3602 (13.4)	1355 (8.1)	2247 (22.3)
5—7	4093 (15.3)	2222 (13.3)	1871 (18.5)
8—9	2880 (10.8)	1793 (10.7)	1087 (10.8)
10—11	2862 (10.7)	1837 (11)	1025 (10.2)
12—14	3791 (14.2)	2525 (15.1)	1266 (12.5)
≥ 15	9564 (35.7)	6965 (41.7)	2599 (25.8)
Nodal Status			
Negative	10,095 (37.7)	0 (0)	10,095 (100)
Positive	16,697 (62.3)	16,697 (100)	0 (0)
Tumor Size	33.9 (26.7)	34.8 (24)	32.2 (30.7)
Surgery Procedure of Primary Site			
Local/Partial Pancreatectomy	26,792 (100)	16,697 (100)	10,095 (100)
Chemotherapy	14,447 (56.9)	9712 (61.8)	4735 (48.9)
Radiation	9922 (37.3)	6520 (39.4)	3402 (33.9)
Margin Status			
Negative	20,165 (75.3)	11,824 (70.8)	8341 (82.6)
Positive	6627 (24.7)	4873 (29.2)	1754 (17.4)
Facility Type			
Other	10,327 (38.6)	6417 (38.4)	3910 (38.7)
Academic	16,465 (61.5)	10,280 (61.6)	6185 (61.3)
Readmission	2195 (11.1)	1423 (11.4)	772 (10.7)
Length of Stay (days)	12.9 (10.8)	12.7 (10.5)	13.2 (11.3)
Neoadjuvant Chemotherapy or XRT	1630 (6.1)	699 (4.2)	931 (9.2)
Post operative survival ≥ 90 days	24,425 (91.2)	15,178 (90.9)	9247 (91.6)