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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.

Keywords

Pancreatic cancer; National Cancer Data Base; lymphadenectomy

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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 approximately 70% of the newly diagnosed cancer cases nationwide in over 1,500 CoC facilities.[21]

Material & Methods

Patient Selection

Patients with primary adenocarcinoma were identified from the NCDB data set from 1998–2011. 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.

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 9.4 (SAS Institute, Cary, NC, USA), and SPSS version 22 (IBM Corp., Armonk, NY, USA). This study was approved by the University of Alabama at Birmingham Institutional Review Board.

Results

Patient and tumor characteristics

After applying the specified selection criteria, 27,752 patients with pancreatic adenocarcinoma underwent PD from 1,268 institutions (17,048 patients had PD performed at academic/research programs, and 10,704 patients had PD performed at comprehensive community cancer programs or community cancer programs). Definitive data relating to pathologic margin status was available for 96.5% of patients. Margins status was recorded as “cannot be evaluated” for 960 (3.5%) patients; these cases were excluded for a total of 26,792 patients. Median age was 65.9 years (range 18–90 years), 50.7% were male and 49.3% female [Table 1]. Mean tumor size was 33.9 mm (range 10 mm to 99 mm), and 75.3% were resected with negative surgical margins. PD including partial gastrectomy was the most common operation performed (79%), followed by a pylorus-sparing technique (12.6%), and PD not otherwise specified (8.4%). 62.3% (16,697/26,792) had LN metastasis and 56.9% of patients received adjuvant chemotherapy.

Lymphadenectomy parameters

The median number of LN examined was 11 (range 1–90). The mean number of LN retrieved in patients who underwent standard PD was slightly lower than with pylorus-sparing PD (12.9 versus 13.7, $P<0.0001$). The mean number of LN retrieved at academic centers is greater than at non-academic centers (13.9 vs 11.5, $P<0.0001$). Patients with LN metastasis had a greater number of nodes examined (10.8 total nodes examined in LN negative patients versus 14.4 total nodes examined in LN positive patients, $P<0.0001$). Patients with greater than 10 LN retrieved had a greater number of metastatic lymph nodes (mean of 2.8 versus 1.1 positive LN, $P<0.0001$). A greater number of LN examined was an independent predictor of identifying a positive node (adjusted OR 1.06, 95% CI 1.05–1.06, $P<0.0001$) [Table 2].

Multivariable predictors of increased risk of negative microscopic margins include AJCC tumor stage, number of LN examined, nodal status, and resection at an academic facility [Table 3].

Inpatient hospital course

Overall, the NCDB inpatient length of stay field was complete for 71.6% of cases (71.1% LN+ patients, 68.1% LN− patients); patients with incomplete length of stay data were excluded from this portion of the analysis. Patients with negative LN had a length of stay of 13.2 days versus 12.7 for LN+ patients, P<0.0001. The number of postoperative inpatient days until hospital discharge was investigated as a surrogate for the physiologic demands of the pancreatic resection. We hypothesized that if a more aggressive lymphadenectomy significantly increased the PD morbidity, then this may be reflected in the duration of inpatient stay following pancreatectomy. This idea is supported by data from a randomized controlled trial which showed that patients who underwent pancreaticoduodenectomy with extended lymphadenectomy demonstrated a statistically significant increase in postoperative length of hospital days and risk for postoperative complication compared to patients who underwent a standard lymphadenectomy.[12] Our data showed that a greater number of lymph nodes examined was an independent predictor of fewer postoperative inpatient days (β-coefficient - 0.05, 95% CI (−0.07, −0.03), P<0.0001); this relationship was preserved for all patients, node9 positive patients, and node-negative patients [Table 4]. Irrespective of nodal status, other multivariable predictors of fewer postoperative inpatient days included younger patient age, increased tumor size, negative margin status, and academic facility type [Table 4]. In the nodenegative subset, only the number of LN examined and academic facility type were predictive of decreased postoperative inpatient days.

Data pertaining to 30-day hospital readmission following PD was complete for 75.3% of cases; patients with incomplete hospital readmission data were excluded from this analysis. There were small differences in the proportion of patients who had an unplanned hospital readmission recorded when comparing LN+ and LN- patients (8.5% versus 8.0%, P<0.0001). In all patients and in node-negative patients, both a greater number of lymph nodes examined and negative margin status were significant multivariable predictors of decreased hospital readmission [Table 5].

Survival analysis

Node-negative patients have an increased median survival compared to node-positive patients (24.5 months versus 15.1 months, respectively, P<0.0001; Figure 1). The optimal threshold for defining adequate lymph node retrieval was examined using the methodology set forth by Tomlinson et al.[20] We dichotomized the node-negative subset of patients based on several lymph node retrieval thresholds; a lymph node threshold of 10 demonstrated the greatest statistical significance when evaluating log-rank x^2 values of univariate Kaplan-Meier survival curves [Table 6]. Overall, the relationship between LN retrieval and median survival is a linear trend (P<0.0001, r=0.89; Figure 2). The survival of patients who underwent PD at academic/research programs had an increased median survival compared to patients who had PD performed at non-academic/research programs (19.4 versus 15.2 months, P<0.0001). The multivariable predictors of mortality after pancreatectomy include advanced patient age, higher tumor grade, increasing AJCC stage, fewer number of lymph nodes examined, positive nodal status, increasing number of positive LN, no adjuvant chemotherapy, positive margin status, increased length of stay, and resection at a non-academic facility [Table 7]. These multivariable relationships with respect to mortality after pancreatectomy are preserved among all patients, node-positive patients, and node-negative patients. We then excluded patients who had AJCC stage IV pancreatic cancer, and examined multivariable predictors of mortality after pancreatectomy. The results were very similar to those displayed in Table 7 for all patients, node-positive patients, and node-negative patients. This was expected since there were just 1214 patients (4.5% of the total number of patients) with stage IV pancreatic cancer, of which 859 were node-positive patients (0.5% of the total number of node-positive patients) and 355 were node-negative patients (3.5% of the total number of node-negative patients) [data not shown].

Discussion

Compared to other gastrointestinal malignancies, pancreatic adenocarcinoma remains a challenging disease on account of its often late presentation and limited efficacy of systemic chemotherapy. Multiple series, ours included, have demonstrated that node-negative patients have a superior survival compared to node-positive patients after PD. In addition, there is ample evidence that among the node-negative subset, increasing lymph node retrieval counts are associated with increased survival.[22–26] Despite having been proposed as a quality benchmark by a number of relevant societies,[1–3, 6] little has been published exploring the relationship between adequacy of lymphadenectomy and other important PD outcomes such as frequency of negative microscopic margins, postoperative length of inpatient stay, and hospital readmission rate.

While the long-term benefit of adequate lymphadenectomy on survival has been demonstrated, the effect of lymphadenectomy on short-term outcomes has not been explored. Consistent with its adoption as a quality measure, we demonstrate that an increasing number of LN examined is a multivariable predictor of achieving a negative microscopic margin status. An adjusted odds ratio of 1.02 translates into a 2% increase in the probability of achieving a negative surgical margin for each additional lymph node examined. The NCDB structure does not allow us to establish whether the relationship between extent of lymphadenectomy and microscopic margin status is attributable to more aggressive surgical dissection, more thorough pathologic evaluation, or both. Further reinforcing the importance of adequate lymphadenectomy, we demonstrate that increased lymph node retrieval is associated with a decreased length of postoperative stay, along with several other parameters. Obtaining a negative surgical margin is another measure of quality control in oncologic surgery. A negative margin resection was associated with decreased length of postoperative stay in our analysis. The increased risk of hospital readmission demonstrated on multivariable analysis with respect to increased lymph node retrieval is small, but may reflect the physiologic stress of a thorough and complete lymphadenectomy.

Our data detail several PD performance characteristics of academic versus non-academic facilities. Patients who underwent PD at an academic facility had a greater number of lymph nodes retrieved versus those at non-academic facilities. Likewise, on multivariable analysis performance of PD at an academic facility increased the probability of obtaining a negative surgical margin. While the length of postoperative stay was shorter, the probability of hospital readmission was greater at academic facilities compared to non-academic facilities. The risk of mortality was decreased in patients undergoing PD at academic versus non-academic facilities in a multivariable model. Further study is necessary to determine whether the superior performance characteristics are attributable to the higher patient volumes found at academic facilities or to other factors not captured in the NCDB data set.

Beyond its retrospective nature, our study has several potential limitations. This data set that includes 27,752 patients provides robust statistical power which can over-emphasize small, clinically irrelevant differences.[27, 28] For example, the small difference in the mean number of lymph nodes retrieved in patients who underwent PD with standard antrectomy versus pyloruspreservation was statistically significant (12.9 versus 13.7, P<0.0001). Consequently, discretion must be used in interpreting over-powered data such as these. Another limitation of our study is that not all fields in the NCDB data set are uniformly populated. For example, definitive data relating to pathology margin status was not available for 3.5% of patients while 30-day readmission data was missing for 26.3% patients. Commission on Cancer designation requires hospitals to provide various elements of cancer care infrastructure, and as such, the NCDB data set may not represent a true cross section of all hospitals performing PD in the United States.[29] Cancer antigen 19-9 levels have often been associated with pancreatic cancer stage and likely impacts multiple parameters included in this study. We did not utilize cancer antigen 19-9 values because in the NCDB data set any value of 99 cannot be distinguished from patients with any value greater than 98.[30] A small proportion of our dataset, 1,330 (4.8%), has AJCC Stage IV disease. Presumably these patients had unplanned intra- or post-operative diagnosis of metastasis, and were initially included in order to preserve a “real world” approach to our data analysis. The multivariable logistic regression analysis was repeated after omitting the Stage IV patients; this did not significantly impact our results [data not shown]. Data regarding tumor recurrence is not available through the NCDB, an inherent limitation of studies utilizing this otherwise valuable data set. The lack of NCDB morbidity data fields motivates the hypothesis that a more aggressive lymphadenectomy may result in an increased postoperative stay, and is supported by data from a randomized controlled trial.[12]

The main goal of this study was to use the NCDB data set to re-evaluate what constitutes an adequate lymphadenectomy. Previous studies largely rely on either single-institution or SEER data. An advantage of the NCDB is that, while SEER covers an estimated 28% of the United States population, the NCDB data set includes approximately 70% of all new cancer diagnoses.[31] SEER data is limited in that it does not report the pathologic margin status, another key PD quality measure. Our data demonstrate that an increasing number of lymph nodes examined was a multivariable predictor of identifying a positive lymph node. The optimal threshold for defining adequate lymph node retrieval was examined using the methodology set forth by Tomlinson et al; a lymph node threshold of 10 demonstrated the greatest statistical significance when evaluating log-rank x^2 values of univariate Kaplan-Meier survival curves, in comparison to a previously published threshold of 15 LN [Table 6].[20] The more aggressive nodal retrieval cutoff thresholds had greater separation in median survival, but their diminishing x^2 values are likely due to the fact that these survival curves intersect as one progresses past the point of median survival. These relationships challenge the notion of defining the adequacy of lymphadenectomy with a discrete number. This point is highlighted by a nearly linear plot of lymph node retrieval versus median survival time; there is no LN retrieval threshold which is associated with a sharp inflection in survival [Figure 2]. The difference in survival curves at specific lymph node retrieval thresholds is also likely attributable to the stage migration phenomenon. For patients who undergo resection as their initial treatment modality, adjuvant therapy is indicated for all patients following PD independent of the nodal status even if an inadequate lymphadenectomy failed to reveal a metastatic LN.[32] Therefore a more robust nodal evaluation is unlikely to alter postoperative treatment recommendations. Because LN retrieval is associated with an increased probability of a negative surgical margin and a decreased length of stay, a robust LN retrieval should be regarded as one of several indicators of a high quality PD. Our data show that 40% of patients had fewer than 10 LN retrieved during PD [Table 1], which is an opportunity for improvement. Instead of motivating a specific lymphadenectomy policy definition, perhaps the greatest benefit of these data is to promote the collaboration of surgeons and pathologists in the resection and identification of lymph nodes as one facet of a high quality pancreatic cancer program.

Conclusion

Because LN retrieval is associated with an increased probability of a negative surgical margin and a decreased length of stay, a robust LN retrieval should be regarded as one of several indicators of a high quality PD. Our data show that 40% of patients had fewer than 10 LN retrieved during PD [Table 1], which is an opportunity for improvement. Instead of motivating a specific lymphadenectomy policy definition, perhaps the greatest benefit of these data is to promote the collaboration of surgeons and pathologists in the resection and identification of lymph nodes as one facet of a high quality pancreatic cancer program.

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Synopsis

Accurate staging of the regional lymph nodes is crucial in determining prognosis following pancreaticoduodenectomy for adenocarcinoma. The National Cancer Data Base was utilized to evaluate the short- and long-term benefits of a robust lymphadenectomy.

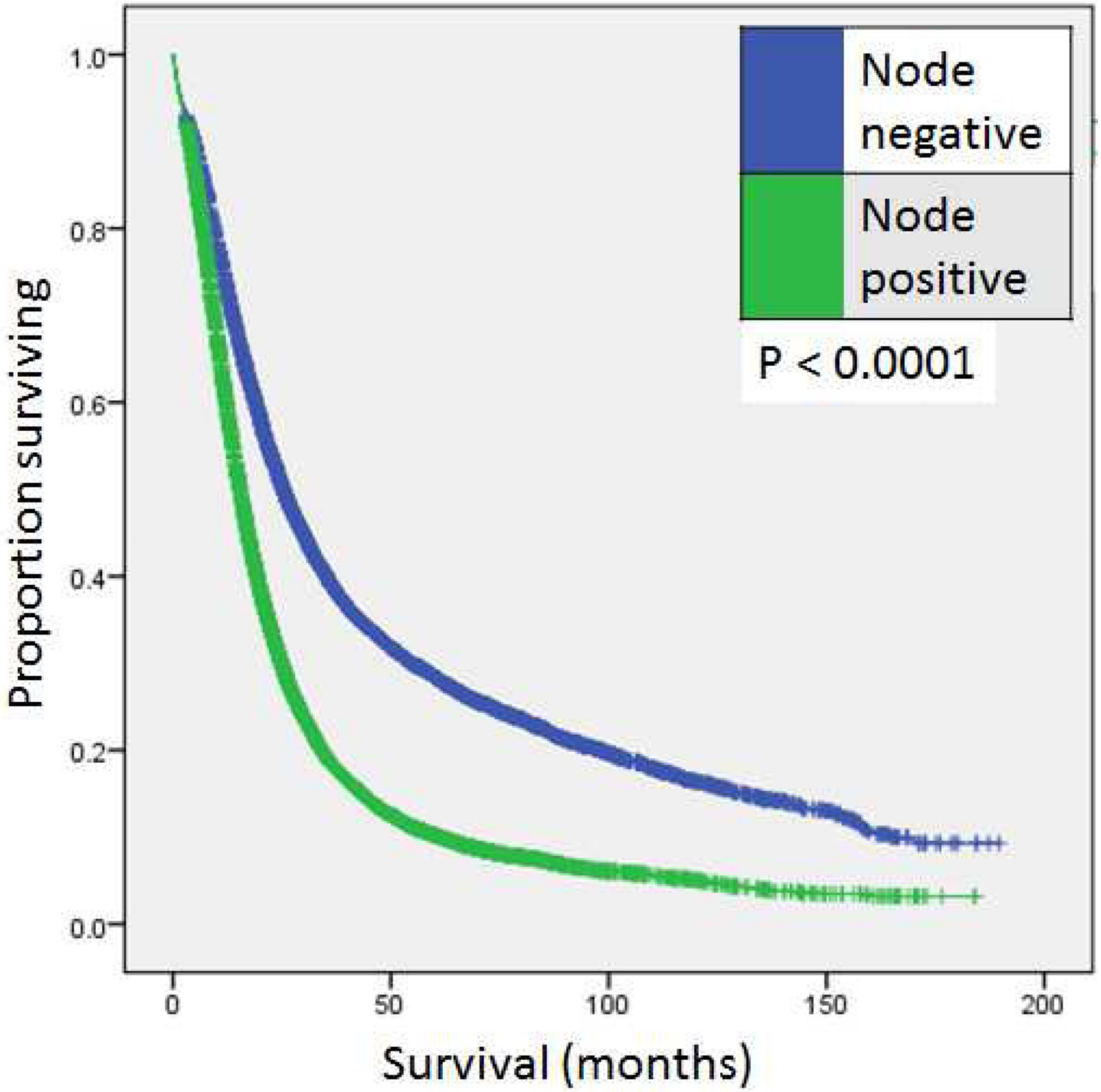

Figure 1.
Kaplan-Meier survival curves of all patients stratified by nodal status (negative lymph nodes versus 1 or more positive lymph nodes). The p value is from the log-rank test comparing the two curves.

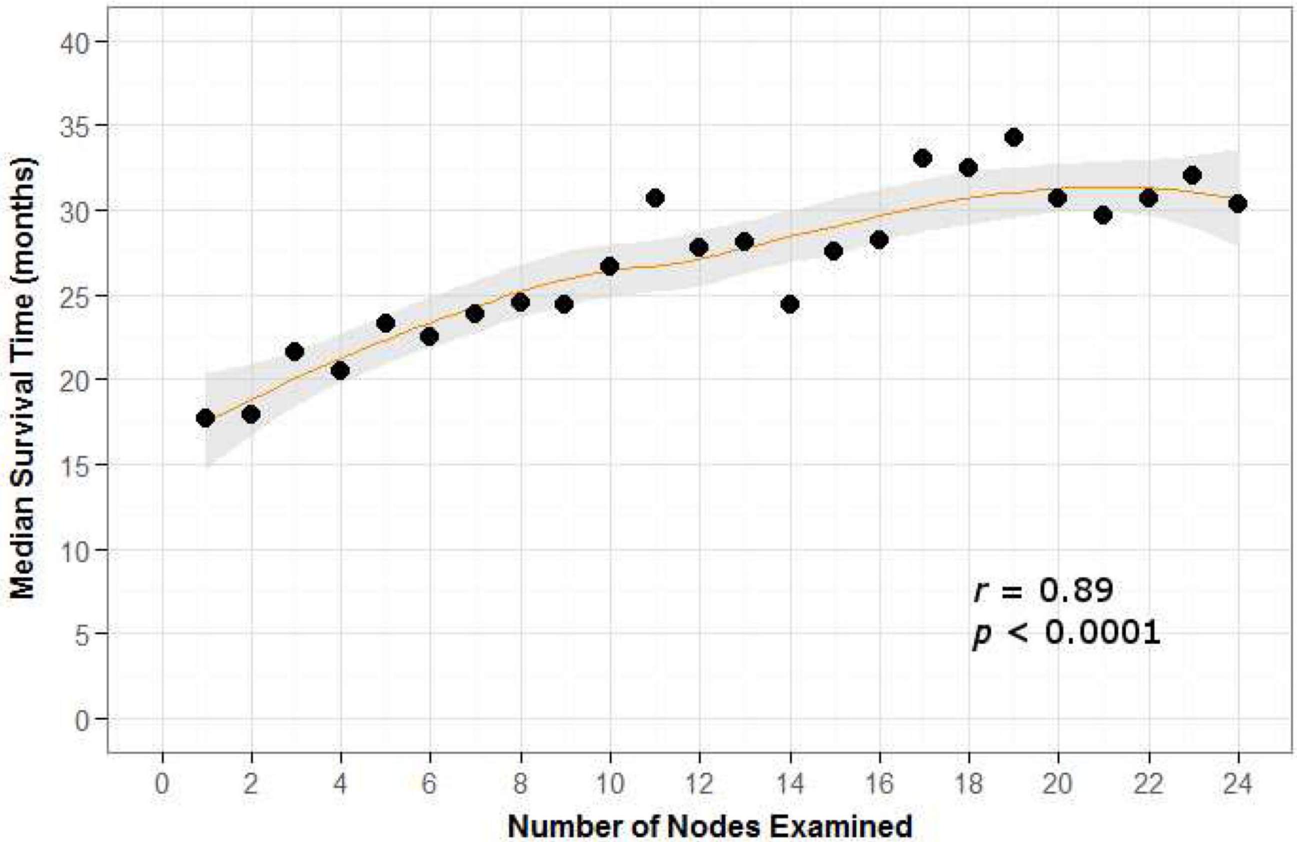

Figure 2.

Scatter plot of median survival time versus number of LN examined with a fitted LOESS[33] curve and 95% CI for lymph node negative patients.

Table 1

Patient and tumor characteristics

Characteristics	All (N=26792)	Node Positive (n=16697)	Node Negative (n=10095)
Demographics	***n (%)***	***n (%)***	***n (%)***
Age, mean (SD)	65.9 (10.8)	65.6 (10.7)	66.4 (32.2)
Gender			
Male	13583 (50.7)	8549 (51.2)	5034 (49.9)
Female	13209 (49.3)	8148 (48.8)	5061 (50.1)
Race			
White	23261 (86.8)	14565 (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	12518 (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	16224 (62.6)	11256 (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	10095 (37.7)	0 (0)	10095 (100)
Positive	16697 (62.3)	16697 (100)	0 (0)
Tumor Size	33.9 (26.7)	34.8 (24)	32.2 (30.7)
Surgery Procedure of Primary Site			
Local/Partial Pancreatectomy	26792 (100)	16697 (100)	10095 (100)
Chemotherapy	14447 (56.9)	9712 (61.8)	4735 (48.9)
Radiation	9922 (37.3)	6520 (39.4)	3402 (33.9)
Margin Status			

Characteristics	All (N=26792)	Node Positive (n=16697)	Node Negative (n=10095)
Demographics	***n (%)***	***n (%)***	***n (%)***
Negative	20165 (75.3)	11824 (70.8)	8341 (82.6)
Positive	6627 (24.7)	4873 (29.2)	1754 (17.4)
Facility Type			
Other	10327 (38.6)	6417 (38.4)	3910 (38.7)
Academic	16465 (61.5)	10280 (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	24425 (91.2)	15178 (90.9)	9247 (91.6)

Table 2

Multivariable logistic regression analysis evaluating the likelihood of lymph node metastasis. This includes both lymph node positive and lymph node negative patients.

Characteristics		**All (N=26792)**	
Demographics	***adj. OR***	***95% C.I.***	***p***
Age	1	(0.99, 1)	0.009
Health Status and Treatments			
Grade			<.0001
Undifferentiated	ref	ref	
Well Differentiated	0.59	(0.42, 0.82)	
Moderately Differentiated	0.77	(0.54, 1.12)	
Poorly Differentiated	0.91	(0.63, 1.32)	
AJCC Stage			<.0001
0	ref	ref	
I	1.09	(0.33, 3.57)	
II	62.6	(19.5, 201.6)	
III	45.4	(13.9, 148)	
IV	70.4	(21.5, 231.2)	
Nodes Examined	1.06	(1.05, 1.06)	<.0001
Tumor Size	1	(1, 1)	0.7
Margin Status			<.0001
Negative	ref	ref	
Positive	1.64	(1.5, 1.8)	
Facility Type			0.09
Other	ref	ref	
Academic	0.93	(0.86, 1.01)	

Table 3

Multivariable logistic regression analysis evaluating the likelihood of positive surgical margin. This analysis includes both lymph node positive and lymph node negative patients.

Characteristics	**All (N=26792)**		
Demographics	***adj. OR***	***95% C.I.***	***p***
Age	1	(1, 1.01)	0.2
Health Status and Treatments			
Grade			0.026
Undifferentiated	ref	ref	
Well Differentiated	0.86	(0.6, 1.22)	
Moderately Differentiated	0.86	(0.61, 1.21	
Poorly Differentiated	0.78	(0.55, 1.09)	
AJCC Stage			<.0001
0	ref	ref	
I	1.14	(0.54, 2.42)	
II	0.53	(0.25, 1.12)	
III	0.19	(0.09, 0.42)	
IV	0.3	(0.14, 0.64)	
Nodes Examined	1.02	(1.01, 1.02)	<.0001
Nodes Positive	0.94	(0.93, 0.96)	<.0001
Tumor Size	0.99	(0.99, 1)	<.0001
Facility Type			<.0001
Other	ref	ref	
Academic	1.3	(1.2, 1.4)	
Nodal Status			<.0001
Negative	ref	ref	
Positive	0.73	(0.66, 0.81)	

Table 4

Multivariable logistic regression analysis evaluating the factors associated with increased likelihood of length of stay. This analysis includes both lymph node positive and lymph node negative patients.

Characteristics	All (N=26792)			Node Positive (n=16697)			Node Negative (n=10095)		
Demographics	***Estimate***	***95% C.I.***	***p***	***Estimate***	***95% C.I.***	***p***	***Estimate***	***95% C.I.***	***p***
Age[1]	0.07	(0.05, 0.08)	<.0001	0.07	(0.05, 0.09)	<.0001	0.06	(0.04, 0.09)	<.0001
Health Status and Treatments									
Grade			0.59			0.67			0.84
Undifferentiated	ref	ref		ref	ref		ref	ref	
Well Differentiated	0.99	(−1.04, 3.02)		1.21	(−1.29, 3.71)		0.54	(−2.96, 4.05)	
Moderately Differentiated	0.8	(−1.13, 2.74)		1.06	(−1.27, 3.43)		0.31	(−3.09, 3.72)	
Poorly Differentiated	0.72	(−1.22, 2.67)		1.03	(−1.33, 3.38)		0.12	(−3.31, 3.55)	
AJCC Stage			0.25			0.008			0.33
0	ref	ref		ref	ref		ref	ref	
I	−0.1	(−3.72, 3.51)		8.11	(−8.47, 24.7)		−0.47	(−4.38, 3.43)	
II	0.25	(−3.34, 3.85)		5.55	(−10.8, 21.9)		0.14	(−3.76, 4.03)	
III	0.13	(−3.66, 3.92)		5.12	(−11.3, 21.5)		0.85	(−3.72, 5.43)	
IV	1.19	(−2.64, 5.02)		6.91	(−9.49, 23.3)		−0.46	(−5.38, 5.43)	
Nodes Examined[1]	−0.05	(−0.07, −0.03)	<.0001	−0.04	(−0.06, −0.02)	0.0005	−0.09	(−0.13, −0.05)	<.0001
Nodes Positive[1]	−0.01	(−0.08, 0.06)	0.77	na	na	na	na	na	na
Tumor Size[1]	−0.01	(−0.02, −0.003)	0.006	−0.01	(−0.02, −0.002)	0.02	−0.008	(−0.02, 0.002)	0.1
Margin Status			0.07			0.21			0.2
Negative	ref	ref		ref	ref		ref	ref	
Positive	0.35	(−0.03, 0.74)		0.28	(−0.16, 0.71)		0.53	(−0.28, 1.33)	
Facility Type			<.0001			<.0001			<.0001
Other	ref	ref		ref	ref		ref	ref	
Academic	−1.46	(−1.81, -1.12)		−1.51	(−1.92, -1.1)		−1.35	(−1.97, −0.73)	
Nodal Status			0.05			na			na
Negative	ref	ref		ref	ref		ref	ref	

Characteristics	All (N=26792)			Node Positive (n=16697)			Node Negative (n=10095)		
Demographics	***Estimate***	***95% C.I.***	***p***	***Estimate***	***95% C.I.***	***p***	***Estimate***	***95% C.I.***	***p***
Positive	−0.46	(−0.93, 0.002)		na	na		na	na	

na: indicates that this parameter was not included in the multivariable analysis for the indicated patient subset.

[1] Estimate represents the slope (B-coefficient) of the regression line.

Table 5

Multivariable logistic regression analysis evaluating the factors associated with increased likelihood of 30-day hospital readmission. This analysis includes both lymph node positive and lymph node negative patients.

Characteristics	All (N=26792)			Node Positive (n=16697)			Node Negative (n=10095)		
Demographics	***adj. OR***	***95% C.I.***	***p***	***adj. OR***	***95% C.I.***	***p***	***adj. OR***	***95% C.I.***	***p***
Age	1	(1, 1.01)	0.35	1	(1, 1.01)	0.86	1.01	(1, 1.01)	0.19
Health Status and Treatments									
Grade			0.33			0.46			0.38
Undifferentiated	ref	ref		ref	ref		ref	ref	
Well Differentiated	0.76	(0.45, 1.28)		0.8	(0.43, 1.5)		0.72	(0.29, 1.78)	
Moderately Differentiated	0.68	(0.41, 1.13)		0.73	(0.41, 1.33)		0.65	(0.27, 1.57)	
Poorly Differentiated	0.7	(0.42, 1.16)		0.79	(0.44, 1.44)		0.59	(0.24, 1.44)	
AJCC Stage			0.45			0.35			0.5
0	ref	ref		ref	ref		ref	ref	
I	1.27	(0.6, 2.71)		2.68	(0.08, 91.5)		1.41	(0.67, 2.98)	
II	1.13	(0.53, 2.39)		1.18	(0.04, 36.3)		1.3	(0.62, 2.73)	
III	1.1	(0.5, 2.43)		1.08	(0.04, 33.4)		1.51	(0.62, 3.69)	
IV	1.39	(0.62, 3.12)		1.34	(0.04, 41.7)		2.2	(0.77, 6.29)	
Nodes Examined	1.01	(1.01, 1.02)	0.0007	1.01	(1, 1.02)	0.005	1.02	(1, 1.03)	0.009
Nodes Positive	1.01	(0.99, 1.03)	0.28	na	na	na	na	na	na
Tumor Size	1	(1, 1)	0.99	1	(1, 1)	0.052	1.01	(1, 1.01)	0.07
Margin Status			0.002			0.07			0.003
Negative	ref	ref		ref	ref		ref	ref	
Positive	0.84	(0.75, 0.94)		0.89	(0.78, 1.01)		0.72	(0.58, 0.89)	
Facility Type			0.4			0.55			0.59
Other	ref	ref		ref	ref		ref	ref	
Academic	0.96	(0.86, 1.06)		0.96	(0.85, 1.09)		0.95	(0.8, 1.14)	
Length of Stay (days)	1	(0.99, 1)	0.019	1	(0.99, 1)	0.057	1	(0.99, 1)	0.13
Nodal Status			0.17			na			na
Negative	ref	ref		ref	ref		ref	ref	

Characteristics	All (N=26792)			Node Positive (n=16697)			Node Negative (n=10095)		
Demographics	***adj. OR***	***95% C.I.***	***p***	***adj. OR***	***95% C.I.***	***p***	***adj. OR***	***95% C.I.***	***p***
Positive	0.91	(0.79, 1.04)		na	na		na	na	

na: indicates that this parameter was not included in the multivariable analysis for the indicated patient subset.

Table 6

Performance of multiple cutoffs for minimum lymph node retrieval in node-negative patients.

Cutoff point, lymph nodes retrieved	Below nodal cutoff		At or above nodal cutoff		Difference in median survival, months	Log-rank test statistic	p
	Patients	Median survival, months	Patients	Median survival, months			
5	2247	19.8	7848	27.2	7.4	84.9	<0.0001
8	4118	21.3	5977	28.5	7.2	83.4	<0.0001
10	5205	22.1	4890	29.3	7.2	85.9	<0.0001
12	6230	22.9	3865	29.7	6.8	76.9	<0.0001
15	7496	23.7	2599	31.8	8.1	79.3	<0.0001
18	8393	24.1	1702	33.5	9.4	68.8	<0.0001
21	9015	24.5	1080	33.5	9.0	46.5	<0.0001
24	9428	24.8	667	38.4	13.6	36.5	<0.0001

Table 7

Multivariable logistic regression analysis evaluating the factors associated with increased likelihood of mortality. This analysis includes both lymph node positive and lymph node negative patients.

Characteristics	All (N=26792)			Node Positive (n=16697)			Node Negative (n=10095)		
Demographics	*adj. OR*	*95% C.I.*	*p*	*adj. OR*	*95% C.I.*	*p*	*adj. OR*	*95% C.I.*	*p*
Age	1.01	(1.01, 1.02)	<.0001	na	na	na	1.02	(1.02, 1.03)	<.0001
Health Status and Treatments									
Grade			<.0001			<.0001			<.0001
Undifferentiated	ref	ref		ref	ref		ref	ref	
Well Differentiated	0.85	(0.61, 1.2)		0.96	(0.61, 1.53)		0.78	(0.47, 1.31)	
Moderately Differentiated	1.39	(1, 1.93)		1.42	(0.92, 2.19)		1.34	(0.81, 2.2)	
Poorly Differentiated	1.79	(1.29, 2.49)		1.72	(1.11, 2.67)		1.9	(1.14, 3.15)	
AJCC Stage			<.0001			na			<.0001
0	ref	ref		ref	ref		ref	ref	
I	7.21	(3.94, 13.2)		na	na		7.36	(3.87, 14)	
II	9.36	(5.12, 17.1)		na	na		9.54	(5.01, 18.2)	
III	13.9	(7.23, 26.6)		na	na		15.1	(7.02, 32.5)	
IV	19.4	(9.79, 38.5)		na	na		22.3	(9.24, 53.8)	
Nodes Examined	0.97	(0.96, 0.97)	<.0001	0.97	(0.96, 0.97)	<.0001	0.97	(0.96, 0.98)	<.0001
Nodes Positive	1.11	(1.08, 1.13)	<.0001	1.11	(1.08, 1.13)	<.0001	na	na	na
Tumor Size	1.01	(1.01, 1.01)	<.0001	1.01	(1.01, 1.02)	<.0001	na	na	na
Chemotherapy	0.61	(0.56, 0.67)	<.0001	0.51	(0.45, 0.58)	<.0001	0.71	(0.62, 0.81)	<.0001
Margin Status			<.0001			<.0001			<.0001
Negative	ref	ref		ref	ref		ref	ref	
Positive	1.64	(1.47, 1.82)		1.61	(1.41, 1.83)		1.8	(1.49, 2.17)	
Facility Type			<.0001			<.0001			na
Other	ref	ref		ref	ref		ref	ref	
Academic	0.81	(0.74, 0.88)		0.78	(0.69, 0.87)		na	na	
Length of Stay (days)	1.02	(1.01, 1.02)	<.0001	1.02	(1.01, 1.03)	<.0001	1.02	(1.01, 1.03)	<.0001
Nodal Status			<.0001			na			na

Characteristics	All (N=26792)			Node Positive (n=16697)			Node Negative (n=10095)		
Demographics	***adj. OR***	***95% C.I.***	***p***	***adj. OR***	***95% C.I.***	***p***	***adj. OR***	***95% C.I.***	***p***
Negative	ref	ref		ref	ref		ref	ref	
Positive	1.46	(1.3, 1.64)		na	na		na	na	

na: indicates that this parameter was not included in the multivariable analysis for the indicated patient subset.