Lymph node evaluation for treatment of adenocarcinoma of the pancreas

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ABSTRACT

Background: Increased lymph node evaluation has been associated with improved survival rates in patients with pancreatic cancer. We sought to evaluate the trends and factors associated with lymph node examination over time and the effects on survival.

Methods: Using the Surveillance, Epidemiology and End Results database, we conducted an analysis of adults with adenocarcinoma of the pancreas who underwent surgical resection. Using the Cochrane Armitage test for trend and logistic regression we identified factors associated with lymph node evaluation. Kaplan–Meier and Cox proportional hazards modeling were used to examine survival.

Results: We identified 4831 patients who underwent surgical resection from 1990 to 2010. The proportion of patients with 15 or more lymph nodes evaluated increased from 16% to 42% (p < 0.05) and the median number of lymph nodes examined increased from 7 to 15 nodes (p < 0.05) during the study period. Overall, 56% of patients had lymph node metastases; this proportion significantly increased during the study period. Factors that were independently associated with less than 15 lymph nodes evaluated included male gender, receipt of pre-operative radiation therapy, early year of diagnosis, older age, and missing information on tumor grade and size (p < 0.05). Survival rates significantly improved when 15 or more lymph nodes were examined.

Conclusion: We observed a significant increase in the number of lymph nodes evaluated with pancreas cancer resection over time. Lymph node evaluation was significantly associated with patient, tumor, and treatment characteristics. Our results suggest that adequate lymph node evaluation is associated with improved survival.

Synopsis

Lymph node evaluation for adenocarcinoma of the pancreas significantly improved in the United States from 1991 to 2010. Survival rates were significantly improved for both node positive and node negative patients when more than 15 lymph nodes were examined.

1. Introduction

Pancreas cancer is one of the leading causes of cancer death for both men and women in the United States [1]. Five-year and median overall survival rates after surgery remain poor despite the use of multimodality therapy [1]. Over the last several decades, quality measures and guidelines have rapidly become commonplace for all facets of care. Quality improvement efforts in cancer care have specifically advocated for a meaningful mechanism or measure that adequately evaluates appropriate staging and therapy [2–6]. Given the particularly low survival rates for pancreas cancer, quality measures are necessary for improving care by accurately staging patients to reduce the risk of inappropriate treatment or inappropriate denial of treatment. Adequacy of lymph node evaluation is one such quality improvement measure that has been used for gastrointestinal malignancies such as colorectal and gastric cancer [2–5]. For pancreatic cancer, several studies have reported a significant association between extent of lymph node evaluation and survival [6–14].

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The recommended number of nodes evaluated for pancreatic adenocarcinoma varies [6–14]. The National Comprehensive Cancer Network (NCCN) recommends that 11–17 nodes be examined to avoid stage migration while others have advocated for the surgical evaluation of 12 or more lymph nodes for staging of pancreas cancer [13,15]. In four recent institutional trials, the mean number of lymph nodes evaluated ranged from 13 to 17 [16–19]. A recent expert consensus statement recommended that ≥15 nodes to be examined [7]. Of note, no adjuvant treatment guidelines incorporate lymph node evaluation or positivity in decision making. The purpose of our study was to evaluate lymph node evaluation patterns and trends in the United States and to determine the factors associated with lymph node evaluation over time. We also examined the association between adequate lymph node evaluation and survival for the entire cohort as well as a number of sub-populations including

patients that underwent a Whipple procedure, patients with node-negative disease and patients with node-positive disease.

2. Methods

2.1. Data

We used the Surveillance Epidemiology and End Results (SEER) database (SEER 9 Registries). The SEER cancer registries provide population-based cancer surveillance for 18 areas that represent approximately 28% of the United States [16]. SEER collects patient demographic and tumor characteristics, including age at diagnosis, race, primary tumor site, tumor laterality, histology type, tumor stage, tumor grade, diagnostic confirmation, type of surgery, radiation, vital status, and cause of death.

Table 1
Patient characteristics 1990–2010.

N = 4831	All patients		<15 nodes examined		≥15 nodes examined		P-Value
	N	%	%	%	N	%	
Year							<0.0001
1990–1994	601	12	504	84	97	16	
1995–1999	924	19	755	82	169	18	
2000–2004	1249	26	908	73	341	27	
2005–2010	2057	43	1198	58	859	42	
Age							0.4
18–39	92	2	65	71	27	29	
40–59	1439	30	994	69	445	31	
60–79	2944	61	2044	69	900	31	
80+	356	7	262	74	94	26	
Gender							0.0023
Male	2459	51	1762	72	697	28	
Female	2372	49	1603	68	769	32	
Race							0.2489
Non-Hispanic White	3880	80	2682	69	1198	31	
Black	532	11	385	72	147	28	
Other or Unknown	419	9	298	71	121	29	
Tumor Size							<0.0001
<2 cm	522	11	381	73	141	27	
≥2 cm	3960	82	2679	68	1281	32	
Missing	349	7	305	87	44	13	
Tumor Grade							<0.0001
I or II	2741	57	1921	70	820	30	
III	1514	31	994	66	520	34	
IV	67	1	52	78	15	22	
Missing/Unknown	509	10	398	78	111	22	
T-Stage							<0.0001
I and II	1323	27	989	75	334	25	
III	3256	67	2183	67	1073	33	
IV	252	5	193	77	59	23	
Surgery Type							<0.0001
Whipple	3480	72	2438	70	1042	30	
Total Pancreatectomy	368	8	220	60	148	40	
Other	983	20	707	72	276	28	
Radiation/Surgery Sequence							0.0084
No Radiation-Surgery Only	2674	55	1875	70	799	30	
Radiation before Surgery	180	4	142	79	38	21	
Radiation after Surgery	1997	41	1348	68	629	32	
Node Positive							<0.0001
No	2115	44	1705	81	410	19	
Yes	2716	56	1660	61	1056	39	
Registry							<0.0001
San Francisco–Oakland	714	15	519	73	195	27	
Connecticut	781	16	492	63	289	37	
Metropolitan Detroit	961	20	664	69	297	31	
Hawaii	290	6	195	67	95	33	
Iowa	543	11	417	77	126	23	
New Mexico	212	4	155	73	57	27	
Seattle (Puget Sound)	612	13	434	71	178	29	
Utah	306	6	197	64	109	36	
Metropolitan Atlanta	412	9	292	71	120	29	