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Trends in lymph node excision and impact of positive lymph node ratio in patients with colectomy for primary colon adenocarcinoma: Population based study 1988 to 2011

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ABSTRACT

Background: Studies suggest increased lymph node excision in patients with colon cancer portends improved survival. Guidelines recommend excising 12 or more lymph nodes during colectomy. There is an inverse correlation between the positive lymph node ratio and survival in patients of these patients.
Objective: We sought to determine whether colon cancer patients have adequate lymph node excision and whether positive lymph node ratio can be used as a guiding factor for their treatment plan.
Design: Retrospective, Observational.
Settings: United States, 1988–2011.
Patients: Utilizing the Surveillance, Epidemiology, and End Results registry, we identified 318,323 patients who underwent colectomy for colonic adenocarcinoma. Patients were stratified by age, tumor stage, tumor grade, race, ratio of positive nodes, and year of diagnosis.
Main outcome measures: We determined the percentage of patients undergoing lymph node excision and mean number of nodes excised by year of diagnosis. In patients with adequate lymph node excision, positive lymph node ratio versus overall and cancer-specific survival was evaluated.
Results: 302,620 patients (95%) had at least 1 lymph node excised and 164,583 patients (52%) had 12 or more lymph nodes excised. This correlates to an increase from approximately 30% in 1988 to 80% by 2011. The mean number of nodes excised doubled from 9 to 18 in the entire cohort over the timeframe studied. On multivariate analysis, the 4 year cluster of diagnosis was the largest predictor of receipt of adequate lymph node excision with a 1.68 times higher odds per 4-year increase from 1988 (95% CI 1.67–1.69, $p < 0.001$). Higher positive lymph node ratio correlated with significantly worse overall and cancer-specific survival in those who had 12 or more lymph nodes excised. At a positive lymph node ratio of 0.16, there is a 15.7% increased rate of cancer specific mortality.
Conclusions: Despite improvement in the performance of lymph node excision in patients undergoing colectomy for colon adenocarcinoma since 1988, only 80% of patients had adequate lymph node excision in 2011. Increasing positive lymph node ratio predicts significantly worse cancer-specific survival and a ratio of 0.16 may be considered an indication for a more aggressive therapeutic plan.
Category: Colorectal/Anal Neoplasia.

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1. Background

Lymph node positivity is one of the most important prognostic factors in patients with colon cancer. Colon cancer survival is also independently associated with the number of lymph nodes analyzed at the time of colectomy [1]. Numerous studies have shown that an increase in the number of lymph nodes removed improves survival in both node-positive and node-negative disease, indicating that the benefit is not solely dependent on upstaging and subsequent adjuvant therapy [1–3]. Guidelines established in 1990

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Table 1
Patient characteristics.

		Totals	LND ≥ 12 (#)	LND ≥ 12 (%)	OR (95% CI)	p-value
Yr of diagnosis						
	1988–1992	33,354	10,898	33	Reference 1.0	
	1993–1997	43,058	15,172	35	1.12 (1.09–1.16)	<0.001
	1998–2002	76,311	31,074	41	1.42 (1.38–1.45)	<0.001
	2003–2007	94,238	52,326	56	2.57 (2.51–2.64)	<0.001
	2008–2011	71,362	55,113	77	6.99 (6.79–7.19)	<0.001
TNM stage						
	Tis-T2N0M0	103,663	40,909	39	Reference 1.0	
	T3-4N0M0	114,441	62,617	55	1.85 (1.82–1.89)	<0.001
	N + M0	100,219	61,057	61	2.39 (2.35–2.43)	<0.001
Grade						
	1	30,975	13,497	44	Reference 1.0	
	2	209,648	111,328	53	1.47 (1.43–1.50)	<0.001
	3	50,674	30,145	59	1.90 (1.85–1.96)	<0.001
	4	3182	2204	69	2.92 (2.70–3.16)	<0.001
	Unknown	23,844	7355	31	0.58 (0.56–0.60)	<0.001
Race						
	White	261,601	134,238	51	Reference 1.0	
	Black	32,308	17,189	53	1.08 (1.05–1.10)	<0.001
	Other	23,498	12,590	54	1.10 (1.07–1.12)	<0.001
	Unknown	916	566	62	1.53 (1.34–1.75)	<0.001
Age group						
	<50	22,684	14,883	66	Reference 1.0	
	50–59	45,768	26,020	57	0.69 (0.67–0.71)	<0.001
	60–69	73,660	37,514	51	0.54 (0.53–0.56)	<0.001
	70–79	97,743	47,582	49	0.50 (0.48–0.51)	<0.001
	80+	78,468	38,584	49	0.51 (0.49–0.52)	<0.001
+LN density						
	0	202,401	103,526	51		
	>0–0.5	80,048	53,814	67		
	≥0.5	20,171	7243	36		
	No nodes examined	15,703	0	0		
Totals		318,323	164,583	52		

Table 2
Multivariable logistic regression evaluating effect of year of diagnosis, stage, age group, grade, and race on the likelihood of having LNE ≥ 12 nodes (with unknowns excluded).

	OR (95% CI)	p-value
Year group	1.68 (1.67–1.69)	<0.001
TNM stage	1.47 (1.46–1.49)	<0.001
Grade	1.21 (1.20–1.23)	<0.001
Age group	0.88 (0.88–0.89)	<0.001
Race	0.98 (0.97–0.99)	0.007

at the World Congress of Gastroenterology in Sydney denote the examination of at least 12 lymph nodes as a benchmark to ensure an appropriate resection and adequate staging [1,4,5]. Subsequent analyses of positive lymph node ratio have identified predictive ratios (from 20 to 40% positivity cutpoints) as independent and accurate survival prognostic factors in patients with colon cancer [6–13]. However, this relationship has yet to be studied in a large-scale, population-based study in the United States. Using the SEER database, we aimed to track the trend and factors of incorporation of lymph node excision into colectomy for colon cancer, and how the positive lymph node ratio correlates with survival. Using the results, we aimed to determine a cutoff ratio after which a more aggressive therapeutic plan should be considered.

2. Materials and methods

2.1. Subjects and databases

Data for this analysis was abstracted from the SEER database, a publicly-available cancer registry maintained by the National Cancer Institute that includes approximately 26% of the United States population from 1973 to 2011 (Connecticut, Iowa, rural Georgia, Alaska, New Mexico, Greater California, Utah, Hawaii, Kentucky, New Jersey and Louisiana as well as the metropolitan areas of Detroit, San Francisco-Oakland, Seattle [Puget Sound], Metropolitan Atlanta, Los Angeles and San Jose-Monterey) [14]. Records before 1988 were excluded as the SEER registry did not collect detailed lymph node data from 1973 to 1987.

2.2. Lymph node data

We included patients of any age who underwent colectomy for primary colon adenocarcinoma diagnosed between 1988 and 2011. We incorporated patients with a primary tumor site between the cecum and rectosigmoid junction, including large intestinal tumors not otherwise specified. Surgical procedures in the analysis included partial colectomy, subtotal/hemicolectomy, total colectomy, total proctocolectomy, and colectomy or coloproctectomy with resection of contiguous organs.

Patients were excluded if either the number of nodes excised or the number of positive nodes were unknown. Additionally, patients with known metastases were excluded as some of these patients may have undergone palliative resection and thus may not have received therapeutic lymph node excision.

Based on guidelines noted above, patients were grouped into 1 or more (LNE ≥ 1), 12 or more (LNE ≥ 12) and 20 or more (LNE ≥ 20) nodes excised, and were grouped by age (<50, 50–59, 60–69, 70–79, and 80 years or older), race (white, black, other and unknown), tumor stage (Tis-T2N0M0, T3-T4N0M0, and N + M0), ratio of positive lymph nodes (0, >0–0.5, and ≥0.5), and grade (1–4 and unknown). SEER does not formally categorize patients as having