Surgical Oncology 27 (2018) 449–455

Contents lists available at ScienceDirect

Surgical Oncology

journal homepage: www.elsevier.com/locate/suronc

Lower survival after right-sided versus left-sided colon cancers: Is an extended lymphadenectomy the answer?

Lawrence Lee[a,b,*], Arman Erkan[a], Noura Alhassan[b], Justin J. Kelly[a], George J. Nassif[a], Matthew R. Albert[a], John RT Monson[a]

[a] Center for Colon and Rectal Surgery, Florida Hospital, Orlando, FL, USA
[b] Department of Surgery, McGill University Health Centre, Montreal, QC, Canada

ARTICLE INFO

Keywords:
Colon cancer
Tumor location
Lymph node harvest

ABSTRACT

Introduction: Tumour location may affect oncologic outcomes for colon adenocarcinoma due to different levels of vascular ligation and nodal harvest, but the data are equivocal. The objective of this study is to determine the effect of tumor location and lymph node yield on overall survival(OS) in stage I-III colon adenocarcinoma.
Methods: The 2004–2014 National Cancer Database was queried for colectomies for non-metastatic colon adenocarcinoma, excluding transverse colon and rectal cancer. Patients were grouped based on left/right tumor location. Main outcome measure was 5-year OS. Propensity score matching created balanced cohorts. Multilevel survival analysis determined the independent effect of tumor location and nodal harvest on OS.
Results: There were 504,958 patients (273,198 right; 231,760 left) in the entire cohort: 26.4% stage-I, 37.3% stage-II, and 36.3% stage-III (equal distribution left/right). After 1:1 matching(n = 297,080), right cancers were associated with worse 5-year overall survival for stage-II (66% vs. 70%, $p < 0.001$) and -III (56% vs. 60%, $p < 0.001$) despite similar nodal harvest and proportion receiving systemic therapy. On multivariate analysis, right-sided cancers (HR 1.12, 95%CI 1.06–1.19) had worse OS, independent of stage and nodal harvest. Nodal harvest ≥22 nodes had the highest OS (HR 0.71, 95%CI 0.68–0.75). There was an interaction between right-sided cancer and > 22 lymph node harvest towards increased survival (HR 0.86, 95%CI 0.80–0.92).
Conclusions: Right-sided cancers are associated with worse oncologic outcomes compared to left-sided tumors but a higher lymph node yield improves survival. These data provide indirect evidence for a higher lymphatic harvest to improve survival.

1. Introduction

There is an increase in the incidence of right-sided colon cancer [1,2]. There are certain important differences between right- and left-sided cancers. Tumors located in the proximal colon tend to occur in older patients, present with more advanced stages, and have mucinous histology and poor differentiation [3]. There are also important molecular biological differences [4]. However, the effect of these differences and the tumor location within the colon has not been well described. Past studies have generally demonstrated worse outcomes for proximal colon cancers compared to more distal lesions, but many of these studies have been limited to single centre studies with relatively small sample sizes or have used study cohorts before the introduction of modern chemotherapy regimens [5].

Tumour location may affect oncologic outcomes for colon adenocarcinoma due to different levels of vascular ligation and nodal harvest, but the data are equivocal [6,7]. For left-sided cancers, a high vascular ligation of the inferior mesenteric artery is often performed, whereas routine high ligation of the ileocolic pedicle (i.e. D3 dissection) is not performed in right-sided cancers. This may result in different nodal harvest patterns between the proximal and distal cancers [8], which may have prognostic implications. Therefore, the objective of this study is to determine the effect of tumor location and lymph node yield on overall survival(OS) in stage I-III colon adenocarcinoma.

2. Methods

2.1. Data source & study subjects

The National Cancer Database (NCDB) is a cancer registry sponsored by the American College of Surgeons, the Commission on Cancer (CoC), and the American Cancer Society. It includes approximately 70% of all

* Corresponding author. Colon and Rectal SurgeryAssistant Professor of SurgeryMcGill University Health Centre, 1001 Decarie Blvd, DS1-3310, Montreal, QC, H4A 3J1, Canada.
E-mail address: larry.lee@mcgill.ca (L. Lee).

https://doi.org/10.1016/j.suronc.2018.05.031
Received 5 March 2018; Accepted 28 May 2018

Table 1
Comparison of patient and facility characteristics. The matched cohort is a subset of the overall cohort.

	Overall Cohort			Matched Cohort		
	Left N = 231,760	Right N = 273,198	*p*	Left N = 148,540	Right N = 148,540	*p*
Mean age, years (SD)	65.7 (13.4)	71.2 (12.5)	< 0.001	68.7 (12.0)	68.7 (11.9)	0.820
Male	123650 (53%)	122063 (45%)	< 0.001	74767 (50%)	74720 (50%)	0.863
Charlson-Deyo score			< 0.001			0.356
0	165676 (72%)	181380 (66%)		101930 (69%)	102026 (69%)	
1	49457 (21%)	65734 (24%)		34313 (23%)	34428 (23%)	
2	16627 (7%)	26084 (10%)		12297 (8%)	12086 (8%)	
Race/ethnicity			< 0.001			0.606
White	193402 (83%)	232032 (85%)		125243 (84%)	125498 (84%)	
Black	25306 (11%)	31801 (12%)		17070 (11%)	16843 (11%)	
Hispanic	8463 (4%)	5200 (2%)		3743 (3%)	3727 (3%)	
Other/unknown	4469 (2%)	4106 (1%)		2484 (2%)	2472 (2%)	
Insurance			< 0.001			0.733
No insurance	7486 (3%)	5901 (2%)		4138 (3%)	4119 (3%)	
Private insurance	92178 (40%)	75983 (28%)		50062 (34%)	50037 (34%)	
Medicare/Medicaid	128446 (55%)	187437 (69%)		92146 (62%)	92116 (62%)	
Unknown/Missing	3650 (2%)	3877 (1%)		2194 (1%)	2268 (1%)	
Median household income			0.017			0.528
< $38,000	40692 (18%)	47311 (17%)		26488 (18%)	26647 (18%)	
$38,000-$47,999	53859 (23%)	63826 (23%)		35332 (24%)	35391 (24%)	
$48,000-$62,999	61369 (26%)	72994 (27%)		39832 (27%)	39979 (27%)	
$63,000+	73063 (32%)	85641 (31%)		46888 (31%)	46523 (31%)	
Unknown/Missing	2777 (1%)	3426 (1%)				
Without high-school degree			< 0.001			0.257
≥21%	41246 (18%)	43840 (16%)		25554 (17%)	25738 (17%)	
13%–20.9%	60228 (26%)	69955 (26%)		38905 (26%)	39101 (26%)	
7%–12.9%	74932 (32%)	91258 (33%)		49361 (33%)	49424 (33%)	
< 7%	52678 (23%)	64850 (24%)		34720 (23%)	34277 (23%)	
Unknown/Missing	2676 (1%)	3295 (1%)		–	–	
Distance traveled			< 0.001			0.615
< 30 miles	197803 (85%)	236017 (86%)		128933 (87%)	128731 (87%)	
30–60 miles	19221 (8%)	20691 (8%)		12010 (8%)	12167 (8%)	
60–100 miles	6529 (3%)	7126 (3%)		4084 (3%)	4065 (3%)	
> 100 miles	8207 (4%)	9364 (3%)		3513 (2%)	3577 (2%)	
Facility type			< 0.001			0.633
Community	31663 (14%)	37554 (14%)		20677 (14%)	20843 (14%)	
Comprehensive	109484 (47%)	134226 (49%)		72925 (49%)	72594 (49%)	
Academic/research	59486 (26%)	68063 (25%)		38540 (26%)	38621 (26%)	
Integrated	24732 (11%)	29613 (11%)		16398 (11%)	16482 (11%)	
Unknown/missing	6395 (3%)	3742 (1%)		–	–	
Population density			0.078			0.841
Metro	190462 (82%)	225003 (82%)		124243 (83%)	123315 (83%)	
Urban	29728 (13%)	34402 (13%)		19341 (13%)	19344 (13%)	
Rural	4280 (2%)	5077 (2%)		2808 (2%)	2804 (2%)	
Unknown	7290 (3%)	8716 (3%)		3148 (2%)	3077 (2%)	
High volume hospital (≥90 cases per year)	117343 (51%)	137308 (50%)	0.008	74534 (50%)	74500 (50%)	0.901

new cancer diagnoses in the United States consisting of over 1 million new cases per year form 1500 hospitals [9]. All Commission on Cancer accredited hospitals are required to include all new cancer diagnoses to the NCDB. Data is entered based on the CoC facility oncology registry standards manual, a coding manual specifically for this purpose [10]. The NCDB has also performs yearly data-quality reviews to ensure its quality and validity [9,11]. For this study, the 2004–2014 colon and rectosigmoid junction cancer participant user file (PUF) was used. These PUFs do not include rectal cancer. Patients were further excluded if they had metastatic disease at diagnosis, neoadjuvant therapy, no surgery was performed, or for histology other than colonic adenocarcinoma. Variable definitions can be found at http://ncdbpuf.facs.org/node/259. Patient characteristics included age, gender, race/ethnicity, comorbidities, insurance status, median household income, population density and education distribution of the patient's zip code, and distance traveled to the reporting institution. Patient comorbidities were defined according to the Deyo classification of the Charlson Comorbidity Index [12]. The NCDB does not provide more detailed information on specific comorbidities or body mass index. Hospital characteristics included hospital type and facility location. Facility is defined as per CoC accreditation criteria, based on total number of new cancer diagnoses, diagnostic and treatment services, research participation, and resident training. Hospital location is based on US census information. Annual hospital volume was divided based on the median number of colon cancer cases per year (90 resections) and divided into low- (fewer than 90 cases) and high-volume (90 or more cases) status. Tumor-related variables included tumor size, grade, location, lymphovascular and perineural invasion. Lymphovascular and perineural invasion were only included in the NCDB after 2010. Treatment-related variables included primary surgical procedure and approach, lymph node yield, margin status, length of primary inpatient stay, 30-day readmissions, 30- and 90-day mortality, and vital status at last contact. Lymph node yield was further subdivided into 3 categories: < 12 nodes, 12 to 21 nodes, and 22 or more nodes. Patients were divided into two groups based on their tumor location: right and left. Right-sided tumors included those with International Classification of Disease for Oncology (ICD-O) location codes listed as cecum, ascending colon, and hepatic flexure. Left-sided tumors included those in the splenic flexure, descending colon, sigmoid colon, and rectosigmoid junction. Transverse colon and rectal tumors were excluded to minimize misclassification bias, as the diagnosis codes for these lesions do not provide their exact location. Patients that had received neoadjuvant therapy were also