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Prognostic Impact of Lymph Node Ratio in Obstructive Colorectal Cancer

Jacquelyn Turner[1], Lampros Liasis[2], George Malietzis[3], Ayana Chase[1], E. Shyam P. Reddy[4], Joel Okoli[1], Veena N. Rao[4] and Clarence Clark[1*]

[1]Morehouse School of Medicine, Department of Surgery, 720 Westview Dr, Atlanta, GA 30310
[2]North West London Hospitals NHS Trust
[3]St. Marks Hospital, London
[4]Morehouse School of Medicine, Department of Obstetrics and Gynecology

***Corresponding author**: Clarence Clark, MD, FACS, FASCRS, Department of Surgery, Morehouse School of Medicine, 720 Westview Dr, Atlanta, GA 30310, USA; E mail: cclark@msm.edu

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Abstract

Background: An estimated 15% to 20% of patients with colorectal cancers present with intestinal obstruction. Although colorectal cancer patients with lower lymph node ratios (LNR) have been shown to have a higher overall survival and disease free survival, this finding has not been clearly defined in patients with obstructive colorectal cancer. Here, we examine the impact of LNR on oncologic outcomes of colorectal cancer patients with and without obstruction.

Methods: A total of 143 patients who underwent surgery for colorectal cancer at a single urban safety-net hospital were identified, retrospectively, from 1999-2009. These patients were divided into two groups: Group A, obstructive colorectal cancer (OC) (n=37) and Group B, non-obstructive colorectal cancer (NOC) (n=106). Clinicopathologic data were compared between the two groups including lymph node ratio (LNR) and overall survival.

Results: Demographics such as age, sex, and race were similar between the OC and NOC cohorts. The location of obstructing colon cancers were more often found in the sigmoid colon (29.7%). Whereas, the location of non-obstructing colon cancers occurred more often in the cecum (48.1%). Overall 5-year survival was 47.1% for OC group and 52.5% for the NOC group. There was no difference in the total number of lymph nodes harvested or the average LNR between the two groups. In a multivariate analysis, sex, race, emergent operation, and tumor-node-metastasis (TNM) stage were adverse factors for survival. In a multivariate analysis, male sex was favorably predictive of overall survival while LNR was not.

Conclusion: LNR is not predictive of overall survival when an adequate number of lymph nodes are harvested in the setting of obstructive colon cancer.

Keywords: Colon cancer, Rectal cancer, Obstructive cancer, Lymph node ratio.

Abbreviations: LNR = Lymph node ratio; OC = Obstructive colon cancer; NOC = Non-obstructive colon cancer; TMN = Tumor, node, metastasis; AJCC = American Joint Committee on Cancer; SD = Standard deviation; NS = Non-significant.

Unit of Measurements: System International units.

Introduction

An estimated 15% to 20% of patients with colorectal cancers present with intestinal obstruction [1]. Obstructing colorectal cancers can present as a challenge when curative oncologic outcomes are desired. Often times, obstructing colorectal cancers are more advanced, associated with a higher incidence of distant metastasis, and associated with emergent operations which may affect the number of lymph nodes harvested compared to non-obstructing cancers [2].

Currently, the tumor, node, metastasis (TNM) staging system is the strongest predictor of survival for colorectal cancers. Of the TNM parameters, nodal status is the strongest predictor of survival. The College of American Pathologists [3] endorses the pathologic examination of a minimum of 12 lymph nodes based on the 7th edition of the American Joint Committee on Cancer (AJCC) Staging Manual [4]. Factors that impact lymph node retrieval include age, immune response, tumor location, hospital volume, emergent cases, and tumor size [4,5]. Other prognostic factors such as lymph node ratio (LNR) have been described to further predict outcomes of patients with colorectal cancer [6]. LNR is defined as the number of positive lymph nodes identified divided by the total lymph nodes examined. Lower LNR indicates a better prognosis with a higher overall and disease-free survival [5,7,8]. Some studies have shown LNR to

be a valid prognostic indicator when compared to conventional nodal staging [9]. This finding, however, has not been elucidated in the setting of obstructive colon cancer to our knowledge. Therefore, the yield of lymph nodes harvested and the LNR in obstructing colorectal cancer should be evaluated. Our aim is to determine the prognostic implications of LNR with obstructing colon cancers.

Methods

Approval for this retrospective review was obtained from an institutional review board. Colorectal cancer data was retrieved from our local tumor registry from 1999-2009. Demographics and clinical data included age at diagnosis, race, sex, payer summary, tumor site and size, presence of obstruction from the cancer, diagnosis date, AJCC stage, TNM data including number of harvested lymph nodes and number of positive lymph nodes, surgical approach, chemotherapy and radiation therapy details, vital status, recurrence, last contact, and date of death. Patients with incomplete data and patients who did not undergo surgery were excluded.

The relationship between LNR and other clinicopathological parameters were assessed using nonparametric statistics. Categorical data were analyzed using Pearson chi-square test and Fisher's exact test while continuous variables were analyzed using t-test. Clinical outcomes were assessed using the Kaplan-Meier survival curves. Stepwise multivariate Cox proportion analysis was performed. The statistical significance for all tests used was set at $p< 0.05$. All analyses were performed using the statistical software, Statistical Package for the Social Sciences, version 20.0 (SPSS, Inc, Chicago, IL).

Results

Demographics

Our search revealed 143 patients who underwent surgery for colorectal cancer at a single urban teaching hospital. There were 37 patients with obstructive colorectal cancer (OC) at the time of surgery and 107 patients without a bowel obstruction (NOC) at the time of surgery. No difference was seen in age (OC, mean 61.32 years versus NOC, mean 59.47 years, p=0.461), sex (Males: 54.1% in OC group versus 49.2% in NOC group, p=0.449), and race (Table 1). Tumor site was analyzed next. OC patients had a higher rate of descending and sigmoid colon cancers (54% versus 29.3% in NOC) while NOC patients showed a higher rate of right and transverse colon cancers (64.1% versus 40.5 in OC). When comparing overall distribution of tumor site, there was a significant difference seen between the two groups (Table 1). No difference in mean tumor size (5.5 cm versus 5.9 cm) or average number of lymph nodes harvested (16.1 versus. 16.05)

Table 1: Distribution of age, sex, race, tumor size, number of total nodes harvested, tumor location, AJCC stage

	OC (N=37)	NOC (N=106)	p Value
Age, y, mean (SD)	61.32 (1.87)	59.47 (1.33)	NS
Sex, n (%)			NS
Male	20 (54.1%)	49 (46.2%)	
Female	17 (45.9%)	57 (53.8%)	
Race, n (%)			NS
Black	33 (89.2%)	96 (90.7%)	
White	3 (8.1%)	7 (6.5%)	
Other	1 (2.7%)	3 (2.8%)	
Tumor Size cm, mean (SD)	5.5 (2.95)	5.9 (3.0)	NS
Lymph Node Harvested, mean (SD)	16.1 (11.85)	16.05 (11.42)	NS
Tumor Site, n (%)			0.0464
Cecum/Ascending colon	8 (21.6%)	51 (48.1%)	
Transverse	7 (18.9%)	17 (16.0%)	
Descending	9 (24.3%)	15 (14.2%)	
Sigmoid	11 (29.7%)	16 (15.1%)	
Rectum	2 (5.4%)	7 (6.6%)	
AJCC stage, n (%)			NS
1	4 (10.8%)	11 (10.4%)	
2	12 (32.4%)	50 (47.2%)	
3	18 (48.7%)	39 (36.8%)	
4	3 (8.1%)	6 (5.6%)	

was seen between the OC and NOC groups, respectively. There was also no difference in staging between the two groups with the majority of patients having stage 2 or 3 disease (Table 1).

Lymph Node Ratio

The mean LNR for the OC group was 0.1341 which was similar to that of the NOC group at 0.1474 (Table 2). We further analyzed LNR by categorizing patients based on quartile distribution: 0 – 0.24, 0.25– 0.49, 0.50– 0.74, and 0.75– 1.0. There was no difference in distribution of LNR between the two groups with the majority of patients falling in the 0 – 0.24 category (OC 81.1% and NOC 77.1%).

Table 2: Lymph node ratio with distribution

	OC	NOC	P
LN ratio, mean (SD)	0.1341 (0.232)	0.1474 (0.239)	NS
LN ratio distribution, n (%)			
0 - 0.24	30 (81.1%)	81 (77.1%)	
0.25 – 0.49	3 (8.1%)	12 (11.4%)	
0.5 – 0.74	3(8.1%)	6 (5.7%)	
0.75 – 1.0	1 (2.7%)	6 (5.7%)	

Oncologic Outcomes

Analysis of the survival data demonstrated that the 1, 3, and 5 year overall survival rates of the OC group were 83.6%, 66.4%, and 52%, respectively (Figure 1). These findings are lower compared to the 1, 3, and 5 year overall survival rates of the NOC group which were 90.3%, 75.1%, and 54.8%, respectively. Factors predictive of survival were then examined including presence of obstruction, LNR, age, gender, stage, and tumor site to determine the significance to survival outcomes. Specifically, the prognostic value of the LNR was assessed in the presence of possible confounding covariates by Cox multivariate regression to achieve this aim. The only variable associated with improved survival in our model was male gender ([HR]: 0.559 [95%CI: 0.312-1.000], p=.050) (Figure 2). No significant trend was seen in regard to LNR as a prognostic indicator in patients with obstructive colon cancer at the time of diagnosis.

Discussion

Obstructive colorectal cancers often present as a challenge especially when curative resection is the goal. Despite the TNM tumor staging being the standard for determining prognosis while guiding treatment, LNR has emerged as an alternative prognostic indicator for colon and rectal cancer [4,10]. This study's aim, to assess whether or not LNR is prognostic in obstructive colorectal cancers, has yet to be elucidated in the literature. Here, we found an average positive LNR for OC and NOC groups of 0.13 and 0.15 respectively. This value is critical given the recent findings of Gracia et al on the trends of positive LNR in patients with colectomy. They reported a positive LNR starting at 0.16 increased the cancer specific mortality by 15.7% while a ratio greater than 0.21 increased the overall mortality by 16.6% in a large population base study [11]. Because 80.1% of our OC and 77.1% of our NOC patients were below LNR

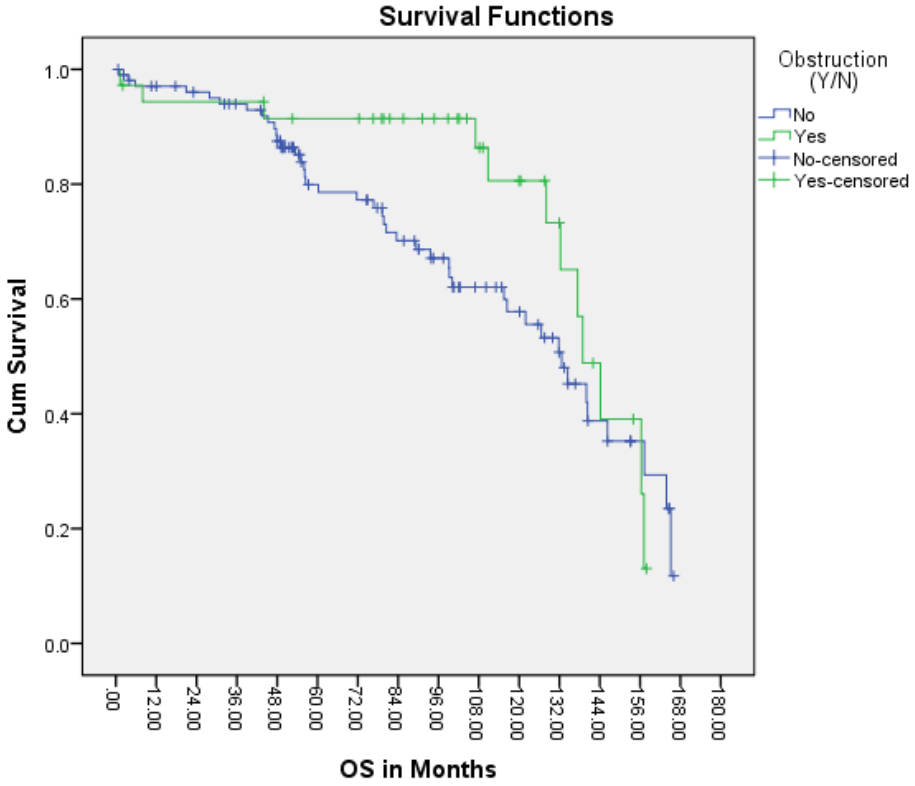

Figure 1: Kaplan-Meier Survival Curve

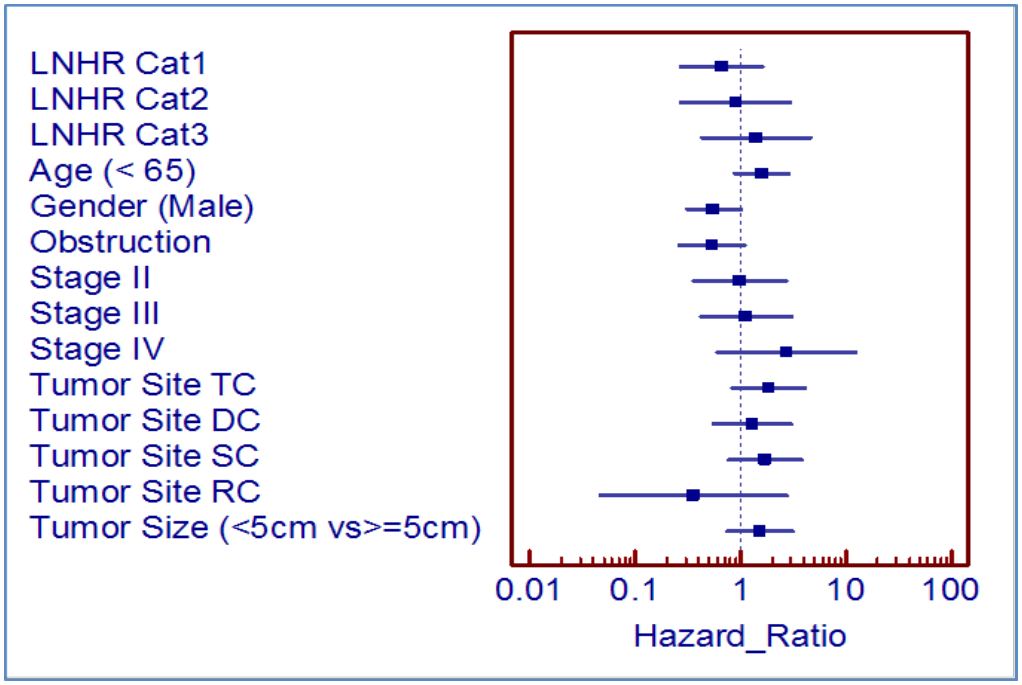

Figure 2: Multivariate Cox Regression analysis results

of 0.24 using a quartile distribution, it is difficult to determine whether a similar trend would be seen in our cohort of patients. Therefore, categorizing patients as described by Rosenberg et al [12] (<0.1, 0.1– 0.17, 0.18 – 0.41, 0.42 – 0.69, and > 0.7) may be advantageous for future studies. Despite this finding, we did not find a correlation between overall survival and LNR in a multivariate regression analysis.

These results should not underestimate the potential value of LNR in colorectal cancer. For example, Huh et al revealed that LNR is more useful when a suboptimal number (<11) of lymph nodes are retrieved and LNR is an independent prognostic factor for survival [13]. In our study, neither group (OC or NOC) had suboptimal lymph nodes harvested with an average retrieval of 16.1 for the OC group versus 16.05 for the NOC group. This finding may play a role in LNR not being prognostic in both cohorts of patients. Berger et al had a similar finding in their study of patients with inadequate lymph retrieval [14]. Future studies are needed to investigate the accuracy and precision of LNR when lymph node harvest is less than 11 in the setting of colorectal obstruction.

There were several limitations of our study. This study is a retrospective review, which is subject to selection bias. In addition, this study is limited by small sample size. Furthermore, as noted by Huh et al, an accepted specific value for LNR is unknown [13]. In addition the optimal distribution of LNR to stratify patients is unclear.

Conclusion

LNR is not predictive of overall survival when an adequate number of lymph nodes are harvested in the setting of obstructive colon cancer.

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References

1. Lee YM, Law WL, Chu KW, Poon RT. Emergency Surgery for obstructing colorectal cancer: A comparison between right sided and left sided lesions. J Am Coll Surg. 2001; 192(6):719-25.
2. Baccari P, Bisagni P, Crippa S, Sampietro R, Staudacher C. Operative and long-term results after one-stage surgery for obstructing colonic cancer. Hepatogastroenterology. 2006; 53(71):698-701.
3. Cap.org. Protocol for the Examination from Patients with Primary Carcinoma of the Colon and Rectum: College of American Pathologists; 2016. Available from: http://www.cap.org/ShowProperty?nodePath=/UCMCon/Contribution%20Folders/WebContent/pdf/cp-colon-16protocol-3400.pdf
4. Veen T, Nedrebø BS, Stormark K, Søreide JA, Kørner H, Søreide K. Qualitative and Quantitative Issues of Lymph Nodes as Prognostic Factor in Colon Cancer. Dig Surg. 2013; 30(1):1-11. doi: 10.1159/000349923.
5. Lu YJ, Lin PC, Lin CC, Wang HS, Yang SH, Jiang JK, et al. The impact of the lymph node ratio is greater than traditional lymph node status in stage III colorectal cancer patients. World J Surg. 2013; 37(8):1927-33. doi: 10.1007/s00268-013-2051-4.
6. Poritz LS, Sehgal R, Hartnett K, Berg A, Koltun WA. Tumor volume and percent positive lymph nodes as a predictor of 5-year survival in colorectal cancer. Surgery. 2011; 150(4):649-55. doi: 10.1016/j.surg.2011.07.049.
7. Medani M, Kelly N, Samaha G, Duff G, Healy V, Mulcahy E, et al. An appraisal of lymph node ratio in colon and rectal cancer: not one size fits all. Int J Colorectal Dis. 2013; 28(10):1377-84. doi: 10.1007/s00384-013-1707-8.

8. Allaix ME, Arezzo A, Cassoni P, Mistrangelo M, Giraudo G, Morino M. Metastatic lymph node ratio as a prognostic factor after laparoscopic total mesorectal excision for extraperitoneal rectal cancer. Surg Endosc. 2013; 27(6):1957-67. doi: 10.1007/s00464-012-2694-5.

9. Lykke J, Jess P, Roikjaer O, Danish Colorectal Cancer Group. The prognostic value of lymph node ratio in a national cohort of rectal cancer patients. Eur J Surg Oncol. 2016; 42(4):504-12. doi: 10.1016/j.ejso.2016.01.012.

10. Manilich EA, Kiran RP, Radivoyevitch T, Lavery I, Fazio VW, Remzi FH. A novel-driven prognostic model for staging of colorectal cancer. J Am Coll Surg. 2011; 213(5):579-88. doi: 10.1016/j.jamcollsurg.2011.08.006.

11. Garcia B, Guzman C, Johnson C, Hellenthal NJ, Monie D, Monzon JR. 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 20177. Surg Oncol. 2016; 25(3):158-63. doi: 10.1016/j.suronc.2016.05.013.

12. Rosenberg R, Friederichs J, Schuster T, Gertler R, Maak M, Becker K, et al. Prognosis of patients with colorectal cancer is associated lymph node ratio: a single-center analysis of 3,026 patients over a 25-year time period. Ann Surg. 2008; 248(6):968-78. doi: 10.1097/SLA.0b013e318190eddc.

13. Huh JS, Kim CH, Kim HR, Kim YJ. Factors predicting oncologic outcomes in patients with fewer than 12 lymph nodes retrieved after curative resection for colon cancer. J Surg Oncol. 2012; 105(2):125-29. doi: 10.1002/jso.22072.

14. Berger AC, Sigurdson ER, LeVoyer T, Hanlon A, Mayer RJ, Macdonald JS, et al. Colon cancer survival is associated with decreasing ratio of metastatic to examined lymph nodes. J Clin Oncol. 2005; 23(34):8706-12.