Impact of Tumour Properties in Lymph Node Harvesting along with Colorectal Cancer Reseetiows: A Prospective Study

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ABSTRACT

Introduction: Colorectal cancer is one of the common cancers worldwide. The prognosis for patients with colorectal cancer is related to the stage of disease at diagnosis and tumor histology, including differentiation, lymphatic invasion, and extent of tumor-free surgical resection margins.
Materials and methods: Digital rectal exam was done. Barium enema with or without air contrast was done to mainly locate deformities of intestinal topography. Sigmoidoscopy, colonoscopy and CT scan was done for direct visualization and grading the tumor. Histopathological examination of the specimen was done to evaluate the size of the tumour, histological grade, depth and lymph node score.
Results: The mean age of the patients in the study was 52.3± 13.08 with most of the patients being between 41 to 60 years of age. In most of the patients, i.e.,41 (45.6%), the site of tumour was in the rectum. The second most common site of carcinoma was caecum and ascending colon. 83.3% of the patients had opted for elective surgeries, while in 16.7%, it was an emergency. The mean lymph nodes harvested among the patients was 32 ± 7.10 with15 of them positive.
Conclusion: This study reveals that the number of lymph nodes harvested is independent of the size and grading of the tumor. Colon cancers in total are commoner than rectal cancers. There is trend of increased right colon tumors.

Keywords: Colorectal Cancer, Lymph Node, Grading of Cancer

INTRODUCTION

Colorectal cancer is one of the common cancers worldwide. It is the fourth leading cause of death due to cancer worldwide, third most common in males and second most in females[1,2]. India stands 9th in the incidence of colon cancers and 10th in rectal cancers. The highest incidence in India was observed in Thiruvananthapuram, followed by Bengaluru, Mumbai. In women, the highest rate was observed in Nagaland and Aizwal[3]. The highest incidences have been observed in Australia/ New Zealand, Europe and the lowest in seen in Africa and South Central Asia[4]. In the Asian countries, the incidence of the colorectal cancer is higher in the developed countries such as Japan, Singapore and South Korea compared to the developing countries such as Malaysia and other developing countries[5]. This is probably due to better screening and treatment methods used in the developed countries than their counterparts. Although the incidence rate of CRC in India is low compared to western countries, they are still major health care burden considering the population of our country, and have mortality rate comparable to the west[2,6]. By the end of 2030, the rate of colorectal cancer is expected to increase to more than 2.2 million new cases and the death rate is expected to be 1.1 million[7,8].

The colorectal cancer occurs when genetic or epigenetic mutations occur on the epithelial cells of the colon and begin to multiply abnormally, thus giving rise to benign adenoma, which further develops into carcinoma over decades[9,10]. There are a few known risk factors which can accelerate the mutation process such as smoking, high alcohol consumption, unhealthy diet, obesity, physical inactivity etc, which make this condition preventable[11].

The prognosis for patients with colorectal cancer is related to the stage of disease at diagnosis and tumor histology, including differentiation, lymphatic invasion, and extent of tumor-free surgical resection margins[12]. Of these lymph node (LN) metastasis is most important predictor of survival and prognosis[13-15].

In India most of patients present late in disease further underlines the importance of LN harvest in patients undergoing surgery in our country[16]. Over the past two decades several studies have been done to determine the number of LNs to be harvested in resection specimen for prognostication of CRC. The prognosis and survival of the patients is proportional to number of LNs harvested along the specimen. The operating surgeon, pathologist and a number of patient and tumor related factors affect the number of LNs recovered. We in this study aim to study the factors that modify LN harvest independently.

This study was therefore done to determine the impact of tumor location, length, depth, grading and pre-op, post- op CEA levels and to assess the need of emergency or elective surgery on LN recovery in colorectal resection specimens.

MATERIAL AND METHODS

This prospective study was done by the Department of Surgery at Apolo KH Hospital, Velloreand Sandhya Hospital, Vellore from August 2012 to August 2019. 90 patients of all ages, who came to the Surgery department with carcinoma of the colon were included into the study. Patients who had Stage IV colorectal carcinoma were excluded from the study.

The nature of the study was explained to the patient and the relatives in detail and informed consent was taken. A thorough medical and clinical examination was done to all the patients. Digital rectal exam was done. Barium enema with or without air contrast was done to mainly locate deformities of intestinal topography. Sigmoidoscopy, colonoscopy and CT scan was done where necessary. Sigmoidoscopy was done to visualize the local rectal tumors or for routine screening. Colonoscopy was for the direct visual examination of the colon and rectum for early polypoid tumors preoperatively and recurrences post-resection. For staging of the disease, Computed tomography was done.

Base line investigations of the patients including Hb, TLC, DLC, ESR, platelet count, Na^+/K^+, random sugar, urea, creatinine, total protein/Albumin/Globulin, A:G ratio, ECG, chest X-ray were done.

CEA levels before the surgery and after the surgery were evaluated. Histopathological examination of the specimen was done to evaluate the size of the tumour, histological grade, depth and lymph node score.

Statistical analysis was done using SPSS software and correlating with the number of lymph nodes harvested.

RESULTS

Out of the 90 patients included in our study, most of the patients (28 (31.1%)) belonged to the age group 51-60 years, followed by 22 (24.4%) in the 41-50 age group. 17 (18.9%) of them belonged to 431-40 years and 13(14.4%) belonged to 61-70 years. The mean age of the patients in the study was 52.3± 13.08 (Table:1)

57 (63.3%) of the patients in our study were males and 33 (36.7%) were females, showing that males were the predominant population in our study (Fig: 1).

In most of the patients, i.e.41 (45.6%), the site of tumour was in the rectum. The second most common site of carcinoma was caecum and ascending colon, in 13 (14.4%), followed by 11 (12.2%) in caecum, 10 (11.1%) in sigmoid colon (fig:2)

70 (77.8%) of the tumours were found in the subserosal level, 15 (16.7%) in the serosa and 5 (5.5%) in the muscular layer (Fig: 3)

The grading of the tumour was M in 42 (46.7%) of the patients, W in 19 (21.1%), P in 11 (12.2%) patients (Fig:4)

75 patients (83.3%) had opted for elective surgeries, while in 15 (16.7%), it was an emergency (Table: 2).

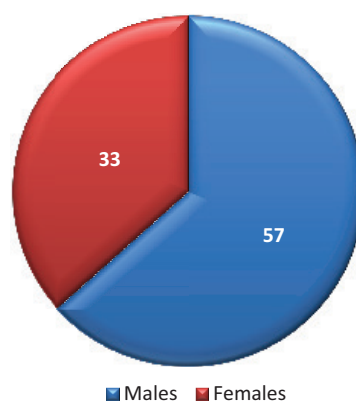The mean lymph nodes harvested among the patients was 32 ± 7.10 with15 of them positive (Table : 3)

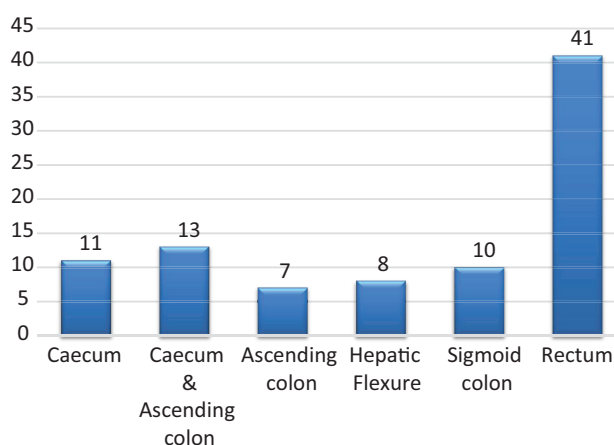**Figure-1:** Distribution of patients according to gender
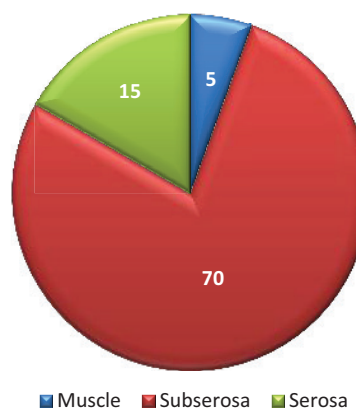

Figure-2: Site of tumour

Figure-3: Depth of tumour
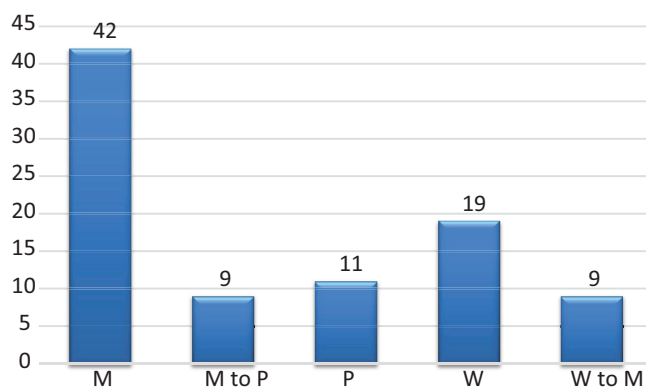
Figure-4: Distribution of patients according to grading of tumour

Age	Number	Percentage
<30	2	2.2%
31-40	17	18.9%
41-50	22	24.4%
51-60	28	31.1%
61-70	13	14.4%
>70	8	8.9%
Total	90	100%

Table-1: Agewise distribution of the patients

Type of surgery	Number	Percentage
Elective	75	83.3%
Emergency	15	16.7%
Total	90	100%

Table-2: Type of surgery

Lymph Nodes	Mean	Standard Deviation
Lymph nodes harvested	32	7.10
Positive lymph nodes	15	6.75

Table-3: Description of Lymph nodes harvested

LN Harvested	Number	Percentage
Adequate (≥12 nodes)	49	54.4%
Not Adequate (<12 nodes)	41	45.6%

Table-4: Distribution of patients according to lymph nodes harvested

Multivariate logistic regression was done for ers and the odds rario for site of tumeour was 1.56 (1.07-3.95), 2.01 (1.90-5.19), 1 (Referent), in the right, left and rectal tumours respectively. This was found to be statistically significant. The depth of the tumour was seen in mainly the subserosal level in 70 cases and 38 (54.3%) of them had harvested more than 12 lymph nodes. This was followed by 15 patients with tumor in the serosa and 8 (53.3%) of them had more than 12 lyomh nodes harvested. These values were statistically significant (Table 5)

Neoadjuvant therapy was given to 15 (16.7%) of the patietns and not given to 75 (83.3%) Table: 6/

DISCUSSION

In the present study 90 patients who met with the criteria of CRC were included. The mean age of the study population was 52.3± 13.08 (S.D.). The range was from 27 years to 77 years. More number of patietns 31.1% were in the age group of 51-60 years followed by 24.4% in the 61-70 years age group. 18.9% of them belonged to 31-40 years and 14.4% belonged to 61-70 years. There was a steady rise in the incidence of CRCs after the age of 30 years. In a study by Suryadeva et al, a majority of their patiens belonged to the 45-64 years age group, corroborating our study[17]. The mean age in a study by Peedikayil et al was 58.4 years, which was also similar to our study[18].

The predominant gender in our study was males with 63.3% and the females were 36.7%, showing a male to female ratio of 1.72:1. A study by Halder et al also had a male predominance

Vaiables	Independent variables (N)	Dependent variables (≥12 LN) N(%)	Odds ratio (95% CI)	P value	Significance
Size of tumour	-	-	0.98 (0.96-1.01)	0.423	NS
Site of Tumour	Right (39)	26(66.5%)	1.56 (1.07-3.95)	0.025	S
	Left (10)	6(60%)	2.01 (1.90-5.19)	0.036	S
	Rectum (41)	17(41.5%)	1 (Referent)		
Depth of Tumour	Subserosa (70)	38(54.3%)	1.16(1.0-4.51)	0.031	S
	Muscle (5)	3(60%)	1.07(1.0-7.52)	0.047	S
	Serosa (15)	8(53.3%)	1 (Referent)		
Type of Surgery	Elective (75)	45(60%)	0.16 (0.01-1.71)	0.132	NS
	Emergency (15)	4(26.7%)	1 (Referent)		
Grading of Tumour	M (51)	30(58.8%)	0.7(0.1-4.5)	0.708	NS
	P (20)	9(45%)	1.3(0.15-11.9)	0.797	NS
	W (19)	10(52.6%)	1 (Referent)		

Table-5: Multivariate logistic regression models of lymph node harvested

Neoadjuvant therapy	Number	Percent (%)
Given	15	16.7
Not given	75	83.3
Total	30	100

Table-6: Number of patietns with neoadjuvant treatment given

The lymph nodes harvested were more than 12 nodes and adequate in 49 (54.4%) of the cases and non adequate and less than 12 in 41 (45.6%) of the cases (Table : 4)

compared to the females, with a ration of 1.85:1 among the patients >35 years[16]. A study by Suryadevara et al reported a male : female of 1.24:1[17].

Majority of patients (45.6%) had rectal cancer. Caecum, ascending colon, hepatic flexure and sigmoid colon contributed to 26.7%, 7.8%, 8.9% and 11.1% of cases respectively. Predominant type of cancer in a study by Suryadevera was rectal cancer in 80% of the cases[17]. In a study by Peedikayil, most of the cancers were located below the splenic flexure[18]. Similar results were observed in other studies[12,19,20].

Out of the 90 patietns, 15 of them required emergency surgeries for intestinal obstruction, while 75 were operated with full pre-operative evaluation and bowel preparation.

The presence of lymph node metastasis has important implications in the prognosis and treatment of patients with colorectal cancer[21]. Observational studies indicate that the number of lymph nodes assessed by pathological examination (in particular, the negative node count) is associated with longer survival in colorectal cancer[22]. Thus, along with disease stage and tumor molecular features, the node count is often used for treatment decision making by oncologists. The mean for lymph nodes harvested was 14 ± 7.10 (SD) with 30 being highest and 5 being lowest. Adequate LN harvest was performed in 54.4% patients. The total number of LN harvested was significantly related to location and depth of invasion of tumor. Tumor located in ascending colon and hepatic flexure and late T stage were associated with increased LN yield. LN harvest was not adequate in 45.6% patients. Tumor located in caecum, sigmoid colon and rectum and early T stage were associated with decreased LN yield. The length of tumor, grade of tumor and CEA levels were not significantly related to LN harvest. There was no statistical difference of LN yield between patients undergoing emergency and elective surgery. According to Morikawa et al specimen length, tumor size, T3N0M0 stage, ascending colon tumor location, and year of diagnosis were positively associated with the negative node count[23].

A study by Betge et al emphasizes the significance of >12 lyph nodes harvest for the prognosis in advanced CRC. They also reported that the high tumor classification and size and stage were associated with the lymph node count[24].

CONCLUSION

This study reveals that the number of lymph nodes harvested is independent of the length and grading of the tumor. this lymph node burden is inclusive of both metastatic and reactive hyperplasia which may also be an integral part of the body's innate defence mechanisms. We also found CRCs tend to occur in younger age group with male predominance in India. Colon cancers are commoner than rectal cancers. There is trend of increased right colon tumors, signifying the need for evaluation of etiological factors and biological behaviour of tumors specific to subsites in future studies.

REFERENCES

1. K. M. Mohandas Colorectal cancer in India: controversies, enigmas and primary prevention Indian J Gastroenterol 2011;30(1):3–6.
2. Indian Council of Medical Research consensus document for the management of colorectal cancer. Bhawna Sirohi, Shailesh V. Shrikhande, Benjamin Perakath, Digumarti Raghunandharao, Pramod Kumar Julka, Vikram Lele, Arvind Chaturvedi, Ambakumar Nandakumar, M Ramadwar, Vikram Bhatia, Rohin Mittal, Tanvir Kaur, Deepak Kumar Shukla, and Goura Kishor Rath. Indian J Med Paediatr Oncol. 2014; 35(3): 192–196.
3. National Cancer Registry Programme, Indian Council of Medical Research: Three Year Report of Population Based Cancer Registries. 2009-2011.
4. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. 2010;127:2893–917
5. J.J.Y. Sung, S.C. Ng, F.K.L. Chan, et al.An updated Asia Pacific Consensus recommendations on colorectal cancer screening Gut, 64 (2015), pp. 121-132.
6. GLOBOCAN 2008 (http://globocan.iarc.fr/factsheets/cancers/colorectal.asp) (2008).
7. L.A. Torre, F. Bray, R.L. Siegel, J. Ferlay, J. Lortet-Tieulent, A. JemalGlobal cancer statistics, 2012. CA Cancer J Clin 2015;65(3):87-108
8. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Gut 2017;66(6):683–691.
9. Ewing I, Hurley JJ, Josephides E, Millar A. The molecular genetics of colorectal cancer. Frontline Gastroenterol. 2014;5(1):26–30.
10. Vogelstein B, Fearon ER, Hamilton SR, et al. Genetic alterations during colorectal-tumor development. N Engl J Med. 1988;319(4):525–32.
11. Islami F, Goding Sauer A, Miller KD, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA Cancer J Clin. 2018;68(5):31-54.
12. Martin R. Weiser, Mitchell C. Posner, Leonard B. Saltz. Adenocarcinoma of the Colon and Rectum. In. Charles J. Yeo, Jeffrey H. Peters, David W. McFadden, Jeffrey B. Matthews, John H. Pemberton, editors. Shackelford's Surgery Of The Alimentary Tract, 7th ed, Saunders; 2013; p2051.
13. Hsiang-Lin Tsai & Yung-Sung Yeh & Fang-Jung Yu & Chien-Yu Lu & Chin-Fan Chen & Chao-Wen Chen & Yu-Tang Chang & Jaw-Yuan Wang. Predicting factors of postoperative relapse in T2-4N0M0 colorectal cancer patients via harvesting a minimum of 12 lymph nodes. Int J Colorectal Dis 2009;24(2):177–183.
14. Tsai HL, Lu CY, Hsieh JS, Wu DC, Jan CM, Chai CY, Chu KS, Chan HM, Wang JY. The prognostic significance of total lymph node harvest in patients with T2-4N0M0 colorectal cancer. J Gastrointest Surg 11:660–665
15. Zlobec I, Lugli A. Prognostic and predictive factors in colorectal cancer. Postgrad Med J 2008;84(4): 403-401.
16. Shyamal Kumar Halder, Prosanta Kumar Bhattacharjee, Partha Bhar, Anadi Pachaury, Ranu Roy Biswas, Tapas Majhi, Pranjal Pandey. Epidemiological, Clinico-Pathological Profile and Management of Colorectal Carcinoma in a Tertiary Referral Center of Eastern India. JKIMSU, Vol. 2, No. 1, Jan-June 2013.
17. Sailaja Suryadevara, Veerendra Kumar KV, Pampanagouda SKM, Ravi Arjun, Vijalakshmi Deshmani. Colorectal Cancer Profile in a Tertiary Care Centre, Bangalore, India. Online Journal of Health and

Allied Sciences Volume 13, Issue 1; Jan-Mar 2014

18. Musthafa Chalikandy Peedikayil, Prem Nair, S. M. Seena, Lakshmi Radhakrishnan, Shine Sadasivan, V. A. Naryanan, V. Balakrishnan. Colorectal cancer distribution in 220 Indian patients undergoing colonoscopy. Indian J Gastroenterol 2009;28(6):212–215.

19. Inger Kristin Larsen and Freddie Bray. Trends in colorectal cancer incidence in Norway 1962–2006: an interpretation of the temporal patterns by anatomic subsite. Int. J. Cancer 2010;126(2):721–732.

20. M. Ponz de Leon, M. Marino, P. Benatti, G. Rossi, M. Menigatti, M. Pedroni, C. Di Gregorio, L. Losi, F. Borghi, A. Scarselli, G. Ponti, B. Roncari, G. Zangardi, G. Abbati, E. Ascari & L. Roncucci. Trend of incidence, subsite distribution and staging of colorectal neoplasms in the 15-year experience of a specialised cancer registry. Annals of Oncology 2004;15(3): 940–946.

21. Compton CC. Optimal pathologic staging: defining stage II disease. Clin Cancer Res. 2007;13(22):6862s-6870s.

22. Chang GJ, Rodriguez-Bigas MA, Skibber JM, Moyer VA. Lymph node evaluation and survival after curative resection of colon cancer: systematic review. J Natl Cancer Inst. 2007;99(6):433-441.

23. Teppei Morikawa, Noriko Tanaka, Aya Kuchiba, Katsuhiko Nosho, Mai Yamauchi, Jason L. Hornick, Richard S. Swanson, Andrew T. Chan, Jeffrey A. Meyerhardt, Curtis Huttenhower, Deborah Schrag, Charles S. Fuchs, Shuji Ogino. Predictors of Lymph Node Count in Colorectal Cancer Resections ARCH SURG/VOL 147 (NO. 8), AUG 2012

24. Betge J, Harbaum L, Pollheimer MJ, et al. Lymph node retrieval in colorectal cancer: determining factors and prognostic significance. Int J Colorectal Dis. 2017;32(7):991-998.