Journal of Cancer and Tumor International

11(3): 14-24, 2021; Article no.JCTI.68424
ISSN: 2454-7360

Audit of Lymph Node Sampling in Colorectal Carcinoma Resections-implication for Prognosis and Management

Uchenna Simon Ezenkwa[1], Omenogor Alexander Odigwe[1], Sebastian Anebuokhae Omenai[1], Temitope O. Ogunsanya[1], Omolade O. Adegoke[1] and Olufemi John Ogunbiyi[1*]

[1]Department of Pathology, University College Hospital, Ibadan Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. Authors USE, SAO, OOA and OJO conceived and designed the study. Data review and statistical analysis was performed by authors USE, OAO and TOO. The first draft manuscript was by author USE. All authors reviewed and corrected the first draft manuscript. Author OJO managed the analyses of the study. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JCTI/2021/v11i330152
Editor(s):
(1) Dr. Nicole D. Riddle, Tampa General Hospital, USA.
Reviewers:
(1) Arun Kumar Barad, ESI Medical College Hospital, India.
(2) Vimal. M, Sri Manakula Vinayagar Medical College and Hospital, India.
Complete Peer review History: http://www.sdiarticle4.com/review-history/68424

Original Research Article

Received 22 March 2021
Accepted 27 May 2021
Published 02 June 2021

ABSTRACT

Aims: To review lymph node yield in colorectal carcinoma (CRC) resections and its associated factors in a Nigerian Teaching Hospital practice.
Study design: This was a retrospective cross-sectional study.
Place and duration of study: Department of Pathology, University College Hospital Ibadan Nigeria and colectomies from January 2014 to December 2018 were reviewed.
Methodology: Surgical Pathology reports of CRC resections at the University College Hospital Ibadan over 5 years (2014-2018) were reviewed. Colectomy lengths, tumour location (colon/rectum), tumour size, comment on presence of lymph node (yes/no), lymph node count, presence of attached mesentery (yes/no), histological subtype, tumour grade, presence of tumour-positive node and count, and pT stage were documented. Fisher's Exact test was employed to test the effects of these variables on presence of lymph node and tumour-positive node at histology using SPSS 20. Significance level was set at $P < .05$.

**Corresponding author: Email: fogunbiyi@gmail.com;*

Results: Of 66 histology reports retrieved, 62 (93.9%) had comments on search for lymph nodes and attached mesentery was documented in 25 (37.9%). The median colectomy length and tumour size were 25cm (6cm-152cm) and 6.75cm (3-30cm) respectively. Lymph nodes were present in 52 (78.8%) specimens; 28 (53.8%) of these had tumour-positive lymph nodes. Adenocarcinoma NOS was the commonest histological subtype 53 (80.3%), mucinous carcinoma 12 (18.2%) and signet ring carcinoma 1 (1.5%). Eighteen, 9 and 1of adenocarcinoma NOS, mucinous carcinoma, and signet ring carcinoma respectively had tumour-positive lymph nodes. Finding of lymph node was significantly associated with comment on search for lymph node ($p < .01$) while finding tumour-positive nodes was associated with histological subtype, presence of mesentery, late tumour stage and lymph node count ≥ 12 ($p < .05$).

Conclusion: If lymph nodes were present, more than likely there will be metastatic involvement. To increase Lymph node yield in CRC resections, submission of mesentery and search for lymph nodes is indicated. When nodes are absent, a mention is required for practice audit. It is imperative to include both clinical and grossing notes for lymph nodes to certify and guide precise staging of the cancer.

Keywords: Audit; lymph node yield; lymph node count; Colorectal carcinoma; tumour staging.

1. INTRODUCTION

In both genders, colorectal carcinoma is the third commonest cancer in the world but ranks second in terms of mortality [1]. It is estimated that over 1.9 million new cancer cases and 935,000 deaths were attributed to this disease in 2020 [1]. In Ibadan, southwestern Nigeria, it ranks first after gender-based cancers (breast, cervix and prostate) [2]. The incidence is on the increase in emerging economies of the world owing to increase in the adoption of westernized lifestyle [1,3,4]. Overall survival is also worse in these countries attributable to late presentation, weak health systems, poverty with consequent lack of access to chemotherapy [5]. It is therefore imperative that patients who receive surgical resections are assessed comprehensively to limit the risk of residual tumour. Examination of a minimum of 12 lymph nodes following surgical resection of the tumour has been adjudged sufficient for reliable tumour staging [6]. Studies have shown that examination of ≥ 12 lymph nodes is associated with improved patient survival [7,8]. This suggests that finding of no lymph node or less number of lymph nodes could give rise to false tumour-node negativity and such patients might have tumour recurrence with poorer prognosis [9]. Lymph node-yield from resection specimen is determined by the diligence of the Surgeon and Pathologist in searching for lymph nodes and also by patient (tumour) factors [10]. Given that the Surgeon and Pathologist factors are modifiable but not the tumour factors, it has been advocated that lower number of lymph nodes after satisfactory search for lymph nodes might be sufficient in some cases [10,11]. Wu et al*.,* showed that there is a 90% level of confidence of finding tumour-positive nodes when 3 lymph nodes are examined for a pT1 patient. This same level of confidence is achieved when 8 nodes are examined for a pT2 patient [11]. Local practices may differ with care adapted to prevailing expertise and available health system support. With this in mind, this study was conceived to determine the lymph node yield in colorectal carcinoma resections in our local practice and factors associated with it, and to determine factors associated with finding tumour-positive nodes.

2. MATERIALS AND METHODS

2.1 Study Location and Case Selection

Surgical Pathology requests forms and histopathological reports of CRC resections at the University College Hospital Ibadan over 5 years (2014-2018) were reviewed retrospectively.

2.2 Data Acquisition

Patient age, gender, tumour location (colon/rectum), colectomy length (cm) tumour size (cm), comment on presence of lymph node (yes/no), lymph node count, presence of attached mesentery (yes/no), were retrieved. The tumour histological subtype (adenocarcinoma not otherwise specified, mucinous carcinoma, signet ring cell carcinoma) [12], tumour grade (well differentiated, moderately differentiated, poorly differentiated and undifferentiated) [12], presence of tumour-positive node and count, and pathological tumour staging (pT stage) [6], were

also retrieved from the surgical pathology reports, and, where any of these were not documented, the H&E stained tissue slides were retrieved and reviewed microscopically. Tumour histological subtypes other than adenocarcinoma (NOS) were not further graded. Patient age and tumour size were further categorized into age < 60 years/≥ 60 years and < 5cm/≥ 5cm respectively, while histologic subtype, tumour grade and pT stage were categorized into adenocarcinoma/others, low grade (well and moderately differentiated)/high grade (poorly differentiated and undifferentiated), and early stage (pT1-pT2)/late stage (pT3-pT4) respectively.

2.3 Statistical Data Analysis

Descriptive statistics were used to classify the data into categories and/or median. The continuous variables were further analyzed using Pearson's correlation and multiple linear regression statistics. Fisher's Exact test was applied on the categorical variables to test for associations between variables and presence of lymph nodes, finding of tumour positive lymph nodes and finding of ≥ 10 or 12 nodes. The test statistical package used was IBM SPSS version 20. The level of significance was set at $p < .05$.

3. RESULTS AND DISCUSSION

3.1 Results

3.1.1 Demographic and histopathological parameters

Sixty six cases were retrieved and included in this study and their clinicopathological parameters are as shown in Table 1. There were 34 males and 32 females with a male-female ratio of 1.1:1 and a median age of 60 years (12-85years). Thirty-six (54.5%) of the patients were younger than 60 years. Forty-nine (74.2%) tumours were located in the colon whilst 17 (25.8%) were in the rectum, with median resection length of 24.5cm (6cm-152cm). Median tumour size was 6.5cm (3-30cm), with 42 (63.2%) being ≥ 5cm in widest dimension. Comment on the presence or otherwise of lymph nodes was made in 62 (93.9%) of cases, 52 (78.8%) had lymph nodes, and 28 (53.8%) out of these 52 cases had tumour metastasis in one or more lymph nodes. Seventeen (25.8%) had lymph node yield ≥ 10 counts whilst 11 (16.7%) had count ≥ 12. Overall median lymph node count was 4 lymph nodes (0-40) with an average of 6 lymph nodes per specimen. Low grade tumour differentiation (well and moderate differentiation) was predominant 49 (74.2%) whilst high grade differentiation (poorly differentiated) was seen in 4 (6.1%). No undifferentiated tumour was seen.

3.1.2 Lymph node yield and clinic pathological factors

Table 2 shows association between clinicopathological parameters and finding of lymph nodes. Only comment on search for lymph nodes was significantly associated with finding a lymph node at surgical cut-up. All the 4 cases with no comment on lymph nodes had no lymph nodes; one of these involved a resection length of 6cm. Twelve out of the 13 mucinous and signet ring cell carcinoma histologic subtypes had lymph nodes whilst 40 out of the 53 adenocarcinomas NOS had lymph nodes. Lymph nodes were found more frequently among tumours with size ≥ 5cm and late pT stage (pT3-pT4). Two out of the 3 tumours with pT1 stage had lymph nodes while 10 of the 11 tumours with pT4 stage had lymph nodes. The highest pT stage was pT3 with 42 cases.

Lymph node count ≥10 was significantly associated with presence of mesentery, histologic subtype, pT tumour stage and tumour size ≥ 5cm, but not with gender, age </≥ 60 years, tumour location, comment on lymph nodes and tumour grade (Table 3). Thirty six cases had no statement on presence of mesentery, 15 of these involved rectal resections. Finding a minimum of 12 lymph nodes was associated with age </≥ 60 years and tumour size ≥ 5cm but not with the other clinicopatholoical parameters (Table 4).

3.1.3 Tumour-positive lymph nodes and lymph node count

Table 5 shows associations between clinicopathological parameters and finding of tumour positive lymph nodes. Significant associations were observed for presence of mesentery, histologic subtype, pT tumour stage, minimum of 10 and 12 lymph node yields. Fig. 1 below shows a tumour-positive lymph node with complete effacement of the nodal architecture by tumor cells.

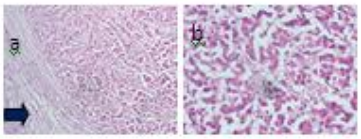

Fig. 1. Tumour-positive lymph nodes. The lymph node tissue has been replaced by malignant epithelial cells from the colon. Note the nodal capsule (arrow). H&E (a) x 40, (b) x 100

Pearson's correlation analysis showed a significant inverse relationship between number of lymph nodes and patient age at $p < .01$ level ($r = -0.370$; $p < .002$) and a positive relationship between resection length and number of lymph nodes at $p < .05$ level ($r = 0.317$; $p < .010$). Correlation between number of lymph nodes and tumour size was non-significant ($r = 0.224$; $p < .078$).

Table 1. Patients and histopathological characteristics distribution of the colorectal carcinomas

	Frequency	Percentage
Gender		
Female	32	48.5
Male	34	51.5
Age		
<60 years	36	54.5
≥60 years	30	45.5
Tumour size		
< 5cm	21	31.8
≥ 5cm	42	63.6
Missing	3	4.5
Tumour location		
Colon	49	74.2
Rectum	17	25.8
pT stage		
pT1	3	4.5
pT2	10	15.2
pT3	42	63.6
pT4	11	16.7
Presence of lymph node		
Yes	52	78.8
No	14	21.2
Tumour positive nodes		
Yes	28	42.2
No	38	57.6
Presence of mesentery		
Yes	25	37.9
No	5	7.6
Missing	36	54.5
Comment on lymph nodes		
Yes	62	93.9%
No	4	6.1
Histologic subtype		
Adenocarcinoma	53	80.3
Mucinous carcinoma	12	18.2
Signet ring cell carcinoma	1	1.5

	Frequency	Percentage
Tumour grade		
Well differentiated	34	51.5
Moderately differentiated	15	22.7
Poorly differentiated	4	6.1
Lymph node count ≥10		
< 10 nodes	49	74.2
≥10 nodes	17	25.8
Lymph node count ≥12		
<12 nodes	55	83.3
≥12 nodes	11	16.7

Table 2. Clinicopathological and their associations with finding lymph nodes following colorectal tumour resections

	Presence of lymph nodes		*P* value
	Yes	**No**	
Age (years)			.768
<60	29	7	
≥60	23	7	
Gender			.766
Female	6	26	
Male	8	26	
Tumour location			.516
Colon	10	39	
Rectum	4	13	
Tumour size			.198
<5cm	7	14	
≥5cm	7	35	
Histological subtype			.269
Adenocarcinoma	13	40	
Others	1	12	
Tumour grade			.688
Low grade	12	37	
High grade	1	3	
pT stage			.450
pT1-pT2	4	9	
pT3-pT4	10	43	
Comment on lymph nodes			.001*
No	4	0	
Yes	10	52	
Presence of mesentery			.066
No	3	2	
Yes	3	22	

**p value significant at <0.05*

Table 3. Factors associate with low or high lymph node counts in colorectal carcinomas resections

	Lymph node yield		*P* value
	Low (<10counts)	**High (≥10counts)**	
Gender			1.000
Female	24	8	
Male	25	9	

	Lymph node yield		*P* value
	Low (<10counts)	**High (≥10counts)**	
Age (years)			.162
< 60	24	12	
≥60	25	5	
Tumour location			.525
Colon	35	14	
Rectum	14	3	
Presence of mesentery			.006*
Yes	13	12	
No	5	0	
Not stated	31	5	
Tumour size			.013*
<5cm	20	1	
≥5cm	28	14	
Histologic subtype			.029*
Adenocarcinoma	43	10	
Others	6	7	
Tumour grade			1.000
Low grade	40	9	
High grade	3	1	
pT Stage			.015*
pT1-pT2	13	0	
pT3-pT4	36	17	
Comment on lymph nodes			.565
No	4	0	
Yes	45	17	

**p is significant at < .05*

Table 4. Lymph node yield set at a minimum of 12 counts as correlated with clinicopathological parameters

	Lymph node yield at a minimum of 12 counts		*P* value
	< 12counts	**≥12 counts**	
Gender			0.748
Female	26	6	
Male	29	5	
Age (years)			0.017*
<60	26	10	
≥60	29	1	
Tumour location			1.000
Colon	41	8	
Rectum	14	3	
Presence of mesentery			0.443
No	5	0	
Yes	19	6	
Not stated	31	5	
Tumour size			0.023*
<5cm	21	0	
≥5cm	33	9	

	Lymph node yield at a minimum of 12 counts		*P* value
	< 12counts	**≥12 counts**	
Comment on lymph nodes			
No	4	0	1.000
Yes	51	11	
pT stage			0.104
pT1-pT2	13	0	
pT3-pT4	42	11	

**p value significant at < .05*

Table 5. Tumour positive lymph nodes detected at histology and the associated clinicopathological factors

	Tumour positive lymph nodes		*P* value
	No	**Yes**	
Gender			.465
Female	20	12	
Male	18	16	
Age (years)			.805
<60	20	16	
≥60	18	12	
Tumour size			.060
<5cm	16	5	
≥5cm	21	21	
Tumour location			
Colon	29	20	.778
Rectum	9	8	
Histological subtype			.010*
Adenocarcinoma	35	18	
Others	3	10	
Tumour grade			1.000
Low grade	32	17	
High grade	3	1	
pT stage			.032*
pT1-pT2	11	2	
pT3-pT4	27	26	
Comment on lymph nodes			.131
No	4	0	
Yes	34	28	
Lymph node count at cut off count 10			.001*
<10	35	14	
≥10	3	14	
Lymph node count at cut off count 12			
<12	36	19	.006*
≥12	2	9	
Presence of mesentery			.021*
No	4	1	
Yes	9	16	
Not stated	25	11	

**p value significant at <.05*

Table 6. Multiple linear regression showing predictors of lymph nodes among patient age, colorectal resection length, and tumour length

	Odds Ratio	95% confidence interval	*P* value
Age (Years)	-0.292	-0.283 - -0.021	.024*
Resection length (cm)	0.156	-0.026 – 0.114	.217
Tumour length (cm)	0.170	-0.122 – 0.716	.161

**p value is significant at < .05*

3.1.4 Predicting lymph node yield in colorectal carcinoma colectomies

On multiple linear regression analysis, only patient age predicted lymph node number (Table 6). A higher proportion of these cases had a younger age at diagnosis. The older the individual the less likely to find lymph nodes within the resected tissue.

3.2 Discussion

Lymph nodes in colorectal carcinoma resections are assessed to determine tumour spread beyond the gut wall. Node-negative tumours are believed to confer better patient overall survival [13]. Lack of/or few lymph node retrieval will therefore give a false negative staging as such patients may harbor tumour-positive nodes, which may be a source of tumour recurrence and metastasis as the study by Lykke et al suggested [11,14]. A minimum of 12 lymph nodes examined was therefore set as a cut off due to finding an association between tumour-habouring lymph nodes and improved overall survival [7,8]. The finding in this study of 21.2% colectomies without accompanying lymph nodes suggests that nearly one out of every 4 CRC patients could be inadequately staged, predisposing to a higher risk of tumour recurrence. Of all the clinicopathological factors examined, only comment on the presence or otherwise of lymph nodes during surgical pathology grossing is associated with finding a lymph node. As expected, such comments represents unequivocal evidence that attempt had been made to search for the lymph nodes. This though does not imply that searching for nodes would lead to its retrieval as has been shown here that 10 out of the 62 cases with search for lymph nodes yielded none. Diligence is therefore advocated at grossing to attempt a near accurate staging of these tumours.

About 42.4% of the cases in this study had tumour-positive lymph nodes. Finding tumour positive lymph nodes was associated with presence of mesentery, tumour histological subtype, advanced tumour stage and high lymph node count. Adequate search for lymph nodes is therefore required both at surgery and grossing to achieve high lymph node count, which would increase the chances of harvesting tumour positive nodes in the patient whilst ensuring proper tumour staging, even in patients with neoadjuvant chemotherapy [15,16]. It also suggests that even when all efforts have been made in search of lymph nodes, tumour characteristics could lead to fewer but true node-negative tumours.

Our results also show a low lymph node count with a median count of 4. This contrasts with a median of 12 lymph nodes counted in the study by da Costa et al in the Netherlands [15]. About 17% of our colectomies had a minimum of 12 lymph nodes and this is similar though slightly higher than the result of the study by Orsenigo et al in Milan, but lower than 49% documented by Elsheikh and Zaitoun in Nottingham [17,18]. Examining a minimum of 10 lymph nodes increased the percentage to 25.8% in the present study. Observation of the factors associated with finding a minimum of 10 lymph nodes in this study shows that tumour characteristics and human factors could contribute to this low lymph node yield as has been found in a Danish study [15]. The human factor in our study included having mesentery attached to the resection specimen while the tumour factors included histologic subtype, pT stage of the tumour, and tumour size greater than 5cm. In the Danish study, the human factors were surgeons' experience and diligence in lymph node search at specimen grossing, while the tumour factors were tumour location, and size [15]. Whilst diligent search for lymph nodes by the pathologist contributes to the finding of lymph nodes, our study suggests that identification of lymph nodes within the mesentery at surgery and including these to the resection specimen could increase the lymph node yield significantly. Resection length was also correlated with lymph

node number, again supporting the notion that human factors influence lymph node yield [13,15,19]. Resection lengths of 6cm, 22 and 24 cm were among those without lymph nodes. While decision on the length of bowel to be resected is patient dependent, shorter lengths may lead to under staging of the tumours thereafter.

Besides patient age, we did not find an additional clinicopathological factor associated with finding a minimum lymph node count of 12. Age was also significantly correlated with lymph node number and remained so on multiple regression analysis. This finding suggests that younger patients may have more lymph node yield in our environment. However, we have observed that a minimum count of 10 lymph nodes could perform well in determining adequate lymph node count just as a minimum count of 12 lymph nodes would, especially in early pT stage tumours. Other researchers have shared this view previously, more so as lymph node yield is also influenced by tumour characteristics, which are non-modifiable [13,15, 20].

In a nut shell, this study has made some observations. First, occasional grossing reports lacked information on lymph node assessment during grossing by the pathologist. We therefore recommend that histopathological reports should be deemed incomplete without lymph node examination unless comment on lymph node search has been documented. This would serve as an audit for colorectal interventions in our environment. Secondly, a minimum count of 10 lymph nodes per resection specimen performed similarly as 12 node counts in determining tumour-positive nodes. Thirdly, tumour characteristics could make insistence on 12 lymph node count unattainable especially in pT1 and pT2 tumours. And fourthly, we have shown that at least half of CRC resections in this environment either have no mesentery attached to the specimen or its presence is not documented. Given the role it could play in identifying higher lymph node count and tumour-positive nodes, local surgical practice may need to review mesenteric resection guidelines to ensure adequate tumour lymph nodal staging. The benefits of extended mesenteric or colectomy length resections, especially for the sake of high lymph node yield, have been questioned [15]. However, more recent studies have shown not only higher lymph node count, but also improved patient outcome and similar tolerability of complete mesocolic with central vascular ligation excision and mesorectal excision with lateral lymph node dissection when compared with conventional surgery [21-24]. We therefore recommend that as indicated, efforts to achieve complete mesocolic resection be implemented.

In other words, to improve nodal staging in CRC colectomies, the surgeon would need to be intentional about the length and extent of mesocolic and or mesorectal excisions. Hence, dissecting along anatomical landmarks with regional meso-colic or rectal resections would be advantageous in ensuring complete locoregional lymph node harvest for examination. Where these are lacking due to specimen lacking mesentery, or too short a specimen length, finding adequate lymph nodes for reliable tumour staging may prove difficult.

Surgeon's expertise and level of experience will also determine how effectively practice recommendations are put into effect [25]. Being a retrospective study, assessing accurately surgeons' expertise was difficult and could prove unreliable, hence it was omitted. Since this treatment modality has curative intent, uniformity with recommended international guidelines would ensure that all patients receive acceptable care. However, regular training on modules emphasizing practice changes needs to be a routine so as to raise the standard of practice continually.

A major limitation to this study was the lack of survival data to examine patient outcome in high and low lymph node yield tumours. Collection of follow-up data is inefficient in this community [26]. More needs to be done as this data helps to evaluate outcome of health system interventions. Also, treatment with neo-adjuvant chemotherapy was not documented for these patients. A prospective study design would help to take these into consideration to further determine their relevance in lymph staging in CRCs.

4. CONCLUSION

Lymph node yield in CRC colectomy specimens in our practice is low and could be improved by observing human factors involved in specimen handling. Finding node positive tumour may be influenced by tumour factors. Local practice settings with similar low node yield may benefit from improved diligence in lymph node search in the specimens thereby ensuring proper tumour staging. These findings have necessitated a call

to practicing pathologists and trainees to proactively audit practice guideline in their own and other healthcare units in the hospital to foster uniformity of patient care.

CONSENT

Not applicable.

ETHICAL APPROVAL

Data for this study was completely anonymized prior to accessing them. No patient identifiers have been added to this study. Being an audit study, names of the personnel were also anonymized. Institutional ethical review board approval was obtained from the hospital ethics committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Sung H, Ferlay J, Siejel RL, Soerjomataram I, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020 : GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;(71):209–249.
2. Ogunbiyi JO, Fabowale AO, Ladipo AA, Ogun GO, Adeyemi AO BO. Cancer incidence and Top ten Cancers in Ibadan (Eleven Local Government Area), Childhood Cancers -Nigeria, 2009-2012; 2016.
3. Rafiemanesh H, Mohammadian-hafshejani A, Sepehri Z, Shamlou R, Salehiniya H, Makhsosi BR. Incidence and Mortality of Colorectal Cancer and Relationships with the Human Development Index across the World. Acian Pac J Cancer Prev. 2016;17(5):2465–73.
4. Jemal A, Smith RA, Ward E. Worldwide Variations in Colorectal Cancer. CA Cancer J Clin. 2009;59:366–78.
5. Sylla BS, Wild CP. A million Africans a year dying from cancer by 2030: what can cancer research and control offer to the continent ? IJC. 2012;250:245–50.
6. Brierley JD, Gospodarowicz MK, Wittekind C. Colon and Rectum. In: TNM Classification of Malignant Tumours. 8th ed. 2017;84–8.
7. Tsai H, Huang C, Yeh Y, Ma C, Chen C. Factors affecting number of lymph nodes harvested and the impact of examining a minimum of 12 lymph nodes in stage I-III colorectal cancer patients : a retrospective single institution cohort study of 1167 consecutive patients. BMC Surg [Internet]. 2016;1–9. Available:http://dx.doi.org/10.1186/s12893-016-0132-7
8. Chen HH, K DC. Pathological examination of 12 regional lymph nodes and long-term survival in stages I – III colon cancer patients: An analysis of 2 , 056 consecutive patients in two branches of same institution. 2010;1333–41.
9. Joseph NE, Sigurdson ER, Hanlon AL, Wang H, Mayer RJ, Macdonald JS, et al. Accuracy of Determining Nodal Negativity in Colorectal Cancer on the Basis of the Number of Nodes Retrieved on Resection. 2003;10(3):213–8.
10. Shia J, Wang H, Nash GM, Klimstra DS. Lymph Node Staging in Colorectal Cancer : Revisiting the Benchmark of at Least 12 Lymph Nodes in R0 Resection. ACS [Internet]. 2012;214(3):348–55. Available:http://dx.doi.org/10.1016/j.jamcollsurg.2011.11.010
11. Wu Z, Qin G, Zhao N, Jia H, Zheng X. Assessing the adequacy of lymph node yield for different tumor stages of colon cancer by nodal staging scores. 2017;1–7.
12. Hamilton SR, Bosman FT, Boffetta P, Ilyas M, Morreau H, Naakamura SI, et al. Tumours of the colon and rectum. In: WHO Classification of Tumours of the Digestive System. 2010;131–82.
13. Ong MLH, Schofield JB, Ong MLH, Schofield JB, Hospital M, Me K. Assessment of lymph node involvement in colorectal cancer. World J Gastrointest Surg. 2016;8(3):179–92.
14. Lykke J, Rosenberg J, Jess P, Roikjaer O, Colorectal D, Group C. Lymph node yield and tumour subsite are associated with survival in stage I – III colon cancer: Results from a national cohort study. 2019;1–8.
15. Da Costa DW, van Dekken H, Witte BI, van Wagensveld BA, van Tets WF, Van Vrouenraets BC. Lymph Node Yield in Colon Cancer: Individuals Can Make the Difference. Dig Surg. 2015;32:269–74.
16. Lykke J, Jess P, Roikjaer O. Increased Lymph Node Yield Is Associated With

Improved Survival in Rectal Cancer Irrespective of Neoadjuvant Treatment: Results From a National Cohort Study. Dis Colon Rectum. 2015;58(9):823–30.
17. Orsenigo E, Gasparini G, Carlucci M. Clinicopathological Factors Influencing Lymph Node Yield in Colorectal Cancer: A Retrospective Study. Gastroenterol Res Pract; 2019.
18. Elsheikh S, Zaitoun M. Factors Influence Lymph Node Retrieval after Resection for Rectal Cancer. J Adenocarcinoma. 2016;1(2):1–7.
19. Destri GL, Carlo I Di, Scilletta R, Scilletta B, Puleo S, Destri GL, et al. Colorectal cancer and lymph nodes : The obsession with the number 12. World J Gastroenterol. 2014;20(8):1951–60.
20. Backes Y, Elias SG, Bhoelan BS, Groen JN, Bergeijk J Van, Seerden TCJ, et al. The prognostic value of lymph node yield in the earliest stage of colorectal cancer : a multicenter cohort study. 2017;1–11.
21. Fujita S, Akasu T, Mizusawa J, Saito N, Kinugasa Y, Kanemitsu Y, et al. Postoperative morbidity and mortality after mesorectal excision with and without lateral lymph node dissection for clinical stage II or stage III lower rectal cancer (JCOG0212): Results from a multicentre , randomised controlled , non-inferiority trial. Lancet Oncol [Internet]. 2012;13(6):616–21.
Available:http://dx.doi.org/10.1016/S1470-2045(12)70158-4
22. Fugita S, Mizusawa J, Kanemitsu Y, Ito M, Kinugasa Y, Komori K, et al. Mesorectal excision with or without lateral lymph node dissection for clinical stage II / III Lower Rectal Cancer (JCOG0212). Ann Surg. 2017;266(2):201–7.
23. Abdelkhalek M, Setit A, Bianco F, Belli A, Denewer A, Youssef TF, et al. Coloproctology complete mesocolic excision with central vascular ligation in comparison with conventional surgery for patients with colon cancer – the experiences at two centers coloproctology. Ann Coloproctol. 2018;34(4):180–6.
24. Perrakis A, Vassos N, Weber K, Matzel KE, Papadopoulos K, Koukis G, et al. Clinical research Introduction of complete mesocolic excision with central vascular ligation as standardized surgical treatment for colon cancer in Greece. Results of a pilot study and bi-institutional cooperation. Arch Med Sci. 2019;15(5):1269–77.
25. Hsu T, Lu H, Wei C, Yin W, Chang C, Chiou W, et al. Clinical and pathologic factors affecting lymph node yields in colorectal cancer. PLoS One. 2013;8(7):7–11.
26. Allemani C, Weir HK, Carreira H, Harewood R, Spika D, Wang X, et al. Global surveillance of cancer survival 1995 – 2009: Analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet [Internet]. 2015;385(9972):977–1010.
Available:http://dx.doi.org/10.1016/S0140-6736(14)62038-9

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/68424