

Comparison of different lymph node staging systems for predicting prognosis in patients with colon cancer who have undergone surgical resection

ANNA MADEJ-MIERZWA¹, MARIUSZ SZAJEWSKI^{1,2} and WIESŁAW JANUSZ KRUSZEWSKI^{1,2}

¹Department of Oncological Surgery, Gdynia Centre of Oncology, Pomeranian Hospitals, Gdynia 81-519;

²Division of Propedeutics of Oncology, Medical University of Gdańsk, Gdańsk 80-210, Poland

Received January 21, 2022; Accepted March 17, 2022

DOI: 10.3892/ol.2022.13296

Abstract. At present, the most widely used lymph node (LN) staging system in colon cancer is number of metastatic LNs in pathological assessment (pN) from the 8th edition of the TNM American Joint Committee on Cancer/Union for International Cancer Control staging system, which considers the number of metastatic LNs, omitting the total number of dissected LNs. The aim of the present study was to compare the prognostic performance of pN with alternative LN staging systems, including LN ratio (LNR) and log odds of positive LNs (LODDS). The clinical and histopathological data of 298 patients with colon cancer who underwent elective surgical resection in a single surgical centre were analysed. LNR and LODDS cut-off values according to two previous studies were selected to separate patients into different subgroups. Univariate and multivariate analyses were performed to distinguish prognostic factors. The three-step multivariate analysis showed that LNR was a superior prognostic indicator compared with pN and LODDS. Additionally, the Akaike Information Criterion, a measure of the relative quality of statistical models, confirmed that LNR displayed the best prognostic performance. Similarly, in a subpopulation of patients with number of dissected LNs (NDLN) ≥ 12 , LNR was the most accurate LN staging system in relation to prognosis. In a subpopulation with NDLN < 12 , there was no significant difference in LN classification prognosis of 5-year overall survival; however, LNR and LODDS

were more independent of NDLN than pN. Among the three LN classifications, LNR is the most accurate LN staging system for predicting prognosis for patients with colon cancer who have undergone surgical resection, particularly those with metastatic LNs subjected to adequate lymphadenectomy.

Introduction

Lymph node (LN) status is a key prognostic factor in colon cancer (1). Staging accuracy and prognosis improve with increased numbers of dissected and examined LNs, both in stage II and III colon cancer (2). At present, the most widely used LN staging system is number of metastatic LNs in pathological assessment (pN) from the 8th edition of the TNM American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) staging system, which takes into account the number of metastatic LNs (3). To evaluate LN status, the AJCC/UICC guidelines recommend resection and assessment of ≥ 12 LNs. Nevertheless, as reported by numerous studies, the LN yield from a colectomy varies and may not be sufficient to meet these recommendations (4,5); this is because LN yield depends on various factors, such as surgical technique and differences in pathological procedure for obtaining LNs from the specimen (5,6).

Evaluation of LN status based only on the number of metastatic LNs and omitting the total number of dissected LNs (as in pN) may be insufficient and lead to understaging. For that reason, two novel systems analysing not only the number of positive LNs, but also number of dissected LNs (NDLNs) were developed: LN ratio (LNR) (7) and log odds of positive LNs (LODDS) (8). LNR is the ratio of positive LNs divided by the total number of dissected LNs, which reflects the probability of metastatic LNs in the LN yield. LNR has been reported to be a strong independent prognostic factor in rectal and colon cancer (9,10), as well as multiple types of solid malignant tumors, such as breast, pancreatic, gastric, lung and bladder cancer (11-14). LODDS is another LN staging system that has been proved to be a strong prognostic factor in colon and rectal cancer (8,15-17). This staging system is particularly useful for patients without metastases to regional LNs. In patients with node-negative cancer, LNR is zero and does not provide any additional information in comparison with

Correspondence to: Dr Anna Madej-Mierzwa, Department of Oncological Surgery, Gdynia Centre of Oncology, Pomeranian Hospitals, 1 Powstania Styczniowego Street, Gdynia 81-519, Poland
E-mail: anna.madejj@gmail.com

Abbreviations: LN, lymph node; LNR, lymph node ratio; LODDS, log odds of positive lymph nodes; AJCC/UICC, American Joint Committee on Cancer/Union for International Cancer Control; AIC, Akaike Information Criterion; NDLN, number of dissected lymph nodes

Key words: colon cancer, LNR, LODDS, survival analysis, prognostic factor

pN0 from TNM classification, whereas LODDS may stratify patients according to prognosis in this group (15-17).

The aim of the present study was to compare three LN staging systems in patients with colon cancer who underwent elective tumour resection.

Materials and methods

Patients. The present study recruited 298 patients who were operated on between September 2006 and May 2014 in the Department of Oncological Surgery, Gdynia Centre of Oncology, Pomeranian Hospitals, Poland. The inclusion criteria were as follows: Patients aged >18 years; histologically proven adenocarcinoma of the colon; curative surgical tumor resection and minimal follow-up period of 65 months or until death. Patients with *in situ* disease, other malignancy, lack of complete information about LN status or follow-up and neoadjuvant treatment were excluded. The present study was approved by the Independent Ethics Committee of the Regional Medical Chamber in Gdańsk (approval no. KB-2/20). Because of the retrospective design of the study based on data analysis, the requirement for informed consent was waived. The patient data included age at diagnosis, sex, primary tumor site, details of surgical procedure, pathological grade (G), postoperative tumor staging (pT stage), presence of distant metastasis (M stage), number of retrieved LNs, number of metastatic LNs (pN stage) and follow-up. The follow-up of all investigated cases proceeded until death or October 2019. The caecum, ascending colon, hepatic flexure and proximal two-thirds of the transverse colon were defined as the right colon. The distal one-third of the transverse colon, splenic flexure, descending colon, sigmoid and rectosigmoid junction were defined as the left colon. In some cases, groups were combined due to minor abundance (e.g., pT1 + pT2, pT3 + pT4, G1 + G2 and G3 + G4). The clinical and histopathological characteristics of the study population are presented in Table I.

Definition of LN classifications. LN status according to pN from TNM staging system is defined by the number of metastatic LNs (Table II) (3).

LNR is defined as the ratio of metastatic to examined LNs. Previous studies used distinct methods to determine LNR cut-off values to discriminate patients by their prognosis, with only a few studies using statistical methods (9,16,18). The majority of previous studies used quartiles, mean values or arbitrary classification. The present study used cut-off values developed by Rosenberg *et al* (9), which were established using statistical methods (classification and regression trees technique) and evaluated using a large population of patients with colorectal cancer (n=17,309) (19). This classification divides patients into five subgroups according to LNR (Table II).

LODDS is the log of the ratio between the numbers of positive and negative LNs: $\log_e [(pN + 0.5)/(nN + 0.5)]$, where pN is the number of positive LNs and nN is the number of negative LNs and 0.5 is added to both the numerator and denominator to avoid an infinite value. In the present study, cut-off values determined statistically by Zhang *et al* (20) using a large group of patients (n=240,898) were used to stratify the patients. The prognostic cut-off values were determined as -2.18 and -0.23 and subgroups are presented in Table II.

Statistical analysis. Statistical analysis was performed using Statistica (version 13; TIBCO Software, Inc.). Pearson's χ^2 test was performed to evaluate the association between clinical and histopathological parameters and investigate the LN staging systems. Univariate analysis of survival was performed using the Kaplan-Meier method and differences in survival rates between subgroups were compared using log-rank test. The end point of the present study was 5-year overall survival (OS). A multivariate analysis was conducted using the Cox proportional hazard model. The three-step multivariate analysis was applied to assess the prognostic discriminating power of different LN staging systems. In step one, all relevant factors from the univariate analysis were encompassed, including pN, but excluding LNR and LODDS. In step 2, LODDS was added, but not LNR. In step 3, all three LN classifications were included. Additionally, Akaike Information Criterion (AIC) was used to assess which model fit best. Principally, the predictive model with the lowest AIC displayed the best fit. The correlation between different LN classifications was analysed using Pearson correlation coefficient. $P < 0.05$ was considered to indicate a statistically significant difference.

Results

The results of the univariate analysis of survival and 5-year OS rates are presented in Table I. Age (>71 years), pT, M stage and pathological grade were significantly negatively associated with patient prognosis. Furthermore, the analysis demonstrated a significant association between increasing number of metastatic LN and worse prognosis (Fig. 1); this was also observed for increasing LNR (Fig. 2) and increasing LODDS (Fig. 3). Multivariate analysis was performed in three steps. In step 1 (Model 1), pN was identified as an independent prognostic factor. In step 2 (Model 2), when LODDS was added, pN was displaced by LODDS, which became a significant independent prognostic factor in relation to prognosis. In step 3 (Model 3), when all three classifications were included, pN and LODDS were replaced by LNR. The results of the multivariate analysis are shown in Table III. Additionally, the AIC confirmed that the LNR staging system displayed the best performance in relation to prognosis among all three classifications (AIC for Model 1, 2 and 3, 1012.022, 1010.827 and 1004.578, respectively). The scatter plots of the correlation between different LN classifications are presented in Figs. 4 and 5. Patients with the same number of metastatic LNs can be assigned to different LNR values ($r=0.77$, $P < 0.001$) (Fig. 4). LODDS and LNR were closely correlated ($r=0.9$, $P < 0.001$), despite the situation when LNR is close to 0 or 1. In this case the value of LODDS is still heterogeneous (Fig. 5).

Further analysis was performed in subpopulations of patients with $NDLN \geq 12$ and < 12 . In univariate analysis in both subpopulations, all three LN classifications were significant prognostic factors. In the multivariate analysis of patients with $NDLN \geq 12$, the best LN staging system was LNR. In the multivariate analysis of patients with $NDLN < 12$, when all three LN classifications were included, none of them displayed significant differences between levels of staging. However, when 5-year OS (according to pN) was directly compared in subgroups pN1b and pN2a, the prognosis was

Table I. Univariate survival analysis.

Parameter	n	5-year OS probability	P-value
Age, years (median, 71 years)			0.0005
≤71	156	0.75	
>71	142	0.57	
Sex			0.5000
Female	143	0.69	
Male	155	0.65	
Location			0.4000
Right colon	138	0.68	
Left colon	160	0.65	
Depth of invasion, pT			0.0200
1 + 2	50	0.80	
3 + 4a + 4b	248	0.64	
pN			<0.0001
pN0	181	0.80	
pN1a	27	0.66	
pN1b	49	0.46	
pN2a	17	0.35	
pN2b	24	0.29	
LNR			<0.0001
LNR0	182	0.80	
LNR1	51	0.62	
LNR2	32	0.43	
LNR3	21	0.33	
LNR4	12	0.08	
LODDS			<0.0001
LODDS1	190	0.79	
LODDS2	78	0.55	
LODDS3	30	0.23	
Distant metastasis			<0.0001
M0	274	0.71	
M1a + 1b + 1c	24	0.20	
Number of nodes retrieved by lymphadenectomy			0.1000
<12	123	0.62	
≥12	175	0.70	
World Health Organization histological grade			0.0200
G1 + G2	264	0.69	
G3 + G4	34	0.50	

pN, pN from pTNM; LODDS, Log odds of positive lymph nodes; LNR, lymph node ratio.

significantly worse in patients with inadequate lymphadenectomy (NDLN<12) compared with that in patients with adequate lymphadenectomy (NDLN≥12; Table IV). By contrast, when comparing LNR and LODDS subgroups, prognosis was similar in patients with inadequate and adequate lymph node dissection (Table IV).

Table II. Classification of LN staging systems.

A, pN	
Stage	Value (number of metastatic LN)
pN0	0
pN1a	1
pN1b	2-3
pN1c	No metastatic LN but there are tumor deposits
pN2a	4-6
pN2b	≥7
B, LNR	
Stage	Values
LNR0	0.00
LNR1	0.01-0.17
LNR2	0.18-0.41
LNR3	0.42-0.69
LNR4	≥0.70
C, LODDS	
Stage	Values
LODDS1	<-2.18
LODDS2	-(2.18-0.23)
LODDS3	>-0.23

The pN classification was obtained from 8th edition of the TNM American Joint Committee on Cancer/Union for International Cancer Control. LNR classification was obtained from Rosenberg *et al* (9) LODDS classification was obtained from Zhang *et al* (20) LN, lymph node; LNR, LN ratio; LODDS, log odds of positive LNs.

Discussion

The prognostic value of LNR and LODDS have been investigated and proven by numerous researchers (7-10,15-21). pN from TNM is still the most widely used classification despite only considering the number of metastatic LNs. A potential limitation of this classification is that its prognostic power is highly affected by the number of examined LNs. Dissection of ≥12 LNs is enough to evaluate LN status (3). However, inadequate lymphadenectomy during colon cancer surgery is commonly observed (4,5). Here, LNR and LODDS were shown to be more accurate LN staging systems compared with pN, potentially due to decreased dependence on the number of dissected LNs.

Numerous studies have investigated the prognostic value of each LN staging system assessed in the present study, but few surveys that have directly compared the three staging systems (16,18,21). As their results have not reached a consensus, the differences may be an outcome of different

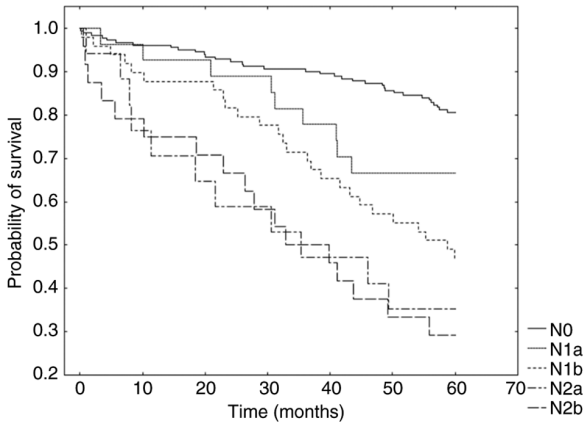


Figure 1. Kaplan-Meier curves of 5-year overall survival for patients stratified by pN, according to pTNM 8th edition American Joint Committee on Cancer/Union for International Cancer Control staging system.

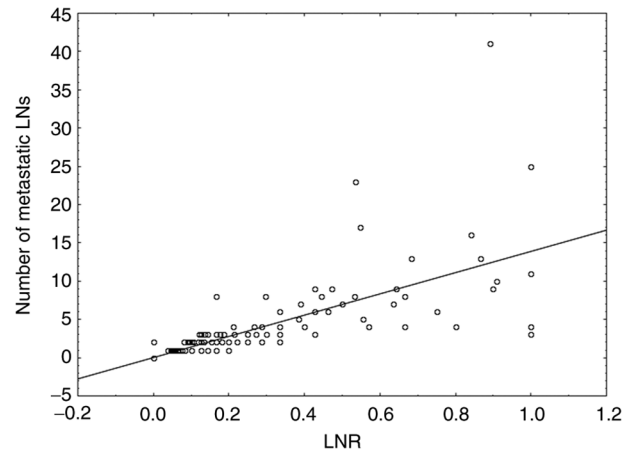


Figure 4. Scatter plot of the distribution of LNR vs. number of metastatic LNs ($r=0.77$, $P<0.001$). LN, lymph node; LNR, LN ratio.

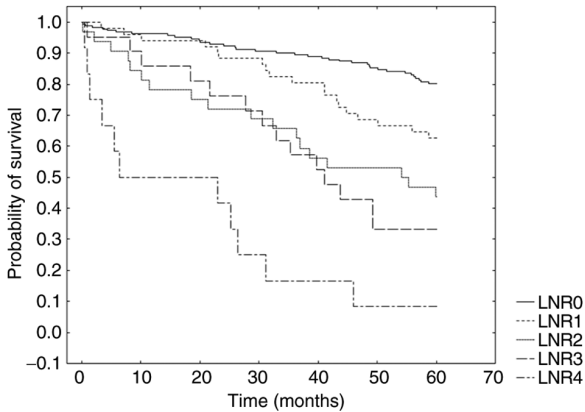


Figure 2. Kaplan-Meier curves of 5-year overall survival for patients stratified by LNR. LNR, lymph node ratio.

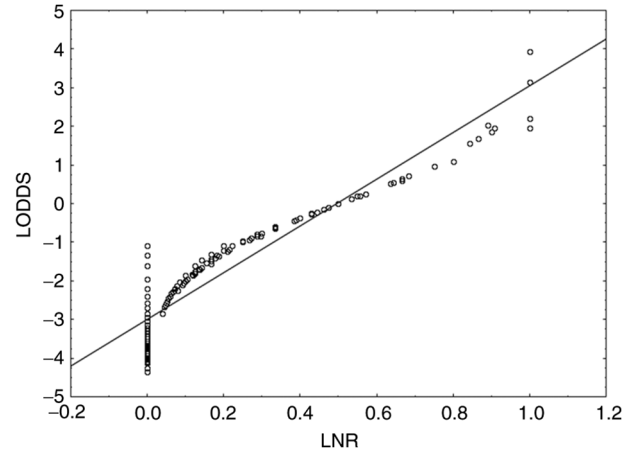


Figure 5. Scatter plot of the distribution of LNR vs. LODDS ($r=0.9$, $P<0.001$). LNR, lymph node ratio; LODDS, log odds of positive lymph nodes.

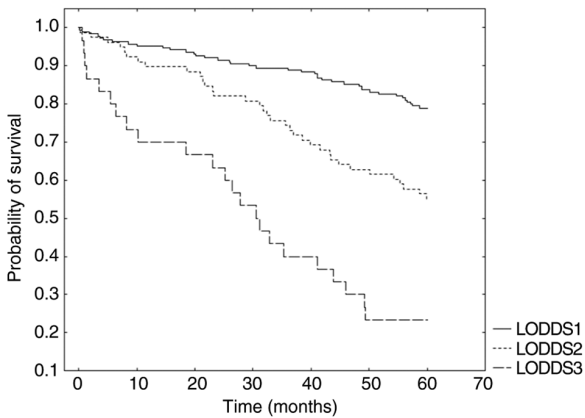


Figure 3. Kaplan-Meier curves of 5-year overall survival for patients stratified by LODDS. LODDS, log odds of positive LNs.

statistical methods, cut-off values and populations of patients. Song *et al* (18) ($n=1,297$) concluded that among all three LN staging systems, LNR was superior to the other two classifications. Moreover, for patients in each LNR subgroup, prognosis was highly homologous between those in different pN or LODDS subgroups. However, for patients in particular

pN and LODDS subgroups, significant differences in survival were identified between patients in different LNR subgroups.

Fang *et al* (16) performed multivariate analysis in a smaller sample of patients ($n=192$), which showed that LODDS was a better prognostic factor compared with LNR and pN and that LODDS was more efficient in differentiating patients with different outcomes, particularly when the ratio of metastatic LNs was close to 0 or 1.

Pei *et al* (21) compared all three LN staging systems using a large group of patients with colorectal cancer ($n=56,747$), analysing pN, LNR and LODDS as both continuous and categorical variables. When investigated as a categorical variable, cut-off values from Berger *et al* (7) and Rosenberg *et al* (9) were used for the LNR staging system, whereas cut-off values from Wang *et al* (8) and Persiani *et al* (15) were implemented for the LODDS staging system. The analysis showed that, when considered as a categorical variable, LNR using Rosenberg's cut-off values exhibited the best prognostic performance in the whole population of patients. This was also true for the subpopulation with $N_{DLN}<12$, whereas for the subpopulation with $N_{DLN}\geq 12$, pN was the best prognostic model. When investigated as a continuous variable, the LODDS staging

Table III. Three-step multivariate analysis (Cox proportional hazards model).

Parameter	Model 1			Model 2			Model 3		
	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value
Median age, years	0.45	-1.220--0.380	0.0001	0.40	-1.330--0.480	<0.0001	0.37	-1.410--0.550	<0.0001
World Health Organization histological grade	1.57	-0.080-0.980	0.0900	1.55	-0.090-0.970	0.1000	1.67	-0.010-1.050	0.0500
Depth of invasion, pT	1.28	-0.420-0.920	0.4600	1.52	-0.260-1.100	0.2000	1.52	-0.250-1.100	0.2000
Distant metastasis, M	4.54	0.960-2.060	<0.0001	3.84	0.770-1.910	<0.0001	3.41	0.660-1.800	<0.0001
pN from pTNM	1.01	0.005-0.010	<0.0001	1.00	-0.002-0.009	0.3000	0.99	-0.007-0.006	0.8000
LODDS	-	-	-	1.87	0.200-1.040	0.0030	0.89	-0.740-0.530	0.7000
LNR	-	-	-	-	-	-	1.88	0.200-1.050	0.0030

LODDS, Log odds of positive lymph nodes; LNR, lymph node ratio.

system was superior to the others. However, according to Pei *et al* (21) LODDS as a continuous variable would be impractical to apply in clinical practice; thus, it should be changed into a categorical variable by calculating the optimal cut-off values to make it applicable for clinical use.

As aforementioned, the most suitable cut-off values for LNR and LODDS are still under discussion. In the present study, cut-off values developed by Rosenberg *et al* (9) were used for LNR, whereas cut-off points determined by Zhang *et al* (20) were used for LODDS. These cut-off values were selected because they were established statistically using large populations of patients with colorectal cancer. The results of the present study confirmed the usefulness of these cut-off values and, in our opinion, they should be tested in consecutive studies and then considered for use in wide clinical practice. In the present study, LNR was identified as the best LN staging system, both for the whole population of patients and for the subpopulation with $NDLN \geq 12$. In multivariate analysis of the subpopulation with $NDLN < 12$, none of three LN classifications provided significantly different prognostic results in the context of 5-year OS. This may be due to the small number of patients in subgroups. However, there were significant differences between pN1b and pN2a subgroups in 5-year OS for patients with adequate and inadequate lymphadenectomy. These differences were not observed for LNR and LODDS, which suggested that LNR and LODDS were more independent of number of dissected LNs, as previously hypothesized (15,22).

A scatter plot demonstrated an association between LODDS and LNR. LODDS value was heterogeneous only when LNR was close to 0 or 1. This indicated that LODDS was particularly valuable in patients without metastatic LNs because when LNR and pN for all patients was 0, LODDS classification still divided patients into subgroups with different prognoses.

The present study has certain limitations because it was single centre retrospective study that included a relatively limited number of patients. Therefore, multicentre studies on larger populations of patients should be performed to verify the present conclusions. Patients without metastatic LNs could not be used for full analysis of prognosis according to LODDS

Table IV. Univariate analysis of 5-year OS depending on extent of lymphadenectomy.

A, pN			
Parameter	5-year OS probability		P-value
	$NDLN < 12$	$NDLN \geq 12$	
pN0	0.77	0.83	0.40
pN1a	0.62	0.68	0.80
pN1b	0.30	0.60	0.02
pN2a	0.11	0.62	0.02
pN2b	0.40	0.26	0.70
B, LNR			
Parameter	5-year OS probability		P-value
	$NDLN < 12$	$NDLN \geq 12$	
LNR0	0.76	0.83	0.30
LNR1	0.57	0.63	0.70
LNR2	0.31	0.61	0.10
LNR3	0.42	0.28	0.80
LNR4	0.12	<0.001	0.10
C, LODDS			
Parameter	5-year OS probability		P-value
	$NDLN < 12$	$NDLN \geq 12$	
LODDS1	0.75	0.81	0.4
LODDS2	0.51	0.58	0.5
LODDS3	0.21	0.25	0.6

LNR, lymph node ratio; LODDS, log odds of positive lymph nodes; OS, overall survival.

due to small sample size of LODDS subgroups. Therefore, further studies on larger populations of patients are required to test the prognostic value of LODDS in pN0 patients operated on for colon adenocarcinoma.

In conclusion, the present study indicated that LNR is the most accurate LN staging system for predicting prognosis for patients with colon cancer who have undergone surgical resection, especially those with metastatic LNs subjected to adequate lymphadenectomy. Due to the limitations of LNR in pN0 patients and the promising prognostic results for LODDS, further studies are required in this group. Subsequent studies should also be performed to investigate patients with NDLN <12, as LNR or LODDS might be more suitable in estimating prognosis in this group than LN staging using pN from TNM.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

AMM conceptualized and designed the present study, collected and interpreted data and drafted the manuscript. MS analysed the data, generated figures and tables and drafted the manuscript. WJK conceived the study and revised the manuscript. AMM and MS confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Independent Ethics Committee of the Regional Medical Chamber in Gdańsk (approval no. KB-2/20). Due to the retrospective design of the study based on data analysis, the requirement for informed consent was waived.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

- Compton CC, Fielding LP, Burgart LJ, Conley B, Cooper HS, Hamilton SR, Hammond ME, Henson DE, Hutter RV, Nagle RB, *et al*: Prognostic factors in colorectal cancer. College of American Pathologists Consensus Statement 1999. Arch Pathol Lab Med 124: 979-994, 2000.
- Chang GJ, Rodriguez-Bigas MA, Skibber JM and Moyer VA: Lymph node evaluation and survival after curative resection of colon cancer: Systematic review. J Natl Cancer Inst 99: 433-441, 2007.
- Weiser MR: AJCC 8th Edition: Colorectal Cancer. Ann Surg Oncol 25: 1454-1455, 2018.
- Ostadi MA, Harnish JL, Stegienko S and Urbach DR: Factors affecting the number of lymph nodes retrieved in colorectal cancer specimens. Surg Endosc 21: 2142-2146, 2007.
- Leung AM, Scharf AW and Vu HN: Factors affecting number of lymph nodes harvested in colorectal cancer. J Surg Res 168: 224-230, 2011.
- Jestin P, Pählman L, Glimelius B and Gunnarsson U: Cancer staging and survival in colon cancer is dependent on the quality of the pathologists' specimen examination. Eur J Cancer 41: 2071-2078, 2005.
- Berger AC, Sigurdson ER, LeVoyer T, Hanlon A, Mayer RJ, Macdonald JS, Catalano PJ and Haller DG: Colon cancer survival is associated with decreasing ratio of metastatic to examined lymph nodes. J Clin Oncol 23: 8706-8712, 2005.
- Wang J, Hassett JM, Dayton MT and Kulaylat MN: The prognostic superiority of log odds of positive lymph nodes in stage III colon cancer. J Gastrointest Surg 12: 1790-1796, 2008.
- Rosenberg R, Friederichs J, Schuster T, Gertler R, Maak M, Becker K, Grebner A, Ulm K, Höfler H, Nekarda H and Siewert JR: Prognosis of patients with colorectal cancer is associated with lymph node ratio: A single-center analysis of 3,026 patients over a 25-year time period. Ann Surg 248: 968-978, 2008.
- Zhang CH, Li YY, Zhang QW, Biondi A, Fico V, Persiani R, Ni XC and Luo M: The prognostic impact of the metastatic lymph nodes ratio in colorectal cancer. Front Oncol 8: 628, 2018.
- Ataseven B, Kümmel S, Weikel W, Heitz F, Holtschmidt J, Lorenz-Salehi F, Kümmel A, Traut A, Blohmer J, Harter P and du Bois A: Additional prognostic value of lymph node ratio over pN staging in different breast cancer subtypes based on the results of 1,656 patients. Arch Gynecol Obstet 291: 1153-1166, 2015.
- Smith DD, Nelson RA and Schwarz RE: A comparison of five competing lymph node staging schemes in a cohort of resectable gastric cancer patients. Ann Surg Oncol 21: 875-882, 2014.
- Tamura M, Matsumoto I, Saito D, Yoshida S, Takata M and Takemura H: Lymph node ratio as a prognostic factor in patients with pathological N2 non-small cell lung cancer. World J Surg Oncol 14: 295, 2016.
- Herr HW: Superiority of ratio based lymph node staging for bladder cancer. J Urol 169: 943-945, 2003.
- Persiani R, Cananzi FC, Biondi A, Paliani G, Tufo A, Ferrara F, Vigorita V and D'Ugo D: Log odds of positive lymph nodes in colon cancer: A meaningful ratio-based lymph node classification system. World J Surg 36: 667-674, 2012.
- Fang HY, Yang H, He ZS, Zhao H, Fu ZM, Zhou FX and Zhou YF: Log odds of positive lymph nodes is superior to the number- and ratio-based lymph node classification systems for colorectal cancer patients undergoing curative (R0) resection. Mol Clin Oncol 6: 782-788, 2017.
- Arslan NC, Sokmen S, Canda AE, Terzi C and Sarioglu S: The prognostic impact of the log odds of positive lymph nodes in colon cancer. Colorectal Dis 16: O386-O392, 2014.
- Song YX, Gao P, Wang ZN, Tong LL, Xu YY, Sun Z, Xing CZ and Xu HM: Which is the most suitable classification for colorectal cancer, log odds, the number or the ratio of positive lymph nodes? PLoS One 6: e28937, 2011.
- Rosenberg R, Engel J, Bruns C, Heitland W, Hermes N, Jauch KW, Kopp R, Pütterich E, Ruppert R, Schuster T, *et al*: The prognostic value of lymph node ratio in a population-based collective of colorectal cancer patients. Ann Surg 251: 1070-1078, 2010.
- Zhang QW, Zhang CH, Pan YB, Biondi A, Fico V, Persiani R, Wu S, Gao YJ, Chen HM, Shi OM, *et al*: Prognosis of colorectal cancer patients is associated with the novel log odds of positive lymph nodes scheme: Derivation and external validation. J Cancer 11: 1702-1711, 2020.
- Pei JP, Zhang CD, Fan YC and Dai DQ: Comparison of different lymph node staging systems in patients with resectable colorectal cancer. Front Oncol 8: 671, 2019.
- Rausei S, Iovino D, Tenconi S, Mangano A, Inversini D, Boni L, Rovera F, Dionigi G and Dionigi R: Impact of lymph node ratio on survival of colorectal cancer patients. Int J Surg 11 (Suppl 1): S95-S99, 2013.