Original Article

Lymph Node Ratio as a Prognostic Determinant Following Neoadjuvant Chemoradiation and Rectal Cancer Surgery

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Key Words
Rectal cancer;
Chemoradiation;
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Lymph node

Purpose. The purpose of this retrospective study was to compare the lymph node ratios (LNRs) of patients with rectal cancer who underwent neoadjuvant chemoradiation followed by total mesorectal excision (TME) in order to examine the applicability of this ratio as an indicator for the prognosis of rectal cancer.

Methods. Lymph node ratio refers to the number of positive lymph nodes divided by the total number of lymph nodes within a given sample. Patients were categorized into three groups: LNR = 0, $0 < \text{LNR} \leqq 0.125$, and LNR > 0.125. Differences in demographic distributions and clinical characteristics among the groups were detected using the Kruskal-Wallis test for continuous variables as well as the Chi-square test or Fisher's exact test for categorical variables. Survival curves were constructed according to the Kaplan-Meier method using the log-rank test to detect the difference between three LNR groups. Cox's proportional hazard regression model was used to calculate crude and adjusted hazard ratios (HR), with 95% confidence intervals (CIs), regarding the influence of LNR and other prognostic factors on overall survival (OS) and disease-free survival (DFS), respectively. Statistical analysis was performed using SAS software version 9.2 (SAS Institute Inc., Cary, NC). Two-tailed $p < 0.05$ indicated statistical significance.

Results. The distributions of pT stage ($p = 0.019$), pN stage ($p < 0.001$), and pTNM stage ($p < 0.001$) differed significantly among the three LNR groups. Cases of more advanced stages of the disease were observed in groups with higher LNR. Patients with higher LNR had a greater number of lymph nodes examined ($p = 0.002$), higher number of positive lymph nodes ($p < 0.001$), and a greater proportion of positive LVSI ($p < 0.001$). The DFS curves among the three LNR groups differed significantly (log-rank test, $p < 0.0001$); however, the OS curves did not reach significance ($p = 0.065$). Survival curves indicated that patients with LNR > 0.125 had a worse prognosis than patients in the other two groups. However, the differences in OS and DFS between groups with LNR = 0 and $0 < \text{LNR} \leqq 0.125$ were not significant.

Conclusion. This study indicates that LNR is an important prognostic indicator of disease-free survival among patients who undergo neoadjuvant chemoradiation followed by TME for rectal cancer.

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Neoadjuvant chemoradiation with total mesorectal excision (TME) and adjuvant chemotherapy represents standard management for patients with advanced rectal cancer.[1-3] Disease stage is the most important prognostic factor for colorectal cancer and a crucial determinant of treatment. Preoperative radiotherapy can reduce the number of lymph nodes harvested, which is an independent prognostic factor for the overall survival of patients with colorectal cancer.[4-6] The five-year survival of patients without lymph node metastasis is greater than 60 percent, which declines to just 30 percent among patients with positive lymph nodes. The American Joint Committee on Cancer and the International Union Against Cancer estimated that 12 is the minimum number of lymph nodes required for the accurate staging of nodal status.[7-12] Neoadjuvant chemoradiation has been shown to produce a significant decrease in both the size and number of lymph nodes available for examination following resection.[13-16] As a result, the number of lymph nodes that are actually examined is frequently below the recommended value, regardless of the quality of surgery and pathologic analysis.[5-7] Considering the decrease in total lymph node harvest, it is possible that the prognostic value of metastatic lymph nodes may also be diminished. This fact underscores the need for a prognostic factor with greater applicability to the selection of patients with rectal cancer. Lymph node ratio (LNR), which is the absolute number of positive lymph nodes (LNP) divided by total lymph node harvest (LNT), has proven an important prognostic factor in various types of cancer.[9] The aim of the current study was to compare the LNRs of patients with rectal cancer who underwent neoadjuvant chemoradiation followed by TME in order to determine whether this ratio is a useful assessment tool for the prognosis of rectal cancer.

Materials and Methods

Patients

The records of patients who underwent neoadjuvant chemoradiation and TME for rectal cancer between 2005 and 2010 were obtained from the Cancer Registry of the Tri-Service General Hospital (TSGH). A total of 126 patients were included in the study. Data were retrospectively collected from electronic medical records and chart reviews. Patients who underwent rectal resection with total mesorectal excision with curative intent were included. Patients with concomitant distant metastases to lung, liver, or bones were excluded. Preoperative tumor assessment included digital examination, colonoscopy, barium enema, and computed tomography of the abdomen and pelvis. TNM stage was determined through assessment by the radiologist, oncologist, and surgeon. Preoperative chemotherapy (5-fluorouracil and leucovorin) was provided to patients with clinically advanced rectal cancer, T3, T4, and/or lymph node involvement. All patients underwent total mesorectal excision at TSGH. Patients underwent surgery 6 to 8 weeks following the completion of neoadjuvant radiotherapy. Surgery included low anterior resection with/without diverting colostomy and abdominoperineal resection. All surgical specimens were dissected by a fixed team of gastrointestinal pathologists within the hospital. Tumors were staged on the basis of TNM classification. Reports included resection margins, vascular and lymphovascular invasion, TNM stage, histological type, total number of retrieved regional lymph nodes in the specimen, and number of tumor-positive lymph nodes. Follow-up was conducted in three-month intervals over a period of two years, six-month intervals for the succeeding three years, and annually thereafter. Follow-up indicators consisted of fecal occult blood tests, abdominal sonography, chest X-ray, serum tumor marker (CEA) level, colonoscopy, and CT scans of the abdomen and pelvis. Colonoscopies were performed three months after surgery and annually thereafter. Local and distant recurrences were defined as recurrent tumors within or outside the pelvis. Biopsies were performed for the purpose of confirmation in all cases of suspicious recurrence. Adjuvant treatment was provided in accordance with performance status and institutional protocol.

Statistical analysis

Continuous variables were summarized according

to the median using inter-quartile range (IQR – the range between the 25th and 75th percentiles) to account for non-normal distribution; categorical variables were expressed according to frequencies and percentages. The 1st, 2nd and 3rd quintiles of LNR were 0, and the 4th quintile was 0.125. Patients were categorized into three groups: LNR = 0, 0 < LNR $\leqq$ 0.125, and LNR > 0.125. Differences among patients with regard to demographic distribution and clinical characteristics were detected using the Kruskal-Wallis test for continuous variables, the Chi-square test, or Fisher's exact test for categorical variables.

Overall survival (OS) time was measured from the date of surgery to the date of death or last follow-up. Patients were censored in the analysis of disease-free survival (DFS) if they were disease-free at the last visit; however, death was counted as an event in DFS analysis. Survival curves were constructed using the Kaplan-Meier method with the log-rank test used to detect differences between the three LNR groups with regard to OS and DFS, respectively.

The Cox proportional hazard regression model was used to calculate crude and adjusted hazard ratios (HR), with 95% confidence interval (CIs), to determine the influence of LNR and other prognostic factors on OS and DFS, respectively. In the multivariate Cox proportional hazard regressions, the significant variables in univariate analysis were candidates in the backward selection procedure, wherein variables that did not improve model fit at $p < 0.05$ were discarded. Nonetheless, age and sex were retained within the model for adjustment purposes. All statistical analysis was performed using SAS software version 9.2 (SAS Institute Inc., Cary, NC). Two-tailed $p < 0.05$ indicated statistical significance.

Results

The demographic and clinical characteristics of patients are summarized in Table 1. A total of 126 patients were recruited, including 72 (57.1%) males and 54 (42.9%) females. The median age was 64 years (IQR: 51-72 years). The medians of pre-tx CEA level were significantly different among the three LNR groups ($p = 0.029$). The distributions of pT stage ($p = 0.019$), pN stage ($p < 0.001$), and pTNM stage ($p < 0.001$) were significantly different among the three LNR groups. Cases of cancer in more advanced stages were observed in groups with higher LNR. Patients with higher LNR also presented a higher number of lymph nodes examined ($p = 0.002$), a higher number of positive lymph nodes ($p < 0.001$), and a greater proportion of positive LVSI ($p < 0.001$). All patients in the group with LNR = 0 presented a complete pathological response, while those in the groups with higher LNR had no response ($p < 0.001$). The distributions of age, gender, and other demographic and clinical characteristics were comparable among the three LNR groups (Table 1).

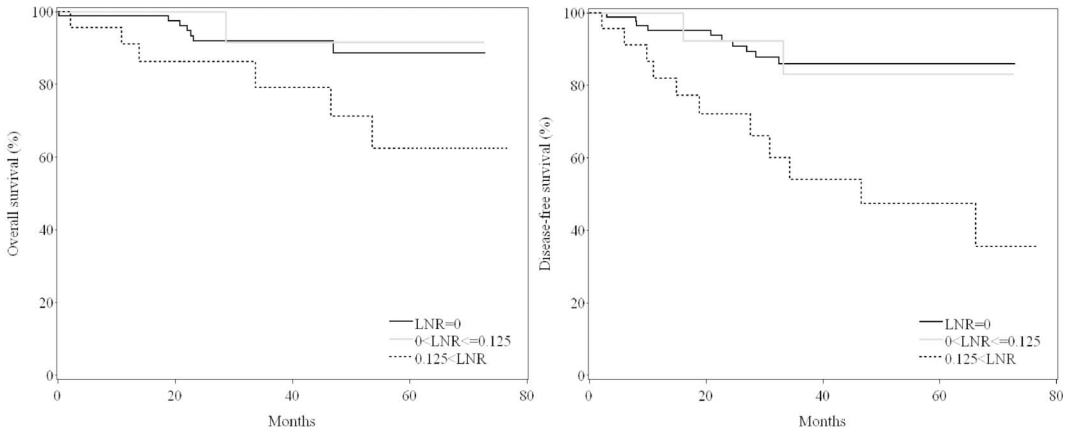
The OS and DFS curves obtained using the Kaplan-Meier method are presented according to the three LNR groups (Fig. 1). The DFS curves among the three LNR groups presented significant differences (log-rank test, $p < 0.0001$); however, the OS curves did not ($p = 0.065$). The DFS curves indicated that patients with LNR > 0.125 had a worse prognosis than patients in the other two LNR groups. However, the difference in OS and DFS between groups with LNR = 0 and 0 < LNR $\leqq$ 0.125 failed to reach significance.

According to univariate Cox regression analysis for OS, elevated pN, LNR > 0.125, and well-differentiated tumors were significantly associated with a higher risk of death (Table 2). Following the backward selection procedure, only age and differentiation remained significant ($p < 0.05$) in the final multivariate Cox proportional hazard model. Compared to the group with LNR = 0, the adjusted HR of the group with LNR > 0.125 was 3.25 (95% CI: 0.89-11.89, $p = 0.074$); however, this was not significant. After controlling for other variables in the final model, patients older than 65 years faced a significantly higher risk of death compared to younger patients (adjusted HR = 4.00, 95% CI: 1.15-13.91, $p = 0.029$). Patients with moderately differentiated tumors had a significantly lower risk of death, compared to those with well-differentiated tumors (adjusted HR = 0.11, 95% CI: 0.02-0.59, $p = 0.010$).

Table 1. Patient characteristics in groups assigned according lymph node ratio (LNR)

Characteristics	Total (n = 126)	LNR = 0 (n = 86)	0 < LNR ≦ 0.125 (n = 15)	LNR > 0.125 (n = 25)	*p*-value
Age (years)					
Median (IQR)	64 (51-72)	64 (52-74)	66 (53-71)	61 (47-71)	0.557†
Gender, n (%)					
Male	72 (57.1)	46 (53.5)	9 (61.5)	17 (69.6)	0.364‡
Female	54 (42.9)	40 (46.5)	6 (38.5)	8 (30.4)	
CEA level (ng/mL)					
Pre-tx[a], median (IQR)	1.75 (1.41-0.31)	1.75 (1.40-0.31)	1.54 (1.27-1.09)	3.28 (1.78-1.50)	0.029†
Post-tx[b], median (IQR)	2.00 (1.41-1.07)	2.00 (1.33-1.07)	1.68 (1.55-1.41)	2.18 (1.42-1.12)	0.827†
cT stage, n (%)					
1	2 (1.6)	1 (1.1)	1 (6.7)	0 (0.0)	0.736¶
2	14 (11.1)	9 (10.5)	3 (20.0)	2 (8.0)	
3	99 (78.6)	67 (77.9)	10 (66.7)	22 (88.0)	
4	11 (8.7)	9 (10.5)	1 (6.7)	1 (4.0)	
cN stage, n (%)					
0	45 (35.7)	34 (39.5)	6 (40.0)	5 (20.0)	0.187¶
1	63 (50.0)	41 (47.7)	9 (60.0)	13 (52.0)	
2	18 (14.3)	11 (12.8)	0 (0.0)	7 (28.0)	
cTNM stage, n (%)					
1	6 (4.7)	4 (4.7)	2 (13.3)	0 (0.0)	0.415¶
2	40 (31.7)	31 (36.0)	4 (26.7)	5 (20.0)	
3	80 (63.4)	51 (59.3)	9 (60.0)	20 (80.0)	
pT stage, n (%)					
0	19 (15.1)	18 (20.9)	1 (6.7)	0 (0.0)	0.019¶
1	6 (4.8)	5 (5.8)	1 (6.7)	0 (0.0)	
2	26 (20.6)	20 (23.3)	3 (20.0)	3 (12.0)	
3	62 (49.2)	34 (39.5)	9 (60.0)	19 (76.0)	
4	13 (10.3)	9 (10.5)	1 (6.7)	3 (12.0)	
pN stage, n (%)					
0	83 (65.9)	83 (96.5)	0 (0.0)	0 (0.0)	< 0.001¶
1	26 (20.6)	2 (2.3)	15 (100.0)	9 (36.0)	
2	17 (13.5)	1 (1.2)	0 (0.0)	16 (64.0)	
pTNM stage, n (%)					
1	33 (26.2)	33 (38.4)	0 (0.0)	0 (0.0)	< 0.001¶
2	46 (36.5)	46 (53.5)	0 (0.0)	0 (0.0)	
3	47 (37.3)	7 (8.1)	15 (100.0)	25 (100.0)	
LNs examined					
Median (IQR)	10 (6-13)	9 (5-12)	12 (10-17)	11 (7-14)	0.002†
LNs positive					
Median (IQR)	0 (0-1)	0 (0-0)	1 (1-1)	4 (3-7)	< 0.001†
Differentiation, n (%)					
Good	5 (4.0)	4 (4.7)	0 (0.0)	1 (4.0)	0.055¶
Moderate	108 (85.7)	77 (89.5)	13 (86.7)	18 (72.0)	
Poor	13 (10.3)	5 (5.8)	2 (13.3)	6 (24.0)	
LVSI, n (%)					
N	111 (88.1)	83 (96.5)	9 (60.0)	19 (76.0)	< 0.001¶
P	15 (11.9)	3 (3.5)	6 (40.0)	6 (24.0)	
Complete pathological response, n (%)					
X (No)	40 (31.7)	0 (0.0)	15 (100.0)	25 (100.0)	< 0.001¶
O (Yes)	86 (68.3)	86 (100.0)	0 (0.0)	0 (0.0)	
Operation, n (%)					
APR	24 (19.0)	21 (24.4)	1 (6.7)	2 (8.0)	0.484¶
LAR	102 (81.0)	65 (75.6)	14 (93.3)	23 (92.0)	

† Kruskal-Wallis test; ‡ Chi-square test; ¶ Fisher's exact test; [a] n = 74; [b] n = 52.



(A) Overall survival (B) Disease-free survival

Fig. 1. Kaplan-Meier survival curve according to lymph note ratio (LNR) for (A) overall survival (log-rank test, $p = 0.065$); (B) disease-free survival (log-rank test, $p = 0.001$).

Table 2. Univariate and multivariate Cox proportional hazard regression models for overall survival (n = 126)

Characteristics	Univariate		Multivariate	
	Crude HR (95% CI)	*p*-value	Adjusted HR	*p*-value
Age (years)				
≦ 65	1.00 (reference)	–	1.00 (reference)	–
> 65	2.36 (0.79-7.06)	0.125	4.00 (1.15-13.91)	0.029
Gender				
Male	1.00 (reference)	–	1.00 (reference)	–
Female	0.89 (0.31-2.59)	0.834	1.28 (0.39-4.18)	0.680
Pre-tx CEA level (ng/mL)				
≦ 2.5	1.00 (reference)	–		
> 2.5	NA	0.998		
pT stage				
0	1.00 (reference)	–		
1	NA	0.995		
2	0.66 (0.04-10.63)	0.771		
3	1.15 (0.13-10.17)	0.900		
4	6.38 (0.72-56.19)	0.095		
pN stage				
0	1.00 (reference)	–		
1	0.67 (0.08-5.73)	0.713		
2	5.20 (1.56-17.28)	0.007		
pTNM stage				
1	1.00 (reference)	–		
2	1.60 (0.17-15.49)	0.686		
3	3.63 (0.44-29.70)	0.229		
LNR				
LNR = 0	1.00 (reference)	–	1.00 (reference)	–
0 < LNR ≦ 0.125	0.81 (0.10-6.60)	0.844	0.99 (0.11-8.65)	0.994
0.125 < LNR	3.24 (1.08-9.75)	0.037	3.25 (0.89-11.89)	0.074
Differentiation				
Good	1.00 (reference)	–	1.00 (reference)	–
Moderate	0.17 (0.04-0.81)	0.027	0.11 (0.02-0.59)	0.010
Poor	0.70 (0.13-3.87)	0.685	0.54 (0.07-3.99)	0.545
LVSI				
N	1.00 (reference)	–		
P	1.53 (0.19-12.46)	0.691		
Complete pathological response				
X (No)	2.14 (0.75-6.13)	0.157		
O (Yes)	1.00 (reference)	–		

HR: hazard ratio; CI: confidence interval; NA: unavailable because of unstable estimates.

In univariate Cox proportional hazard regression for DFS, pre-tx CEA level > 2.5, higher pN, LNR > 0.125, positive LVSI, and a lack of complete pathological response were significantly associated with a higher risk of recurrence (Table 3). Following the backward selection procedure, only the designation of LNR group remained significant ($p < 0.05$). Compared to the group with LNR = 0, the adjusted HRs of the groups with $0 < \text{LNR} \leqq 0.125$ and LNR > 0.125 were 1.09 (95% CI: 0.24-4.97, $p = 0.915$) and 4.56 (95% CI: 1.88-11.03, $p = 0.001$), respectively.

Discussion

This study used a retrospective review of three trials in the North Central Cancer Treatment Group to demonstrate that LNR is an independent prognostic factor of both local recurrence and overall survival.[17] This study categorized 126 patients according to LNR: LNR = 0 (n = 86), $0 < \text{LNR} \leqq 0.125$ (n = 15), and LNR > 0.125 (n = 25). Cases of more advanced cancer were observed in groups with higher LNR. The DFS survival curves among the three LNR groups dif-

Table 3. Univariate and multivariate Cox proportional hazard regression models for disease-free survival (n = 126)

Characteristics	Univariate		Multivariate	
	Crude HR (95% CI)	*p*-value	Adjusted HR	*p*-value
Age (years)				
≦ 65	1.00 (reference)	–	1.00 (reference)	–
> 65	0.99 (0.43-2.26)	0.974	1.11 (0.47-2.61)	0.811
Gender				
Male	1.00 (reference)	–	1.00 (reference)	–
Female	0.69 (0.29-1.62)	0.393	0.82 (0.34-2.00)	0.668
Pre-tx CEA level (ng/mL)				
≦ 2.5	1.00 (reference)	–		
> 2.5	3.41 (1.08-10.76)	0.036		
pT stage				
0	1.00 (reference)	–		
1	NA	0.991		
2	2.02 (0.21-19.49)	0.543		
3	3.60 (0.47-27.77)	0.219		
4	8.28 (0.96-71.33)	0.054		
pN stage				
0	1.00 (reference)	–		
1	1.76 (0.59-5.24)	0.313		
2	4.34 (1.65-11.41)	0.003		
pTNM stage				
1	1.00 (reference)	–		
2	1.93 (0.39-9.56)	0.423		
3	3.75 (0.84-16.67)	0.083		
LNR				
LNR = 0	1.00 (reference)	–	1.00 (reference)	–
$0 < \text{LNR} \leqq 0.125$	1.10 (0.24-5.01)	0.906	1.09 (0.24-4.97)	0.915
$0.125 < \text{LNR}$	4.61 (1.94-10.96)	0.001	4.56 (1.88-11.03)	0.001
Differentiation				
Good	1.00 (reference)	–		
Moderate	0.68 (0.09-5.14)	0.707		
Poor	2.11 (0.25-17.51)	0.490		
LVSI				
N	1.00 (reference)	–		
P	4.66 (1.62-13.45)	0.004		
Complete pathological response				
X (No)	2.86 (1.25-6.57)	0.013		
O (Yes)	1.00 (reference)	–		

HR: hazard ratio; CI: confidence interval; NA: unavailable because of unstable estimates.

fered significantly (log-rank test, $p < 0.0001$). Patients with LNR > 0.125 had a worse prognosis than those in the other two groups.

Numerous advanced techniques have been developed for the treatment of patients with rectal cancer, including TME resection and detailed search methods for metastatic lymph nodes. All patients in this study underwent standard total mesorectal excision. The total number of nodes examined varied between 5 and 17. This wide range can be attributed to preoperative treatment, which has been shown to reduce the number and size of LN available for pathologic examination.[13-16]

A number of limitations should be noted in this retrospective study. The follow-up period was only five years, which is a relatively short period for a disease of this type. In addition, surgical operations were performed by five different surgeons, which may have contributed to variations in the results.

LNT is not always the best way to stage patients who undergo neoadjuvant therapy. Risk assessment in terms of LNPs categorized according to absolute values can result in understaging, especially in situations where lymph nodes are rare. The intervals selected for LNR staging were determined according to the significance of HR compared with N0 patients. In a different cohort, other LNR intervals might be preferable or result in different risk categories.

In conclusion, this study has demonstrated the importance of LNR as a prognostic factor in patients with rectal cancer who underwent TME followed by neoadjuvant chemoradiation. In future trials, LNR could be considered in the stratification of patients to evaluate the benefits of adjuvant chemotherapy following curative resection of rectal cancer.

References

1. Kapiteijn E, Marijnen CA, Nagtegaal ID, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *N Engl J Med* 2001;345:638-46.
2. Sauer R, Becker H, Hohenberger W, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. *N Engl J Med*. 2004;351:1731-40.
3. Parfitt JR, Driman DK. The total mesorectal excision specimen for rectal cancer: a review of its pathological assessment. *J Clin Pathol* 2007;60:849-55.
4. Doll D, Gertler R, Maak M, et al. Reduced lymph node yield in rectal carcinoma specimen after neo-adjuvant radiochemotherapy has no prognostic relevance. *World J Surg* 2008;33: 340-47.
5. Kim J, Huynh R, Abraham I, Kim E, Kumar RR. Number of lymph nodes examined and its impact on colorectal cancer staging. *Am Surg* 2006;72:902-5.
6. Thorn CC, Woodcock NP, Scott N, Verbeke C, Scott SB, Ambrose NS. What factors affect lymph node yield in surgery for rectal cancer? *Colorectal Dis* 2004;6:356-61.
7. Kim YW, Kim NK, Min BS, Lee KY, Sohn SK, Cho CH. The influence of the number of retrieved lymph nodes on staging and survival in patients with stage II and stage III rectal cancer undergoing tumor-specific mesorectal excision. *Ann Surg 2*009;249:965-72.
8. Kim NK, Kim YW, Min BS, Lee KY, Sohn SK, Cho CH. Factors associated with local recurrence after neoadjuvant chemoradiation with total mesorectal excision for rectal cancer. *World J Surg* 2009;33:1741-9.
9. Kim YS, Kim JH, Yoon SM, et al. Lymph node ratio as a prognostic factor in patients with stage III rectal cancer treated with total mesorectal excision followed by chemoradiotherapy. *Int J Radiat Oncol Biol Phys* 2009;74:796-802.
10. Washington K, Berlin J, Branton P, et al. Protocol for the examination of specimens from patients with primary carcinomas of the colon and rectum. *Arch Pathol Lab Med* 2009; 133:1539-51.
11. Nelson H, Petrelli N, Carlin A, et al. Guidelines 2000 for colon and rectal cancer surgery. *J Natl Cancer Inst* 2001;93: 583-96.
12. de la Fuente SG, Manson RJ, Ludwig KA, Mantyh CR. Neoadjuvant chemoradiation for rectal cancer reduces lymph node harvest in proctectomy specimens. *J Gastrointest Surg* 2009;13:269-74.
13. Wichmann MW, Muller C, Meyer G, et al. Effect of preoperative radiochemotherapy on lymph node retrieval after resection of rectal cancer. *Arch Surg* 2002;137:206-10.
14. Scott N, Thorne C, Jayne D. Lymph node retrieval after neoadjuvant radiotherapy for rectal adenocarcinoma. *J Clin Pathol* 2004;57:335-6.
15. Baxter NN, Virnig DJ, Rothenberger DA, et al. Lymph node evaluation in colorectal cancer patients: a population-based study. *J Natl Cancer Inst* 2005;97:219-25.
16. Rullier A, Laurent C, Capdepont M, et al. Lymph nodes after preoperative chemoradiotherapy for rectal carcinoma: number, status, and impact on survival. *Am J Surg Pathol* 2008; 32:45-50.
17. Stocchi L, Nelson H, Sargent DJ, et al. Impact of surgical and pathologic variables in rectal cancer: A United States community and cooperative group report. *J Clin Oncol* 2001;19: 3895-902.

原　著

直腸癌經手術前化放療及手術後淋巴結比率的預後重要性

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目的　這項回顧性研究目的是比較淋巴結比率在直腸癌患者接受術前化放療以及接著全直腸繫膜切除，並確定此比率是否為有用的直腸癌預後評估。

方法　淋巴結比率是由同樣本內陽性淋巴結的數目除以淋巴結的總數。患者被分為 3 組：淋巴結比率 = 0，0 < 淋巴結比率 ≦ 0.125 還有淋巴結比率 > 0.125。三組的人口統計學與臨床特徵之間的分佈差異由 Kruskal-Wallis 檢驗來進行連續變量檢測，並通過卡方檢驗或 Fisher 精確檢驗分類變量。生存曲線通過 Kaplan-Meier 法，log-rank 檢驗檢測 3 組之間的差異。Cox 比例風險回歸分別進行計算淋巴結比率和其他預後因素影響總體生存率和無病生存率的原始和調整後的危險比和 95% 信賴區間。統計分析由 SAS 軟體版本 9.2 進行。雙尾 *p* 值 < 0.05 為差異有統計學意義。

結果　pT 分期 (*p* 值 = 0.019)，pN 分期和 pTNM 分期 (*p* 值均 < 0.001) 的分佈在三組具有顯著性差異。較高分期的群體具有較高的淋巴結比率。淋巴結比率較高的患者也有更高的淋巴結檢查數量 (*p* 值 = 0.002)，陽性淋巴結的數目較高、較大比例的淋巴血管間隙浸潤陽性 (*p* 值均 < 0.001)。無病生存率曲線在三組有顯著差異。生存曲線表示淋巴結比率 > 0.125 的患者預後較其他兩組差。

結論　淋巴結比率對於接受術前化放療以及接著全直腸繫膜切除的直腸癌患者的無病生存率是一個重要的預後因素。

關鍵詞　直腸癌、化放療、預後、淋巴結。