International Journal of Colorectal Disease (2025) 40:55
https://doi.org/10.1007/s00384-025-04839-4

RESEARCH

Optimal cutpoint of preoperative neutrophil–lymphocyte ratio and associated postoperative prognosis in colorectal cancer patients

Tai-Jan Chiu[1,2] · Ting-Ting Liu[3,4] · Ching-Di Chang[5] · Wan-Hsiang Hu[2,6]

Accepted: 16 February 2025

Abstract

Purpose As the role of systemic inflammation in cancer progression, the neutrophil-to-lymphocyte ratio (NLR) is easily evaluated and predicts prognosis in solid cancers. However, the optimal cutpoint for NLR in colorectal cancer patients remains unclear.

Methods This retrospective cohort study was based on the Chang Gung Research Database. Participants included colorectal cancer patients who received operation and preoperative complete blood counts with differentiation from 2007 to 2017. The cutpoint of NLR was calculated by SAS macro (%FINGCUT).

Results A total of 16,990 colorectal patients were included, and 4961 (29.1%) were identified as the high NLR group (≥ 3.59). Poor clinical characteristics were significantly predominant in the patients with high NLR. The patients with high NLR were associated with worse 5-year disease-free survival and overall survival ($p < 0.0001$). Multivariate Cox regression survival analysis still showed poor 5-year disease-free survival (HR = 1.319, $p < 0.0001$) and overall survival (HR = 1.611, $p < 0.0001$) in the high NLR group after adjustment. Patients with high NLR and hypoalbuminemia had the worst disease-free survival and overall survival ($p < 0.0001$). In subgroup analysis, stage II colon cancer patients with low NLR had better survival than those with high NLR ($p < 0.0001$). The hazard ratios of without chemotherapy in disease-free survival and overall survival were higher in the patients with high NLR.

Conclusions High NLR was associated with worse clinical characteristics and an independent predictor of poor survival. After adjuvant chemotherapy for stage II colon cancer, more benefits of improving survival were demonstrated in the patients with high NLR.

Keywords Neutrophil/lymphocyte ratio · Colorectal cancer · Survival · Cancer inflammation · Malnutrition

✉ Wan-Hsiang Hu
gary.hu0805@gmail.com

[1] Division of Hematology Oncology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung 833, Taiwan

[2] Graduate Institute of Clinical Medical Science, College of Medicine, Chang Gung University, Kaohsiung 833, Taiwan

[3] Department of Pathology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung 833, Taiwan

[4] Department of Medical Laboratory Science, I-Shou University, Kaohsiung 833, Taiwan

[5] Department of Radiology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung 833, Taiwan

[6] Department of Colorectal Surgery, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, 123, Ta-Pei Rd., Niao-Sung District, Kaohsiung 833, Taiwan

Published online: 26 February 2025

Introduction

The connection between inflammation and carcinogenesis has been well-discussed [1, 2]. The strong association is the evidence of colorectal cancer developing from inflammatory bowel disease [3, 4]. The cytokines linking inflammation and cancer stimulate the bone marrow to increase the number of neutrophils [5, 6] and inhibit circulating cytotoxic lymphocyte [7], which reflect elevated neutrophil–lymphocyte ratio (NLR) serving as a biomarker of systemic inflammation in colorectal cancer.

Among colorectal cancer patients, high NLR was investigated as an adverse prognostic predictor of survival analyses [8–10]. However, the optimal cutoff point of NLR still remains unclear based on the published studies of relatively limited sample sizes, using either median values or receiver operating characteristic analysis [11]. The correlation between NLR and nutrition markers [12, 13] and the role of NLR in the decision of postoperative adjuvant chemotherapy for stage II colorectal cancer patients [14, 15] were seldom discussed.

The incidence of colorectal cancer ranks third in the USA and global cancer survey [16, 17]; however, it is the most common cancer in Taiwan for years [18]. In this study, we used the Chang Gung Research Database (CGRD), a multi-institutional database of Taiwan [19], to demonstrate the exact and specific role of NLR in predicting the prognosis of colorectal cancer patients.

Material and methods

Study design and participants

This study was approved by the Chang Gung Medical Foundation Institutional Review Board. Based on the multi-institutional Chang Gung Research Database [19], patients with colorectal cancer who underwent surgical resection were enrolled from 2007 to 2017. Clinicopathological features including age, gender, body mass index (BMI), preoperative blood tests, American Joint Committee on Cancer (AJCC) TNM stage, chemotherapy, and survival were recorded. Hypoalbuminemia was defined as if serum albumin level was less than 3.5 g/dl [20]. Disease-free survival was defined as the length of survival without any clinical evidence of residual colorectal cancer. The protocol of chemotherapy was based on the National Comprehensive Cancer Network (NCCN) guidelines and monitored by the Cancer Center of Chung Gung Memorial Hospital. The STROBE checklist was finished (Supplementary).

Cutpoint of neutrophil–lymphocyte ratio

Neutrophil–lymphocyte ratio (NLR) was calculated from preoperative routine complete blood counts (CBC) with differentiation. The patients without available NLR data were excluded. An SAS macro (%FINGCUT) [21, 22] was used to investigate the clinically significant cutpoint of NLR in the survival analyses. After calculation, the cutpoint of NLR was defined as 3.59.

Statistical analyses

An unpaired *t*-test was computed for the continuous variables. A chi-square test was performed for univariate analysis. Kaplan–Meier curves were used to visualize the differences between groups for 5-year disease-free survival and overall survival of the patients, and the significance was calculated using a log-rank test. Multiple linear regression was applied for collinearity diagnostics, and variance inflation factors were calculated between the variables and NLR. Multivariate Cox regression survival analysis was used to compute hazard ratios and interaction between clinical factors. Pearson correlation was calculated for the relationship of two continuous variables. Statistical significance was set at a p value of < 0.05. All analyses were performed using Prism 6 and SPSS version 24.

Results

Clinicopathological characteristics of the study population

Among the total of 16,990 colorectal patients included in the study, 4961 (29.1%) were identified as the high NLR group according to the cutoff point (3.59). The differences in clinical characteristics between low and high NLR are shown in Table 1. Patients with high NLR were more likely to be older, male, and had less body mass index, hemoglobin, albumin, and prealbumin. High CEA (carcinoembryonic antigen) and PLR (platelet-lymphocyte ratio), advanced stage, and more chemotherapy were also significantly noted in the high NLR group ($p < 0.001$).

NLR and survival outcome

In the univariate analysis, 5-year disease-free survival rates were 44.7% in the high NLR group and 68.1% in the low NLR group (hazard ratio, 2.085; 95% CI, 1.969–2.207; $p < 0.0001$) (Fig. 1A). Overall survival rates at 5 years were 50.1% in patients with high NLR and 73.6% in

Table 1 Clinicopathological characteristic of colorectal cancer patients stratified by the NLR group

Characteristic	Low NLR (< 3.59) (*N* = 12,029)	High NLR (≥ 3.59) (*N* = 4961)	*p* value
Age, mean (SD), years	63 (12.6)	65 (14.3)	< 0.0001
Gender, No. (%)			< 0.0001
Male	6686 (55.6)	2914 (58.7)	
Female	5343 (44.4)	2047 (41.3)	
BMI, mean (SD)	24.51 (3.9)	23.23 (3.92)	< 0.0001
Hemoglobin, mean (SD)	12.56 (1.97)	11.62 (2.15)	< 0.0001
Albumin, mean (SD)	4.08 (0.5)	3.58 (0.71)	< 0.0001
Prealbumin, mean (SD)	16.13 (6.26)	13.40 (6.39)	< 0.0001
CEA, mean (SD)	22.87 (425.72)	76.15 (716.85)	< 0.0001
PLR, mean (SD)	1.38 (0.61)	2.98 (2.6)	< 0.0001
TNM stage, No. (%)			< 0.0001
0	980 (8.1)	223 (4.5)	
I	2656 (22.1)	505 (10.2)	
II	3114 (25.9)	1538 (31)	
III	3758 (31.2)	1502 (30.3)	
IV	1521 (12.6)	1193 (24)	
Chemotherapy, No. (%)	5490 (47.8)	2460 (54)	< 0.0001

BMI body mass index, *CEA* carcinoembryonic antigen, *PLR* platelet-lymphocyte ratio, *TNM stage* American Joint Committee on Cancer (AJCC) TNM system

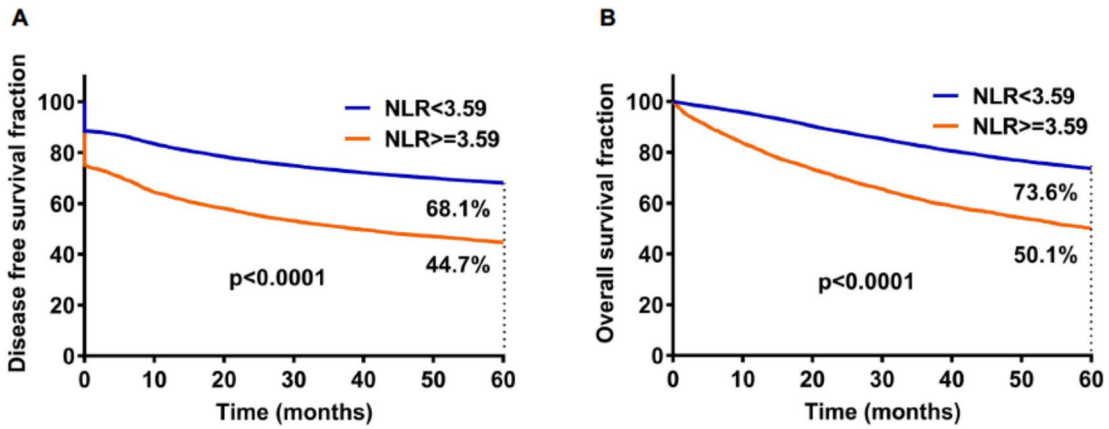

Fig. 1 Kaplan–Meier plots of 5-year survival in colorectal cancer. Significant difference was noted between the patients' groups stratified by the neutrophil–lymphocyte ratio (NLR) in disease-free survival (**A**) and overall survival (**B**)

those with low NLR (HR, 2.423; 95% CI, 2.272–2.584; $p < 0.0001$) (Fig. 1B). In subgroup analyses divided by stage, high NLR was also associated with poor 5-year disease-free and overall survival from stage 0 to IV (Supplementary Figs. 1 and 2). Multivariate Cox regression survival analysis showed poor 5-year disease-free survival

Table 2 Multivariate Cox regression survival analysis of high NLR for 5-year disease-free survival and overall survival after adjustment

5-year survival	Hazard ratio	95% CI	*p* value
Disease-free survival	1.319	1.176–1.48	< 0.0001
Overall survival	1.611	1.413–1.838	< 0.0001

Adjusted factors: age, gender, BMI, hemoglobin, hypoalbuminemia, CEA, PLR, TNM stage, and chemotherapy

(HR = 1.319, $p < 0.0001$) and overall survival (HR = 1.611, $p < 0.0001$) in the high NLR group after adjusting for age, gender, BMI, hemoglobin, hypoalbuminemia, CEA, PLR, TNM stage, and chemotherapy (Table 2).

NLR and hypoalbuminemia

As observed from the survival Kaplan–Meier curve (Fig. 2), patients with NLR of less than 3.59 and no hypoalbuminemia survived the longest, whereas patients with NLR of 3.59 or greater than 3.59 and hypoalbuminemia had the worst disease-free survival and overall survival (log-rank $p < 0.0001$). A negative correlation was significantly noted between NLR and albuminemia in colorectal cancer survival analysis ($r = -0.32$, $p < 0.0001$).

NLR and chemotherapy

In subgroup analysis, the patients with stage II colon cancer ($n = 3116$) were selected and divided into four groups using NLR and chemotherapy. The Kaplan–Meier curve (Fig. 3) demonstrated that patients with low NLR (< 3.5) had still better 5-year disease-free survival and overall survival than those with high NLR (≥ 3.5) ($p < 0.0001$). The hazard ratios of without chemotherapy were significantly higher in the high NLR group than those in the low NLR group regardless of disease-free survival or overall survival (Table 3).

Discussion

To our knowledge, this is the largest retrospective cohort study to evaluate the association between preoperative NLR and the survival prognosis of colorectal cancer patients receiving surgical intervention. High NLR was demonstrated as an independent, adverse prognostic predictor for disease-free and overall survival. It was also associated with nutrition marker and high-risk evaluation about further adjuvant chemotherapy for stage II colorectal cancer patients.

Our finding and most prior studies consistently showed high NLR was associated with poor survival in colorectal cancer patients, although some study did not conclude the same result [23, 24]. Some published literature enrolled

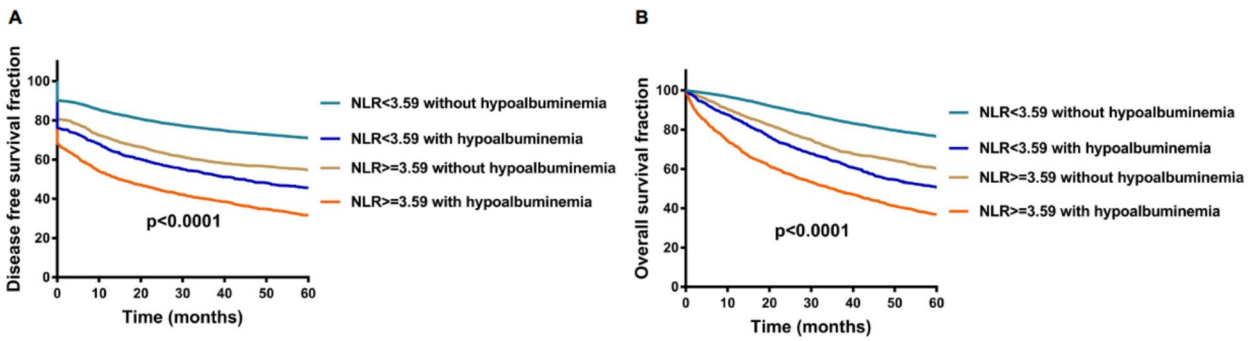

Fig. 2 Kaplan–Meier plots of 5-year survival in colorectal cancer. Significant difference was noted between the patients' groups stratified by NLR and hypoalbuminemia in disease-free survival (**A**) and overall survival (**B**)

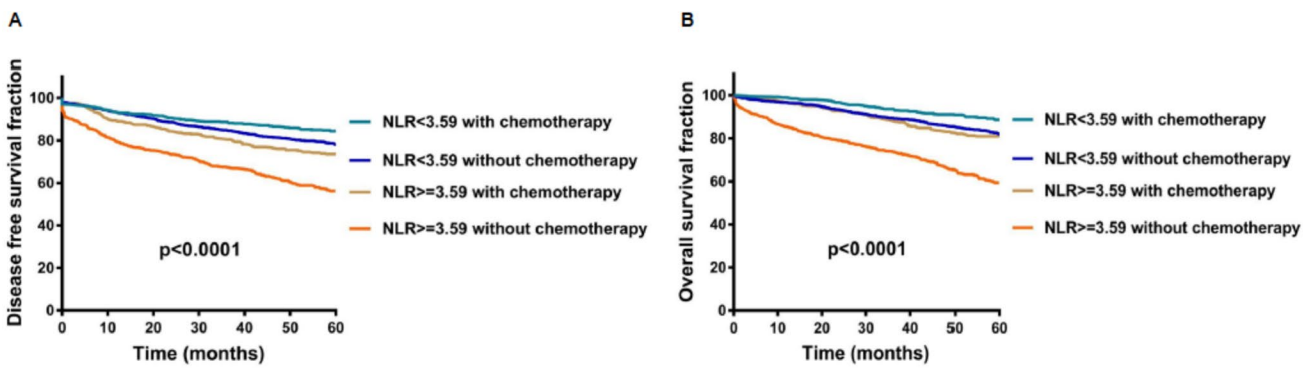

Fig. 3 Kaplan–Meier plots of 5-year survival in colorectal cancer. Significant difference was noted between the patients' groups stratified by the neutrophil–lymphocyte ratio (NLR) and chemotherapy in disease-free survival (**A**) and overall survival (**B**)

Table 3 Multivariate Cox regression survival analysis of chemotherapy for 5-year disease-free survival and overall survival in high and low NLR patients

5-year survival		NLR	Hazard ratio*	95% CI	*p* value
Disease-free survival	Crude	High	1.875	1.498–2.346	< 0.0001
		Low	1.401	1.121–1.751	0.003
	Adjusted**	High	1.497	0.924–2.425	0.101
		Low	1.157	0.766–1.747	0.49
Overall survival	Crude	High	1.875	1.498–2.346	< 0.0001
		Low	1.664	1.275–2.17	< 0.0001
	Adjusted**	High	1.872	1.039–3.37	0.037
		Low	1.052	0.631–1.751	0.847

*Without chemotherapy, reference: with chemotherapy

**Adjusted factors: age, gender, BMI, hemoglobin, hypoalbuminemia, CEA, and PLR

only the patients with specific stages [9, 25–29]. The studies including all stages of patients did not show the individual predictor role of NLR in each stage [13, 30–36] or only identified NLR as an associated survival risk factor in some stages [37].

There was no uniform cutpoint for NLR to divide the colorectal cancer patients into high and low NLR groups in survival analyses. In the published literature, the methods used to determine the cutpoint included receiver operating characteristic (ROC) [25, 27, 33, 37–45], referring to previous reports [26, 28, 46–48], mean of NLR, [49], and X-tile program [50, 51]. The optimal cutpoint for survival analyses must statistically provide the threshold value of the continuous covariates in events (death or recurrence) and time. In this study, we applied %FINDCUT SAS macro [21, 52] developed from the Contal and O'Quigley's approach [53] using log-rank statistics to demonstrate a cutpoint when a significant difference between groups in survival measured as time-to-event is identified. Exact dichotomization of a continuous variable into groups, which is based on a large sample size and optimal cutpoint, improves predictive valve for interpretation and treatment decision-making in medical practice. Further studies are necessary to standard cohort cutpoint of NLR in survival analyses.

Serum albumin level serves as a marker not only of nutritional status but also of systemic inflammation. Patients with higher NLR had lower serum albumin level [54], consistent with the findings of this study. Hypoalbuminemia was an independent risk factor of myopenia [55], associated with sarcopenia which predicted the worst survival in nonmetastatic colorectal cancer with co-occurrence of high NLR [54] and cytokine (interleukin-23) [56]. In this study, compared patients classified according to NLR and hypoalbuminemia, disease-free and overall survival were also poor in the group with both elevated NLR and hypoalbuminemia.

The mechanisms associated with the prognostic effect of NLR in colorectal cancer had been studied. A high NLR correlates with many kinds of cytokines, including interleukin 6 (IL-6), IL-8, and growth factors, which are related to key biological processes involved in carcinogenesis [46]. NLR was associated with pro-inflammatory cytokines and used as a simple measure of the systemic inflammatory response which activated intracellular pathways like NF-kB and affected tumor growth and progression [57]. On the other hand, increasing tumor-infiltrating lymphocytes seemed to be associated with represented cytotoxic lymphocyte aggregation and had better outcomes [58]. The future study combining the inflammation process with tumor-infiltrating lymphocytes would offer more comprehensive valuable information and insights in the role of NLR and colorectal cancer prognosis.

For stage II colon cancer, high-risk factors associated with recurrence and survival have been identified and used as the guideline for decision-making of adjuvant chemotherapy [14]. Not all high-risk features have the similar survival benefit from adjuvant chemotherapy [59]. We demonstrated that adjuvant chemotherapy increased more survival benefits in the patients with high NLR compared to those with low NLR. Further studies are needed to confirm NLR as high risk when recommending adjuvant chemotherapy in stage II colon cancer patients.

Several limitations should be considered in this database research. First, the retrospective study was based on routine clinical practice and laboratory test results. Some kinds of markers of systemic inflammation, like C-reactive protein, were not available in all patients and therefore used in this study. Second, some variables including infection and post-chemotherapy neutropenia have not been recorded in our study. Third, the database only included the patients treated in Taiwan. Our conclusions may not be applied generally to other populations with different treatment guidelines and racial backgrounds. Additionally, the type and the cycles of the chemotherapy regimen administered were not included in this analysis.

Conclusion

Our findings confirmed that high NLR was associated with poor outcomes in survival analyses of colorectal cancer patients. Postoperative adjuvant chemotherapy for stage II colon cancer brings more benefits of improving survival to the patients with high NLR. NLR would be a simple and warranted method to stratify the patients for tailored treatments.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00384-025-04839-4.

Author contributions Study concepts: T.J.C, W.H.H, Study design: T.J.C, W.H.H, Data acquisition: T.J.C, T.T.L, C.D.C, W.H.H, Data analysis and interpretation: T.J.C, T.T.L, C.D.C, W.H.H, Manuscript writing: T.J.C, W.H.H, Manuscript editing: T.J.C, W.H.H, All authors reviewed the manuscript.

Funding This study was supported by the Chang Gung Memorial Hospital grant CFRPG8J0171 and CMRPG8L0621.

Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

References

1. Coussens LM, Werb Z (2002) Inflammation and cancer. Nature 420(6917):860–867
2. Terzić J, Grivennikov S, Karin E, Karin M (2010) Inflammation and colon cancer. Gastroenterology 138(6):2101-2114.e5
3. Sebastian S, Hernández V, Myrelid P et al (2014) Colorectal cancer in inflammatory bowel disease: results of the 3rd ECCO pathogenesis scientific workshop (I). J Crohns Colitis 8(1):5–18
4. Borowczak J, Szczerbowski K, Maniewski M et al (2022) The role of inflammatory cytokines in the pathogenesis of colorectal carcinoma—recent findings and review. Biomedicines 10(7):1670
5. Ocana A, Nieto-Jiménez C, Pandiella A, Templeton AJ (2017) Neutrophils in cancer: prognostic role and therapeutic strategies. Mol Cancer 16(1):137
6. Ma SJ, Yu H, Khan M et al (2022) Evaluation of optimal threshold of neutrophil-lymphocyte ratio and its association with survival outcomes among patients with head and neck cancer. JAMA Netw Open 5(4):e227567–e227567
7. Bhat AA, Nisar S, Singh M et al (2022) Cytokine- and chemokine-induced inflammatory colorectal tumor microenvironment: emerging avenue for targeted therapy. Cancer Commun (Lond) 42(8):689–715
8. Haram A, Boland MR, Kelly ME, Bolger JC, Waldron RM, Kerin MJ (2017) The prognostic value of neutrophil-to-lymphocyte ratio in colorectal cancer: a systematic review. J Surg Oncol 115(4):470–479
9. Dell'Aquila E, Cremolini C, Zeppola T et al (2018) Prognostic and predictive role of neutrophil/lymphocytes ratio in metastatic colorectal cancer: a retrospective analysis of the TRIBE study by GONO. Ann Oncol 29(4):924–930
10. Ma CJ, Hu WH, Huang MC et al (2021) Taiwan Society of Colon and Rectum Surgeons (TSCRS) consensus for anti-inflammatory nutritional intervention in colorectal cancer. Front Oncol 11:819742
11. Naszai M, Kurjan A, Maughan TS (2021) The prognostic utility of pre-treatment neutrophil-to-lymphocyte-ratio (NLR) in colorectal cancer: a systematic review and meta-analysis. Cancer Med 10(17):5983–5997
12. Wang F, He W, Jiang C et al (2018) Prognostic value of inflammation-based scores in patients receiving radical resection for colorectal cancer. BMC Cancer 18(1):1102
13. Zhang N, Ning F, Guo R et al (2020) Prognostic values of preoperative inflammatory and nutritional markers for colorectal cancer. Front Oncol 10:585083
14. Taieb J, Karoui M, Basile D (2021) How I treat stage II colon cancer patients. ESMO Open 6(4):100184
15. Ginesi MC, Bliggenstorfer JT, Kwesiga DM et al (2023) Factors associated with receipt of adjuvant chemotherapy in stage II colon cancer. Ann Surg Oncol 30(9):5511–5518
16. Siegel RL, Giaquinto AN, Jemal A (2024) Cancer statistics, 2024. CA: A Cancer J Clin 74(1):12–49
17. Bray F, Laversanne M, Sung H et al (2024) Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer J Clin 74(3):229–263
18. Huang YC, Chen YH (2020) Cancer incidence characteristic evolution based on the national cancer registry in Taiwan. J Oncol 2020:1408793
19. Tsai MS, Lin MH, Lee CP et al (2017) Chang Gung Research Database: a multi-institutional database consisting of original medical records. Biomed J 40(5):263–269
20. Hu WH, Cajas-Monson LC, Eisenstein S, Parry L, Cosman B, Ramamoorthy S (2015) Preoperative malnutrition assessments as predictors of postoperative mortality and morbidity in colorectal cancer: an analysis of ACS-NSQIP. Nutr J 14:91
21. Meyers JP, Mandrekar J (2015) Cutpoint determination methods in survival analysis using SAS®: updated %FINDCUT macro
22. Brown JD, Alipour-Haris G, Pahor M, Manini TM (2020) Association between a deficit accumulation frailty index and mobility outcomes in older adults: secondary analysis of the lifestyle interventions and independence for elders (LIFE) study. J Clin Med 9(11):3757
23. Yatabe S, Eto K, Haruki K et al (2020) Signification of Systemic Immune-Inflammation Index for prediction of prognosis after resecting in patients with colorectal cancer. Int J Colorectal Dis 35(8):1549–1555
24. Choi KW, Hong SW, Chang YG et al (2014) Inflammation-based score (Glasgow prognostic score) as an independent prognostic factor in colorectal cancer patients. Ann Surg Treat Res 86(6):309–313
25. Dimitriou N, Felekouras E, Karavokyros I, Alexandrou A, Pikoulis E, Griniatsos J (2018) Neutrophils to lymphocytes ratio as a useful

prognosticator for stage II colorectal cancer patients. BMC Cancer 18(1):1202
26. Ashizawa N, Furuya S, Katsutoshi S et al (2020) Clinical significance of dynamic neutrophil-lymphocyte ratio changes in patients with colorectal cancer. Anticancer Res 40(4):2311–2317
27. Mazaki J, Katsumata K, Kasahara K et al (2020) Neutrophil-to-lymphocyte ratio is a prognostic factor for colon cancer: a propensity score analysis. BMC Cancer 20(1):922
28. Murray NP, Villalon R, Orrego S, Guzman E (2021) The association of the neutrophil-lymphocyte ratio with the presence of minimal residual disease and outcome in patients with stage II colon cancer treated with surgery alone. Colorectal Dis 23(4):805–813
29. Polk N, Budai B, Hitre E, Patócs A, Mersich T (2022) High neutrophil-to-lymphocyte ratio (NLR) and systemic immune-inflammation index (SII) are markers of longer survival after metastasectomy of patients with liver-only metastasis of rectal cancer. Original research. Pathol Oncol Res 28:. https://doi.org/10.3389/pore.2022.1610315
30. Liu H, Liu G, Bao Q et al (2010) The baseline ratio of neutrophils to lymphocytes is associated with patient prognosis in rectal carcinoma. J Gastrointest Cancer 41(2):116–120
31. Guthrie GJ, Roxburgh CS, Farhan-Alanie OM, Horgan PG, McMillan DC (2013) Comparison of the prognostic value of longitudinal measurements of systemic inflammation in patients undergoing curative resection of colorectal cancer. Br J Cancer 109(1):24–28
32. Mallappa S, Sinha A, Gupta S, Chadwick SJ (2013) Preoperative neutrophil to lymphocyte ratio >5 is a prognostic factor for recurrent colorectal cancer. Colorectal Dis 15(3):323–328
33. Balde AI, Fang S, He L et al (2017) Propensity score analysis of recurrence for neutrophil-to-lymphocyte ratio in colorectal cancer. J Surg Res 219:244–252
34. Song Y, Yang Y, Gao P et al (2017) The preoperative neutrophil to lymphocyte ratio is a superior indicator of prognosis compared with other inflammatory biomarkers in resectable colorectal cancer. BMC Cancer 17(1):744
35. Hachiya H, Ishizuka M, Takagi K et al (2018) Clinical significance of the globulin-to-albumin ratio for prediction of postoperative survival in patients with colorectal cancer. Ann Gastroenterol Surg 2(6):434–441
36. Zhang X, Hu D, Lin X et al (2019) Prognostic value of an inflammation-related index in 6,865 Chinese patients with postoperative digestive tract cancers: the FIESTA study. Front Oncol 9:427
37. Kubo H, Murayama Y, Arita T, Kuriu Y, Nakanishi M, Otsuji E (2016) The prognostic value of preoperative neutrophil-to-lymphocyte ratio in colorectal cancer. World J Surg 40(11):1
38. Malietzis G, Giacometti M, Askari A et al (2014) A preoperative neutrophil to lymphocyte ratio of 3 predicts disease-free survival after curative elective colorectal cancer surgery. Ann Surg 260(2):287–292
39. Choi WJ, Cleghorn MC, Jiang H, Jackson TD, Okrainec A, Quereshy FA (2015) Preoperative neutrophil-to-lymphocyte ratio is a better prognostic serum biomarker than platelet-to-lymphocyte ratio in patients undergoing resection for nonmetastatic colorectal cancer. Ann Surg Oncol 22(Suppl 3):S603-13
40. Khan M, Hakeem A, Scott N, Botterill I (2015) PTH-298 Preoperative neutrophil lymphocyte ratio (NLR) is a poor predictor of response to neo-adjuvant chemo-radiotherapy in rectal cancer resection. Gut 64(Suppl 1):A541–A542
41. Tohme S, Sukato D, Chalhoub D et al (2015) Neutrophil-lymphocyte ratio is a simple and novel biomarker for prediction of survival after radioembolization for metastatic colorectal cancer. Ann Surg Oncol 22(5):1701–1707
42. Grenader T, Nash S, Adams R et al (2016) Derived neutrophil lymphocyte ratio is predictive of survival from intermittent therapy in advanced colorectal cancer: a post hoc analysis of the MRC COIN study. Br J Cancer 114(6):612–615
43. McCluney SJ, Giakoustidis A, Segler A et al (2018) Neutrophil: lymphocyte ratio as a method of predicting complications following hepatic resection for colorectal liver metastasis. J Surg Oncol 117(5):1058–1065
44. Kim H, Jung HI, Kwon SH et al (2019) Preoperative neutrophil-lymphocyte ratio and CEA is associated with poor prognosis in patients with synchronous colorectal cancer liver metastasis. Ann Surg Treat Res 96(4):191–200
45. Sagawa M, Yokomizo H, Yoshimatsu K et al (2020) Significance of neutrophil-lymphocyte ratio (NLR) as a prognostic factor in stage II colorectal cancer. Int Surg 105(1–3):552–558
46. Chen ZY, Raghav K, Lieu CH et al (2015) Cytokine profile and prognostic significance of high neutrophil-lymphocyte ratio in colorectal cancer. Br J Cancer 112(6):1088–1097
47. Patel M, McSorley ST, Park JH et al (2018) The relationship between right-sided tumour location, tumour microenvironment, systemic inflammation, adjuvant therapy and survival in patients undergoing surgery for colon and rectal cancer. Br J Cancer 118(5):705–712
48. Cha YJ, Park EJ, Baik SH, Lee KY, Kang J (2019) Prognostic impact of persistent lower neutrophil-to-lymphocyte ratio during preoperative chemoradiotherapy in locally advanced rectal cancer patients: a propensity score matching analysis. PLoS ONE 14(3):e0214415
49. Ke T-M, Lin L-C, Huang C-C, Chien Y-W, Ting W-C, Yang C-C (2020) High neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio predict poor survival in rectal cancer patients receiving neoadjuvant concurrent chemoradiotherapy. Medicine 99(17):e19877
50. Li Y, Jia H, Yu W et al (2016) Nomograms for predicting prognostic value of inflammatory biomarkers in colorectal cancer patients after radical resection. Int J Cancer 139(1):220–231
51. Ouyang H, Xiao B, Huang Y, Wang Z (2023) Baseline and early changes in the neutrophil-lymphocyte ratio (NLR) predict survival outcomes in advanced colorectal cancer patients treated with immunotherapy. Int Immunopharmacol 123:110703
52. Williams BA, Mandrekar J, Mandrekar S, Cha S, Furth A (2006) Finding optimal cutpoints for continuous covariates with binary and time-to-event outcomes
53. Contal C, O'Quigley J (1999) An application of changepoint methods in studying the effect of age on survival in breast cancer. Comput Stat Data Anal 30(3):253–270
54. Cespedes Feliciano EM, Kroenke CH, Meyerhardt JA et al (2017) Association of systemic inflammation and sarcopenia with survival in nonmetastatic colorectal cancer: results from the C SCANS study. JAMA Oncol 3(12):e172319–e172319
55. Malietzis G, Johns N, Al-Hassi HO et al (2016) Low muscularity and myosteatosis is related to the host systemic inflammatory response in patients undergoing surgery for colorectal cancer. Ann Surg 263(2):320–325
56. Hu WH, Chang CD, Liu TT et al (2021) Association of sarcopenia and expression of interleukin-23 in colorectal cancer survival. Clin Nutr 40:5322–5326
57. Pine JK, Morris E, Hutchins GG et al (2015) Systemic neutrophil to-lymphocyte ratio in colorectal cancer: the relationship to patient survival, tumour biology and local lymphocytic response to tumour. Br J Cancer 113(2):204–211
58. Hu WH, Miyai K, Cajas-Monson LC, Luo L, Liu L, Ramamoorthy SL (2015) Tumor-infiltrating CD8(+) T lymphocytes associated with clinical outcome in anal squamous cell carcinoma. J Surg Oncol 112(4):421–426
59. Babcock BD, Aljehani MA, Jabo B et al (2018) High-risk stage II colon cancer: not all risks are created equal. Ann Surg Oncol 25:1980–1985