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INFLAMMATORY MARKERS AS PREDICTORS OF RECURRENCE OF COLORECTAL CANCER. LITERATURE REVIEW

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Abstract. The urgent requirement for biological markers capable of indicating a high risk of recurrence persists for colorectal cancer (CRC) patients.

The aim of the study. To evaluate the prognostic value of inflammatory markers (IM) as disease course predictors for CRC patients based on the results of scientific research on this topic.

The search of literature sources on the selected topic was performed in the Web of Science, Scopus and Pubmed databases. Keywords for the search were: "inflammatory markers", "colorectal cancer", "survival", "prognosis", "neutrophils", "lymphocytes", "monocytes", "platelets", "albumin", "C-reactive protein".

Even though the design of the reviewed studies was different by the quantitative and qualitative composition of the cohorts and time points for marker determination, it was possible to single out the most frequently used IM and their main characteristics. The neutrophils-to-lymphocytes ratio (NLR) was found to be one of the most common markers. Patients with high NLR showed worse recurrence-free and overall survival. Most of the works devoted to this IM assess its level for predicting the course of CRC after radical surgery.

In contrast to NLR, patients with a high lymphocyte-to-monocyte ratio (LMR) had better overall survival. In addition, the researchers established a relationship between the level of this marker and the grade of tumor differentiation. The Systemic Inflammatory Score (SIS) reflects the combined prognostic value of LMR and albumin. Its high levels are associated with worse prognosis. High levels of PLR (platelet-to-lymphocyte ratio) and PNLR (platelet-to-neutrophil-to-lymphocyte ratio), or as it is also called systemic inflammatory index (SII), are independent predictors of poor prognosis. Classic and modified Glasgow scales (GPS and mGPS) are used for predicting the course of the disease, both in the postoperative period and for metastatic cancer. As well as the scales, the PNI marker (prognostic nutritional index) is associated with the albumin level. The decrease in its level is associated with poor prognosis. A particular focus was given to the novel marker, "LA", which was used for patients with rectal cancer. Its high levels, in contrast to PNI, proved to be a predictor of a good prognosis. The prognostic inflammatory index (IPI) proved to be a statistically better predictor of relapse than the mGPS described above. And the ALI (Inflammatory Index of Advanced Lung Cancer), low values of which indicate poor overall survival, was found to be more sensitive than the IPI. Unfavorable prognosis is also associated with low levels of the albumin-globulin ratio (AGR). High CAR levels (CRP-albumin ratio) and low LCR levels (lymphocyte-CRP ratio) are associated with shorter recurrence-free and overall survival.

The results of the performed scientific search made it possible to establish a statistically significant prognostic value of IM as disease course predictors for CRC patients. The absolute advantage of IM is their accessibility, as the majority of indicators are determined in routine practice. Additionally, it offers ease of use as its calculation based on simple mathematical formulas. Cut-off values for each marker may differ depending on the stage of the disease in the studied cohort, the time points of determining the value of the marker, use of therapy. There might be a dependence on other parameters that have not yet been investigated.

Keywords: inflammatory markers, colorectal cancer, survival, NLR, LMR, SIS, PLR, GPS, LA, ALI, CRP.

Introduction. Colorectal cancer remains among the leaders in terms of the number of the caused deaths. This pattern persists, particularly due to the high rate of relapse, which occurs even after radical treatment and significantly deteriorates patient's prognosis [1]. Therefore, the search for new tools for monitoring and predicting the course of colorectal cancer is an extremely urgent issue.

The course of cancer is determined by the complex interaction between the tumor and the patient's organism. A reflection of this interaction is a systemic inflammatory response. It has important clinical value because it can be assessed with the help of clinical and biochemical blood tests obtained during a routine examination [2]. For example, high levels of neutrophils and monocytes can promote tumor metastasis [3-4]. Lymphocytes can influence disease relapse and promote a cytotoxic immune response. Scientists believe that a low level of lymphocytes in blood serum worsens the prognosis of patients with colorectal cancer [5]. Platelets are able to release pro-angiogenic proteins and stimulate angiogenesis, which in turn promotes the growth of malignant tumors. In addition, cytokines and chemokines produced by them support chronic inflammation associated with the tumor existence [6].

Albumin is an important laboratory indicator that belongs to acute phase proteins. Its concentration can vary depending on the level of nutrition and the intensity of the systemic inflammatory response. A low level of albumin indicates malnutrition and may be the result of existing inflammation [7].

Hence, even isolated levels of blood indicators possess clinical significance. Nevertheless, studies of the

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systemic inflammatory response demonstrate that their combined analysis is significantly informative [8]. Inflammatory markers (IM) are the tools of this analysis. Their features and prognostic value will be discussed below.

The aim of the study is to evaluate the prognostic value of inflammatory markers (IM) as disease course predictors for CRC patients based on the results of scientific research on this topic.

Materials and methods. The search of literature on the selected theme was performed in the Web of Science, Scopus and Pubmed databases. Keywords for the search were: "inflammatory markers", "colorectal cancer", "survival", "prognosis", "neutrophils", "lymphocytes", "monocytes", "platelets", "albumin", "C-reactive protein".

Research results and discussion.

- **Inflammatory markers associated with neutrophils**

One of the most common inflammatory markers is the neutrophil-to-lymphocyte ratio (NLR). Proctor et al. [9] analyzed 1413 patients with colorectal cancer and found that NLR is a significant marker of survival. The research team of Li et al. [10] studied 5336 patients with stage I–III malignancy who underwent radical surgical treatment and reported that NLR > 2.72 is an independent predictor of recurrence-free survival.

Dell'Aquila et al. [11] studied a cohort of patients (n=413) with metastatic colorectal cancer treated with FOLFOXIRI or FOLFIRI and bevacizumab. Scientists have observed that NLR > 3.0 is an independent predictor of overall survival.

Partykevych [12] in his study demonstrated that 5-year predicted overall and recurrence-free survival was 21.9 % and 28 % higher for the group with low NLR (1.2) compared to the group with high NLR (9).

It is noteworthy that the majority of works are devoted to the investigation of NLR before surgical treatment. However, Yasui et al. [13] studied the relationship of this inflammatory marker with recurrence, examining the value of the marker before and after surgery. It was established that patients with neutrophils and lymphocytes within the normal range had significantly better survival. A similar research design was followed by other scientists, and the results were similar [14, 15]. In a cohort of 2280 people, it was confirmed that patients with a high preoperative and postoperative neutrophil-lymphocyte ratio (greater than 3.75) have extremely poor overall survival. Low NLR scores (≤3.75) were clearly associated with better survival.

The value of the NLR marker at different time points (from 0 to 3 months after the operation) was examined by other scientists who tackled the issue more thoroughly. It was established that a high level of NLR 57–90 days after surgery (> 1.57) indicates a low recurrence-free survival [16].

A neutrophil-lymphocyte ratio greater than 3.0 before surgery is considered a risk factor for extrahepatic recurrence [17]. Moreover, high NLR can reduce tumor sensitivity to oxaliplatin [18]. Numerous studies have demonstrated that NLR is an independent predictor of survival in patients with colorectal cancer, although the data may vary depending on the stage of the disease, the time points of the inflammatory index study, and the chemotherapy regimens used.

- **Markers associated with monocytes**

In this particular context, the prognostic potential of the lymphocyte-monocyte ratio (LMR) was taken into account. It is believed that a low LMR may indicate the presence of an active inflammatory process within the patient's body, given that a low level of lymphocytes is observed in contrast to a high number of monocytes.

One study assessed 1,623 individuals with all stages of colorectal cancer who underwent curative resection and found that an increase in LMR (>2.38) was independently associated with a longer life expectancy [19]. In addition, they monitored the relationship between the degree of tumor differentiation and the value of the LMR marker. A significant difference between groups has been established. It appears that highly differentiated tumors were found to be associated with low LMR, while patients with high LMR had poorly differentiated tumors.

Mai et al. [20] performed a meta-analysis that included 3,089 patients with metastatic colorectal cancer. Obtained results show that high LMR was associated with favorable prognosis in terms of progression-free and overall survival.

Furthermore, studies have been performed to investigate the combined effect of serum albumin levels and the LMR. This index is called the systemic inflammatory scale (SIS). Suzuki et al. [21] scored points as follows: patients with albumin > 4.0 g/dL and LMR > 4.44 received 0 points, patients with albumin < 4.0 g/dL and LMR < 4.44 received a score of 2 points, and all others received 1 point. According to this criterion, 727 patients with colorectal cancer of all stages who underwent curative resection were evaluated.

It is also important to note the prognostic value of isolated levels of lymphocytes and monocytes. So, for example, Noh et al. [22] studied a group of 231 patients who received radical surgery and adjuvant chemotherapy. It was found that patients who had sufficiently high levels of lymphocytes (≥1.78 × 109/l) after chemotherapy had significantly better recurrence-free survival.

The research team of Zhang et al. [23] reported that an elevated monocyte count (>595/mm3) significantly shortened the recurrence-free survival period in patients with rectal cancer (T3N0M0) who underwent radical surgery. Haruki et al. [24] examined the clinical blood analysis of 64 patients with liver metastases of colorectal cancer. They discovered that an increase in serum monocyte count less than in two times prior and after surgery was independently associated with recurrence-free survival.

- **Markers associated with platelets**

Platelet-to-lymphocyte ratio (PLR) is another well-known prognostic marker for survival in patients with colorectal cancer. An increase in platelet number against the background of a decrease in lymphocyte number creates high values of the PLR index. Higher levels indicate a worse patient's prognosis. Kim et al. [25] established a PLR cut-off value of 160. Higher values in patients with stages III and IV were independent predictors of poor recurrence-free and overall survival. The value of the marker was also studied for 151 patients with colorectal cancer and liver metastases. PLR ≥ 220 and NLR ≥ 5 were found to be independent predictors of a poor prognosis [26]. Ma et al. [27] provided a wide meta-analysis of 23 observation studies that included 7577 colorectal cancer patients who

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had undergone surgery. Similarly, to previous examples, a significant association between high PLR and worse overall survival was found, but in contrast, no association between PLR level and disease-free survival was observed.

The research team of Mercier et al. [28] demonstrated another prognostic marker – platelet-to-neutrophil-to-lymphocyte ratio (PNLR). An increase in the number of neutrophils and platelets leads to an increase in PNLR. Scientists studied the results of analyses of 305 patients with an advanced colorectal cancer and found that a high PNLR (≥2000) is an independent predictor of low recurrence-free and overall survival. Another team of scientists called this ratio as the systemic inflammatory index (SII) and investigated the prognostic value of the marker among 1,383 patients who underwent radical surgery for colorectal cancer. SII had a higher diagnostic efficiency compared to NLR and PLR. This index was recognized as an independent predictor of low overall survival [29].

Studies that determined the prognosis directly by the number of blood platelets were also noted. Ishizuka et al. [30] reported that in a cohort study of 453 patients with colorectal cancer, it was established that an elevated platelet count (>300 × 109/L) was an independent predictor of poor prognosis and poor overall survival. Similar results were obtained among patients with stage IV colorectal cancer. The number of platelets up to 350 × 109/l was considered acceptable. Higher scores were a significant prognostic factor for poor survival [31].

- **Inflammatory markers associated with albumin**

The Glasgow Prognostic Scale (GPS) is an indicator that considers the concentration of C-reactive protein (CRP) and albumin. A study examining the results of analyses of 448 patients found that a high GPS was significantly associated with recurrence-free survival [32]. Scientists analyzed 1590 patients with completely resected colorectal cancer and found that GPS 1 or 2 can be considered an independent predictor of recurrence-free survival [33].

The GPS is used to determine the prognosis of metastatic colorectal cancer. Kobayashi et al. collected data from 99 patients with lung metastases who underwent curative resection and found that GPS was an independent predictor of overall survival [34].

In addition to the classic version of GPS, a modified version of it is also used. Park et al. [35] calculated the mGPS as follows: CRP ≤ 1.0 mg/dL is classified as score 0, CRP > 1.0 mg/dL and albumin ≥ 3.5 g/dL is score 1, and CRP > 1.0 mg/dL and albumin < 3.5 g/dL is 2 points. Scientists have proven that the combination of mGPS and TNM stage can be used to determine the postoperative prognosis.

In addition to GPS, other prognostic markers associated with albumin are used. For example, the prognostic nutrition index (PNI), which is widely used in Japan. The index is calculated as "albumin level (g/l) + 0.005 × number of lymphocytes." Scientists believe that a decreased PNI is associated with a poor prognosis for patients with colorectal cancer. In a group of 468 patients undergoing radical surgery, PNI was found to be more sensitive than mGPS. This index can be considered a predictor of recurrence-free and overall survival in patients with colorectal cancer [36].

Tominaga et al. [37] studied 84 patients above the age of 85 years who were treated for colorectal cancer. The optimal limit value of PNI is set at the level of 42.4. PNI values lower than this value are associated with better recurrence-free survival.

Recently, a new prognostic marker "LA" was discovered. It is defined as "number of lymphocytes × albumin level (g/dL)" [38]. Scientists collected retrospective data and evaluated the value of the marker in 448 patients with stage II and III rectal cancer. It has been established that a score lower than 5950 can be a predictor of a good prognosis, long-term recurrence-free survival, and overall survival of patients. The calculation of LA is somewhat easier than the calculation of PNI. However, since the study was conducted among patients with rectal cancer, it is not known if it can be applied to colorectal cancer in general.

The research team of Wang et al. [39] analyzed 877 patients with stages I–III colorectal cancer who received radical surgical treatment. The study examined the impact of a combination of variables, including neutrophil-lymphocyte ratio and serum albumin level. It was found that the combination of a high level of NLR (≥2.39) and hypoalbuminemia (<39.75 g/L) can be considered a predictor of poor overall survival.

Hong et al. [40] considered the NLR-to-albumin ratio as a prognostic inflammatory index (IPI) and tried to evaluate its impact on prognosis in individuals with colorectal cancer. According to blood parameters the appropriate score was established: an IPI score of 0 was given to patients with NLR ≤ 3.0 and albumin ≥ 35 g/l, score 1 to patients with NLR ≤ 3.0 or albumin < 35 g/l, and score 2 to patients with NLR > 3.0 and albumin < 35 g/l. 571 patients were evaluated and found that IPI was a statistically better predictor of relapse than mGPS.

An even more difficult marker for calculation is the ALI (Inflammation Index of Advanced Lung Cancer), which is also used for patients with colorectal cancer [41]. To calculate this index, the product of the patient's body mass index (BMI) and serum albumin concentration is calculated, which is then divided by the NLR. The cut-off value for ALI was found to be 28.9 in the considered study, using ROC analysis. Indicators that are lower than the specified value indicate low overall survival. The study was conducted on a group of 159 patients with metastatic colorectal cancer. As indicated above, sarcopenia has a negative impact on the prognosis of the course of the disease. Usually, a low BMI is associated with insufficient nutrition and a sarcopenic state of the patient. The researchers concluded that ALI is a more sensitive marker than IPI.

Fujikawa et al. [42] proved that the albumin-to-globulin ratio (AGR) can also be used to predict the course of colorectal cancer. A low AGR indicates hypoalbuminemia and hyperglobulinemia. Both indicators are associated with systemic inflammation. A retrospective study of 248 patients with stage I-III colon cancer undergoing curative surgery found that AGR was independently associated with overall and recurrence-free survival.

In addition to already described markers, Liu et al. [43] reported about the controlling nutritional status (CONUT) score. Serum albumin level, lymphocyte count and total cholesterol level were used for appropriate calculation. In a retrospective analysis of 217 patients with newly diagnosed colorectal cancer, the group with high CONUT had worse overall and relapse-free survival.

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Moreover, it was demonstrated that CONUT was superior to mGPS, PNI and NLR.

- **Markers associated with C-reactive protein**

C-reactive protein is considered one of the most modern and effective indicators for assessing the level of inflammation in cancer patients before or after surgery. But CRP does not belong to the indicators performed in routine oncological practice. This statement, however, is not applicable to Japan. That is why numerous studies devoted to the prognostic potential of CRP have been conducted in this country. For example, Koike et al. [44] evaluated the preoperative CRP level in 300 patients with colorectal cancer. The scientists concluded that a high level of CRP (>0.5 mg/dL) can be considered an independent predictor of a negative prognosis.

Matsuoka et al. [45] studied the mutual influence of CRP and hypoalbuminemia. In a group of 133 patients who underwent radical surgery for stage III colorectal cancer, it was proved that this marker is effective enough to determine the prognosis. Postoperative CRP-to-albumin ratio (CAR) values greater than 0.035 indicated significantly shorter recurrence-free and overall survival. Another study examined the association of CAR with prognosis in patients with rectal cancer who underwent neoadjuvant chemoradiotherapy and radical surgery. It was established that CAR ≥ 0.049 before chemotherapy is an independent predictor of recurrence-free and overall survival [46]. The scientific team of Dolan et al. [47] obtained different results. CAR > 0.22 was found to be an independent predictor of survival.

Besides the ratio of CRP-to-albumin, some scientists studied the ratio of CRP and almost all indicators of clinical blood analysis. For instance, Suzuki et al. [48] studied 16 markers of inflammation: NLR, PLR, PNI, LMR, CAR, lymphocyte-to-CRP ratio (LCR), monocytes-to-albumin ratio (MAR), neutrophils-to-albumin ratio (NAR), neutrophils-to-monocytes ratio (NMR), neutrophils-to-CRP ratio, (NCR), platelets-to-albumin ratio (PAR), neutrophils-to- platelets ratio (NTR), monocytes-to-platelets ratio (MPR), monocytes-to-CRP ratio (MCR). The study was conducted with the participation of 1,303 patients with II-III stages of colorectal cancer. The LCR cutoff was set at 12,980. Values below this range indicated poor recurrence-free and overall survival.

Okugawa et al. [49] confirmed the prognostic value of LCR in their own study with the participation of 373 patients. Furthermore, scientists have established that a low LCR can indicate the risk for postoperative infectious complications. Scientists noted that the ratio of lymphocytes to CRP is an effective marker of long-term and short-term prognosis for colorectal cancer patients.

In the latest publication, Takeda et al. [50] described a novel CRP-albumin-lymphocyte (CALLY) index. The results of the retrospective study, which included 578 patients with stage II-III colorectal cancer who underwent curative resection, showed that CALLY <2 was associated with significantly poorer disease-free and overall survival. So, CALLY was named as one more independent prognostic biomarker for colorectal cancer patients.

Conclusions. The results of the conducted scientific search made it possible to establish a statistically significant prognostic value of IM as disease course predictors for CRC patients. The absolute advantage of IM is their accessibility, as the majority of indicators are determined in routine practice. Additionally, it offers ease of use as its calculation based on simple mathematical formulas. Cut-off values for each marker may differ depending on the stage of the disease in the studied cohort, the time points of determining the value of the marker, use of chemotherapy or radiation therapy. There might be a dependence on other parameters that have not yet been investigated.

References:

1. Dakui L, Yufei Y, Zezhi S, Qi L, Sanjun C, Qingguo L, et al. Clinicopathological Features of Stage I–III Colorectal cancer recurrence over 5 years after radical surgery without receiving neoadjuvant therapy: evidence from a large sample study. Frontiers in Surg. 2021; 8. DOI: 10.3389/fsurg.2021.666400
2. Schmitt M, Greten FR. The inflammatory pathogenesis of colorectal cancer. Nat. Rev. Immunol. 2021; 21:653-667. DOI: 10.1038/s41577-021-00534-x
3. Yang J, Guo X, Wang M, Ma X, Ye X, Lin P. Pretreatment inflammatory indexes as predictors of survival and cetuximab efficacy in metastatic colorectal cancer patients with wild-type RAS. Sci Rep. 2017 Dec 7; 7(1):17166. DOI: 10.1038/s41598-017-17130-6
4. Dallavalasa S, Beeraka NM, Basavaraju CG, Tulimilli SV, Sadhu SP, Rajesh K, et al. The Role of Tumor Associated Macrophages (TAMs) in Cancer Progression, Chemoresistance, Angiogenesis and Metastasis - Current Status. Current Medicinal Chemistry. 2021; 28(39):8203-8236. DOI: 10.2174/0929867328666210720143721
5. Naszai M, Kurjan A, Maughan TS. The prognostic utility of pre-treatment neutrophil-to-lymphocyte-ratio (NLR) in colorectal cancer: A systematic review and meta-analysis. Cancer Med. 2021; 10: 5983-5997. DOI: 10.1002/cam4.4143
6. Bulut G, Ozdemir ZN. Prognostic Significance of Neutrophil-Lymphocyte Ratio and Platelet-Lymphocyte Ratio in Metastatic Colorectal Cancer. J Gastrointest Canc. 2022; 53: 1-6. DOI: 10.1007/s12029-021-00616-y
7. Christina NM, Tjahyanto TB, Lie JG, Santoso TA, Albertus H, Octavianus D, et al. Hypoalbuminemia and colorectal cancer patients: Any correlation?: A systematic review and meta-analysis. Medicine. 2023; 102(8):e32938. DOI: 10.1097/MD.0000000000032938
8. Nøst TH, Alcala K, Urbarova I, et al. Systemic inflammation markers and cancer incidence in the UK Biobank. Eur. J. Epidemiol. 2021; 36:841-848. DOI: 10.1007/s10654-021-00752-6
9. Proctor MJ, Morrison DS, Talwar D, Balmer SM, Fletcher CD, O'Reilly DS, et al. A comparison of inflammation-based prognostic scores in patients with cancer. A Glasgow Inflammation Outcome Study. Eur J Cancer. 2011 Nov; 47(17):2633-41. DOI: 10.1016/j.ejca.2011.03.028
10. Li Y, Jia H, Yu W, Xu Y, Li X, Li Q, et al. Nomograms for predicting prognostic value of inflammatory biomarkers in colorectal cancer patients after radical resection. Int J Cancer. 2016 Jul 1; 139(1):220-31. DOI: 10.1002/ijc.30071

ISSN 2521-1455 (Print)
ISSN 2523-4250 (Online)

11. Dell'Aquila E, Cremolini C, Zeppola T, Lonardi S, Bergamo F, Masi G, et al. Prognostic and predictive role of neutrophil/lymphocytes ratio in metastatic colorectal cancer: a retrospective analysis of the TRIBE study by GONO. Ann Oncol. 2018 Apr 1; 29(4):924-930. DOI: 10.1093/annonc/mdy004
12. Partykevych YD. Analysis of treatment outcomes in patients with rectal cancer. Prognostic influence of neutrophillymphocyte index on survival. Clinical Oncology. 2024 Apr; 14 (2 (54)):1-6). DOI: 10.32471/clinicaloncology.2663-466X.54-2.32108
13. Yasui K, Shida D, Nakamura Y, Ahiko Y, Tsukamoto S, Kanemitsu Y. Postoperative, but not preoperative, inflammation-based prognostic markers are prognostic factors in stage III colorectal cancer patients. Br J Cancer. 2021 Mar; 124(5):933-941. DOI: 10.1038/s41416-020-01189-6
14. Li Z, Zhao R, Cui Y, Zhou Y, Wu X. The dynamic change of neutrophil to lymphocyte ratio can predict clinical outcome in stage I–III colon cancer. Sci Rep. 2018 Jun 21; 8(1):9453. DOI: 10.1038/s41598-018–27896-y
15. Chan JCY, Diakos CI, Chan DLH, Engel A, Pavlakis N, Gill A, Clarke SJ. A Longitudinal Investigation of Inflammatory Markers in Colorectal Cancer Patients Perioperatively Demonstrates Benefit in Serial Remeasurement. Ann Surg. 2018 Jun; 267(6):1119-1125. DOI: 10.1097/SLA.0000000000002251
16. Thiagarajan S, Tan JW, Zhou S, Tan QX, Hendrikson J, Ng WH, et al. Postoperative Inflammatory Marker Surveillance in Colorectal Peritoneal Carcinomatosis. Ann Surg Oncol. 2021 Oct; 28(11):6625-6635. DOI: 10.1245/s10434-020–09544-w
17. Verter E, Berger Y, Perl G, Peretz I, Tovar A, Morgenstern S, et al. Neutrophil-to-Lymphocyte Ratio Predicts Recurrence Pattern in Patients with Resectable Colorectal Liver Metastases. Ann Surg Oncol. 2021 Aug; 28(8):4320-4329. DOI: 10.1245/s10434-021-10000-6
18. Xun F, Jiang W, Sha M, Wang W, Xia Y, Hu H, et al. Neutrophil-to-lymphocyte ratio in colorectal tissue affects prognosis in patients with colorectal cancer. Pathology. 2024 Aug; 56(5):643-652. DOI: 10.1016/j.pathol.2024.03.003
19. Chan JC, Chan DL, Diakos CI, Engel A, Pavlakis N, Gill A, Clarke SJ. The Lymphocyte-to-Monocyte Ratio is a Superior Predictor of Overall Survival in Comparison to Established Biomarkers of Resectable Colorectal Cancer. Ann Surg. 2017 Mar; 265(3):539-546. DOI: 10.1097/SLA.0000000000001743
20. Mei P, Huang L, Lin L, Chen Y, Guo X. The prognostic utility of the ratio of lymphocyte to monocyte in patients with metastatic colorectal cancer: a systematic review and meta-analysis. Front Oncol. 2025 Feb 3; 15:1394154. DOI: 10.3389/fonc.2025.1394154
21. Suzuki Y, Okabayashi K, Hasegawa H, Tsuruta M, Shigeta K, Kondo T, Kitagawa Y. Comparison of Preoperative Inflammation-based Prognostic Scores in Patients With Colorectal Cancer. Ann Surg. 2018 Mar; 267(3):527-531. DOI: 10.1097/SLA.0000000000002115
22. Noh OK, Oh SY, Kim YB, Suh KW. Prognostic Significance of Lymphocyte Counts in Colon Cancer Patients Treated with FOLFOX Chemotherapy. World J Surg. 2017 Nov; 41(11):2898-2905. DOI: 10.1007/s00268-017-4104-6
23. Zhang LN, Xiao W, OuYang PY, You K, Zeng ZF, Ding PR, et al. The prognostic impact of preoperative blood monocyte count in pathological T3N0M0 rectal cancer without neoadjuvant chemoradiotherapy. Tumour Biol. 2015 Sep; 36(10):8213-9. DOI: 10.1007/s13277-015-3560-6
24. Haruki K, Shiba H, Fujiwara Y, Furukawa K, Wakiyama S, Ogawa M, et al. Perioperative change in peripheral blood monocyte count may predict prognosis in patients with colorectal liver metastasis after hepatic resection. J Surg Oncol. 2012 Jul 1; 106(1):31-5. DOI: 10.1002/jso.23033
25. Kim JH, Lee JY, Kim HK, Lee JW, Jung SG, Jung K, et al. Prognostic significance of the neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in patients with stage III and IV colorectal cancer. World J Gastroenterol. 2017 Jan 21; 23(3):505-515. DOI: 10.3748/wjg. v23.i3.505
26. Erstad DJ, Taylor MS, Qadan M, Axtell AL, Fuchs BC, Berger DL, et al. Platelet and neutrophil to lymphocyte ratios predict survival in patients with resectable colorectal liver metastases. Am J Surg. 2020 Dec; 220(6):1579-1585. DOI: 10.1016/j.amjsurg.2020.05.003
27. Ma L, Yang F, Guo W, Tang S, Ling Y. Prognostic role of platelet-to-lymphocyte ratio in patients with rectal cancer undergoing resection: a systematic review and meta-analysis. Front Oncol. 2024 Sep 30; 14:1415443. DOI: 10.3389/fonc.2024.1415443
28. Mercier J, Voutsadakis IA. The platelets-neutrophils to lymphocytes ratio: a new prognostic marker in metastatic colorectal cancer. J Gastrointest Oncol. 2018 Jun; 9(3):478-486. DOI: 10.21037/jgo.2018.03.13
29. Chen JH, Zhai ET, Yuan YJ, Wu KM, Xu JB, Peng JJ, et al. Systemic immune-inflammation index for predicting prognosis of colorectal cancer. World J Gastroenterol. 2017 Sep 14; 23(34):6261-6272. DOI: 10.3748/wjg. v23.i34.6261
30. Ishizuka M, Nagata H, Takagi K, Iwasaki Y, Kubota K. Preoperative thrombocytosis is associated with survival after surgery for colorectal cancer. J Surg Oncol. 2012 Dec; 106(7):887-91. DOI: 10.1002/jso.23163
31. Pedrazzani C, Mantovani G, Fernandes E, Bagante F, Luca Salvagno G, Surci N, et al. Assessment of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and platelet count as predictors of long-term outcome after R0 resection for colorectal cancer. Sci Rep. 2017 May 4; 7(1):1494. DOI: 10.1038/s41598-017-01652-0
32. Inamoto S, Kawada K, Okamura R, Hida K, Sakai Y. Prognostic impact of the combination of neutrophil-to-lymphocyte ratio and Glasgow prognostic score in colorectal cancer: a retrospective cohort study. Int J Colorectal Dis. 2019 Jul; 34(7):1303-1315. DOI: 10.1007/s00384-019–03316-z
33. Lee SC, Huh JW, Lee WY, Yun SH, Kim HC, Cho YB, et al. Prognostic value of serum inflammatory markers in colorectal cancer. Int J Colorectal Dis. 2020 Jul;

ISSN 2521-1455 (Print)
ISSN 2523-4250 (Online)

35(7):1211-1219. DOI: 10.1007/s00384-020-03591-1. Epub 2020 Apr 18. PMID: 32306074.
34. Kobayashi S, Karube Y, Nishihira M, Inoue T, Araki O, Sado T, Chida M. Usefulness of Inflammation-Based Prognostic Score in Patients Undergoing Lung Metastasectomy for Colorectal Carcinoma. World J Surg. 2016 Jul; 40(7):1632-7. DOI: 10.1007/s00268-016-3459-4. PMID: 26908239.
35. Park JH, Watt DG, Roxburgh CS, Horgan PG, McMillan DC. Colorectal Cancer, Systemic Inflammation, and Outcome: Staging the Tumor and Staging the Host. Ann Surg. 2016 Feb; 263(2):326-36. DOI: 10.1097/SLA.0000000000001122
36. Tokunaga R, Sakamoto Y, Nakagawa S, Izumi D, Kosumi K, Taki K, et al. Comparison of systemic inflammatory and nutritional scores in colorectal cancer patients who underwent potentially curative resection. Int J Clin Oncol. 2017 Aug; 22(4):740-748. DOI: 10.1007/s10147-017-1102-5
37. Tominaga T, Nonaka T, Hisanaga M, Fukuda A, Tanoue Y, Yoshimoto T, et al. Prognostic value of the preoperative prognostic nutritional index in oldest-old patients with colorectal cancer. Surg Today. 2020 May; 50(5):449-459. DOI: 10.1007/s00595-019–01910-w
38. Yamamoto T, Kawada K, Hida K, Matsusue R, Itatani Y, Mizuno R, et al. Combination of lymphocyte count and albumin concentration as a new prognostic biomarker for rectal cancer. Sci Rep. 2021 Mar 3; 11(1):5027. DOI: 10.1038/s41598-021-84475-4
39. Wang F, He W, Jiang C, Guo G, Ke B, Dai Q, et al. Prognostic value of inflammation-based scores in patients receiving radical resection for colorectal cancer. BMC Cancer. 2018 Nov 12; 18(1):1102. DOI: 10.1186/s12885-018-4842-3
40. Hong T, Shen D, Chen X, Cai D, Wu X, Hua D. A novel systematic inflammation related index is prognostic in curatively resected non-metastatic colorectal cancer. Am J Surg. 2018 Sep; 216(3):450-457. DOI: 10.1016/j.amjsurg.2017.07.021
41. Shibutani M, Maeda K, Nagahara H, Fukuoka T, Matsutani S, Kimura K, et al. The prognostic significance of the advanced lung cancer inflammation index in patients with unresectable metastatic colorectal cancer: a retrospective study. BMC Cancer. 2019 Mar 18; 19(1):241. DOI: 10.1186/s12885-019-5468-9
42. Fujikawa H, Toiyama Y, Inoue Y, Imaoka H, Shimura T, Okigami M, et al. Prognostic Impact of Preoperative Albumin-to-Globulin Ratio in Patients with Colon Cancer Undergoing Surgery with Curative Intent. Anticancer Res. 2017 Mar; 37(3):1335-1342. DOI: 10.21873/anticanres.11452
43. Liu LX, Wang H, Gao B, Xu TT, Yuan QG, Zhou SZ, Ding C, Miao J, Guan WX. Preoperative controlling nutritional status as an optimal prognostic nutritional index to predict the outcome for colorectal cancer. World J Gastrointest Oncol. 2024 Feb 15; 16(2):343-353. DOI: 10.4251/wjgo.v16.i2.343
44. Koike Y, Miki C, Okugawa Y, Yokoe T, Toiyama Y, Tanaka K, et al. Preoperative C-reactive protein as a prognostic and therapeutic marker for colorectal cancer. J Surg Oncol. 2008 Dec 1; 98(7):540-4. DOI: 10.1002/jso.21154
45. Matsuoka H, Ando K, Hu Q, Zaitsu Y, Tsuda Y, Hisamatsu Y, et al. Postoperative C-reactive protein/albumin ratio is a biomarker of risk of recurrence and need for adjuvant chemotherapy for stage III colorectal cancer. Int J Clin Oncol. 2020 Jul; 25(7):1318-1326. DOI: 10.1007/s10147-020-01672-3
46. Ide S, Toiyama Y, Okugawa Y, Oki S, Yasuda H, Fujikawa H, et al. Clinical Significance of C-Reactive Protein-to-Albumin Ratio with Rectal Cancer Patient Undergoing Chemoradiotherapy Followed by Surgery. Anticancer Res. 2017 Oct; 37(10):5797-5804. DOI: 10.21873/anticanres.12022
47. Dolan RD, McSorley ST, Park JH, Watt DG, Roxburgh CS, Horgan PG, McMillan DC. The prognostic value of systemic inflammation in patients undergoing surgery for colon cancer: comparison of composite ratios and cumulative scores. Br J Cancer. 2018 Jul; 119(1):40-51. DOI: 10.1038/s41416-018-0095-9
48. Suzuki S, Akiyoshi T, Oba K, Otsuka F, Tominaga T, Nagasaki T, et al. Comprehensive Comparative Analysis of Prognostic Value of Systemic Inflammatory Biomarkers for Patients with Stage II/III Colon Cancer. Ann Surg Oncol. 2020 Mar; 27(3):844-852. DOI: 10.1245/s10434-019-07904-9
49. Okugawa Y, Toiyama Y, Yamamoto A, Shigemori T, Ide S, Kitajima T, et al. Lymphocyte-C-reactive Protein Ratio as Promising New Marker for Predicting Surgical and Oncological Outcomes in Colorectal Cancer. Ann Surg. 2020 Aug; 272(2):342-351. DOI: 10.1097/SLA.0000000000003239
50. Takeda Y, Sugano H, Okamoto A, Nakano T, Shimoyama Y, Takada N, et al. Prognostic usefulness of the C-reactive protein-albumin-lymphocyte (CALLY) index as a novel biomarker in patients undergoing colorectal cancer surgery. Asian J Surg. 2024 Aug; 47(8):3492-3498. doi: 10.1016/j.asjsur.2024.03.054

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МАРКЕРИ ЗАПАЛЕННЯ ЯК ПРЕДИКТОРИ РЕЦИДИВУ КОЛОРЕКТАЛЬНОГО РАКУ. (ОГЛЯД ЛІТЕРАТУРИ)

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Резюме. Пошук біологічних маркерів рецидиву захворювання залишається актуальним для пацієнтів з колоректальним раком (КРР).

Метою роботи була оцінка прогностичної цінності маркерів запалення (МЗ) для пацієнтів з КРР на основі результатів наукового пошуку.

Пошук даних проводився в базах Web of Sciense, Scopus та Pubmed. Ключові слова: «маркери запалення», «колоректальний рак», «виживаність», «прогнозування», «нейтрофіли», «лімфоцити»,

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«моноцити», «тромбоцити», «альбумін», «С-реактивний білок».

Одним з популярних МЗ виявилося співвідношення нейтрофілів та лімфоцитів (NLR). Пацієнти з високим рівнем NLR продемонстрували гіршу безрецидивну (БРВ) та загальну виживаність (ЗВ).

На противагу NLR пацієнти з високим рівнем лімфоцитарно-моноцитарного співвідношення (LMR) мали кращу ЗВ. Системна запальна шкала (SIS) відображає сумісне значення LMR та альбуміну для прогнозування. Високі її показники пов'язані з гіршим прогнозом. Високі рівні PLR (тромбоцитарно-лімфоцитарного співвідношення) та PNLR (тромбоцитарно-нейтрофільно-лімфоцитарного співвідношення) є незалежними предикторами поганого прогнозу. Класична та модифікована шкали Глазго (GPS та mGPS) застосовуються як в післяопераційному періоді, так і для прогнозування перебігу метастатичного раку. Зі зниженням PNI (прогностичного нутритивного індексу) асоційовано поганий прогноз для пацієнтів. Окремо відзначено новий маркер «LA». Високі його значення виявилися предиктором гарного прогнозу. Прогностичний запальний індекс (IPI) виявився кращим предиктором рецидиву ніж mGPS. Прогностично несприятливими є низькі рівні співвідношення альбумін-глобулін (AGR) та ALI (індекс запалення прогресуючого раку легень). Високий CAR (співвідношення СРБ–альбумін) та низький LCR (співвідношення лімфоцитів та СРБ) свідчать про гіршу БРВ та ЗВ.

Результати проведеного наукового пошуку дозволили встановити статистично значущу прогностичну цінність МЗ для прогнозування перебігу КРР.

Ключові слова: маркери запалення, колоректальний рак, виживаність, NLR, LMR, SIS, PLR, GPS, LA, ALI, CRP.

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