

The contribution of hematological parameters to prediction of the phase in stage 2 and stage 3 colon cancers

Erkan Karacan¹, Eyüp Murat Yılmaz², Buse Yildiz², Ahmet Ender Demirkiran²

¹Department of General Surgery, Aydın State Hospital, Aydın, Turkey

²Department of General Surgery, Faculty of Medicine, Adnan Menderes University, Aydın, Turkey



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Corresponding Author: Erkan Karacan, Department of General Surgery, Aydın State Hospital, Aydın, Turkey.

Tel.: +905075657221,

E-mail: erkan8806@gmail.com

Abstract

Purpose: Colorectal cancers are a significant cause of cancer-related deaths around the world. In the preoperative staging of colon cancers, radiological images and various blood tests are used. However, it is both difficult and expensive to apply radiological examinations. In our study, we aimed at predicting the stage of colon cancers by preoperatively viewing the hematological parameters, which are simple, cheap and easy to apply.

Material and methods: The patients, who had been operated due to colon cancer by a single surgeon in the General Surgery Clinic between January 2015 and January 2020, were divided into two groups as stage 2 and stage 3 according to the tumor-nodule-metastases classification. In these groups, preoperative mean platelet volume, carcinoembryonic antigen, platelet/lymphocyte count ratio and neutrophil/lymphocyte count ratios were checked and evaluated in terms of staging and significance according to postoperative pathology results. According to the tumor-nodule-metastases classification, Stage 1-4 patients, emergency cases, patients with an inflammatory disease and rectal cancer were excluded from the study.

Results: In the study, 38 of 59 patients who had been operated between January 2015 and January 2020 were found to be at stage 2 (group 1), and 21 patients at stage 3 (group 2). While no significant difference was found between carcinoembryonic antigen and neutrophil/lymphocyte levels between group 1 and group 2, a proportional increase was observed between the increase in platelet/lymphocyte ratio and staging ($p=0.041$). Mean platelet volume was seen to be proportional to stage progression ($p=0.03$).

Conclusion: We think that platelet/lymphocyte ratio and mean platelet volume levels can easily be applied as a cheap and simple test in the prediction of the preoperative stage in stage 2-3 colon cancers.

Key words: colon cancer, neutrophil lymphocyte ratio, platelet lymphocyte ratio, mean platelet volume

2-ШІ ЖӘНЕ 3-ШІ КЕЗЕҢДЕРІНДЕГІ ТОҚ ІШЕК ОБЫРЫНЫҢ ФАЗАЛАРЫН БОЛЖАУДАҒЫ ГЕМАТОЛОГИЯЛЫҚ ПАРАМЕТРЛЕРДІҢ РӨЛІ

Э. Карачан¹, Э.М. Йылмаз², Б. Йылдыз², А.Э. Демиркиран²

¹Жалпы хирургия бөлімшесі, Айдын мемлекеттік ауруханасы, Айдын, Түркия

²Жалпы хирургия бөлімшесі, Медицина факультеті, Аднан Мендерес атындағы университет, Айдын, Түркия

ТҰЖЫРЫМДАМА

Мақсаты: Тоқ ішек пен тік ішек обыры - бүкіл әлемде қатерлі ісік ауруларының өлімінің маңызды себебі. Ішектің қатерлі ісігінің операцияға дейінгі кезеңінде рентген және түрлі қан анализдері қолданылады. Алайда, рентгендік зерттеулерді қолдану қиын және қымбат. Бұл зерттеудің мақсаты гематологиялық параметрлерді алдын-ала қарастыратын ішек қатерлі ісігінің сатысын болжау болды, оны қолдану қарапайым.

Материалы және әдістері: Жалпы хирургиялық клиникада бір хирургке тоқ ішектің қатерлі ісігіне байланысты ота жасатқан науқастар қатерлі ісік сатыларының жіктелуіне сәйкес 2-ші және 3-ші кезеңдерге бөлінді. Бұл топтарда операциядан кейінгі патологияның нәтижелері бойынша тромбоциттердің орташа көлемінің, карциноэмбрионды антигеннің, тромбоциттер / лимфоциттер және нейтрофилдер / лимфоциттер санының арақатынасы мен кезеңге қатынасы тексерілді және бағаланды. Қатерлі ісік сатыларының жіктелуіне сәйкес 1-4 сатысы бар науқастар, төтенше жағдайлар, қабыну аурулары және тік ішектің қатерлі ісік ауруы бар науқастар зерттеуден шығарылды.

Нәтижелері: Зерттеу нәтижелері бойынша 2015 жылдың қаңтарынан бастап 2020 жылдың қаңтарына дейін операция жасалынған 59 науқастың 38-і 2-ші сатыға (1-топ), 21-і 3-кезеңге (2-топ) ие болды. 1-ші және 2-ші топ арасында канциноэмбрионды антиген мен нейтрофилдердің лимфоциттердің деңгейлері арасында айтарлықтай айырмашылық болмағанмен, тромбоциттер/лимфоциттердің арақатынасы мен сатысы арасындағы пропорционалды өсу байқалады ($p = 0.041$). Ортаңғы тромбоциттер деңгейі сатының өсуіне пропорционалды болды ($p = 0.03$).

Қорытынды: Біз тромбоциттер мен лимфоциттердің қатынасы мен тромбоциттердің орташа мөлшерін 2-3 сатылардағы операция алдындағы кезеңді болжау үшін арзан әрі қарапайым тест ретінде оңай қолдануға болады деп санаймыз.

Негізгі сөздер: тоқ ішек қатерлі ісігі, нейтрофил/лимфоциттердің қатынасы, тромбоциттер/лимфоциттердің қатынасы, тромбоциттердің орташа мөлшері

РОЛЬ ГЕМАТОЛОГИЧЕСКИХ ПАРАМЕТРОВ В ПРОГНОЗИРОВАНИИ ФАЗЫ ПРИ РАКЕ ТОЛСТОЙ КИШКИ 2 И 3 СТАДИИ

Э. Карачан¹, Э.М. Йылмаз², Б. Йылдыз², А.Э. Демиркиран²

¹Отделение общей хирургии, Государственная больница Айдын, Айдын, Турция

²Отделение общей хирургии, Факультет медицины, Университет имени Аднана Мендереса, Айдын, Турция

РЕЗЮМЕ

Цель: Рак ободочной и прямой кишки является важной причиной смертности от рака во всем мире. В предоперационной стадии рака толстой кишки используются рентгенологические снимки и различные анализы крови. Однако применять рентгенологические исследования сложно и дорого. Целью настоящего исследования стало прогнозирование стадии рака толстой кишки, предварительно просматривая гематологические параметры, применение которых является простым и дешевым.

Материал и методы: Пациенты, которые были прооперированы в связи с раком толстой кишки одним хирургом в клинике общей хирургии в период с января 2015 года по январь 2020 года, были разделены на две группы: стадия 2 и стадия 3, в соответствии с классификацией стадий злокачественных новообразований. В этих группах проверены и оценены предоперационные значения среднего объема тромбоцитов, карциноэмбрионального антигена, соотношение количества тромбоцитов/лимфоцитов и нейтрофилов/лимфоцитов с точки зрения стадии и значимости, согласно результатам послеоперационной патологии. Согласно классификации стадий злокачественных новообразований, пациенты с 1-4 стадиями, неотложные случаи, пациенты с воспалительным заболеванием и раком прямой кишки были исключены из исследования.

Результаты: В ходе исследования было установлено, что у 38 из 59 пациентов, которые были прооперированы в период с января 2015 года по январь 2020 года, была стадия 2 (группа 1), и у 21 пациента стадия 3 (группа 2). Хотя не было обнаружено существенного различия между уровнями карциноэмбрионального антигена и уровня нейтрофилов/лимфоцитов между группой 1 и группой 2, наблюдается пропорциональное увеличение между увеличением соотношения тромбоцитов/лимфоцитов и стадированием ($p=0.041$). Средний объем тромбоцитов был пропорционален прогрессированию стадии ($p=0.03$).

Заключение: Мы полагаем, что значения соотношения тромбоцитов/лимфоцитов и уровня среднего объема тромбоцитов можно легко применять в качестве дешевого и простого теста для прогнозирования предоперационной стадии при раке толстой кишки 2-3 стадии.

Ключевые слова: рак толстой кишки, соотношение нейтрофилов/лимфоцитов, соотношение тромбоцитов/лимфоцитов, средний объем тромбоцитов

Introduction

Colorectal cancers are a significant cause of cancer-related deaths around the world [1]. In addition to imaging methods such as computed tomography (CT), colonoscopy, Positron emission tomography (PET-CT), Magnetic resonance (MR), transrectal ultrasound, markers such as carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (Ca 19-9) and fecal occult blood test are checked in staging colon cancers [2,3].

More efficient markers are needed for early diagnostic staging in colon cancers. Biomarkers such as neutrophil/lymphocyte (N/L) ratio, mean platelet volume (MPV) and platelet/lymphocyte (P/L) ratio may have properties to predict preop staging [4,5]. In our study, we aimed at checking whether there was a significant relationship between the patients with stage 2 and stage 3 colon cancer by looking at the N/L ratio, P/L ratio and MPV, which might be low-cost and easy-to-apply predictors to help us predict the preoperative staging.

Material and methods

Patients who had been operated by a single surgeon for colon cancer at the General Surgery Clinic between January 2015 and January 2020 were included in the study. Patients operated for colon cancer were divided into two groups as stage 2 and stage 3 according to the tumor-nodule-metastases (TNM) classification. In these groups, the preoperative mean platelet volume (MPV), carcinoembryonic antigen (CEA), platelet/lymphocyte ratio (P/L), and neutrophil/lymphocyte (N/L) ratios were checked. The distribution between the groups was assessed. These results were compared to the stage that emerged from the postoperative pathology results and evaluated for correlation. According to the TNM classification, Stage 1-4

patients, emergency cases, patients with an inflammatory disease and rectal cancer were excluded from the study.

Statistical analysis

The statistical packaged software SPSS 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) was used for the evaluation of the data. For the variables, mean±standard deviation, percentage and frequency values were used. The variables were evaluated after the prerequisites for normality and homogeneity of variances were checked (Shapiro-Wilk and Levene's Test). In data analysis, the Independent two-group t-test (Student's t-test) was used for the comparison of two groups, and the Mann-Whitney U test was carried out when the prerequisites were not met. The relationship between the two continuous variables was evaluated with the Pearson Correlation Coefficient, and the Spearman Correlation Coefficient when the prerequisites for parametric testing were not met. Categorical data were analyzed with Fisher's Exact Test and Chi-Square test. When the expected frequency was less than 20%, evaluation was made via the "Monte Carlo Simulation Method" to include these frequencies in the analysis. For the significance level of the tests, $p<0.05$ was accepted.

Results

In the study, 38 (64%) of 59 patients who had been operated between January 2015 and January 2020 were found to be at stage 2 (group 1), and 21 (36%) patients at stage 3 (group 2). 23 (60%) of 38 patients in Group 1 were operated laparoscopically, and 15 (40%) patients had open operation. 13 (61%) of 21 patients in Group 2 were operated laparoscopically, and 8 (39%) patients had open operation. While the mean P/L ratio of group 1 was 36.03 ± 13.02 , the mean P/L ratio of group 2

Table 1 Mean values of hematological parameters

	N	Minimum	Maximum	Mean	Std. Deviation
P/L	59	14.58	83.44	38.20	13.15
N/L	59	0.51	0.93	0.67	0.10
MPV	59	7.4	12.5	9.87	0.99
CEA	59	0.71	73.82	7.52	12.01

was calculated as 39.77 ± 13.9 ($p < 0.05$). While the mean N/L ratio of group 1 was 0.66 ± 0.1 , the mean ratio of group 2 was found to be 0.67 ± 0.1 ($p = 0.741$) (Table 1). No significant correlation was detected between the N/L ratio and staging. The mean MPV was determined as 9.83 ± 1.03 in group 1 and 9.83 ± 1.03 in group 2 ($p < 0.05$). A significant correlation was discovered between the MPV values and staging. The mean CEA was 8.62 ± 14.55 in group 1, and 5.8 ± 5.14 in group 2 ($p = 0.29$) (Table 2). No significant correlation was observed between CEA and staging.

Discussion

Previously, systemic inflammation was reported in many studies as one of the important parts of the carcinogenesis process [6,7]. Inflammatory processes play a significant role in the development of colon cancer [8]. One of the important factors that affect survival in colon cancers is the stage of the tumor [9]. Today, the usage of simple, easy-to-apply, cheap and non-invasive tests has become desirable in preop staging of colorectal cancers [10]. The fact that hematological parameters are simple, cheap and easily accessible methods increase their applicability. For this reason, hematological parameters are becoming more and more popular today.

In the literature, there is a low number of studies comparing the N/L ratio to the TNM staging of colon cancers, however, in a study conducted by Roxburgh et al., it was revealed that high N/L ratios are not only an indicator in cancer types, but also an independent factors in short survival [11]. In the study by Absenger et al., the increased N/L ratio was shown to be correlated with an advanced TNM stage, early recurrence and bad survival [12]. However, no statistically significant correlation could be found between the N/L ratio and staging in our study. We assume that this may result from the low number of patients in our study.

In a study, Szkandera et al. reported that the P/L ratio was detected higher in patients with increased stage 3 colon cancer compared to stage 2 patients, and the cancer recurrence was observed earlier in patients with high P/L ratios [13]. In a study conducted by You et al. on patients with colorectal cancer, it was stated that the P/R ratio was an independent factor in terms of advanced tumor stage (III, IV), however, the increased preoperative P/L ratio was correlated with decreased survival, and the P/L ratio could be used as a prognostic marker [14]. There are meta-analysis studies in which the P/L ratio is also attributed to survival in cancer types other than colorectal cancers [15]. In a study involving 376 cases, Jia et al. observed a correlation between the increase in the P/L ratio and the increase in T staging in colorectal cancers, but could not find any correlation with the TNM stage of the tumor. However, they stated that these ratios were promising that they could be used to predict the prognosis in colorectal cancers [16]. In our study, the P/L ratios were found in correlation with the increase in stage, and a statistically and significantly higher P/L ratio was found in stage 3 patients compared to stage 2 patients.

MPV is the value that refers to the average volume of the platelets in the blood, and routinely checked in blood

Table 2 Comparison of parameters between groups

	Stage 2 n=38	Stage 3 n=21	p
P/L	36.03 ± 13.02	39.77 ± 13.9	0.041*
N/L	0.66 ± 0.1	0.67 ± 0.1	0.740
MPV	9.83 ± 1.03	10.89 ± 0.95	0.030*
CEA	8.62 ± 14.55	5.8 ± 5.14	0.290

* $p < 0.05$

parameters. In the literature, there are few studies directly comparing the relationship between MPV and TNM. MPV has emerged as an early diagnostic parameter in the detection of colon, pancreas, stomach and hepatocellular cancers [17]. In another study by Kilincalp et al., no significant correlation was discovered between the N/L, P/L, MPV values and TNM stage, however, it was stated that these values were higher in patients with colorectal cancer, and these values dropped back to normal values after curative resection [18]. In their study, Ying Li et al. expressed that a positive correlation was detected between the preoperative MPV value and TNM in patients with colon cancer, and the MPV values dropped back to the normal level after curative resection [19]. In their study, Zhu et al. could not establish a correlation between MPV and TNM stage, but a positive correlation was found between the increased MPV value and perivascular invasion [20]. Therefore, they stated that MPV could be used as a biomarker with potential to predict the prognosis. In our study, advanced stage correlated with increased MPV, i.e. poorer prognosis was encountered in patients with colon cancer.

Even though CEA is generally used in the postoperative follow-up of patients with colon cancer in terms of recurrence, there are studies suggesting that it may contribute to staging preoperatively [21]. Lalosevic et al. stated that the levels of Ca 19-9 and CEA were found higher in patients with colorectal cancer and in patients with lymph node metastasis and distant metastasis, and the preoperative CEA levels could predict the stage [22]. Another study suggested that increased CEA levels did not have any significant contribution in terms of lymph-node metastasis in preoperative staging, apart from detecting the cases with colorectal cancer with liver metastasis and indicating a poor prognosis [23]. In our study, no significant correlation was discovered between CEA antigen levels and staging. We think that the sensitivity of CEA levels is low in preoperative staging. However, its preoperative high level can be considered as an indicator of a poor prognosis since it may point at liver metastasis.

Limitations in the study

Because the number of patients in the study was low, we could not classify the patients according to the localization area of colorectal cancers.

Conclusion

The preoperative usage of P/L and MPV in colon cancers can be possible with prospective studies on larger patient groups. Even though the N/L ratio does not predict staging in patients with colon cancer, it may be useful for predicting the prognosis and survival. Prospective studies with larger groups are needed to increase the usability of these markers. CEA is preoperatively found high while its effectiveness is low in preoperative staging, which can be considered as an indicator of a poor prognosis since it is highly associated with liver metastasis.

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