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Prognostic importance of neutrophil / lymphocyte and lymphocyte / crp ratio in cases with malignant bowel obstruction

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Abstract

The aim of this study is to present the importance of systemic inflammatory markers in patients with malignant bowel obstruction (MBO) due to intra-abdominal tumor metastasis. Patients who developed MBO due to end-stage intra-abdominal metastatic tumoral disease between October 2010 and September 2018 were retrospectively investigated. Clinical data such as age, sex, histopathological diagnosis of primary tumor and the level of obstruction due to tumor metastasis were recorded. Patients who were still receiving chemotherapy and had no metastatic involvement in the abdomen were excluded from the study. Patients with MBO who developed intra-abdominal metastasis from non-abdominal tumors were included. In the determination of the patients, whether or not the patient had previously operated for primary tumor was not taken into consideration. Neutrophil, lymphocyte ratio (NLR) and lymphocyte CRP ratio (LCR) were determined using laboratory data including the results of neutrophil, lymphocyte, C-reactive protein (CRP) and other basic hematological parameters. The effect of these values on survival as a prognostic factor was compared with statistical methods. There were 74 patients (28 females, 46 males) aged 60.5 ± 12.8 years (27-88) who developed MBO due to tumor metastasis in the abdomen. It was detected that the diagnosis of MBO developed an average of 11±7.5 months after the primary diagnosis. As a result of statistical evaluations, we found a positive correlation between serum LCR and survival (r=0.433; p=0.001) and a negative correlation between serum NLR and survival (r=-0.202; p=0.085). According to the Cox regression analysis, high NLR increases mortality risk (p= 0.01, OR = 1.050 [CI: 1.020-1.081]) and LCR increases the survival rate (p=0.02, OR = 0.014 [C: 0.000 to 0.503]). NLR and LCR in metastatic tumor patients are closely related to the prognosis of the disease. High NLR and low LCR values can be used as an indicator to determine the poor prognosis of malignant patients. NLR and LCR can be used as a simple, fast and cost-effective biomarker. For this, further studies are needed.

Keywords: Malignant bowel obstruction, NLR, LCR, CRP, survival

Introduction

The relationship between inflammation and cancer was first expressed by Rudolph Virchow in 1863. Virchow has suggested that leukocyte, lymphocyte and monocyte infiltration secondary to chronic inflammation develops in neoplastic tissues [1]. As a result of the increasing number of tumor-related studies , inflammation has been shown to play an important role in the development and progression of cancer [2].

The inflammatory response in the organism inhibits apoptosis and stimulates angiogenesis. Inflammatory cytokines stimulate DNA damage and inhibit DNA repair [3,4]. Increased tumor cell growth, invasion and metastasis are observed due to mediators released from inflammatory cells such as interleukin-6 (IL-6), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF) [3,5]. In many studies published in the literature NLR and CRP elevation has been reported to related with short survival time and to be a poor prognostic marker for colorectal cancer, gastric cancer, lung cancer, and pancreatic cancer [6-10].

Despite modern diagnostic and therapeutic approaches, the prognosis of end-stage intra-abdominal tumors diseases are poor. The aim of this study is to evaluate the relationship between life expectancy and systemic inflammatory markers in patients with malignant bowel obstruction (MBO).

Material and Methods

The study was approved by Gaziosmanpaşa University Clinical Research Ethics Committee with registration number 19-KAEK-

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229. Between October 2010 and September 2018 the patients with MBO developed due to end-stage intra-abdominal metastatic disease were identified and recorded. Clinical data including age, sex, histopathological diagnosis of primary tumor and the level of bowel obstruction, morbidity and mortality findings were recorded retrospectively. Patients who were still receiving chemotherapy and had no metastatic involvement in the abdomen were excluded from the study. Patients with MBO who developed intra-abdominal metastasis from non-abdominal tumors were included . In the determination of the patients, whether or not the patient had previously operated for primary tumor was not taken into consideration.

Laboratory data including neutrophils, lymphocytes counts and CRP level and other basic hematological parameters were measured at the time of diagnosis of MBO. NLR was defined as the absolute number of neutrophils divided by absolute lymphocyte count. LCR was defined as the absolute CRP value divided by the absolute number of lymphocytes.

Statistical Analysis

Descriptive analyses were performed to provide information on general characteristics of the study population. Kaplan Meier method was used for determining survival probabilities and survival curves. Spearman correlation coefficient was used for bivarite correlation of variables. A p-value <0.05 was considered significant. Analyses were performed using SPSS 19 (IBM SPSS Statistics 19, SPSS inc., an IBM Co., Somers, NY).

Results

There were 74 patients (28 females, 46 males) aged 60.5 ± 12.8 years (27-88) who developed MBO. The diagnosis of MBO established after an average of 11± 7.5months after the primary diagnosis. Demographic data of patients are summarized in Table 1.

Table 1. Gender distribution, obstruction level and etiologic causes of patients

		n	%
Female	Female	28	37.8
Male	Male	46	62.2
	Gastric outlet	9	12.2
Total (p<0.05)	Small intestine	42	56.8
	Large intestine	23	31.1
	Stomach	26	35.1
	Colon-Rectum	32	43.2
Adenocarcinoma	Pancreas	4	5.4
	Over	3	4
	Small intestine	2	2.7
Invasive ductal carcinoma	Breast	3	4
Metastatic epithelial tumor	Renal cell ca	2	2.7
Sarcoma	Rectum	1	1.3
	Small intestine	1	1.3
Neuroendocrine tumor	Rectum	1	1.3
Lymphoma	Small intestine	1	1.3

As a result of statistical evaluations, we found a positive correlation between serum LCR and survival time (r=0.433; p=0.001) and a negative correlation between serum NLR (r=-0.202; p=0.085). According to the Cox regression analysis where life expectancy is modelled, high NLR increases mortality risk (p=0.01, OR=1.050 [CI: 1.020-1.081]) and increase in LCR increases the survival rate (p=0.02, OR=0.014 [C:0.000-0.503]). According to these results, LCR and NLR were found as prognostic factors in survival time analyzes (Table 2) (Figure 1,2). In addition, there was an inverse correlation between NLR and LCR (Figure 3).

Table 1. Cox regression model between LCR, NLR and life expectancy

	p	Odds ratio	Lower	Upper
				Upper
NLR	.001	1.050	1.020	1.081
LCR	.020	.014	.000	.503

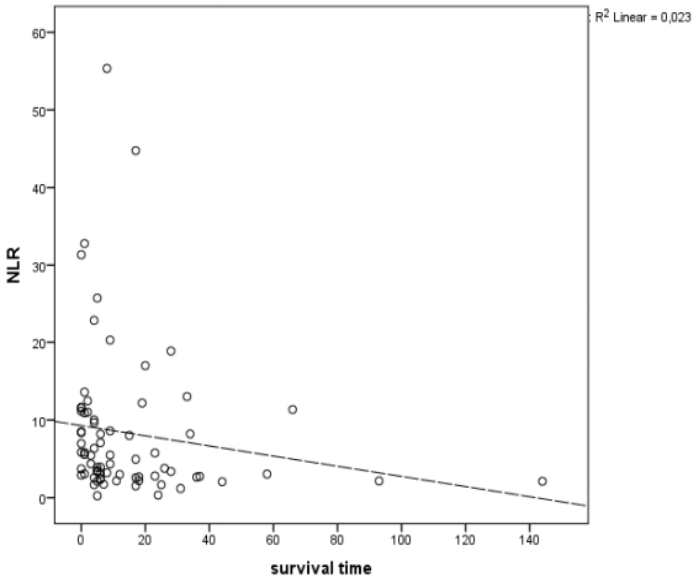

Figure 1. Positive correlation between neutrophil/lymphocyte ratio (NLR) and survival time in patients with malignant bowel obstruction

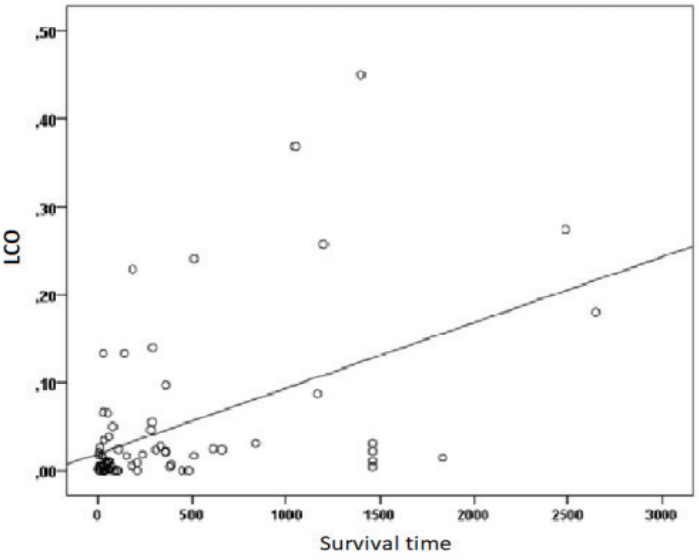

Figure 2. Positive correlation between Lymphocyte/CRP ratio (LCR) and survival time in patients with malignant bowel obstruction

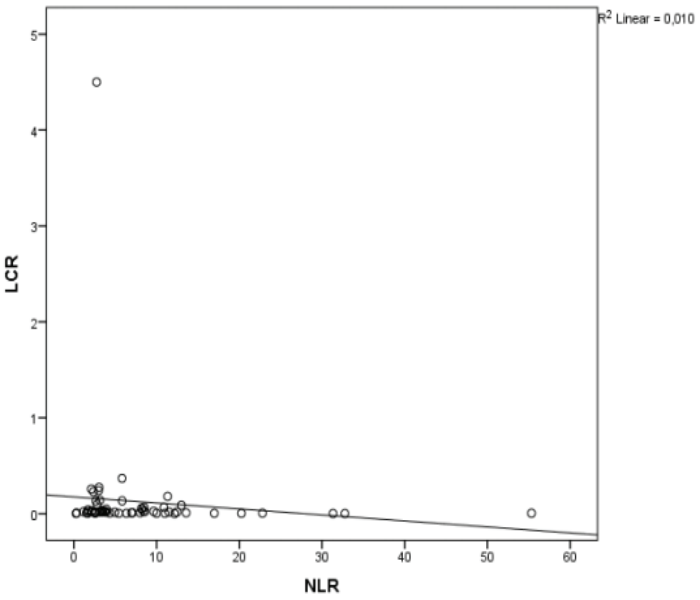

Figure 3. Correlation between NLR and LCR in patients with malignant bowel obstruction

Discussion

Inflammation is characterized with release of mediators from cells that cause increase in number of neutrophils and decrease in lymphocytes [11]. Neutrophils stimulate angiogenesis by angiogenic factors such as vascular endothelial growth factor (VEGF), triggering tumor growth and metastasis [12]. Lymphocytes, on the other hand, play an important role in tumor-related immunology due to the strong antitumoral immune function that prevents the progression of the tumor. Increase in lymphocyte count has been reported to be related with favorable prognosis of various tumors. Lymphocyte depletion can accelerate tumor progression by reducing the anti-tumoral immune response. In addition, systemic inflammation is associated with poor prognosis due to nutritional status and decreased organ function in cancer patients. The effects of anti-inflammatory drugs on tumor formation and progression have been studied extensively. For example, prophylactic administration of non-steroid anti-inflammatory drugs (NSAIDs) may reduce the incidence of colon cancer by 40-50%. NSAIDs have also preventive effects on lung cancer, esophageal cancer, and stomach cancer [16,17]. In addition, vaccination studies are being conducted to increase the immune response of lymphocytes against tumors, thus improving the prognosis of the patient [18]. Therefore, NLR can be used as a good indicator of systemic inflammatory status of cancer patients. In the literature, there are reports that NLR elevation is closely related to poor prognosis in various malignant tumors such as liver cancer, colorectal cancer, breast cancer, bladder cancer [4,19-21]. Jung et al [22] and Shimada et al [11] stated that high NLR was associated with poor prognosis and short life span in patients with gastric cancer. In these studies, NLR was defined as an independent prognostic factor affecting survival. Similarly, there are publications showing that high NLR affects disease-free survival and overall survival in patients with advanced gastric cancer [23,24]. In our study, we found that NLR elevation had a negative effect on survival in patients with MBO due to intra-abdominal metastasis in end stage tumors (p=0,01, OR=1,050 [CI: 1,020-1,081]) (Table 2, Figure 1). Therefore, we think that high NLR may be a useful indicator for determining poor prognosis in these patients.

Serum CRP is an acute phase protein commonly used for the detection of acute and chronic infections. CRP is synthesized by hepatocytes as part of the inflammatory response to tissue damage caused by infection, trauma and malignant diseases. CRP is produced and released from the liver cells in early stages against inflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6) and tumor necrosis factor (TNF-α) in trauma, infection and malignant diseases. Therefore, it is a non-specific serum biological marker that is sensitive to inflammation and tissue damage. Chronic inflammation occurs due to increased CRP, leukocytes, lymphocytes and macrophages in the tissue where tumor tissue is formed. This microenvironment may contribute to carcinogenesis through induction of genomic imbalance, epigenetic changes and subsequent induction of inappropriate gene expression. This leads to increased proliferation of tumor cells, resistance to apoptosis, formation of neovascularization and metastasis of cancer cells. The tumor microenvironment may confer resistance to the host's immune response and compromise the effects of chemotherapeutic agents. Elevated CRP is probably a secondary response to tumor necrosis, local tissue damage, and malignancy-related inflammation [25,26]. Inflammatory response indicators, such as CRP levels and platelet count, are generally higher in patients with end stage cancers and are associated with poor prognosis. The prognostic significance of serum CRP has been demonstrated in patients with primary malignancies including esophagogastric, colorectal, hepatocellular, pancreatic, prostate, bladder, ovarian and cervical cancers, melanoma and thymoma. [27-29]. Wang et al [29] reported that preoperative serum CRP elevation in gastric cancer patients was associated with bigger tumor size,wide spread and poor prognosis . In our study, the high LCR value was positively correlated with the lifespan (p=0.02, OR=0.014 [CI:0.000-0.503]) (Table 1) (Figure 2). This situation is consistent with the literature. Our study carries the risks of retrospective studies and there are some limitations in this study. These include low number of patients and removal of malignant patients presenting with intestinal obstruction.

Conclusion

NLR and LCR in metastatic tumor patients are closely related to the prognosis of the disease. High NLR and low LCR values can be used as an indicator to determine the poor prognosis of cancer patients. NLR and LCR can be used as a simple, fast and cost-effective prognostic biomarkers in patients with advanced malignant disease. New prospective studies can be beneficial with this subject.

Competing interests
The authors declare that they have no competing interests.

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Ethical approval
Before the study, permissions were obtained from the local ethical committee.

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