Survey of Neutrophil to Lymphocyte Ratio as Prognostic Factor in Colorectal Cancer

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Abstract

Background: Neutrophil-lymphocyte ratio (NLR) is derived from the neutrophil and lymphocyte count obtained from routine complete blood count with the differential test (CBC/diff). The aim of the present study is to determine the relationship between NLR with prognostic factors in colorectal cancer.

Material and Methods: A total of 70 patients with colorectal cancer were studied according to the research objectives. Independent T-test and Mann-Whitney U Mann-Whitney test were used to compare the NLR with qualitative variables such as pathology type. Pearson or Spearman correlation coefficient was used for correlating the quantitative variables. The significance level was considered as $P<0.05$.

Results: Most of the enrolled patients were in the age group of 60-69 years (31.5%). The mean and standard deviation of NLR was 2.1 ± 0.1. Only 4.3% of the subjects had NLR greater than 5. The association between NLR with N-stage ($P=0.005$) and inflammatory factor (CRP) was statistically significant ($P = 0.016$). The correlation between NLR and these variables showed that Grade ($P=0.091$), PNI ($P=0.093$), LDH ($P=0.20$), diabetes ($P=0.264$), M-stage ($P=0.282$), ESR ($P=0.386$), LVSI ($P=0.473$), T-stage ($P=0.527$), CEA ($P=0.582$), and BMI ($P=0.681$) with NLR was not meaningful.

Conclusion: NLR can be associated with prognosis and risk of disease progression, especially in lymph nodes. Since NLR does not require additional testing and request and is quite easy and cost-effective, it is recommended considering this ratio during the initial assessment and the classification of the risk and stage of the disease.

Keywords: Colorectal cancer (CRC), Neutrophil-lymphocyte ratio (NLR), Prognostic Factor

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Introduction

Colorectal cancer (CRC) is the fourth most frequent malignancy in men and the third among women.[1] Identification of prognostic factors is an important step to assess clinical outcome in the treatment of CRC. Tumor stage, tumor grade, number of resected lymph nodes, peri-neural or vascular invasion, and also the carcinoembryonic antigen (CEA) level have been introduced as prognostic markers in previous studies.[2] The circulating neutrophil-lymphocyte ratio (NLR) which is derived from the neutrophil and lymphocyte count, which is obtained from routine complete blood count with the differential test (CBC w/diff). NLR as a reliable and readily available prognostic marker in various tumor types including CRC, reflects a systemic inflammatory response.[3] Based on multiple studies, high NLR is associated with low survival in multiple cancers including breast, pancreatic, gastric, renal, and CRC.[4] Increased NLR has been associated with adverse clinicopathological parameters and poor survival rates in CRC[5] and suggested as a simple index of systemic inflammatory response in seriously ill patients.[6]

The aim of the present study is to determine the relationship between NLR with prognostic factors in CRC.

Material and Methods

In this descriptive cross-sectional study, 70 patients with CRC were recruited according to the research objectives. A questionnaire was designed for data collection related to the objectives of this study. Information was collected by filling out the forms from patients' files for each individual and some of the variables were obtained with appropriate tests. After completing the data collection form, the information obtained was entered into SPSS software version 20 and analyzed. Descriptive statistics including calculating numerical indices such as mean and standard deviation for quantitative traits and percentage for qualitative traits were used to summarize. Independent T-test and Mann-Whitney U test were used to compare the NLR with qualitative variables such as pathology type. Pearson or Spearman correlation coefficient was used for correlating the quantitative variables. The significance level was considered as $P<0.05$. The ethics committee of Kermanshah University of Medical Sciences (KUMS) approved this study (Approved research plan No.: 95016).

Results

According to table 1, most of the patients were in the age group of 60-69 years (31.5%). Also, 47.1% of the enrolled patients were female and 52.9% were male. The mean and standard deviation (SD) of NLR was 2.1±0.1. Only 4.3% of the subjects had NLR greater than 5. In the age group under 50 years of age, the mean±SD of NLR was 9.9±0.8. The mean±SD of NLR was 0.9±0.6 and 2.3±1.1 in the age groups 50-60 and 70-69 years, respectively. Also, in the age group older than 70 years, the mean±SD of NLR was 2.4±1.3. Regarding these results, although with increasing age, the NLR was slightly decreased, the statistical test did not show any significant difference.

As shown in table 1, 50% of the patients had grade 1 tumor. Also, 77.1% had stage 3, 57.1% had no lymph node involvement, and only 4 had metastasis (M1). The correlation between NLR and these variables showed that Grade ($P=0.091$), T-stage ($P=0.527$), and M-stage ($P=0.282$) had no statistically significant relationship with NLR, but the relationship between NLR with N-stage was statistically significant ($P=0.005$). According to table 1, 45.7% of the cases had negative CRP. The mean and standard deviation of ESR was 31.6±24.6 mm/h. The relation between ESR and NLR was not statistically significant ($P=0.386$), but the one between NLR and CRP was statistically significant ($P=0.016$). The association between ESR and CRP was also assessed by NLR.

Results showed that none of the two LVSI factors ($P=0.473$) and PNI ($P=0.093$) had a significant relation with NLR. Table 1 shows that 15.7% of the patients had a mucosal pathology and 84.3% of non-muscular pathology, and only 11.4%

Table 1. Clinical characteristics of the enrolled patients and clinicopathological findings

Gender			LVSI		
	Male	37 (47.1%)		Positive	11 (16%)
	Female	33 (52.9%)		Negative	59 (84%)
Age			**PNI**		
	<50	13 (18.5%)		Positive	23 (33%)
	50-59	18 (25.7%)		Negative	47 (67%)
	60-69	22 (31.5%)			
	>70	17 (24.2%)			
BMI			**LDH**	<200	02 (3%)
				200-300	32 (46%)
	<20	05 (7%)		300-400	28 (40%)
	20-25	43 (61.5%)		>400	08 (11%)
	25-30	19 (27%)			
	>30	03 (4.5%)			
Diabetes			**CEA**	<3	29 (41.5%)
				3-6	20 (28.5%)
	Positive	08 (11.5%)		>6	21 (30%)
	Negative	62 (88.5%)			
Type of Pathology			**ESR**	<20	27 (38.5%)
	Mucinous	11 (16%)		20-69	37 (53%)
	Non-mucinous	59 (84%)		>70	06 (8.5%)
Grade	1	35 (50%)	**CPR**	-	32 (46%)
	2	29 (41.5%)		+	26 (37%)
	3	06 (8.5%)		++	10 (14%)
	4	00 (0%)		+++	02 (3%)
T-stage					
	1	01 (1.5%)			
	2	01 (1.5%)			
	3	54 (77%)			
	4	14 (20%)			
Node Involvement					
	Yes	30 (43%)			
	No	40 (47%)			
Metastasis					
	Yes	04 (6%)			
	No	66 (94%)			

of the patients had diabetes. Also, there was no significant relationship between the two pathologic factors (P=0.827) and diabetes (P=0.264) with NLR. The mean and standard deviation of BMI in the study population was 23.9±3.33 and the highest frequency was in the 25-20 group with 61.4%. The mean and standard deviation of LDH and CEA were 317.75±7.7 and 16.5±39.1, respectively. The association of these three factors with NLR was investigated and it was found that the relationship between the three, BMI (P=0.681), LDH (P=0.20), and CEA (P=0.582) and NLR was not meaningful.

Discussion

Identifying the prognostic and predictive factors of CRC plays a key role in determining the most effective treatment. However, there are still pending satisfactory detecting prognostic markers. According to study on the prognostic impact of increased NLR in multiple settings of CRC, it was found that increased NLR leads to poor prognosis in CRC and NLR associated with the highest degree of discrimination of outcomes.[7] Recently, two meta-analyses showed significant evidence to support the association between high

NLR and poor prognosis in patients with CRC.[8,9] Previous studies have shown the role of albumin, serum CRP, CEA, absolute neutrophil counts, and NLR in predicting the clinical outcomes of patients with CRC diagnosis.[10] Several studies have demonstrated the role of NLR as a prognostic factor in CRC patients.[11] Immune cells reflect tumor development while NLR acts closely with the systematic inflammatory response.

In the present study, we surveyed patients with CRC, most of them being stage III and not having metastasis. The relation of stage and CEA with NLR and some variables and a number of other previously expressed variables, were studied as well.

Carruthers et al. found no correlation between NLR and tumor downstaging.[12] However, in another study, it was associated with T4 stage cancer.[13] Based on the results of the current study, the correlation between NLR and N-stage was statistically significant. Tumor differentiation data were available from three studies involving 1329 CRC patients. Based on the overall estimates, NLR greater than 5 is associated with low tumor differentiation with no meaningful heterogeneity displayed that CRC patients with NLR>5 were expected to be in T4 stage.[8]

Previous studies reported that NLR could be an independent prognostic factor to predict long-term outcomes in stage III and II CRC, and also an important predictive marker in stage IV CRC.[2] Several researchers have reported the relationship between NLR and CEA level before cancer therapy. The pooled estimates presented a significant relationship between NLR>5 and higher CEA level (>5). Elsewhere, pooled OR was 1.59 without significant heterogeneity.[14-16,17] However, according to the data of the present study, the relationship between the three BMI, LDH, and CEA with NLR was not meaningful.

Conclusion

NLR can be associated with prognosis and risk of disease progression, especially in lymph nodes. Since NLR does not require additional testing and request and is quite easy and cost-effective, it is recommended to consider this ratio during the initial assessment and the classification of the risk and stage of the disease.

The evaluation of the NLR factor can be useful in determining the risk and progression of the disease and should be considered in treatment decisions.

In the current study, due to the limited numbers of patients, the optimal cut-off of NLR was not achieved. It would be possible to achieve an optimal cut-off for this ratio, as a better prognostic marker, in other studies with more sample sizes. Furthermore, it seems necessary to perform similar studies to follow up the survival of patients and determine the relationship between NLR with the survival rate in order to reveal the prognostic importance of this marker.

Conflict of Interest

None declared.

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