

Simple Laboratory Parameters Predict Peritoneal Involvement in Colorectal Cancer Patients Who Underwent Curative Surgery

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Abstract

Objective: Recent studies have suggested that the preoperative neutrophil-platelet score (NPS) predicted survival in colorectal cancer patients. In this study, we aimed to examine whether this score were predictive of tumor stage in a group of Turkish patients with colorectal cancer.

Methods: A total of 105 patients who underwent curative surgery for colorectal cancer were included in this study.

Results: NPS was significantly correlated with TNM stage ($p = 0.009$), presence of venous invasion ($p = 0.022$) and presence of peritoneal involvement ($p = 0.03$).

Conclusion: NPS is a supportive scoring system in predicting stage of the disease, especially peritoneal involvement, in patients with colorectal cancer.

Keywords: Colorectal Cancer; Stage; Metastases; Neutrophil-Platelet Score

Introduction

Colorectal cancer (CRC) is still one of the most frequent causes of cancer death worldwide. Although recent developments in the imaging techniques made early diagnosis of cancer possible and led to decrease in mortality rates, nearly half of patients will die due to the complications of their disease. Today, surgery remains the main curative method in these patients [1].

In patients with CRC, presence of a preoperative systemic inflammatory response has a crucial role in disease progression and worse outcomes, regardless of tumor stage [1]. Studies conducted in recent years argued that there should be an interaction between neutrophil and thrombocytes during early inflammatory process [2-5]. Previously Watt, *et al.* demonstrated the prognostic significance of preoperative Neutrophil-Platelet Score (NPS) in patients undergoing potentially curative surgery for CRC, independent of classic TNM stage [1].

Aim of the Study

The aim of this study was to investigate correlation between NPS and tumor stage in a group of Turkish patients who underwent curative surgery for CRC.

Material and Methods

A total of 105 patients who underwent curative surgery for colorectal adenocarcinoma in between January 2014 and January 2016 were included in this clinical study. This research was performed according to the World Medical Association Declaration of Helsinki. Informed consent was not received due to the retrospective nature of the study.

Demographic characteristics of the patients (age, gender) preoperative liver and renal function tests, Complete blood count (CBC), serum tumor markers (CEA, Ca 19-9, Alpha fetoprotein), preoperative radiologic findings (Abdominal, pelvic and thoracic computerized tomography), type of operations, intra-operative findings (presence of peritoneal involvement and organ invasions), and pathologic findings (TNM stage, grade, venous and neural invasion) were collected retrospectively.

NPS was calculated and subclassified with formulas as follows: if neutrophil count is $\leq 7.5 \times 10^9/L$ and thrombocyte count is $\leq 400 \times 10^9/L$ then score is 0; if neutrophil is $> 7.5 \times 10^9/L$ or thrombocyte is $> 400 \times 10^9/L$ then score is 1; if both neutrophil is $> 7.5 \times 10^9/L$ and thrombocyte counts is $> 400 \times 10^9/L$ then score is calculated as 2 (Table 1). Accordingly, the patients in the present study were divided into 3 groups as NPS 0, NPS 1 and NPS 2.

NPS 0	Neutrophil $\leq 7.5 \times 10^9/L$ and platelet $\leq 400 \times 10^9/L$
NPS 1	Neutrophil $> 7.5 \times 10^9/L$ or platelet $> 400 \times 10^9/L$
NPS 2	Neutrophil $> 7.5 \times 10^9/L$ and platelet $> 400 \times 10^9/L$

Table 1: Neutrophil-Platelet Score (NPS).

Statistical analysis

Numerical data are expressed as mean \pm standard deviation (SD) or median (with minimum–maximum range), depending on normal distribution (Shapiro–Wilk test). Unpaired t-test and Mann–Whitney U test were used for determination of differences between two groups. Categorical variables were expressed as proportions or percentages. The significance of differences between proportions or percentages was determined by the Chi-square test or Fisher’s exact test. Analyses were performed using SPSS 18.0 (SPSS Inc., Chicago, IL).

Results

Sixty-one (58.1%) patients were male, 44 (41.9%) were female. The median age was 60 (min: 22, max: 81). Median follow-up period of the patients was 11 months (min: 1, max: 26).

When patients were classified according to localization of tumor; 52 (49.5%) cases had rectal. 45 (42.9%) cases had colonic and 8 (7.6%) cases had multiple involvement. Fifty-two (49.5%) operations were laparoscopic operations while 46 (43.8%) were open surgeries. In 7 (6.7%) patients, the operation was converted to open operation. In 21 (20%) patients, early complications were observed. Three (2.9%) patients died during early postoperative course due to causes other than cancer (pulmonary insufficiency, cardiac arrest dysrhythmia, and etc).

Well differentiated tumors were detected in 86 (68.4%) patients, while poorly differentiated tumors were detected in 12 (12.2%). In 38 (36.2%) patients, lymph node metastasis was detected. Peritoneal involvement was detected intraoperatively in 13 (12.4%).

According to AJCC 7th edition; 7 (6.7%) patients were accepted as Stage 0, 18 (17.1%) patients were accepted as Stage 1, 35 (33.3%) patients were accepted as Stage 2, 26 (24.8%) patients were accepted as Stage 3, and 10 (9.5%) patients were accepted as Stage 4. Sixty-four (61%) patients had adjuvant therapy, 15 (14.3%) patients had neo-adjuvant therapy. During 2-year follow-up period, recurrence was detected in only 2 (1.9%) patients. Four (3.8%) patients died in the late stage due to reasons associated with cancer.

After the patients were classified according to the NPS score, NPS was significantly correlated with TNM stage ($p = 0.009$), presence of venous invasion ($p = 0.022$) and presence of peritoneal involvement ($p = 0.03$).

n (%)		All	NPS 0	NPS 1	NPS 2	p value
		105	58	36	11	
Tumor site	Colon	45 (42,9)	23 (39,7)	14 (38,9)	8 (72,7)	0,258
	Rectum	52 (49,5)	31 (53,4)	18 (50)	3 (27,3)	
	Multiple	8 (7,6)	4 (6,9)	4 (11,1)	0 (0)	
t Stage	0	14 (13,3)	11 (19)	2 (5,6)	1 (9,1)	0,131
	1	7 (6,7)	4 (6,9)	2 (5,6)	1 (9,1)	
	2	14 (13,3)	9 (15,5)	5 (13,9)	0 (0)	
	3	62 (59)	32 (55,2)	24 (66,7)	6 (54,5)	
	4	8 (7,6)	2 (3,4)	3 (8,3)	3 (27,3)	
n Stage	0	68 (64,8)	51 (87,9)	13 (36,1)	4 (36,4)	0,000
	1	28 (26,7)	6 (10,3)	19 (52,8)	3 (27,3)	
	2	9 (8,6)	1 (1,7)	4 (11,1)	4 (36,4)	
TNM Stage	0	7 (6,5)	6 (10,3)	1 (2,8)	0 (0)	0,009
	1	18 (17,1)	14 (22,4)	4 (11,1)	2 (18,2)	
	2	39 (37,1)	27 (44,8)	10 (29,2)	3 (27,3)	
	3	26 (24,8)	7 (10,3)	16 (44,4)	4 (36,4)	
	4	10 (9,5)	4 (5,2)	5 (13,9)	2 (18,2)	
Venous invasion	No	91 (86,7)	55 (94,8)	28 (77,8)	8 (72,7)	0,022
	Yes	14 (13,3)	3 (5,2)	8 (22,2)	3 (27,3)	
Peritonea linvolvment	No	92 (87,6)	56 (96,6)	29 (80,6)	7 (63,6)	0,03
	Yes	13 (12,4)	2 (3,4)	7 (19,4)	4 (36,4)	
Metastatic lymph node ratio			0,00	0,05	0,09	0,00

Table 2: Relationship between NPS and clinical characteristics of patients.

Discussion

Neutrophils arising from injured tissues and activated platelets during inflammatory processes migrate to intravascular area. This demonstrates importance of immune system in development of systemic inflammatory response [3].

In our study, NPS scores of patients for whom elective surgery is planned due to colorectal cancer were calculated using preoperative neutrophil and platelet counts. We showed that this latter could be used to predict TNM stage, presence of metastatic lymph nodes, peritoneal involvement and venous invasion. The possibility that prediction of peritoneal involvement which is difficult to diagnose even with advanced imaging methods could be achieved with a simple calculation such as NPS score. This would provide the surgical team an opportunity for HIPEC and peritonectomy planning preoperatively as an alternative treatment modality. In addition, there are other studies showing the relationship of NPS score with prediction of survival in colorectal and other common cancers [4].

When relationship between Stage 4 and NPS score was examined; while 5.2% of the patients with NPS 0 were Stage 4, 13.9% of the patients were with NPS1 and 18.2% of the patients with NPS 2 consisted of Stage 4 patients. In advanced stage tumors, higher NPS was observed. Similarly, when relationship between peritoneal involvement and NPS was analyzed; while peritoneal involvement was observed in 3.4% of the patients with NPS 0, this value was 36.4% in the group with NPS 2. This situation clearly shows the relationship between increased NPS and peritoneal involvement. Increased systemic inflammatory responses and neutrophil and platelet counts may lead to cellular distortion and deterioration of tissue re-modeling system. Neutrophils contain many enzymes directly affecting cancer cells such as myeloperoxidase, collagenase and IL-6 which may lead to spread of cancer cells [1-5]. Also, activated platelets containing significant amounts of IL-6 and secreting vascular endothelial growth factor providing angiogenesis might prevent immune system from recognizing cancer cells. Moreover, both thrombocytes and neutrophils are stimulated by IL-6 [6,7]. This may provide a clue about spread of the disease and progression of metastatic disease [8].

In patients with high NPS scores, increased metastatic lymph node rate can also be explained with this high NPS score. In advanced stage diseases, NPS score rises and this will raise a possibility of explorative laparoscopy.

Conclusion

NPS score can be a supportive parameter in decision making along with imaging methods in cases with trivial peritoneal involvement in patients with colorectal cancer.

Conflict of Interest Statement

The authors declare no conflicts of interest.

Financial Disclosure

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