

ORIGINAL ARTICLE

HEMATOLOGICAL PARAMETERS AND TUMOR SIZE IN RECTAL CANCER**O. Andronic^{1,2}, Georgiana Radu¹, D.N. Păduraru^{1,2}, D. Ion^{1,2}, S.M. Oprescu^{1,2}**¹The University of Medicine and Pharmacy “Carol Davila” Bucharest²Emergency University Hospital Bucharest, Romania

Corresponding author: Octavian Andronic

Phone no.: 0040724024019

E-mail: andronicoctavian@gmail.com

Abstract

Rectal cancer is a pathology that still has a high incidence, mortality and morbidity all around the world. As with other types of neoplasm, researchers all around the world are attempting to find statistically significant linkages between easy and inexpensive hematological parameters and the progression of this disease which is affecting approximately 1.8 million individuals. The present study aims to investigate whether biological parameters measured in rectal cancer patients change significantly with tumor growth. The results show a significant change in WBC (white blood cell counts) ($p = 0.002$).

Keywords: *rectal cancer, WBC, Leukocytes, tumor size, hematological parameters***Introduction**

Rectal cancer is a disease with a growing incidence, especially in highly developed countries. As for the general population, it is the third in the line of incidence and the second in the line of mortality of all known types of neoplasms. The latest WHO data from the International Agency for Cancer Research announces the occurrence of more than 1.8 million new cases of colorectal cancer and over 881,000 deaths due to this pathology worldwide [1]. The average age when rectal cancer mostly occurs is 70 years, but in recent decades there has been an alarming increase in the incidence of this type of neoplasm in younger individuals (between 20-50 years) [2–4].

Currently, the etiology of rectal cancer is considered to be multifactorial. In addition, although the etiology of rectal cancer was initially thought to be the same as that of colon cancer, it seems that the evidence found in recent

years indicates the existence of different origins. Among the most often criminalized risk factors that can lead to the development of rectal cancer we can find: hereditary conditions (non-polyposis hereditary colorectal cancer, familial adenomatous polyposis, Peutz-Jeghers syndrome, etc.), chronic intestinal inflammatory diseases, age, sex, a diet low in fiber and rich in red meat and fats, alcohol, tobacco, obesity and pelvic irradiation [5,6,15,16,7–14].

Recently, a high interest in this pathology due to an increased incidence and high mortality and morbidity rates, has led to spectacular advances in the management of rectal cancer. Initially, the purpose of surgery was to save the patient's life. This came at the cost of drastically decreasing the quality of his life after the surgical cure. Now, one of the primary therapeutic goals is to increase the patient's quality of life after having completely treated the tumour. There has been a shift in the focus of the medical professional's

attention to increasing the patient's quality of life, early detection of the tumor and, why not, finding some factors / markers that can help prevent or manage this pathology. Hence the idea of finding correlations between easy and inexpensive to test haematological parameters and aspects of great importance in the management of the patient with rectal neoplasm such as tumor size, disease progression, survival rate etc.

Right now we have no biological, haematological or histopathological marker that can predict (even with minimal accuracy) the occurrence or evolution of rectal cancer. The purpose of this study is to analyze the hematological parameters of patients with rectal cancer in the search for a routinely evaluated parameter that may predict changes in tumour growth.

Materials and methods

The present research was based on the retrospective analysis of the patients admitted to a general surgery service within a period of 2 years – from the 1st of January 2017 to the 31st of December 2018 – having a diagnosis of stage I, II or III rectal neoplasm.

Results

From the demographic point of view, the analyzed group was composed of 21 women and 31 men, aged 37-86 years, with an average age of 62.75 years (Tables no. 1 and 2).

The values of the evaluated biological parameters are presented in Table no. 2. The data were correlated with the size of the tumour to see whether the changes that occurred are dependent on the tumor stage. The size of the tumor formations ranged between 1 and 14 cm, with an average of 4.93 cm. Of all parameters, the only one which demonstrated a correlation (Pearson correlation coefficient $r = 0.560$) with statistical significance ($p < 0.01$) was the number of leukocytes (Table no. 2 and Figure no. 1).

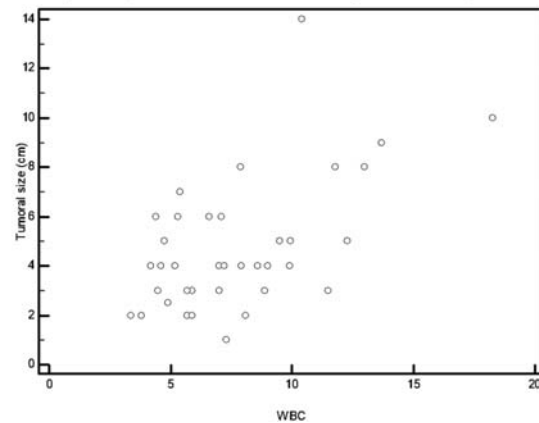


Figure no. 1 –The graphic representation of tumor size and WBC

	Mean	SD	Median	Minimum	Maximum	Normal*
ALT	28.731	10.3699	27.500	10.000	53.000	52
AST	29.212	30.3434	22.000	10.000	179.000	47
aPTT	29.837	5.9321	28.450	20.400	56.100	44
Cholesterol	185.769	38.5017	180.000	84.000	300.000	42
Glucose	110.058	29.4368	103.500	72.000	220.000	40
HGB	12.267	2.5153	12.300	6.000	16.710	42
Ht	36.797	6.6481	37.300	19.700	47.600	39
INR	1.331	1.6275	1.080	0.900	12.800	35
Thrombocytes	286621.154	104150.8565	256600.000	112000.000	640000.000	49
Urea	36.878	20.6836	33.140	17.000	154.000	42
WBC	7.798	3.0067	7.210	3.370	18.260	40
Fibrinogen	426.923	120.3096	388.310	242.000	737.000	33
Erythrocytes	4.328	0.5392	4.370	3.230	5.590	43

*Number of patients with normal value of the parameter

Table no. 1 –Statistical data about the analyzed biological parameters

		Size(cm)
ALT	Correlation Coefficient	0.043
	Significance Level P	0.7953
aPTT	Correlation Coefficient	0.124
	Significance Level P	0.4536
AST	Correlation Coefficient	-0.138
	Significance Level P	0.4032
Coolesterol	Correlation Coefficient	0.259
	Significance Level P	0.1112
Creatinină	Correlation Coefficient	-0.026
	Significance Level P	0.8749
Eritrocite	Correlation Coefficient	-0.092
	Significance Level P	0.5769
Fibrinogen	Correlation Coefficient	0.068
	Significance Level P	0.6800
Glucoza	Correlation Coefficient	0.320
	Significance Level P	0.0473
HGB	Correlation Coefficient	-0.279
	Significance Level P	0.0857
Ht	Correlation Coefficient	-0.258
	Significance Level P	0.1123
INR	Correlation Coefficient	0.347
	Significance Level P	0.0304
PT	Correlation Coefficient	-0.131
	Significance Level P	0.4277
Trombocite	Correlation Coefficient	0.355
	Significance Level P	0.0268
Uree	Correlation Coefficient	0.202
	Significance Level P	0.2179
WBC	Correlation Coefficient	0.560
	Significance Level P	0.0002

*Pearson correlation coefficient

Table no. 2 – Parameters' correlation with the tumor size

Discussions

The possibility to use standard, inexpensive, easy-to-measure and non-invasive tests (such as hematological parameters normally investigated for any patient who enters a hospital) to predict the evolution of a rectal tumor is a desideratum that deserves to be pursued. In addition to the economic benefits of discovering these indices, another major advantage would be the psychological one for both the physician and the patient. Patients diagnosed with any type of neoplasm suffer, on one hand, from the shock of the diagnosis, and on the other hand because of the general uncertainty surrounding the odds of survival. Any information that can increase the

level of assurance that a certain therapeutic behavior is the right one relieves a burden for the patient, the family and the physician.

In other types of cancer there are already some factors which correlate positively with various aspects of the disease such as its evolution, response to treatment, survival, or time to progression to another stage. In small cell lung cancer, Sumithra J. Mandrekar et. al have identified BMI, WBC, Hgh and PLT as significant predictors of OS (overall survival) and TTP (time to progression) [17]. In metastatic pancreatic cancer, colleagues at the Institute of Oncology from the University of Istanbul have found that age is a major prognostic factor that affects survival [18]. Thrombocytosis was found

to be an independent prognostic indicator for the survival of patients with gastric cancer [19] or even as a predictor of malignancy in women with a pelvic mass [20].

Colleagues G. Ramsay et al. have successfully investigated if hematological parameters sampled prior to the initiation of neo-adjuvant treatment in rectal cancer patients can have a positive predictive value in determining the response to this treatment. The results of the research have shown that a patient with a leukocyte count of less than $8 \times 10^9/L$ is more likely to obtain a favorable post-neo-adjuvant treatment response and a significant improvement in survival compared to patients who have had a higher value [21].

The discovery of such markers that can decisively influence the moment of diagnosis and the progression of rectal cancer would be a real revolution for patients. Also, this would increase the possibility of such indices to exist for other neoplasms. In addition, predictive equations and personalized scores based on the individual prognosis of each patient can be developed, thus increasing their chances of survival. Certainly in the future these parameters will be used in routine clinical practice and it is only a matter of time until the data collected about the patient at the time of presentation will be used to predict his response to treatment and the disease progression.

The limitation of our study is given by the small group of patients.

Conclusions

We found a statistically significant correlation between WBC value and tumor size regarding the patients in the present study but, due to limited patients group, further research is, however, needed to confirm it.

References

- [1] Bray F, Ferlay J, Soerjomataram I. Global Cancer Statistics 2018 : GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. 2018;394-424. doi:10.3322/caac.21492
- [2] Jacobs D, Zhu R, Luo J, et al. Defining Early-Onset Colon and Rectal Cancers. 2018;8(November):1-9. doi:10.3389/fonc.2018.00504
- [3] Kasi PM, Shahjehan F, Cochuyt JJ, Li Z, Colibaseanu DT, Merchea A. Rising Proportion of Young Individuals With Rectal and Colon Cancer. *Clin Colorectal Cancer*. 2018. doi:10.1016/j.clcc.2018.10.002
- [4] Siegel RL, Fedewa SA, Anderson WF, et al. Colorectal Cancer Incidence Patterns in the United States. 2017;109:27-32. doi:10.1093/jnci/djw322
- [5] Baxter NN, Tepper JE, Durham SB, Rothenberger DA, Virmig BA. Increased risk of rectal cancer after prostate radiation: A population-based study. *Gastroenterology*. 2005;128(4):819-824.
- [6] Larsson SC, Wolk A. Obesity and colon and rectal cancer risk : a meta-analysis of. 2007:556-565.
- [7] Slattery ML, Ph D, Wolff RK, et al. changes. 2011;53(8):1182-1189. doi:10.1007/DCR.0b013e3181d325db.Alcohol
- [8] Pericleous M, Mandair D, Caplin ME. Diet and supplements and their impact on colorectal cancer. *J Gastrointest Oncol*. 2013;4(4):409-423. doi:10.3978/j.issn.2078-6891.2013.003
- [9] Aykan NF. Red meat and colorectal cancer. *Oncol Rev*. 2015;9(1):38-44. doi:10.4081/oncol.2015.288
- [10] Ryan-Harshman M, Walid Aldoori. Diet and colorectal cancer. *Can Fam Physician*. 2007;53:1913-1920.
- [11] Lewis JD, Deren JJ, Lichtenstein GR. Cancer risk in patients with inflammatory bowel disease. *Gastroenterol Clin North Am*. 1999;28(2):459-477. doi:10.1016/S0889-8553(05)70065-0
- [12] Aihara H, Kumar N, Thompson CC. Diagnosis, surveillance, and treatment strategies for familial adenomatous polyposis: Rationale and update. *Eur J Gastroenterol Hepatol*. 2014;26(3):255-262. doi:10.1097/MEG.000000000000010
- [13] Carayol J, Khlal M, Maccario J, Bonaiti-Pellié C. Hereditary non-polyposis colorectal cancer: current risks of colorectal cancer largely overestimated. *Medicine (Baltimore)*. 2003;1:913-917. doi:10.1136/jmg.2003.013029
- [14] Berger MD, Yang D, Sunakawa Y, et al. Impact of sex, age, and ethnicity/race on the survival of patients with rectal cancer in the United States from 1988 to 2012. *Oncotarget*. 2016;7(33):53668-53678. doi:10.18632/oncotarget.10696
- [15] Ngeow J, Eng C. Rectal Cancer: Age Matters in the Affairs of Stage. *J Natl Cancer Inst*. 2016;108(1):1-2. doi:10.1093/jnci/djv325
- [16] Institutet K, Institutet K. LONG-TERM TOBACCO SMOKING AND COLORECTAL CANCER. 2001;587(September 2000):585-587.
- [17] Cancer CL, Schild SE, Hillman SL, et al. A Prognostic Model for Advanced Stage Non-small. 2006;(July). doi:10.1002/cncr.22049

[18]Tas F, Sen F, Keskin S, Kilic L, Yildiz I. Prognostic factors in metastatic pancreatic cancer : Older patients are associated with reduced overall survival. 2013;788-792. doi:10.3892/mco.2013.131
[19]M. I, H. F, H. I et al. Poor prognosis associated with thrombocytosis in patients with gastric cancer. *Ann Surg Oncol.* 2002;9(3):287–291.

[20]T. KJ, A. FM. Thrombocytosis as a predictor of malignancy in women with a pelvic mass. *J Reprod Med.* 2000;54(11):929-932.
[21]Ramsay G, Ritchie T, Mackay C, Murray G. Can Haematology Blood Tests at Time of Diagnosis Predict Response to Neoadjuvant Treatment in Locally Advanced Rectal Cancer ? 2018:1-7. doi:10.1159/000493433