

**HEALTH, ENVIRONMENT, DEVELOPMENT****MORPHOMETRIC INDICES OF ERYTHROCYTES IN DIFFERENT FORMS OF IRON DEFICIENCY ANEMIA AND MALIGNANT ANEMIA IN COLORECTAL CANCER****Artem Andriiaka**

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**Summary**

Due to the growing incidence of cancer in the world, it is becoming more relevant to study the indicators of secondary changes in blood in malignancies to use them as diagnostic and prognostic markers. The objective of the work is to conduct a morphometric analysis of peripheral blood erythrocytes in patients with iron deficiency anemia (IDA) and malignant anemia in colorectal cancer to identify specific changes and use them in a differential diagnostic practice. As the study material blood of 110 patients (58 men and 52 women) was taken. Among them 53 patients (31 women and 22 men) with IDA were examined, they formed the first (I) observation group and 57 patients (36 men and 21 women) with colorectal cancer, where the course of the underlying disease was burdened by malignant anemia second (II) observation group. The age of the patients under the survey is from 22 to 69 years. All patients were examined before any treatment was prescribed. The control group consisted of 50 healthy primary donors. Results. The data on the clinical significance of laboratory determination of morphometric changes in peripheral blood erythrocytes is highlighted in this paper. Differential-diagnostic and prognostic value of morphometric changes of erythrocytes in peripheral blood with iron deficiency anemia and anemia of malignancies is discussed. Indicators of morphometric characteristics of erythrocytes can be used in the differential diagnosis of anemia.

**Keywords:** peripheral blood, cancer detection, differential diagnosis, cancer control.

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**1. Introduction**

Colorectal cancer takes a leading place in the structure of cancer incidence in Ukraine – the second one among men and the third one among women, in the structure of mortality, it takes the second place in both men and women. Dynamic models of colorectal cancer incidence in Ukraine for the last 20 years show a steady increase in both male and female population, with the predominance in men. The peak incidence of colorectal cancer is registered in the older

groups. The average mortality-to-incidence ratio in Ukraine ranges from 51,8 to 57,3 % with an increase of this value in some region to 76,0 %. Significant shortcomings in the prevention, diagnosis and treatment of patients with colorectal cancer lead to the fact that 27,6 – 33,3 % of them died within one year since the time of diagnosis, and in some areas, this rate exceeds 40 %. Survival of persons with colorectal cancer directly depends on the timeliness of cancer detection, therefore, the 5-year relative survival rate of patients with early stages of the cancer is 8-10 times higher than of those with advanced stages (*Fedorenko et al., 2019*).

The anemic syndrome often occurs as a result of the development and progression of the tumor process, and chemotherapy and (or) radiation therapy used to treat cancer, the presence of hemolysis, splenomegaly, hemorrhagic syndrome, hemodilution, ineffective erythropoiesis, the cascade of disorders in iron metabolism regulation in the body of the patient, whose key link is now considered to be the changes in the synthesis of hepcidin (*Andriiaka, 2018, Atanasiu, 2007, Vydyborets, 2017*). In the erythrocytes of a person in the course of his life changes occur due to gender, age-specific features of metabolism, hematopoiesis (*Matlan, 2015, Shparyk, 2015*). In the hematopoiesis system itself, when pathological conditions and disease development occur, certain functional and morphological changes appear (*Andriiaka, 2018, Green, 2014*). Iron deficiency anemia (IDA) is a disease that is accompanied by significant changes in erythropoiesis, qualitative and quantitative changes in erythrocytes, impaired functioning of organs and systems (*Green, 2014, Popovych, 2020*). Fundamentally different mechanisms of formation have anemia of malignancies, which, no doubt, should affect the particular qualities of erythropoiesis (*Andriiaka, 2018, Matlan, 2015*). Colorectal cancer is a malignance which can lead to mortal complications even without significant tumor progression. Colorectal cancer can be also characterized by rapid spreading (*Fedorenko et al., 2019*). In the available literature, we have not encountered data on the comparison of morphometric changes in erythrocytes in patients with IDA and patients with malignant anemia in malignant diseases of the colorectal cancer, so it prompted us to conduct appropriate study.

The objective of the work is to conduct a morphometric analysis of peripheral blood erythrocytes in patients with iron deficiency anemia (IDA) and malignant anemia in colorectal cancer to identify specific changes and use them in a differential diagnostic practice.

## 2. Material and methods

As the study material blood of 110 patients (58 men and 52 women) was taken. Among them 53 patients (31 women and 22 men) with IDA were examined, they formed the first (I) observation group and 57 patients (36 men and 21 women) with colorectal cancer, where the course of the underlying disease was burdened by malignant anemia second (II) observation group. The age of the patients under the survey is from 22 to 69 years. All patients were examined before any treatment was prescribed.

The diagnosis of IDA was verified based on a typical clinical picture (signs of anemic hypoxia and sideropenic syndrome), typical hematologic picture of peripheral blood and indicators of iron metabolism.

The severity of anemia was defined according to the criteria proposed by the National Cancer Institute (USA) as follows: mild hemoglobin (Hb) from 10 to 12 g/dL, moderate Hb from 8 to 10 g/dL; severe Hb from 6,5 g/dL to 8 g/dl, life-threatening Hb below 6,5 g/dL. Among the patients with IDA, 19 were diagnosed with a mild type, 15 with a moderate, 11 with severe, and 8 with a life-threatening one. Among the patients with malignant anemia 29 were diagnosed with a mild type, 12 with moderate, 10 with severe, and 6 with life-threatening.

The study was conducted in compliance with the main provisions of the Council of Europe Convention on Human Rights and Biomedicine, Declaration of Helsinki Ethical Principles for Medical Research and (1964, with further additions, including 2000 version) and the Ministry of Health of Ukraine Order No. 690 dated September 23, 2009. All patients admitted to the hospital were examined with the use of clinical, laboratory, instrumental and special research methods, and were consulted by specialists of related specialties, if necessary. The examination and treatment of patients were performed in accordance with the World Medical Association Declaration of Helsinki (*Seoul, 2008*), and the relevant orders of the Ministry of Health of Ukraine (No. 281 from 01.11. 2000, No. 355 from 25.09.2002, No. 356 from 22.05.2009 in revision of the Ministry of Health of Ukraine Order No. 574 of 5 August 2009, No. 1118 of 21 December 2012).

The control group consisted of 50 healthy primary donors who had no history of cancer or chronic inflammatory disease. All donors were examined at the State Institution "Blood Transfusion Station of the Southwestern Railway" following the requirements of the "Procedure of medical examination of blood donors and (or) its components", approved by the Order of the Ministry of Health of Ukraine dated 01.08.2005 under No. 385 "On infectious safety of donor blood and its components".

Patients with colorectal cancer were conducted with a thorough histological examination of the drugs, taking into account the nature of the tumor margins with the surrounding tissues, the severity of infiltration, the presence of tumor cells in the vessels, the number of mitoses, including atypical ones. In addition, the cellular elements of different maturity (in %): low differentiated (LD), moderately differentiated (MD), highly differentiated (HD) cells were determined in tumors. The degree of malignancy and histologic type of the tumor were evaluated according to the generally accepted criteria.

The research materials were statistically processed according to the relevant programs (*Khalafian, 2014*). The significance of the difference was assessed using the Student's Difference Factor t-test ( $p < 0,05$ ).

### 3. Results of the study and discussion

When analyzing the obtained data, it was found that the erythrocyte indicators in the examined patients were as follows (Table 1).

Table 1

#### Erythrocyte indicators in the examined patients and healthy people ( $X \pm m$ )

Indicator	Control group (n=50)	I group (n=53)	II group (n=57)
RBC, $10^{12}/L$	4,62±0,05	3,19±0,14*	3,30±0,15*
MCV, fl	86,01±0,47	80,11±0,74*	81,21±0,41*
MCP, pg	28,95±0,11	27,71±0,43	27,73±0,37
MCHC, g/dL	33,12±0,12	34,61±0,04*	34,31±0,04*
RDW, %	13,21±0,06	14,25±0,21*	13,99±0,09*

\* $p < 0,05$  compared with indicators in control group.

As it is seen from the data above, significant changes in the morphometric parameters in patients with IDA and malignant anemia with colorectal cancer were found in the peripheral blood link. Besides, patients from group I showed a significant ( $p < 0,01$ ) increase in RDW

compared with patients from group II. We have not found any significant changes in the above indicators depending on the sex and age of the patients from the observation groups I and II ( $p < 0,05$ ). Data on the erythrocyte cytometry indicators in patients under the observation is given in Table 2.

Table 2

**Indicators of erythrocyte cytometry in patients under the observation ( $\bar{X} \pm m$ )**

Indicator	Control group (n=50)	I group (n=53)	II group (n=57)
Average diameter erythrocytes, $\mu\text{m}^3$	7,22±0,04	6,21±0,12*	6,31±0,03*
Share of micro- and schizocytes, fl	4,81±0,11	30,39±0,63*	14,21±0,23*
Anisocytosis indicator, %	4,01±0,12	17,33±0,12*	7,76±0,13*
Discocytes, %	80,91±0,47	54,29±0,15*	65,11±0,08*
Anomalous forms,%	19,07±0,52	45,71±0,14*	34,79±0,11*

\* $p < 0,05$  compared with indicators in control group.

As it is seen from data in table 2, patients in both groups showed a significant increase in the number of transformed erythrocytes (stomatocytes, echinocytes, etc.), and, accordingly, a decrease in the number of normal discocytes. A more significant decrease in the average diameter of erythrocytes, an increase in the proportion of microcytes and an increase in the level of anisocytosis ( $p < 0,05$ ) was found in patients from a group I. In addition, a clear poikilocytosis was found in patients from group I, that showed a significant decrease in the number of discocytes, an increase in the number of echinocytes and irreversibly altered pre-hemolysed forms of erythrocytes.

An increase in the number of echinocytes is always accompanied by an increase in blood viscosity. Moreover, rigid erythrocyte forms, due to their loose contact with the vessel wall, cannot fully participate in a gas exchange, which enhances tissue hypoxic processes. The movement of these cells in the total volume of capillary blood flow slows down, which can create a favorable background for the formation of microtubules. If we take into account that these processes occur in the vessel crease, where pathophysiological and pathobiochemical shifts occur, the significance of these disorders in the formation of anemic hypoxia syndrome in the examined patients of both groups will become more obvious. In the erythrocyte formula in patients from group I, against the background of a decrease in the average size of erythrocyte cell diameter and an increase in anisocytosis due to an increase in the number of microcytes we observed a significant decrease ( $p < 0,01$ ) in the number of discocytes, an increase in the number of echinocytes and irreversibly changed prehemolized erythrocyte forms, that can obviously affect the life span of erythrocytes.

#### 4. Conclusions

1. Malignant anemia is an urgent problem in the modern oncology clinic since anemic syndrome is one of the common complications of cancer. Instead, the number of studies highlighting this problem in cancer of the urinary system is limited. Also, the issues of secondary metabolic disorders in anemic hypoxia in combination with tumor intoxication are insufficiently covered.

2. Malignant anemia at colorectal cancer is accompanied by significant changes in the morphometric characteristics of erythrocytes, which is manifested by a decrease in the proportion of discocytes, an increase in the proportion of echinocytes and irreversibly altered prehemolytic forms of erythrocytes.

3. The changes that we have detected in the erythrocyte link of peripheral blood, on the one hand, is a reflection of the peculiarities of hematopoiesis and, in particular, erythropoiesis, and on the other, evidence of deeper pathophysiological disorders in people with malignant anemia while colorectal cancer.

4. IDA is characterized by changes in morphometric parameters: a decrease in the average diameter of erythrocytes, an increase in the number of microcytes and an increase in the level of anisocytosis, clear poikilocytosis, which showed a significant decrease in the number of discocytes, an increase in the number of echinocytes and irreversibly changed prehemolyzed erythrocyte forms.

5. Further study of the pathophysiological and biochemical changes in the erythrocyte link of hematopoiesis with IDA and malignant anemia is a promising area of scientific research. Its implementation will allow optimizing diagnostics, differential diagnosis and pathogenetic treatment regimens in these categories of patients, which, in the end, will obviously lead to an improvement in their quality of life.

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