



Research article

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## STUDY OF ELECTRO-PHYSICAL, RHEOLOGICAL PROPERTIES ON THE BACKGROUND OF INVESTIGATING IRON METABOLISM IN PATIENTS WITH GASTRIC CANCER

E. Labadze<sup>1</sup>, N. Narsia<sup>1</sup>, A. Tsalugelashvili<sup>2</sup>, C. Saldanha<sup>3</sup>, G. Kuchava<sup>4</sup>,  
N. Momtselidze<sup>4,5</sup>, M. Mantskava<sup>4,6</sup>

<sup>1</sup> Tbilisi State Medical University, Tbilisi, Georgia

<sup>2</sup> MMT Hospital, Tbilisi, Georgia

<sup>3</sup> University of Lisbon, Lisbon, Portugal

<sup>4</sup> Ivane Beritashvili Experimental Center of Biomedicine, Tbilisi, Georgia

<sup>5</sup> Kutaisi University, Kutaisi, Georgia

<sup>6</sup> European University, Tbilisi, Georgia

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### ABSTRACT

It is crucial to conduct research on clinical parameters of different body systems in gastric cancer as it is one of the most serious diseases in the modern world. The aim of our work was to study the rheological properties of blood in gastric cancer, along with the electrophysical properties of blood and iron metabolism in patients with gastric cancer. The research methods were modern and innovative. The study included patients with stomach cancer and a control group of healthy volunteers. The average age in the studied groups was similar. In all cases participants' informed consent was obtained. In patients with gastric cancer before surgery the iron and hemoglobin levels were low, transferrin and ferritin remained within normal limits. On the 7th day after the operation, ferritin increased twice, hemoglobin was close to control values. Transferrin and iron remained reduced on the 7th postoperative day. The erythrocyte aggregability index in patients with gastric cancer before surgery was 1.5 times higher compared to the control group. On the 7th day after the operation, the erythrocyte aggregability index improved and increased by only 30 % compared to the control. The index of electrophysical properties in gastric cancer before surgery was changed compared to control values, on the 7th day after surgery, it was also changed. This approach, along with a thorough study of these routine analyzes in gastric cancer, is very important. It turned out that the seven-day postoperative interval was insufficient to normalize the studied parameters. The analysis of such data will make it possible to personalize the therapy of patients with stomach cancer, which is very important for each patient and public health in general.

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© Ekaterine Labadze – PhD Student, e-mail: [labadze@gmail.com](mailto:labadze@gmail.com) iD: 0000-0001-7103-3190

© Nugzar Narsia – Professor, e-mail: [n.narsia@tsmu.edu](mailto:n.narsia@tsmu.edu)

© Alexander Tsalugelashvili – Professor, e-mail: [tsalugelashvili@mmt.ge](mailto:tsalugelashvili@mmt.ge)

© Carlota Saldanha – Professor, e-mail: [carlotasaldanha@un.lis.edu](mailto:carlotasaldanha@un.lis.edu) iD: 0000-0002-5058-2112

© Giorgi Kuchava – Associate Professor, e-mail: [g.kuchava@gmail.com](mailto:g.kuchava@gmail.com) iD: 0000-0001-6907-2000

© Nana Momtselidze – Associate Professor, e-mail: [nana.momtseliidze@unik.edu.ge](mailto:nana.momtseliidze@unik.edu.ge) iD: 0000-0003-3065-1405

© Maia Mantskava – Professor, e-mail: [maia.mantskava@eu.edu.ge](mailto:maia.mantskava@eu.edu.ge) iD: 0000-0002-4632-3097



## Introduction

Today, gastric cancer is one of the most common cancers in the modern world. Important and topical are all the fundamental and applied papers devoted to the issues. The rheological parameters of blood play a special role in the functioning of organs, tissues, and body systems. The amount of iron in the blood, as well as the electrophysical properties of the blood, determine the profile of the blood flow, which cannot but affect the rheological status. In oncological diseases, the violation of blood circulation and blood flow has a certain character. These changes affect the transport of toxic agents and may contribute to the spread of the tumor. The course of gastric cancer is often accompanied by anemia and changes in iron metabolism. It is also known that erythrocyte aggregation is impaired in gastric cancer. This is the basis of the violation of blood rheology. On the other hand, the electrophysical properties of blood cells determine the kinetics of aggregation processes suspension stability of blood [4; 6], blood viscosity and the nature of the dependence of viscosity on shear rate [10], the processes of blood coagulation, vascular thrombosis, and any others [12; 13; 19]. All this forms the fluidity of the blood, which affects its flow and biomechanical behavior [8; 9]. The electromagnetic properties of cells affect the features of the flow of cell suspensions. For its part, iron deficiency anemia significantly worsens the condition of patients with gastric cancer and complicates antitumor therapy [5]. At the same time, excess iron may be involved in the development of the malignant process [3; 11; 15–18]. Our work aimed to study the rheological properties of blood in gastric cancer, along with the little-studied electrophysical properties of blood and iron metabolism in patients with gastric cancer. In such a causal relationship, this issue has not been considered in modern literature. The relevance of the topic is primarily associated with the spread of stomach cancer, with high mortality and the percentage of disability in the population from stomach cancer. Along with the standard routine parameters that are examined by patients with gastric cancer, it is very interesting to monitor the rheological, electrophysical properties, as well as to investigate the iron metabolism in the blood of such patients. Research in all areas that will shed light on the pathogenesis of the disease, as well as give practical recommendations to oncologists, chemotherapists, radiologists, and clinical rheologists, is especially timely and valuable.

## Materials and methods

By the official standard of healthcare, patients need a set of certain tests to manifest stomach cancer. Before being included in our study, all patients underwent the following routine laboratory and instrumental analyzes: endoscopy with biopsy of stomach tissue, general and biochemical blood test, ultrasound of the abdominal organs, X-ray of the digestive tract, computed tomography, tumor markers: Cancer Antigen 19-9, Gastrointestinal Cancer Antigen, Carcino Embryonic Antigen. It is a

clinical standard, and its application is outside the scope of our study. Our focus was on a new complex study, which united the erythrocyte aggregation index as the rheological marker and electrophysical properties, as well as investigated the iron metabolism such as hemoglobin, transferrin, ferritin, iron in the blood in patients group with stomach cancer. The target group of the study was men and women with cancer gastric. The average age of the control group strictly corresponded to the mean age of the patient group, and the distribution of men and women in the control group was the same as in the patient group. The study included data on 20 patients with stage II–III locally advanced gastric cancer who underwent radical interventions: subtotal resection or gastrectomy combined with extended D2 lymphadenectomy. We studied the laboratory data before the operation and 7 days after surgery. As a comparison group (control group), 20 people without oncological diseases were invited to participate. The average age in the study group was  $54 \pm 9.1$  years, and the average age in the control group was  $50 \pm 6.1$  years. In blood serum, ferritin (in ng/mL), transferrin (in g/L), and iron (in  $\mu\text{mol/L}$ ) were determined using a Cobas Integra 400 plus analyzer (Roche Diagnostics, Switzerland). The indicators were analyzed using Excel applications. The clinical parameter of erythrocyte aggregation was studied using the "Georgian method". RBC aggregation index counts as the area of aggregated erythrocytes divided by the full area of the erythrocytes in the volume unit. This new innovative method is famous in the world as a direct, numeral, and exact; it has the name of the Georgian method. Blood samples were centrifuged and about 0.1 ml blood was diluted 1:200 in own plasma in the Thoma pipettes preliminary rinsed with 5 % sodium citrate solution without addition of any other anticoagulants to the blood under study. Following standard mixing the diluted blood was placed into a glass chamber 0.1 mm high. The quantitative index of erythrocyte aggregation, which was assessed with a special program at the Texture Analysis System (TAS-plus, Leitz, Germany), represented itself the relationship of the aggregated and unaggregated red cells [14]. A rotational viscometer Contraves LS30 (Switzerland) with MS 1/1 standard measurement system and the concurrent measuring system MS 1/1 was used to investigate electrophysical properties of blood simultaneously [2]. Time variation of whole blood conductivity  $\sigma$  and shear stresses under transient flow at rectangular and trapezium-shaped Couette viscometric flow were investigated under an electric field of 2 kHz. after being subjected to shearing for 30 seconds to disperse all aggregates, RBC suspension was stopped or decreased to allow RBCs aggregation. Immediately after beginning and complete stoppage of shearing kinetics of conductivity and torque signals were recorded. If the higher shear rates had no further effect on  $\sigma$  values measured during shearing, the applied shear rate was sufficiently high for complete dispersion of the aggregates [1; 2; 7]. This process was described by the so-called index of electrophysical properties. The obtained data on the kinetics of the whole blood conductivity in both studied groups of patients with gastric cancer before surgery, 7 days after surgery, and in blood samples of patients from the control group.

**Results**

We examined patients with stomach cancer before surgery and after surgery on the 7th day. The same indicators were studied in the control group (Table).

In patients with gastric cancer before surgery, the content of iron and hemoglobin was reduced, transferrin and ferritin remained within normal limits.

On the 7th day after the operation, ferritin increased twice, hemoglobin was close to control values. Transferrin and iron remained reduced on the 7th postoperative day.

The erythrocyte aggregability index in patients with gastric cancer before surgery was one and a half times higher than in the control group. On the 7th day after the operation, the erythrocyte aggregability index improved and was only 30 % higher relative to its value in the control group.

The index of electrophysical properties in gastric cancer before surgery was different from the control values, on the 7th day after surgery, it was also different (Figs 1–4).

**Properties in group with patients with stomach cancer before surgery and after surgery and in control group**  
*M ± m*

Parameters	Before surgery	After surgery 7th day	Control group (cancer)
Hemoglobin, g/l	110 ± 5*	122 ± 2	124 ± 6
Transferrin, g/l	2.7 ± 0.62	2.9 ± 0.5	2.9 ± 0.5
Ferritin, ng/ml	119 ± 26	300 ± 68*	116 ± 30
Iron, μmol/l	8.9 ± 6.1 *	9.1 ± 5.0*	17 ± 5.0
RBC aggregation index, %	45 ± 4.6*	41 ± 3.1*	30 ± 2.1
Index of electrophysical properties	2.4 ± 0.06	2.5 ± 0.05	1.5 ± 0.04

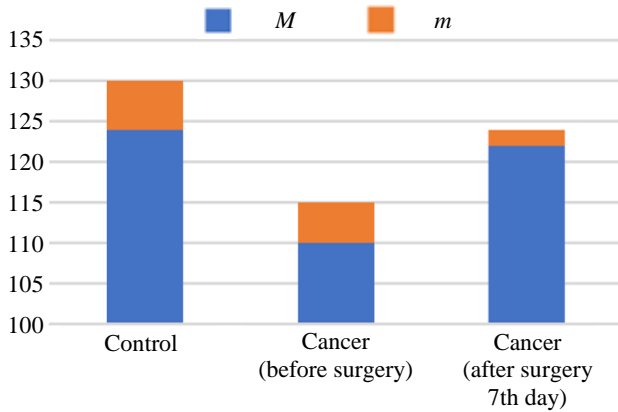


Fig. 1. Mean of hemoglobin (g/l) in the control group, and in patients with stomach cancer before surgery and on the 7th day after surgery (*M ± m*); *p* < 0.05 (between results of control and patients group in before surgery period)

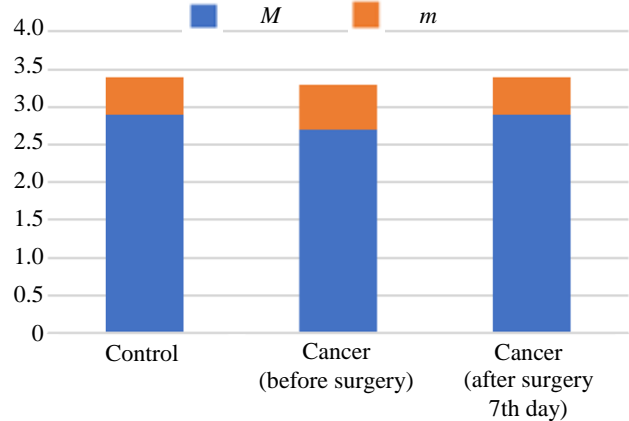


Fig. 2. Mean of transferrin (g/l) in the control group, and in patients with stomach cancer before surgery and on the 7th day after surgery (*M ± m*); *p* ≈ 0.78 (between results of control and patients group in the period after surgery)

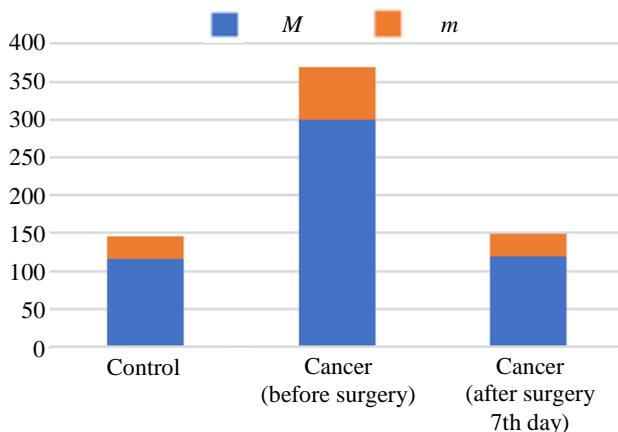


Fig. 3. Mean of ferritin (ng/ml) in the control group, and in patients with stomach cancer before surgery and on the 7th day after surgery (*M ± m*); *p* < 0.05 (between results of control and patients group in period before surgery); *p* < 0.05 (between results of patients group before and after surgery periods)

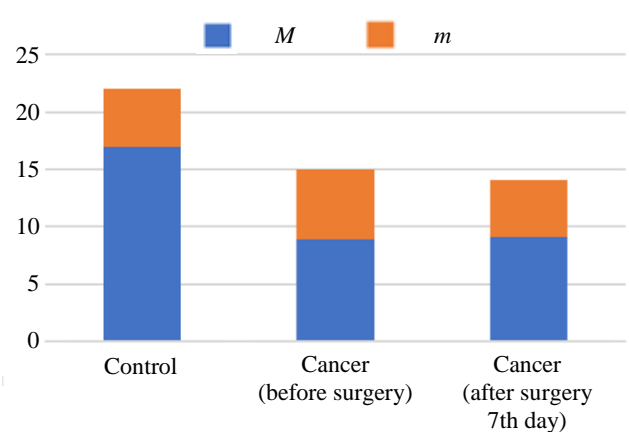


Fig. 4. Mean of iron (μmol/l) in the control group, and in patients with stomach cancer before surgery and on the 7th day after surgery (*M ± m*); *p* < 0.05 (between results of control and patients group in the period before surgery); *p* < 0.05 (between results of control and patients group in the period after surgery)

## Discussion

A comprehensive analysis of iron metabolism, erythrocyte aggregation, and electrophysical properties of blood in patients with gastric cancer before and 7 days after surgery showed significant changes in the content of iron and proteins of the iron metabolism system, which may be a response reaction to stress connected with surgery.

This may be due to the mechanism of ferritin synthesis, as well as due to the release of intracellular ferritin into the serum, where it has attached iron to itself. According to some authors, this can explain the sharp decrease in iron content. Considering the detoxifying role of ferritin, it can be concluded that the detoxifying ability of the body increases in the postoperative period. The cytotoxic effect of ferritin on many cell types is also known [5]. In patients with gastric cancer compared with controls, blood aggregation was increased. However, on the 7th day after the operation, aggregation remained increased, but there was a trend of improvement compared with the preoperative period in patients with gastric cancer. This is possibly caused by the removal of the tumor. Apparently, a smaller number of toxic substances, which contribute to the enhancement of the aggregation process, enter the bloodstream. The electrophysical properties of blood in patients with gastric cancer were disturbed before surgery compared to the norm and almost did not improve on the 7th day after surgery. Apparently, gastric cancer, as well as any pathological processes, is accompanied by cell damage and hydration, which leads to a change in the capacity of the cell and intracellular membranes. There is an additional macrostructural polarization in the blood. Macrostructural polarization ensures the movement of positive and negative ions [5]. They move under the action of an external electric field in opposite directions, reach the surface of impenetrable objects, where they accumulate, creating additional dipole moments. The relaxation times of the macrostructural polarization are not very long ( $10^{-3}$ – $10^{-8}$  sec), therefore, at the corresponding low frequencies, a significant reactive (capacitive) resistance is manifested in biological media. It was assumed that erythrocytes, their total volume and total area play an important role in the formation of the physicoelectric properties of blood [7]. But we saw that with the improvement of aggregability on the 7th day after the operation, the electrophysical properties of the blood did not approach the control values. The degree of activity of inflammatory processes correlates with the content of leukocytes and protein molecules with characteristic electrical conductivity. Apparently, those are leukocytes that form changes in the conductive and dielectric properties of blood. This work describes for the first time a comprehensive study of the electrophysical properties of blood along with monitoring of iron metabolism and blood rheology (by the example of erythrocyte aggregation) before surgery and on the 7th day after surgery. This approach, along with a thorough study of these routine analyzes in gastric cancer, is very important. It turned out that the seven-day postoperative interval was insufficient to normalize the studied parameters. We cannot be sure, whether the slight improvement that we observed on the 7th day after the operation was the beginning of the iron regulation, erythrocyte and electrophysical properties aggregation, or whether it was just a temporary improve-

ment. It is necessary to monitor the proposed parameters on the 14th, and 21st days after the operation. The analysis of such data will make it possible to personalize the therapy of patients with stomach cancer, which is very important for each patient and public health in general.

## Conclusions

The aim of our work was to study the rheological properties of blood in gastric cancer, along with the electrophysical properties of blood and iron metabolism in patients with gastric cancer. In patients with gastric cancer before surgery, there was a decreased level of iron and hemoglobin; transferrin and ferritin remained within normal limits. On the 7th day after the operation, ferritin increased twice, hemoglobin was close to control values. Transferrin and iron remained reduced on the 7th postoperative day. The erythrocyte aggregability index in patients with gastric cancer before surgery was one and a half times higher in comparison with the control group. On the 7th day after the operation, the erythrocyte aggregability index improved and was only 30 % higher compared to its value in the control group. The index of electrophysical properties in gastric cancer before surgery was different from the control values, on the 7th day after surgery, it was also different. This approach, along with a thorough study of these routine analyzes in gastric cancer, is very important. It turned out that the seven-day postoperative interval was insufficient to normalize the studied parameters.

The analysis of such data will make it possible to personalize the therapy of patients with stomach cancer, which is very important for each patient and public health in general. Continuation of research in this direction is very promising in medicine for assessing the structure, condition, and viability of tissues, as well as determining the intensity of the pathophysiological processes occurring in them.

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