Impact of preoperative immunonutrition on thrombocyte phagocytic activity and early postoperative outcomes in invasive gastric cancer patients.

Zbigniew Kamocki (zkamocki@gmail.com)
Uniwersytet Medyczny w Bialymstoku https://orcid.org/0000-0002-4414-9304

Joanna Matowicka
Uniwersytet Medyczny w Bialymstoku

Anna Jurczuk
Uniwersytet Medyczny w Bialymstoku

Anna Milewska
Uniwersytet Medyczny w Bialymstoku

Anna Kamocka
Imperial College London Faculty of Medicine

Boguslaw Kedra
Uniwersytet Medyczny w Bialymstoku

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Abstract

Background:The aim was to determine the phagocytic activity of thrombocytes in patients with gastric cancer and to assess the effect of oral and parenteral preoperative glutamine-based immunonutrition on nutritional status, thrombocyte phagocytic activity and early postoperative outcomes.

Methods:Patients suffer from invasive gastric cancer had been treated with preoperative immunonutrition with glutamine and they were compared to patients without nutritional treatment. Nutritional status, percentage of weight loss and BMI were assessed. Levels of total protein, albumin, cholesterol, triglycerides, platelets and their phagocytic ability were measured twice. Postsurgical complications were assessed via Claven-Dindo classification.

Results:Group I-20 patients with an oral glutamine, Group II-38 patients received an intravenous glutamine. Group III-25 patients did not receive preoperative immunonutrition. 47% patients Group I, 54% patients Group II and 33% patients Group III were malnourished. In Group I, percentage of phagocytizing platelet (%PhP) was 1.1 pre- and 1.2 postoperatively. Phagocytic index (PhI) was 1.0 and 1.1. In Group II, %PhP was 1.1 and 1.2. PhI was 1.0 and 1.1. In Group III %PhP was 1.0 and1.2. PhI was 1.0 and 1.1. An increase in triglyceride level was observed in both immunonutrition groups. There was a fall in total protein, albumin level in Group II. In Group III there was a decline in total protein, albumin and cholesterol level. Total platelet count, and PhI was increased in both immunonutrition groups. There was also a rise in %PhP in Group II. In Group III there was no change in blood plateles level, %PhP and PhI. Complications rate was 53% in Group I, 29 % in Group II, 40% in Group III.

Conclusions:In invasive gastric cancer, laboratory nutritional parameters are significantly reduced, causing malnutrition in 45.7% of patients. Oral glutamine supplementation inhibited the postoperative decline in protein metabolism parameters, however, this did not affect the reduction of the percentage of postoperative complications. Glutamine used preoperatively significantly reduced the percentage of serious surgical complications, regardless of the way it was supplemented. Patients with invasive gastric cancer have a significant decrease in platelet phagocytic activity. Immunonutrition based on intravenous form of glutamine allows to improve the phagocytic activity of platelets.

Background:

Gastric cancer incidence worldwide has declined significantly over the last 30 years. Nevertheless, it still constitutes a significant clinical problem. Only in 2015 stomach cancer caused 754 000 deaths globally, which makes it fourth cancer-related mortality [1, 2]. Despite progress in diagnostic and therapeutic management, therapy of invasive gastric cancer is associated with high morbidity rate and often low quality of life. Postoperative complication rate after total gastrectomy ranges from 9 to 47.5% and reported mortality rate varies between 1.1 and 10.8% [3–6]. Causes of poor outcomes are late diagnosis, pre-operative malnutrition and impaired immune system being one of the most important causes. Even eighty-five percent of patients undergoing surgery for gastric cancer are malnourished [7]. It is a result of

tumour-related cachexia and decreased food intake due to anorexia. Moreover, host immune response is impaired [8]. The outcomes of cancer treatment can be optimised by maintaining an unharmed immune system and using immunogenic therapies to re-establish anti-tumour immune response. Glutamine plays a major role as a fuel source for macrophages, lymphocytes, and enterocytes. As the energy substrate for intestinal epithelial cells, it also protects the intestinal immune barrier against microbes.

Role of various blood cells in host response to cancer has been thoroughly investigated. Platelets (thrombocytes) are predominantly known for their role in coagulation. What is less commonly known is their ability to phagocytise, first reported by Mustard et al. in1968. These nonnuclear blood cells have the potential for chemotaxis and diapedesis [9]. They are able to phagocytise bacteria, viruses, antibody complexes, collagen and latex particles, working both as single platelets as well as in aggregates [10, 11]. Upon activation, the thrombocyte changes its shape from discoid to an irregular one with numerous projections. This morphological change is accompanied by intensification of energetic processes and enhanced protein anabolism inside the activated platelet [12].

Aim:

The aim of the study was to determine the impact of preoperative glutamine-based immunonutrition on phagocytic activity of blood platelets in patients with gastric cancer. Effects of both, intravenous infusion of glutamine and oral supplementation, were assessed.

Methods

Study population

Patients with gastric cancer were enrolled in the study. The only inclusion criterion was an operable gastric cancer. The stage of gastric cancer was based on the TMN classification. Patients were divided into three randomized research groups. Group I and II was received preoperative glutamine-based immunonutrition, Group III did not receive preoperative immunonutrition. Patients receiving preoperative nutritional treatment were divided into two groups depending on the route of glutamine supply. Patients in Group I were fed a regular hospital diet enriched with an oral glutamine solution twice a day. Additionally, an infusion of three-chamber parenteral feeding bag (1447 mls) daily plus one ampoule of vitamins was administered. Group II was also on a regular diet supplemented with three-chamber parenteral feeding bag Smofkabiven Peripheral (1447 mls) fortified with one ampoule of vitamins but also with an intravenous solution of glutamine – 100 ml of – N(2)-L-alanyl-L-glutamine dipeptide (20 g N(2)-L-alanyl-L-glutamine, 8.2 g L – alanyl and 13.46 g L- glutamine) with 0.2 g/ml of the medicinal product. Group III was fed only by natural regular hospital diet supplemented with three-chamber parenteral feeding bag Smofkabiven Peripheral (1447 mls) fortified with one ampoule of vitamins.

Exclusion criteria were inoperable gastric cancer and impaired gastric empting in the oral glutamine supply group. Due to the small number of early gastric cancer patients in clinical stage I were excluded

from further analysis. Figure 1 shows

Data collection

On admission to hospital, each patient was evaluated for nutritional status using SGA. The percentage of unintentional weight loss and BMI were calculated. Each patient had total protein, albumin, total cholesterol, triglyceride, platelet count and phagocytic activity assessed. Laboratory tests and phagocytic activity were reassessed 12 days after the surgery. Similar examination was performed in patients without preoperative immunonutrition.

In both groups, the duration of preoperative immunonutrition was 8 to 14 days (mean 12). Postoperative artificial nutrition without glutamine (three chamber bag + early postoperative enteral nutrition) was continued for 5–6 days after the surgery (mean 5.4) and it was the same in each group. Operation included stomach resection with excise of regional lymph nodes in the D2 range or above D2. Nasojejunal feeding tube was placed intraoperatively. Early postoperative enteral nutrition with semi-elemental, normocaloric, low fat diet was started 20 hours post-surgery. Three patients with type 2 diabetes mellitus received a special diet normalizing glycaemia.

Imaging technique and imaging analysis

Phagocytic activity of blood platelets was determined against Staphylococcus aureus ATCC 653P bacterial strain, according to Mantur`s et al. method [13].

Statistical analysis

Results were compared to a control group with was consisted of 30 healthy individuals. The results were analysed using the Statistica 13.1 program, $p < 0.05$.

The study has been approved by Bioethical Commission at Medical University of Bialystok No.: R-I-022/149/2007.

Results:

Eighty-three patients with resectable invasive gastric cancer were recruited from the 2nd Department of General and Gastroenterological Surgery, Medical University of Bialystok from 2007 to 2015. There were 25 females (30%) and 58 men (70%) aged 27 to 84 (mean 63.5 ± 14). Patients were divided into three groups.

Distribution of clinical stages in particular groups is presented in Figure.

In Group I the percentage of invasive gastric cancer is 92%, in Group II – 85%, in Group III – 66%. Early Gastric Cancer were detected in 3 patients of Group I, in 3 of Group II, and in 10 of Group III.

Preoperatively

Group I included 20 patients (7 women, 13 men) aged from 34 to 82 years (65.2 ± 11.9). Unintentional weight loss above 10% was demonstrated in patients 7 (35%). Percentage of body weight ranged from 10 to 25% (15.3% ± 6). Body mass index was from 16 to 28 (26.3 ± 7.29). Low protein level was found in 9 patients, in 16 patients a low albumin level. Lower triglyceride value was observed in 1 patient as well lower cholesterol level.

A preoperative level of total protein, albumin and triglyceride were significantly lover in comparison to control group. There was no statistically differences in total cholesterol level. Preoperative serum levels of total protein, albumin, cholesterol and triglyceride in patients of Group I are shown in Table 1. Malnutrition was found in 47% patients.

Table 1
Preoperative serum levels of total protein, albumin, cholesterol and triglyceride in patients of Group I in comparison to control group.

	Min	Max	Mean	SD	p
Total protein (g/dl)	4.6	7.0	6.0	0.5	0.000
Albumin (g/dl)	2.6	4.0	3.2	0.3	0.000
Cholesterol (mg/dl)	102	232	159	32	0.153
Triglyceride (mg/dl)	34	205	103	56	0.043

No statistically differences of a total count of blood platelets in Group I and control group was observed. A preoperative phagocytic activity of blood platelets and phagocytic index were relevantly lover in comparison to healthy individuals. Preoperative phagocytic activity and phagocytic index are shown in Table 2.

Table 2
The number of blood platelets, the number of phagocytizing platelets, and phagocytic index in Group I before surgery in comparison to control group.

	Min	Max	Mean	SD	p
Platelets	110000	450000	268500	84082.5	0.544
Phagocytizing platelets	1	1.2	1.1	0.1	0.000
Phagocytic index	1	1.1	1	0.1	0.000

Group II consisted of 38 patients (8 women, 30 men) aged from 45 to 84 years (66.9 + 10.4). Unintentional weight loss above 10% was demonstrated in 15 patients (50%). Percentage of body weight

ranged from 10 to 30% (15.7%+6.1). Body mass index was from 18 to 40 (24 + 4.2). Low protein level was found in 17 patients, in 19 patients a low albumin level. Lower triglyceride value was observed in 1 patient. No patient had low cholesterol level. As in Group I the level of total protein, albumin and triglyceride were significantly lover in comparison to control group. There was no statistically differences in total cholesterol level. Preoperative serum levels of total protein, albumin, cholesterol and triglyceride in patients of Group II are shown in Table 3. Malnutrition was observed in 54% patients.

Table 3
Preoperative serum levels of total protein, albumin, cholesterol and triglyceride in patients of Group II in comparison to control group.

	Min	Max	Mean	SD	P
Total protein (g/dl)	5.3	8.0	6.1	0.6	0.000
Albumin (g/dl)	1.9	4.0	3.4	0.5	0.000
Cholesterol (mg/dl)	79	264	168	43	0.376
Triglyceride (mg/dl)	37	175	102	37	0.015

No statistically differences of a total count of blood platelets in Group II and control group was observed. A preoperative phagocytic activity of blood platelets and phagocytic index were relevantly lover in comparison to healthy individuals.

Preoperative number of total count of platelets, their phagocytic activity and phagocytic index are shown in Table 4.

Table 4
The number of blood platelets, the number of phagocytizing platelets, and phagocytic index in Group II before surgery in comparison to control group.

	Min	Max	Mean	SD	p
Platelets	132000	532000	262111	104378	0.059
Phagocytizing platelets	1	1.2	1.1	0.1	0.000
Phagocytic index	0.8	1.1	1.0	0.1	0.000

Group III consisted of 25 patients (10 women, 15 men) aged from 27 to 83 years (63.5 + 13.8). Unintentional weight loss above 10% was demonstrated in 4 patients (16%). Percentage of body weight ranged from 10 to 15% (12.5%+2.9). Body mass index was from 19 to 35 (25.2 + 4.0). Low protein level was found in 5 patients, in 8 patients a low albumin level. No patient had low cholesterol and triglyceride

level. As in previous groups the total protein, albumin and triglyceride level was relevantly lover in comparison to control group. There was also a statistical difference in cholesterol level. In 33% patients malnutrition was observed. Preoperative serum levels of total protein, albumin, cholesterol and triglyceride in patients of Group III are shown in Table 5. No statistically differences of a total count of blood platelets in Group III and control group was observed. A preoperative phagocytic activity of blood platelets and phagocytic index were relevantly lover in comparison to healthy individuals. The number of blood platelets, the number of phagocytizing platelets and phagocytic index in Group III before surgery are presented in Table 6.

Table 5
Preoperative serum levels of total protein, albumin, cholesterol and triglyceride in patients of Group III in comparison to control group.

	Min	Max	Mean	SD	P
Total protein (g/dl)	5.3	7.0	6.4	0.6	0.002
Albumin (g/dl)	2.7	5.0	3.6	0.4	0.000
Cholesterol (mg/dl)	110	264	171	36	0.418
Triglyceride (mg/dl)	31	197	100	36	0.001

Table 6
The number of blood platelets, the number of phagocytizing platelets, and phagocytic index in Group III before surgery in comparison to control group.

	Min	Max	Mean	SD	p
Platelets	98000	353000	233040	57866	0.303
Phagocytizing platelets	0.9	1.2	1	0.1	0.000
Phagocytic index	0.9	1.1	1	0.1	0.000

Postoperatively

In Group I postoperatively a significant increase of triglyceride level was observed. There was no relevant changes in total protein, albumin and cholesterol levels.

Postoperative serum levels of total protein, albumin, cholesterol and triglyceride in patients of Group I are shown in Table 7. The total protein, albumin and triglyceride level did not change in relation to Group III. However a significant reduction in cholesterol level was found.

Table 7
Postoperative serum levels of total protein, albumin, cholesterol and triglyceride in patients of Group I.

	Min	Max	Mean	SD	p
Total protein (g/dl)	4.8	7.0	5.8	0.6	0.066
Albumin (g/dl)	2.2	4.0	2.9	0.5	0.068
Cholesterol (mg/dl)	84	195	153	30	0.398
Triglyceride (mg/dl)	67	218	139	49	0.041

A relevant increase of total count of platelets and index was noticed. There was no significant changes in phagocytic activity of blood platelets but phagocytic index was statistically increased. Postoperative total count of platelets, their phagocytic activity and phagocytic index are show in Table 8.

Table 8
The number of blood platelets, the number of phagocytizing platelets, and phagocytic index in Group I after surgery.

	Min	Max	Mean	SD	P
Platelets	265000	1093000	657750	271598	0.018
Phagocytizing platelets	1.1	1.3	1.2	0.1	0.068
Phagocytic index	1	1.2	1.1	0.1	0.043

In Group II a relevant fall in total protein, albumin, and cholesterol level was observed. There was no significant changes in triglyceride level in this group of patients.

Postoperative serum levels of total protein, albumin, cholesterol and triglyceride in patients of Group II are shown in Table 9. The total protein, albumin and cholesterol level did not change in comparison to Group III. There was a relevant increase in triglyceride level. There was a statistical increase in postoperative number of total count of platelets, their phagocytic activity and phagocytic index. Postoperative number of total count of platelets, their phagocytic activity and phagocytic index are shown in Table 10.

Table 9
Postoperative serum levels of total protein, albumin, cholesterol and triglyceride in patients of Group II.

	Min	Max	Mean	SD	P
Total protein (g/dl)	5.0	7.0	5.9	0.6	0.009
Albumin (g/dl)	2.0	4.0	2.9	0.5	0.000
Cholesterol (mg/dl)	78	212	143	33	0.000
Triglyceride (mg/dl)	51	188	109	31	0.194

Table 10
The number of blood platelets, the number of phagocytizing platelets, and phagocytic index in Group II after surgery.

	Min	Max	Mean	SD	P
Platelets	180000	1152000	643368	288018	0.000
Phagocytizing platelets	1	1.4	1.2	0.1	0.013
Phagocytic index	0.8	1.2	1.1	0.1	0.024

Group III - there was a relevant decline in total protein, albumin and cholesterol level in patients without immunonutrition. There was a significant rise in triglyceride level.

Postoperative serum levels of total protein, albumin, cholesterol and triglyceride in patients of Group III are shown in Table 11.

Table 11
Postoperative serum levels of total protein, albumin, cholesterol and triglyceride in patients of Group III.

	Min	Max	Mean	SD	P
Total protein (g/dl)	4.4	7.0	5.9	0.7	0.192
Albumin (g/dl)	1.9	4.0	2.9	0.5	0.009
Cholesterol (mg/dl)	62	232	137	36	0.016
Triglyceride (mg/dl)	56	243	138	52	0.037

Postoperatively, the number of total blood platelets increased. There was no significant changes thrombocytes ability to phagocyte bacteria. Postoperative number of total count of platelets, their phagocytic activity and phagocytic index are shown in Table 12

Table 12
Table 11. The number of blood platelets, the number of phagocytizing platelets, and phagocytic index in Group III after surgery.

	Min	Max	Mean	SD	P
Platelets	123000	1189000	564416	320658	0.050
Phagocytizing platelets	1	1.4	1.2	0.1	0.059
Phagocytic index	0.9	1.1	1.1	0.1	0.075

Complications

In Group I overall postoperative complication rate was 53% with major complications of 33%. 30-day mortality was 12%.

In Group II overall postoperative complication rate was 29% with major complications of 40%. 30-day mortality was 6%.

In Group III overall postoperative complication rate was 40% with major complications of 83%. 30-day mortality was 6%.

Table 13. shows surgical complications in examined groups according to Clavien-Dindo classification.

Table 13
Postoperative complications in both groups according to Clavien-Dindo classification (14).

Grade	Group I	Group II	Group III
I	1	2	-
II	5	5	-
IIIa	-	1	1
IIIb	-	1	1
IVa	1	-	1
IVb	-	1	2
V	2	2	1

Dicussion:

Different surgical techniques have various local and general imbroglios [6]. One of the most important problem in the treatment of patients suffering from stomach cancer is their proper preoperative preparation. Malignancy process is associated with malnutrition, as well as with impairment of the host immune defence. Furthermore, the increase in energy-protein expenditure during the surgery increases malnutrition and exacerbates the risk of perioperative complications. Excessive loss of protein and energy observed in patients with advanced cancer is associated with increased morbidity, poor response to chemotherapy and a shorter survival time [15]. Li et al. reported cachexia in 73.3% of patients with gastric cancer [16]. Even prolonged malnutrition during early life may increase the risk of stomach cancer mortality in later life [17]. Hence nutritional status needs to be optimised in the preoperative period. Fukuda et al. analysed 800 gastric cancer patients who had undergone gastrectomy. They classified 19% patients as a malnourished. In multivariate analysis malnutrition was independent factor postoperative fewer infections. Based on the assessment of nutritional status based on biochemical analysis, malnutrition was found in 47% patients in Group I, 54% patients in Group II, 33% patients in Group III. Well–managed preoperative nutritional support decreased

the incidence of postoperative surgical site infections [18]. The current ESPEN guidelines recommends about a 10–14 day period of feeding with immunologically active compounds [19]. In the present study, malnutrition has also been reported. Unintentional weight loss above 10% of body weight in last 6 months was found in 34% patients. The main unintentional weight loss was 13.7 kg. Biochemical analysis shown similar values of examined parameters in all groups of patients.

In Group I low protein level was found in 9 patients, in 16 patients a low albumin level. Lower triglyceride value was observed in 1 patient as well lower cholesterol level. In Group II low protein level was found in 17 patients, in 19 patients a low albumin level. Lower triglyceride value was observed in 1 patient. No patient had low cholesterol level. As in previous groups in group without immunonutrition the total protein, albumin and triglyceride level was relevantly lover in comparison to control group. There was also a statistical difference in cholesterol level. It was found that in all patients, body mass index correlated with an unintentional weight loss and serum albumin concentrations. Moreover, the percentage of unintentional weight loss negatively correlated with total preoperative protein and triglyceride levels. Furthermore, total protein concentration was positively correlated with albumin concentration and triglycerides. Liu et al found that preoperative BMI was positively correlated with albumin and triglyceride levels and preoperative albumin levels were positively correlated with triglycerides. Therefore, serum albumin level is not only a window into the patients' nutritional status but is also a useful factor for predicting prognosis [20]. Poor survival was also observed in gastric cancer patients with lower levels of BMI, albumin, and triglyceride [21]. Because low levels of serum albumin are associated with poor outcomes in cancer patients, they can be used as an independent indicator when assessing the need for aggressive nutritional intervention [22].

Glutamine-supplemented perioperative nutrition has been investigated in patients with

a variety of diseases but the effects have not been conclusively established [23]. In our study, interesting results in two different models of preoperative immunonutrition were observed.

In Group I the increased triglyceride level was observed. In Group II the total protein, albumin and cholesterol level was declined. In Group III both groups the decreased total protein after the surgery was noticed but albumin level was similar before and after surgery.

In Group I the total protein, albumin and triglyceride level did not change in relation to Group III. However a significant reduction in cholesterol level was found. In Group II The total protein, albumin and cholesterol level did not change in comparison to Group III. There was a relevant increase in triglyceride level.

We can say that glutamine using during preoperative immunonutrition helped to sustain higher albumin levels whilst on the other hand, a decrease in total protein level was recorded. Tue et al have also observed an improvement in postoperative cumulative nitrogen balance with perioperative parenteral nutrition supplemented with glutamine in patients undergoing abdominal surgery [24]. One explanation for this protein metabolism may be a reduced production of proinflammatory cytokines. In a previous study of our group, we found elevated levels of interleukin 6 (IL-6) in gastric cancer patients which correlated negatively with the disease stage. Its values were highest in patients with early gastric cancer [25]. Administration of the preoperative parenteral glutamine immunonutrition results in normalization of cholesterol and triglycerides by increasing or decreasing their levels to achieve the normal range. In oral glutamine supplementation model, there were no significant changes in total protein, albumin and cholesterol levels. Glutamine enriched nutrition support in surgical patient’s remains controversial. The meta-analysis thirteen randomized controlled trials showed improving immune function, reducing incidence of infectious complications and shortening the length of hospital stay [26]. Jiang et al noticed alanyl-glutamine supplemented parenteral nutrition clinically safe with better nitrogen balance, and maintained intestinal permeability in postoperative patients than patients who received isonitrogenous and isocaloric parenteral nutrition [27]. The highest percentage of postoperative complications was found in Group I and it was almost twice as high compared to patients in Group II. Perhaps this is due to the different numbers of patients. However, an interesting result is a similar percentage of severe complications in both groups with preoperative immunonutrition. Major postoperative complications were almost three times more common in patients without preoperative immunonutrition. Giannotti et al did not report better surgery outcomes with parenteral glutamine supplementation in well-nourished patients with gastrointestinal cancer [28].

High number and wide distribution within the circulatory system make thrombocytes

an important component of immune system but their role in immune response is not yet fully understood. Platelet granules contain: peroxidase, acid phosphatase, cationic proteins

and proteolytic enzymes. These substances represent high activity for bacteria phagocytosis. Furthermore, platelets exert cytotoxic effects on cancer cells by adhering to them via antigenic determinants. Then characteristic structural changes, such as Golgi apparatus hypertrophy, increase in

secretory granulations and displacing them towards contact zone with a neoplastic cell are observed. Platelet cytotoxicity ensues from their ability to product and release lytic mediators [29]. Additionally, platelets play an important role in tumour metastasis. Platelet-delivered proteolytic enzymes facilitate the release and migration of tumour cells across

the vessel wall [30]. Furthermore, activated platelets release substances which increase vascular permeability, factors stimulating myocytes proliferation, platelet activating factor, prostaglandins, histamine and serotonin. The substances above facilitate an implantation

and growth of metastatic tumour [31]. In our last studies we found that the fraction of phagocytizing platelets and their phagocytic index in gastric cancer patients was markedly impaired as compared to healthy individuals [32]. Current work confirms impaired phagocytic activity in patients with gastric cancer. A decreased phagocytic activity can influence inflammatory processes as well as cancer growth [25]. In this study, impact of immunonutrition on phagocytic activity of platelets was evaluated. Glutamine is an essential amino acid for fast-dividing immune cells, epithelial cells of the gastrointestinal tract, fibroblasts and reticulocytes. It is a precursor of protein and nucleotide synthesis, it is also involved in hepatic gluconeogenesis and glutathione synthesis. Its high concentration was found in the intestinal mucosa cells. Glutamine and glutamate are amino acids responsible for the transport of nitrogen and detoxification of ammonia. The consequence of inhibition of glutathione synthesis is mucosal destruction, diarrhoea, and growth inhibition. Parenteral supplementation of glutamine in rats demonstrated its protective role against bacterial translocation [33]. Glutamine impact on blood platelets phagocytic activity is unknown.

In our study in all groups showed severe impairment of thrombocyte phagocytic activity. The significant decline in phagocytic activity of blood platelets and their phagocytic index in all patients was observed. In patients with oral glutamine supplementation the percentage of blood platelets and their phagocytic index was increased. In patients with intravenous glutamine administration both total count of platelets, their phagocytic activity and index was improved. There was no improvement in platelet phagocytic activity in patients without immunonutrition.

Authors had previously reported partial improved thrombocyte phagocytic activity in gastric cancer patients as a result of perioperative immunonutrition enriched with glutamine and ω-3 fatty acids both in local disease and in peritoneal dissemination [32] but this is the first study analysing blood platelets phagocytic activity in gastric cancer patients receiving enteral glutamine diet preoperatively.

Conclusions:

In invasive gastric cancer, laboratory nutritional parameters are significantly reduced, causing malnutrition in 45.7% of patients. Oral glutamine supplementation used in preoperative nutritional therapy inhibited the postoperative decline in protein metabolism parameters, however, this did not affect the reduction of the percentage of postoperative complications. Glutamine used in preoperative immunonutrition significantly reduced the percentage of serious surgical complications, regardless of the

way it was supplemented. Patients with invasive gastric cancer have a significant decrease in platelet phagocytic activity. Immunonutrition based on intravenous form of glutamine allows to improve the phagocytic activity of platelets.

Abbreviations

SGA- Subjective Global Assessment

BMI-Body Mass Index

TNM- Classification of Malignant Tumours

PhIT-phagocytic index

PhT%-percentage of phagocytizing thrombocytes

ESPEN- European Society for Clinical Nutrition and Metabolism

Declarations

Trial has been registered with Clinicaltrials.gov – NCT01704664 registered October 11.2012,

Title of registration: Perioperative Immunonutrition, Phagocytic and Bactericidal Activity of Blood Platelets in Gastric Cancer Patients

URL: https://clinicaltrials.gov/ct2/show/NCT01704664?term=NCT01704664&cond=Gastric+Cancer&draw=2&rank=1

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Authors Contributions

All authors have read and approved the manuscript.

ZK concept and design of study, interpretation of data, finalizing manuscript, JMK assessment of blood platelets phagocytic activity, AJ interpretation data and preparing manuscript, AM statistical data, AK interpretation data, preparing manuscript, fluent in English edition, BK design of study.

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Availability of data and material

The raw data generated and analysed in the current study are not publicly available due to appropriate protection of patient personal information but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent to be included in the study, or the equivalent, was obtained from all patients. Informed consent obtained from study participants was in written form.

Consent to Publish

Not Applicable.

Competing Interests

The authors declare that they have no conflict of interest.

Authors details

- Second Department of General and Gastroenterological Surgery, Medical University of Bialystok, Poland
- Department of Clinical Laboratory Diagnostics, Medical University of Bialystok, Poland
- Department of Statistic and Medical Informatics, Medical University of Bialystok, Poland
- Department of Investigative Medicine, Imperial College London, United Kingdom

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Figures

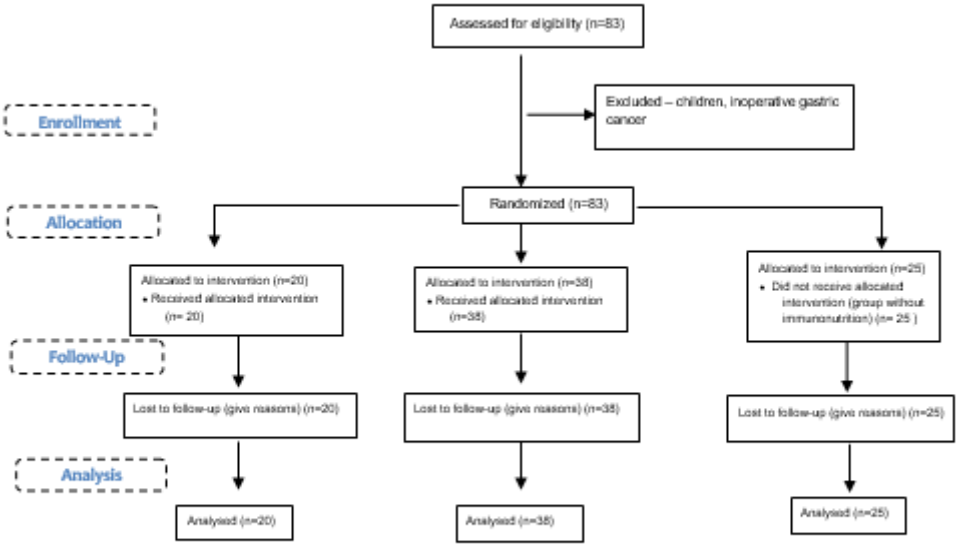

Figure 1

Clinical stages of Gastric Cancer in examined particular groups of patients

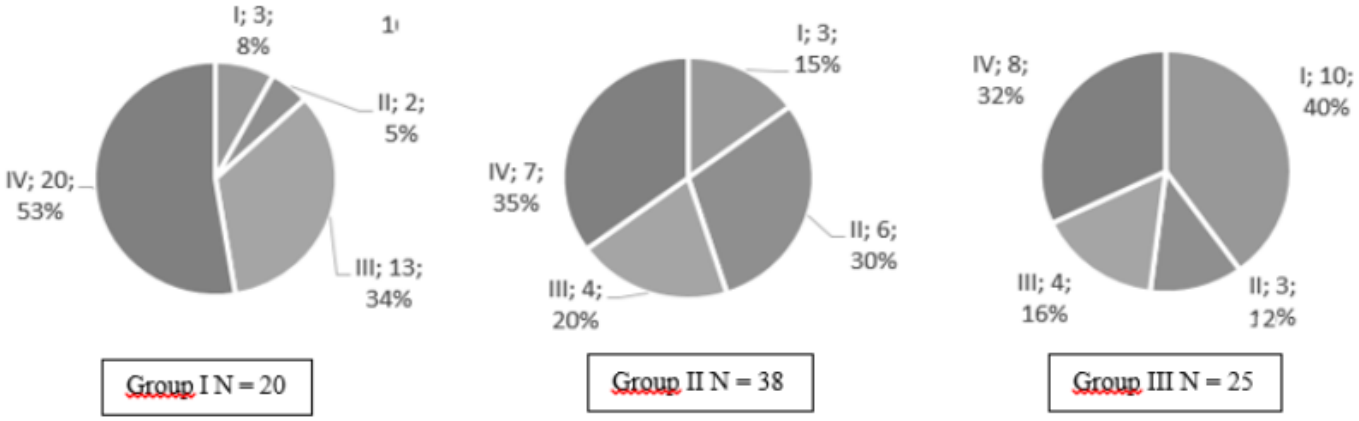

Figure 2

Clinical stages of Gastric Cancer in examined particular groups of patients

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