

CLINICAL STUDY

Hyponutrition among newly diagnosed gastric cancer

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ABSTRACT

OBJECTIVES: This study aims to determine the malnutrition status among Vietnamese patients newly diagnosed with gastric cancer (GC).

BACKGROUND: GC remains the top rank of common and deadly diseases. With limited clinical manifestation, most GC patients were diagnosed at late stages when tumor is not radically resected. Malnutrition was associated with poor prognosis of GC, such as prolonged hospitalization, limited treatment efficacy and low survival rate.

METHODS: The cross-sectional descriptive study recruited 77 patients newly diagnosed with GC and 90 healthy individuals (HC). The data used for this study were approved by the local Ethical Committee. The data were analysed on STATA 14.0 and GraphPad Prism 8.0.

RESULTS: We observed the male dominant distribution in GC cohort and over 65% of GC were firstly diagnosed at advanced stages (III and IV). Anemia was detected in about 50% of GC patients. Hyponutrition was prevalent in newly diagnosed GC. We found the decreased tendency of anemia related indexes from HC to early stages (I and II) and advanced stages (III and IV) of GC patients.

CONCLUSION: Anemia and hypoproteinemia occurred frequently among Vietnamese newly diagnosed GC. The nutrition therapy would benefit GC patients (*Tab. 4, Fig. 4, Ref. 20*). Text in PDF www.elis.sk

KEY WORDS: hyponutrition, gastric cancer, anemia, hypoproteinaemia.

Abbreviations: Area under ROC curve (AUR), Gastric cancer (GC), Healthy individuals (HC), White Blood Cell count (WBC), Red blood cells (RBC), Hemoglobin (HBG), Hematocrit (HCT), Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC)

Introduction

Gastric cancer (GC) remains the common and deadly cancer, ranking at the 5th of incidence and the 3rd of mortality worldwide (1). Over one million new GC cases were diagnosed and 768,793 cases were died in 2020 worldwide (2). Despite of the

steadily declined incidence and mortality over the last 50 years, GC remains the leading health burden and is estimated to reach 1.3 million deaths and 1.8 million new cases by 2040 (1, 3, 4). Among several risk factors reported, the most attributable influences of GC are *Helicobacter pylori* infection, *Human gamma-herpesvirus 4* infection, genetic susceptibility, high-salt foods and salt-preserved foods (5). The strong association between GC and its common modifiable risk factors hints it a significantly preventable disease (6). With limited clinical manifestation, most GC patients are diagnosed at late stages when tumor is not radically resected (5). Disregarding stages, the five-year survival rates of GC are 31% in the United States, 19% in the United Kingdom and 26% in Europe (3). Localized, regional and distant GC showed 72%, 33% and 6% of five-year survival rate, respectively (7). The most countries showed about 20–30% of the five-year survival rate of GC, excluding Japan and Korea (8).

Besides stage-dependence, GC prognosis depends on nutritional status, as well. About 31–87% newly diagnosed cancer presents weight loss, whereas 80% of advanced GC experienced malnutrition (9). The stomach stores, crushes and mechanically disrupts the intake foods, directly impact digestion and absorption (10). In addition, acid and pepsin secreted in stomach digests food, especially peptide food and absorption of vitamin B12. Given the most important role in the digestive system, undernutrition occurs commonly among GC patients. Malnutrition was detected in up to 85% GC patients and associated with poor prognosis, such as: increased morbidity and mortality, prolonged hospitalization, limited treatment efficacy and low survival rate (11). GC surgery

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Acknowledgements: This research is funded by Vietnam National Foundation for Science and Technology Development (NAFOSTED) under grant number 108.02–2019.324. The funder had no role in the study design, data collection and analysis, decision to publish or preparation of the manuscript.

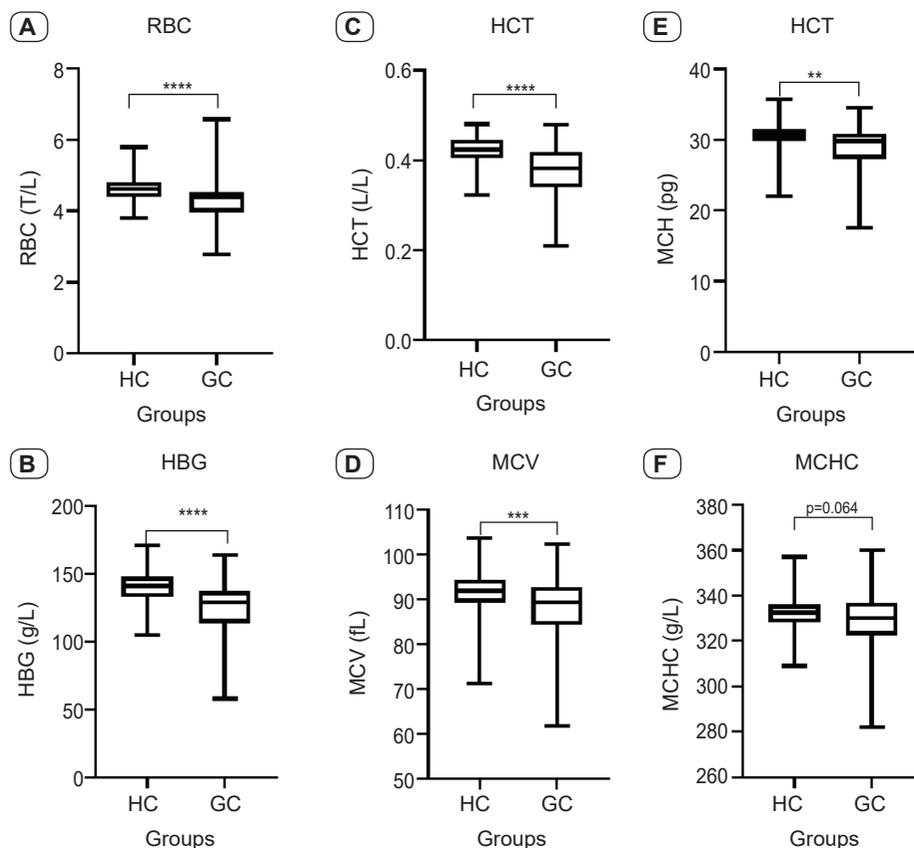


Fig. 1. The relationship between anemia-related indexes and gastric cancer patients (GC). Anemia-related indexes significant decreased in GC, compared to healthy control (HC). (A) Red blood cell (RBC); (B) Hemoglobin (HGB); (C) Hematocrit (HCT); (D) The mean corpuscular volume (MCV); (E) The mean corpuscular hemoglobin (MCH); (F) The mean corpuscular hemoglobin concentration (MCHC).

removes partly or totally gastric, directly reduces digestive activity, leading to the deficient intake and uptake. Nutrition supplement not only replenishes deficient intake but also imposes the recovery after the operation (12). Early detection and appropriate nutrition supplement improve the postoperative outcome (11). The superior life quality is an additional concern of malnutrition among patients with GC (11). Thus, the determination of undernutrition of newly diagnosed GC patients to supply nutrition appropriately is needed to improve their prognosis. Thus, this study aims to determine the

malnutrition status among Vietnamese patients newly diagnosed with GC for further nutrition strategy.

Materials and methods

Patient consent and ethical approval

All participants were informed and agreed with the collection and reporting their clinical data in this study. The recruitment and execution of this study were approved by the Ethical Committee,

Tab. 1. Referent range to categorize the level of anemia-related index.

Index	Decrease	Normal range	Increase
Red blood cell (RBC)	Male: <4.2	Male: 4.2–5.4	Male: >5.4
	Female: <4.0	Female: 4–4.9	Female: >4.9
Hemoglobin (HGB)	Male: <130	Male: 130–160	Male: >160
	Female: <120	Female: 120–150	Female: >150
Hematocrit (HCT)	Male: <0.4	Male: 0.4–0.47	Male: >0.47
	Female: <0.37	Female: 0.37–0.42	Female: >0.42
Mean corpuscular volume (MCV)	<85	85–95	>95
Mean corpuscular hemoglobin (MCH)	<28	28–32	>32
Mean corpuscular hemoglobin concentration (MCHC)	<320	320–360	>360
Protein (Pro)	<66	66–83	>83
Albumin (Alb)	<35	35–52	>52

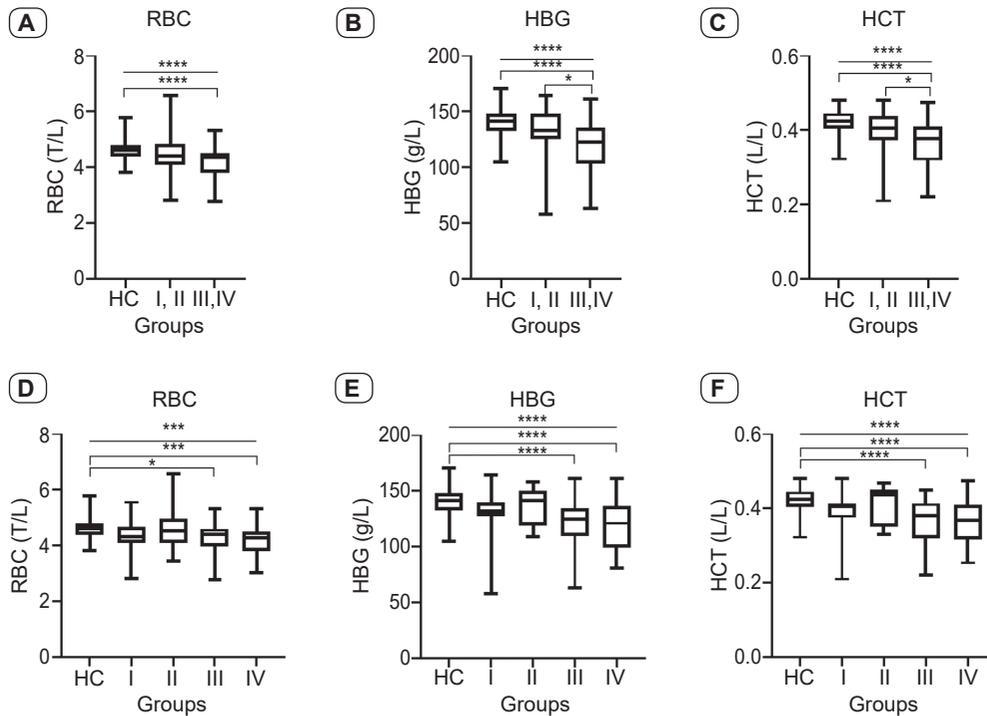


Fig. 2. The anemia-related indexes among healthy control (HC) and different stages of gastric cancer patients (GC). Different anemia-related indexes were compared between different stages of GC and HC. (A, D) Red blood cell count (RBC); (B, E) Hemoglobin (HBG); (C, F) Hematocrit (HCT).

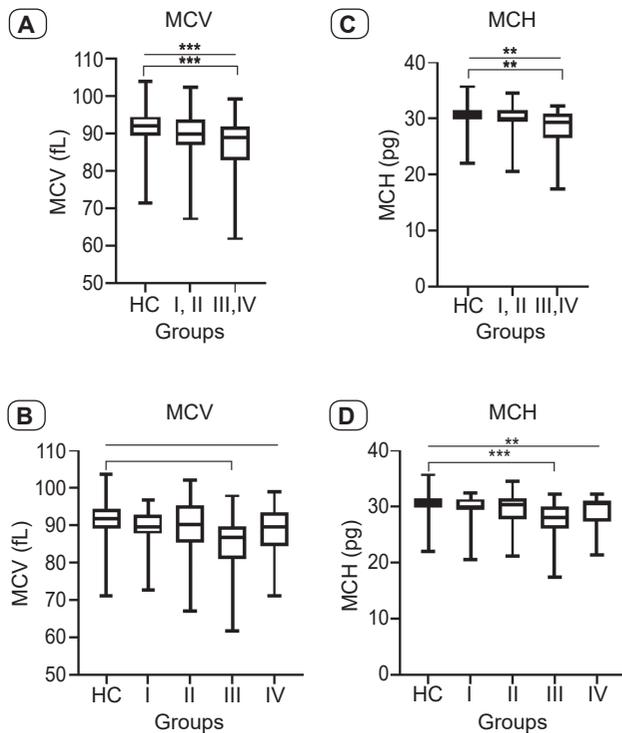


Fig. 3. The mean corpuscular hemoglobin (MCV) and the mean corpuscular hemoglobin concentration (MCH) among healthy control (HC) and different stages of gastric cancer patients (GC). (A, B) The mean corpuscular hemoglobin (MCH); (C, D) The mean corpuscular hemoglobin concentration (MCHC).

Vietnam Military Medical University, Hanoi, Vietnam. All participants signed the consent agreement form.

Data collection and study design

This is a cross-sectional descriptive study. The study recruited 77 hospitalized patients who were firstly diagnosed with GC at Military Hospital 103 from June 2020 to September 2022. Patients is selected if fulfilled eligibility criteria: firstly confirmed diagnosis with GC, hospitalized patients and participant agreement. The healthy control (HC) group included 90 people who visited Military Hospital 103 for regular health check and did not detected disease after examination and willing to participate in the study. All participants were explained clearly about the purpose of the study and participated voluntarily. The clinical and preclinical data of participants were collected from Hospital Information Management System. Based on the absolute concentration, the preclinical data were also categorized to different levels according to the referent range (Tab. 1). The results accuracy of preclinical parameter using in the study was controlled and warranted by ISO 15189 standard.

Statistical analysis

The statistical analysis was performed using GraphPad Prism 8.0 (GraphPad Software, USA) and Stata 14.0 (Stata Software, USA). The distribution of all variables were determined via Skewness test. The difference between more-than-two groups was analysed by one-way of variance (ANOVA) if the variable follows normal distribution or Kruskal–Wallis if the variable

does not follow normal distribution. The difference between two groups was analysed by unpaired t-test or Mann–Whitney if the variable follows and not follow normal distribution, respectively. The association between two categorical variables was checked by Chi-square (Fisher exact). The difference was referred significance *, **, *** and **** if $p < 0.05$, $p < 0.01$, $p < 0.001$ and $p < 0.0001$, respectively.

Results

Description of study cohort

This study recruited 77 GC patients including 15 stage I-GC (19.5%), 12 stage II-GC (15.5%), 27 stage III-GC (35.1%) and 23 stage IV-GC (29.9%). The male patients were predominant with 51 patients (66.23%). HC group had 90 healthy individuals, the male was predominant with 55 individuals (61.11%). The age and gender distribution of the study cohort were reported previously (13).

Anemia among GC patients in comparison to HC

To determine the nutrient status of GC, we compared the anemia-related indicators, including Red blood cell (RBC), Hemoglobin (HGB), Hematocrit (HCT), The Mean corpuscular volume (MCV), The Mean corpuscular hemoglobin (MCH), and The Mean corpuscular hemoglobin concentration (MCHC) between GC and HC. Our results consistently showed the lower level of RBC, HGB, HCT, MCV, MCH and MCHC of GC pa-

tients, compared to HC (Fig. 1 A-F). In addition, we categorized participants into increased, normal and decreased levels, based on their absolute value in comparison to referent range (Tab. 1). The rate of decreased RBC, HGB and HCT were respectively 33.77%, 53.25% and 58.44%, indicating the frequent anemia occurring

Tab. 2. The changes of anemia-related indexes in early and late stages of gastric cancer.

Indexes	Levels	Stages		p
		I+II	III+IV	
Change RBC	Decrease	27	43	0.041
		100	86	
	Normal	0	7	
		0	14	
Total	27	50	100	100
Change HGB	Decrease	8	27	0.111
		29.63	54	
	Increase	1	2	
		3.7	4	
Normal	18	21	66.67	42
Total	27	50	100	100
Change HCT	Decrease	8	30	0.014
		29.63	60	
	Increase	1	4	
		3.7	8	
Normal	18	16	66.67	32
Total	27	50	100	100
Change MCV	Decrease	5	17	0.273
		18.52	34	
	Increase	5	5	
		18.52	10	
Normal	17	28	62.96	56
Total	27	50	100	100
Change MCH	Decrease	4	20	0.075
		14.81	40	
	Increase	3	4	
		11.11	8	
Normal	20	26	74.07	52
Total	27	50	100	100
Change MCHC	Decrease	3	13	0.124
		11.11	26	
	Normal	24	37	
		88.89	74	
Total	27	50	100	100

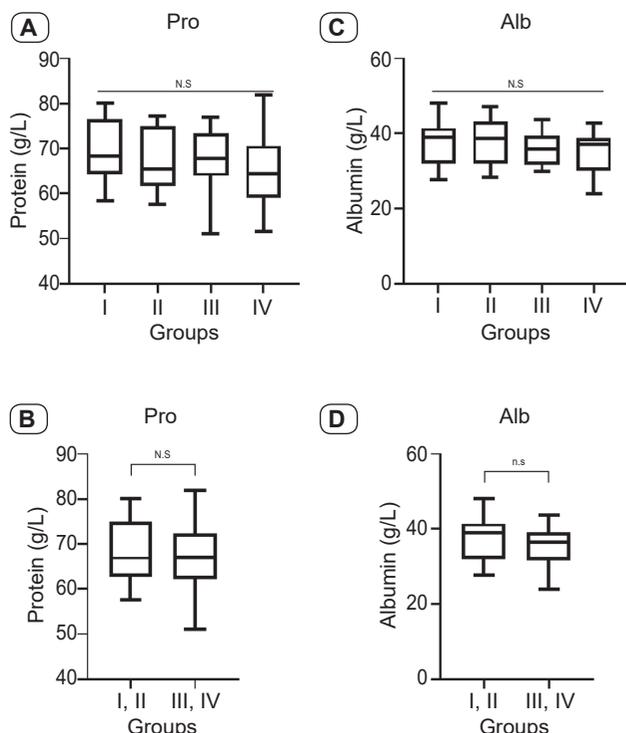


Fig. 4. The hypoproteinemia among different stages of gastric cancer patients (GC). The comparison of the plasma protein (Pro) concentration (A, B) and plasma albumin (Alb) concentration (C, D) between GC in different stages.

Red blood cell (RBC), Hemoglobin (HGB), Hematocrit (HCT), Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC)

among newly diagnosed GC. Our analysis showed the significant association between the decrease of RBC, HGB, HCT, MCV, MCH and MCHC and GC (The results indicated the frequent anemia among newly diagnosed GC patients) (Tab. 2).

The comparison between anemia levels and GC stages

To determine the change of hematological system during GC progress, we compared some hematological indexes between HC, early and late stages of GC. We found the decreased tendency of some anemia-related indexes (including RBC, HGB and HCT) from HC to GC early stages (I, II) to GC late stages (III, IV) (Fig. 2 A-C). These anemia-related indexes gradually decreased from HC to GC stage I, II, III, IV (Fig. 2 D-F). Similar pattern was observed in the mean corpuscular hemoglobin (MCV) (Fig. 3 A, B) and the mean corpuscular hemoglobin concentration (MCHC) (Fig. 3 C, D). All anemia-related investigation indexes gradually decreased from HC to GC stage I, II, III, IV. Basically, the significant decrease was observed between stage III and IV, compared to HC, but not between HC and early GC stages (I, II). Thus, the data showed worse anemia during the GC progression.

Hypoproteinemia among GC patients and association with GC stages

To determine the nutrient status of GC, we categorized the GC patients depending on their levels of nutrient-related indicators, including protein and albumin concentration in plasma. We found that the decreased protein and albumin was observed in 44.29% and 34.67% of GC patients, respectively (Tab. 3).

In addition, we compared the protein and albumin concentration between different GC stages. The results showed a comparable level of protein and albumin between GC stage I, II, III, IV as well as between early and advanced GC (Fig. 4 A-D). Additionally, we determined the association between hypoproteinemia and GC stages. No association between protein and albumin levels and GC stage was found (Tab. 3). Briefly, anemia and insufficient protein, the indicator of malnutrition occurred in around 40–50% of GC patients.

The distribution of anemia-related indexes with age

To determine the interference of age on malnutrition-related indexes, such as RBC, HGB, HCT, MCV, MCH, MCHC, protein and albumin, their mean value were compared between age groups.

Our analysis showed the equal value of above indexes between different age groups. Among GC, the absolute value of RBC, HGB, HCT, MCV, MCH, MCHC, protein and albumin were comparable between different age groups (Tab. 4). Among HC, the value of MCV were slightly lower in elder group (≥ 60 years old), compared to the younger groups. Our analysis showed the equal value of almost investigated hypoproteinemia indexes (except MCV) among different age groups.

Tab. 3. The changes of protein and albumin concentration in different stages of gastric cancer.

Indexes	Levels	Stages				Total	p	
		I	II	III	IV			
Change Pro	Decrease	n	4	6	10	11	31	0.437
		%	30.77	54.55	38.46	55	44.29	
	Normal	n	9	5	16	9	39	
		%	69.23	45.45	61.54	45	55.71	
	Total	n	13	11	26	20	70	
		%	100	100	100	100	100	
Indexes	Levels	I+II		III+IV		Total	p	
Change Pro	Decrease	n	10		21		31	0.75
		%	41.67		45.65		0.44	
	Normal	n	14		25		39	
		%	58.33		54.35		0.56	
	Total	n	24		46		70	
		%	100		100		100	
Indexes	Levels	Stages				Total	p	
		I	II	III	IV			
Change Alb	Decrease	n	4	4	11	7	26	0.828
		%	26.67	33.33	40.74	33.33	34.67	
	Normal	n	11	8	16	14	49	
		%	73.33	66.67	59.26	66.67	65.33	
	Total	n	15	12	27	21	75	
		%	100	100	100	100	100	
Indexes	Levels	I+II		III+IV		Total	p	
Change Alb	Decrease	n	8		18		26	0.75
		%	29.63		37.5		0.35	
	Normal	n	19		30		49	
		%	70.37		62.5		0.65	
	Total	n	27		48		75	
		%	100		100		100	

Protein (Pro), Albumin (Alb)

Discussion

Being the prevalent malignancy for many decades, GC showed poor and stage-dependent prognosis (3). Patients with operable GC have a longer overall survival compared to inoperable GC. Meanwhile, preoperative and postoperative nutritional supplement reduces the length of hospitalization, complications and support the recovery (9). Nutrition not only supports the recovery, incision healing and combat against cancer postoperatively but also affects treatment tolerance and response to the systematic treatment therapy. Thus, malnutrition is an important concern of cancer treatment, especially with GC due to its digestive function.

Several indicators have been used to evaluate the nutritional status, but none of them present enough reliability (11). The

prognostic value of serum hepatic proteins, such as albumin, prealbumin, and transferrin relating to nutrition is restricted by their decrease in other dysregulation, such as infection, injury, inflammation, kidney and liver failure (11, 14). Thus, the combination of different indexes to build the nutritional scores increase the reliability of investigation. Unfortunately, our study lack the nutritional evaluation by nutritional scores (nutritional screening and nutritional assessment tools) and mainly focused on some basic and convenient malnutrition-related tests, such as complete blood count (CBC), protein and albumin tests (11). However, these cheap and common tests gave the useful information relating nutrition status among the newly diagnosed GC patients.

Malnutrition occurs frequently in chronic syndromes including cancer. Stomach is a key organ of digestive system, and GC progress directly affect nutritional absorption. Thus, the determination of nutritional status provides information for nutritional therapy which benefits patient during operation, post-operation, systematic treatment tolerance. The malnutrition occurs among 65% to 85% of GC with deteriorate tendency after hospitalization (11). The possible culprits of malnutrition in GC are the poor nutrition diet, the deficient digestion and absorption and the impaired metabolism. Nutrition deficiency related to the poor treatment response and quality of life, shorter survival, increased morbidity and mortality, prolonged hospitalization and serious postoperative complications (11, 15). Malnutrition is exacerbated by treatment or pathological disease itself, especially in case of gastric resection (12, 16). Malnutrition is an independent prevalent concern of postoperative subtotal and total gastrectomy, requiring intensive nutritional management in follow-up period (17, 18). GC patients in this study presented the significant low RBC, HCT, HGB, MCV, MCH and MCHC, compared to HC. Anemia occurred up to 50% of the newly diagnosed GC patients. Also, the value of the anemia-related indexes was the lowest on late-stage GC, followed by early-stage GC and HC. Thus, our analysis showed the high rate of anemia among GC with late stage being the aggravation. We additionally investigated the change of protein and albumin concentration among patients with different GC stages. We found that hypoproteinemia and hypoalbuminemia occurred around 45% and 35%, respectively. Taken the role of protein on health and wound healing, the hypoproteinemia and hypoalbuminemia hints the necessary to supply nutrition for GC patients. The preoperative malnutrition of GC related to a greater morbidity and mortality, lower survival, increased infective complications (19). The malnutrition might be exacerbated and impose complication, such as infection and malnourishment postoperatively (19). The nutrient status support the recovery after surgery and systematic treatment of chemotherapy. Thus, pre-surgical nutritional treatment and post-surgical nutritional therapy were highly recommended for GC patients (19). The preoperatively insufficient nutrition predicts the poor postoperative survival of GC (20). Although, our results was only restricted in pre-clinical signs of malnutrition, without clinical signs, the malnutrition was evidenced, and intensive nutrient supplement is needed.

Tab. 4. The distribution of malnutrition-related indexes with age.

Indexes	Group	Age groups			p
		≤50	50-60	≥60	
RBC	GC	4.2±0.2	4±0.6	4.3±0.7	0.27
	HC	4.6±0.4	4.6±0.4	4.7±0.3	0.91
HGB	GC	116.5±17.5	119.2±21.6	125±24.4	0.38
	HC	139.8±11.7	140.6±11.7	139.6±9.4	0.95
HCT	GC	0.36±0.04	0.36±0.06	0.38±0.06	0.38
	HC	0.42±0.04	0.42±0.05	0.42±0.06	0.96
MCV	GC	85.0±10.41	90.4±4.5	87±8.0	0.46
	HC	91.5±4.0	91.9±4.9	86.4±1.9	0.02
MCH	GC	27.6±4.4	29.8±1.7	28.7±3.5	0.62
	HC	30.4±1.4	30.6±1.9	29±1.6	0.087
MCHC	GC	322.7±15.6	330.3±10.0	328.5±15.0	0.63
	HC	331.9±5.2	332.8±7.4	336±11.6	0.55
Pro	GC	70.2±7.8	64.6±9.1	67.4±6.9	0.37
Alb	GC	39.2±3.4	35.6±5.6	36.1±5.2	0.32

Red blood cell (RBC), Hemoglobin (HGB), Hematocrit (HCT), Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC), Protein (Pro), Albumin (Alb)

Briefly, the anemia and hypoproteinemia occurred frequently among Vietnamese patients newly diagnosed with GC. The early evaluations of nutritional status, followed by early appropriate nutritional supplement potentially benefits both operable and advanced GC patients.

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Received November 13, 2023.

Accepted December 11, 2023.