

# Nutritional status of patients with ovarian cancer and associated factors

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**Abstract.** Malnutrition associated with cancer is a common concern and negatively affects the resilience of patients. The method of assessing nutrition based on serum blood albumin levels is considered to be an objective one. However, due to the long half-life, specificity is also controversial. The present study cross-sectional study was conducted to assess the nutritional status of patients with ovarian cancer (OC) assessed according to the serum albumin levels of from 2018 to 2021. For this purpose, the medical records of 129 patients with OC were selected. As a result, the malnutrition rate by serum albumin accounted for 17.1%. The rate of malnutrition in patients with OC at stages III and IV (35.9%), was almost 5-fold higher than that of patients with OC at stages I and II (7.9%). At the time of testing, post-operative malnutrition accounted for 56.2%, >2-fold higher than the pre-operative malnutrition rate. Subclinical indicators, including the numbers of red blood cells, hematocrit and hemoglobin levels, neutrophil percentage, lymphocyte percentage, neutrophil, lymphocyte, monocyte and platelet counts, glucose and creatinine levels, Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup> and total calcium levels were found to be significantly associated with the changes in nutritional status according to serum albumin levels. On the whole, the findings of the present study may assist healthcare professionals to improve the nutritional status of patients, and also suggests the possible use of serum albumin in assessing the nutritional status.

## Introduction

Ovarian cancer (OC) is caused by the abnormal growth of cells formed in the ovaries. Their rapid development can lead

to the destruction of healthy body tissues. In 2020, ~21,750 new cases of OC were identified, accounting for 1.2% of all cancer types (1). OC is the second most common type of malignancy affecting women >40 years of age, particularly in developing countries (2). Of note, only ~15% of OC cases are diagnosed when the disease is localized (1). Moreover, ~60% of OC cases are detected at the metastatic stage (1). This is perhaps the reason that OC is becoming the leading cause of cancer-related mortality among women with gynecological cancer worldwide (1,2). OC has been proven to be in the list of top five common cancers among women in Southeast Asian countries, including Vietnam (3). The majority of patients are diagnosed at a late stage. Therefore, the treatment of OC is a particular concern nowadays.

Malnutrition is the most common nutritional concern of patients with cancer and OC (4). In patients with OC, the metabolic effects of large tumors and intestinal obstruction lead to a poor nutritional status (5). A previous study also demonstrated that >50% of patients with OC are at risk of developing malnutrition (6). This condition negatively affects the treatment efficacy, causing pain to patients, and increasing the mortality and morbidity rates (6). In addition, the nutritional status also significantly affects the occurrence of post-operative complications (7). However, in Vietnam, the nutritional status of patients with OC has not been studied to date, at least to the best of our knowledge.

Currently, a number of methods are used to assess and screen nutrition in patients with OC. In recent years, clinicians have used the albumin-based nutrition assessment method. When the serum albumin level is <35 g/l, the patient is considered to be at risk of malnutrition (8). Serum albumin is considered an indicator for convenient and objective nutrition evaluation for clinicians. However, its specificity in nutrition assessment is controversial worldwide (9). Currently, studies using albumin levels to assess nutritional status are encouraged to verify the reliability of this approach. Moreover, an overview of the nutritional status of patients with OC through albumin levels can help healthcare professionals assess and take measures to improve the nutritional status of patients.

Therefore, the present study aimed to assess the scientific basis of the nutrition assessment method based on serum albumin levels. In addition, the present study determined the

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nutritional status of patients with OC and related factors based on this method.

### Patients and methods

**Research subjects.** The medical records of patients treated for OC at K Hospital in Tan Trieu, Vietnam, from January, 2018 to December, 2021 were obtained. The present study was approved by the Institute of Genome Research Institutional Review Board, Vietnam Academy of Science and Technology, according to the decision number: 02-2022/NCHG-HĐĐĐ on March 09, 2022.

**Study procedure.** The present cross-sectional study was carried out between October, 2021 and June, 2022. The study was performed at K Hospital. The convenience sampling method was used for the study. All medical records of patients treated for OC at K Hospital between January, 2018 and December, 2021 were obtained. Retrospective information was collected based on the medical records of patients with OC. All written medical records of the patient were photographed. Medical records with information about the characteristics of patients, indicators of total peripheral blood cell analysis, blood biochemical indicators and electrolyte indexes were selected. The medical records of 129 patients with OC with a median age of 52 years were selected. The nutritional status of the patients with OC was divided into three stages based on serum albumin levels as follows: 36-48 g/l, normal; 21-35.9 g/l, mild and moderate malnutrition; and <21 g/l, severe malnutrition. The subclinical indicators used to identify factors affecting the nutritional status and its classification as normal and abnormal are presented in Table SI.

**Statistical analysis.** The data were checked, cleaned, encrypted and entered using Excel software, then processed statistically using SPSS volume 20 software (IBM Corp.). Descriptive and inferential statistical tests (Chi-squared and Fisher's exact tests) were used for data analysis. A value of  $P < 0.05$  was considered to indicate a statistically significant difference. The following principles were applied when analyzing data: i) For a description of the general nutritional status of the study subject, the nutritional status by age, self-history, family history and the stage of OC was considered. The test results of serum albumin levels at the first test after admission were used to avoid the effects of treatment interventions. ii) For the description of nutritional status at the time of pre-and post-operative testing, and the association between nutritional status and this factor, the test results of serum albumin levels were used immediately before and after surgery. iii) For determining the association between nutritional status and subclinical indicators, the serum albumin levels from all tests were used where that subclinical index was present.

### Results

From the 129 patients with OC, 22 patients had mild and moderate malnutrition (17.1%). Patients <60 years of age accounted for 68.2% of the study population, with a median age of 52 years. Of note, >75% of the study subjects had no comorbidities (78.3%), and the proportion of study subjects with one and

Table I. Characteristics of the patients in the present study.

Characteristic	No. of patients	%
Nutritional status		
Normal	107	82.9
Mild and moderate malnutrition	22	17.1
Severe malnutrition	0	0
Age, years		
<60	88	68.2
≥60	41	31.8
Median (interquartile range)	52 (39-61.5)	
Comorbidities		
0	101	78.3
1	25	19.4
2	3	2.3
Family history		
No	118	91.5
Yes	11	8.5
Self-history		
No	59	45.7
Yes	70	54.3
Allergies		
No	121	93.8
Yes	4	3.1

two comorbidities was 19.4 and 2.3%, respectively. Only 8.5% of the total study subjects had a family history of OC. More than half of the patients had a history that could lead to a risk of developing OC and could affect their OC condition (54.3%). Subjects with allergies accounted for only 3.1% (Table I).

Of the 129 patients with OC included in the present study, information regarding the stage of OC was available for only 77 subjects. Patients with stage I and III OC accounted for the same proportion (40%) of the study population, followed by patients with stage IV OC; this subpopulation accounted for 11% of the total study population, whereas patients with stage II OC accounted for 9% of the total study population (Fig. 1).

The stage of OC and testing time were factors that were found to affect the nutritional status of patients, as determined by the serum albumin levels ( $P < 0.01$ ;  $P = 0.005$  and  $0.003$ , respectively). For patients with stage III and IV OC, the rate of malnutrition was 35.9%, almost 5-fold higher than that of patients with stage I and II OC (7.9%). As regards the time of testing, post-operative malnutrition accounted for 56.2%, >2-fold higher than the pre-operative malnutrition rate (Table II).

Indicators, including red blood cell count, hemoglobin levels, hematocrit, white blood cell count, neutrophil and lymphocyte percentage, neutrophil, lymphocyte, monocyte and platelet count were found to significantly affect the nutritional status of patients ( $P < 0.05$ ). In particular, the malnutrition rate was higher when the levels of these indicators were abnormal (Table III).

The creatinine and glucose levels were also found to significantly affect the nutritional status of patients ( $P < 0.01$ ). The malnutrition rate was higher when the levels of these

Table II. Factors associated with the nutritional status of patients with ovarian cancer.

Factor	Normal		Malnutrition		P-value
	No. of patients	%	No. of patients	%	
Age, years					
<60	76	87.4	11	12.6	0.079
≥60	31	73.8	11	26.2	
Stage of OC					
I and II	35	92.1	3	7.9	<b>0.005<sup>a</sup></b>
III and IV	25	64.1	14	35.9	
Family history					
No	97	82.2	21	17.8	0.689
Yes	10	90.9	1	9.1	
Self-history					
No	46	78	13	22	0.167
Yes	61	87.1	9	12.9	
Time of testing					
Pre-operative	36	75	12	25	<b>0.003<sup>b</sup></b>
Post-operative	21	43.8	27	56.2	

Values in bold font indicate statistically significant differences (<sup>a</sup>P<0.05, as determined using Fisher's exact test; <sup>b</sup>P<0.05, as determined using the Chi-squared test).

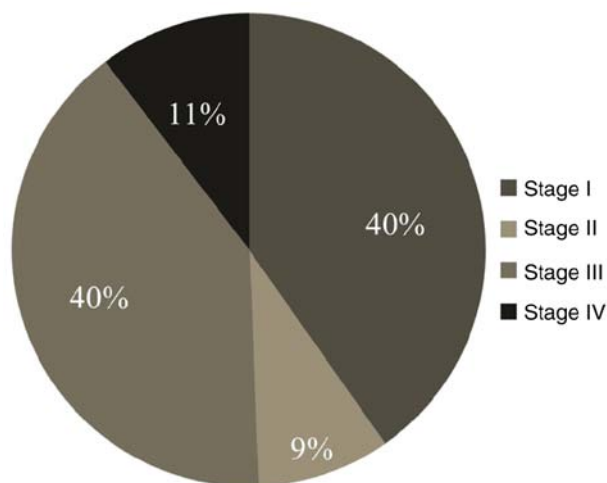


Figure 1. Pie chart demonstrating the stages of patients with ovarian cancer in the present study.

indicators were abnormal (48.1 and 59.3% compared with 22.6 and 15.3%) (Table IV).

It was also found that electrolyte indices, including Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup> and total calcium levels, were significantly associated with the malnutrition status (P<0.05). In particular, the malnutrition rate was higher when the levels of these indicators were abnormal (Table V).

## Discussion

The present cross-sectional study of 129 patients with OC found that 17.1% were malnourished using an albumin-based

nutrition assessment method. This ratio appears to be low when compared to the study of Le NTA *et al* (70.3%) (10). The different research subjects used may be the cause for this disparity. The present study was conducted only on patients with OC and small sample sizes. By contrast, the study of Le NTA *et al* (70.3%) was conducted on a larger sample size with a variety of cancer types. In particular, weight loss and malnutrition rates were obtained for patients with liver, stomach, mouth, pharyngeal and tonsil cancer. Therefore, the rate of malnutrition was higher than the one obtained in the present study.

In the present study, the malnutrition rate of the patients aged ≥60 years was >2-fold higher than that patients <60 years of age, although this difference was not statistically significant (P>0.05). Older patients often experience physiological aging associated with changes that render them more susceptible to nutritional risks (11). They often suffer from a number of diseases, such as high blood pressure, diabetes, dental deterioration, issues related to memory loss, etc., along with the weakening of the digestive system, which makes the ability to tolerate nutrients. Furthermore, the presence of OC cells leads to the metabolic effects of tumor enlargement and intestinal obstruction, which aggravate malnutrition (5).

In the present study, patients with stage III and IV OC were found to have a 5-fold higher malnutrition rate than patients with stage I and II OC (P=0.005). This is true of the current understanding of OC. The majority of research often focuses on studying the nutritional status and improvement measures in patients with late-stage OC than those with early-stage OC (12,13). In the early stages of the disease, symptoms and physical changes are often unclear. However, changes in the body's condition are strongly manifested when the disease

Table III. Association between indicators of total peripheral blood cell analysis and the nutritional status of patients with ovarian cancer.

Indicator	Normal		Malnutrition		P-value
	No. of testing times	%	No. of testing times	%	
Red blood cell count					
Normal	138	79.8	35	20.2	<b>0.001</b>
Abnormal	73	62.4	44	37.6	
Hemoglobin levels					
Normal	79	84	15	16	<b>0.003</b>
Abnormal	132	67.4	64	32.6	
Hematocrit					
Normal	128	80.5	31	19.5	<b>0.001</b>
Abnormal	83	63.4	48	36.6	
Mean corpuscular hemoglobin concentration					
Normal	158	74.9	53	25.1	0.292
Abnormal	55	68.8	25	31.2	
Mean corpuscular hemoglobin					
Normal	162	73	60	27	0.878
Abnormal	51	73.9	18	26.1	
Red cell distribution width					
Normal	123	70.3	52	29.7	0.227
Abnormal	86	76.8	26	23.2	
Red cell distribution width-standard deviation					
Normal	94	65.3	50	34.7	0.120
Abnormal	66	75	22	25	
White blood cell count					
Normal	152	86.4	24	13.6	<b>0.001</b>
Abnormal	57	51.4	54	48.6	
Neutrophil percentage					
Normal	118	89.4	14	10.6	<b>0.001</b>
Abnormal	95	59.8	64	40.2	
Lymphocyte percentage					
Normal	148	94.9	8	5.1	<b>0.001</b>
Abnormal	65	48.2	70	51.8	
Eosinophil percentage					
Normal	201	71.8	79	28.2	0.075
Abnormal	11	100	0	0	
Basophil percentage					
Normal	195	71.7	77	28.3	0.113
Abnormal	17	89.5	2	10.5	
Neutrophil count					
Normal	155	87.6	22	12.4	<b>0.001</b>
Abnormal	55	49.6	56	50.4	
Lymphocyte count					
Normal	187	82	41	18	<b>0.001</b>
Abnormal	23	38.3	37	61.7	
Monocyte count					
Normal	178	76.4	55	23.6	<b>0.008</b>
Abnormal	32	58.2	23	41.8	
Eosinophil count					
Normal	206	72.8	77	27.2	0.666
Abnormal	4	66.7	2	33.3	

Table III. Continued.

Indicator	Normal		Malnutrition		P-value
	No. of testing times	%	No. of testing times	%	
Basophil count					
Normal	201	72	78	28	0.452
Abnormal	8	88.9	1	11.1	
Platelet count					
Normal	184	80	46	20	<b>0.001</b>
Abnormal	22	41.5	31	58.5	

Values in bold font indicate a statistically significant difference ( $P<0.05$ ) determined using the Chi-squared test.

Table IV. Association between blood biochemical indicators and the nutritional status of patients with ovarian cancer.

Related biochemical indicator	Normal		Malnutrition		P-value
	No. of testing times	%	No. of testing times	%	
Creatinine levels					
Normal	205	77.4	60	22.6	<b>0.001</b>
Abnormal	28	51.9	26	48.1	
Glucose level					
Normal	199	84.7	36	15.3	<b>0.001</b>
Abnormal	33	40.7	48	59.3	
Glutamic-oxaloacetic transaminase					
Normal	206	74.4	71	25.6	0.401
Abnormal	23	67.7	11	32.3	
Urea levels					
Normal	215	74.7	73	25.3	0.537
Abnormal	8	66.7	4	33.3	

Values in bold font indicate a statistically significant difference ( $P<0.05$ ) determined using the Chi-squared test.

progresses to the late stages. The rapid growth and spread of tumors lead to metabolic disturbances in the body due to a greater anabolism than catabolism (14). Furthermore, patients in the terminal stage are prone to malignant bowel obstruction and gastrointestinal metastases accompanied by tumor expansion, leading to mechanical obstruction of the gastrointestinal tract, placing the patient at high risk of falling into a state of exhaustion (14). It was demonstrated that using serum albumin levels for nutritional assessment can also yield results similar to current knowledge. Assessing the nutritional status through serum albumin levels is thus reliable.

In the present study, albumin levels were used to measure the nutritional status. However, other factors, such as inflammation, liver function and hydration status have been considered to influence albumin levels. On the other hand, these factors can exhibit major variations before and after surgery. Therefore, the present study demonstrated the albumin levels before or after surgery to partially shed light on this matter. The results revealed that the rate of post-operative malnutrition accounted

for 56.2%, which was >2-fold higher than the pre-operative malnutrition rate. This indicates that the albumin level was significantly decreased following surgery. The leading causes of a sharp decrease in albumin levels following surgery include hypoalbuminemia immediately before surgery, blood loss or blood dilution, and a systemic inflammatory response. This result is similar to that of the study of Motamed *et al* (15); following surgery for breast cancer, the serum albumin levels were shown to be reduced by 40% compared to those prior to surgery. Post-operative low serum albumin levels have been found to be significantly associated with mortality within the first 6 months post-operatively, as well as with poor peri-operative outcomes (hospital length of stay is longer; other complications after surgery), particularly for patients with late-stage OC (16).

In the present study, indicators related to erythrocytes, including red blood cell count, hemoglobin, and hematocrit levels, were found to significantly influence malnutrition, as determined using serum albumin levels ( $P=0.001$ ,  $0.003$

Table V. Association between electrolyte indexes and nutritional status.

Related electrolyte index	Normal		Malnutrition		P-value
	No. of testing times	%	No. of testing times	%	
Na <sup>+</sup>					
Normal	217	77.2	64	22.8	<b>0.001</b>
Abnormal	6	31.6	13	68.4	
K <sup>+</sup>					
Normal	199	78.7	54	21.3	<b>0.001</b>
Abnormal	24	51.1	23	48.9	
Cl <sup>-</sup>					
Normal	203	76.3	63	23.7	<b>0.028</b>
Abnormal	20	58.8	14	41.2	
Bilirubin					
Normal	131	84	25	16	0.421
Abnormal	9	75	3	25	
Total calcium levels					
Normal	168	94.4	10	5.6	<b>0.001</b>
Abnormal	18	22.8	61	77.2	

Values in bold font indicate a statistically significant difference ( $P < 0.05$ ) determined using the Chi-squared test.

and 0.001, respectively). When the levels of these indicators are abnormal, the rate of malnutrition increases. These are specific indicators which can be used to determine anemia or the hemoconcentration in patients. An increased red blood cell count indicates hemoconcentration or polycythemia, while a decreased red blood cell count is associated with hemodilution. The amount of hemoglobin is the most characteristic indicator of anemia; it is a relatively reliable and accurate baseline indicator. Red blood cell volume or hematocrit levels are valuable in assessing and monitoring anemia. Decreased serum albumin levels may result from hemoconcentration, hemodilution, or anemia. Therefore, any abnormality in the red blood cell count, hemoglobin and hematocrit levels can cause a decrease in serum albumin levels. This suggests that the prevalence of malnutrition is determined by serum albumin levels, which influence red blood cell count, hemoglobin and hematocrit indices. Furthermore, iron- or zinc-deficiency anemia cases are considered to be related to the body's under-nutrition. Therefore, diets and interventions to improve these indicators are essential to avoid the depletion of patients with OC and harmful post-operative complications.

In the present study, the white blood cell counts, neutrophil percentage, lymphocyte percentage, neutrophils count, lymphocyte count and monocyte count also yielded similar results (all,  $P < 0.001$ ; monocyte count,  $P = 0.008$ ). The increased white blood cell count can be caused by inflammation; the decreased white blood cell count is related to a lack of nutrients, such as vitamin B12. Neutrophils are also elevated in cancer infections. Monocytes are increased in infections, anemia due to bone marrow failure, cancer, etc. Therefore, it is reasonable that these indicators are related to the nutritional status, as determined by serum albumin levels. Inflammatory reactions that occur will cause the potent inhibition of organ

protein synthesis, leading to malnutrition (9). Anemia for a number of days is also the cause of exhaustion and reduced nutrition in the body. Abnormal lymphocyte counts are associated with cancer and infections. The lymphocyte percentage and lymphocyte count are also used to assess and predict the nutritional status of patients. Low lymphocyte counts are used to assess and predict the risk of malnutrition (17). Moreover, herein, anomalies in creatinine and glucose levels also led to a significant increase in malnutrition rates ( $P < 0.001$ ). Creatinine is also considered a sign of malnutrition due to creatinine levels being an indicator of musculoskeletal rotation (9). Typically, creatinine levels decrease in cases of low muscle mass (18). The cause of low muscle mass in the body is malnutrition (19). Therefore, malnutrition can lead to a low muscle mass status and low creatinine levels. In addition, glucose is the body's leading energy supplier. Poor metabolism and glucose absorption cause abnormalities in blood glucose levels that lead to a lack of energy and malnutrition. Excessive blood glucose levels can lead to organ damage, such as the liver, kidneys, etc (20). Albumin production in the liver is also then disrupted, leading to a decrease in levels (21). In the present study, electrolyte indices including Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup> and total calcium were all significantly associated with malnutrition, as determined using the serum albumin levels. Disorders in the indicators of electrolytes are often related to damage to the liver and kidneys. In particular, dyskalemia may be caused by malabsorption. As is known, the liver is the site of albumin synthesis; thus, when the liver and kidney function is damaged, this leads to a decrease in albumin synthesis, resulting in low serum albumin levels (22). It is responsible for the higher prevalence of malnutrition as determined by higher serum albumin levels. In addition, poor absorption also directly affects the patient's nutritional status (23). Patients with late-stage OC also suffer

from intestinal obstruction and tumors compressing the digestive tract, lead to an even more severe condition (24). These results suggest that a nutritional assessment based on serum albumin levels may still be reliable. However, it can be combined with other methods to determine the accuracy.

The present study had certain limitations which should be mentioned. Firstly, data availability was one of the limitations. The data collected was from written medical records; thus, only information on the characteristics of patients, indicators of total peripheral blood cell analysis, blood biochemical indicators and electrolyte indices was only collected. In addition, some old medical records from 2018 to 2019 had been torn and information was lost; thus, some medical records were incomplete. Therefore, during the analysis, the research object was divided into a number of subgroups. In addition, the collection of patient medical records in the period from 2018-2021 was a volatile period due to the impact of COVID-19. Therefore, the present study had a small sample size. Finally, studies in Vietnam on the nutritional status of cancer patients mainly focus on stomach and esophageal cancers; studies on OC often focus on understanding the influence of genes on patients; thus, it is difficult to compare the study results.

In conclusion, in the present study, of the 129 study subjects, malnutrition or the risk of malnutrition accounted for a low rate (17.1%). In particular, the malnutrition rate in the group aged  $\geq 60$  years, in patients with stage III and IV OC, and the post-operative malnutrition rate was markedly higher compared the other groups (2.1-, 4.5- and 2.2-fold higher than the other groups, respectively). Patients with stage III and IV OC and the post-operative time point, were significantly associated with an increased prevalence of malnutrition ( $P=0.005$  and  $0.003$ , respectively). Some subclinical indicators were also significantly related to the nutritional status of patients with OC. The lymphocyte counts and hematocrit levels were prominent indicators significantly related to the increased rate of malnutrition of the study subjects when levels were abnormal (61.7 vs. 6 vs. 19.5%). This evidence may help healthcare professionals improve the nutritional status of patients with OC, as well as provide evidence for the use of serum albumin to assess the nutritional status. The findings presented herein may provide the basis for future studies on the nutritional status of patients with OC and the reliability testing of nutritional assessment methods by serum blood albumin.

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### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Authors' contributions

DTC and LTN conceived and designed the study. THNT and BPV provided the medical records of the patients. All authors collected the patient data. LTN and HVT analyzed the data. DTC, LTN and HVT drafted the manuscript. DTC and HVT revised and edited the manuscript. DTC, NKD and BPV supervised the study. THNT, BPV and LTN confirm the authenticity of all the raw data. All authors have read and agreed to the published version of the manuscript.

### Ethics approval

The present study was approved by the Institute of Genome Research Institutional Review Board, Vietnam Academy of Science and Technology according to the decision number: 02-2022/NCHG-HĐĐĐ on March 09, 2022.

### Patient consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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