Original Article

Prevalence of Malnourished Status and its Relationship to Surgical Outcomes in Women Undergoing Surgery for Gynecologic Cancers

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Background: Malnutrition in cancer patients is an important problem and is associated with adverse clinical outcomes.

Objective: To determine the prevalence of malnutrition in women with gynecologic cancers undergoing surgery in Rajavithi Hospital, Thailand, and to identify malnutrition-associated risk factors for adverse surgical outcomes.

Materials and Methods: This prospective study was conducted on 200 women with gynecologic cancer undergoing elective surgery at Rajavithi Hospital between November 26th, 2015 and March 10th, 2016. The nutritional status of participants, assessed by subjective global assessment, length of hospital stay and postoperative complications at 7 and 30 days post-surgery, were recorded. Postoperative complications were classified according to the Clavien classification system.

Results: Malnourished patients accounted for 25.5% of participants. Factors associated with malnutrition status included ovarian, Fallopian tube and peritoneal cancers, advanced or recurrent stage of disease, high Eastern Cooperative Oncology Group score, low serum albumin concentrations, and a high platelet-to-lymphocyte ratio. A statistical interaction between subjective global assessment and serum albumin was a significant prognostic factor for postoperative complications (adjusted odds ratio 10.9, $p = 0.018$) and length of hospital stay (adjusted mean difference 8.3 days, $p<0.001$). Respiratory complications were more common in moderately-malnourished than in well-nourished participants (22.0 vs. 3.8%, $p<0.001$).

Conclusion: Malnutrition is a significant problem which is found in approximately 21% of gynecologic cancer patients. Pre-operative malnutrition is an important predictor of poor clinical outcomes in those undergoing surgery.

Keywords: Nutrition, Operative outcomes, Gynecologic cancer

J Med Assoc Thai 2019;102(Suppl.4):61-8
Website: http://www.jmatonline.com

Malnutrition is a common problem in hospitalized patients, especially in cancer and older patients. The prevalence of malnutrition in hospitalized patients is high, reportedly ranging from 20.0 to 50.0%[1-4]. Malnutrition is a multifactorial condition, caused by the metabolic effects of underlying diseases and reduced nutritional intake. It is associated with adverse clinical outcomes such as morbidity, disability, prolonged length of hospital stays and increased hospital costs. It has been suggested that up to 20.0% of cancer patients may die from the effects of malnutrition rather than from the malignancy itself[5].

Patients who undergo abdominal surgery are at greater risk of malnutrition because of the prolonged periods of starvation required before and after operations, and increased post-surgery catabolism. Patients with a degree of preoperative malnutrition therefore have a higher risk of developing postoperative complications than those who are well-nourished. The prevalence of malnutrition in surgical patients has been reported by previous studies as ranging from 40% to 65%[6-9]. This high prevalence suggests that it is important to screen cancer patients for malnutrition to provide early nutritional support and treatment. However, data on nutritional status and the prevalence of malnutrition in Thai gynecologic cancer patients are limited.

The objective of the present study was to determine the prevalence of malnutrition in Thai women with gynecologic cancer undergoing surgery in Rajavithi Hospital, Thailand, and to identify malnutrition-associated risk factors for adverse surgical outcomes.

Materials and Methods

This prospective study was conducted at the Department of Obstetrics and Gynecology, Rajavithi Hospital, from November 26th, 2015 and March 10th, 2016. After Institutional Review Board approval had been obtained, gynecologic cancer patients with scheduled elective gynecologic surgery were prospectively enrolled, and all

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How to cite this article: Yanaranop M, Nutcharas T. Prevalence of Malnourished Status and its Relationship to Surgical Outcomes in Women Undergoing Surgery for Gynecologic Cancers. J Med Assoc Thai 2019;102(Suppl.4):61-8.

participants gave written informed consent.

Participants were admitted for preoperative preparation at least 24 hours prior to surgery. Clinical data were collected including age, body mass index (BMI), gynecologic cancer types and International Federation of Gynecologists and Obstetricians staging, underlying diseases, American Society of Anesthesiologists (ASA) physical status classification, and Eastern Cooperative Oncology Group (ECOG) performance status score. Pre-operative nutritional evaluation was conducted using subjective global assessment (SGA), and blood samples for complete blood count (CBC) including hemoglobin concentration, platelet count, white blood cell count, absolute neutrophil count, total lymphocyte count (TLC), serum albumin and ferritin were drawn in the 24 hours prior to surgery. The neutrophil-to-lymphocyte ratio (NLR) was defined as the absolute neutrophil count divided by the TLC, and the platelet-to-lymphocyte ratio (PLR) was defined as the platelet count divided by the TLC. In the postoperative period, all participants followed up for surgical complications at 7 and 30 days after surgery, and the length of postoperative hospital stay (LOS) was recorded. Those women who underwent emergency surgery, had no nutritional assessment conducted, had no CBC, serum albumin or serum ferritin results, had no gynecologic cancer, who cancelled surgery, or were lost to follow-up, were excluded. To determine a participant's nutritional status according to SGA, the authors obtained clinical history information including weight loss, changes in dietary intake, gastrointestinal symptoms and functional capacity, as well as information from a physical examination including muscle wasting, and edema or ascites. On the basis of SGA, participants were classified as category A (well-nourished), category B (moderately malnourished), or category C (severely malnourished)[10-12].

Five ml of blood was collected in a tube that allowed clotting and 5 ml into an EDTA tube. Blood tubes were processed immediately or stored at -20°C until analysis. Clotted blood tubes were centrifuged at 800 g for 10 min and serum was collected. Serum albumin concentrations were analyzed using a Cobas c701/c702 series analyzer (Roche Diagnostics, Indianapolis, IN, USA) and serum ferritin concentrations were analyzed using a Cobas e602 series analyzer (Roche Diagnostics). For CBC, 3 ml of blood was collected by peripheral venous puncture into an EDTA tube. CBC was analyzed using the UniCel® DxH 800 Coulter® cellular analysis system (Beckman Coulter; Miami, FL, USA). The Clavien classification system[13] was chosen for use as a standardized classification system to monitor postoperative complications. In this system, the severity grading is based on the type of therapy used to correct a specific complication as follows: grade 1, minor risk events that do not require any specific therapy; grade 2, complications that are effectively treated with drugs, blood transfusion, physiotherapy or nutritional support; grade 3, complications that require intervention treatment; grade 4, life-threatening complications requiring ICU management; grade 5, complications resulting in the death of the patient.

Sample size calculation was performed using the formula for estimating proportion[14] "$N = (Z_{\alpha/2})^2 p(1-p)/d^2$" with a type I error of 0.05. The authors incorporated the relative incidence of malnutrition in gynecologic cancer patients from the study of Hertlein et al[15] into the calculation. The output indicated that at least 143 subjects were required for the study, suggesting that at least 179 subjects be enrolled in anticipation of a dropout rate of 20%.

Data were analyzed using IBM SPSS Statistics version 22.0. Continuous data were assessed for normality with the Shapiro-Wilk test. Characteristics of participants, serum biomarkers and predictive scores were summarized using mean (SD) for normally distributed continuous variables, median and interquartile range (IQR) for non-normally distributed continuous variables, and percentage for categorical variables. Comparisons of continuous variables were performed using the Student's t-test or Mann-Whitney U test, as appropriate. Comparisons of categorical variables were performed using the binomial test, Chi-square test or Fisher's exact test, as appropriate. Stratified analyses were performed for the assessment of confounding factors and statistical interactions. Risk factors for malnutrition and surgical outcomes were analyzed using the univariate and multivariate binary logistic, ordinal logistic and linear regression tests. A probability (*p*-value) of less than 0.05 was considered significant.

Results

During the study period, a total of 215 patients were enrolled. Of these, 15 were excluded as follows: 8 cases did not undergo SGA assessment before surgery, 4 cases were not diagnosed as having gynecologic cancer, and 3 cases cancelled their surgery.

Of the remaining 200 participants, 159 (79.5%) presented as well-nourished (SGA-A) and 41 (20.5%) as moderately malnourished (SGA-B) at the time of admission. No participants were severely malnourished (SGA-C). Results of the comparison between SGA-A and SGA-B participants of clinical characteristics and laboratory assessments are presented in Table 1. There were no significant differences between groups in age, BMI or underlying diseases, which were most commonly diabetes mellitus and/or chronic hypertension. However, compared with SGA-A, SGA-B participants had the following significant results: a greater frequency of ovarian/tube/peritoneal cancers and advanced or recurrent disease; a higher ASA physical status classification and ECOG performance status score; lower serum albumin concentrations, hemoglobin levels and TLC; and higher PLR, NLR, and serum ferritin concentrations. The following were significantly associated with malnutrition (Table 2): ovarian/tube/peritoneal cancers (adjusted odds ratio (aOR) 7.0, 95% CI 2.6 to 18.9, $p<0.001$); advanced or recurrent disease (aOR 4.8, 95% CI 1.8 to 12.7, $p = 0.001$); higher ECOG performance status score (ECOG = 1: aOR 4.1, 95% CI 1.1 to 15.1, $p = 0.034$; ECOG = 2: aOR 10.3, 95% CI 1.9 to 58.6, $p = 0.008$); lower serum albumin concentrations (aOR 0.4, 95% CI 0.2 to 0.9, $p = 0.017$); and higher PLR

Table 1. Baseline characteristics of well-nourished (subjective global assessment (SGA) category A) and moderately malnourished (SGA-B) gynecologic cancer patients

Variables	SGA-A (n = 159)	SGA-B (n = 41)	*p*-value
Age (years)	52.83±11.71	54.52±9.24	0.377
<50	64 (40.3)	14 (34.1)	0.475
>50	95 (59.7)	27 (65.9)	
BMI (kg/m^2), mean (SD)	25.53±5.91	25.51±6.63	0.978
<18.5	14 (8.8)	4 (9.8)	0.447
18.5 to 24.9	67 (42.1)	21 (51.2)	
25 to 29.9	51 (32.1)	8 (19.5)	
>30	27 (17.0)	8 (19.5)	
Cancer			<0.001*
Uterine cervix	49 (30.8)	1 (2.4)	
Uterine corpus	58 (36.5)	6 (14.6)	
Ovary/tube/peritoneum	46 (28.9)	31 (75.6)	
Other	6 (3.8)	3 (7.3)	
Staging			<0.001*
Early	120 (75.5)	12 (29.3)	
Advanced/recurrent	39 (24.5)	29 70.7)	
Underlying disease			0.861
No	80 (50.3)	20 (48.8)	
Yes	79 (49.7)	21 (51.2)	
ECOG performance status			<0.001*
0	71 (44.7)	5 (12.2)	
1	82 (51.6)	26 (63.4)	
2	6 (3.8)	10 (24.4)	
ASA physical status classification			<0.001*
1	43 (27.0)	4 (9.8)	
2	102 (64.2)	24 (58.5)	
3 to 4	14 (8.8)	13 (31.7)	
Serum albumin (g/dL)	4.16±0.47	3.63±0.75	<0.001*
≤3.5 (%)	16 (10.1)	18 (43.9)	<0.001*
>3.5 (%)	143 (89.9)	23 (56.1)	
Hemoglobin (g/dL)	11.53±1.44	10.51±1.52	<0.001*
TLC (x10^3/mm^3)	2.14±0.82	1.83±0.71	0.019*
PLR, median	168.84 (82.91)	277.03 (235.72)	<0.001*
NLR, median	2.24 (2.03)	4.91 (3.72)	<0.001*
Log (serum ferritin, µg/L)	2.01±0.42	2.24±0.51	0.005*

ASA = American society of anesthesiologists; BMI = body mass index; ECOG = eastern cooperative oncology group; IQR = interquartile range; NLR = neutrophil-to-lymphocyte ratio; PLR = platelet-to-lymphocyte ratio; SD = standard deviation; TLC = total lymphocyte count. Values were represented as n (%), mean ± SD, median (IQR), * Significant at $p<0.05$

(aOR 1.7, 95% CI 1.2–2.4, $p = 0.004$).

The frequency of postoperative complications in SGA-B participants tended to be higher than in SGA-A participants (36.6% vs. 22.0%, $p = 0.055$) (Table 3). Respiratory complications including atelectasis, pneumonia, bronchiectasis and pleural effusion were significantly more common in SGA-B than SGA-A participants (22.0% vs. 3.8%, $p < 0.001$). Using the Clavien classification system for surgical complications, the severity of complications was significantly greater in SGA-B than SGA-A participants (Grade 2, RR 1.5; Grade 3, RR 3.2; $p = 0.003$).

The following were found to be significant prognostic factors for surgical complications (Table 4): SGA status, serum albumin concentration, and ASA physical status classification. From multivariate analysis, the significant prognostic factors for the more severe Clavien grades were statistical interaction between SGA and serum albumin (aOR 10.9, 95% CI 1.5 to 78.9, $p = 0.018$), and ASA physical status classification (ASA 2, aOR 4.1, 95% CI 1.2 to 14.5, $p = 0.028$; ASA 3 to 4, aOR 8.1, 95% CI 1.9 to 34.7, $p = 0.005$).

The following were found to be significant prognostic factors for LOS (Table 5): SGA status and serum albumin concentration. There was a significant statistical interaction between SGA status and serum albumin concentration associated with LOS (adjusted MD 8.3 days, 95% CI 4.1 to 12.6, $p<0.001$).

Discussion

Postoperative morbidity is an important problem, and it is increasingly being acknowledged that postoperative

Table 2. Risk factors significantly associated with malnutrition in gynecologic cancer patients identified by multivariate binary logistic regression analysis

Variables	Total	SGA-B (n = 41)				
		%	cOR	aOR	95%CI	p-value
Ovarian/Tube/Peritoneal cancer	77	40.3	7.6	7.0	2.6 to 18.9	<0.001*
Advanced stage/Recurrence	68	42.7	7.4	4.8	1.8 to 12.7	0.001*
ECOG = 1	108	24.1	4.5	4.1	1.1 to 15.1	0.034*
ECOG = 2	16	62.5	23.7	10.3	1.9 to 58.6	0.008*
Serum albumin (every 1 g/dL increase)	200	20.5	0.2	0.4	0.2 to 0.9	0.017*
PLR (every 100 increase)	200	20.5	2.0	1.7	1.2 to 2.4	0.004*

aOR = adjusted odds ratio; CI = confidence interval; cOR = crude odds ratio; ECOG = eastern cooperative oncology group; OR = odds ratio; PLR = platelet-to-lymphocyte ratio; SGA = subjective global assessment; SGA-B = moderately malnourished status
* Significant at p<0.05

Table 3. Comparison of surgical complications between well-nourished (subjective global assessment (SGA) category A) and moderately malnourished (SGA-B) gynecologic cancer patients

Surgical outcomes	SGA-A (n = 159)	SGA-B (n = 41)	RR	95% CI	p-value
Post-operative complications (%)	35 (22.0)	15 (36.6)	1.7	1.0 to 3.0	0.055
Wound	8 (5.0)	4 (9.8)	1.7	0.7 to 4.0	0.256
Cardiac	1 (0.6)	1 (2.4)	2.5	0.6 to 10.2	0.299
Respiratory	6 (3.8)	9 (22.0)	3.5	2.1 to 5.8	<0.001*
Neurological	2 (1.3)	0 (0.0)			1.000
Gastrointestinal	2 (1.3)	1 (2.4)	1.6	0.3 to 8.3	0.579
Renal	17 (10.7)	2 (4.9)	0.5	0.1 to 1.9	0.258
VTE	4 (2.5)	1 (2.4)	1.0	0.2 to 5.8	0.978
Other	1 (0.6)	2 (4.9)	3.4	1.4 to 7.9	0.046*
Clavien classification of surgical complication (%)					0.003*
Grade 1	131 (82.4)	26 (63.4)	-		
Grade 2	21 (13.2)	8 (17.1)	1.5	0.7 to 3.1	
Grade 3 to 4	7 (4.4)	7 (19.5)	3.2	1.8 to 5.8	

CI = confidence interval; RR = relative risk; VTE = venous thromboembolism
* Significant at p<0.05

complications are not solely related to the type of surgery. Malnutrition is potentially reversible, so its early recognition and effective treatment may play a pivotal role in reducing postoperative complications[16].

There is little information available on the assessment of nutritional status of patients with gynecologic cancers[17-20]. Malnutrition was found in approximately 20.5% of 200 study participants, and these participants had a higher postoperative complication rate and a longer LOS. The prevalence of malnutrition in this study is comparable to that reported by studies of hospitalized patients in general, i.e., 20 to 50%[1-4], but less than that reported by studies of surgical patients specifically i.e., 40 to 65[6-9]. Hertlein et al[15] evaluated the nutritional status of gynecologic patients using the Nutritional Risk Screening (2002) system and found that 35.8% were severely malnourished (nutritional risk screening score ≥3).

Risk factors significantly associated with malnutrition in the present study were ovarian/tube/peritoneal cancers, advanced or recurrent disease, high ECOG performance status score, low serum albumin concentration, and high PLR. A study of gynecologic cancer patients by Laky et al[20] reported that ovarian cancer (OR 19.8, 95% CI 3.0 to 129.8, p = 0.002) and serum albumin concentration (OR 0.7, 95% CI 0.6 to 0.9, p<0.001) were significant factors predicting moderate malnutrition. Albumin is an objective parameter often used in clinical studies to measure long-standing malnutrition. Systematic inflammatory response (SIR) is closely associated with malnutrition and cancer cachexia, and NLR and PLR have been shown to act as indicators of SIR[21]. Clinical evidence has shown that activation of the SIR is one of the earliest and most important factors contributing to cachexia[22].

Postoperative complications in the present study were found in 25.0% of participants, and moderately malnourished participants had a 36.6% risk of developing

Table 4. Significant prognostic factors for postoperative complications in gynecologic cancer patients identified by univariate and multivariate ordinal logistic regression analysis

Variables	Clavien classification (Grade)			cOR	(95%CI)	p-value	aOR	(95%CI)	p-value
	1 (%)	2 (%)	3 to 4 (%)						
Nutrition status									
SGA-A	131 (82.4)	21 (13.2)	7 (4.4)	1.0			1.0		
SGA-B	26 (63.4)	7 (17.1)	8 (19.5)	3.0 (1.4, 6.3)	0.004*	0.8	(0.2, 2.4)	0.629	
Serum albumin (g/dL)									
> 3.5	137 (82.5)	22 (13.3)	7 (4.2)	1.0			1.0		
≤ 3.5	20 (58.8)	6 (17.6)	8 (23.5)	3.8	(1.8, 4.3)	0.001*	0.9	(0.2, 3.3)	0.845
Nutrition status x Serum albumin	7 (38.9)	3 (16.7)	8 (44.4)	5.5	(2.5-12.1)	<0.001*	10.9	(1.5, 78.9)	0.018*
ASA physical status classification									
1	44 (93.6)	3 (6.4)	0 (0.0)	1.0			1.0		
2	98 (77.8)	19 (15.1)	9 (7.1)	4.3	(1.2, 14.8)	0.022*	4.1	(1.2, 14.5)	0.028*
3 to 4	15 (55.6)	6 (22.2)	6 (22.2)	12.9	(3.2, 51.4)	<0.001*	8.1	(1.9, 34.7)	0.005*
ECOG performance status									
0	67 (88.2)	6 (7.9)	3 (3.9)	1.0					
1	80 (74.1)	20 (18.5)	8 (7.4)	2.5	(1.1, 5.7)	0.025*			
2	10 (62.5)	2 (12.2)	4 (25.0)	5.3	(1.5, 18.1)	0.008*			
Staging									
Early	111 (84.1)	15 (11.4)	6 (4.5)						
Advanced/Recurrent	46 (67.6)	13 (19.1)	9 (13.2)	2.6	(1.3, 5.1)	0.006*			

aOR = adjusted odds ratio; ASA = American Society of Anesthesiologists; CI = confidence interval; cOR = crude odds ratio; ECOG = Eastern Cooperative Oncology Group; OR = odds ratio; SGA = subjective global assessment; SGA-A = well-nourished status; SGA-B = moderately malnourished status; x = statistical interaction. * Significant at $p<0.05$

Table 5. Significant prognostic factors for length of hospital stay in gynecologic cancer patients identified by univariate and multivariate linear regression analysis

Variables	LOS (days)		MD	(95% CI)	*p*-value	Adjusted MD	(95% CI)	*p*-value
	Mean	SD						
Nutrition status					0.029*			0.250
SGA-A	8.1	4.5						
SGA-B	10.3	8.3	2.1	(0.2, 4.0)		-1.4	(-3.7, 1.0)	
Serum albumin (g/dL)								0.656
>3.5	8.0	4.4						
≤3.5	11.3	8.9	3.3	(1.3, 5.3)	0.001*	-0.6	(-3.3, 2.1)	
Nutrition status x Serum albumin	14.6	11.0	5.1	(4.1, 9.1)	<0.001*	8.3	(4.1, 12.6)	<0.001*
ASA physical status classification								
1	7.4	3.4	Ref.					
2	8.3	5.2	1.0	(-0.9, 2.8)	0.301			
3 to 4	11.5	8.4	4.1	(1.6, 6.7)	0.002*			
Staging					0.007*			
Early	7.8	4.4						
Advanced/recurrent	10.0	7.0	2.2	(0.6, 3.8)				

ASA = American society of Anesthesiologists; CI = confidence interval; LOS = length of hospital stays; MD = mean difference; SD = standard deviation; SGA = subjective global assessment; SGA-A = well-nourished status; SGA-B = moderately malnourished status; x = statistical interaction

* Significant at $p<0.05$

these problems after surgery. This was higher than the 22.8% complication risk for malnourished patients reported by Hertlein et al[15]. A statistical interaction between SGA and serum albumin concentration was a significant prognostic factor for postoperative complications (adjusted OR 10.9, $p = 0.018$) and LOS (adjusted mean difference 8.3 days, $p<0.001$). The risk of respiratory complications was significantly higher for our moderately malnourished participants than our well-nourished participants. This was similar to the findings of the study of Lunardi et al[23], in which the risk of respiratory complications for patients undergoing upper abdominal surgery was higher in the malnourished group (31%) than in the control group (11%) ($p = 0.050$). In patients undergoing abdominal surgery, malnutrition is associated with weakness of expiratory muscles, decreased chest wall expansion, and increased incidence of pulmonary complications[23].

LOS is associated with cancer patients' well-being during hospital treatment. Reducing LOS has the potential to lower the risk of infection and other hospital-acquired diseases, to improve patients' quality of life and to reduce healthcare costs. Previous studies have reported that malnutrition is associated with prolonged LOS in hospitalized patients requiring treatment for various types of cancer[10, 24]. Laky et al[25] found that malnutrition, low quality of life scores, and advanced stages of ovarian cancer were the major determinants of a prolonged LOS among gynecologic cancer patients.

Both subjective and objective nutritional assessment tools can serve as predictors of postoperative morbidity and mortality. In a study by Kathiresan et al[19], serum albumin concentration was identified as a nutritional parameter of gynecologic cancer patients where decreased albumin was significantly associated with more postoperative complications, hospital readmissions, reoperations and ICU admissions. In another study by Hertlein et al[15], gynecologic patients with a severe risk of malnutrition had a significantly higher complication rate than those with good nutritional status (22.8% vs. 7.8%, $p<0.001$) and their median LOS increased significantly from 7 to 10 days ($p<0.001$).

The ASA physical status classification is the most widely used patient assessment scheme in anesthesia. In the present study, ASA classification was an important prognostic factor for postoperative complications. Associations between ASA classification and surgical complications and outcomes have been reported in the literature[26]; for instance, Wolters et al[27] found a significant association between ASA classification and postoperative outcomes in a prospective study of 6,301 surgical patients.

The present study had some limitations. In particular, the nutritional assessments were performed as static evaluations before surgery, and no dynamic evaluations, which may be more informative for the study of associations between malnutrition and clinical outcomes, were performed after surgery. However, prospective studies like the present one are useful for determining temporal sequences and reducing information bias. In addition, the present study incorporated nutritional assessment parameters and other comorbidity variables. The authors found that nutritional status had a separate influence on clinical outcomes in gynecologic cancer patients. Interventional studies providing nutritional support to malnourished gynecologic patients are thus required, and the authors believe they have the potential

to guide patient management strategies.

In conclusion, malnutrition is a common problem found in approximately 21% of patients, and it is an important prognostic factor for adverse surgical outcomes in gynecologic cancer patients. Screening for risk of malnutrition should be integrated into the overall assessment of gynecologic cancer patients to identify those patients for whom nutritional support before surgery should be considered. SGA and serum albumin concentration are two simple nutritional assessment tools suitable for clinical practice.

What is already known on this topic?

Malnutrition is significantly related to higher postoperative complications and longer length of hospital stay.

What this study adds?

In the present study, malnutrition was a significant problem for women with gynecologic cancer, and it was found in 20.5% of gynecologic cancer patients undergoing elective surgery. Ovarian/tube/peritoneal cancer, advanced or recurrent disease, higher ECOG performance status, low serum albumin concentration and higher platelet-to-lymphocyte ratio were significantly associated with malnutrition status. Preoperative assessment of subjective global assessment accompanied with serum albumin concentration is a significant predictor for postoperative complications and length of hospital stay. Postoperative pulmonary complications were found to be significantly more common in malnourished patients.

Potential conflict of interest

The authors declare no conflicts of interest.

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