Assessment of nutritional status, performance status scores, Glasgow prognostic score
and their relationship in advanced squamous carcinoma of the esophagus

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A Thesis Submitted in Partial Fulfillment of the Requirements
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การประเมินและการหาความสัมพันธ์ของภาวะโภชนาการในโรคมะเร็งหลอดอาหารแบบแอด
วานซ์สเควมัสคาร์สิโนมา เพอร์ฟอร์มานซ์สเตตัสสกอร์และกลาสโกว์พรอกโนสติกสกอร์

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แทรน โชว หยูเจิ้น : การประเมินและการหาความสัมพันธ์ของภาวะโภชนาการในโรคมะเร็งหลอดอาหาร แบบแอควานซ์สเควมัสคาร์สิโนมา เพอร์ฟอร์มานซ์สเตตัสสกอร์และกลาสโกว์พรอกโนสติกสกอร์ (Assessment of nutritional status, performance status scores, Glasgow prognostic score and their relationship in advanced squamous carcinoma of the esophagus) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: รศ. ดร. จงจิตร อังคทะวานิช, อ.ที่ปรึกษาวิทยานิพนธ์ร่วม: Do Anh Tu,Ph.D., 137 หน้า.

ที่มาและความสำคัญ : มะเร็งหลอดอาหารเป็นมะเร็งที่พบมากเป็นอันดับที่แปดในกลุ่มโรคมะเร็งทั่วโลกและมีอุบัติการณ์เพิ่มขึ้นอย่างรวดเร็ว ผู้ป่วยมะเร็งหลอดอาหารนั้นมักมาพบแพทย์เมื่อความรุนแรงดำเนินไปจนถึงระยะท้ายๆ ซึ่งผู้ป่วยเหล่านี้มักมีภาวะทุพโภชนาการและมีความผิดปกติในการกลืนอาหารแล้ว ฉะนั้นจึงมีความจำเป็นในการการประเมินความรุนแรงของภาวะทุพโภชนาการในคนไข้กลุ่มนี้และแสวงหาสิ่งบ่งชี้ที่เกี่ยวข้องกับภาวะ โภชนาการเพื่อช่วยในการระบุปัญหาทางคลินิก

จุดประสงค์ : เพื่อประเมินภาวะโภชนาการของผู้ป่วยมะเร็งหลอดอาหาร และศึกษาความสัมพันธ์ระหว่างภาวะโภชนาการ คะแนนประเมินความสามารถของกิจกรรมทางกายผู้ป่วย และคะแนนการพยากรณ์โรค

กลุ่มตัวอย่างและวิธีศึกษา

การศึกษาทางคลินิก ชนิดการวิจัยแบบตัดขวาง ดำเนินการระหว่างเดือนสิงหาคม 2557 ถึงเดือนกุมภาพันธ์ 2558 ณ โรงพยาบาลมะเร็งแห่งชาติ กรุงฮานอย ประเทศเวียดนาม ผู้ป่วยเพศชายที่มีมะเร็งหลอดอาหารในระยะที่สามและสี่จะถูกประเมินภาวะโภชนาการโดยการใช้แบบสอบถามพีจีเอสจีเอ เอสจีเอ ดัชนีมวลกาย ค่างรอบขนาดของแขนท่อนบน พลังงานและโปรตีนที่ได้รับต่อวัน การเปลี่ยนแปลงของน้ำหนักตัว คะแนนประเมินของคานอฟสกี้ คะแนนอีซีโอจี และคะแนนการพยากรณ์โรคของกลาสโกว์

ผลการศึกษา

จากการศึกษาผู้ป่วยชายจำนวน 64 ราย พบว่าค่าเฉลี่ยบวกลบส่วนเบี่ยงเบนมาตรฐานของคะแนนพีจีเอสจีเอมีค่าเท่ากับ 9.88 ± 4.41 ซึ่งมีผู้ป่วยที่ได้รับการประเมินเอสจีเอและจัดอยู่ในระดับบี คิดเป็นร้อยละ 44 และระดับซีคิดเป็นร้อยละ 6.2 การประเมินค่าดัชนีมวลกายพบว่ามีผู้ป่วยที่อยู่ในเกณฑ์น้ำหนักตัวต่ำกว่ามาตรฐานคิดเป็นร้อยละ 43.8 การประเมินค่างรอบขนาดของแขนท่อนบนพบว่ามีผู้ป่วยที่มีภาวะทุพโภชนาการคิดเป็นร้อยละ 29.7 การประเมินการได้รับพลังงาน พบว่ามีผู้ป่วยร้อยละ 54.7 ที่ได้รับพลังงานต่ำกว่า 25 กิโลแคลอรีต่อน้ำหนักตัว 1 กิโลกรัมและมีผู้ป่วยร้อยละ 48.4 ที่ได้รับโปรตีนต่ำกว่า 1 กรัมต่อน้ำหนักตัว 1 กิโลกรัม มีการสูญเสียน้ำหนักตัวภายในช่วงเวลาต่างๆ ก่อนการประเมิน โดยน้ำหนักลดในช่วงสองสัปดาห์คิดเป็นร้อยละ 68.8 ในช่วง 1 เดือนคิดเป็นร้อยละ 84.4 และในช่วง 6 เดือนคิดเป็นร้อยละ 92.2 จากผลดังกล่าวพบว่าคะแนนพีจีเอสจีเอและเอสจีเอมีความสัมพันธ์อย่างมากกับคะแนนเคพีเอส (สัมประสิทธิ์ความสัมพันธ์คิดเป็น 0.717 และ 0.632 ตามลำดับ ที่ระดับนัยสำคัญต่ำกว่า 0.001) และคะแนนอีซีโอจี (สัมประสิทธิ์ความสัมพันธ์คิดเป็น 0.672 และ 0.626 ที่ระดับนัยสำคัญต่ำกว่า 0.001) แต่คะแนนพีจีเอสจีเอและเอสจีเอกลับมีความสัมพันธ์น้อยกับคะแนนการพยากรณ์โรคของกลาสโกว์ (สัมประสิทธิ์ความสัมพันธ์คิดเป็น 0.332 ที่ระดับนัยสำคัญน้อยกว่า 0.01) นอกจากนี้ไม่พบความสัมพันธ์ระหว่างคะแนนการพยากรณ์โรคของกลาสโกว์ กับค่าต่อไปนี้: คะแนนประเมินของคานอฟสกี้ คะแนนอีซีโอจี ค่าดัชนีมวลกาย ค่างรอบขนาดของแขนท่อนบน การได้รับพลังงานและโปรตีนต่อวันและการเปลี่ยนแปลงของน้ำหนักตัว

สรุปผลการศึกษา

ภาวะทุพโภชนาการ การเปลี่ยนแปลงของน้ำหนักตัวและการได้รับพลังงานและโปรตีน ไม่เพียงพอถือว่าเป็นประเด็นที่สำคัญในผู้ป่วยมะเร็งหลอดอาหาร การประเมินคะแนนพีจีเอสจีเอและเอสจีเอ มีความสัมพันธ์อย่างมากกับคะแนนการประเมินคานอฟสกี้แต่มีความสัมพันธ์น้อยกับดัชนีชี้วัดการพยากรณ์โรค

คำสำคัญ

มะเร็งหลอดอาหาร ภาวะโภชนาการ คะแนนประเมินของคานอฟสกี้ คะแนนอีซีโอจี คะแนนการพยากรณ์โรคของกลาสโกว์ น้ำหนักลด

ภาควิชา	โภชนาการและการกำหนดอาหาร	ลายมือชื่อนิสิต _____
สาขาวิชา	อาหารและโภชนาการ	ลายมือชื่อ อ.ที่ปรึกษาหลัก _____
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5676855837 : MAJOR FOOD AND NUTRITION

KEYWORDS: ESOPHAGEAL CANCER, NUTRITION STATUS, PERFORMANCE SCORE, PROGNOSTIC SCORE, WEIGHT LOSS

TRAN CHAU QUYEN: Assessment of nutritional status, performance status scores, Glasgow prognostic score and their relationship in advanced squamous carcinoma of the esophagus. ADVISOR: ASSOC. PROF. JONGJIT ANGKATAVANICH, Ph.D., CO-ADVISOR: DO ANH TU, Ph.D., 137 pp.

Background: Esophageal was the eighth of leading kinds of cancer all over the world and the incidence rate is increasing rapidly. Most of esophageal cancer patients present with late stages at the point of admissions, when they had malnutrition and dysphagia. There is a need for determination of the magnitude of poor nutrition status in these patients and find the other helpful indicators associated with it to help in clinical detection.

Objectives: To determine the nutrition status of esophageal cancer patients and investigate the relationship between nutrition status, performance status scores and prognosis score.

Subjects and methods: A clinical, cross-sectional study was conducted from August 2014 to February 2015 at National Cancer Hospital, Hanoi, Vietnam. Male esophageal cancer patients stage III/IV were assessed for nutritional status (patient-generated subjective global assessment-PG-SGA score), SGA, BMI, mid-arm circumference-MAC, energy and protein intakes, weight change), Karnofsky Performance Score (KPS) and Eastern Cooperative Oncology Group- ECOG, and Glasgow prognostic the incidence rate is increasing rapidly Results: Sixty-four male patients enrolled in the study. The mean $\pm$ SD of PG-SGA score was 9.88 $\pm$ 4.41. Forty-four% of patients had class B and 6.2% in class C by SGA. Using BMI, 43.8% patients were underweight. By MAC, 29.7% patients were undernourished. Patients having energy intakes below 25 kcal/kg/d were 54.7%, and 48.4% consumed protein below 1g/kg/d. Weight loss in the past two weeks, one month, and six months occurred in 68.8%, 84.4% and 92.2% patients, respectively. PG-SGA and SGA correlated well with KPS ($r = -0.717$ and 0.632; $p < 0.001$) and ECOG ($r = 0.672$ and 0.626; $p < 0.001$) but weakly correlated with GPS ($r = 0.332$, $p < 0.01$ and 0.278, $p < 0.05$). KPS, ECOG, BMI, MAC, energy and protein intakes, and weight change did not correlate with GPS.

Conclusions: Malnutrition, weight change, and insufficient energy and protein intakes were noteworthy in esophageal cancer patients. Good correlation between PG-SGA and SGA with performance status were documented and to a lesser extent with prognosis index.

Department:	Nutrition and Dietetics	Student's Signature ....
Field of Study:	Food and Nutrition	Advisor's Signature ....
Academic Year:	2014	Co-Advisor's Signature ....

ACKNOWLEDGEMENTS

CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF DIAGRAMS

CHAPTER 1.

INTRODUCTION

1. Background of the study

1.1. Epidemiology of cancer

Cancer, along with cardiovascular diseases, diabetes and chronic respiratory diseases, are causes of an estimate of 35 million deaths in 2005 ([1]) Based on the GLOBOCAN 2008 estimates, about 12.7 million cancer cases and 7.6 million cancer related deaths occurred in 2008 worldwide; of these, 56% of the cases and 64% of the deaths occurred in the economically developing world ([2]).

Esophageal cancer has been ranking as the eighth of leading cancers all over the world with the incidence of 482,000 (3.8% of total) and was one of six leading causes of death due to cancer with 407,000 cases (5.4%) in 2008 ([2]). It is noticeable that most of incident and mortality cases (83% and 86%) were found in developing countries, which males are 2 to 4 times more common than females. The highest rates were found in Southern, Eastern Africa and Eastern Asia, and the lowest rate were observed in Western, Middle Africa and Central America in both males and females. In the South East Asia area, esophageal cancer rates are 2.6/100,000 in males and 1.3/100,000 in female; the incidence of this disease for males and females in 2008 was 6.7 and 3.8 thousand people, respectively; the mortality rate was 5.8 and 3.4 thousand people, respectively ([3]). In Vietnam, the overall age-standardized mortality rates in 2008 was estimated at 2.3/100,000 in males and 0.8/100,000 in females ([4]). It is undoubtable that the esophageal cancer trend is increasing rapidly when looking at the ratio between two periods of 2006-2007 and 1993-1998 (2.34: 1 in male and 1.43:1 in female) ([5]).

1.2. Malnutrition among cancer and esophageal cancer patients

Malnutrition is a common problem among cancer patients. The prevalence in earlier researches has ranged from 9% up to 85% ([6], [7]), depending on age, living areas, the tumor size, stage of disease, and type of treatment ([6], [8]). It can give a negative impact on patients' response to therapy. Consequently, it may increase the incidence of treatment related side effects and decreases survival ([7]). Malnutrition occurred in 60-

85% of esophageal cancer patients, and this was one of the main causes of treatment failure ([6]),([9]). Malnutrition may be due to tumor biology, pathophysiology of the disease, the side effects of cancer treatment and other unknown mechanisms. The most leading cause of malnutrition is cachexia, which includes anorexia, early satiety, tiredness, anemia, edema, weight loss, and loss of muscle ([9]). All cancer patients should be screened for malnutrition; those at risk should be referred to further assessment, and appropriate nutrition support plan would be developed accordingly ([10], [11]).

1.3. Characteristic of the patients

Most of esophageal cancer patients present with stage III/IV at the point of admissions ([12]), when they have dysphagia (74%) and weight loss (57%) ([13]). The late diagnosis leads to poor prognosis and the high morbidity/mortality rates ([14]). The pretreatment performance status in association with poor nutrition status resulted in early mortality has been shown in patients with locally advanced head and neck cancer undergoing concurrent chemo-radiation ([15]).

1.4. Performance status

Performance status is described as an assessment of the patients' actual function and their capability of self-care ([16]). Functional status assessment, including physical performance measures, have been recommended as a part of nutrition assessment for decades ([17]) . Among a number of metrics which have been developed to quantify performance status, the Eastern Cooperative Oncology Group performance score (ECOG) and Karnofsky performance score (KPS) are commonly used in cancer researches ([16]). Both KPS and ECOG are considered as prognostic factors in patient assessment ([18]).

1.5. Prognostic score

In clinical practice, prognostic tools will help health care staff in their clinical decisions. Complicated indices were less used or assessed inadequately. A preferred alternative is a single prognostic index, or perhaps a tool with a small number of indices ([19]). Over the past decades, the Glasgow Prognostic score, basing on serum albumin and C- reactive protein (CRP), has been considered as the most extensively

validated tool and therefore being used in routine clinical assessment activities for patients with cancer (20) and was considered as a nutrition-based management in cancer patients (21).

2. Problem justification

- The current situation in Vietnam: Hospital overload has become a significant challenge for the health sector in the recent years. Hospital overload is particularly serious at central hospitals and in big cities. According to the project report of Ministry of Health"Reducing hospital overload 2013 -2020", there is 6.74 doctors/10,000 population; one doctor have to examine from 60 to 80 patients/8 working hours/day (as reported in The Vietnam Annual health statistics 2012); Ideally, a doctor should be responsible for not more than 50 patients/8 working hours/day in 2015 (22). The National cancer hospital now do not have dietitian. The doctors also have to take care of patient's nutritional needs and the patients provide food for themselves (self prepared). Therefore, specific factors that provide the most useful information about the nutrition status of the patients and correlation between the current situation to the prognosis and treatment planning are nesscessary to be studied.

- For esophageal cancer: currently, the PG-SGA is still not routinely being used in clinical practice, and there is rarely published report on current nutritional status of esophageal cancer patients. Furthermore, there is no study showing the correlation between nutritional status, performance scores and Glasgow prognostic score in esophageal cancer patients.

3. Study objectives

The ESPEN guidelines 2014 on nutrition for cancer recommended the necessity of objective and quantitative assessments for nutritional intake, physical performance and the systemic inflammation among patients with abnormal screening (23). This study aimed to determine the nutrition status of esophageal cancer patients stage III/IV using Subjective Global Assessment (SGA), the Patient Generated Subjective Global Assessment (PG-SGA), anthropometric measurements (weight, height, BMI, mid arm circumference, triceps skinfold thickness, mid arm muscle area), energy and

protein intake assessment, in order to explore the relationship between nutrition status and performance scores such as Karnofsky performance score (KPS) and Eastern Cooperative Oncology Group (ECOG) and the Glasgow prognostic score (GPS).

This study aimed to:

1. Studied and evaluated nutrition status, performance status scores, and prognostic score of patients with esophageal cancer using Karnofsky performance score, Eastern Cooperative Oncology Group performance score and Glasgow prognostic score upon admission (pretreatment period).

2. Examined the relationship between nutritional status, performance status scores and Glasgow prognostic score in esophageal cancer patients.

In more details:

Step 1:

1. Evaluated nutrition status of esophageal cancer patient using full assessments (anthropometrics measurement, laboratory test, clinical assessment, 24- hour dietary intake assessment), and perform SGA, PG-SGA assessments upon admission (pretreatment period).

2. Assessed the performance status score using Karnofsky performance score and Eastern Cooperative Oncology Group performance score of esophageal cancer patient upon admission (pretreatment period).

3. Evaluated the prognosis in patients with esophageal cancer upon admission (pretreatment period) using Glasgow prognostic score.

Step 2:

Based on the results of step 1, the relationship between nutritional status, performance status scores and the Glasgow prognostic score were identified as described in this figure:
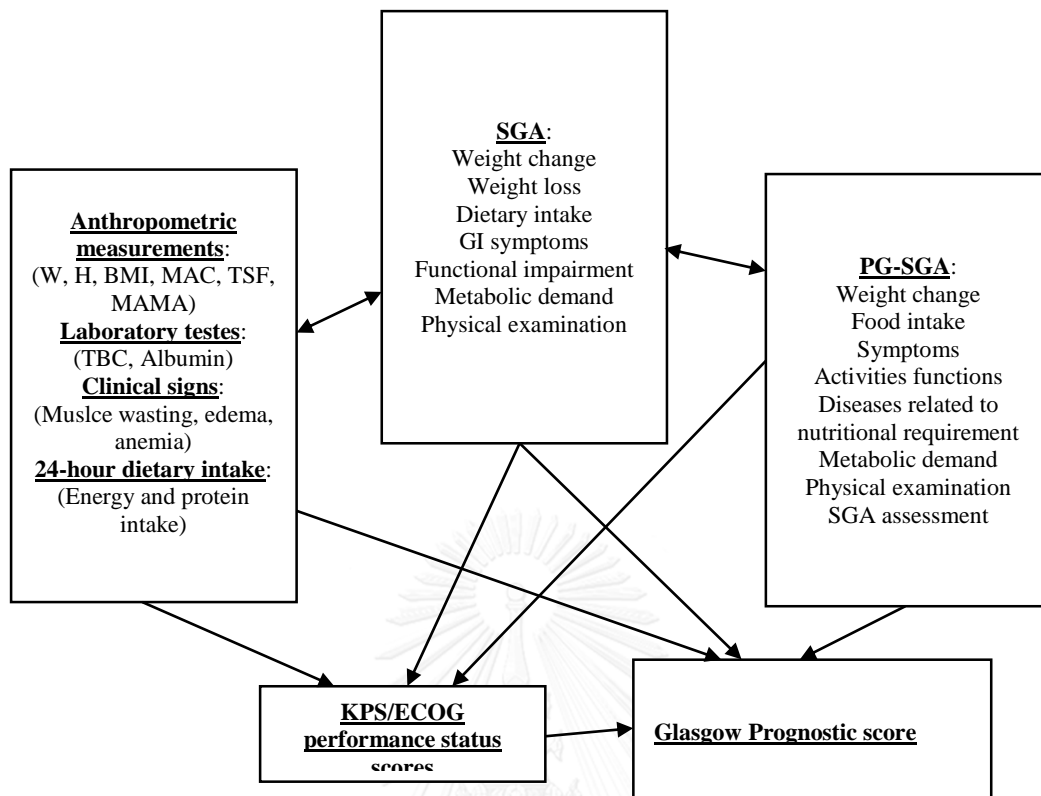
Diagram 1. Study objective

Step 3: Suggested nutrition indicators should be applied in clinical practice to find out the patients with advance esophageal cancer at high risk of nutrition malnutrition or require nutrition intervention.

4. Benefit of this study

The results of this study provided the picture of nutrition status, performance status scores, and also the Glasgow prognostic score of advanced esophageal cancer patients in Vietnam. The determined relationship between these indicators helped suggest the useful nutritional indicators so that practitioners can apply in their daily working to identify the patients at high risk or require nutrition intervention.

CHAPTER 2.

LITERATURE REVIEW

2. Overview on esophagus and esophageal cancer

2.1. Anatomy of the esophagus

The esophagus is a muscular tube that begins as the continuation of the pharynx in the neck (lower border of the sixth cervical vertebra), descends anteriorly to the vertebral column through the middle mediastinum and traverses the diaphragmatic hiatus into the abdomen at the level of the tenth thoracic. The length of the entire esophagus ranges from 19 to 25 cm (median 22 cm) in men, and 18 to 22 cm (median 21 cm) in women. Topographically, the esophagus is divided into 3 regions: cervical, thoracic, and abdominal. The wall of the esophagus consists of 4 layers: mucosa (epithelium, lamina propria, and muscularis mucosa), submucosa (which separates the mucosa and the muscularis propria; contains blood vessels, lymph vessels, nerves,elastic, and collagen fibers), muscularis propria (consists of an internal layer of circular fibers and an external layer of longitudinal fibers), and adventitia (a fibrous layer that covers the esophagus, connecting it with neighboring structures). Unlike other areas of the gastrointestinal tract it does not have a serosal layer. The esophagus has 2 intrinsic high-pressure zones called the upper esophageal sphincter the lower esophageal sphincter, which prevent reflux from the esophagus into the hypopharynx and from the stomach into the esophagus (24).

2.2. Pathology of esophageal cancer

Esophageal cancer has two common kinds of histopathology: Squamous cell carcinoma (SCC) and Adenocarcinoma. Other rarelies are melanoma, leiomyo sarcoma, and small-cell carcinoma. Squamous cell carcinoma (but not adenocarcinoma) is clearly linked to a low socioeconomic status.The risk factors are also different between these two kinds of cancer. Smoking, alcohol consumption, alcohol metabolism gene mutation, history of radiotherapy in the chest area, low social-economic situation, bad mouth hygien, and malnutrition are risk factors for squamous cell carcinoma. But for adenocarcinoma, the common risk factors are Gastro esophageal reflux disease (GERD) and Barret's esophagus disease (13, 25).

2.3. Clinical presentation

Dysphagia is the most common symptom of oesophageal carcinoma. In patients with SCC, the most common presentation is dysphagia, typically accompanied by weight loss and a history of smoking and alcohol intake. By contrast, most patients with adenocarcinoma are white men with a history of GERD who have recently developed dysphagia. Weight loss is not a frequent finding (25).

2.4. Staging of esophageal cancer

The International Union Against Cancer (UICC) and American Joint Committee on Cancer (AJCC) have staged esophageal cancer using the TNM system whereby T categorizes the depth of invasion into or through the esophageal wall, N is the status of regional lymph nodes, and M metastases to distant sites (27).

Table 1. TNM system

Primary tumor (T)

T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor confined to mucosa or invades lamina propria or submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades adventitia
T4	Tumor invades adjacent structures

Regional lymph nodes (N)

N0	No regional lymph node metastasis
N1	Regional lymph node metastasis

Distant metastasis

M0	No distant metastasis
M1	Distant metastasis

Table 2. Stage grouping

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2	N0	M0
	T3	N0	M0
Stage IIB	T1	N1	M0
	T2	N1	M0
Stage III	T3	N1	M0
	T4	Any N	M0
Stage IV	Any T	Any N	M1
Stage IVa	Any T	Any N	M1a
Stage IVb	Any T	Any N	M1b

Table 3. M categories

Tumors of the upper thoracic esophagus

M1a   Metastasis in cervical nodes

M1b   Other distance metastasis

Tumors of the mid-thoracic esophagus

M1a   Not applicable

M1b   Non-regional lymph nodes and/or other distant metastasis

Tumors of the lower thoracic esophagus

M1a   Metastasis in celiac lymph nodes

M1b   Other distant metastasis

According to European Society for Medical Oncology (ESMO group), optimal clinical staging for esophageal cancer should include clinical examination, blood counts, liver, pulmonary and renal function tests, endoscopy (including upper-aerodigestive tract endoscopy in case of tumors at or above the tracheal bifurcation), and a CT scan of chest and abdomen. In candidates for surgical resection endoscopic ultrasound has to be added to evaluate the T (and N) stage of the tumor; an esophagogram can be performed to assist in the planning of the surgical procedure (II, B). When available, positron emission tomography (PET) may be helpful in

identifying otherwise undetected distant metastases or in diagnosis of suspected recurrence. PET/CT is preferred over PET alone. In locally advanced (T3/T4) adenocarcinomas of the esophago-gastric junction (EGJ) infiltrating the anatomic cardia, laparoscopy can rule out peritoneal metastases. For selection of local treatments, the tumors should be assigned to the cervical or intrathoracic esophagus or to the EGJ. The stage is to be given to the TNM system with corresponding American Joint Committee on Cancer stage grouping (28).

The American National Comprehensive Cancer Network suggested to add endoscopies to determined the presence and location of esophageal cancer, to provide accurate T staging, including degree of differentiation and vascular and or lymphatic invasion (29).

2. Nutrition in esophageal cancer patient

Esophageal cancer patients are at the high risk of malnutrition. Tumor-related causes of malnutrition are more complex. Mechanical causes include dysphagia, food avoidance, and diet change to avoid foods known to cause dysphagia. Additionally, metabolic complications caused by tumor presence exist as well. Carbohydrate turnover is increased, insulin resistance occurs, and increased wasting of lactate occurs due to maladaptation of the Cori cycle. Derangements in protein metabolism include decreased catabolism, decreased synthesis, increased degradation, and an increase in the ubiquitin pathway for protein breakdown; all contribute to loss of skeletal and visceral muscle mass. Tumors produce lipid mobilizing factor, increase lipolysis, and decrease overall fat intake, resulting in loss of adipose tissue stores. Tumor treatment is also the cause of malnutrition. Surgical causes stress and malnutrition causes slowly wound healing. Chemotherapy attacks to the rapidly proliferating cells that cause damage the gastrointestinal cells; the lower red blood cells lead to increase the risk of infection and increase metabolism rates. Radiotherapy can cause malnutrition when combination with the chemotherapy, depending on the duration and position of treatment (9). Early nutrition support and routine follow up help improve the effectiveness of radiochemotherapy in esophageal cancer patients (30). Many clincal nutrition organizations worldwide have guidelines on nutrition support and/or nutrition care for esophageal cancer patients such as

ASPEN, ESPEN, ESMO, etc. In general, these organization requires the nutrition assessment, which includes anthropometry assessment, related biochemistry indices assessment, the patient's clinical situation assessment, dietary assessment and also the nutrition screening/assessment tools (such as SGA, PG-SGA). Patiens must be followed up on nutrition tollerance, the changes on anthropometry and biochemical indexes and clinical situation. These follow up may be daily, weekly or monthly, depending on each case (31), (29), (28), (32).

2.1. The anthropometric assessment

Anthropometric measurements provide basic information about nutrition status of patients. This is one of components of nutrition assessment process. Practically, anthropometric measurement includes weight, height, and BMI calculation. More specifically, some other information such as demispan, mid upper arm circumference (MUAC), hip circumference, calf circumference, biceps skinfold, triceps skinfold (TSF), subscapular skinfold, suprailiac skinfold, and medial calf skinfold are required. But all these measurements have potential errors in nutritional assessment (33). For hospitalized patients, some measurements often used are weight, height, BMI, MAMC and TSF (34). Anthropometric measurements are relatively quick, simple, cheap and non invasive. Its limitations include the extent to which measurement error can influence interpretation, and the length of time needed to take measurements (33).

Information from weight and height measurement is not enough and it normally requires more comprehensive measurement sets which include skinfolds and circumferences. But these techniques require trained staff and the more complicated measurement, the more bias we have (33). Jacquelin-Ravel (2012) had a review on body composition and oncology, the authorfound that BMI linked with treatment toxicity, but suggested that BMI was hard to use at least alone (35). Ryu (2010) concluded in a study on malnutrition among gastric cancer patients that a combination of objective and subjective assessments is needed for the early detection of the nutritional status in case of gastric cancer patients after gastrectomy (36).

Mid arm circumference (MAC) measurement is also the easy, cheap and invasivemethod in anthropometric assessment. The technique is simple with trained

staff with a tape measure. Tartari (2013) found that there was a relationship between MAC and the prognosis of non small cell lung cancer in patients at stage IV (37).

Triceps skin fold (TSF) measurement is a practical, inexpensive, and objective assessment of nutritional status. It measures subcutaneous fat and can evaluate both body fat and caloric stores (38).

Based on the MAC and TSF measurements, the Mid arm muscle area (MAMA) index can be calculated by a technique popularized by Jelliffe and co-workers, which described in previous study (37). This index, in combination with MAC and TSF, reflexes the muscle wasting and protein-calorie malnutrition (38).

2.2. The PG-SGA (Patient Generated- Subjective Global Assessment)

Both SGA and PG-SGA are suggested by The American Society for Parenteral & Enteral Nutrition (ASPEN) in cancer patient nutrition screening and assessment (10). These tools represent a good option for assessing nutritional status in various clinical situations, but its sensitivity is sub-optimal (39). Laky (2008) reported the PG-SGA significantly associated with subjective and objective parameters and is a widely recognized, clinically relevant method of evaluating nutritional status. PG-SGA seemed to be the most appropriate tool to identify malnourishment in gynecologic cancer patients (40). Bauer found that PG-SGA has more advantages than SGA in cancer patients (41). When comparing the three methods (SGA, MNA, PG SGA), Kubrak (2007) found that the PG-SGA had the most diagnostic value for patients with cancer (42).

2.3. Twenty four hour recall dietary intake

The twenty four hour (24-hour) recall dietary intake also has important role in nutrition assessment and is one of requirements on nutrition care process that suggested on current guidelines (10, 32, 43). This technique may be administered by a person with less training and in a short of time. The subject is required to recall his intake within last 24 hours (44). It provided rich detail about the types and amounts of foods consumed and the primary instrument used in surveillance. But the information was collected only within 24 hours, so it did not reflect the usual consumption. To treat the errors happened, it requires some techniques and some methods to control the

errors. To fulfill this gap, normally they combine 24-hour recall and food frequency questionnaire. However, the food frequency questionnaire is limited to a finite list of foods and are hampered by the inability of individuals to accurately report their food intake retrospectively over a long period of time. So the food frequency questionnair is more effective in epidemiology study. Another way is implement the multiple (two to seven) 24-hour recalls per respondent. But this causes unsatisfactory due to high respondent burden and low quality of reported information. Moreover, averages over a small number of days do not adequately represent individual usual intakes (44, 45).

2.4. Studies on nutrition status assessment using anthropometric measurements, dietary assessment, PG-SGA

PG-SGA has been validated in some kind of cancer, but in some other kinds, it requires combination PG-SGA with some other nutrition indicators. The change in PG-SGA score can be used to predict the change in quality of life and also carried prognostic information. But many question related to PG-SGA and nutrition status of the patient need to be answer, such as the validation of PG-SGA in esophageal cancer patients, the correlation between PG-SGA with quality of life scores and prognostic score, which appeared in previous studies's recommendation. Moreover, up till now, there is no published paper use PG-SGA as a tool in nutrition assessment in Vietnames cancer population. Table 4 below shows the summarized of studies which use PG-SGA and some nutrition assessment/screening tools in their research on cancer patients.

Table 4. Summarized studies on PG-SGA in cancer patients

Author	Design and sample	Conclusion	Limitation	Recommend.
Elisabeth Isenring (2006) (46); Australia	Observational, cross-sectional study; Australian public hospital; 50 oncology outpatients receiving chemotherapy; Using PG SGA, MST and BMI	According to PG-SGA global rating, the prevalence of malnutrition was 26%; MST has acceptable relative validity, inter-rater reliability, sensitivity, and specificity relative	Limit sample size	Larger sample size

		to the scored PG-SGA to identify chemotherapy outpatients at risk of malnutrition		
Brenda Laky (2008) (47) ; Australia	Assessed the nutritional status of 194 patients with suspected or proven gynecologic cancer according to the SGA and the scored PG-SGA, and skin fold-thickness (n=145) before primary treatment	The PG-SGA is significantly associated with subjective and objective parameters and is a widely recognized, clinically relevant method of evaluating nutritional status		Needed to assess whether the scored PG-SGA can predict which patients are at risk of adverse clinical outcomes and how well it serves in monitoring nutritional interventions, especially for malnourished ovarian cancer patients
Rong Li (2011) (48); China	Total of 96 newly diagnosed primary lung cancer patients in stage IIIB/IV and 52 benign lung disease patients nutritional status were assessed according to the SGA, the scored PG-SGA, and serum albumin, pre-albumin, transferrin, hemoglobin, total lymphocyte count, body mass index	In compared with serum albumin, pre-albumin, transferrin, hemoglobin, total lymphocyte count, body mass index (BMI) and weight, the scored PG-SGA and SGA are both accurate and simple nutritional assessment tools that are suitable for clinical practice. Lung cancer patients can be differentiated from benign conditions by PG-SGA	Compared all nutritional variables with the SGA; the comparison between the scored PG-SGA and SGA is not clear-cut	Pay attention to whether cancer patients' nutritional status is related to prognosis

	(BMI), and weight.			
Faith D Ottery (1996) (49); American	186 patients (from 1987 to 1994); aim to defined a proactive, standardized assessment and interventional approach	The use of a standardized nutritional assessment tool and a standardized interventional approach is defined which allows pro-active rather than re-active approaches to the prevention and management of cancer cachexia. The approach is appropriate to general patient care, cooperative oncology group protocols, and clinical trials of nutritional intervention.	The PG-SGA can be used in define a standardized interventional approach in oncology patients, in clinical practice, cooperative oncology group protocols, and clinical trials of nutritional intervention regimens.	
Mariana Ramosc haves (2010) (50); Portugal	Cross-sectional study; 450 non-selected cancer patients (aged 18 –95 years) at referral for radiotherapy; Nutritional status assessment included recent weight changes, BMI categorized by World Health Organization's age/sex criteria, and PG-SGA	Both under nutrition and overweight/obesity have very distinct implications and associations in cancer; Although BMI and PG-SGA are global assessment methods, thus potentially influenced by clinical parameters, both are easy to use in the clinical setting. They provide valuable	Not measure actual body composition, the degree of depletion, and/or excess of body compartments	Malnutrition, whether by deficit or excess, and because of its major negative impact on treatment, prognosis, and quality of life, is always a decisive factor in the overall treatment of cancer patients.

		information on the patients' global condition and both are validated and have been categorized according to the most appropriate standards		
Angel Segura (2005) (51); Spain	An epidemiological, observational, cross-sectional and multi-centered study; 781 patients with advanced cancer representative from the whole of Spain; evaluation of the patient's physical status according to the ECOG/WHO guidelines and the Karnosfky scale, parameters of nutrition and attitudes that could have nutritional repercussions; the questionnaire concluded with a question relating to the subjective importance that the patient assigned to food intake as part of general well-being and	The scored PG-SGA is a very useful tool. It is easy to use by health-care professionals who are not nutrition experts and enables the conduct of screening for malnutrition in patients with cancer additional information can be derived on the nutritional recommendations that each patient may need.	Few patients in the diagnostic phase	Identification of nutrition status as early as possible is essential if nutritional treatment is to be implemented so as to assist the cancer treatment, and to improve the patient's quality of life

	current physical status; PG SGA			
J Bauer (2002) (41); Australia	An observational study; 71 cancer patients, aged 18 – 92; compared PG-SGA with SGA in sensitivity and specificity.	The scored PG-SGA is an easy to use nutrition assessment tool that allows quick identification and prioritisation of malnutrition in hospitalised patients with cancer	PG-SGA was only applied at one time point	PG-SGA applied at multiple time points to determine if the PG-SGA score may be able to demonstrate the effect of nutrition support on outcomes in cancer patients
Arribas L (2013) (52); Spain	64 patients; estimated the prevalence of malnutrition and evaluate the independent prognostic factors for malnutrition from PG-SGA	From PG-SGA, the main prognostic factors ($p < 0.001$) were the percentage of weight loss, serum albumin levels, BMI and the presence of dysphagia or/and anorexia prior diagnosis		
Negar Shahmoradi (2009) (53); Malaysia	Cross-sectional study examined the association between global quality of life and its various subscales with nutritional status among 61 (33 females and 28 males) advanced cancer patients; (PG-SGA) and the Hospice Quality of Life Index (HQLI)	Able to establish the association between quality of life and its three domains with PG-SGA score as nutritional assessment tool among cancer patients in hospice home care	The small sample size and excluded of subjects with emotional, cognitive or physical problems that prevented them from completing the HQLI and PGSGA questionnaire	Further studies in cancer patients in hospice setting is necessary
N. Khoshnevis	The PG-SGA standard questionnaire	The average PG-SGA score was 10.1 with 49		Investigate the factors affecting more nutritional

(2010) (54); Iran	was administered to 416 cancer patients to evaluate their nutrition status and determine the frequency of each malnutrition stage	being the highest; 46.1% of the patients scored over 9 (requiring critical nutrient intervention)		symptoms and the prevalence of depression and anorexia
Z. Malihi (2013) (55); Malaysia	A prospective study; 63 acute leukaemia patients (65% men and 35% women); Used the PG SGA questionnaire and the EORTC assessment for the quality of life (QOL-C30, version 3); Objective assessment of nutritional status was also analysed within selected biochemical parameters (i.e. C-reactive protein (CRP) and serum albumin.	PG-SGA score and SGA rating showed a significant change after chemotherapy compared to that before the treatment; Serum albumin values correlated with the PG-SGA scores; the mean score of overall quality of life decreased significantly after the induction chemotherapy.	The duration of follow-up procedures in the present study could not be extended as a result of some logistical constraints such as time and human resource; Lengthening the span of time required for each patient assessment (45 mins) would likely lead to poorer patient tolerance; ethical considerations prevented from adding some objective assessment tools.	Further investigations could be conducted to further delineate the most effective approach in improving nutritional status in this patient population; nutritional status and quality of life would be further amplified by a longer study period; using a larger patient sample size
Digant Gupta (2011) (56);	Systematic review; there were 21 of the total 149	Validated nutritional tools such as SGA/PG-SGA are better	Potential publication bias (unpublished	

American	articles met the selection criteria. Of the 21 studies, 10 studies investigated gastrointestinal cancer patients, 4 gynecological cancers, and 7 heterogeneous cancers. Eight studies used subjective global assessment (SGA) or PG-SGA, nine articles used serum albumin and/or BMI, and 4 used other methods of nutritional assessment.	predictors of length of stay in gastrointestinal cancers requiring surgery than in nonsurgical gastrointestinal cancer patients.	studies; language bias)	
P. Ravasco (2003) (57); Portugal	Prospective, cross-sectional study; 205 consecutive patients (133 men and 72 women) with head and neck, gastro-esophageal, colon and rectum cancer, age 33–86 years, referred for radiotherapy; nutritional status (percentage of weight loss, PG-SGA assessment and	% weight loss is a sensitive and specific tool that can screen and identify malnutrition effectively; the results revealed high sensitivity and specificity for PG-SGA, indicating a high performance and a strong capacity to detect patients at high nutritional risk and malnutrition effectively		

	body mass index), nutritional requirements, usual diet intake (diet history) and current intake (24-h recall)			
Tzu‑Hao Huang (2014) (58); Taiwan	Retrospective study; PG‑SGA in 86 adult patients who had undergone an open appendectomy within 24 hours of admission	The scored PG‑SGA in adults receiving an appendectomy is significantly associated with length of hospital stay, and is an effective tool for assessing the nutritional status of patients with cancer and chronic illness, as well as of patients with acute surgical abdomen	The severity of acute appendicitis not examined whether affected length of stay (LOS), although longer LOS in participants with complicated appendicitis has been well‑known	
E Isenring (2003) (59); Australia	A prospective 4 week study assessing the nutritional status and QoL of ambulatory patients receiving radiation therapy to the head, neck, rectal or abdominal area; Sixty cancer patients aged 24–85 y	The scored PG-SGA is a nutrition assessment tool that enables malnourished ambulatory patients with cancer to be identified and triaged for nutrition support. It is suitable for use as an outcome measure in clinical nutrition practice and is associated with QoL in ambulatory patients receiving radiotherapy to	The exclusion of subjects with physical, cognitive, language or emotional problems that prevented them from completing the PG-SGA	

		the head, neck, abdominal or rectal area. Additionally, changes in PG-SGA score can be used to predict the direction and magnitude of change in QoL		
Elnaz Faramarzi (2013) (60); Iran	52 volunteer colorectal cancer patients referred to an radiotherapy center; NRI and PG SGA	NRI method had low sensitivity and specificity in assessing nutritional status of patients with cancer in comparison with PG-SGA; the combination of anthropometric, laboratory parameters and a subjective scoring system may be helpful tools in screening of malnutrition in cancer patients.		
Marta Alexandra Correira Pereira (2014) (61); Portugal	A descriptive-correlational Observational study, to be undertaken in a hospital setting; 42 head or neck cancer patients in a single moment, using the scored PG-SGA survey. In the same assessment day, a blood sample was collected for serum albumin and	In PEG fed head or neck cancer patients, PG-SGA was practicable and useful, even in patients with impaired speaking skills; albumin and transferrin levels showed relation with scored PG-SGA and should be considered as nutritional biomarkers		

	transferrin evaluation			
Giorgio Capuano (2010) (62); Italia	61 consecutive outpatients with locally advanced HNC; evaluated for malnutrition (UWL), nutritional intake (by diet history), nutritional status (PG-SGA), serum pre-albumin, hemoglobin level, C-reactive protein, QoL (EORTC QLQ) C-30 v. 3.0), and ECOG before treatment.	Early and intensive nutritional support might reduce weight loss before, during, and after treatment completion, improving outcome, QoL, and performance score		
C. Persson (1999) (63); Swedish	87 patients with gastrointestinal (n=54) and urological tumors (n=33) were assessed at the outpatient unit; PG-SGA was translated into Swedish	The PG-SGA is useful for the assessment of nutritional status. Patients had no problems in answering the questions. The PG-SGA also carried prognostic information.	Number of discrepancies was limited	
Nicole Barthele my (2014) (64); Belgiu m	47 lung cancer patients treated with curative intent were evaluated before radiotherapy and after completion of the treatment; PG-SGA and NRS-2002;	This is the first study establishing malnutrition before radiotherapy and predicting it after radiation based on data collected prior to treatment.		These two scores need to be validated in a larger cohort of lung cancer patient. Its application to other cancers also requires further investigation.

	BMI, weight loss, MUAC,TSF, KPS and the WHO performance status; diet history covering the last month; albumin, pre-albumin, creatinine, lymphocytes, transferrin, and total cholesterol			
Catherine Kubrak (2007) (42); Canada	Articles reviewed from 23 empirical reports, 4 reviews, and 3 reports from professional associations	Of the 3 recommended tools, the PG-SGA has the most diagnostic value for patients with cancer. The PG-SGA has been validated in both inpatient and outpatient settings and a variety of oncology patient groups. In addition, the PG-SGA directs clinicians to a plan of nutrition care and assessment of clinical outcomes; The MNA and MST have had limited evaluation in the cancer population		Further study of these tools is recommended
Ushashree Das (2014) (65); India	Observational, cross-sectional study; 60 gynecological cancer patients were assessed	Any correlations between PG-SGA and the other diagnostic tools here analyzed (BMI,	Selection bias introduced involuntarily by the exclusion of patients with	

	for their nutritional status using BMI, serum albumin, hemoglobin, percentage weight lost in last 1 month, and scored PG‑SGA. Correlation, sensitivity, specificity, and predictive values of the former four parameters compared to scored PG‑SGA were calculated	hemoglobin, albumin, and weight loss)	physical, cognitive, or emotional problems that prevented them from completing the scored PG-SGA form	
M. Cristina G (2008) (<u>66</u>); Brazil	Review article	PG-SGA, a scored version, could be repeated at intervals and subtle changes in the nutritional status could be evaluated in response to intervention but other studies are necessary to prove the usefulness of this assessment in other clinical situations; Visceral proteins should not be referred as nutritional markers, as they are associated to nutritional status only in the presence of stable		Future studies may show which method is more suitable to evaluate the response to this treatment

		inflammatory parameters		
Ang Yee Kwang (2010) (67); Malaysia	58 patients with advanced cancers; Nutritional status was assessed by 2 different methods (1) anthropometric measurements that were BMI, MUAC, triceps skin fold (TSF) thickness, MAC, and the percentage change in body weight within 1 month or 6 months and (2) the scored PG-SGA tool	PG-SGA is a quick and easily applied technique to assess the nutritional status of patients with cancer and accordingly stage them into well nourished, moderately malnourished, and severely malnourished categories. This instrument correlates significantly with objective nutritional indices and thus indicates that it is a good alternative to anthropometric measurements and could be used routinely in busy palliative care settings.	Relatively small sample size that may not allow the generalizability of the results to the nutritional status of patients with cancer in other palliative cares of the country; exclusion of objective biochemical parameters such as inflammatory activity biomarkers (serum pre-albumin and high sensitivity C-reactive protein) also restricted a more comprehensive evaluation of the methods used and further understanding of the etiology of malnutrition in these patients.	A larger prospective study is suggested to confirm the prevalence of malnutrition in patients with cancer in palliative care.
Susan S. Morelan	Systematic review; 11 articles that	In three articles, the PG-SGA was used to establish		

d (2010) (68); America	remained were used in this review + one additional relevant article was found by hand-searching in the articles' references. Of those 12 articles, one was a randomized, controlled trial; eight were non-experimental or qualitative, and three were written by nationally recognized experts or were based on no research evidence	whether the patient was well nourished, suspected malnourished, or severely malnourished; Anthropometric measurements (i.e., skin-fold measurements and body circumference) were done with the scored PG-SGA and in three other studies to evaluate nutrition status		
Ji-Yeon Kim (2011) (69); Korea	1057 patients was assessed by the Scored Patient-Generated Subjective Global Assessment (PG-SGA)	PG-SGA as gold standard for malnutrition screening tool for cancer patients (MSTC) equation;	Interviewer bias due to variation in the style of questioning; patients answering queries differently depending on varying states of alertness and medical conditions on the day of assessment; the MST includes indicators that are supposed to be collected by	Further studies on consistency between dietitians and nurses who perform the survey are necessary

			trained registered dietitians, whereas nurses are more likely to perform such a survey in practice	

3. Performance status

Karnofsky and Eastern Cooperative Oncology Group performance scores were widely used. However, limited data exist documenting their reliability and validity.

3.1. Karnofsky performance score

The Karnofsky performance score developed by Dr. David A. Karnofsky in 1948 with Joseph H. Burchenal, MD, of the Sloan-Kettering Institute for Cancer Research. The scale was created in an attempt to evaluate the results of chemotherapy in a more objective manner (70, 71). The scores run from 100% (perfect health) to 0% (death) as shown below (72):

Table 5.Karnofsky performance score

	Condition	Performance status (%)	Comments
A	Able to carry on normal activity and to work. No special care is needed.	100	Normal. No complaints. No evidence of disease.
		90	Able to carry on normal activity. Minor signs or symptoms of disease.
		80	Normal activity with effort. Some signs or symptoms of disease.
B	Unable to work. Able to live at home, care for most personal needs. A varying degree of assistance is needed.	70	Care of self. Unable to carry on normal activity or to do active work.
		60	Requires occasional assisstance, but is able to care for most of his needs.
		50	Requires considerable assistance and frequent medical care.
C	Unable to care for self. Requires equivalent of institutional or hospital care. Disease may be progressing rapidly	40	Disabled. Requires special care and assistance.
		30	Severe disabled. Hospitalization is indicated although death not imminent.
		20	Hospitalization neccessary, very sick active supportive treatment neccessary.
		10	Moribund. Fatal processes progressing rapidly.
		0	Dead.

Since then, it has been widely used in numourous studies on health related, especialy in cancer research. Kenneth E (1980) found that Karnofsky performance score was one of the three most important prognostic factors affecting survival among seventy-seven prognostic factors were considered in an evaluation of more than 5,000 patients with operable bronchogenic carcinoma of the lung (73). Cyndie Coscarelli Schag

(1984) used several analyses to evaluate the interrater reliability and construct validity of the KPS in 293 cancer patients from three healthcare settings in American. The KPS was shown to have good reliability and validity (74). Vincent Mor (1984) examined KPS about its reliability and validity in a research setting. The findings suggested the utility of the KPS as a valuable research tool when employed by trained observers (72). Yuji Murakami (2007) announced the results of the 1999–2001 Japanese patterns of care study for patients receiving definitive radiation therapy without surgery for esophageal cancer. Of the 621 patients receiving radiotherapy, 385 non-surgical patients were analysed. KPS was ≥ 80 in 71% and better in T1 cases than in T2–4 cases (75). Shirley S.Hwang (2004) used KPS to defined the role of KPS and quality of life, symptom distress on predict survival for advanced cancer patients. The author found that the combination of these three tools provided the prognosis (76). Karis K.F. Cheng (2011) used KPS in assessing the effects of pain, fatigue, insomnia, mood disturbance on functional status, and quality of life of elderly patients with cancer. This cross-sectional study used secondary data from a convenience sample of 120 patients 65 years of age or older with colorectal, lung, head/neck, breast, gynecological, prostate or esophageal cancer receiving chemotherapy or radiotherapy at an oncology unit of a regional hospital in Hong Kong. The study sample was drawn from a previously conducted observational validation study. The rated Karnofsky Performance Scale (KPS) was used to measure functional status (77). Ameer L. Elaimy (2011) assessed the clinical outcomes of stereotactic radiosurgery in the treatment of patients with metastatic brain tumors. Modern literature was reviewed for studies on Stereotactic Radiosurgery (SRS) in the treatment of patients with metastatic brain tumors. Patients who did not require urgent focal treatment for an acute neurological deficit, have KPS ≥ 70 . The results showed that patients with 1 to 4 brain metastases who have a KPS ≥ 70, the addition of SRS to whole brain radiation therapy (WBRT) produces increased levels of survival and local tumor control when compared with patients treated with whole brain radiation therapy alone (78). Carsten Timmermann (2012), in the paper "Just give me the best quality of life questionnaire", reviewed the Karnofsky scale and the history of quality of life measurements in cancer trials. All articles referring to the Karnofsky scale and quality of life measurements published from the 1940s to the 1990s were identified by

searching databases and screening journals, and analysed using close-reading techniques. The results showed that The Karnofsky scale was devised for a different purpose than measuring quality of life as a standardisation device that helped quantify effects of chemotherapeutic agents less easily measurable than survival time (71). Hailang He (2013) in a review article used meta-analysis of randomized trials on couse of Astragalus-containing Chinese herbal prescriptions and radiotherapy benefit to non-small-cell lung cancer treatment. Among 29 studies met the criteria, 8 studies reported performance status, 6 studies showed improved Karnofsky performance status in 615 patients (79).

Karnofsky performance score also has been used in some research on cancer in Thailand. Ubolrat Piamjariyakul (2010) used KPS in a report on cancer therapy-related symptoms and self-care in Thailand. This was a descriptive study using a cross-sectional design. A convenient sample (n=202) was drawn from both in-patients and out-patients undergoing radiation therapy and chemotherapy at the National Cancer Institute, Bangkok (n = 127), and at the Lopburi Cancer Center (n=75). Patients with GI track cancer was 32% of total patients, which included esophageal cancer; Patients on combined radio-chemotherapy reported more symptoms on the Therapy-Related Symptom Checklist (TRSC), with greater severity than those receiving radiotherapy or chemotherapy alone (F = 7.2); and lower Karnofsky score (F = 4.2); Karnofsky and TRSC scores were inversely correlated (80). Permsak Paholpak (2012) in a retrospective study on prevalence of known and unknown primary tumor sites in 82 spinal metastasis patients who had not received a previous diagnosis of carcinoma. The KPS was one of parameters. The mean performance status score was of an intermediate level (53.15 ± 12.19) (81). Sakarunchai (2013) in a retrospective study on free survival time of recurrence and malignant transformation and associated factors in patients with supratentorial low-grade gliomas; 77 patients who underwent surgery and were diagnosed with low-grade gliomas between January 2000 and October 2009 were recruited; KPS was one of factors associated with tumor recurrence (82).

Some papers of the Vietnamese authors used KPS in their research, but those studies did not show the KPS was applied in Vietnamese patients or not. Nguyen Thi PL et al

(2002) in the paper named "Factors determining inpatient satisfaction with care" aimed to identify factors associated with satisfaction among inpatients receiving medical and surgical care for cardiovascular, respiratory, urinary and locomotor system diseases. The Karnofsky scores of more than 70 is one of the specific predictors for certain dimensions of satisfaction (83). Tran Chi Minh Chau, Felix Sundram et al (2004) in a multicentre study sponsored by the International Atomic Energy Agency (Vienna) assessed the safety and efficacy of trans-arterial rhenium-188 HDD conjugated lipiodol (radioconjugate) in the treatment of patients with inoperable hepatocellular carcinoma (HCC), in which Karnofsky performance status was one of clinical parameters (84). Ngo T. Trang, Dirk Rades et al (2013) in "A new survival score for patients with brain metastases who received whole-brain radiotherapy (WBRT) alone" (a multicenter study with a total of 882 patients from seven institutions who received 10 x 3 Gy of WBRT alone for brain metastases between 1998 and 2012; patients were randomly assigned to the test group (n= 441) or the validation group (n= 441) using the excel random number generator), the Karnofsky Performance Score (KPS < 70 vs KPS > 70) was one of nine potential prognostic factors in the test group (85). The application of KPS in Vietnamese patients was found in a master of science thesis in Vietnamese inpatients at Ho Chi Minh city Oncology hospital by Sherry Linn Priebe (2009) from The University of British Columbia (Vancouver). This thesis about oral squamous cell carcinoma and culture risk factors in patients at Oncology hospital in Ho Chi Minh city, Vietnam. Patients included 106 males and 55 females, from 24 to 85 year olds. Of all examined, 90% of the subjects had a value on the KPS scale between 80% and 90% regarding their general status (86).

Focus on esophageal cancer, KPS was found in some researches. H. Bergquist (2008) studied factors predicting survival in 96 patients with advanced oesophageal cancer; the KPS was used in analysis of factors predictive of survival, sociodemographic data. This is a randomized-controlled trials of palliative treatment in patients with incurable cancer of the oesophagus. Results shown KPS ranged between 30 and 100 with a mean of 73; KPS and CT-assessed size measurement of the primary tumour were found to correlate to survival but had no predictive value of their own (87). Hai-Qin Zhang (2012) used KPS in the study on evaluate the prognostic value of serum

CYFRA21-1, CEA and hemoglobin levels regarding long-term survival of patients with esophageal squamous cell carcinoma (ESCC) treated with concurrent chemoradiotherapy (CRT) ([88](#)). Daniel E. Spratt (2012) assessed time course and predictors for cancer-related fatigue in a series of oropharyngeal cancer patients treated with chemoradiation therapy. There were 87 consecutive oropharyngeal carcinoma patients underwent definitive radiotherapy; weight, KPS, scores, and pain scores were collected at each appointment. All patients had KPS $\geq$ 70, and performance scores had a mild trend toward predicting cancer related fatique (p =0.12) (did not correlated) ([89](#)). Yipeng Song (2013) used KPS as an inclusion criteria (KPS > 70%) in his study on assess the application of serial section method to determine the radiotherapy target volume for esophageal squamous carcinoma ([90](#)). M.-P. Vasson (2014) use KPS in assess the role of immunenutrition in functional capacities in head and neck and esophageal cancer patients undergoing radiochemotherapy. This is a double-blind clinical trial and 37 patients aged more than 18 years were randomized. KPS was used as a clinical outcome ([91](#)).

In summary, KPS had widely been used in many countries all over the world and in many kinds of diseases. But KPS did not appeared in well known published paper on Vietnamese population. Moreover, there is no paper on the correlation between KPS and nutritional status and/or prognostic score in esophageal cancer patients.

3.2. Eastern Cooperative Oncology Group performance score

Eastern Cooperative Oncology Group performance score also has a wide history applied in research on cancer worldwide. This tool was published the first time in 1982 by Oken MM in the paper named 'Toxicity and response criteria of the Eastern Cooperative Oncology Group" ([92](#)). The score runs from 0 (denote perfect health) to 5 (death) which was below:

Table 6. Eastern Cooperative Oncology Group performance score

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Compeletely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

G. Buccheri (1996) compared the predict validity of KPS and ECOG and suggested a table presenting the transformation between these tools. The study conducted in 536 consecutive lung cancer patients. The study shown that ECOG should be preferred to KPS due to ECOG ability to discriminate patients with different prognosis (93). Forrest LM (2004) studied on comparison of GPS with ECOG in 190 patients receiving platinum based chemotherapy for in operable small cell lung cancer. Chang XJ (2011) used ECOG in assess the predictive efficacy of cryoblation in patients of advance hepato-carcinoma. He found that ECOG is one of important predictors for survival time in this group of patients (94). Sitthinamsuwan B (2014) used ECOG in a study on Therapeutic and survival outcomes following treatment of primary central nervous system lymphoma. This is a twelve-year case study with total 85 participants. The result shown that patients with ECOG > 1 and elevated cerebrospinal fluid protein level > 45 mg/dl were significant prognostic factors of poor survival outcome as estimated by Cox regression analysis (95). Qiu-Huan Kong (2014) did a prospective analysis of the risk factors for falls in 203 lymphoma patients. The univariate regression analysis showed ECOG is one of the risk factors for falls in

lymphoma patients ([96]). Kultida Klarod (2011) used ECOG to assess the performance of patient in his study on serum antioxidant levels and nutritional status in early and advanced stage lung cancer patients. The author found that there was a significantly lower levels of antioxidants and selenium were found in lung cancer patients compared to healthy controls and more interestingly, levels of some antioxidants and minerals differed among categories of BMI, SGA categories, or ECOG performance status ([97]). In summarize, although there were limit study that validate ECOG performance score, this is still useful and practical tool.

4. Glassgow Prognostic score

From 2003, Forrest et al fisrt build the prognostic tool, which based on CRP (C Reactive Protein) and Albumin for patients with small cell lung cancer ([98]). Since then, this tool was used in many researches on cancer, especially to have the factor that affect quality of life or to have the patient's prognosis and define the impact on the patient's health.

Table 7. Systemic inflammation based prognostic scores, the Glasgow prognostic scores

The Glasgow Prognostic score	Point allocated
CRP ≤ 10 mg/l and Albumin ≥ 35 g/l	0
CRP > 10 mg/l	1
Albumin < 35 g/l	1
CRP > 10 mg/l and albumin < 35 g/l	2
The modified Glasgow Prognostic Score (mGPS	
CRP ≤ 10 mg/l and Albumin ≥ 35 g/l	0
CRP > 10 mg/l or Albumin < 35 g/l	1
CRP > 10 mg/l and albumin < 35 g/l	2

Recently, Michael J. Proctor et al (2013) wished to optimized the GPS. He used the cut off point for CRP of 3mg/L (instead of 10mg/L) and addition of addition of neutrophil and platelet counts. The studied conducted in 12,119 patients. Results shown that the addition of neutrophil and platelet counts, as well as a high-sensitivity C-reactive protein measurement, enhanced the prognostic value of the mGPS (99). Once more, Shinsuke Takeno (2014) improved this investigation that "the high-sensitivity modified Glasgow prognostic score (HS-mGPS) is superior to the modified Glasgow prognostic Score as a prognostic predictor in patients with resectable gastric cancer", by the author's study on 552 patients with gastric cancer who underwent gastrectomy at the Fukuoka University Hospital (100).

4.1. The C Reactive Protein- CRP:

CRP is a serum protein, mainly produced by liver cells, but other cells in human body can produced this protein and many of them are still unknown nowadays. There are 3 subtypes of CRP, include conventional CRP, high sensitive CRP (hs CRP) and cardiac CRP (cCRP). The table 9 below outlines similarities and differences between these 3 types of assays, in terms of intended use and performance features:

Table 8. Summarize and differences between 3 types of CRP (101)

	Conventional CRP	**hsCRP**	**cCRP**
Intended use	For evaluation of infection, tissue injury, and inflammatory disorders; Provides information for the diagnosis, therapy, and monitoring of inflammatory disorders.	For evaluation of conditions thought to be associated with inflammation, in otherwise healthy individuals	For aid in identification and stratification of individuals at risk for cardiovascular disease. When used in conjunction with traditional clinical laboratory evaluation of acute coronary syndromes, cCRP

			may be useful as an independent marker of prognosis for recurrent events, in patients with stable coronary disease or acute coronary syndrome.
Typical clinical cutoff concentrations	Cut-off: approximately 10mg/L; Apparently healthy individuals: ≤ 5mg/L; Acute range: 20-500 mg/L	Cut-off: ≤ 1.0 mg/L	Cut-off: ≤ 1.0 mg/L
Appropriate assay measuring range	≥ 5mg/L to upper range of the assay	< 1.0 mg/L to ≤ 10.0 mg/L	< 1.0 mg/L to ≤ 10.0mg/L
Analytical sensitivity information	Describe performance at the low end of claimed assay range	Determine limit of quantitation (functional sensitivity)	Determine limit of quantitation (functional sensitivity)
Clinical or method comparison	Comparison of new device to a predicate device	Comparison of new device to a predicate device	Comparison of new device to a predicate device whose clinical utility and cutoff has been demonstrated or

informat ion			Presentation of results from literature describing clinical utility of the new device or Clinical studies for the new device.

Normally, the CRP level increase when human in inflammation situation. Especially, in acute inflamation phage, CRP increase incombination with decrease albumin level (102). Recently, CRP level showed the validity in cancer diagnosis and prognosis. The increase of CRP level causes increase the risk of some kind of cancer and lowel level CRP relates with increase treatment outcome and better prognosis; high level CRP relates with increases the risk of death of breast cancer women (103).

Marta Łukaszewicz-Zajac et al demonstrated the relation between CRP and different subtypes esophageal cancer, and realized that the CRP concentration has relationship with other tumor indexes, suggested CRP is a low cost but effectiveness tool in esophageal cancer clinical diagnosis and follow up (104); Magdalena Groblewska (2012) also reports the CRP level relates with pathology of esophageal cancer such as the stage of disease, the invasive of tumor and lymph nodes metastasis. This finding suggested CRP level was the potential prognostic factor in survival outcome of esophageal cancer patients (105); Guillem and Triboulet also published the increase CRP level related to bad prognosis in esophageal cancer patients (106). The serum CRP level can be lowered by aspirin, antiplatelet agents, lipid lowering agents, anti-diabetes agents, estrogens, beta-Adrenoreceptor antagonists, antioxidants, inhibitors of Renin-Angiotensin System (107) and curcuminoids (108).

4.2. Albumin

Albumin is a protein produced by the liver cell and is one of main protein in serum. Albumin helps in balance intravascular fluid, and keeps asmospheric plasma presure, vitamins and ions transportation, hormonal transportation, and blood cloth. In acute phage inflamation, the decreased level of albumin paralei with increased level of CRP

(102). Chang-Yu Wang et al (2009) showed the correlation between low level serum albumin combined with high level CRP and the poor prognosis in esophageal cancer patients treatment with radiotherapy (109).

4.3. Glasgow Prognostic score (GPS)

GPS has been shown in many studies on cancer. Most recently, X Jiang (2012) published a paper on prognostic importance of the inflammation-based Glasgow prognostic score in 1710 patients with gastric cancer who underwent surgery between January 2000 and December 2007. The results claimed that GPS is a simple and useful prognostic factor for post-operative survival in patients with gastric cancer (110). Johann Dreanic (2013) had a research to identified prognostic value of the Glasgow prognostic score in 49 patients with metastatic colorectal cancer (mCRC) in the era of anti-EGFR therapies. This study confirmed that the GPS is still a simple and effective prognostic factor in the era of cetuximab therapy in mCRC patients (111). Akiyoshi Kinoshita (2013) assessed GPS in predicted survival in patients with hepatocellular carcinoma (HCC). Total 150 patients with newly diagnosed HCC were prospectively evaluated. The results demonstrated that the GPS can serve as an independent marker of poor prognosis in patients with HCC in various stages of disease and different liver functional status (112). Qun-Xiong Pan (2014) aimed to find if GPS was an independent prognostic predictor of hepatocellular carcinoma following radical resection. The study based on infomation collected from 171 cases selected retrospectively. The GPS showed an independent biomarker for prognostic prediction of HCC following radical resection (113). Martin HL (2014) investigated the prognostic significance of three systemic inflammation-based factors: neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and modified Glasgow Prognostic Score (mGPS) in patients with advanced pancreatic cancer. Data was evaluated for 124 patients. Findings suggest that the NLR, PLR and mGPS derived from routine blood tests can be used as clinically meaningful biomarkers to stratify advanced pancreatic cancer patients into different prognostic groups. Ai-Gui Jiang (2014) assessed the predictive value of survival in patients with advanced non-small cell lung cancer (NSCLC) treated with cisplatin-based first-line chemotherapy in 138

consecutive patients. Study conclusion announced GPS can be used as an independent predictor for survival in patients with advanced NSCLC (114).

Focus on esophageal cancer, Vashist studied this tool in patients with only surgical treatment and found that this tool had strong abilily in post operative morbidity and long term effectiveness in resected esophageal cancer patients without neoadjuvant or adjuvant treatment (115); Takashi Kobayashi also showed GPS is an independent prognosis tool in squamous cell carcinoma esophageal cancer (116). Yogesh K (2011) had a research on Glasgow Prognostic Score as a predictor of perioperative and long-term outcome in patients with only surgically treated esophageal cancer, aimed to evaluate the potential prognostic role of GPS in a homogeneous population of esophageal cancer (EC) patients undergoing only resection. The results indicated GPS represents a strong prognosticator of perioperative morbidity and long-term outcome in resected EC patients without neoadjuvant or adjuvant treatment (115). Sumanta Dutta (2012) compared of the prognostic value of tumour and patient related factors in patients undergoing potentially curative resection of gastric cancer. This study aimed to compare the prognostic value of selected markers of systemic inflammation in 112 patients who underwent surgical resection for oesophageal cancer. Patients had laboratory measurement of white cells, neutrophils, lymphocytes, platelet counts, albumin, and C-reactive protein. Glasgow Prognostic Score (mGPS), neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), and metastatic lymph node ratio (LNR) were calculated. The results indicated that the mGPS better predicts cancer survival compared with the cellular components of systemic inflammation in patients with oesophageal carcinoma (117). Ji-Feng Feng (2014) identified prognostic significance of GPS in total of 1048 patients undergoing esophagectomy for esophageal squamous cell carcinoma. For evaluation of the GPS, blood test results from the day before surgery were used. High levels of GPS is associated with tumor progression. GPS can be considered as an independent prognostic factor in patients who underwent esophagectomy for ESCC (118).

So untill now, there are only two studies on HS-mGPS, and there is no cut off point for the number of lymphocyte count and platelet count, so HS-mGPS need further

evidence to conclude about the effective on prognosis for cancer patient. And currently, GPS and mGPS still more advantage in clinical practice.

5. The correlation between nutrition status, the Karnofsky performance score and the Glassgow Prognostic score

Luca Cozzaqlio (1997) identified the outcome of cancer patients receiving home parenteral nutrition (Italia) in his retrospective study of 75 cancer patients from nine institutions. Weight, height, lymphocyte count, serum albumin, and KPS. There was a positive effect of home parenteral nutrition (HPN) on nutritional status and quality of life in patients who survived > 3 months and suggested that HPN should be avoided when KPS < 50 ([119]). Donald C. McMillan (2009) published a literature review on systemic inflammation, nutritional status and survival in patients with cancer. This study showed GPS not only identify patients at risk but also provided well defined therapeutic targets for future clinical trials targeting nutritional decline ([120]). DAC Deans (2009) assessed the influence of systemic inflammation, dietary intake and stage of disease on rate of weight loss in 220 patients diagnosed with gastric or oesophageal cancer. An assessment of their nutritional status at the time of diagnosis (calculation of BMI, estimation of weight loss, estimated dietary intake), determinded serum acute-phase protein concentrations, KPS. This study concluded weight loss associated with poor performance status, advanced disease stage, dysphagia, reduced dietary intake and elevated serum C-reactive protein (CRP) concentrations; systemic inflammation plays a role in nutritional depletion and may informed the development of appropriate therapeutic strategies to ameliorate weight loss, making patients more tolerant of cancer-modifying treatments such as chemotherapy ([121]). RJE Skipworth (2010) announced that plasma MIC-1 correlated with systemic inflammation but is not an independent determinant of nutritional status or survival in oesophago-gastric cancer patients. The study based on information of patients with a new histological diagnosis of OGC (n = 293; 198 males and 95 females). Data collection included nutrition assessment (height, weight, MAC, TSF, MAMC); Karnofsky performance score; dietary intake; Plasma CRP and albumin concentrations. The median BMI, MAMC, and TSF measures were lower than those reported in healthy elderly

populations; both CRP and mGPS correlated with weight loss, and mGPS also correlated negatively with MAMC; a highly significant increase in CRP and mGPS between patients who had $\geq 10\%$ weight loss in compared with those who had not; percentage weight loss, diet score and KPS found to correlated with CRP (122). K. V. Gomes de Lima (2012) examined the co-relation between nutritional status, systemic inflammation and prognosis of patients with gastrointestinal cancer. A case series study was carried out involving 30 male and female adults and elderly patients with no prior treatment sent consecutively for surgery. Nutritional status was assessed using subjective and objective methods. Inflammatory response and prognosis were assessed through the determination of CRP, the GPS and CRP/Albumin ratio. Results showed that nutritional status is related to inflammation markers and prognosis in patients with gastrointestinal cancer, which suggested that the diagnosis and attenuation of systemic inflammation should be part of the nutritional care of these patients (123). Mauricio SF (2013) discorvered the relationship between nutritional status and the Glasgow Prognostic Score in patients with colorectal cancer. A cross-sectional, prospective, and descriptive study concruited 70 patients met the study criteria, the nutritional status was defined by the SGA, anthropometric measurements such as BMI, TSF, MAC, MAMA, adductor pollicis muscle thickness, and the severity of inflammation defined by GPS. The complications were classified using the Common Toxicity Criteria, version 3. This study shown that the nutritional status was associated with the GPS (124). Carla Alberici Pastore (2013) reported the association between an inflammatory-nutritional index and nutritional status in cancer patients. This is a cross sectional study, included 74 patients with gastrointestinal and lung cancer of a public chemotherapy service in Brazil. Anthropometric data, SGA, BMI, serum CRP, albumin, the Inflammatory-Nutritional Index (INI) was calculated using the formula: INI = Albumin/CRP, estimated the GPS. When nutritional status was evaluated by SGA, there was an increase of CRP levels as nutritional status declined; The albumin/CRP ratio was associated with SGA nutritional status, independent of systemic inflammation status. As the ratio decreased, patient's nutritional state worsened. So, these parameters (CRP and albumin), appraised routinely in cancer patients, could be used to build a nutritional indicator; More studies, with larger sample size, are necessary to evaluate the usefulness and reliability of this method as

an indicator of nutritional status, and to determine logical end-points for nutritional risk categories (125). Tora S Solheim (2014) questioned on weight loss, appetite loss and food intake in cancer patients with cancer cachexia whether it is such as three peas in a pod. By an analysis from a multi-center cross sectional study and 1070 patients with incurable cancer, the analyse based on PG-SGA, weight, height, weight loss, change in dietary, KPS. The results showed mean KPS was 72; there was correlation between weight loss and food intake with r = 0.34. F. Bozzetti1 (2014) studied the prognosis of incurable cachectic cancer patients on home parenteral nutrition in his multi-centre observational study with prospective follow-up of 414 patients. On each patient's discharge, participating centres were asked to fill up an ad hoc form including data on demographic, nutrition status (usual and current body weight, BMI), clinical oncology related index (life expectancy, KPS, site of primary, histopathology, tumour spread and vital organ involvement, previous oncologic treatments), biochemical variables (blood cell count, serum albumin, C-reactive protein (CRP)), indications for HPN, start date, end date and method of HPN administration and management, and date of death. At the multivariable analysis, the variables significantly associated with 3- and 6-months survival were GPS, KPS, and tumour spread (126).

As showed previously, GPS was used in many research on cancer, but still limitted in esophageal cancer studies. In addition, there was no research on the inter-relationship between GPS, performance status and nutrition status of esophageal cancer patients.

CHAPTER 3.

METHODOLOGY

1. Conceptual framework
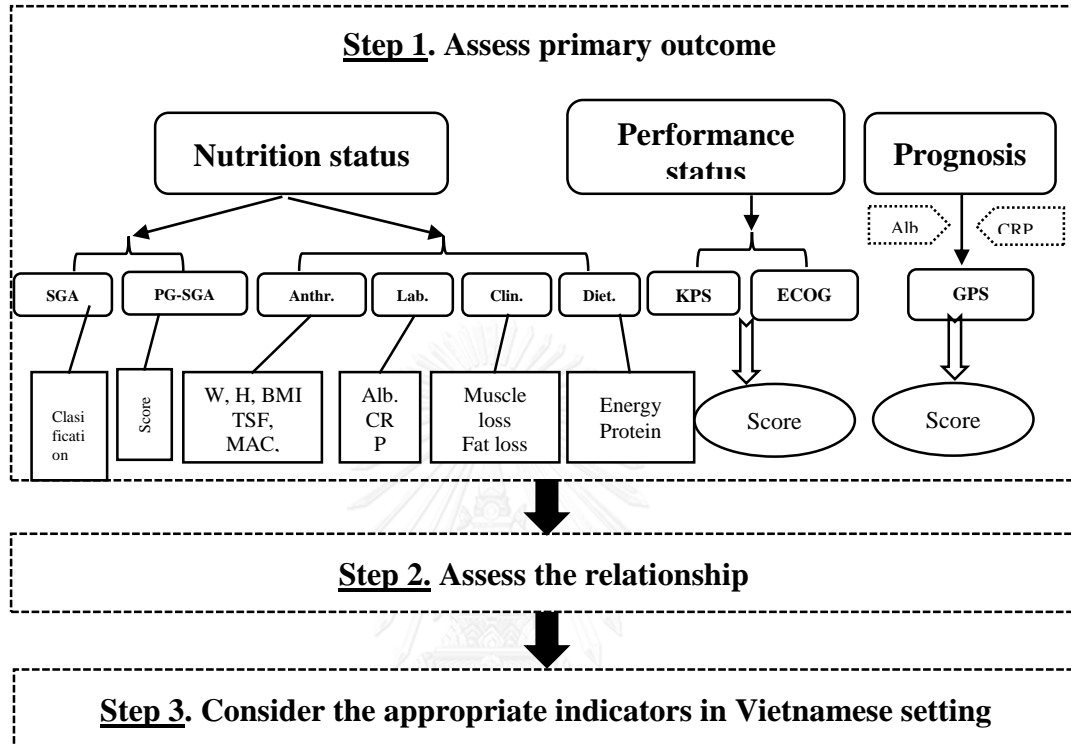
2. Study hypothesis

Malnutrition rate in esophageal cancer patients may or may not be higher than the rate in general patients

- PG-SGA may or may not correlate with anthropometric measurements, biochemistry values, clinical signs and 24-hour dietary recall in esophageal cancer patients.

- PG-SGA may or may not correlate with KPS/ECOG score and GPS score in esophageal cancer patients

- KPS/ECOG scores may or may not correlates with anthropometric measurements, biochemistry values, clinical signs and 24-hour dietary recall in esophageal cancer patients.

- GPS score may or may not correlate with anthropometric measurements, biochemistry values, clinical signs and 24hours dietary recall in esophageal cancer patients

- Appropriate indicators in clinical practice in Vietnamese setting for esophageal cancer patients are PG-SGA and GPS

3. Limitation of this study

This study does not follow up the patients to assess the relation between PG-SGA, pre-treatment nutrition assessments to the length of survival. Further study is required to solve this problem.

4. Future perspectives

The result of this study will be translated into clinical practice by:

- Present the result in the conferences

- Dissemination the result to cancer hospitals and National Institute of Nutrition

- Training clinical staffs to use the research tools in Vietnamese version.

5. Patients selection and study method

5.1. Patients selection

This study enrolls patients registered/admitted to the National Cancer Hospital (NCH) with the diagnosis as esophageal cancer from August 2014 to February 2015. The NCH is a national oncology hospital located in Hanoi and receives referral cases from other surrounding Northern provinces of Vietnam. In addition, the NCH is also playing a role as a teaching hospital for Hanoi Medical University. In Vietnam, most of esophageal cancer patients stage III/IV have the chemo-radiation therapy treatment. Therefore, right after admitted to the hospital, the patients are usually referred to the Radiotherapy ward for the chemotherapy treatment at the same time with the radiotherapy. In this study, the patients were followed up consecutively within 48 hours since admission, at the Radiotherapy ward.

Inclusion criteria

Aged from 18 to 65, both male and female

Patients diagnosed with esophageal cancer stage III/IV, diagnosed by histopathology with Squamous cell carcinoma or Adenocarcinoma

Patients at pretreatment period (not have any kind of treatment and medical therapy before data collection) (patients were at first day and second day of admission)

Patient have good mind, can read and write adequately

Received consent from the patients

Exclution criteria

- History and treatment of GI diseases, chronic liver diseases, kidney diseases, heart failure, total or partial paralized before diagnosed of esophageal cancer.

- History treatment with Aspirin/NSAIDs, and/or omega 3 supplement

- Recurrent esophageal cancer diagnosis

- Presented sepsis symptoms (have at least two of the following symptoms) ([127]):

* Body temperature above 38^0C or below 36^0C;

* Heart rate higher than 90 beats a minute or or arterial carbon dioxide tension (PaCO 2) of less than 32 mm Hg;

* Respiratory rate higher than 20 breaths a minute;

* Abnormal white blood cell count (>12,000/µL or < 4,000/µL or >10% immature forms)

- Not sign into the inform consent

5.2. Study methods

5.2.1. Study design

Clinical cross sectional study

5.2.2. Sample size

Method 1

This study aimed to assess the nutrition status of the patients with esophageal cancer stage III and IV, and found out the interrelationship between the nutrition status,

performance score and Glasgow prognogstic score. The equation that helped to identify the representative of population in data collection ([128]) was the equation:

$$N = \frac{p(1-p)*D*Z^2_{\alpha/2}}{E^2}$$

Where:

P: the prevalence of the esophageal cancer patient at stage III/IV;

E: the precision (or margin of error) with which want to measure; generally E equals to 10% of P;

$Z_{\alpha/2}$: Normal deviate for two-tailed alternative hypothesis at a level of significance

D was the design effect reflects the sampling design used in the survey type of study. This was 1 for simple random sampling and higher values (usually 1 to 2) for other designs such as stratified, systematic, cluster random sampling etc, estimated to compensate for deviation from simple random sampling procedure. The design effect for cluster random sampling was taken as 1.5 to 2.

In previous study, the prevalence of esophageal cancer at stage III/IV was 87.5% ([12]), so P =0.875 and (1-P) = (1-0.875) = 0.125;

E = 10% of P = 0.1 * 0.875 = 0.0875

Choose α = 0.05 (the normal deviates for type 1 error), so $Z_{\alpha/2}$= 1.96;

Choose D = 1 for simple random sampling

$$N = \frac{0,875(1-0.875)*1*1.96^2}{(0.1*0.875)^2} = 54.88$$

Estimate 10% refused to participate or dropped out before the study ends, so the sample size was achieved:

$$N = \frac{54.88}{1-0.1} = 60.97 \approx 61 \; patients$$

Method 2:

Use the equation for unknown population (more than 200) ([129]):

$$N = \left(\frac{Z_{\alpha/2}}{E}\sigma\right)^2$$

$Z_{\alpha/2}$ was known as the critical value, it was 1.96 for alpha = 0.05;

σ: The standard deviation

E = margin of error (maximum difference between the observed mean) = mean x precision while Precision = relative error of estimation = proportion of difference of sample mean of population, example 10% (0.1), 15% (0.15).

According to last study from Malaysian population ([67])

	Z	SD	Mean	% precision	Calculated	Add 10%	Sample size
BMI	1.96	3.98	20.9	0.05	56	5.6	62
MAC	1.96	37.3	217.5	0.05	45	4.5	50

Choose the max sample size, so the sample size for this study was 62 patients who met the inclusion criteria.

Sample size in some other researches on correlation between nutritional status/performance score/prognostic score:

Table 9. Number of subjects in previous researches

Name of study	Measurements	Author (year)	Number of subject
Nutritional status, systemic inflammation and prognosis of patients with gastrointestinal cancer	W,H,TSF,MAC, BMI, MAMC, Hb, Hct, TLC, CRP, albumin, 24hrs dietary recall, PG SGA	K. V. Gomes de Lima (2012)	30
Association between an inflammatory-nutritional index and nutritional status in cancer patients	BMI, SGA, CRP, albumin, GPS, INI = Albumin/CRP ration	Carla Alberici Pastore (2013)	74
Immuno-nutrition improves functional capacities in head and neck and esophageal cancer patients undergoing radio-chemotherapy: A randomized clinical trial	KPS, ECOG, 24hrs dietary recall, W, BMI, NRI	M.-P. Vasson (2013)	37

5.3. Data collection:

Within 48 hours since patients admitted to the Radiotherapy ward, they were screened for the study inclusion criteria. The enrolled patients were asked to sign informed consent to join the research, and then they would be introduced to fill in the first part of PG-SGA form (the rest then would be completed by a physician). In the next day, the patient's blood sample would be collected in the early morning according to hospital's procedure and other information such as anthropometric measures, 24 hours

dietary record would be collected as well. SGA, PG-SGA, KPS and ECOG scores were assessed by a researcher.

Anthropometric measurements: Body weight was measured using an electronic weighing scale (LAICA S.P.A., Italy) with a precision of 100 gr, in the early morning, after urinate and defecate. Body height was collected by using locally made wooden boards (stadiometer) with a precision of one millimeter. Body Mass Index (BMI) would be calculated based on weight in kilogram divided by height in meters squared (kg/m^2). Patients would be then classified as underweight, in the normal range, overweight or obese using World health organization (WHO) criteria ([130], [131]).

Classification	Principle cut-off points	ASIA population cut-off points
Underweight	BMI < 18.5	BMI < 18.5
Normal range	18.5 ≤ BMI ≤ 24.99	18.5 ≤ BMI ≤ 22.99
Overweight	BMI ≥ 25	23 ≤ BMI ≤ 24.99
Obese	BMI ≥ 30	BMI ≥ 25

- Mid arm circumference (MAC): Measurement tapes were used to measure the left mid-upper arm circumference in centimeters with a precision of one millimeter. For MAC, use the cut-off point of 22 cm for females and 23 cm for males [132].

- Triceps skin fold thickness (TSF), in mm: measured in the left arm, using the Caliper measurement Made in Japan. The patient stands or sits erect with bare arm and shoulder. The arm was held vertically, so as not to rest on any surface. Using the Caliper measurement, read at the 4th second.

- Mid-arm muscle area (MAMA) in cm^2 and calculated by this calculation ([133]):

$$\text{MAMA} = \frac{(MAC - \pi TSF)^2}{4\pi}$$

Reference tables, standardized for age and sex, and validated for normal subjects were used for the classification of individual. A result of MAMA < 15th percentile is indicative of below average, whereas a TSF > 85th percentile is indicative of excess body fat ([134])

MAMA ≤ 5th percentile	Wasted
5 < MAMA ≤ 15th percentile	Below average
15 < MAMA ≤ 85th percentile	Average
85 < MAMA ≤ 95th percentile	Above average
MAMA > 95th percentile	High muscle

- 24-hour dietary recall: Dietary intake was measured by a single dietitian, which included administered 24-hour recall, using food portion size models and illustrated pictures to help patients imagine and understand the estimation. Both oral and tube feeding were noted. Parenteral nutrition was calculated based on information from medical record. Results of the sum of the 24-hour dietary recall and total parenteral nutrition (if possible) were calculated into kcal energy and gram protein intake within 24 hours using the Vietnam National Institute of Nutrition software as well as based on local food composition and nutrition content of parenteral nutrition commercial product. Cut-off points for energy intakes are > 35 kcal/kg/day, 30-35 kcal/kg/day, 25- 30 kcal/kg/day and < 25 kcal/kg/day while thresholds of protein intakes are > 2 g/kg/day, 1.2-2 g/kg/day, 1-1.2 g/kg/day and < 1 g/kg/day, which were based on ESPEN guidelines ([11], [23]).

- PG-SGA: PG-SGA was assessed for all subjects. This tool consists of two sections that would be completed by patient or clinician accordingly. There were four medical components (weight loss, nutrition impact symptoms, intakes and functional capacity) which would be completed by the patient with a check box format. The physician then would score the disease status and its relation to nutritional requirements, metabolic demand and physical examination. The result of PG-SGA score will be classified as introduced in the form. Higher score would reflect a higher risk of malnutrition. The appropriate action plan would be suggested as following: 0-1 score: not require intervention; 2-3 score: patients and their family need a nutrition education and counseling from medical staff (such as dietitian, nurse, medical doctor) and/or pharmacologic intervention as indicated; 4-8 score: require intervention by dietitians

in collaboration with nurses or physicians; ≥ 9 score: a critical need of improving symptom management and/or nutrient intervention options (41).

- SGA: the SGA is assessed by a dietitian and it includes two main components: (1) history of weight loss, dietary intake change, gastrointestinal symptoms, functional capacity, and metabolic demand related to the underlying disease; and (2) physical exam focused in the detection of muscle wasting, loss of subcutaneous fat and the presence of edema. The patients' nutrition status then would be classified as: (A) well-nourished, (B) moderately (or suspected of being) malnourished, or (C) severely malnourished (135).

- Weight change: Weight change was defined as the total weight changed by the number of months (one month and six months). The number appeared positive if patient had weight gain and negative if patient lost their weight.

- Karnofsky performance score: the score ranged from 100% (no complaint and no evidence of diseases) down to 0% (death) and divided by 3 sub-classes: Level A: 100% to 80%: patient able to carry on normal activities and to work. Level B: 70% to 50%: Patients unable to work. Level C: Under 50%: Patients unable to carry themselves (74).

- ECOG performance score: The 5-point ECOG (92) performance status scores ranged from 0 to 5. Patient at scored 0 are fully active and able to carry on all pre-disease performance without restriction; at scored 1, they had restricted in physically strenuous activity but able to carried out work of sedentary nature; scored 2 was gave to patient who ambulatory and capable of all self-care but unable to carried out any work activities, ≥ 50% of waking hours; patient at scored 3 were those capable of only limited self-care, confined to bed or chair ≥ 50% of waking hours; Patients scored 4 were completely disabled and scored 5 if they dead.

- Glasgow prognostic score (GPS) is constructed based on the serum Albumin and C-reactive protein levels. Blood samples (5 mL) were collected from a peripheral vein with a single puncture in the morning (6:00 AM to 7:00 AM), following the standardized procedures of the Clinical analysis laboratory of the NCH. The albumin and CRP blood concentrations were measured using an automated biochemical

analyzer (Olympus AU400 Chemistry Analyzer Tokyo, Japan) with chemical substances of Beckman Coulter Ireland Inc 250s, Lismeehan. GPS point is calculated as 0 (CRP $\leq$ 10mg/L and Albumin $\geq$ 35g/L), 1 (CRP > 10mg/L or Albumin < 35g/L) and 2 (CRP > 10mg/L and Albumin < 35g/L)

5.4. Statistical considerations

Epi data 3.1 software was used to enter the data on demographics, anthropometrics, SGA, PG-SGA, biochemical analysis, KPS, GPS. Data on 24-hour dietary intake was analysed using the Vietnam National Institute of Nutrition dietary analysis software based on Vietnamese food composition. All entered data were converted in to the Statistical Package for the Social Sciences (SPSS) version 16.0 for Windows for statistical analysis. The continuous variables are presented as mean $\pm$ SD (standard deviation); categorical data are showed in number and percentage (N; %). The correlation coefficient between two variables was assessed using Pearson's product-moment correlation coefficient for normal distribution data and Spearman's rho for non-normally distributed data.

CHAPTER 4.

RESULTS

1. General characteristics

1.1. Demographic data

A clinical, cross-sectional study was conducted from August 2014 to February 2015 at National Cancer Hospital, Hanoi, Vietnam. There were 65 patients (64 males and only one female) met the inclusion criteria and involved in the study among total of 266 cases admitted during the period of August 2014 to February 2015. We removed the female from the data set, so that 64 male were selected in data analysis.

All of 64 selected male patients had pathology diagnosis as squamous cell carcinoma. The mean ± SD age was 54.91 ± 6.52, median age was 57 (ranged from 35-64). Most of them (73.4%) have tumor located at the middle of esophagus, 14.1% and 12.5% of the subjects have tumor located at the upper and the lower esophagus, respectively. Thirty-one patients (48.4%) were at stage III, while the rest 33 patients (51.6%) were at stage IV of disease. There were 40 patients (62.5%) been placed PEG. The mean ± SD days of post PEG was 8.6 ± 18.02, the median was 4 days (ranged from 3 to 114 days).

Table 10. Patient demographics

Characteristics	N (%)	Mean ± SD (Range)	Median
Age (years)		54.91 ± 6.52 (35-64)	57
Tumor location in the esophagus			
1/3 upper (N; %)	9 (14.1)		
1/3 middle (N; %)	47 (73.4)		
1/3 upper (N; %)	8 (12.5)		
Stage of esophageal cancer disease			
Stage III (N; %)	31 (48.4)		
Stage IV (N; %)	33 (51.6)		
Pathology diagnosis: SCC (N; %)	64 (100)		
Number of patients had gastrectomy for tube feeding (N; %)	40 (62.5)		
Number of days post placed PEG		8.6 ± 18.02 (3-114)	4
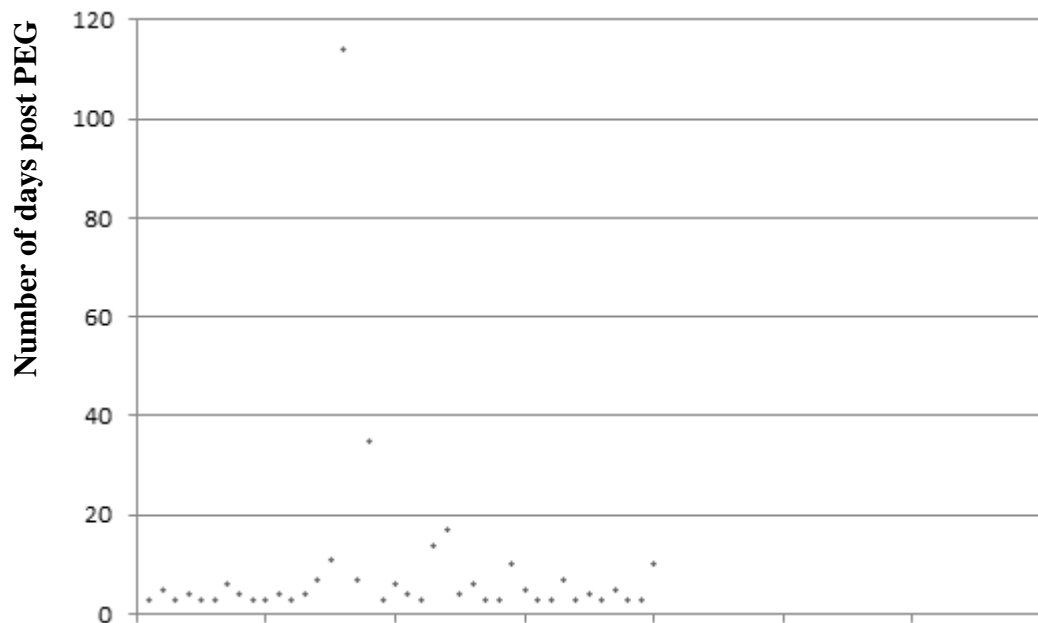
Figure 1. Scatter plot of number of days post- PEG

1.2. Characteristics on nutritional assessments

1.2.1. Anthropometrics measurements

Table 2 depicts anthropometric measurements of patients. Regarding BMI, slight minority (43.8 %) of patients were identified as underweight while in terms of MAC, up to 29.7% of patients were at risk of under-nutrition based on its cut-off point for male.

The results of TSF and MAMA measurement were compared with the US population, using 15th and 85th percentile as cut off point, as described in the study methods. Almost all the patients were classified as below average (85.9% and 96.9% respectively).

Table 11. Characteristics on anthropometric measurements

Characteristics	N (%)	Mean ± SD (Range)	Median
Anthropometric measurements			
Weight (Kg)		49.8 ± 6.8 (37.1 – 73.5)	48.8
Height (cm)		161.5 ± 6.3 (143.2 – 175.3)	162.5
BMI[1]		19.9 ± 2.1 (14.9-25.6)	18.9
BMI classification			
Underweight	28 (43.8)		
18.5 ≤ BMI ≤ 22.99	34 (53.1)		
23 ≤ BMI ≤ 24.99	1 (1.6)		
25 ≤ BMI ≤ 27.49	1 (1.6)		
MAC (mm) [2]		24.0 ± 2.4 (18.8-32.3)	24.1
MAC classification			
Undernutrition (N; %)	19 (29.7)		
Normal (N; %)	45 (70.3)		
TSF[3] (mm)		0.67 ± 0.31 (0.25 – 1.9)	0.6
Below average	55 (85.9)		
Average	9 (14.1)		
MAMA[4] (mm^2)		38.7 ± 7.7 (25.8 – 69.9)	37.6
Below average	62 (96.9)		
Average	2 (3.1)		

1: Body mass index, calculated by Weight (in kg)/(Height (in metters))^2

2: Mid arm circumference

3: Triceps skin fold thickness

4: Mid arm muscle area

1.2.2. Laboratory measurements

Our study population had the median total blood count, serum albumin, and serum CRP in the normal range.

Table 12. Characteristics on total blood count, serum albumin and CRP

Index	Unit	N	Nor. range	Mean ± SD	Med.	Min.	Max.
RBC	T/l	60	4.0 - 5.2	4.40 ± 0.55	4.30	3.17	5.86
Hb	g/l	63	120 - 160	192.5 ± 16.3	130	83	165
Hct	l/l	63	36 - 46	39.61 ± 4.49	40.2	28.2	49.2
MCV	fl	54	80 - 100	88.3 ± 8.54	89.15	63.1	98.8
MCH	pg	63	26 - 34	29.56 ± 3.34	30.1	18.5	37.6
MCHC	g/l	63	315 - 363	326.7 ± 10.8	326	286	363
Platelets	G/l	59	150 - 400	314.1 ± 102.8	303	136	649
WBC	G/l	60	4 - 12	9.6 ± 2.24	9.7	5.3	15.3
Neutro	G/l	62	1.8 - 7.5	5.75 ± 1.87	5.6	2.23	9.78
Eosin	G/l	62	0 - 0.8	0.39 ± 0.39	0.27	0.02	1.87
Baso	G/l	63	0 - 0.1	0.02 ± 0.03	0.01	0	0.22
Mono	G/l	57	0 - 0.8	0.98 ± 0.34	0.98	0.34	2.19
Lympho	G/l	62	1 - 4.5	2.49 ± 0.93	2.32	0.67	6.27
Albumin	g/l	64	35 - 55	41.5 ± 5.35	40.8	29.9	58.0
CRP	g/l	61	< 10	15.97 ± 20.44	7.6	4	74.1

According to total blood count tests, there were 9 patients (15%) had low total red blood cell (RBC), 12 (19%) patients had hemoglobin level (HGB) lower than the normal range, 6 (1.1%) patients had low mean corpuscular volume (MCV) and 5 (7.9%) had low mean corpuscular hemoglobin (MCH). There were 8 (12.9%) patients had total white blood cell higher than normal range and interestingly, there were 36 patients (63.2%) had the number of mono cells higher than the normal range.

There were 6 patients (9.4%) had low serum albumin level as showed in the biochemistry testes.

Table 13. Characteristics on total blood count and serum albumin classification

Index	Unit	N	Results			
			Normal range	Lower N (%)	In the nor. range N (%)	Upper N (%)
RBC	T/l	60	4.0 - 5.2	9 (15)	46 (76.7)	5 (7.8)
Hb	g/l	63	120 – 160	12 (19)	49 (77.8)	2 (3.2)
Hct	l/l	63	36 – 46	10 (15.9)	50 (79.4)	3 (4.8)
MCV	fl	54	80 – 100	6 (11.1)	48 (88.9)	
MCH	pg	63	26 – 34	5 (7.9)	55 (87.3)	3 (4.8)
MCHC	g/l	63	315 – 363	5 (7.9)	58 (92.1)	
Platelets	G/l	59	150 – 400	1 (1.7)	48 (81.4)	10 (16.9)
WBC	G/l	60	4 – 12		54 (87.1)	8 (12.9)
Neutro	G/l	62	1.8 - 7.5		55 (88.7)	7 (11.3)
Eosin	G/l	62	0 - 0.8		54 (87.1)	8 (12.9)
Baso	G/l	63	0 - 0.1		62 (98.4)	1 (1.6)
Mono	G/l	57	0 - 0.8		21 (36.8)	36 (63.2)
Lympho	G/l	62	1 - 4.5	1 (1.6)	60 (96.8)	1 (1.6)
Serum albumin	g/l	64	35 – 55	6 (9.4)	56 (87.5)	2 (3.1)

1.2.3. Clinical assessment

Only 3 patients (4.7%) were assessed anemia in clinical diagnosis. More than a half of patients appeared mild to medium level of fat loss and muscle loss, but none of them got edema and ascites.

According to SGA assessment, there were four GI symptoms persisting for more than two weeks: nausea (6.2%), vomiting (7.8%), diarrhea (0) and anorexia (10.9%). All the patients were diagnosed at low stress level for metabolic demand.

Symptoms related dietary intake based on patient's self-noted in PG-SGA assessment showed almost all the patients complained they had difficult on swallowing (84.4%); 18.8% painful in the throat and chest area when patient eating; other symptoms such as nausea, vomiting, constipation, dry mouth, changing in smell, and feel full quickly were in small scales (under 10% for each). There were 9.4% patient noted they had no problem in eating.

Table 14. Characteristics on clinical presentation

Characteristics	N (%)	Characteristics	N (%)
Anemia	3 (4.7)	**According to PG-SGA assessment**	
According to SGA assessment		No problem eating	6 (9.4)
Fat loss		No appetite	4 (6.2)
No fat loss	22 (34.4)	Nausea	8 (12.5)
Mild to medium	37 (57.8)	Vomiting	5 (7.8)
Severe	5 (7.8)	Constipation	5 (7.8)
Muscle loss		Diarrhea	0
No muscle loss	31 (48.4)	Mouth sores	0
Mild to medium	32 (50.0)	Dry mouth	5 (7.8)
Severe	1 (1.6)	Taste changed	0
		Smell changed	3 (4.7)
No edema	64 (100)	Problem in swallowing	54 (84.4)
No ascites	64 (100)	Feel full quickly	4 (6.2)
Metabolic demand	64 (100)	Pain	12 (18.8)
(Low stress level)			
GI symptoms (for > 2 wks)		Others	2 (3.1)
Nausea	4 (6.2)		
Vomiting	5 (7.8)		
Diarrhea	0		
Anorexia	7 (10.9)		

1.2.4. Dietary assessment

In the SGA assessment, 92.1% patients had change in dietary intake. Among those, 49.1% had suboptimal oral diet, 28.1% had the full liquid diet and 22.8% had hypocaloric liquid diet. Two third of patients noted they had dietary difficulties or reduction of intake but not severe, slight minority one third (23.4%) did not have dietary difficulties or improved at the time of assessment; only 12.5% had severe reduction of intake food.

For the self-report in PG-SGA assessment, three forth patients (76.6%) had food intake less than usual, the percentage of patient had food intake unchanged or more than usual were similar (12.5% and 10.9%, respectively). For the current food intake, there were 45.3% had less food than normal amount; 26.6% noted they just had a little of solid food; 23.4% nourished by only tube feeding, two patients (3.1%) had small amount of food and only one patient (1.6%) had only liquids.

Table 15. Characteristics on intake dietary

Characteristics (On SGA assessment)	N (%)	Characteristics (On PG-SGA assessment)	N (%)
Change in dietary intake	58 (92.1)	**Food intake**	
Suboptimal oral diet	28 (49.1)	Unchanged	8 (12.5)
Full liquid diet	16 (28.1)	More than usual	7 (10.9)
Hypocaloric liquid	13 (22.8)	Less than usual	49 (76.6)
Dietary difficulties or reduction of intake		**Current food intake**	
None or improved	15 (23.4)	Less than normal amount	29 (45.3)
Some but not severe	41 (64.1)	Little solid food	17 (26.6)
Many or severe	8 (12.5)	Only liquids	1 (1.6)
		Only nutritional supplements	0
		Very little of anything	2 (3.1)
		Only tube feeding	15 (23.4)

The energy intake was 24.5 ± 11.2 kcal/kg/d (median was 23.8 kcal/kg/d; ranged from 6.1 to 73.0 kcal/kg/d), and protein intake was 1.1 ± 0.5 g/kg/d (median was 1 g/kg/d; ranged from 0.3 to 3.1 g/kg/d). According to ESPEN recommendation, more than half of the patients (54.7%) had energy intake under 25 kcal/kg/day and nearly half of patients (48.4%) had protein intake under 1 g/kg/d. Even most patients got protein intake lower as the ESPEN recommendation, but the protein from animal still reached 55.4% with the median 47.2g/d.

The median percent energy from CHO and lipid intake were 55.9% (median 158g/d) and 26.1% (median 32g/d), respectively.

Table 16. General characteristics of 24-hour recall dietary intake assessment

Characteristics	N (%)	Mean ± SD (Range)	Median
Energy intake (Kcal/d)		1,208 ± 552	1,116
		(364 – 3,883)	
Energy intake (kcal/kg/d)		24.5 ± 11.2 (6.1- 73)	23.8
Energy intake (kcal/kg/d) classification			
Under 25 kcal/kg/d	35 (54.7)		
25-30 kcal/kg/d	13 (20.3)		
30-35 kcal/kg/d	8 (12.5)		
Over 35 kcal/kg/d	8 (12.5)		
Protein intake (g/d)		53.2 ± 25.1	47.2
		(14.4 - 154.9)	
% Protein from animal		54 ± 1.6 (14.3 - 90)	55.4
% energy from Protein		17.7 ± 3.5 (8.7 – 30.3)	17.1
Protein intake (g/kg/d)		1.1 ± 0.5 (0.3- 3.1)	1.0
classification			
Under 1 g/kg/d	31 (48.4)		
1-1.2 g/kg/d	11 (17.2)		
1.2-1.5 g/kg/d	10 (15.6)		
1.5-2 g/kg/d	10 (15.6)		
Over 2 g/kg/d	2 (3.1)		
CHO intake (g/d)		172 ± 96 (40 - 695)	158
% energy from CHO		55.9 ± 7.3 (39.4 – 79.3)	55.9
Lipid intake (g/d)		34 ± 14 (11 - 67)	32
% energy from lipid		26.5 ± 6.6 (12 – 43.3)	26.1
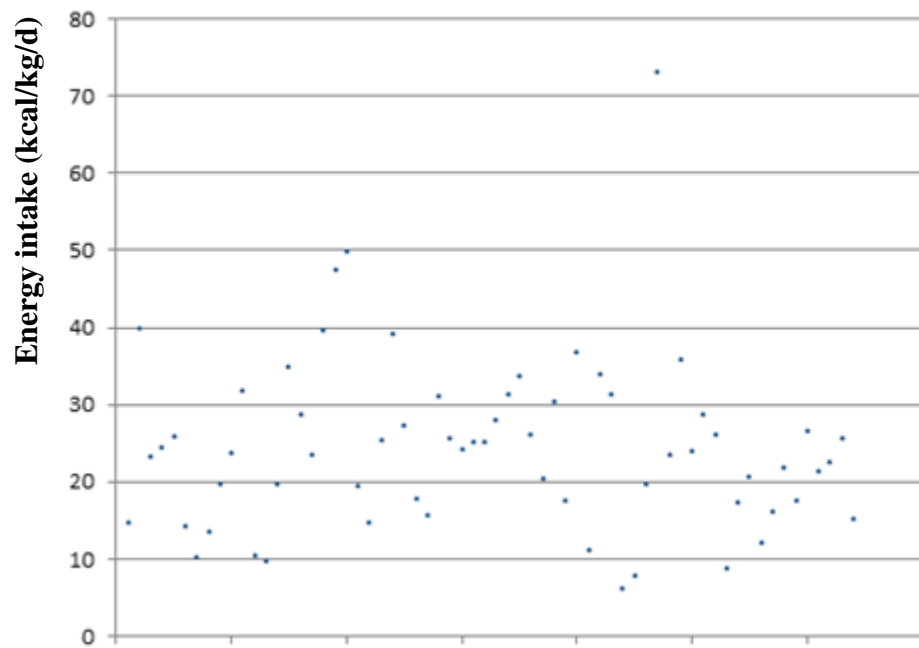
Figure 2. Scatter plot of energy intake
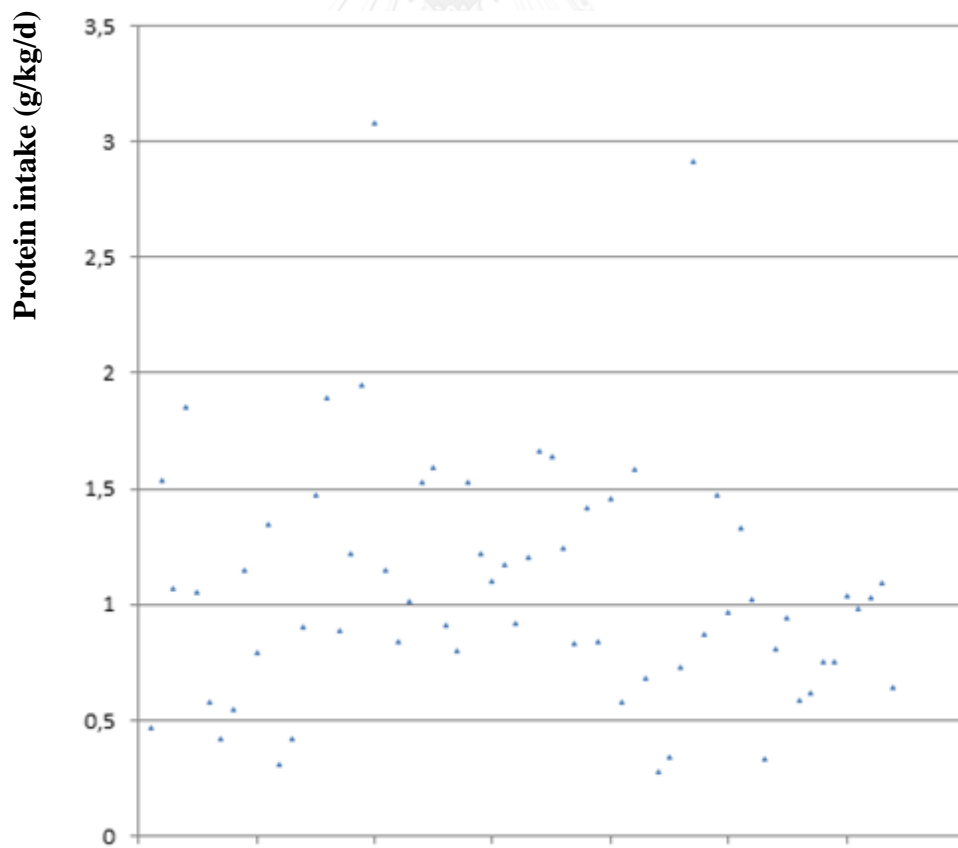
Figure 3. Scatter plot of protein intake

Dietary assessment in 40 patients placed PEG to support feeding

Patients had placed PEG to support feeding even got less energy and protein intake. The energy intake in this population was 21 ± 7.7 kcal/kg/d (median 22) and the protein intake was 0.9 ± 0.4 g/kg/d (median 0.9). In those population, nearly two third (65%) had energy intake under the lower level of ESPEN requirement. The protein intake also had the same situation, which 57.7% patients had lower 1gr/kg/d. Fortunately, the percentage of protein from animal sources still reached about 54% with the median of 45.9g/d. Percentage energy from carbohydrate and lipid were 55% and 27%, respectively.

Table 17. Characteristics of 24-hour recall dietary intake among 40 patients placed PEG

Characteristics	N (%)	Mean ± SD (Range)	Median
Energy intake (Kcal/d)		1,048 ± 384 (363 – 1,981)	1,077
Energy intake (kcal/kg/d)		21 ± 7.7 (6.0- 40)	22
Energy intake (kcal/kg/d) classification			
Under 25 kcal/kg/d	26 (65)		
25-30 kcal/kg/d	10 (25)		
30-35 kcal/kg/d	2 (5)		
Over 35 kcal/kg/d	2 (5)		
Protein intake (g/d)		46.8 ± 1.1 (14.4 – 94.0)	45.9
% Protein from animal		54 ± 1.6 (19.7 - 90)	54
% energy from Protein		17.7 ± 3.5 (11.8 – 30.3)	17.1
Protein intake (g/kg/d) classification		0.9 ± 0.4 (0.3- 1.9)	0.9
Under 1 g/kg/d	23 (57.5)		
1-1.2 g/kg/d	7 (17.5)		
1.2-1.5 g/kg/d	6 (15)		
1.5-2 g/kg/d	10 (10)		
CHO intake (g/d)		143 ± 57 (40 - 293)	145
% energy from CHO		54 ± 6.5 (39 – 68)	55
Lipid intake (g/d)		33 ± 13 (11 - 67)	30
% energy from lipid		28.5 ± 6.2 (12.7 – 43.3)	27

1.2.5. SGA and PG-SGA assessments

The mean ± SD of PG-SGA score was 9.88 ± 4.41 (median was 9). Based on PG-SGA assessment, all patients required nutritional intervention at different levels. The majority of these patients (54.7%) were at critical need for nutrition intervention (PG-SGA score ≥ 9). The SGA determined 43.8% of patients at moderate malnutrition and 6.2% of them at severe malnutrition.

Table 18. Characteristics on PG-SGA and SGA assessment

Characteristics	N (%)	Mean ± SD (Range)
PG-SGA[3] score		9.88 ± 4.41 (2 – 21)
PG-SGA score classification		
2-3	3 (4.7)	
4-8	26 (40.6)	
≥ 9	35 (54.7)	
SGA[4] classification		
A	32 (50)	
B	28 (43.8)	
C	4 (6.2)	

3: Patient generated subjective global assessment

4: Subjective global assessment

1.2.6. Weight change

Mean weight ± SD at admitted was 49.7 ± 9.4 kg. The mean weight change ± SD in the past one and six months were − 2.8 ± 3.1 kg and -5.0 ± 3.7 kg, respectively. Among those who had weight loss, the mean ± SD of weight loss in past one and six months were -3.6 ± 2.7 kg (median was -3.2 kg) and -5.4 ± 3.5 kg (median was -5.0 kg), respectively. The proportions of patients who experienced weight loss pass six months under 5%, 5% to 10%, and above 10% were 17.6%, 39.2% and 43.1%, respectively.

In comparison with two weeks before admitted, it was common that patients got weight loss (68.8 %) while only 2 patients (3.1%) had weight gain. Moreover, the percentage of patients had placed PEG to support feeding even got the weight loss past two weeks higher than in general, with 75%.

Table 19. Characteristics on weight change

Characteristics	N (%)	Mean ± SD (Range)	Median
Weight change past two weeks			
Weight loss	44 (68.8)		
Weight stable	18 (28.1).		
Weight gain	2 (3.1)		
Weight change past two weeks among those placed PEG			
Weight loss	30 (75)		
Weight stable	8 (20)		
Weight gain	2 (5)		
Weight change past one month (kg)		-2.8 ± 3.1 (-12.9 – 2.7)	-2.4
Weight loss past one month (kg)	54 (84.4)	-3.6 (-12.9 - -0.2)	-3.2
Percent weight loss past one month			
Under 5%	24 (44.4)		
From 5% to 10%	20 (37.0)		
Above 10%	10 (18.5)		
Weight change past six months (kg)		-5.0 ± 3.7 (-19.4 – 1.8)	-4.7
Weight loss past six months (kg)	59 (93.7)	-5.4 (-19.4 - -0.2)	-5.0
Percent weight lost past six month			
Under 5%	9 (17.6)		
From 5% to 10%	20 (39.2)		
Above 10%	22 (43.1)		

1.3. Characteristics on performance status

The SGA assessment showed that the nutrition impacted 50% patients in functional impairment. And slightly more than a half of patients (57.8%) reported limitation of usual activities but not severe.

Self-report on activities and function of PG-SGA assessment noted minor half of patients (46.9%) did their activities fairly normal; patients without limitation of their activities were 26.6%; one fifth (18.8%) stayed in bed less than half a day and 7.8% spent most day in bed. There were none patients had to stay whole day in bed.

Table 20. Characteristics on performance status based on SGA, PG-SGA assessment

Characteristics (based on SGA assessment)	N (%)	Characteristics (based on PG-SGA assessment)	N (%)
Functional impairment		**Activities and functions**	
Due to nutrition	32 (50)	Normal without limitation	17 (26.6)
Other diagnosis	32 (50)	Fairly normal	30 (46.9)
Limitation of usual activities		In bed < ½ day	12 (18.8)
None	27 (42.2)	Most day in bed	5 (7.8)
Some but not severe	37 (57.8)	Rarely out of bed	0

The mean of KPS score, a specifically tool in assess the performance status, among study subjects was 77.5 ± 15.1 with the median was 80. The biggest portion (40.6%) belong to patients with KPS = 90 (patients able to carried on normal activities, had minor signs or symptoms of disease). Number of patients had KPS = 60 or 70 or 80 were fairly similarly (15.6%; 15.6% and 21.9%, respectively). Only 4 patients (6.2%) had KPS = 50, means patients required considerable assistance and frequent medical care.

For ECOG assessment (another well-known assessment performance status tool in oncology patients), the mean of score was 1.47 ± 0.67 with the median was 1. These scores reflected the patient's ability to do daily activities themselves. Similarly to KPS assessment, only 5 patients (7.8%) had ECOG score = 3, reflected patients capable of only limited self-care, confined to bed or chair more than 50% of waking hours.

Table 21. Characteristics on performance scores

Characteristics	N (%)	Mean ± SD (Range)	Median
KPS score		77.5 ± 13.1 (50 – 90)	80
KPS = 50	4 (6.2)		
KPS = 60	10 (15.6)		
KPS = 70	10 (15.6)		
KPS = 80	14 (21.9)		
KPS = 90	26 (40.6)		
Characteristics	**N (%)**	**Mean ± SD (Range)**	**Median**
ECOG score		1.47 ± 0.67 (0 – 3)	1
ECOG score = 0	1 (1.6)		
ECOG score = 1	37 (57.8)		
ECOG score = 2	21 (32.8)		
ECOG score = 3	5 (7.8)		

1.4. Characteristics on prognostic score

Most of patients had the GPS equal to 0 and 1 (52.5% and 42.6%, respectively). Only 3 patients (4.9%) had GPS = 2 (serum albumin < 35mg/dl and serum CRP > 10 mg/dl). In sub-class of CRP score, almost all of the patients (90.6%) had serum albumin ≥ 35g/dl. The amount of patients with serum CRP < 10 mg/L or ≥ 10 mg/L were nearly similar (57.4% and 42.6%, respectively).

Table 22. Characteristics on GPS

Characteristics	N (%)
GPS score	
GPS = 0	32 (52.5)
GPS = 1	26 (42.6)
GPS = 2	3 (4.9)
Serum albumin range	
< 35 g/dL	6 (9.4)
≥ 35 g/dL	58 (90.6)
Serum CRP range	
< 10 mg/L	35 (57.4)
≥ 10 mg/L	26 (42.6)

2. Correlation among nutritional scales, performance and prognostic scores

2.1. Correlation between SGA, PG-SGA and anthropometric measurements

BMI had fairly weak negative correlation coefficient with PG-SGA (r = -0.266) while there was no association with SGA. TSF had no correlation coefficient with both SGA and PG-SGA.

Both SGA and PG-SGA had negative correlation with MAC index (r = -0.304; p < 0.05 and r = -0.414, p < 0.01 respectively), and MAMA (r = - 0.313; p < 0.05 and r = -0.388; p < 0.01)

Table 23. Correlation between SGA, PG-SGA and anthropometric measurements

		BMI	MAC	TSF	MAMA
SGA	R	-0.105	-0.304[*]	-0.115	-0.313[*]
	p	0.41	0.015	0.365	0.012
PG-SGA	R	-0.266[*]	-0.414[**]	-0.187	-0.388[**]
	p	0.03	0.001	0.138	0.002

*: Correlation is significant at the 0.05 level (2-tailed)

**: Correlation is significant at the 0.01 level (2-tailed)

Figure 4. Correlation between total PG-SGA score and BMI calculation

MAC (cm)

Figure 5. Correlation between total PG-SGA score and MAC measurement
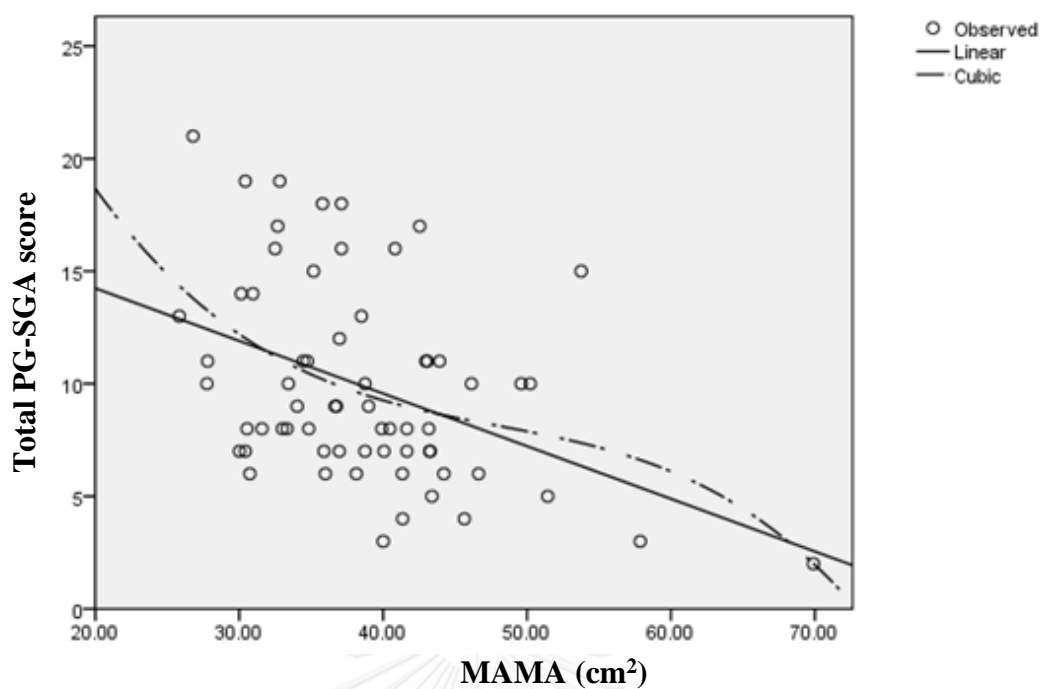
Figure 6. Correlation between total PG-SGA score and MAMA measurement

2.2. Correlation between dietary intake and anthropometric measurements

Both energy intake and protein intake had no correlation coefficient with anthropometric measurements (BMI, MAC, TSF, and MAMA)

Table 24. Correlation between energy, protein intake and anthropometric measurements

		BMI	**MAC**	**TSF**	**MAMA**
Energy intake	R	-0.061	0.029	0.051	0.041
(Kcal/kg/d)	_p_	0.633	0.823	0.686	0.749
Protein intake	R	0.141	-0.043	0.014	0.022
(g/kg/d)	_p_	0.265	0.737	0.914	0.862

2.3. Correlation between dietary intake and SGA, PG-SGA assessments

In contrast, both SGA and PG-SGA had moderate correlation coefficient with energy intake (kcal/kg/d) ($r = -0.448$; $p < 0.001$ and $r = -0.414$; $p < 0.01$) and protein intake (g/kg/d) ($r = -0.468$; $p < 0.001$ and $r = -0.444$; $p < 0.001$)

Table 25. Correlation between energy, protein intake and SGA, PG-SGA assessments

		SGA	PG-SGA
Energy intake (kcal/kg/d)	R	-0.448**	-0.468**
	p	< 0.001	< 0.001
Protein intake (g/kg/d)	R	-0.414**	-0.444**
	p	0.001	< 0.001

*: Correlation is significant at the 0.05 level (2-tailed)

**: Correlation is significant at the 0.01 level (2-tailed)
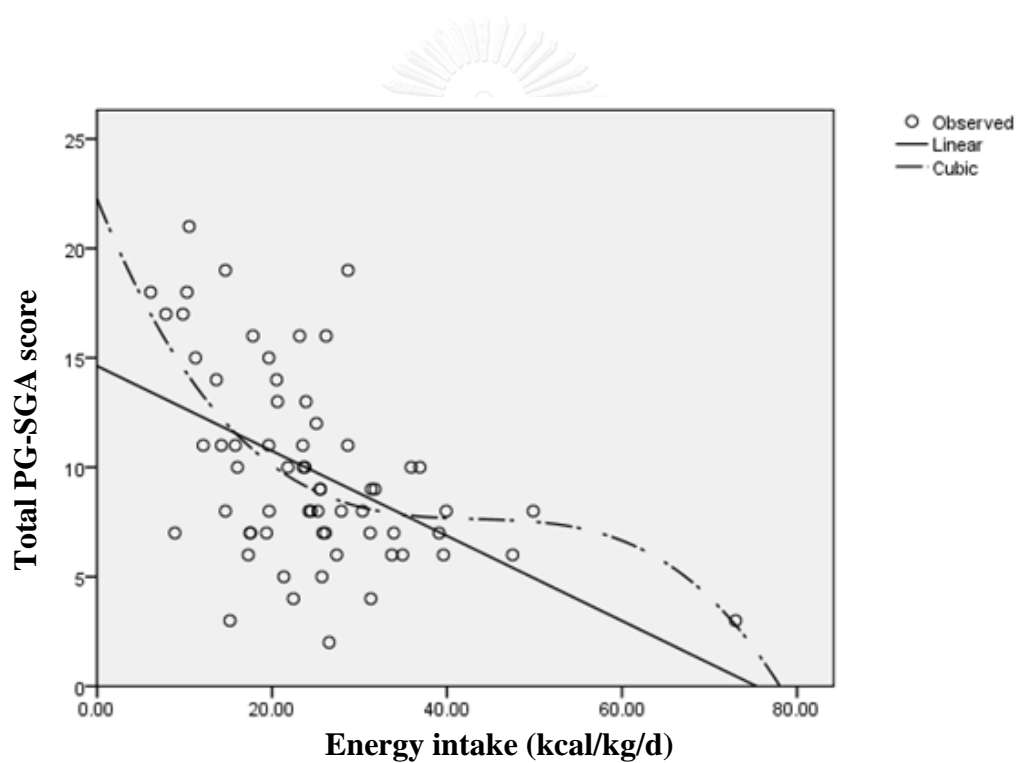
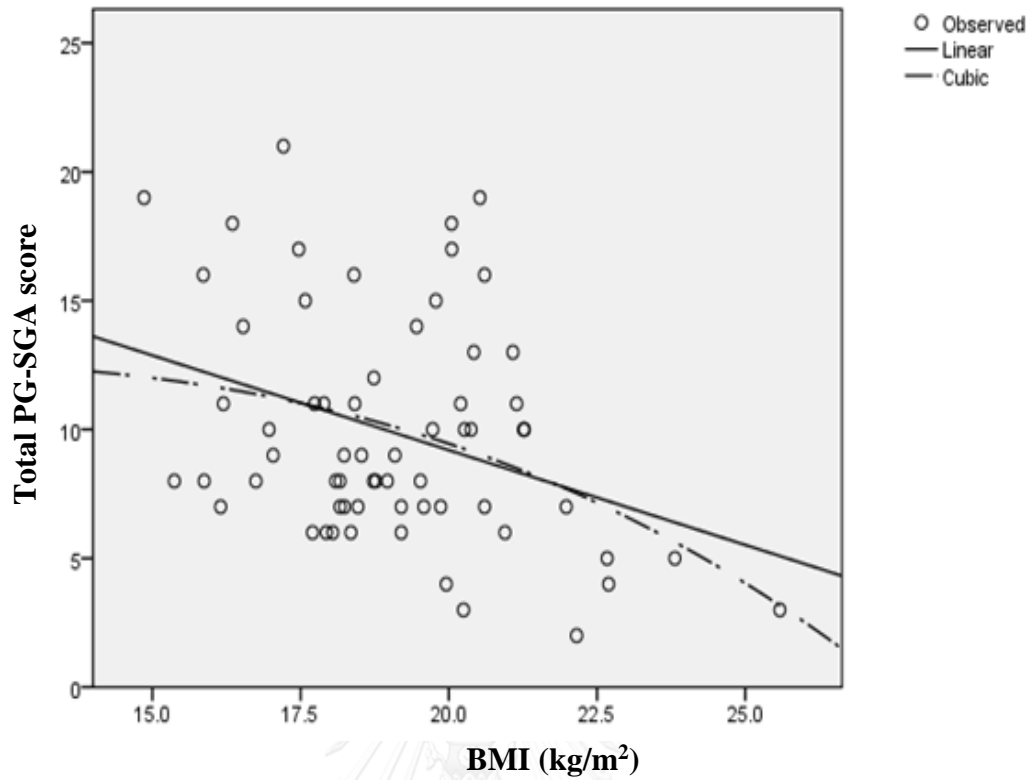**Figure 7. Correlation between total PG-SGA score and energy intake**
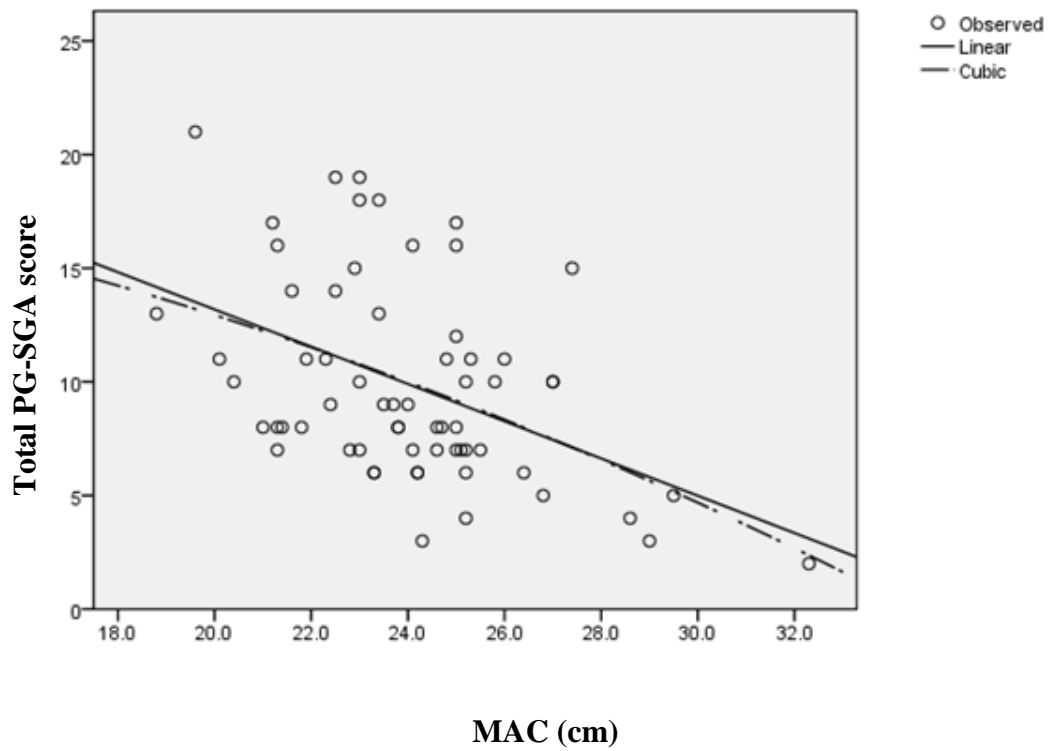
Figure 8. Correlation between total PG-SGA score and protein intake

2.4. Correlation between SGA, PG-SGA and performance scores, GPS, weight change

There was a strong correlation coefficient between SGA, PG-SGA and KPS as well as ECOG. The correlation between SGA, PG-SGA and KPS was negatively (r = - 0.632 and r = -0.717; p < 0.001). There was a positive correlation between SGA, PG-SGA and ECOG with r = 0.626 and r = 0.672; p < 0.001. Both SGA and PG-SGA had weak correlation coefficient with GPS (r = 0.278; p < 0.05 and r = 0.332; p < 0.01, respectively).

Table 26. Correlation between SGA, PG-SGA and performance scores, GPS

		KPS	ECOG	GPS
SGA	R	-0.632[**]	0.626[**]	0.278[*]
	p	< 0.001	< 0.001	0.03
PG-SGA	R	-0.717[**]	0.672[**]	0.332[**]
	p	< 0.001	< 0.001	0.009

*: Correlation is significant at the 0.05 level (2-tailed)

**: Correlation is significant at the 0.01 level (2-tailed)
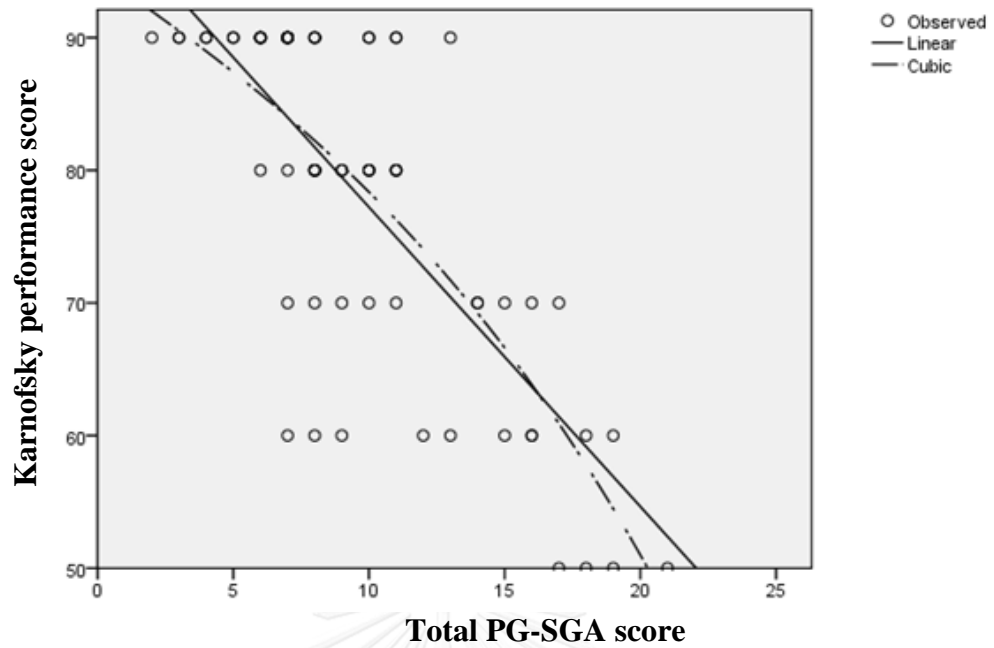
Figure 9. Correlation between total PG-SGA score and KPS
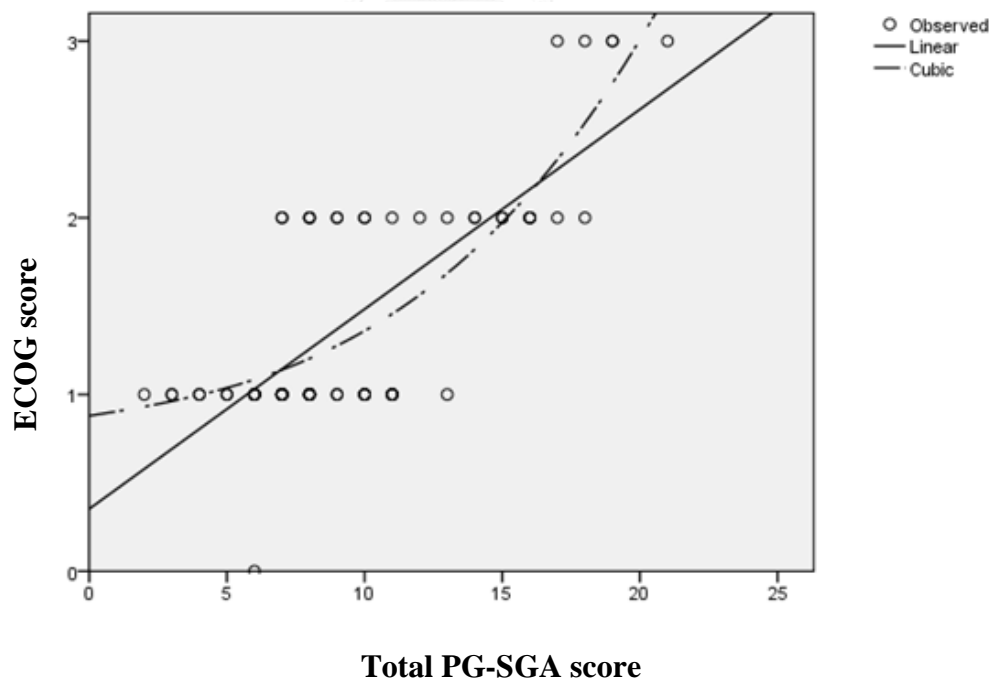
Total PG-SGA score

Figure 10. Correlation between total PG-SGA score and ECOG score
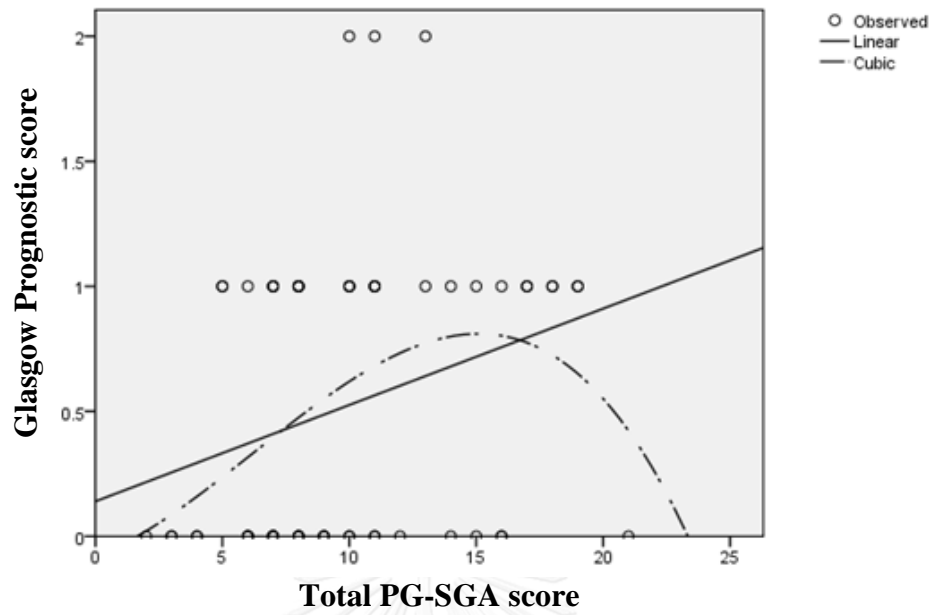
Figure 11. Correlation between total PG-SGA score and Glasgow prognostic score
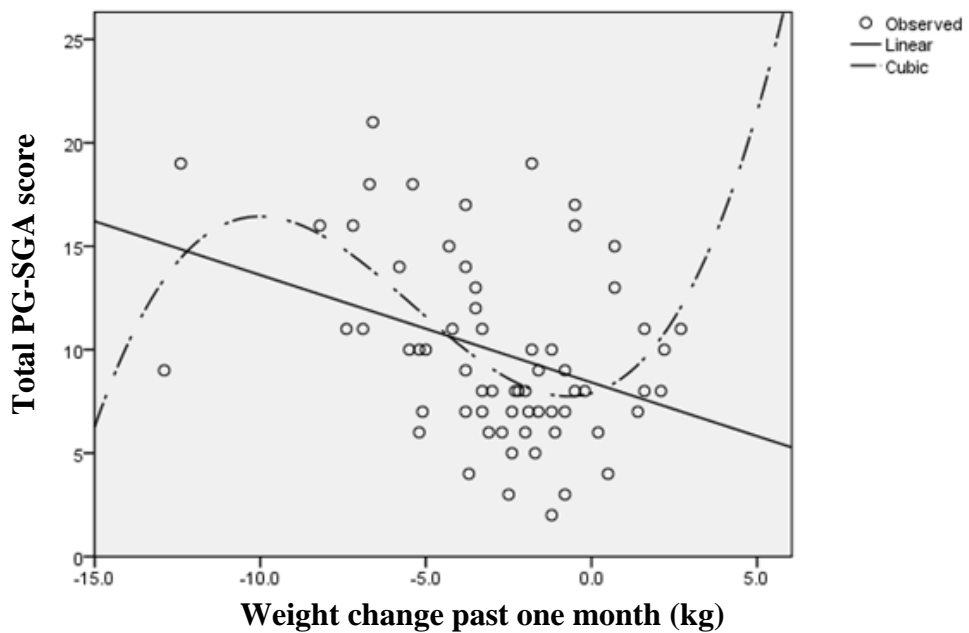
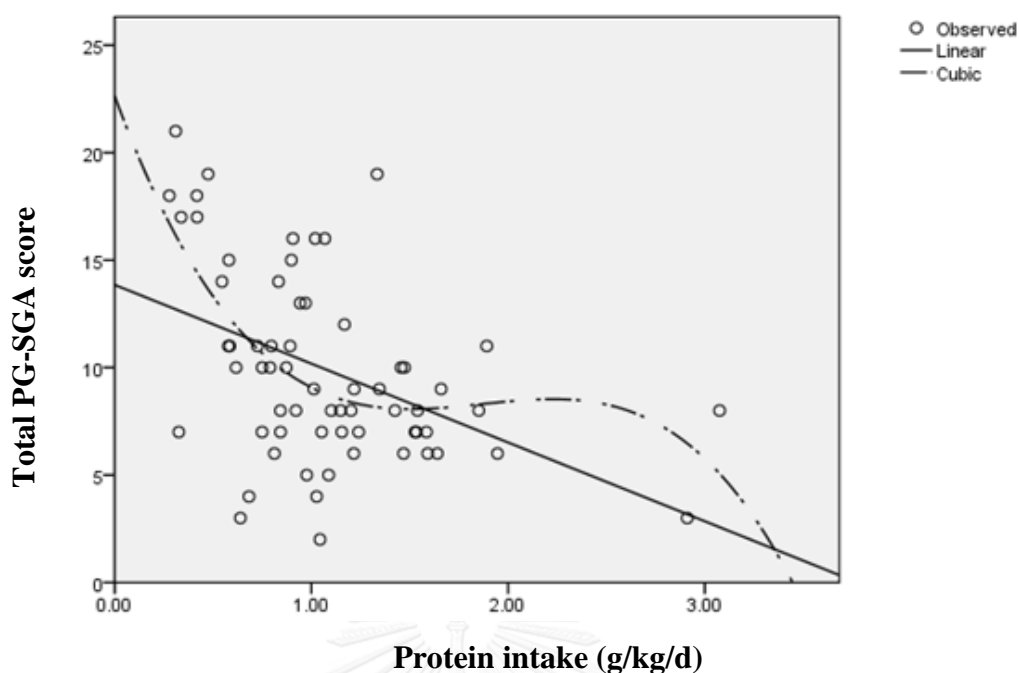**Figure 12. Correlation between total PG-SGA score and weight change past one month**
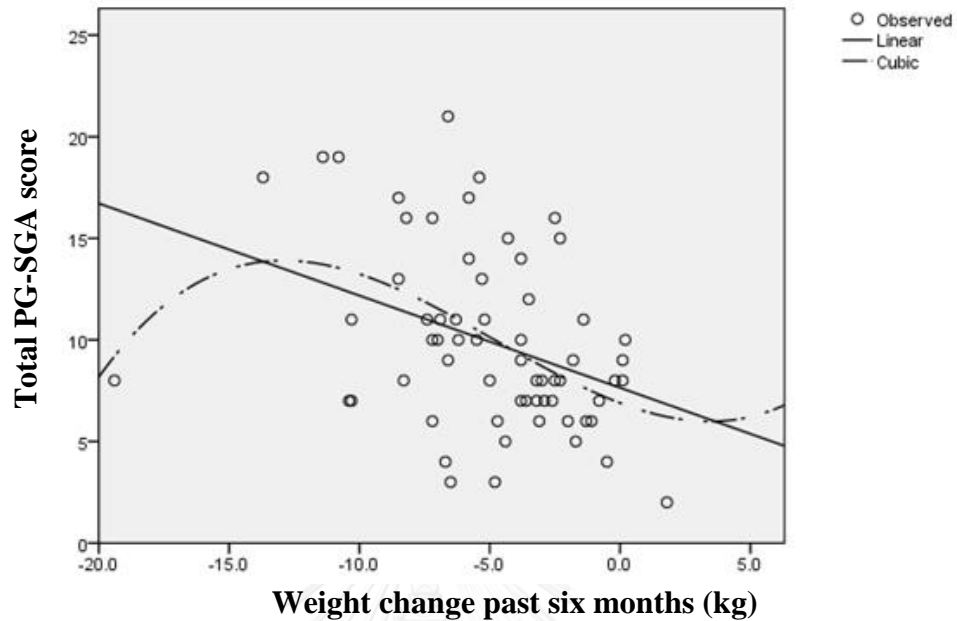
Figure 13. Correlation between total PG-SGA score and weight change past six months

2.5. Correlation between anthropometric measurements, dietary intake and performance scores, GPS

BMI, MAC and TSF did not have a significant correlation coefficient with GPS but MAMA did with r = -0.292, p < 0.05. BMI had weak correlation coefficients with KPS (r = 0.254, p < 0.05) but did not show the correlation with ECOG. MAC and MAMA had moderate correlation coefficient with both KPS and ECOG while TSF completely did not.

Similarly to anthropometric measurements, dietary intake did not show the correlation coefficient with GPS. The correlation between dietary intake and performance scores were moderate, with r value in the range of 0.318 (p < 0.05) to 0.396 (p < 0.01).

Table 27. Correlation between anthropometric measurements and performance scores and GPS

		KPS	ECOG	GPS
BMI	R	0.254[*]	-0.145	0.085
	p	0.042	0.253	0.514
MAC	R	0.391[**]	-0.273[*]	-0.247
	p	0.001	0.029	0.055
TSF	R	0.026	-0.054	0.039
	p	0.841	0.671	0.764
MAMA	R	0.449[**]	-0.307[*]	-0.292[*]
	p	< 0.001	0.014	0.022
Energy intake (Kcal/kg/d)	R	0.375[**]	-0.396[**]	-0.159
	p	0.002	0.001	0.221
Protein intake (g/kg/d)	R	0.318[*]	-0.348[**]	-0.197
	p	0.011	0.005	0.127

*: Correlation is significant at the 0.05 level (2-tailed)

**: Correlation is significant at the 0.01 level (2-tailed)
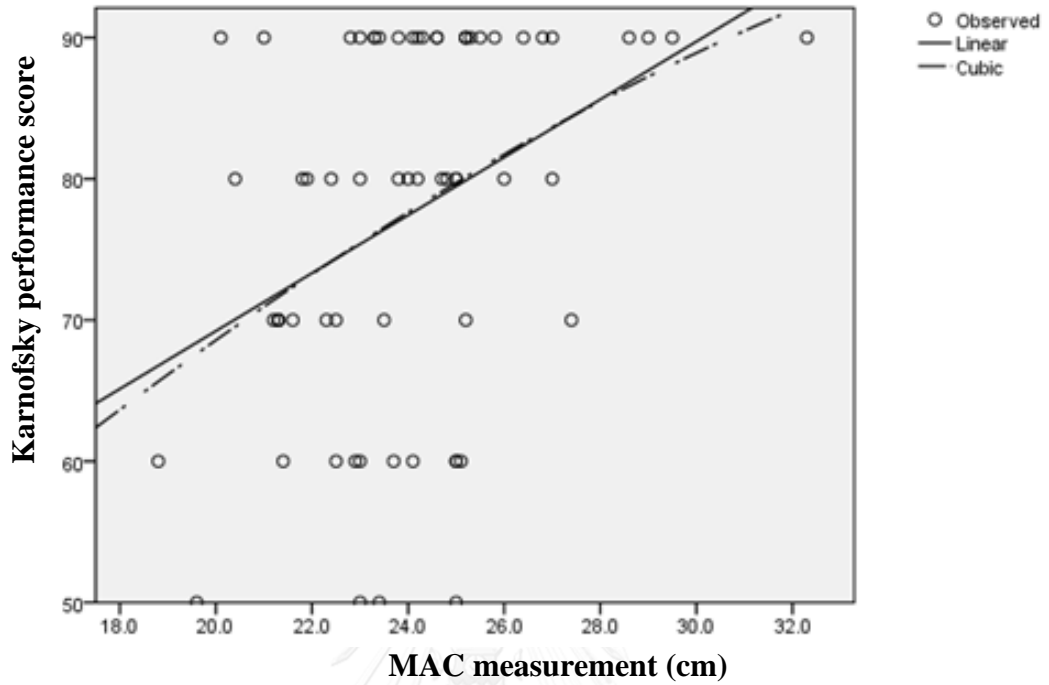
Figure 14. Correlation between KPS and MAC measurement
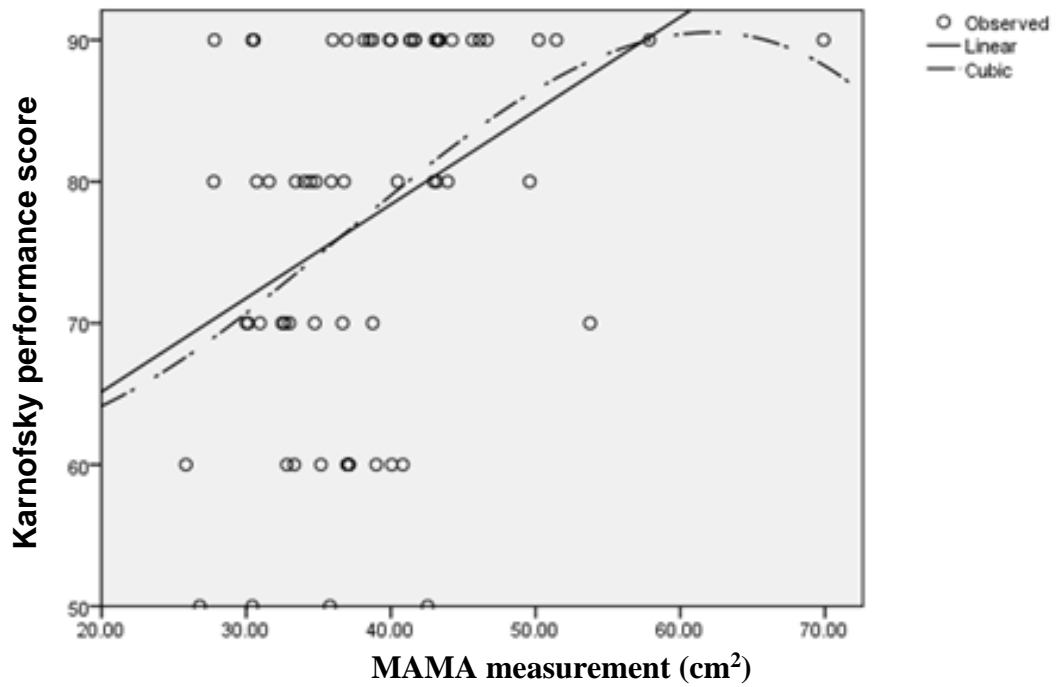

Figure 15. Correlation between KPS and MAMA measurement
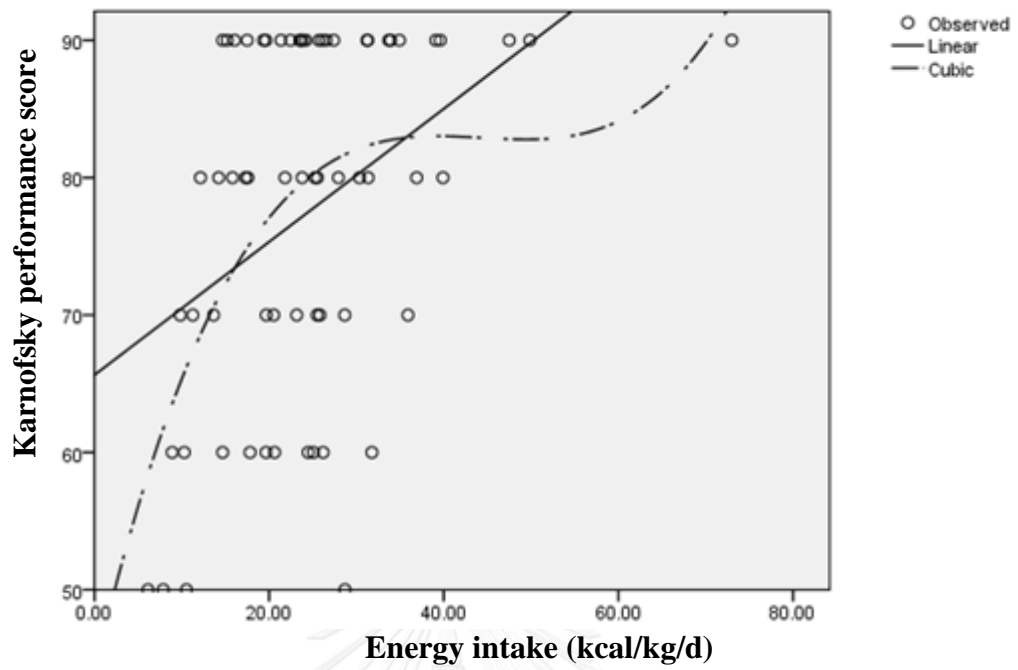
Figure 16. Correlation between KPS and energy intake
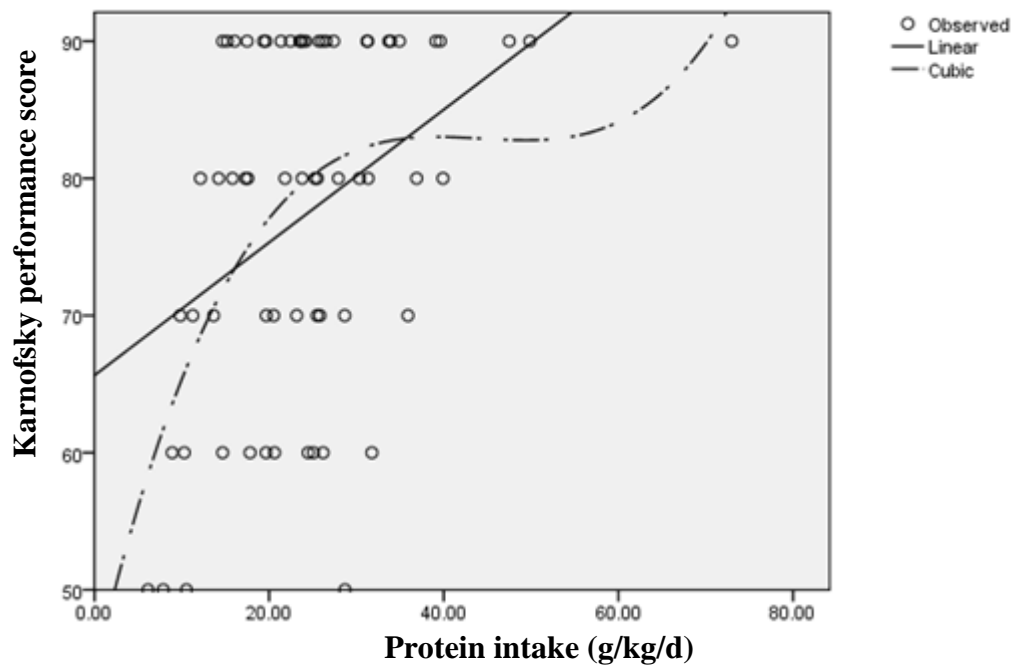
Figure 17. Correlation between KPS and protein intake

2.6. Correlation between GPS and performance scores

Performance scores did not have correlation coefficient with GPS.

Table 28. Correlation between GPS and performance scores

		KPS	ECOG
GPS	R	-0.224	0.219
	p	0.083	0.09

2.7. Correlation between weight change and anthropometric measurements

Weight change past one month did not correlate with both four anthropometric measurements (BMI, MAC, TSF and MAMA). The TSF also had no correlates with weight change past six months. But the weight change past six months correlated significantly with BMI, MAC and MAMA (r = 0.272, p < 0.05; r = 0.360, p < 0.01 and r = 0.326, p < 0.01, respectively).

Table 29. Correlation between weight change and anthropometric measurements

		BMI	MAC	TSF	MAMA
Weight change past one month	R	0.177	0.046	0.036	0.037
	p	0.162	0.716	0.778	0.775
Weight change past six months	R	0.272[*]	0.360[**]	0.185	0.326[**]
	p	0.031	0.004	0.146	0.009

*: Correlation is significant at the 0.05 level (2-tailed)

**: Correlation is significant at the 0.01 level (2-tailed)

Figure 18. Correlation between BMI and weight change past six months
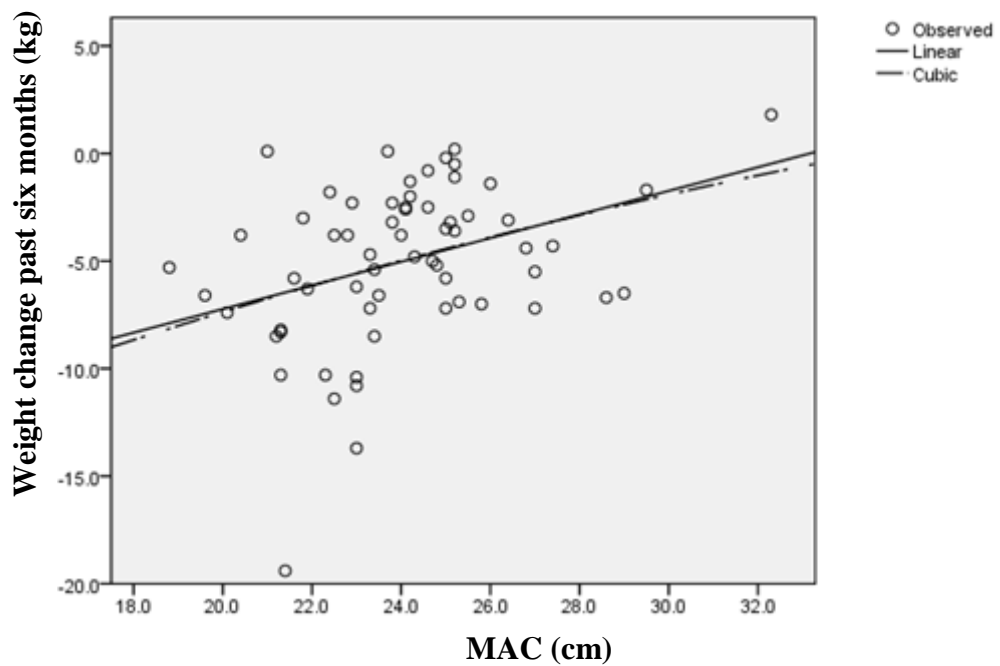
Figure 19. Correlation between MAC and weight change past six months
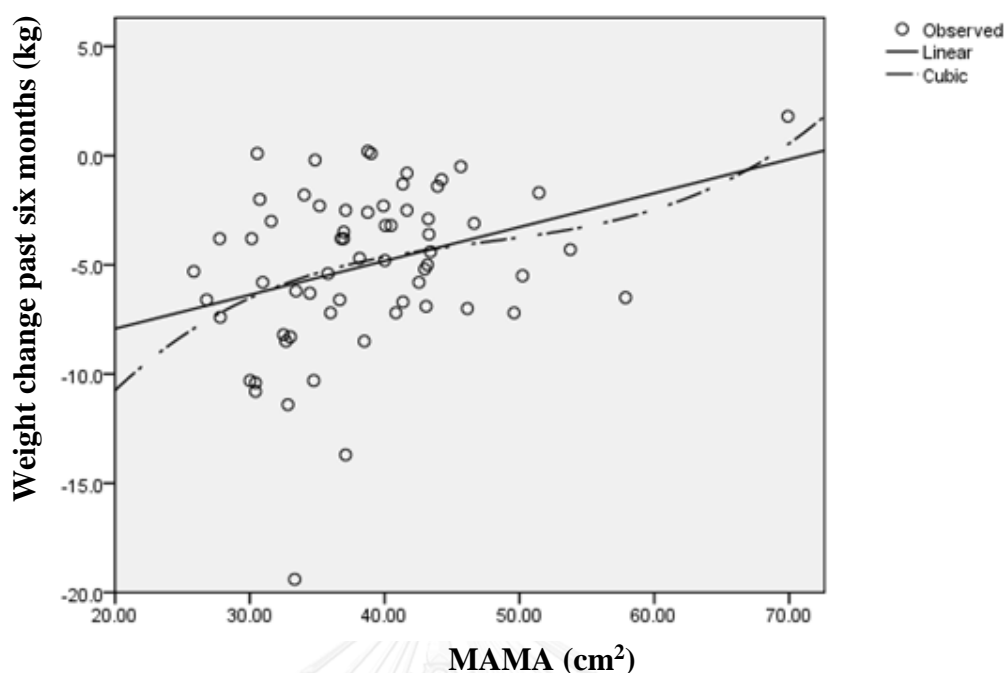
Figure 20. Correlation between MAMA and weight change past six months

2.8. Correlation between weight change and SGA, PG-SGA assessment

The correlation coefficient between SGA, PG-SGA and weight change was negative. SGA did not show significant correlation with weight change in the past one month, while its correlation with weight change in the past six months was moderate ($r = -0.429$; $p < 0.001$). The PG-SGA showed correlation with the weight change in the past one and six months, which $r = -0.318$; $p < 0.05$ and $r = 0.405$; $p < 0.01$, respectively.

Table 30. Correlation between weight change and SGA, PG-SGA assessments

		SGA	PG-SGA
Weight change past one month	R	-0.123	-0.318[*]
	p	0.334	0.01
Weight change past six months	R	-0.429[**]	-0.405[**]
	p	< 0.001	.001

*: Correlation is significant at the 0.05 level (2-tailed)

**: Correlation is significant at the 0.01 level (2-tailed)
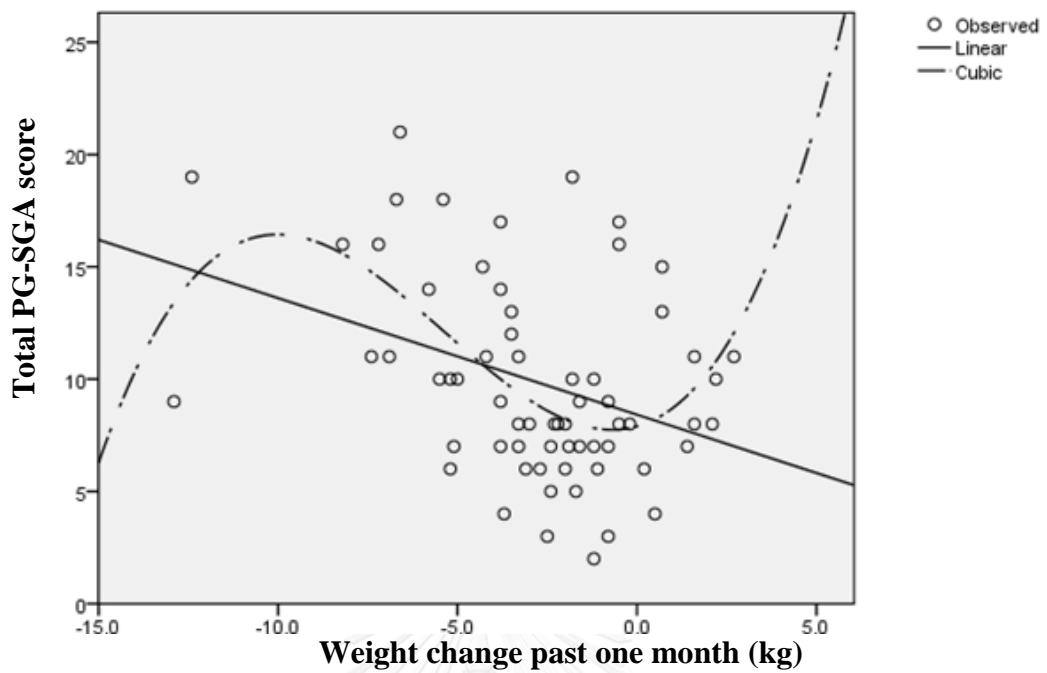
**Figure 21. Correlation between total PG-SGA score and weight change past one month**
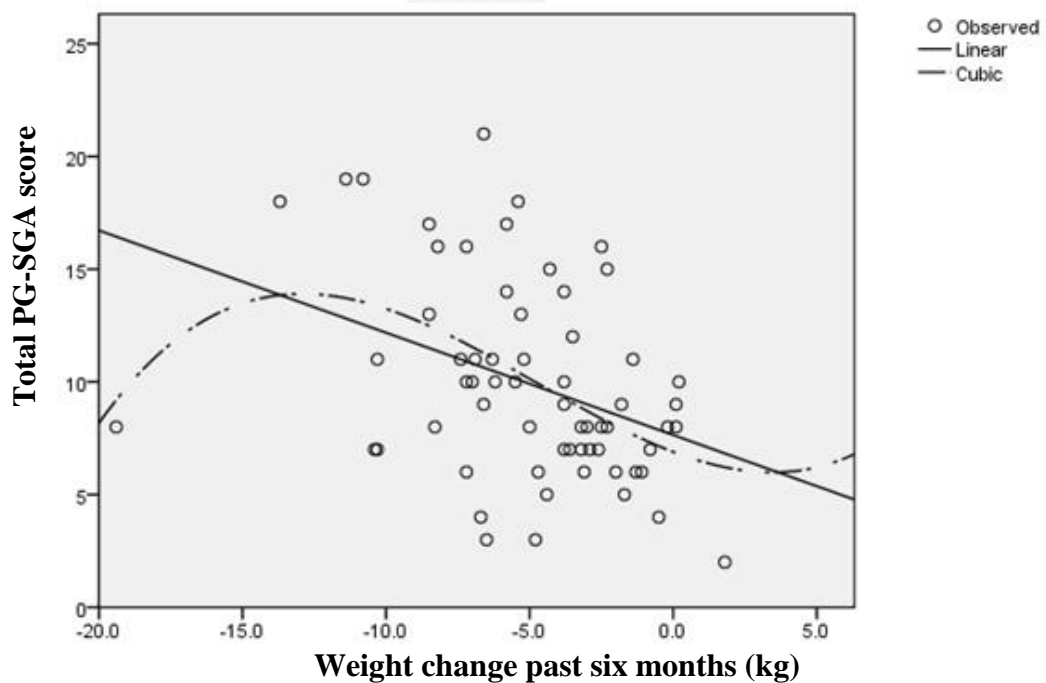

Figure 22. Correlation between total PG-SGA score and weight change past six months

2.9. Correlation between weight change and performance scores, GPS, dietary intake

Weight change in the past one month did not have correlation coefficient with both performance scores and GPS. In addition, the GPS also did not have correlation with weight change in the past six months. The correlation between weight change in the past six months and performance scores were fairly weak, with r = 0.278 (p < 0.05) for KPS and r = -0.352 (p < 0.01) for ECOG.

The weight change in the past one month correlated with energy and protein intake with r=0.307 (p < 0.05) and r = 0.377 (p < 0.01) respectively. Weight change in the past six months correlated with energy intake (r = 0.299; p< 0.05), while not correlated with protein intake.

Table 31. Correlation between weight changed and performance scores, GPS, dietary intake

		KPS	ECOG	GPS	Energy intake (Kcal/kg/d)	Protein intake (g/kg/d)
Weight change	R	0.138	-0.211	0.105	0.307[*]	0.377[**]
past one month	*p*	0.276	0.094	0.422	0.013	0.002
Weight change	R	0.278[*]	-0.352[**]	-0.143	0.299[*]	0.242
past six months	*p*	0.027	0.005	0.275	0.017	0.056

*: Correlation is significant at the 0.05 level (2-tailed)

**: Correlation is significant at the 0.01 level (2-tailed)
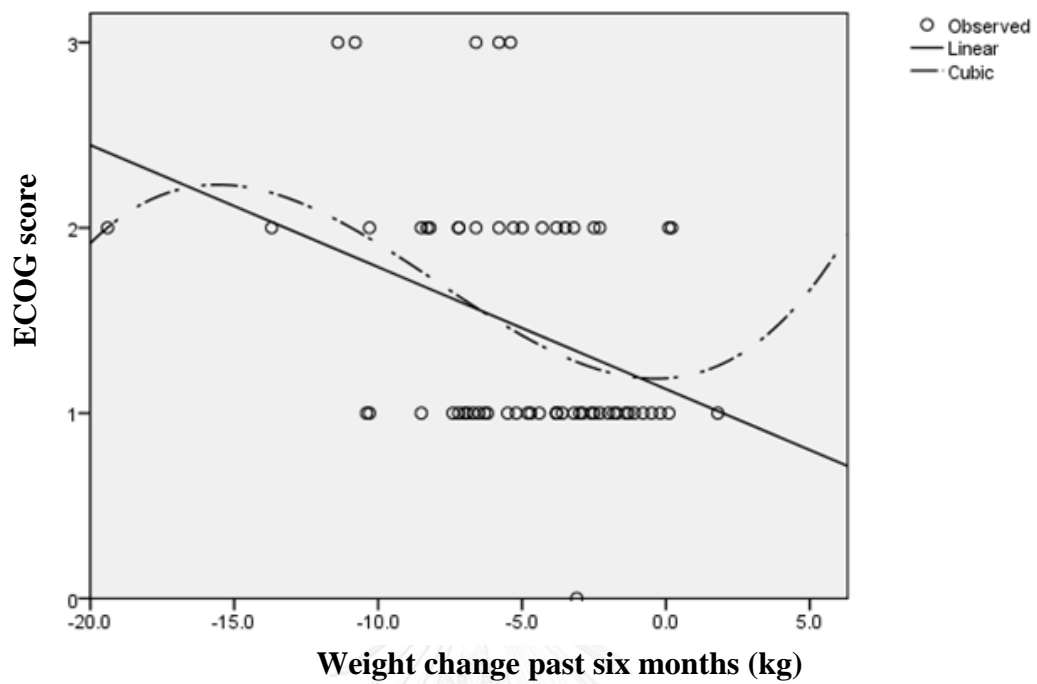
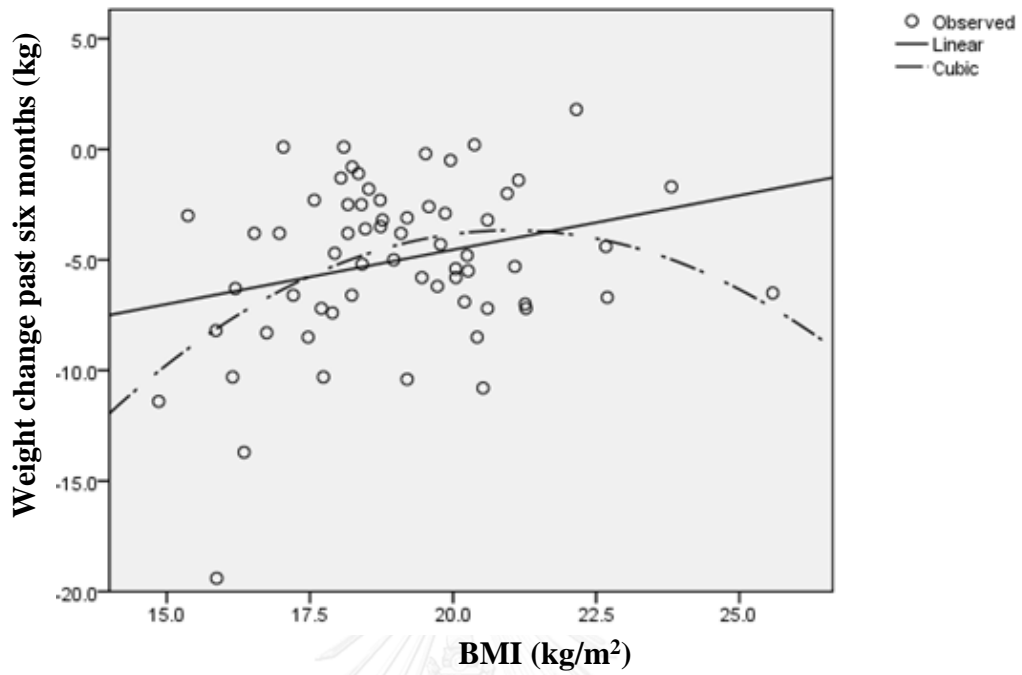**Figure 23. Correlation between total ECOG score and weight change past six months**
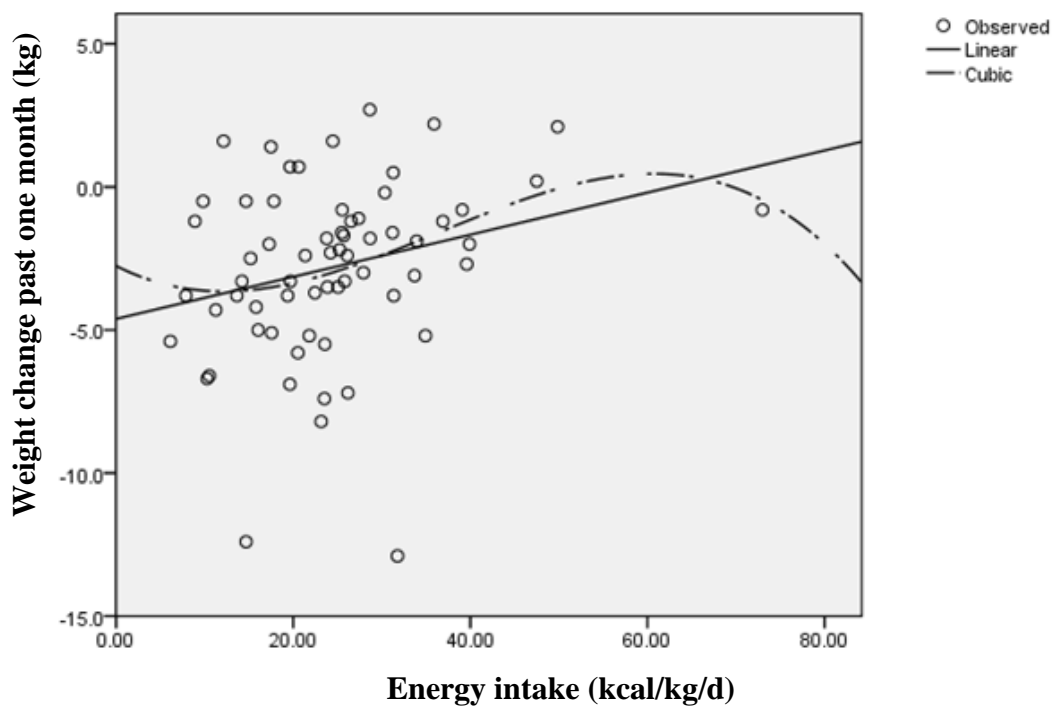
Figure 24. Correlation between weight change past one month and energy intake
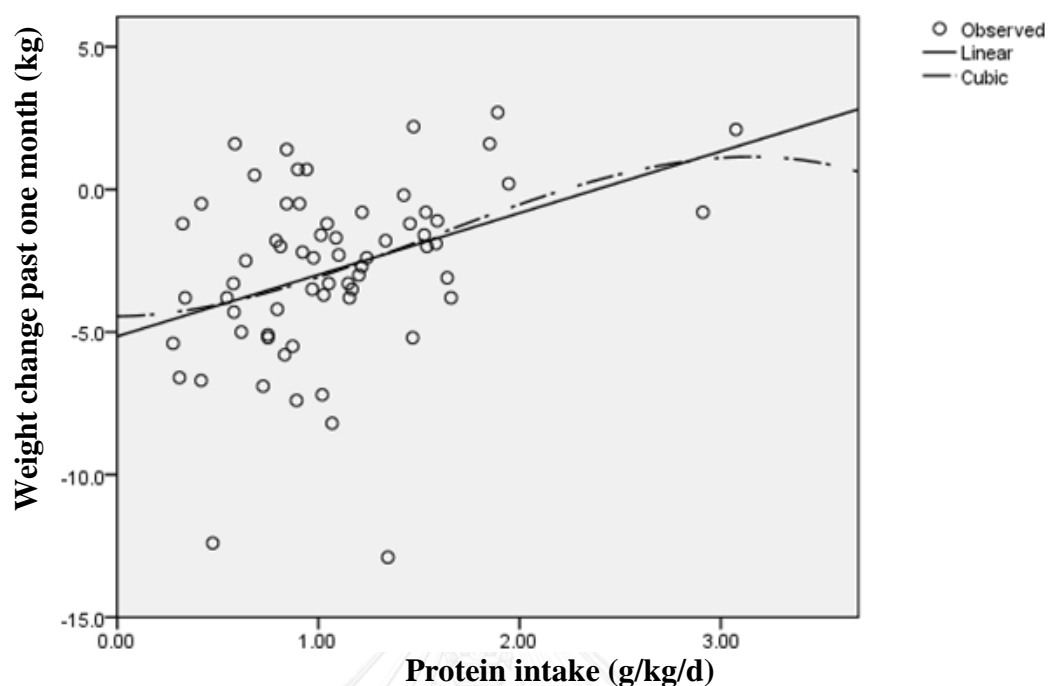
Figure 25. Correlation between weight change past one month and protein intake

3. Other correlations

3.1. Correlation between total white blood cell, serum albumin, and CRP

Total white blood cell correlated significantly with CRP ($r = 0.318$; $p < 0.05$) and GPS ($r = 0.389$; $p < 0.01$).

Table 32. Correlation between total white blood cell, serum albumin, and CRP

		Albumin	CRP	GPS
White blood cell	R	-0.232	0.318*	0.389**
	p	0.07	0.014	0.002

*: Correlation is significant at the 0.05 level (2-tailed)

**: Correlation is significant at the 0.01 level (2-tailed)
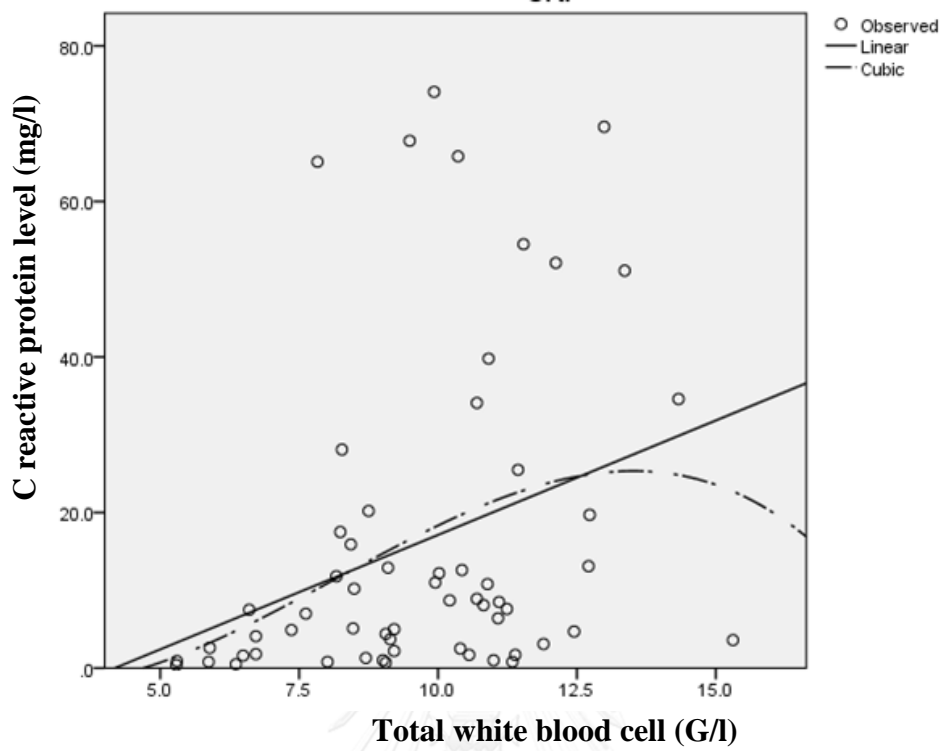
Figure 26. Correlation between serum CRP level and total white blood cell

Total white blood cell (G/l)
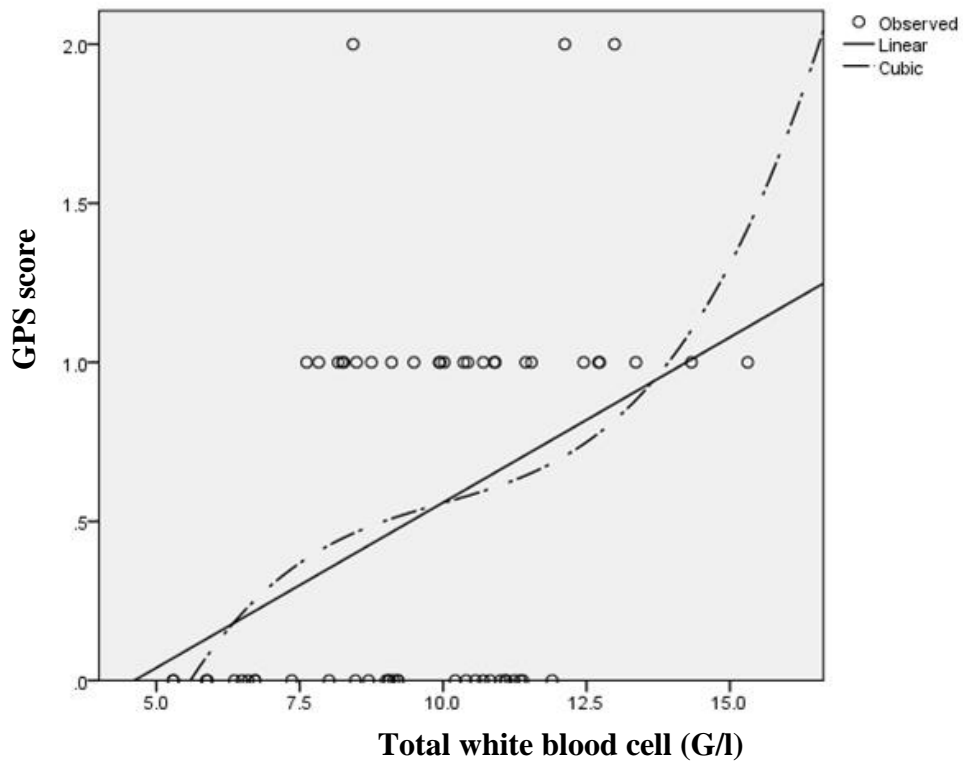
Figure 27. Correlation between GPS score and total white blood cell

3.2. Correlation between protein intake, MAMA, albumin, and CRP

Protein intake did not correlate with MAMA, serum albumin level and serum CRP level. MAMA did not correlate with serum CRP level but correlated significantly with albumin level.

Table 33. Correlation between protein intake, MAMA, albumin, and CRP

		MAMA	Albumin	CRP
Protein intake	R	-0.022	0.131	-0.156
(g/kg/d)	p	0.862	0.301	0.230
MAMA	R		0.302[*]	-0.191
	p		0.015	0.141

*: Correlation is significant at the 0.05 level (2-tailed)

**: Correlation is significant at the 0.01 level (2-tailed)
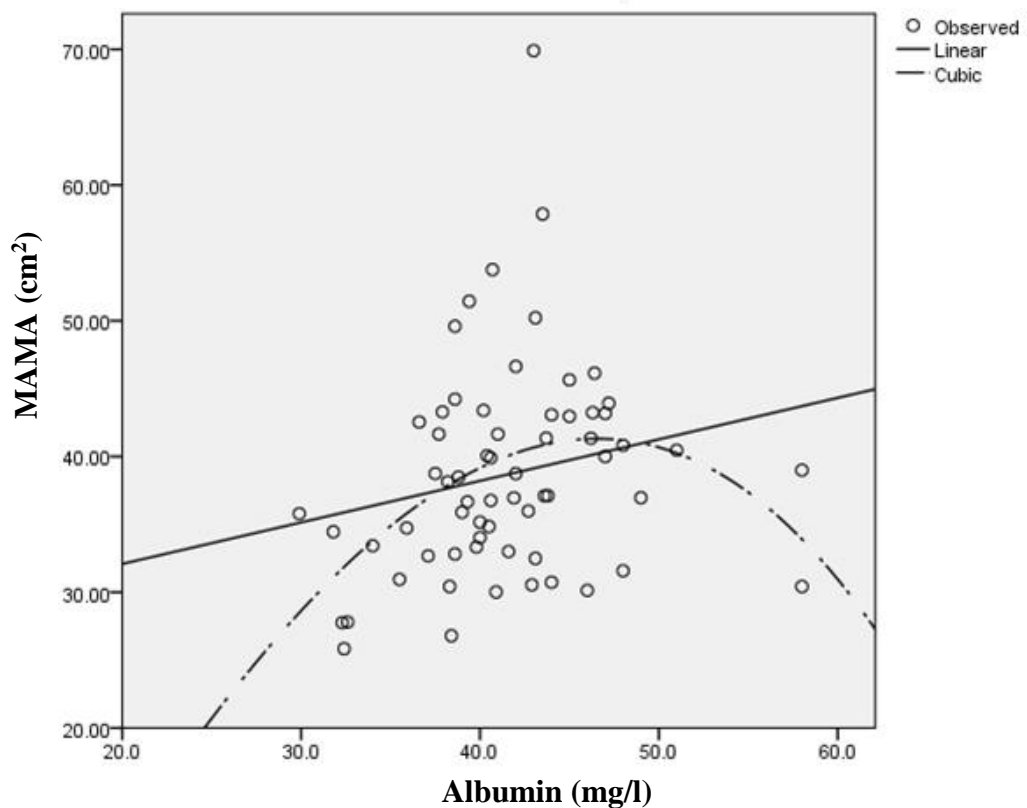
**Figure 28. Correlation between MAMA and albumin**
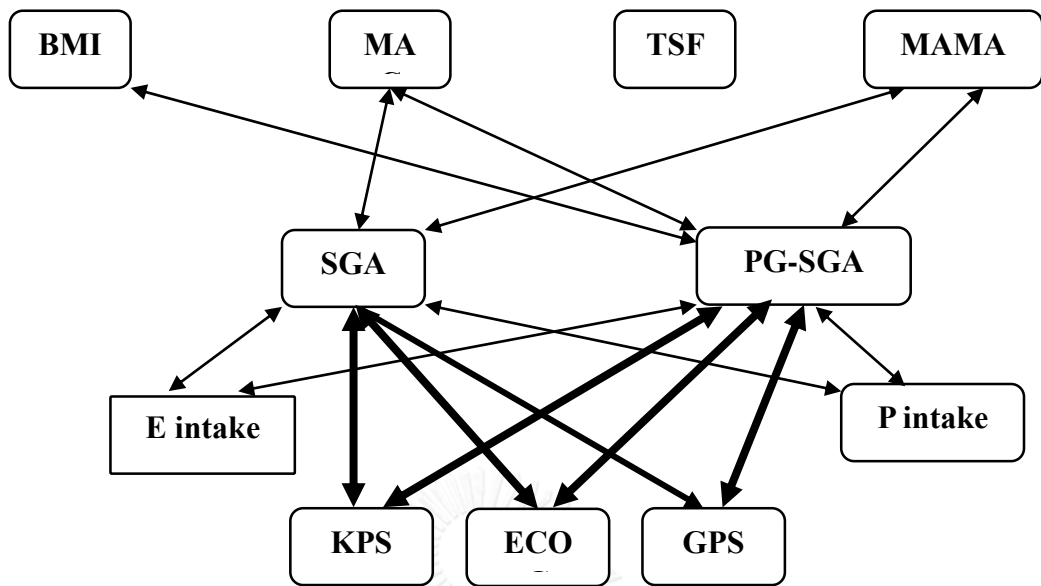
Diagram 2. Correlation between SGA, PG-SGA assessment and anthropometric measurements, dietary intake, performance status scores and GPS
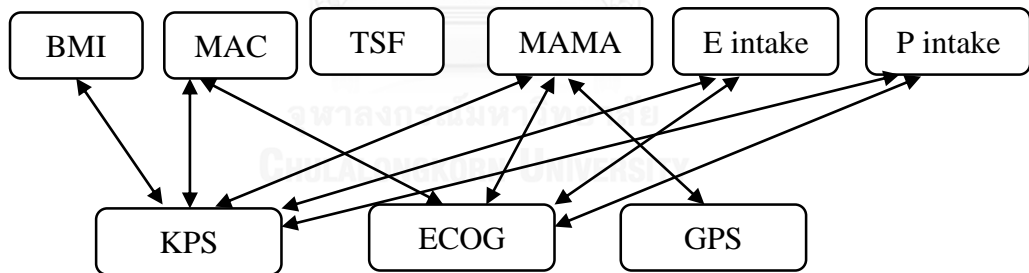
Diagram 3. Correlation between nutrition assessments, performance status scores and GPS
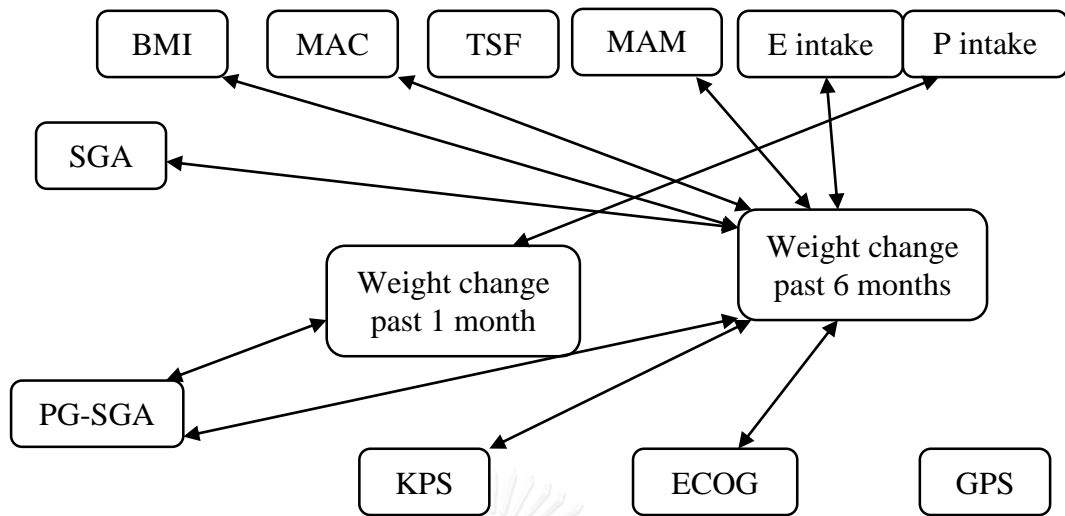
Diagram 4. Correlation between weight change, nutrition assessment, performance status and GPS

CHAPTER 5.

DISCUSSION

In general, most of our study population was at age 50 to 60 and all had squamous cell carcinoma. The mean ± SD of PG-SGA score was 9.88 ± 4.41, which reflected that patients were in needs of nutrition intervention. Most of patients consumed less energy and protein intakes than even the minimum level of recommendation. Almost all of them had experienced weight loss and swallowing problems. More than a half of them got mild to medium fat and muscle loss. The PG-SGA and SGA strongly correlated with performance scores but weakly correlated with GPS. KPS, ECOG, energy and protein intakes, weight change past one and six months did not correlate with GPS.

1. General characteristics

The mean age of this population was 55 ± 7 (range 35- 64). This result was similar to some other researches, such as Kamran A. (Iran, 2014) found that among 69 patients with esophageal cancer, the median age of 58.5 years (range 33 – 84) (14); Yogesh K. (Germany, 2010) announced median age of the study population was 63.2 (range, 34.5–85.2) (115); The Taiwanese population in Chang-Yu W.'s study (Taiwan, 2009) has the median age of 54 years at diagnosis (ranged from 34 to 81 years) (109); Ji-Feng F. (China, 2014) shown the mean age was 59.1 ± 7.9 years, with an age range from 34 to 80 years (118); In Sumanta D.'s study (UK, 2011), 68% patients has age < 65 years old (136); Gholipour. C studied in western side of the Caspian littoral esophageal population (Iran, 2008), the mean age ± SD was 61.7 ± 11.5 among SCC type (137). This might be the epidemiology characteristics of esophageal cancer, which required long term to generate the disease. Although there are many unknown reason to cause esophageal cancer, but known risk factors are poor nutritional status; low intake of fruits and vegetables causing deficiencies of vitamins A, B6, C, riboflavin, thiamine, zinc and molybdenum; nitrosamines (in fermented corn, well water contaminated by animal / human wastes and produced by fungal contaminants), polycyclic aromatic hydrocarbons (138) and drinking beverages at high temperatures (139), smoking(140), food preparation method, drinking water source (141). HPV has been implicated by some investigators. Moreover, in the high risk regions,

detection rates were from 0 to 66%, but most authorities do not believe HPV is etiologically related to the majority of squamous cell carcinomas (142-145). The mechanism of how tobacco and alcohol in combination lead to increased risk of esophageal cancer has been extensively studied. Alcohol can damage the cellular DNA by decreasing metabolic activity within the cell and therefore reduce detoxification function while promoting oxidation. Alcohol is a solvent, specifically of fat-soluble compounds. Therefore, the hazardous carcinogens within tobacco are able to penetrate the esophageal epithelium easier. Some of the carcinogens in tobacco include aromatic amines, nitrosamines, polycyclic aromatic hydrocarbons, aldehydes and phenols. Other carcinogens, such as nitrosamines found in certain salted vegetables and preserved fish, have also been implicated in SCC of the esophagus. The pathogenesis appears to be linked to inflammation of the squamous epithelium that leads to dysplasia and in situ malignant change (146).

All patients in our research has the squamous cell carcinoma. This rate is quite different from other research. Yogesh K. (Germany, 2010) shown 50.7% within population study (patients with histological proven EC and tumor-free resection margins, none of the patients received neoadjuvant or adjuvant therapy) (115). The SCC in Chang Yu W. population's study was 38.8 ± 54.4 (patients with newly diagnosed esophageal SCC or adenocarcinoma undergoing radiotherapy) (109). Gholipour. C shown the number of patients with SCC was much higher than the AC (1405 vs 207 respectively) (137). The study of Gholipour. C (Iran, 2008) showed the result with 86.9% SCC (137). Our result might reflect the trend of SCC in Asian countries due to increase alcohol and tobacco consumption, as described in Taiwan's report (147). It need further study to determine whether Vietnam belongs to the SCC "esophageal cancer belt" (which 90% of cases are SCC) (2) or not.

Esophageal cancer causes the same symptoms and progresses in the same way in both men and women. But globally, the incidence of esophageal cancer in males is 2 to 4 times more common than females. In the South East Asia area, esophageal cancer rates are 2.6/100,000 in males and 1.3/100,000 in female; the incidence of this disease for males and females in 2008 was 6.7 and 3.8 thousand people, respectively (3). In Vietnam, the overall age-standardized mortality rates in 2008 was estimated at

2.3/100,000 in males and 0.8/100,000 in females (4). In our study population, among 65 patients met the inclusion criteria, there were only one female. This might be the lifestyle differences. Since men are more likely to use tobacco, drink excess alcohol, and less intake of vegetables and fruits, so they are at higher risk of esophageal cancer. And because of these reason, the only one female was excluded from data analysis. Further study with larger sample size should be implemented to determine how smoking, alcohol consumption and the difference in dietary intake between the two genders impact nutrition status in esophageal cancer patient and the difference of GPS as well.

The tumor was most located in the one third middle of the esophagus (73.4%). This result was quite different from the report of Gholipour. C (Iran, 2008), in which the tumor located at the middle part of esophagus was only 32.9% (137). This difference might be the result of the inclusion criteria which required tumor located totally in the esophageal cancer. Some cases were excluded due to the tumor located in 1/3 upper or lower spread out of the esophagus. Besides that, another study explained that SCC results from the formation of non-keratinized stratified squamous epithelium and is more common in developing countries. The preferential sites of SCC are the middle and upper thirds of the esophagus (13).

Normally patients at advanced stages of esophageal cancer had difficult in swallowing due to the tumor development that cause esophageal obstruction, so these patients were suggested to place PEG to support feeding. Those with partial obstruction required the specialized dietitian to educate or train them technique to ensure the adequate dietary intake by mouth. But in our study, 84.4% patients reported difficult in swallowing while only 62.5% patient had placed PEG. This might be patient did not follow the surgery indication, or the medical doctor did not understood well about the role of PEG in nutrition intervention to these population. So this problem need further study to determine the exact reason.

2. Characteristics on nutritional assessments

2.1. Malnutrition

According to anthropometric assessment, BMI classification showed that 43.8% of patients were underweight while MAC classification detected the undernourished rate as 29.7%; TSF found 85.9% and MAMA showed 96.9% patients at below average in compared with US population. There were 12 patients (19%) had hemoglobin level and 6 patients (9.4%) had serum albumin level under the normal range in our study. Clinical examination found 4.7% patient had signs of anemia; fat loss happened in 65.6% patients from mild to severe; muscle loss appeared in 51.6% patients. The PG-SGA found 54.7% of patients required nutrition intervention (PG-SGA score $\geq$ 9) while SGA stated this rate at 50% (SGA level B and C). So PG-SGA can determine the larger number of patients who require the nutrition intervention. This finding is similar to other population, such as studies in gynecologic cancer (40), lung cancer (48), head and neck cancer (61), which can be due to the PG-SGA is a more specific nutritional assessment tool for hospitalized cancer patients (41),(58). Previously, the anthropometrics measurements are considered as less credible than PG-SGA in nutritional assessment because of the significance differences between races(148) and nationality(149). Study in lung cancer population also confirmed BMI and weight fail to detect malnutrition when used alone as nutritional variables (48) and highlighted the limitations of using BMI as the sole measure of nutritional status in cancer patients; the scored PG-SGA and SGA are both accurate and simple nutritional assessment tools that are suitable for clinical practice (46).

The nutritional characteristic of esophageal cancer patients also described in previous studies. Study of N. Sarhill (2003) evaluate the nutritional status in advanced metastatic cancer showed the median BMI was 23.6 kg/m^2 (range 12–54 kg/m^2), in the range of normal or high in 87% patients; median MAMA was 32.6 cm^2 (range 11.3–117.9 cm^2); The median TSF was 1.1 cm (range 0.06–2.1 cm); median hemoglobin was 10.6 g/dl (range 6.5–22 g/dl); Most patients (72%) were anemic (hemoglobin <12 g/dl in females and <13.5 g/dl in males); median serum albumin was 3.2 g/dl (range 1.6–4.8 g/dl); The majority of patients (66%) were hypoalbuminemia (normal 3.5–5 g/dl) (150). Even in clinical presentation, only 3

patients were detected anemia, but according to laboratory tests, there were 12 patients with hemoglobin level under normal range. Although the rate of patients with anemia in our study much less than the previous study, but anemia is still a big problem and this may due to the long term reduced food intake and long term development of the disease Malnutrition leads not only to increased morbidity and mortality but also can lead to lower quality of life and a change in self-image. The social aspects of eating are affected by reduced appetite, nausea, or vomiting. Nutrition affects functional status and well-being as malnourished patients experience weakness and fatigue, which can affect the ability to work or carry out activities of daily living. There is overwhelming evidence in the literature that weight loss and malnutrition are adverse prognostic factors in patients with cancer (151). Known causes of malnutrition in pretreatment esophageal cancer patients are: (1) the localized effects of the tumor. Tumors of the esophagus physically interfere with consumption of nutrients, and the resultant malnutrition closely depends on tumor extent. Dysphagia occurs relatively late as the esophagus slowly distends to accommodate the ingestion of food or liquid to pass the tumor. Most cancers involve at least a 4 cm length of the esophagus before diagnosis, and the typical patient will have had 3 to 6 months of dysphagia and some weight loss before first contact to a physician. Other patients report reflux, odynophagia, coughing or choking on food; they are afraid or reluctant to eat, which places them at high risk for malnutrition from the time of diagnosis; (2) the systemic effects of the tumor. Many patients with esophageal cancer develop cachexia at some point in the progression of their disease. Patients with cancer cachexia experience increased rates of glucose turnover, gluconeogenesis, and protein breakdown with an inhibition of lipoprotein lipase. As a result, metabolic rate may increase in spite of decreases in energy intake, thus causing a significant increase in nutritional needs and further nutritional depletion (152).

As shown previously, when compared with the US population, 85.9% patients had the TSF measurement and 96.9% patients had MAMA below the average; the biochemistry test result showed only 9.4% patients had serum albumin level < 35g/dl. The result of serum albumin was consistent to previous studies that patients who present with esophageal cancer are often malnourished but with normal albumin levels and it was explained as this results came from the acute weight loss

experienced in this population and the limited ability of albumin to detect early protein deficiency (152, 153). But as discussed in previous study, it is assumed that the TSF indicates the calorie reserves stored in the form of fat and the MAMA size reflects the reserves of muscle protein (38). The metabolic changes found in cachexia resemble those of infection rather than starvation, and are multifactorial and complex (154). Weight loss from cancer is due to loss of both skeletal muscle and adipose tissue mass, whereas weight loss is mainly from adipose tissue stores in starvation (155). Activation of proteolysis is an early event during tumor growth and it may be present for a long time prior to its clinical manifestation. Protein synthesis may be increased or unchanged (156). Muscles are the largest protein reservoir in the body. Muscles serve as a source of amino acids that can be used for energy production by various organs (including the heart, liver and brain) during catabolic periods, such as in cancer, sepsis, burn injury, heart failure and AIDS. Evidence indicates that two most important cell proteolytic systems that control protein turnover in muscle, play a pivotal role in regulating overall muscle homeostasis: the ubiquitin-proteasome system and the autophagy-lysosome system. The ubiquitin-proteasome system is required to remove sarcomeric proteins upon changes in muscle activity. A decrease in muscle mass is associated with: (1) increased conjugation of ubiquitin to muscle proteins; (2) increased proteasomal ATP-dependent activity; (3) increased protein breakdown that can be efficiently blocked by proteasome inhibitors; and (4) upregulation of transcripts encoding ubiquitin, some ubiquitin-conjugating enzymes (E2), a few ubiquitin-protein ligases (E3) and several proteasome subunits. Autophagy plays a crucial role in the turnover of cell components both in constitutive conditions and in response to various stimuli, such as cellular stress, nutrient deprivation, amino acid starvation and cytokines. Three different mechanisms have been described in mammals for the delivery of the autophagic cargo to lysosomes: macroautophagy, chaperone-mediated autophagy (CMA) and microautophagy. Moreover, many recent findings have highlighted a complex scenario whereby an intricate network of signaling pathways regulates the size of myofibers and the contractile performance of muscle. Intriguingly, these different pathways crosstalk and modulate one another at different levels, coordinating protein synthesis and degradation simultaneously (157). Another study discovered that the protein synthesis

rate per cell was also positively correlated with the cell volume (158). The pathogenesis of cancer cachexia is highly dependent on the patient's immune response. Inflammatory cytokines, procachectic factors, induce muscle degradation even in the face of adequate nutrition. These cytokines are produced by the host in response to the tumor, as well as from tumor factors themselves. IL-6, TNF-α,and PIF are major contributors to the syndrome of muscle wasting (159).

2.2. Dietary intake

Most of our study population experienced a decrease in energy and protein intake compared with the lower level requirements based on the ESPEN guidelines (23) even when they placed PEG to support feeding. As discussed previously, there were only two thirds of patients had PEG to support feeding. And even they had PEG feeding, the dietary intake still did not reach even the lower level requirements.

Nutrition is an important factor that influences patients with esophageal cancer during their perioperative period. Early enteral nutrition was noted to protect the intestinal mucosa, improved the nutritional status, and increased the immune status in patients undergoing esophagostomy. Enteral nutrition protected the intestinal mucosa by maintaining the intestinal barrier against plasma endotoxins (146). The patients had PEG can begin feedings 24 hours later (160). All 40 patients had PEG in our study were assessed 24 hour dietary intake at least at the third day post placed PEG. And some other studies also mentioned that the decreased in food intake among esophageal population due to physical dysfunction of esophagus (161, 162). So the low nutrient intake in patients who had PEG may suggest future studies to determine the reasons of these problems and how to improve accordingly.

According to SGA assessment, 92.1% patients had changed in their dietary intake. Among them, 49.1% had suboptimal oral intake, 28.1% had full liquid and 22.8% had hypocaloric diet. These results were different to M. Al-Sarraf (1997) in a progress report of combined chemo-radio therapy versus radiotherapy alone in patients with esophageal cancer (163), which 23% patients was unrestricted diet, 50% had soft food only and 18% had liquid only in the radiotherapy group and 21%, 33% and 33% in chemo-radio therapy group, respectively. Especially, this report noted only 8% patients cannot swallow in radio therapy group and 10% in chemo-radio therapy

group. As reported in PG-SGA assessment of our study, 84.4% patients had problem in swallowing. This might be the patients in M. Al Sarraf were at earlier stages (patients with TI-3N0-IMO). Hua Lu (2009) assessed the dietary mineral and trace element intake and squamous cell carcinoma of the esophagus in a Chinese Population. Results showed mean ± SD age was 63.67 ± 9.64, similar to our study population, but the average total energy intake for esophageal cancer patients was higher than our population (1,932.4 kcal/day vs 1,208 ± 552) (161).

Numerous studies have proved that dietary nutrition is closely correlated with the esophageal cancer. The author's results show that, in areas with high incidence of esophageal cancer, residents' food is monotonous, grain cereal intake is too much, animal foods, soy foods and fresh fruits, vegetables are in shortage, supply rate of three major nutrients are imbalanced. Unreasonable dietary structure and the intake of nutrients is imbalanced that could be one of the important factors of high incidence of esophageal cancer (164).

2.3. Weight loss

Weight loss is a common symptom among advanced cancer patients (165). Severe weight loss is defined as >1% in one week, > 5% in one month, > 7.5% in three months, and > 10% in six months (166). In our study, more than two-thirds of patients (69%) suffered from weight loss within two weeks prior to the time of hospital admission, 55.6% had weight loss > 5% past one month and 43.1% had weight loss > 10% past six months. The mean ± SD of weight change in the past one month was -2.8 ± 3.1 kg (median was -2.4 kg). Among these patients, 84.4% of them had weight loss and their median weight loss was -3.2 kg. The mean ± SD of weight loss in the past six months was -5.0 ± 3.7 kg (median -3.2 kg) while 93.7% of them had weight loss. This might be the result of the development of the tumor that prevents patients from swallowing when that kind of symptom was reported by up to 84.4 % of patients. With regard to those had placed PEG, weight loss keep orcurred in 75% patients in last two weeks and the nutrient intake in those population was 21 ± 7.7 kcal/kg/day (median = 22) and 0.9 ± 0.4 g/kg/day (median = 0.9) of protein. But the median number of day post-operative was 4 days, so it was undoubtable that patients did not have adequate nutrient intake by enteral tube feeding or not. Nicolas

Magne (2001) assessed weight gain in patients with head and neck cancer with PEG feeding. The results showed the mean increase body weight over 3 weeks was 2.5 kg (range −1 to 6). Only one patient lost weight because of gastro-oesophageal reflux due to a hernia; after conversion of PEG to transgastric jejunostomy, his weight increased by 2 kg within 2 weeks (167). In the N. Sarhill (2003)'s study, 87% patients had weight loss past six months and there were absolute number of GI symptoms correlated (r = 0.8) with severity of weight loss in advanced cancer patients (150). According to Flavia Andreia Marin (2010), disease severity (or late diagnosis) is associated with poor nutritional status, which lead to more complicated postsurgery outcome and mortality. For weight loss, 78% had lost more than 10% in the 6 months prior to disease diagnosis. The most frequent symptom, reported at time of diagnosis, was dysphagia (95%). Most patients had modified their diet consistency from the start and during symptoms, and at moment of disease diagnosis, 83.9% were on a semi-solid diet, 13.9% on paste consistency, and 5.7% on a liquid consistency. Only 2% had not modified their diet and 17.8% reported fasting. The more serious stage (TNM III & IV) presented higher frequency of ostomiasis, hypoalbuminemia, anemia,ly mphopenia, high weight loss, postoperative complications, and low survival. Mean BMI value was 19.7 kg/m^2; most patients with partial or total obstruction suffered significant weight loss, more than 10%, in the period before disease diagnosis (168).

A previous study found that weight loss alone was not an accurate indicator of malnutrition among women with gynecologic cancer (169). The effects of pro-inflammatory cytokines cause hypercatabolism, mainly in advanced phases of the disease, but mechanical obstruction seems to have a major contribution in the installation of cachexia in esophagus cancer; The high percentage of weight loss could be due to the picture of starvation linked with local tumor effect; the metabolic stress caused by cytokine and humoral alterations which lead to hypermetabolism with proteic hypercatabolism and anorexia for patients, and consequently depletion of body compartments (170).

2.4. Clinical presentation

In our study, most of patients had fat loss and muscle loss from mild to medium level, no patients had ascites and edema. This might due to the characteristic of the disease, which the tumor increase gradually and prevent patients from swallowing, so the dietary intake decrease as the tumor get bigger. But the esophageal tumor develops not so quickly (which appeared in the weight loss rate), and the protein synthesis rate per cell was also positively correlated with the cell volume (158), so it make the fat mass and muscle mass reduce from mild to medium level in clinical presentation. And because of the malnutrition is acute, so it not cause the ascites and edema due to protein energy malnutrition.

Even there were 84.4% patients reported they had problems in swallowing in PG-SGA assessment, but 92.1% reported they had changed in dietary intake and 64.1% had difficult in intake food in SGA assessment. This means other symptoms such as loss of appetite, nausea, vomiting, and constipation account for the presented of limitation dietary intake, which not appeared in the SGA form.

Almost patients reported problem in swallowing that prevent patient from intake foods. This is also a characteristic of the pretreatment esophageal cancer patient, that the tumor prevents the patients from having foods, not the change in taste or smell, or anorexia like other kinds of cancer.

2.5. Performance status

KPS is known not to reflect variations in psychological well-being measures, other than those associated with physical disability. However, its evident validity, reliability, and simplicity make it quite helpful as a criterion in clinical trials for patients with cancer (171).

In our study, all the patients had KPS > 60% and ECOG < 3. But according to the functional status self-report by patients in PG-SGA assessment, 26.6% patients did daily activities and work "normal without limitation", 46.9% reported fairly normal, 18.8% had to in bed less than half a day and 7.8% used most day in bed. And for SGA assessment, 57.8% reported patients had some limitation of usual activities but not

severe. This difference might be the sentence described in the form that makes different level in assessment the performance status of the patients.

These results are also in line with other studies on esophageal cancer population. M. Al-Sarraf (1997) reported in 62 patients with TI-3N0-IMO lesions (1983 American Joint Committee staging) with either squamous cell carcinoma or adenocarcinoma of the thoracic esophagus exclusive of gastric involvement. The author's study population also had KPS score ranged from 60- 100 (163). David H. Ilson reported in the phase II trial of weekly Irinotecan plus Cisplatin in advanced esophageal cancer that among thirty-five patients with metastatic or unresectable esophageal adenocarcinoma (23 patients) or squamous cell carcinoma (12 patients), the median KPS was 80 (ranged 70-90) (172). Yuji Murakami (2007) reported the results of the 1999–2001 Japanese patterns of care study for patients receiving definitive radiation therapy without surgery for esophageal cancer, the Karnofsky performance status (KPS) was ≥ 80 in 71% and better in T1 cases than in T2–4 cases. Karis K.F. Cheng (2011) in his cross-sectional study, which used KPS as an instrument to measure functional status of 120 patients, 65 years of age and older, with colorectal, lung, head/neck, breast, gynecological, prostate or esophageal cancer receiving chemotherapy or radiotherapy. The mean KPS score was 87.67±11.8. Among them, eighty-four percent had a KPS score >80; The KPS scores showed a mild to moderate negative correlation with the four symptoms pain, fatigue, insomnia and mood disturbance (77). Kawashima M (1998) reported KPS affect the survival rates of older patients, especially those at stage III/IV (173). Shirley S. Hwang (2004) performed an exploratory recursive partitioning analysis (RPA) in 429 metastatic cancer patients who had completed a functional assessment of cancer therapy general (FACT-G) and a memorial symptom assessment scale-short form (MSASSF) to define survival prognostic groups. Cox models analysis was performed, included Karnofsky performance status (KPS), age, FACT-G subscales, and MSAS-SF subscales as survival predictors. The results confirmed that the KPS was the most significant survival predictor by either RPA or multivariate Cox proportional hazard model (76). Sherry Linn Priebe (2009) in her master of science thesis on oral squamouscell carcinoma; A retrospective clinical study was performed with a data collection from July 1, 2005 to April 1, 2006 at the Ho Chi Minh City (HCMC) Oncology

hospital in Vietnam. Results were 99.3% patients had KPS score 70 to 100%, only one female death so KPS = 0 (86). As discuss previously, Dominik Péus (2013) realised that in the literal sense a KPS of 100% must be considered a true rarity among oncology patients because of the terms of "no evidence of disease" of KPS = 100% (18). This explained why in our study population, there were no patients had KPS = 100%.

Clement Ma (2010) interconverse three measures of performance status (ECOG, KPS and Palliative Performance Scale (PPS)); one of the study perpose was assess whether it was possible to convert ECOG to KPS. Each possible categorisation was separately compared against the ECOG scale using the hit rate and the weighted kappa coefficient.The result of this study showed that the KPS categorisation of 10–30, 40–50, 60–70, 80–90 and 100 had the highest hit rate (75%, ranging among individual physicians from 71% to 79%), and the second highest absolute weighted kappa coefficient (0.84; $p < 0.0001$), indicating a high level of agreement with ECOG scores. There was one other combination (10–40, 50, 60–70, 80–90 and 100) with a slightly higher absolute weighted kappa coefficient (0.85), but the hit rate for that combination was lower at 73%. Our study showed the KPS runs from 50 to 100%, and ECOG score runs from 0 to 3. So if we group as this first categorisation, the results will be:

KPS group (%)	N (%)	ECOG group	N (%)
40 - 50	4 (6.2)	3	5 (7.8)
60 - 70	20 (31.2)	2	21 (32.8)
80 - 90	40 (62.5)	1	37 (57.8)
100	0	0	1 (1.6)

3. Relationship between nutritional status, performance scores and Glasgow prognostic score

3.1. Correlation between SGA, PG-SGA and anthropometric measurements

PG-SGA had mild to moderate correlation with BMI, MAC and MAMA while SGA only correlates with MAC and MAMA in our study results. These results were compatible of previous studies. Arman A. Kahokehr found the PG-SGA correlated

significantly with grip strength, triceps fat fold, arm circumference, arm muscle circumference in acute and elective general surgical patients in a tertiary academic hospital in the South Auckland region of New Zealand (patients had age 52 ± 20.4 and 60 ± 15) (174), but different with Toshitatsu Wakahara (2007)'s research in patients with digestive diseases at Gifu University Hospital, which Spearman's rank correlation analysis revealed a significant correlation between SGA and body mass index, % AMC, and %TSF (median age = 68) (175). Habibe Sahin (2009) conducted a study on 150 patients (84 male, 66 female) on haemodialysis in a hospital of Kayseri, Turkey; the patients aged 50.4 ± 1.14. There were also no correlation between SGA and anthropometric measurements (weight, BMI, lean body mass, % body fat content) (176). Another previous study showed that weight or weight loss was accurate at predicting the SGA global rating or PG-SGA rating for both lung cancer patients and lung benign disease patients, while BMI can only predicted for lung cancer patients. Although the mean BMI of the severely malnourished patients was significantly lower than that of the well-nourished lung cancer patients, the mean BMI of severely malnourished patients still was 21.6, which, according to the World Health Organization is considered to represent normal (48). The mechanism of these difference need further studies.

3.2. Correlation between dietary intake and anthropometric measurements

In our study, both energy and protein intake did not correlate with anthropometric measurements. This might be the data on dietary intake in our study based on 24 hour dietary recall, which reflect the dietary intake at the time of admission. But anthropometric measurements reflect the long term changing of the patient and can be affected by many factors, such as age, nutrition intake for long time, change in dietary, the development of disease and tumor.

3.3. Correlation between dietary intake and SGA, PG-SGA assessments

Our study showed that SGA and PG-SGA had moderate negative correlation with energy and protein intake. In previous study, also from Habibe Sahin (2009), there was a negative correlation between energy, fat intake and SGA score but the correlation between carbohydrate, protein intake and SGA score was not found (176). The correlates between SGA/PG-SGA and dietary intake might be these assessment

tools included the change of dietary intake in general. For specific nutrients (protein, energy, protein intake, vitamin and mineral intake), the correlation might different between studies due to the characteristics of population in each study inclusion criteria.

3.4. Correlation between anthropometric measurements, dietary intake and performance scores, GPS

BMI, MAC and TSF did not have significant correlation with GPS but MAMA did with r = -0.292, p < 0.05; BMI had weak correlation coefficients with KPS (r = 0.254, p < 0.05) but did not show the correlation with ECOG; MAC and MAMA had moderate correlation with both KPS and ECOG while TSF completely did not. And only MAMA correlated with both performance scores and GPS. This might be MAMA reflect the muscle status of the patients. In previous study, RJE Skipworth (2010) also noted that GPS also correlated negatively with MAMC (122). This might be GPS was scored based on serum albumin and CRP level, which both of these are kinds of protein.

Similarly to anthropometric measurements, dietary intake did not show the correlation with GPS. This finding was similar to K. V. Gomes de Lima (2012) in gastro-intestinal cancer population (123). As discussed previously, reduced dietary intake stemming from anorexia may be a response through the intermediation of the action of TNF-α, IL-1, IL-6 and IFN-γ, but a number of gastrointestinal symptoms can affect dietary intake, which is often diminished in the presence of cancer. In the present study, the following symptoms were reported by the patients in the PG-SGA: problem in swallowing (84.4%), loss of appetite (6.2%), nausea (12.5%), vomiting (7.8%), constipation (7.8%), dry mouth (7.8%), changing smell (4.7%), feel full quickly (6.2%).

3.5. Correlation between weight change and performance scores, GPS, dietary intake

There were negative correlation between weight change and dietary intake in our study. These results were in line with Tora S. Solheim's finding (2014), which the correlations between weight loss and food intake was 0.34. Another previous

longitudinal study in gastrointestinal cancer patients has shown that 2.5 kg weight change over 6–8 weeks is sufficient to produce significant changes in performance status; the presence of an inflammatory response is associated with further weight loss and the deterioration of performance status (177). This result was similar as some other studies (178-180). As Tora S Solheim's discussion, these results suggested weight loss is not caused by reduced food intake alone in cancer population. Moreover, the information of dietary intake in this study based on 24 hour dietary intake assessment, which based on patient's self- reported, so this technique itself contain bias. The self-reported question of food intake has not been validated against prospectively collected diet records and there is a possibility that patients have been eating less than they reported; in this case the correlation between weight loss and food intake might have been higher if the information on food intake were based on precise measurements of food intake instead of self-reported information (180). DAC Deans (2009) reported patients diagnosed with gastric or oesophageal cancer (n = 220) who reduced dietary intake was associated with a lower BMI at diagnosis, increased total weight loss and increased rate of weight loss; reduced food intake was associated with reduced Karnofsky performance scores; patients increased rate of weight loss from the time of diagnosis was associated with adverse prognosis (121).

3.6. General relationship between nutritional status, performance scores and GPS

It is well known that cancer promotes release of proinflammatory cytokines from tumor cells. The cytokines interact with immunovascular system and facilitate tumor growth, invasion, and metastasis. Serum albumin participates in systemic inflammatory response and that decline of its serum level is a poor prognostic factor for long-term survival in patients with various cancers. Based on these reports, GPS, incorporating CRP and serum albumin levels, may reflect both the presence of the systemic inflammatory response and the progressive nutritional decline in patients with cancers (21). Recently, another index also uses to assess as a prognostic factor is erythrocyte sedimentation rate (ESR), such as in renal cell carcinoma (181, 182). But previously, other review showed that the ESR might be increased in some unknown or

metastase cancer (183). Further study should determine the ESR in advanced esophageal cancer patients.

Both weakness and dyspnea, rather than disease characteristics, reflect the overall severity of the cancer cachexia and predict survival, particularly in the later stages of terminal cancer. The presence or severity of certain symptoms, such as weakness, dyspnea, and anorexia, may help to identify the patients for whom performance status assessments have greater prognostic value (184). Antonio V. (2000) in his systematic review found that the presence of weight loss, dysphagia, anorexia, xerostomia and dyspnea, along with the clinical estimation of survival, appeared to be among the best prognostic indicators after performance status. Symptoms, such as weight loss, dysphagia, anorexia, xerostomia and dyspnea, rather than disease characteristics (e.g. type of tumor or metastatization), are linked to the prognosis of patients with different end-stage malignancies. To date, performance status, clinical prediction and the presence of cognitive failure, weight loss, dysphagia, anorexia and dyspnea appear to be important prognostic factors for survival in this population (185).

In this study, the results of nutritional assessments at admission (SGA and PG-SGA, BMI and MAC, energy and protein intake) were correlated significantly to performance scores, but had weak relationship with GPS; the performance scores at the time of hospitalization had no correlation with GPS. These findings were different from some previous studies. Kenneth E (1980) reported Karnofsky performance score was one of the three most important prognostic factors affecting survival among seventy-seven prognostic factors in patients within operable bronchogenic carcinoma of the lung (73). Chang XJ (2011) found that ECOG is one of important predictors for survival in patients with advance hepato-carcinoma (94). Sitthinamsuwan B (2014) stated that ECOG > 1 was a significant prognostic factor of poor survival outcomes in patients undertaking treatment of primary central nervous system lymphoma (95). Skipworth RJ (2010) announced KPS correlated with CRP (122). Gomes de Lima KV (2012) claimed that nutritional status was related to inflammation markers and prognosis tools in patients with gastrointestinal cancer (123). Mauricio SF (2013) discovered the association between nutritional status and the GPS (124). Therefore, the results of our study investigated the correlation among three components

(nutritional status, performance status and prognostic) in advanced stages of esophageal cancer male patients. Moreover, our results suggested that there might be many other factors that would affect the prognosis of the patients' treatment outcomes, hence the regular nutrition assessment and adequate nutrition intervention along with the treatment period may help improving in prognosis of the patients' treatment outcomes.

Kenneth E. Stanley (1980) determined the prognostic factors for survival in patients with inoperable lung cancer. Results showed that the interaction between initial performance status and weight loss was statistically significant (73).

Further follow up this study population is necessary to identify the relation between GPS and the survival.

CHAPTER 6.
CONCLUSION

Malnutrition status with weight loss and insufficient dietary intake is the most noteworthy problem in esophageal cancer patients at stage III/IV. The correlation between nutritional status and performance scores was quite strong while the correlation with GPS was minimal. Weight change did not correlate with GPS; only weight change in six months prior to hospital admission had correlation with performance scores but the correlation was weak. PG-SGA is a helpful tool to identify patients who require nutrition intervention; weight loss past six months is a valuable indicator in nutrition assessment. Both KPS and ECOG may be helpful for indirect prompting of nutrition status in the situation with inadequate dietitian in clinical practice such as in Vietnam.
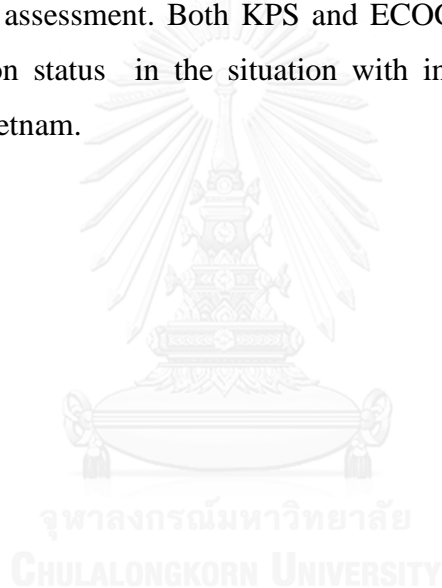
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APPENDIX

Appendix 1. General information and anthropometric measurement

GENERAL INFORMATION AND ANTHROPOMETRIC MEASUREMENT

General information

Fullname: _____   Hospital chart number: _____

Date of birth: ____ ____/____ ____/____ ____   Age:_____   Gender: ☐ Female

☐ Male

Medical insurance number: _____   Not have ☐

Date of admission: ____ ____/____ ____/____ ____

Diagnosed at admission:

       1. _____

       2. _____

       3. _____

Reason for admission: ☐ (1) Radio therapy   ☐ (2) Chemical therapy   ☐ (3) Surgery

       ☐ (4) Others (specify)_____

First time diagnosis: ____ ____/____ ____

Anthropometry

Weight: ☐ Recall: . ____ ____ , ____ kg   ☐ Weight ____ ____ , ____ kg

       ☐ Not weight (*reason*): _____

Height: ☐ Recall: . ____ ____ , ____ kg   ☐ Weight ____ ____ , ____ kg

       ☐ Not Height (*reason*): _____

MUAC: ____ ____ , ____ mm   ☐ Not measure (*reason*): _____

TSF: ____ ____ , ____ mm   ☐ Not measure (*reason*): _____

Appendix 2. Laboratory test

LABORATORY TEST

Date					
Total Blood count					
RBC					
Hemoglobin					
Hematocrit					
MCV					
MCH					
MCHC					
RDW					
Platelets					
WBC					
Neutro					
Lymph					
Mono					
Eosino					
Baso					
Biochemistry					
CRP					
Albumin					

Appendix 3. 24-hour dietary recall

24 HOURS DIETARY RECALL

Time	Name of food/ Food content	Code of food	Amount (sz)	Weight of food

Other supplements:

	Name of product	Amount per day
1		
2		
3		
4		
5		

Appendix 5. SGA assessment

SUBJECTIVE GLOBAL ASSESSMENT

			SGA score	
PATIENT NAME Date (mm/dd/yy)	Patient ID:			
Part 1: Medical History		A	B	C
1. Overall Weight Change: Current wt: …..kg Change in the past 6 m: ……kg				
Percent change in the past 6 months	• <5% loss, stable, or gain			
	• 5 to 10% loss			
	• >10% loss			
2. Recent Weight Loss				
Weight change in the past 2 weeks?	• Weight gain			
	• Stable weight			
	• Weight loss			
3. Dietary Intake: Overall change: • no change • change				
If change, duration: 2 weeks (or -----days), and type of change: • suboptimal oral diet for age • full liquid diet: oral>6m old, tube feeding, PN • hypocaloric liquid • starvation				
Dietary difficulties or reduction of intake	• none or improved			
	• some but not severe			
	• many or severe			
4. Gastrointestinal Symptoms (persisting for >2 weeks)				
• none • nausea • vomiting • diarrhea • anorexia				
Presence of GI symptoms for > 2 wks	• none			
	• some but not severe			
	• many or severe			
5. Functional Impairment • due to poor nutrition • other diagnosis_____				
Limitations of usual activities	• none			
	• some but not severe			
	• severe (bedridden)			
6. Metabolic demand: Primary diagnosis_____				
Stress level	• low			
	• increased			
	• high			

Part 2: Physical Examination				
1. Loss of subcutaneous fat				
Triceps or lower ribs at axillary midline	• none			
	• mild to moderate			
	• severe			
2. Muscle wasting				
Quadriceps or deltoid	• none			
	• mild to moderate			
	• severe			
3. Edema				
Ankle or sacral area	• none			
	• mild to moderate			
	• severe			
4. Ascites				
Exam or history	• none			
	• mild to moderate			
	• severe			
Overall SGA Rating (Check one)				
• A. Not at nutrition risk • B. Low to moderate nutrition risk • C. High nutrition risk				

Appendix 6. KPS score

KARNOFSKY PERFORMANCE STATUS SCORE

	Condition	Performance status (%)	Comments
A	Able to carry on normal activity and to work. No special care is needed.	100	Normal. No complaints. No evidence of disease.
		90	Able to carry on normal activity. Minor signs or symptoms of disease.
		80	Normal activity with effort. Some signs or symptoms of disease.
B	Unable to work. Able to live at home, care for most personal needs. A varying degree of assistance is needed.	70	Care of self. Unable to carry on normal activity or to do active work.
		60	Requires occasional assisstance, but is able to care for most of his needs.
		50	Requires considerable assistance and frequent medical care.
C	Unable to care for self. Requires equivalent of institutional or hospital care. Disease may be progressing rapidly	40	Disabled. Requires special care and assistance.
		30	Severe disabled. Hospitalization is indicated although death not imminent.
		20	Hospitalization neccessary, very sick active supportive treatment neccessary.
		10	Moribund. Fatal processes progressing rapidly.
		0	Dead.

Appendix 7. ECOG score

EASTERN COOPERATIVE ONCOLOGY GROUP
PERFORMANCE SCORE

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Compeletely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

VITA

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Professional Carriers

12/2004- present:　　Researcher at Clinical Nutrition and Dietetics Department,

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Research achievements

Books: in Editorial Board

Food exchange list for diabetic patients. Medical Publisher. 2008 (In Vietnamese)

International publications:

Prevalence of malnutrition in patients admitted to a major urban tertiary care hospital in Hanoi, Vietnam. Huong PT, Lam NT, Thu NN, Quyen TC, Lien DTK, Anh NQ, Elizabeth G., Lauren O., Caroline M., Thomas R., Carine L.Asia Pac J Clin Nutr 2014;23(3).