Comparison of enteral nutrition methods with weight improvement in patients with T4b esophageal squamous cell carcinoma

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Abstract. Enteral nutrition is the preferred method for providing nutrition to patients who can consume food orally or via a feeding tube. In the case of patients with advanced esophageal cancer, tracking nutritional status is critical and weight is a key factor in this regard. Monitoring weight changes is a simple and non-invasive approach that can be easily incorporated into clinical settings. Therefore, the present study aimed to compare different enteral nutrition techniques and assess the efficacy of weight changes in patients with advanced esophageal cancer. A retrospective study was conducted on patients with advanced esophageal squamous cell carcinoma who received enteral nutrition between January 2012 and December 2022, and included the collection of various data, including baseline characteristics, comorbidities, BMI, route of enteral nutrition, tolerable enteral nutrition, total calories per day and mode of treatment via methods such as nasogastric tube (NG), esophageal stent, percutaneous endoscopic gastrostomy (PEG) or open gastrostomy (OG). The study assessed the impact of enteral nutrition on body weight at the 0-, 1-, 3- and 6-month follow-up, as well as the 1-year survival. After a 3-month follow-up, it was observed that patients with advanced esophageal cancer who underwent enteral nutrition exhibited a significant improvement in weight. This improvement trended to be sustained up to the 6-month follow-up. At 3 months, the groups that underwent NG, OG and PEG exhibited significant optimal results compared with the esophageal stent group (P=0.027, P=0.009 and P=0.001, respectively). No significant differences were observed among the NG, OG and PEG methods. The enteral nutrition can aid in weight improvement for patients who suffer from advanced esophageal cancer. Enteral feeding tubes have been demonstrated to be safe and effective options. Within 3 months of beginning nutrition support, there was a trend of weight improvement, which could be maintained up to the 6-month follow-up.

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Abbreviations: NG, nasogastric tube; OG, open gastrostomy; PEG, percutaneous endoscopic gastrostomy

Key words: enteral nutrition, NG, esophageal stent, gastrostomy, PEG, esophageal cancer, weight improvement

Introduction

Esophageal cancer is one of the most important cancer types in the gastrointestinal tract. It is more prevalent in the Asian continent, including Thailand (1,2). Unfortunately, the majority of patients with esophageal cancer are asymptomatic in the early stages and the diagnosis is often made at an advanced stage. This leads to a poor prognosis, notably in patients with malnutrition, who have a lower survival rate (3,4). Esophageal cancer can cause metabolic changes that lead to anoxia and cachexia, in addition to worsening dysphagia (5-7). Nutrition plays a crucial role in any type of treatment and staging, particularly for esophageal cancer. Therefore, it is even more essential to pay attention to nutrition when dealing with this type of cancer (3,7,8).

Enteral nutrition is the preferred method of providing nutrition for patients who can consume food orally or through a feeding tube (3,7-12). In cases of T4b esophageal cancer, feeding is done by passing food through the narrowed esophagus caused by the cancer. There are two main methods for delivering the food: Prepyloric (or gastric) and postpyloric (or jejunum). The prepyloric methods currently in use include nasogastric tube feeding, percutaneous endoscopic gastrostomy (PEG), surgical gastrostomy and esophageal stent. However, there is a lack of comparison between the effectiveness of each method. Different factors can be used to monitor nutritional status, which may vary depending on the type of cancer. For instance, weight plays a crucial role in tracking nutritional status in patients with esophageal cancer (9). Monitoring weight changes is a straightforward and non-invasive approach that can be employed in clinical settings. The aim of the present study was to compare various enteral nutrition techniques and assess the efficacy of weight changes in patients who have advanced esophageal cancer.

Materials and methods

Study design and patients. A study was conducted retrospectively on patients who were referred to the Department of Surgery at Thammasat University Hospital in Pathum Thani, Thailand, for esophageal cancer treatment between January 2012 and December 2022. The patients were treated in accordance with the guidelines set by the National Comprehensive Cancer Network (13) and the Japan Esophageal Society (14,15). The present study included patients aged 18 years or older with stage T4b esophageal cancer and squamous cell carcinoma confirmed by pathology. All enrolled patients received enteral nutrition via methods such as nasogastric tube (NG), esophageal stent, PEG, or open gastrostomy (OG). Patients were excluded if they had no treatment plan due to impending death, or if their Eastern Cooperative Oncology Group Performance Status Score was ≥4. Patients who received parenteral nutrition, had other causes of malnutrition, or altered their enteral method were also excluded from the study. The institutional ethics review committees approved the study. The following reference number was provided by the institutional review board and the Human Ethics Committee of Thammasat University (Faculty of Medicine): MTU-EC-SU-0-262/65.

Data collection. The present study included the collection of various data including baseline characteristics, comorbidities, body mass index (BMI), route of enteral nutrition, tolerable enteral nutrition, total calories per day and mode of treatment. Malnutrition was defined as having a BMI <18.5 kg/m^2 or unintentional weight loss exceeding 10% at any time or exceeding 5% over the last 3 months combined with either a BMI <20 kg/m^2 if the patient was <70 years of age or <22 kg/m^2 if the patient was 70 years of age or older, based on the European Society for Clinical Nutrition and Metabolism guidelines. The present study recorded the patient's body weight at 0-, 1-, 3- and 6-month follow-up visits. In addition, the one-year survival data were also collected.

Statistical analysis. The statistical analysis of data is presented as the mean ± standard error of the mean. The analysis was carried out using various statistical tests such as the χ^2 test for categorical data, and unpaired t-test and one-way ANOVA for continuous data. The analysis was carried out using Fisher's exact test if >20% of the expected counts in the cells of the analyzed contingency table were 5 or fewer. The Bonferroni multiple comparison test was performed in the event of a significant result according to one-way ANOVA. Bonferroni correction was applied after Fisher's exact tests and χ^2 tests for multiple comparisons. The weight changes of all four groups were assessed at 1-, 3- and 6-month follow-up periods using the Kruskal-Wallis test for non-parametric continuous data and Dunn's pairwise comparison between two groups. The data were analyzed using Stata/MP 18.0 for Mac (StataCorp LP). A $P<0.05$ was considered to indicate a significant difference.

Results

Out of 192 patients with esophageal cancer who were screened, only 58 were enrolled in the present study. Among the enrolled patients, 11 (18.97%) received enteral nutrition through the NG route, 4 (6.9%) received an esophageal stent with an oral route, 18 (31.03%) received OG, and 25 (43.1%) received PEG. Table I provides the baseline characteristics of patients with advanced esophageal cancer. On average, the patients were 61.85 years old and 86.21% of them were male. The patients had similar tolerable enteral nutrition and total calorie intake per day. All patients, except for those in the esophageal stent group who received chemotherapy, underwent chemoradiation. Following the improvement in their enteral nutrition status, the one-year survival rate of these patients was 55.17%.

During the study, each patient's weight was monitored at the beginning and subsequently at 1-, 3-, and 6-month follow-up periods. All patients were monitored for 6 months. Fig. 1 illustrates the trend of their body weight throughout the study. Prior to receiving enteral nutrition, the average weight of all patients one year before diagnosis was 57.62±7.41 kg; this value was altered to 42.51.5±8.56 kg. Following administration of enteral nutrition, the average body weight was 42.52±6.16 kg in the 1st month, which was improved to 44.55±6.61 kg in the 3rd month and reached a plateau at ~44.21±6.13 kg in the 6th month. Fig. 2 demonstrated the percentage change in body weight in patients with esophageal cancer who received enteral nutrition via each method. The weight change of patients with advanced esophageal cancer who received enteral nutrition at the 3-month follow-up period indicated significant weight improvement in the NG tube, OG and PEG group compared with that of the esophageal stent group ($P=0.027$, $P=0.009$ and $P=0.001$, respectively). No significant difference was noted between the NG tube, OG and PEG methods. There were statistically significant differences in the mean weight change between the NG and OG methods as well as OG and ES methods at the 1-month follow-up ($P=0.044$ and $P=0.047$, respectively). At the 6-month follow-up, ES methods demonstrated statistically significant difference compared with the NG, OG and PEG methods ($P=0.023$, $P=0.024$ and $P=0.010$, respectively). Table II provides information on detailed comparisons.

Discussion

Dysphagia, or difficulty in swallowing, is a significant symptom that affects both swallowing function and nutrition. It can be indicative of conditions such as esophageal cancer or external pressure on the esophagus, such as from enlarged lymph nodes (13). Advanced esophageal cancer is a significant healthcare issue noted worldwide, particularly in developing countries, such as Thailand (1,2). In the institution in which the present study was performed, a previous study demonstrated that 53.8% of patients exhibited stage 4 cancer (4). Tumors can severely impact swallowing and cause dysphagia, particularly in cases of T4 staging. The systemic effects of cancer can also lead to malnutrition, causing further health deterioration and distress for patients. Patients with T4b esophageal cancer often have large mass effects that affect oral intake and have invaded vital nearby organs; in this clinical status, surgery is not recommended (14-16). Therefore, it was decided that research should be conducted on this group of patients with esophageal cancer.

It is crucial to take into account various factors related to the nutritional status of patients with advanced esophageal cancer,

Table I. Characteristics of patients with advanced esophageal cancer receiving enteral nutrition methods, including nasogastric tube, esophageal stent, open gastrostomy and percutaneous endoscopic gastrostomy.

Characteristics	Enteral nutrition methods				P-value
	NG (n=11)	ES (n=4)	OG (n=18)	PEG (n=25)	
Mean age ± SD, years	60.64±5.54	61.00±6.22	61.94±11.66	62.44±10.76	0.083[a]
Sex, n (%)					0.697
Male	9 (81.82)	3 (75.00)	16 (88.89)	22 (88.00)	
Female	2 (18.18)	1 (25.00)	2 (11.11)	3 (12.00)	
Comorbidities, n (%)					
Hypertension	2 (18.18)	1 (25.00)	4 (22.22)	9 (36.00)	0.586
Diabetes	1 (9.09)	0 (0.00)	2 (11.11)	6 (24.00)	0.235
Dyslipidemia	1 (9.09)	0 (0.00)	2 (11.11)	6 (24.00)	0.235
Coronary artery disease	1 (9.09)	0 (0.00)	0 (0.00)	0 (0.00)	0.259
Atrial fibrillation	1 (9.09)	0 (0.00)	0 (0.00)	0 (0.00)	0.259
Tuberculosis	3 (27.27)	1 (25.00)	3 (16.67)	3 (12.00)	0.599
Chronic obstructive pulmonary disease	1 (9.09)	1 (25.00)	0 (0)	8 (32.00)	0.041; >0.999[b]; >0.999[c]; >0.999[d]; >0.999[e]; >0.999[f]; >0.999[g]
Cirrhosis	0 (0.00)	0 (0.00)	2 (11.11)	0 (0.00)	0.260
Chronic kidney disease	0 (0.00)	0 (0.00)	2 (11.11)	0 (0.00)	0.260
Head and neck cancer	1 (9.09)	0 (0.00)	1 (5.56)	1 (4.00)	0.825
Other	0 (0.00)	1 (25.00)	1 (5.56)	0 (0.00)	0.107
Mean weight 1 year before diagnosis ± SD, kg	54.45±5.52	58.75±5.44	56.06±8.84	59.96±6.79	0.361[a]
Mean weight before enteral nutrition methods ± SD, kg	42.31±5.24	44.75±6.65	40.07±7.76	43.99±3.77	0.018[a]; >0.999[b]; >0.999[c]; >0.999[d]; 0.872[e]; >0.999[f]; 0.186[g]
Weight loss, %	22.34±5.41	23.85±8.00	28.88±6.21	23.23±7.83	0.529[a]
Mean height ± SD, cm	161.27±4.36	163.25±5.38	163.17±4.30	164.08±8.94	0.730[a]
Mean BMI ± SD, kg/m^2	16.28±2.05	16.74±1.69	15.01±2.52	17.12±1.78	0.469[a]
Mean tolerable enteral nutrition total calories per day ± SD, calorie	1,654.55±249.45	1,472.50±166.41	1,757.78±540.89	1,760.04±299.53	0.006[a]; >0.999[b]; >0.999[c]; >0.999[d]; >0.999[e]; >0.999[f]; >0.999[g]
Mean albumin ± SD, g/dl	2.96±0.28	2.85±0.19	2.79±0.61	2.99±0.36	0.011[a]; >0.999[b]; >0.999[c]; >0.999[d]; >0.999[e]; >0.999[f]; 0.784[g]

Table I. Continued.

Characteristics	Enteral nutrition methods				P-value
	NG (n=11)	ES (n=4)	OG (n=18)	PEG (n=25)	
Treatment, n (%)					
Radiation	0 (0.00)	0 (0.00)	2 (11.11)	1 (4.00)	0.665
Chemoradiation	9 (81.82)	0 (0.00)	13 (72.22)	22 (88.00)	0.002; 0.003[b]; >0.999[c]; >0.999[d]; 0.007[e]; <0.001[f]; >0.999[g]
Chemotherapy	2 (18.18)	4 (100.00)	3 (16.67)	2 (8.00)	<0.001; 0.001[b]; >0.999[c]; >0.999[d]; <0.001[e]; <0.001[f]; >0.999[g]
1-year survival, n (%)	6 (54.55)	2 (50.00)	9 (50.00)	15 (60.00)	0.924

[a]One-way ANOVA for continuous data. The Bonferroni post hoc test was used for continuous data. For categorical data, when multiple tests were performed to compare individual groups after a significant result was obtained from the χ^2/Fisher's exact test for all groups, a correction with the Bonferroni test was applied after the χ^2 or Fisher's exact tests. The comparisons were as follows: [b]NG vs. ES, [c]NG vs. OG; [d]NG vs. PEG, [e]ES vs. OG; [f]ES vs. PEG and [g]OG vs. PEG. NG, nasogastric tube; ES, esophageal stent; OG, open gastrostomy; PEG, percutaneous endoscopic gastrostomy.

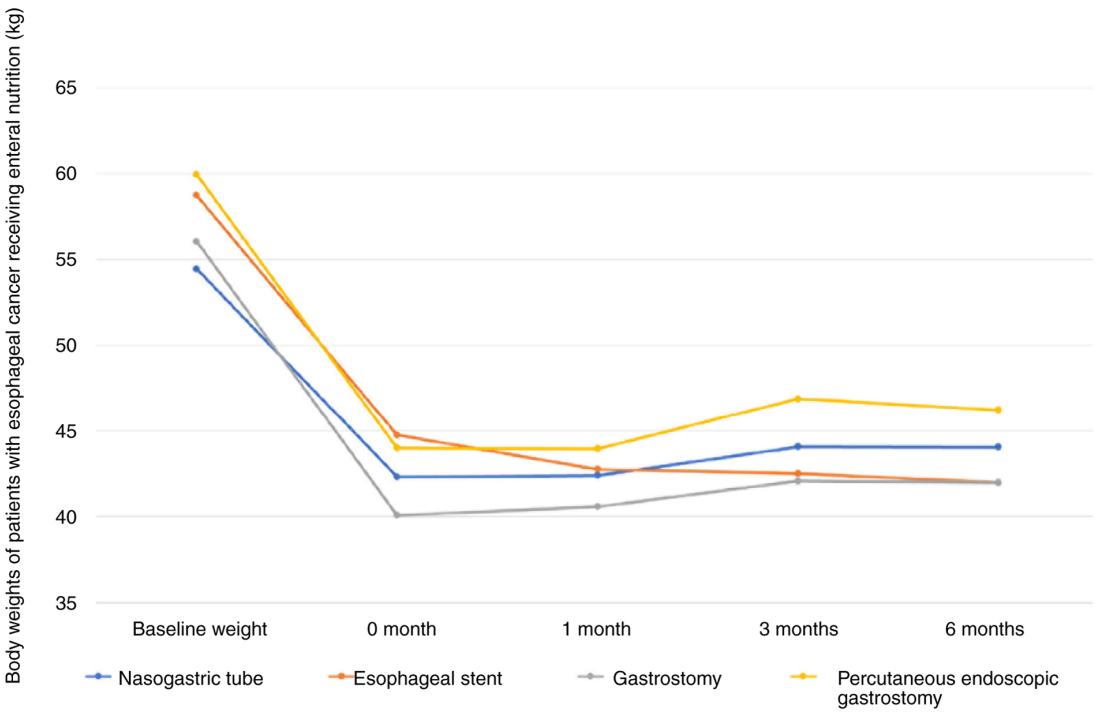

Figure 1. Body weights of patients with esophageal cancer receiving enteral nutrition.

notably their weight, in order to ensure their quality of life, regardless of the treatment method used (8,9,17-21). Weighing of the patients is a simple and effective method that can be easily implemented in clinical practice. Even if the patients

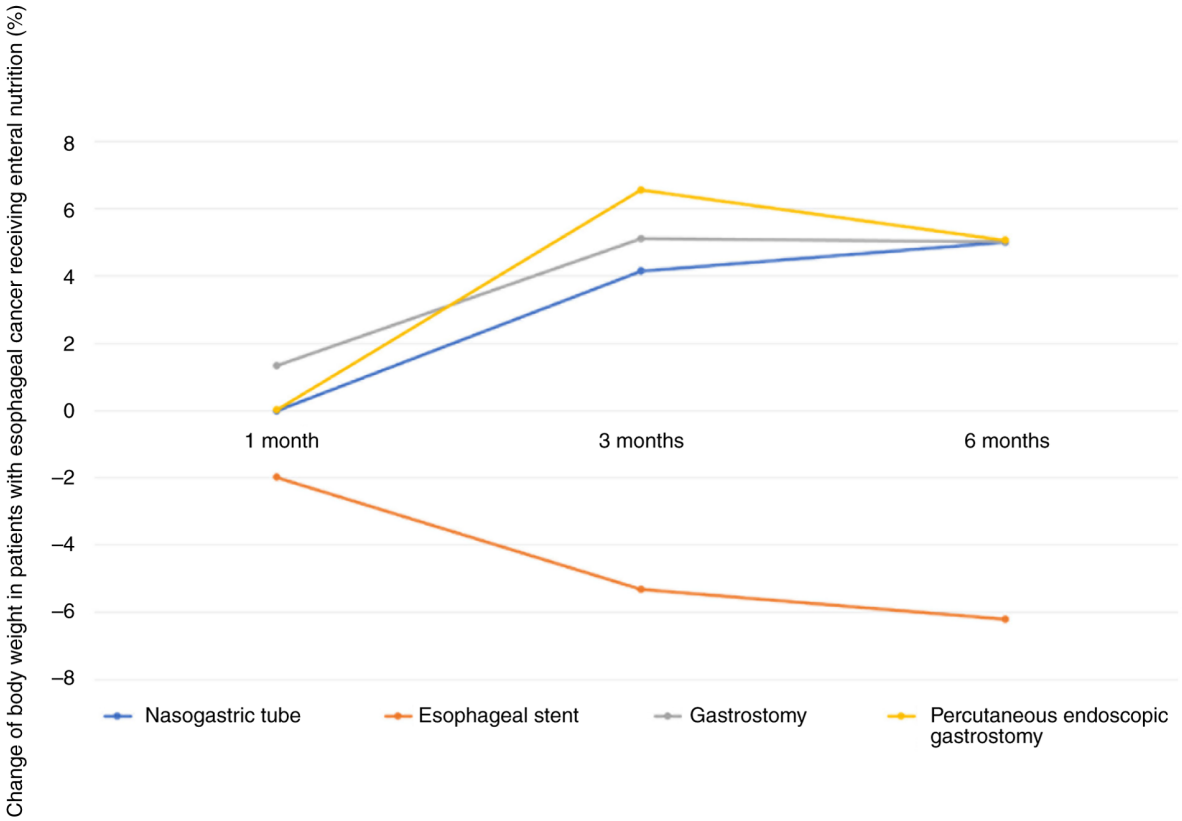

Figure 2. Percentage change of body weight in patients with esophageal cancer receiving enteral nutrition.

are unable to stand, their weight can still be measured using specialized weight machines or by subtracting the weight of their wheelchair using wheelchair scales. In addition, blood chemistry values can also be employed to determine the patient's nutritional status; however, this is an invasive method that may not be comfortable for the patient.

Nutritional support for patients with advanced esophageal cancer requires consideration of various factors, including indications, suitability based on disease staging and cost. There is no one-size-fits-all approach, as each method has its own advantages and disadvantages that must be evaluated on a case-by-case basis. It is important to note that all enteral nutrition methods are classified based on feeding sites in the stomach or prepyloric feeding route. One such method is the NG tube, which involves the use of a pediatric endoscopy with a small diameter and guidewire to pass through the narrowing of the esophageal lumen caused by cancer. While this method is relatively inexpensive, patients may find it uncomfortable to have a nasal tube in their nose and throat and it may impact their self-image from the perception of others (22). An additional method is the esophageal stent, which allows for oral intake without the requirement for tubes or wounds from the procedure. However, this method requires a technical skill and may be more expensive compared with other methods (23,24).

Surgical gastrostomy is a feeding technique that has been in use for a long time. It involves making an opening in the stomach through surgery. However, this procedure carries the risk of complications and abdominal wounds. An innovative method called PEG uses an endoscope to insert the feeding tube. This technique has been developed to minimize the disadvantages associated with surgical gastrostomy. PEG causes lower number of complications and reduced pain and results in a shorter hospital stay. A special technique of PEG has been developed called the push technique, which is used for patients with esophageal cancer. This technique has no risk of cancer seeding to the stroma of the gastrostomy site. All of the patients in the present study were treated by this technique. However, the success of PEG depends on technical practices and experiences, as well as the cost of PEG kits. In addition, if the endoscope is unable to pass through the mass and luminal narrowing in the stomach, an open gastrostomy is still required in such cases. Ultimately, the selection of the method should be based on the individual disease and patient factors and/or circumstances of each disease status (11,12).

According to the findings of the present study, the majority of the participants exhibited malnourished status. In patients with advanced esophageal cancer, enteral nutrition exhibited a modest impact on body weight during the initial month of the study. However, it indicated an inclination towards enhancing body weight in the first 3 months following treatment, and the improvement persisted for the subsequent 6 months of follow-up.

No significant difference was noted in the body weight change between the NG, OG and PEG methods. However, when analyzed with an esophageal stent, three of these methods demonstrated significant improvement in weight. One possible reason for this difference is that all patients in the stent group were treated with chemotherapy, whereas patients who were treated with other enteral nutrition methods mostly received chemoradiation. The present study relates to a previous

Table II. Weight changes of patients with advanced esophageal cancer receiving enteral nutrition methods, including NG, esophageal stent, OG and PEG, at the 1-, 3- and 6-month follow-ups.

	1-month follow-up				3-month follow-up				6-month follow-up			
		P-value (P=0.404[a])				P-value (P=0.020[a,b])				P-value (P=0.146[a])		
Enteral nutrition methods	Mean weight change ± SD, kg	NG vs.	ES vs.	OG vs.	Mean weight change ± SD, kg	NG vs.	ES vs.	OG vs.	Mean weight change ± SD, kg	NG vs.	ES vs.	OG vs.
NG	0.08±2.82				1.76±2.88				1.73±5.47			
ES	-2.00±2.58	0.067			-2.25±2.6	0.027[b]			-2.50±3.70	0.023[b]		
OG	0.49±2.51	0.044[b]	0.047[b]		1.99±2.36	0.326	0.009[b]		19.00±1.12	0.420	0.024[b]	
PEG	-0.06±1.36	0.378	0.079	0.296	2.88±2.05	0.078	0.001[b]	0.136	2.22±2.06	0.414	0.010[b]	0.307

[a]Kruskal-Wallis test for comparisons of non-parametric continuous data among the four groups and Dunn's pairwise comparison test for comparisons between two groups. [b]Statistically significant at P<0.05. NG, nasogastric tube; ES, esophageal stent; OG, open gastrostomy; PEG, percutaneous endoscopic gastrostomy.

publication, which indicates that stents did not prevent weight loss or malnutrition (25,26). By contrast, certain studies have determined that esophageal stents could relieve dysphagia and maintain the nutritional status (27,28). Moreover, the number of stents was very small and further studies in the future will probably provide better answers and evidence on this point. Furthermore, the one-year survival in these patients with enteral nutritional support was 55.17%; in the present study, the range was between 29-76% compared with the one-year overall survival noted in the previous reports (29).

The study's limitation was that it was a single-center and retrospective analysis. The study's conclusion revealed that enteral nutrition can support weight improvement in patients with advanced esophageal cancer. Methods, such as NG, gastrostomy and PEG feeding tubes have been proven to be safe and effective options.

In our study, a trend of weight improvement was observed within 3 months of initiating nutritional support with weight maintenance noted at the 6-month follow-up. Further research is required with multi-center, randomization and blinding protocols, as well as larger population numbers, to confirm the definitive evidence of enteral nutritional options and their effectiveness in treating patients with advanced esophageal cancer.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

PM and BC confirm the authenticity of all the raw data. PM and BC contributed to data analysis, drafting and revising the article, have agreed on the journal to which the article was submitted, and agree to be accountable for all aspects of the work. Both authors have read and approved the final manuscript.

Ethics approval and consent to participate

The institutional ethics review committees approved the study before participation, and it passed the institutional review board and the ethical research process of the Human Ethics Committee of Thammasat University, Amphur Klongluang, Pathum Thani, Thailand (Faculty of Medicine; approval no. M TU-EC-SU-0-262/65). The requirement for informed consent from all patients included in the present study was waived due to the retrospective design.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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