Chapter 6

Nutritional Management of Esophageal Cancer Patients

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Additional information is available at the end of the chapter

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Abstract

Esophageal cancer is associated with malnutrition in the vast majority of patients. This phenomenon is partly attributed to the disease process itself, the location of the tumor and other factors, such as dysphagia which is often accentuated due to chemotherapy/radiotherapy treatment or surgical intervention. The poor nutritional status of these patients is often related to the presence of cancer cachexia, altered metabolism, and tissue wasting. Malnutrition in this patient population affects quality of life, worsens patient's tolerance to chemotherapy and accounts for lower survival. Nutritional management of these patients includes both proper nutritional assessment and support and might prevent, to a certain extent, the manifestation of malnutrition-related consequences. The purpose of this article is to review the current literature in order to focus on the etiology and diagnosis of malnutrition in esophageal cancer patients, emphasizing also on the optimal nutritional support during multimodality treatment.

Keywords: nutritional assessment, nutritional support, perioperative nutritional care, esophageal cancer

1. Introduction

Esophageal cancer is one of the most fatal cancers worldwide as it was ranked ninth for cancer incidence and sixth for cancer death in 2013. In 2013, there were 442,000 new cases of esophageal cancer and 440,000 deaths [1]. There are two main histologic subtypes of esophageal cancer: squamous cell carcinoma and adenocarcinoma, each one of them is related to several risk factors. Among them, modifiable lifestyle factors, such as alcohol consumption, tobacco use, and nutrition should be considered as key points in order to prevent esophageal cancer.

Excess alcohol consumption and consumption of hot food and beverages increase the risk of esophageal squamous cell carcinoma, whereas many components of Western type diet, such as red and processed meat increase the risk of esophageal adenocarcinoma [2–4]. Moreover, obesity, especially central type, and gastroesophageal reflux disease are risk factors toward developing esophageal adenocarcinoma [5, 6]. On the other hand, healthy dietary habits could be a shield against some types of esophageal cancer [7], while nutritional support could be beneficial for the management of these patients after cancer diagnosis.

Esophageal cancer is commonly associated with malnutrition and impaired nutritional intake. Nutritional management of these patients may differ according to the type of therapy and stage of disease, in order to alleviate symptoms, ameliorate nutritional status, and improve quality of life. Furthermore, cancer cachexia affects a great percentage of esophageal cancer patients emerging as a significant factor the multidisciplinary team should deal with [8]. Regarding the perioperative care, the proper type of feeding (i.e. enteral/parenteral nutrition (EN/PN), immunonutrition, oral supplements, etc.) as well as the right time of feeding is a matter of controversy due to lack of consistent evidence for patients undergoing esophagectomy [9]. Special nutritional needs in the long run are also of great significance for patients with both resectable and unresectble disease, bearing in mind that the majority of these patients strive to meet their caloric and protein needs. Considering the treatment approach, nutritional screening and assessment leads to early detection of malnourished patients in need of nutritional support. Taking into account patient's specific needs helps to choose the most suitable routes of delivering nutritional support (nutritional counseling and artificial nutrition). Personalized nutritional support could modify poor nutritional status resulting in reduced postoperative complications and improved survival. Moreover, the implementation of nutritional protocols could reduce toxicity of treatment regimens and in conjunction with nutritional monitoring could have impact on patients' daily living [10]. Therefore, nutritional therapy should be an essential part of a multidisciplinary approach in the clinical setting, in order to improve short- and long-term outcomes.

The aim of the current review is to focus on the etiology of malnutrition, review the various methods of nutritional assessment, and analyze the aspects of nutritional management of esophageal cancer patients as a fundamental part of multimodality therapy.

2. Nutritional status

2.1. Malnutrition rates and weight loss

Esophageal cancer patients often suffer from malnutrition, the manifestation of which is strongly linked to the stage of the disease and therapeutic regimens. Excessive weight loss is partly attributed to the disease process itself and is often deteriorated due to chemotherapy/radiotherapy treatment [11]. Malnutrition occurs in 60–85% of esophageal cancer patients, which is one of the highest reported rates when compared to other malignancies, such as lung, head and neck, stomach, and pancreatic cancers [12]. According to recent publications, 32% of patients who underwent esophagectomy experienced more than 10% weight loss

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preoperatively [13], while 90% of patients had a 5% weight loss at 3 months postoperatively [14]. It is noteworthy that in many patients weight loss persists for at least 3 years after surgical intervention [15]. Another study revealed that 43.8% of patients with esophageal cancer were underweight based on BMI values, 29.7% of patients were undernourished as indicated from anthropometric measurements and 69% had weight loss within 2 weeks before hospital admission [16]. Chemotherapy and radiotherapy affect nutritional status by promoting weight loss and muscle wasting. More specifically, malnutrition developed in 83.8% of patients after the end of radiotherapy [17] and the number of patients requiring nutritional intervention increased from 56 to 75% during induction chemotherapy [10]. These facts highlight the need of nutritional assessment at several time points in order to identify patients who are candidates for nutritional support.

2.2. Methods of nutritional assessment and impact on clinical outcome

There are various methods of nutritional assessment in the clinical setting providing clinicians with tools for the evaluation of the nutritional status and the estimation of nutritional needs of esophageal cancer patients. One commonly used criterion of malnutrition is the percentage of weight loss in a certain period of time. A weight loss of more than 5% in the previous month or more than 10% in the last 3–6 months is considered significant malnutrition [18]. One retrospective study concluded that weight loss <10% and BMI>18 kg/m^2 were significantly correlated with a better response to chemoradiotherapy, while BMI>18 kg/m^2 was predictive of survival at both univariate and multivariate analysis [19]. Other anthropometric measurements, such as mid-arm circumference and mid upper-arm muscle area can give information about the nutritional status and body composition of these patients.

Biochemical markers, such as plasma proteins are often used as nutritional markers. For instance, albumin is commonly used for the assessment of protein status, but given its long half-life (14–20 days), it has a slow response to dietary interventions and cannot detect subtle changes in nutritional status. Furthermore, albumin reflects an acute phase response and is not always a reliable marker of malnutrition [20]. However, albumin is an independent risk factor for complications after esophagectomy, since patients with hypoalbuminemia have twice the risk of postoperative infection and increased incidence of acute respiratory distress syndrome [21]. A recent review examined the association of serum albumin with postoperative complications in patients undergoing esophagectomy, suggesting that low serum albumin does increase the risk of postoperative complications, but there is still conflicting evidence regarding the prognostic value of this biomarker [22].

Other methods of nutritional assessment include questionnaires that incorporate many factors that impede adequate nutritional intake, as well as laboratory parameters, and unintentional weight loss. For example, Subjective Global Assessment (SGA), a questionnaire based on four parameters of patient's history (percentage of weight loss, changes in habitual diet, presence of significant gastrointestinal symptoms, and changes in patient's functional capacity) and three elements of their physical examination (loss of subcutaneous fat, muscle wasting, and presence of edema or ascites) is one the most commonly used tool for nutritional screening in malnourished hospital patients with cancer. SGA is strongly correlated with performance status in esophageal cancer patients [16] as well as with The Glasgow prognostic score and with complications during cancer treatment [23]. Other tools that have been studied in cancer patients is the Prognostic Nutritional Index (PNI), the Nutritional Risk Screening 2002 (NRS 2002), the Controlling Nutritional Status (CONUT) and the Nutritional Risk Index (NRI). Esophagectomized patients with a high Prognostic Nutritional Index—a tool which includes serum albumin and absolute peripheral lymphocyte count—had a higher prevalence of postoperative complications [24]. These results are in accordance with later studies, indicating that nutritional status preoperatively, expressed as PNI, was significantly related with the occurrence of severe complications and was a predictive factor for long-term survival [25, 26]. Nevertheless, Han-Geurts et al. showed that PNI was not associated with postoperative infectious complications in patients who underwent esophageal resection for malignancy [27]. NRS-2002 is recommended by the European Society for Clinical Nutrition and Metabolism as a standard tool for the assessment of surgical patients [28], but it is not tailored to esophageal cancer patients, thus limiting its prognostic value in this population. The CONUT score, which is calculated by serum albumin concentration, total peripheral lymphocyte count, and total cholesterol concentration, was developed as a screening tool for early detection of patients at risk of malnutrition [29]. Patients classified preoperatively as moderate or severe malnourished had a higher incidence of pulmonary and other severe morbidities, surgical site infections, and reoperation. Consequently, the duration of hospital stay in patients with moderate or severe malnutrition was significantly longer compared to well-nourished or slightly malnourished patients [30]. Similarly, Hirahara et al. [31] and Toyokawa et al. [32] demonstrated that CONUT was significantly associated with cancer death and poorer disease-free survival in patients with resectable esophageal squamous cell carcinoma. NRI is another tool used for the assessment of malnutrition based on serum albumin concentration and weight loss. Increased nutritional risk, derived from NRI, is associated with reduced survival in esophageal cancer patients treated with definitive chemoradiotherapy [10, 33], but is not associated with postoperative infectious complications in patients treated with esophagectomy [27]. The Geriatric Nutritional Risk Index (GNRI) is a new index recently introduced for the assessment of nutritional status of elderly patients. Patients diagnosed with poor nutritional status according to GNRI had significantly higher rate of respiratory complications after esophagectomy and gastric tube reconstruction [34]. In conclusion, there are several nutrition assessment tools for esophageal cancer patients, but since many of the studies mentioned above are of retrospective nature, the gold standard for the evaluation of nutritional status in this cancer subpopulation is yet to be determined (**Table 1**).

Percentage of unintentional weight loss	*Biochemical markers* (albumin, prealbumin, total peripheral lymphocyte count)	*Questionnaires and indices:* SGA, NRS2002, CONUT, NRI, PNI, Glasgow Prognostic Score

Table 1. Nutritional assessment of esophageal cancer patients.

2.3. Sarcopenia and cancer cachexia

Patients with esophageal cancer often witness loss of muscle mass and/or muscle strength, a condition described as sarcopenia. Although there are many different definitions of the term sarcopenia, all of them place emphasis on the impaired physical function following decreased muscle mass [35–37]. Sarcopenia is a component of cancer cachexia, especially in advanced stage cancer patients. Cancer cachexia is a complex syndrome which combines anorexia, early satiety, weakness, anemia, inflammation, weight loss, and loss of muscle mass with or without loss of fat mass [38]. A recent study pointed out that the prevalence of cancer cachexia in advanced esophageal cancer patients was 52.9% [39]. There is lack of consensus on the definition, diagnostic criteria, and classification of cancer cachexia, but the most commonly used definition includes one of the following: Weight loss >5% over past 6 months (in absence of simple starvation); or BMI <20 and any degree of weight loss >2%; or appendicular skeletal muscle index consistent with sarcopenia (males <7.26 kg/m^2; females <5.45 kg/m^2),and any degree of weight loss >2% [40]. Furthermore, assessment of sarcopenia plays an emerging role in cancer patients owing to the fact that CT scanning is a gold standard imaging method of body composition analysis at the tissue-organ level [41]. CT scans can identify reduced muscle mass and predict negative cancer outcomes in people with abdominal malignancies, where traditional methods of assessment are less effective [42]. Handgrip strength is another method used to measure muscle strength, which is directly related to the physiologic status of the individual and reflects patient's nutritional status. It could be easily used in patient's nutritional assessment due to the fact that it is an inexpensive and not time-consuming method.

Sarcopenia and cachexia are prognostic factors for surgical complications, decreased survival, and poor response to chemotherapy. More specifically, patients with weak handgrip strength had higher risk of complications and mortality after elective esophagectomy [43]. Decreased muscle mass, assessed by preoperative computed tomography scans, seems to be an independent predictor of both overall survival (**Figure 1**) [44] and disease-free survival, as significant as tumor stage, in patients following esophagectomy [45, 46]. In addition, sarcopenic patients who underwent esophagectomy had significantly higher rate of respiratory complications compared to nonsarcopenic subjects, but there was no difference in the incidence of overall complications between the two groups [47–49]. Sarcopenia has also impact on chemotherapy outcome since decreased muscle mass is associated with dose-limiting toxicity and pathological chemotherapy response in patients receiving neoadjuvant chemotherapy [50–52]. Therefore, it is imperative to estimate patients' muscle mass not only preoperatively but also before the onset of chemotherapy, bearing in mind that sarcopenia is frequently masqued by obesity making it more difficult to define patients' needs for intervention.

2.4. Mechanisms of malnutrition

Malnutrition, as mentioned above, affects a great percentage of esophageal cancer patients. Most patients are not able to achieve a positive energy balance and in many cases, initial body weight cannot even be maintained. This is ascribed mainly to impaired metabolism and side effects caused by esophagectomy or chemotherapy/radiation treatment. Dysphagia is a very common mechanical cause of malnutrition and is accompanied by dietary changes in order to

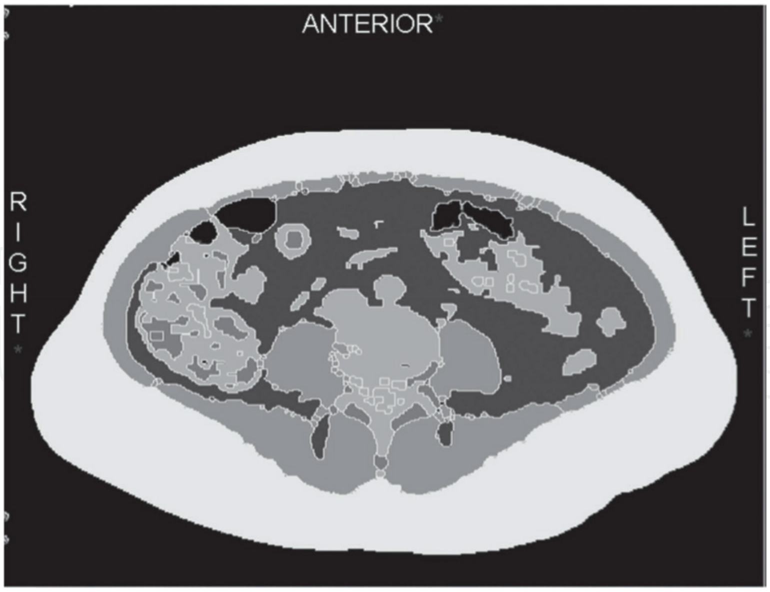

Figure 1. Example of CT scan analysis by the Slice-O-Matic software. Lumbar vertebrae 3 slice with Hounsfield units used to measure area of skeletal muscle, subcutaneous fat and visceral fat. White outer ring, subcutaneous fat; Light grey inner ring, muscle; Dark grey central area, visceral fat. Reproduced from Gibson et al. [42].

avoid foods that worsen symptoms leading to inadequate intake of calories. The surgical procedure often causes deficiencies in macronutrients and micronutrients, with the most prevailing side effects being postprandial dumping syndrome, dysphagia, anorexia, reflux, and early satiety [53–55]. Furthermore, chemotherapy affects rapidly proliferating cells preferentially and, consequently, affects the cells of the gastrointestinal tract. Chemotherapy-related causes of reduced food intake include nausea, vomiting, diarrhea, mucositis, and decreased appetite. Radiotherapy also contributes to malnutrition, and combined with chemotherapy exacerbates patients' nutritional status. Common side effects of radiotherapy include mucositis, esophagitis, odynophagia, mouth and throat soreness, and hypogeusia [56]. Tumor-related causes of malnutrition are also of great significance, but the mechanisms involved are still under investigation. Cancer-induced anorexia may result from circulating factors produced by the tumor or by the host in response to the tumor. For instance, cytokines, such as interleukins (IL) and tumor necrosis factor-alpha (TNF-α) cause anorexia [57], whereas other tumor-secreted factors promote central- and peripheral-mediated cancer cachexia. Tumor growth results in the secretion of pro-inflammatory factors that promote cachexia by signaling anorexia, muscle wasting, and white adipose tissue atrophy. Tumors also secrete both the proteolysis-inducing factor and activin, which promote skeletal muscle degradation and sarcopenia [58, 59].

Even though the mechanisms behind muscle wasting have been widely studied, less is known about the factors implicated in adipose tissue loss in cancer cachectic patients, such as lipid-mobilizing factor, as well as about the derangement in the neuroendocrine regulation of food intake and anorexia [60]. Additionally, changes in carbohydrate, lipid, and protein metabolism account for altered substrate metabolism. Changes in resting energy expenditure (REE) are considered one of the causes of nutritional depletion in cancer. In particular, measured REE by indirect calorimetry (IC) was elevated in patients with newly detected esophageal cancer, compared to healthy individuals [61]. A cross-sectional study involved 30 patients admitted with a diagnosis of squamous cell carcinoma who underwent IC before starting cancer therapy. The basal energy expenditure (BEE) was evaluated using IC and was also estimated using the Harris-Benedict Equation (HBE). The results showed that BEE of patients with squamous cell carcinoma was underestimated when using the HBE [62]. However, current evidence is inconsistent, since some studies suggest that REE is normal and is not affected by stage of disease [63–65]. Consequently, more research should be conducted in order to shed light on this controversial field.

3. Perioperative nutritional care

3.1. Enteral versus parenteral nutrition

Esophagectomy is one of the most invasive and time-consuming operations among gastrointestinal surgical procedures. It induces a strong stress response in the human body [66]. Consequently, patients' nutritional status is deteriorated after surgery, making postoperative nutritional care very important. The use of enteral nutrition (EN) postoperatively is a matter of debate, while scientific research attempts to define the role of enteral and parenteral nutrition (PN) on the clinical outcome of patients undergoing esophagectomy. Enteral feeding is considered the method of choice for the nutritional support of cancer patients with functioning gastrointestinal tract. Enteral nutrition is advantageous over parenteral nutrition for the following reasons: it provides all the necessary micro- and macronutrients in a more intact form, maintains gut mucosal integrity, inhibits the cytokine response, reduces the secretion of stress hormones, inhibits bacterial translocation, has a decreased risk of complications, and is less expensive [67]. Nevertheless, enteral nutrition is often avoided in order to minimize strain to the anastomoses, and reduce the risk of postoperatively impaired gastrointestinal motility. Another concern involves the return of gut motility or peristalsis and the ability of the gut to absorb nutrients. Surgical advances have increased the integrity of all anastomoses, making early oral enteral feeding after surgery a feasible option.

A randomized control trial investigated the outcomes of PN or EN after thoracoscopic esophagectomy. The rate of weight loss at postoperative day (POD) 14 was significantly lower in the EN group than in the PN group. Prealbumin levels at POD 10 showed no differences between the two groups. However, the incidence of postoperative pneumonia was higher in the PN group than in the EN group [68]. The results of another randomized clinical trial showed that there was no significant difference between EN and PN groups in terms of postoperative serum albumin, prealbumin, or transferrin. However, complement component 3 (C3) and 4 (C4) levels were significantly higher in the EN group compared with the PN group, while C-reactive protein level was significantly lower in the enteral feeding group. Bowel movements were restored sooner and costs of treatment were lower in the EN group. Postoperative complications did not differ significantly between the two groups [69]. Results from a recent meta-analysis of 10 randomized controlled trials concerning cancer patients following esophagectomy indicated that early postoperative enteral nutrition could significantly decrease pulmonary complications and anastomotic leakage compared with parenteral nutrition. On the eighth postoperative day, the EN group had higher levels of albumin and prealbumin compared with the PN group, suggesting that postoperative EN support is more effective in maintaining patients' nutritional status than PN support. No difference was observed in digestive complications between these two approaches. However, this meta-analysis is characterized by heterogeneity issues, especially regarding the postoperative nutritional status [70]. Furthermore, others suggest that combination of enteral and parenteral feeding is more beneficial, since total parenteral nutrition (TPN) could lead to hyperglycemia in stressed patients. A combination of EN and TPN might have some benefits when compared to TPN alone, such as improvement of intestinal integrity and stimulation of incretin production contributing to improved glucose control in patients undergoing esophagectomy [71]. Moreover, supplemental parenteral nutrition after esophagectomy contributes to better coverage of patients' calorie requirements, since large amounts of enteral nutrition are not usually tolerated in the first postoperative days [72].

The European Society for Parenteral and Enteral Nutrition (ESPEN) guidelines for nutritional support recommend that interruption of nutritional intake is unnecessary after surgery in most patients and in patients who require postoperative artificial nutrition, enteral feeding, or a combination of enteral and supplementary parenteral feeding is the first choice. Also this combination should be considered in patients in whom more than 60% of energy needs cannot be met via the enteral route. Postoperative parenteral nutrition is beneficial in undernourished patients in whom enteral nutrition is not feasible or not tolerated. In addition, postoperative parenteral nutrition is beneficial in patients with postoperative complications impairing gastrointestinal function that are unable to receive and absorb adequate amounts of oral/enteral feeding for at least 7 days [28]. Moreover, the American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines for critically ill patients recommends that patients who have undergone major upper gastrointestinal tract surgery and EN is not feasible, PN should be initiated (only if the duration of therapy is anticipated to be more than 7 days). Unless the patient is at high nutrition risk, PN should not be started in the immediate postoperative period, but should be delayed for 5–7 days [73]. In conclusion, although enteral nutrition seems to be a safe and feasible option postoperatively in terms of immunological parameters and postoperative complications, no firm conclusion can be drawn regarding postoperative nutritional markers that reflect patients' nutritional status.

3.2. Time of feeding

3.2.1. Early enteral nutrition

The initiation of enteral feeding after esophagectomy remains a controversial topic and many studies examine whether or not early enteral feeding affects negatively or positively the postoperative outcome. One study that investigated early enteral feeding after esophagectomy included 208 patients who received enteral nutrition postoperatively and were divided into three groups (Group 1, 2, and 3) based on whether they received EN within 48 h, 48–72 h or more than 72 h, respectively. The postoperative complications, length of hospital (LOH) stay, days for first fecal passage, cost of hospitalization, and the difference in serum albumin values pre- and postoperatively were all recorded. Group 1 had the lowest thoracic drainage volume, the earliest first fecal passage, and the lowest LOH and hospitalization expenses of all the three groups. The incidence of pneumonia was higher in Group 3. Finally, all postoperative outcomes of nutritional status were worst in Group 3 [74]. Similarly, one systematic review demonstrated that early oral EN was associated with reduced length of stay and did not increase complication rates [75]. More randomized clinical trials are required to confirm the results from retrospective studies that indicated that early EN promotes early recovery of intestinal movement and better recovery from systemic inflammation [66]. In addition, current literature is inconclusive with respect to the right time of EN administration postoperatively, that is, EN initiation within 24 h versus EN initiation during 24–72 h [76, 77].

3.2.2. Enhanced recovery after surgery (ERAS)

Early enteral nutrition is an essential part of fast-track surgery protocols in order to maximize the effects of enhanced recovery. Fast-track programs incorporate new methods regarding anesthesia, nutritional care, pain control, and surgical techniques in the preoperative, intraoperative, and postoperative period, aiming to promote postoperative rehabilitation of patients [78]. ESPEN guidelines recommend that all cancer patients undergoing either curative or palliative surgery should be managed within an enhanced recovery program postoperatively; within this program every patient should be screened for malnutrition and if deemed at risk, given additional nutritional support [79]. Nutritional aspects of ERAS could be summarized as follows: limitation of preoperative fasting, preoperative fluid and carbohydrate loading, and initiation of oral diet on the first postoperative day [80]. A recently published review demonstrated that utilization of enhanced recovery programs in esophageal cancer patients was associated with a reduction in the incidence of anastomotic leak, pulmonary complications, and length of hospital stay, but no significant change was observed in postoperative mortality or readmission rate. Nevertheless, there was significant heterogeneity between the studies in terms of enhanced recovery protocols, surgical approach, and utilization of neoadjuvant therapies that should be taken into account [81]. Results from a randomized controlled clinical study showed that the implementation of a fast-track protocol improved postoperative clinical recovery and cellular and humoral immunity of patients undergoing esophagectomy for esophageal cancer (**Table 2**) [82]. In this context, the implementation of fast-track programs in esophagectomy patients is promising, but the majority of patients included in the studies are relatively healthy patients. More randomized controlled studies and evidence-based research are required in order to justify the routine use of fast-track protocols in esophageal cancer patients [83].

3.3. Perioperative immunonutrition

Immunonutrition is one of the most debated topics in nutritional support of esophageal cancer patients. The term immunonutrition includes formulas that contain immune-modulating substances, such as arginine, glutamine, ribose nucleic acid, and omega-3-fatty acids. A recent review concluded that postoperative enteral immunonutrition could be promising in improving humoral immunity in patients undergoing esophagogastric resection, but this improvement is not related to a reduced hospital stay, nor does it reduce the rate of infections. The authors reported that there is heterogeneity regarding the types of operations undertaken (two studies included patients undergoing esophagectomy, three studied patients undergoing gastrectomy,

Day	FTS pathway
POD1	Jejunostomy tube feeding 500 ml (starting at 20 ml/h)
	Early postoperative mobilization program
	(>2 h out of bed)
	Physical therapy and nebulizers
	Remove urine catheter
	Head of bed put at 30°
	Supply albumin
	Chest tube to suction
	Promoted to lung recruitment
POD2	Jejunostomy tube feeding 1000 ml (40 ml/h)
	Chest tube to suction
	Expand mobilization (>4 h out of bed)
	Continue physical therapy and nebulizers
	Continue supply albumin
POD3	Jejunostomy tube feeding 1500 ml (60–80 ml/h)
	Remove chest tube
	Remove epidural catheter
	Expand mobilization (>6 h out of bed)
	Continue physical therapy and nebulizers
	Continue supply albumin
POD4	Gastrograffin opacification of upper gastrointestine
	If swallow shows no leak, advance patient to oral drink
	Jejunostomy tube feeding 1500 ml (60–80 ml/h)
	Continue physical therapy and nebulizers
	Education on aspiration precaution
	Education on chewing and swallowing
POD5	Jejunostomy tube feeding 1500 ml (60–80 ml/h)
	Advance patient to a full liquid diet
	Continue aspiration precautions
	Continue physical therapy and nebulizers
POD6	Increase liquid diet
	Decrease jejunostomy tube feeding
	(500 or 1000 ml)
	Continue aspiration precautions
	Continue physical therapy and nebulizers
POD7	Remove jejunostomy tube
	Full liquid diet
	Discharge home on soft diet and liquid diet
	Continue aspiration precautions

Note: FTS: Fast track surgery. Adapted from Chen et al. [82].

Table 2. Daily guideline of postoperative care of patients with fast-track surgery pathway.

and one had patients undergoing both operations). Additionally, the included randomized clinical trials used different formulations of enteral immunonutrition and standard enteral nutrition, further limiting the accuracy of the results. Moreover, not all studies reported the same outcomes as far as inflammatory and immunological markers are concerned. Therefore, the authors suggest that there is no convincing evidence in terms of routine immunonutrition in patients undergoing esophageal resection for cancer [84].

On the other hand, preoperative nutritional supplementation with immune-enhancing formulas was associated with reduced infectious complications, duration of hospitalization, improved short-term survival and less mortality in patients with esophageal cancer. These results highlight the possible need to provide immunonutrients before surgery to obtain sufficient levels at the time of surgical stress when there is an increased need for stimulation of the immune system [85]. One meta-analysis that included studies with patients that underwent esophagectomy, gastrectomy and pancreatectomy, demonstrated that patients who received immunonutrition postoperatively, had a significantly lower risk of wound infection and shorter length of hospital stay. No significant effect of immunonutrition on other postoperative morbidities and mortality was noticed [86]. The reduction in hospital stay and/or in postoperative complications seems to compensate for the higher cost of immunonutrition compared to standard enteral feeding in a cost-effectiveness analysis [87]. According to ESPEN guidelines on nutrition in cancer patients, upper gastrointestinal tract cancer patients undergoing surgical resection should receive oral/enteral immunonutrition in the context of traditional perioperative care [79]. Furthermore, ASPEN guidelines suggest the routine use of an immunemodulating formula (containing both arginine and fish oils) in the surgical intensive care unit for the postoperative patient who requires enteral nutrition therapy [73].

Synbiotics, which are a combination of prebiotics and probiotics, are speculated to have beneficial effects on human health, but little is known about their clinical value in patients who have undergone esophagectomy. Administration of synbiotics prevented postoperative deterioration of the intestinal microfloral environment and suppressed excessive inflammatory response, possibly by exerting immunomodulatory effects and by inhibiting bacterial translocation [88, 89]. Additionally, synbiotics led to decreased incidence of severe diarrhea and lower interruption or reduction of enteral nutrition. Passage of flatus postoperatively occurred significantly earlier in patients who received synbiotics than in the control group, suggesting that synbiotics maintain intestinal motility [88]. Taking all the aforementioned things into consideration, larger scale studies are needed in order to define whether or not immunonutrition has beneficial effects on the postoperative outcome of esophageal cancer patients. Future research should focus on the optimal dose of specific immunonutrients, on the timing (preoperatively and/or postoperatively) and duration of immunonutrition delivery and clarify which is the target group the intervention should be addressed to.

3.4. Type of feeding

Enteral feeding postoperatively seems to be the method of choice for uncomplicated esophageal cancer patients. Enteral feeding options after surgery include mainly nasoenteric tubes and jejunostomy catheters, in order to bypass recently constructed anastomoses. However there is no general agreement regarding the best method for postoperative feeding, and the optimal access route remains questionable. Tube-related complications include occlusion, catheter displacement and local cellulitis at the site of insertion. More severe complications include leakage into the peritoneal cavity resulting in peritonitis, volvulus at the point of fixation to the anterior abdominal wall, aspiration pneumonia, necrotizing fasciitis or jejunal necrosis at the site of catheter insertion and septicemia [90, 91].

A retrospective analysis of 90 patients who underwent esophagectomy demonstrated that early enteral nutrition can be administered using three different routes (nasojejunal tube, jejunostomy tube, and pharyngostomy tube) with similar results regarding tube-related complications, length of stay, and 30-day morbidity [92]. Another study of esophageal cancer patients with dysphagia examined the effects of jejunostomy feeding on weight loss and treatment outcomes. The palliative group of patients was able to maintain a stable weight despite the presence of cancer cachexia. This was also evident in the esophagectomy group of patients despite the catabolic effect of the operation, indicating the effectiveness of the jejunostomy feeding catheter as a means of nutritional support. The feeding catheter was well tolerated by the majority of patients (86.8%) and the most frequently occurred complications included catheter clogging (10.1% of the study population) and catheter dislodgement (3.1% of the study population) [93]. A randomized clinical study that compared nasoenteric tubes to jejunostomy feeding in upper gastrointestinal tract cancer patients showed that the length of enteral feeding use was less in the nasoenteric group and parenteral feeding was required more frequently than in jejunostomy feeding group. Complications related to the different feeding routes were similar between the two groups [94]. A recent review investigated the best route for enteral nutrition following esophagectomy (oral intake, jejunostomy, or nasojejunal tube feeding) in terms of postoperative complication rates, percentage of patients meeting their nutritional needs, weight loss, tube feeding complications, mortality, patient satisfaction, and length of hospital stay. Complications and catheter efficacy did not differ between postoperative nasojejunal tube feeding and jejunostomy tube feeding. Moreover, jejunostomy feeding patients were able to meet their short-term nutritional requirements, but data concerning long-term outcomes and patients satisfaction were scarce. This review concluded that the best route for the delivery of early enteral nutrition postoperatively is still unclear [75].

ESPEN guidelines on enteral nutrition in surgical patients recommends that tube feeding should be applied in patients who cannot start early oral nutrition, including those undergoing gastrointestinal surgery for cancer and patients with obvious undernutrition at the time of surgery, in whom oral intake will be inadequate (<60%) for more than 10 days. Initiation of tube feeding should start within 24 h after surgery with a low flow rate (i.e. 10–20 ml/h) due to limited intestinal tolerance. Placement of a needle catheter jejunostomy or nasojejunal tube is recommended for all candidates for tube feeding undergoing major abdominal surgery. When anastomoses of the proximal gastrointestinal tract have been performed, enteral nutrition should be delivered via a tube placed distally to the anastomosis [95].

Postoperative nutritional management of esophageal cancer patients can be summarized as in **Figure 2**.

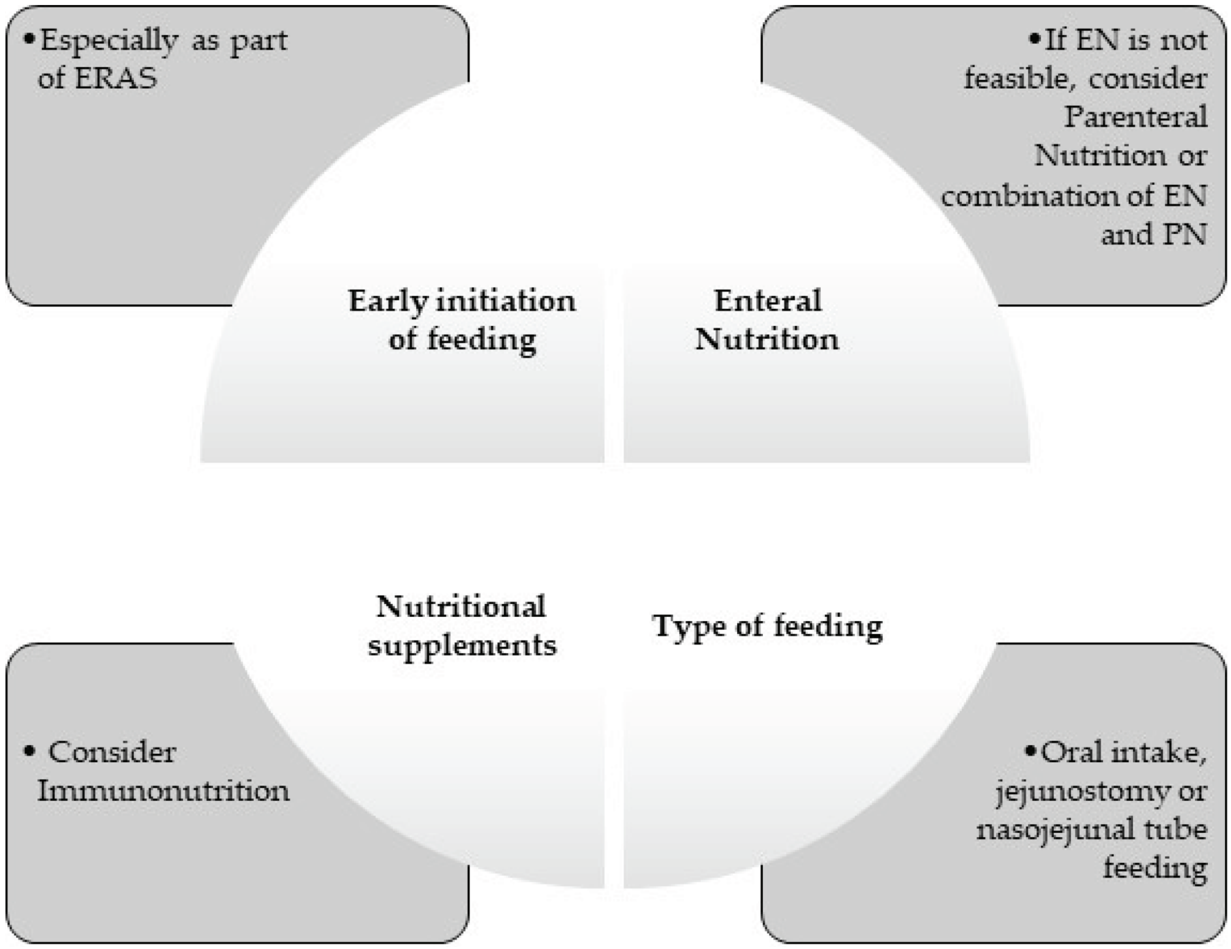

Figure 2. Postoperative nutritional management of esophageal cancer patients.

4. Nutritional care during chemoradiotherapy

4.1. Nutrition issues during chemotherapy and radiotherapy

Currently, perioperative chemotherapy is frequently administered for the treatment of resectable advanced esophageal cancer. The neoadjuvant administration of chemotherapy or chemoradiotherapy preoperatively results in reduced tumor size before surgery. Perioperative chemotherapy improves significantly disease-free survival and overall survival rates compared to surgery alone. However, a great percentage of these patients are not able to complete the planned postoperative chemotherapeutic regimens. This is mainly caused because of postoperative complications and impaired nutritional and physical status [96–98]. Gastrointestinal disorders caused by chemotherapy itself, including nausea, vomiting, diarrhea, and anorexia, negatively affect patients' quality of life and make completion of chemotherapy difficult. Neoadjuvant chemotherapy induces changes in body composition which, in turn have negative impact on clinical outcomes. Results from a small cohort of esophageal cancer patients showed that 26% of patients were sarcopenic before the initiation of neoadjuvant chemotherapy and this percentage increased to 43% after its completion. There was a significant loss of fat mass and skeletal muscle mass which was associated with risk of circumferential resection margin positivity [50]. In another study, sarcopenia was present in 56 and 67% of patients before and after neoadjuvant chemoradiotherapy, respectively. This decrease in muscle mass was predictive of postoperative mortality in the stage III–IV subgroup of patients [99]. Furthermore, most of the radiotherapy-related toxicities are strongly associated with patient's nutritional status. Esophagitis is the main toxicity during radiotherapy in esophageal cancer patients. These patients often suffer from pain and difficulties in swallowing [100]. One study in patients receiving concurrent chemoradiotherapy revealed that malnutrition was observed in 83.8% of patients, while 68.8% of patients developed severe dysphagia. Malnourished patients developed more treatment-related toxicities compared to those without malnutrition. Patients with impaired nutritional status presented severe dysphagia, anorexia, severe nausea/vomiting, and severe hematologic toxicities more frequently than those in a good nutrition status [17]. Although nutritionally related side effects occur frequently, nutritional assessment of patients with cancer receiving chemoradiotherapy is often omitted in the clinical setting. Scientific research has to focus on nutritional interventions during neoadjuvant chemoradiotherapy or postoperative adjuvant therapy that seems to improve patients' nutritional status, alleviate symptoms and increase tolerance to therapies.

4.2. Nutritional interventions during chemoradiotherapy

The type and timing of nutritional interventions during chemoradiotherapy challenge the caregivers, since a multidisciplinary approach seems more effective in managing treatment's side effects. Current literature emphasizes mainly on the immunomodulatory effects of some nutrients, on the impact of oral/tube administration of high-energy, and/or high protein supplements on the clinical outcome and on patients education about selecting an enriched diet. In cancer patients, it has been shown that the use of supplemental formulas and *n*-3 fatty acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), can improve body composition, preserve muscle mass, and possibly reverse or stop the development of cancer cachexia [101]. A controlled, randomized prospective, double-blind, multicenter study investigated the impact of enteral nutrition (via percutaneous endoscopic gastrostomy (PEG)) enriched with EPA and DHA on body composition, nutritional and functional status of esophageal and head and neck cancer patients undergoing concurrent chemoradiotherapy. There was a tendency toward improvement regarding loss of body cell mass and body weight following chemoradiotherapy, but did not reach statistical significance. However, Karnofsky score and subjective parameters, such as the NRS 2002 and the SGA score were significantly improved in the experimental group compared with the control group, indicating improved nutritional and functional status [102]. Similar results reported by another randomized double-blind clinical trial showed that administration of immunonutrition during chemoradiotherapy in head and neck and esophageal cancer patients was advantageous over standard enteral nutrition in terms of body weight, lean body mass, serum albumin levels, NRI assessment, plasma antioxidant capacity, and functional capacity [103].

Moreover, immunonutrition can modulate the immunological and inflammatory systems, thus reducing the risks of concurrent chemoradiotherapy. One randomized clinical trial examined the effects of immunonutrition on serum cytokine and inflammatory markers, and cellular immunity in locally advanced esophageal cancer patients undergoing chemoradiotherapy. The levels of C-Reactive Protein (CRP) and TNF increased more during treatment in the control group (standard enteral nutrition) than in the treatment group, whereas all other markers did not differ significantly between the two groups [104]. In addition, the impact of immunonutrients on immune system of head and neck and esophageal cancer patients during chemoradiotherapy was examined in another randomized clinical trial. Immune cells metabolism and functions were assessed at the initiation and at the completion of treatment. The experimental group had better adaptation to the systematic inflammation and oxidative stress, as indicated by $CD4^+/CD8^+$ T-lymphocyte counts ratio, CD3 membrane expression, polymorphonuclear cells CD62L and CD15 densities, reactive oxygen species (ROS) production, and peripheral blood mononuclear cells production of pro-inflammatory prostaglandin-E2 [105].

Another role of immunonutrition is the potential protection against chemotherapy-induced toxicities. Miyata et al. compared the effects between enteral nutrition rich in *n*-3 fatty acids (900 mg/d) and enteral nutrition poor in *n*-3 fatty acids (250 mg/d) on chemotherapy-related adverse events and inflammatory markers during neoadjuvant chemotherapy in esophageal cancer patients. This randomized control trial showed no significant difference in the incidence of grade 3/4 leukopenia and neutropenia, but stomatitis was observed less frequently in the *n*-3-rich group, than in the *n*-3-poor group. Grade 3/4 diarrhea was also observed less frequently in the *n*-3-rich group than in the *n*-3-poor group, but this was not statistically significant. Moreover, *n*-3-rich enteral nutrition seems to have hepatoprotective properties by preventing an increase of aspartate aminotransferase and alanine aminotransferase values [106].

Synbiotics seem also to mitigate chemotherapy-related side effects through adjustments to the intestinal microbiota. A randomized clinical trial investigated the effects of synbiotics in esophageal cancer patients undergoing neoadjuvant chemotherapy, on the intestinal microbiota, and the adverse events of treatment. Severe lymphopenia and diarrhea were less frequent in patients who received synbiotics than in the control group. Furthermore, febrile neutropenia occurred less in the synbiotics group compared to the control group [107]. Chemotherapy may disturb the intestinal microbiota, leading to reduced production of organic acids in the bowel, impaired mucosal integrity, and increased harmful bacteria. These, in turn, may induce chemotherapy-related toxicities, such as diarrhea and infectious complications [108]. Administration of synbiotics results in increased concentrations of short-chain fatty acids, such as acetate and propionate. These fatty acids are an important energy source of enterocytes, maintain intestinal environment acidity and intestinal motility. Synbiotics also maintain the number of beneficial bacteria and inhibit the overgrowth of possible diarrheal pathogens, thus reducing the incidence of diarrhea [109].

ESPEN guidelines on nutrition in cancer patients recommend the supplementation with long-chain *n*-3 fatty acids or fish oil to stabilize or improve appetite, food intake, lean body mass, and body weight in patients with advanced cancer undergoing chemotherapy and at risk of weight loss or malnourished [79]. It is therefore evident that immunonutrition enhances immune system and exerts anti-inflammatory properties, but the promising effects on clinical outcome during chemoradiotherapy in esophageal cancer are still under investigation. Additional clinical trials are needed to determine the preferred type, timing and duration of immunonutrition required to reduce inflammation and chemotherapy-induced toxicities, and maintain muscle mass.

Nutritional interventions, other than that examining the impact of specific immunonutrients on chemoradiotherapy-related outcomes, include nutritional counseling and/or enteral supplements in order to maintain stable body weight and cope with feeding difficulties (**Table 3**). A recent randomized controlled trial compared the effects of a walk-and-eat intervention versus conventional medical care for patients with esophageal cancer undergoing neoadjuvant chemoradiotherapy. This intervention consisted of a structured walking protocol and weekly nutritional advice including weight and intake evaluation, counseling to overcome feeding difficulties, supplementation, if necessary, with enteral formulas, and patient's education concerning food texture modification and oral care before and after eating. During chemoradiotherapy, the group that received the walk-and-eat intervention had 100-m less decline than controls in walk distance, 3 kg less decrease in handgrip strength, and 2.7 kg less reduction in body weight. Moreover, the experimental group had significantly reduced rates of intravenous nutritional support and wheel chair use [110]. Another randomized trial tested the effects of an interdisciplinary nutrition support team on clinical and hospitalized outcomes of esophageal cancer patients receiving concurrent chemoradiotherapy. Nutritional support included dietary counseling, oral nutritional supplements, enteral nutrition, and parenteral nutrition according to patient's needs. At the completion of treatment, nutritional status of patients in the interventional group was better compared to control group, as demonstrated by prealbumin, transferrin, and albumin levels. Bone marrow suppression and complications related to infections were significantly lower in the nutritional support group. Nutritional intervention was also associated with a lower average length of hospital stay and in-patient cost [111]. Furthermore, nutritional intervention improved survival of esophageal cancer patients treated with definitive chemoradiotherapy. It is noticeable that this effect was observed only if nutritional support was provided at baseline (dietary advice, oral supplementation, or major intervention), and not if provided later in the treatment course [10].

According to ESPEN, in patients receiving radiotherapy, especially radiotherapy of the head and neck, thorax, and gastrointestinal tract, an adequate nutritional intake should be ensured primarily by individualized nutritional counseling and/or with use of oral nutritional

Nutritional counseling
Oral supplementation
Immunonutrition
Synbiotics
Parenteral nutrition support

Table 3. Nutritional interventions during chemoradiotherapy.

supplements, in order to avoid nutritional deterioration, maintain intake, and avoid radiotherapy interruptions. In addition, for patients undergoing curative anticancer drug treatment who cannot meet their nutritional requirements despite counseling and oral nutritional supplements, ESPEN recommends supplemental enteral nutrition or, if this is not sufficient or possible, parenteral nutrition [79]. Therefore, assessment and maintenance of good nutritional status at baseline may be a simple and cost-effective intervention that improves clinical outcomes in esophageal cancer patients during chemoradiotherapy treatment.

4.3. Stent insertion

There are various types of stents available, such as self-expandable metallic stents, self-expandable plastic stents, and biodegradable stents. Esophageal stenting can be implemented to relieve dysphagia during preoperative chemotherapy and/or radiotherapy. A systematic review investigated the impact of stent insertion during neoadjuvant treatment on dysphagia improvement. Placement of an esophageal stent significantly improved overall dysphagia scores in all 12 studies reviewed. However, no consistent improvement in nutritional status was observed, defined by body weight and albumin levels. Moreover, stent insertion was associated with complications, such as migration and chest pain, frequently resulting in stent removal or replacement [112]. The European Society of Gastrointestinal Endoscopy (ESGE) does not recommend self-expandable metal stents placement as a bridge to surgery or prior to preoperative chemoradiotherapy, since it is associated with a high incidence of adverse events. Other options, such as feeding tube placement are preferable and should be considered in dysphagic or malnourished patients in the neoadjuvant setting [113].

5. Palliative care

Management of patients undergoing noncurative treatments due to advanced disease is difficult, since the goals are not to cure patients but to improve length and quality of remaining life. Nutritional support is a crucial part in the palliative care as long as its benefits outweigh its costs. Patients with metastatic disease present for the clinician not only clinical but ethical issues as well. Dysphagia is the main symptom in patients with unresectable disease which aggravates malnutrition and requires nutritional intervention [114]. Nutritional support of these patients includes intravenous fluids for hydration, feeding tubes, parenteral nutrition, and stent placement in order to supplement dietary and caloric intake. Various techniques have been proposed to manage dysphagia, such as brachytherapy, self-expanding metal stents, thermal laser therapy, and photodynamic therapy. Each one of them has specific advantages and risks that should be taken into consideration. The authors of a recent meta-analysis of 53 randomized controlled trials concluded that self-expanding metal stent insertion is safe, effective, and improves dysphagia faster compared to other modalities. High-dose intraluminal brachytherapy is a satisfactory alternative and might provide additional survival benefit with a better quality of life. Combinations of brachytherapy with self-expanding metal stent insertion or radiotherapy seem to be the preferable option addressed to inoperative patients [115]. ESGE recommends placement of partially or fully covered self-expandable metal stents for palliative treatment of malignant dysphagia over laser therapy, photodynamic therapy, and esophageal bypass [113].

Moreover, in esophageal cancer patients with short life expectancy unsuitable for esophageal stenting, percutaneous endoscopic gastrostomy (PEG) may be a suitable means in order to achieve nutritional support, while allowing patients to be at home [116]. Endoscopically assisted nasogastric tube feeding is also a feasible palliative option for nutritional support, with a low complication rate. Tube-feeding patients had significantly higher enteral calorie intake, higher serum albumin, shorter hospital stay, and longer median survival compared to those who received *nil per os*, according to a retrospective study of patients with malignant esophageal obstruction [117]. Palliative care in the terminal phase should be followed in an individualized manner. ESPEN recommends that in dying patients, artificial hydration and nutrition are unlikely to benefit patients. Nevertheless, in acute confusional states, patients might receive a short and limited hydration to rule out dehydration as precipitating cause [79].

6. Conclusion

Esophageal cancer patients suffer from malnutrition and cannot easily meet their nutritional needs. Nutritional assessment, in the perioperative phase, but also in patients undergoing chemoradiotherapy should be performed regularly, in order to identify undernourished patients. Regarding the perioperative management of these patients, early enteral nutrition support seems to be the method of choice in uncomplicated patients, especially as a part of ERAS programs. However, the impact of immunonutrition on clinical outcome is still under investigation. During chemoradiotherapy, prevention of weight loss is of great significance and might be achieved through close nutritional monitoring. Nutritional support mainly encompasses dietary counseling, oral supplementation, tube feeding, and combination of them and has promising results in ameliorating nutritional status and affecting the oncologic outcome. Moreover, patients with terminal-stage esophageal cancer might benefit from early stent insertion in order to reduce dysphagia. Individualized nutritional support should be addressed to every patient who is in need of nutritional intervention.

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References

[1] Global Burden of Disease Cancer Collaboration. The global burden of cancer 2013. JAMA Oncology. 2015;**1**(4):505-527. DOI: 10.1001/jamaoncol.2015.0735

[2] Yang CS, Chen X, Tu S. Etiology and prevention of esophageal cancer. Gastrointestinal Tumors. 2016;**3**(1):3-16. DOI: 10.1159/000443155

[3] Choi Y, Song S, Song Y, Lee JE. Consumption of red and processed meat and esophageal cancer risk: Meta-analysis. World Journal of Gastroenterology. 2013;**19**(7):1020-1029. DOI: 10.3748/wjg.v19.i7.1020

[4] Andrici J, Eslick G. Hot food and beverage consumption and the risk of esophageal cancer. American Journal of Preventive Medicine. 2015;**49**(6):952-960. DOI: 10.1016/j.amepre.2015.07.023

[5] Corley DA, Kubo A, Zhao W. Abdominal obesity and the risk of esophageal and gastric cardia carcinomas. Cancer Epidemiology, Biomarkers & Prevention: A Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology. 2008;**17**(2):352-358. DOI: 10.1158/1055-9965.EPI-07-0748

[6] Cook MB, Corley DA, Murray LJ, et al. Gastroesophageal reflux in relation to adenocarcinomas of the esophagus: A pooled analysis from the Barrett's and Esophageal Adenocarcinoma Consortium (BEACON). Suzuki H, ed. PLoS One. 2014;**9**(7):e103508. DOI: 10.1371/journal.pone.0103508

[7] Kubo A, Block G, Quesenberry CP, et al. Effects of dietary fiber, fats, and meat intakes on the risk of Barrett's esophagus. Nutrition and Cancer. 2009;**61**(5):607-616. DOI: 10.1080/01635580902846585

[8] Anandavadivelan P, Lagergren P. Cachexia in patients with oesophageal cancer. Nature Reviews Clinical Oncology. 2016;**13**(3):185-198. DOI: 10.1038/nrclinonc.2015.200

[9] Llop-Talaveron JM, Farran-Teixidor L, Badia-Tahull MB, et al. Artificial nutritional support in cancer patients after esophagectomy: 11 years of experience. Nutrition and Cancer. 2014;**66**(6):1038-1046. DOI: 10.1080/01635581.2014.939292.

[10] Cox S, Powell C, Carter B, et al. Role of nutritional status and intervention in oesophageal cancer treated with definitive chemoradiotherapy: Outcomes from SCOPE1. British Journal of Cancer. 2016;**115**(2):172-177. DOI: 10.1038/bjc.2016.129

[11] Deans DAC, Tan BH, Wigmore SJ, et al. The influence of systemic inflammation, dietary intake and stage of disease on rate of weight loss in patients with gastro-oesophageal cancer. British Journal of Cancer. 2009;**100**(1):63-69. DOI: 10.1038/sj.bjc.6604828

[12] Riccardi D, Allen K. Nutritional management of patients with esophageal and esophagogastric junction cancer. Cancer Control. 1999;**6**(1):64-72

[13] Bailey SH, Bull DA, Harpole DH, et al. Outcomes after esophagectomy: A ten-year prospective cohort. The Annals of Thoracic Surgery. 2003;**75**(1):217-222

[14] Bower MR, Martin RC. Nutritional management during neoadjuvant therapy for esophageal cancer. Journal of Surgical Oncology. 2009;**100**(1):82-87. DOI: 10.1002/jso.21289

[15] Martin L, Lagergren P. Long-term weight change after oesophageal cancer surgery. British Journal of Surgery. 2009;**96**(11):1308-1314. DOI: 10.1002/bjs.6723

[16] Quyen TC, Angkatavanich J, Thuan TV, et al. Nutrition assessment and its relationship with performance and Glasgow prognostic scores in Vietnamese patients with esophageal cancer. Asia Pacific Journal of Clinical Nutrition. 2017;**26**(1):49-58. DOI: 10.6133/apjcn.122015.02

[17] Pan P, Tao G, Sun X. Subjective global assessment and prealbumin levels of esophageal cancer patients undergoing concurrent chemoradiotherapy. Nutricion Hospitalaria. 2015;**31**(5):2167-2173. DOI: 10.3305/nh.2015.31.5.8596

[18] Nitenberg G, Raynard B. Nutritional support of the cancer patient: Issues and dilemmas. Critical Reviews in Oncology/Hematology. 2000;**34**(3):137-168

[19] DiFiore F, Lecleire S, Pop D, et al. Baseline nutritional status is predictive of response to treatment and survival in patients treated by definitive chemoradiotherapy for a locally advanced esophageal cancer. American Journl of Gastroenterology. 2007;**102**(11):2557-2563. DOI: 10.1111/j.1572-0241.2007.01437.x

[20] National Collaborating Centre for Acute Care. Nutrition Support for Adults Oral Nutrition Support, Enteral Tube Feeding and Parenteral Nutrition Methods, Evidence and Guidance; 1e176. 2006. London: National Collaborating Centre for Acute Care at The Royal College of Surgeons of England; 2011

[21] Ryan AM, Hearty A, Prichard RS, et al. Association of hypoalbuminemia on the first postoperative day and complications following esophagectomy. Journal of Gastrointestinal Surgery. 2007;**11**(10):1355-1360

[22] Goh SL, De Silva RP, Dhital K, et al. Is low serum albumin associated with postoperative complications in patients undergoing oesophagectomy for oesophageal malignancies? Interactive CardioVascular and Thoracic Surgery. 2015;**20**(1):107-113. DOI: 10.1093/icvts/ivu324

[23] da Silva JB, Maurício SF, Bering T, Correia MI. The relationship between nutritional status and the Glasgow prognostic score in patients with cancer of the esophagus and stomach. Nutrition and Cancer. 2013;**65**(1):25-33. DOI: 10.1080/01635581.2013.741755

[24] Nozoe T, Kimura Y, Ishida M, et al. Correlation of pre-operative nutritional condition with post-operative complications in surgical treatment for oesophageal carcinoma. European Journal of Surgical Oncology. 2002;**28**(4):396-400. DOI: 10.1053/ejso.2002.1257

[25] Feng J-F, Chen Q-X. Significance of the prognostic nutritional index in patients with esophageal squamous cell carcinoma. Therapeutics and Clinical Risk Management. 2014;**10**:1-7. DOI: 10.2147/TCRM.S56159

[26] Filip B, Scarpa M, Cavallin F, et al. Postoperative outcome after oesophagectomy for cancer: Nutritional status is the missing ring in the current prognostic scores. European Journal of Surgical Oncology. 2015;**41**(6):787-794. DOI: 10.1016/j.ejso.2015.02.014

[27] Han-Geurts IJ, Hop WC, Tran TC, Tilanus HW. Nutritional status as a risk factor in esophageal surgery. Digestive Surgery. 2006;**23**(3):159-163. DOI: 10.1159/000093756

[28] Braga M, Ljungqvist O, Soeters P, et al. ESPEN guidelines on parenteral nutrition: Surgery. Clinical Nutrition. 2009;**28**(4):378-386. DOI: 10.1016/j.clnu.2009.04.002

[29] Ignacio de Ulibarri J, Gonzalez-Madrono A, de Villar NG, et al. CONUT: A tool for controlling nutritional status. First validation in a hospital population. Nutricion Hospitalaria. 2005;**20**(1):38-45

[30] Yoshida N, Baba Y, Shigaki H, et al. Preoperative nutritional assessment by controlling nutritional status (CONUT) is useful to estimate postoperative morbidity after esophagectomy for esophageal cancer. World Journal of Surgery. 2016;**40**(8):1910-1917. DOI: 10.1007/s00268-016-3549-3

[31] Hirahara N, Matsubara T, Hayashi H, et al. Prognostic importance of controlling nutritional status in patients undergoing curative thoracoscopic esophagectomy for esophageal cancer. American Journal of Therapeutics. 2016;**0**(0):1-9. DOI: 10.1097/MJT.0000000000000414

[32] Toyokawa T, Kubo N, Tamura T, et al. The pretreatment controlling nutritional status (CONUT) score is an independent prognostic factor in patients with resectable thoracic esophageal squamous cell carcinoma: Results from a retrospective study. BMC Cancer. 2016;**16**(1):722. DOI: 10.1186/s12885-016-2696-0

[33] Clavier JB, Antoni D, Atlani D, et al. Baseline nutritional status is prognostic factor after definitive radiochemotherapy for esophageal cancer. Diseases of the Esophagus. 2014;**27**(6):560-567. DOI: 10.1111/j.1442-2050.2012.01441.x

[34] Yamana I, Takeno S, Shibata R, et al. Is the geriatric nutritional risk index a significant predictor of postoperative complications in patients with esophageal cancer undergoing esophagectomy? European Surgical Research. 2015;**55**(1-2):35-42. DOI: 10.1159/000376610

[35] Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis—Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010;**39**(4):412-423. DOI: 10.1093/ageing/afq034

[36] Muscaritoli M, Anker SD, Argiles J, et al. Consensus definition of sarcopenia, cachexia and pre-cachexia: Joint document elaborated by special interest groups (SIG) "cachexia-anorexia in chronic wasting diseases" and "nutrition in geriatrics". Clinical Nutrition. 2010;**29**(2):154-159. DOI: 10.1016/j.clnu.2009.12.004

[37] Fielding RA, Vellas B, Evans WJ, et al. Sarcopenia: An undiagnosed condition in older adults—Current consensus definition: Prevalence, etiology, and consequences. International working group on Sarcopenia. Journal of the American Medical Directors Association. 2011;**12**(4):249-256. DOI: 10.1016/j.jamda.2011.01.003

[38] Argilés JM, Olivan M, Busquets S, López-Soriano FJ. Optimal management of cancer anorexia–cachexia syndrome. Cancer Management and Research. 2010;**2**:27-38

[39] Sun L, Quan XQ, Yu S. An epidemiological survey of cachexia in advanced cancer patients and analysis on its diagnostic and treatment status. Nutrition and Cancer. 2015;**67**(7):1056-1062. DOI: 10.1080/01635581.2015.1073753

[40] Fearon K, Strasser F, Anker SD, et al. Definition and classification of cancer cachexia: An international consensus. Lancet Oncology. 2011;**12**(5):489-495. DOI: 10.1016/S1470-2045(10)70218-7

[41] Prado CM, Birdsell LA, Baracos VE. The emerging role of computerized tomography in assessing cancer cachexia. Current Opinion in Supportive and Palliative Care. 2009;**3**(4):269-275. DOI: 10.1097/SPC.0b013e328331124a

[42] Gibson DJ, Burden ST, Strauss BJ, et al. The role of computed tomography in evaluating body composition and the influence of reduced muscle mass on clinical outcome in abdominal malignancy: A systematic review. European Journal of Clinical Nutrition. 2015;**69**(10):1079-1086. DOI: 10.1038/ejcn.2015.32

[43] Chen CH, Ho-Chang, Huang YZ, Hung TT. Hand-grip strength is a simple and effective outcome predictor in esophageal cancer following esophagectomy with reconstruction: A prospective study. Journal of Cardiothoracic Surgery. 2011;**6**:98. DOI: 10.1186/1749-8090-6-98

[44] Levolger S, van Vugt JL, de Bruin RW, IJzermans JN. Systematic review of sarcopenia in patients operated on for gastrointestinal and hepatopancreatobiliary malignancies. British Journal of Surgery. 2015;**102**(12):1448-1458. DOI: 10.1002/bjs.9893

[45] Sheetz KH, Zhao L, Holcombe SA, et al. Decreased core muscle size is associated with worse patient survival following esophagectomy for cancer. Diseases of the Esophagus. 2013;**26**(7):716-722. DOI: 10.1111/dote.12020

[46] Tamandl D, Paireder M, Asari R, et al. Markers of sarcopenia quantified by computed tomography predict adverse long-term outcome in patients with resected oesophageal or gastro-oesophageal junction cancer. European Radiology. 2016;**26**(5):1359-1367. DOI: 10.1007/s00330-015-3963-1

[47] Ida S, Watanabe M, Yoshida N, et al. Sarcopenia is a predictor of postoperative respiratory complications in patients with esophageal cancer. Annals of Surgical Oncology. 2015;**22**(13):4432-4437. DOI: 10.1245/s10434-015-4559-3

[48] Nishigori T, Okabe H, Tanaka E, et al. Sarcopenia as a predictor of pulmonary complications after esophagectomy for thoracic esophageal cancer. Journal of Surgical Oncology. 2016;**113**(6):678-684. DOI: 10.1002/jso.24214

[49] Makiura D, Ono R, Inoue J, et al. Preoperative sarcopenia is a predictor of postoperative pulmonary complications in esophageal cancer following esophagectomy: A retrospective cohort study. Journal of Geriatric Oncology. 2016;**7**(6):430-436. DOI: 10.1016/j.jgo.2016.07.003

[50] Yip C, Goh V, Davies A, et al. Assessment of sarcopenia and changes in body composition after neoadjuvant chemotherapy and associations with clinical outcomes in oesophageal cancer. European Radiology. 2014;**24**(5):998-1005. DOI: 10.1007/s00330-014-3110-4

[51] Tan BH, Brammer K, Randhawa N, et al. Sarcopenia is associated with toxicity in patients undergoing neo-adjuvant chemotherapy for oesophago-gastric cancer. European Journal of Surgical Oncology. 2015;**41**(3):333-338. DOI: 10.1016/j.ejso.2014.11.040

[52] Anandavadivelan P, Brismar TB, Nilsson M, et al. Sarcopenic obesity: A probable risk factor for dose limiting toxicity during neo-adjuvant chemotherapy in oesophageal cancer patients. Clinical Nutrition. 2016;**35**(3):724-730. DOI: 10.1016/j.clnu.2015.05.011

[53] Aghajanzadeh M, Safarpour F, Koohsari MR, et al. Functional outcome of gastrointestinal tract and quality of life after esophageal reconstruction of esophagus cancer. Saudi Journal of Gastroenterology. 2008;**15**(1):24e8. DOI: 10.4103/1319-3767.45050

[54] Ginex P, Thom B, Jingeleski M, et al. Patterns of symptoms following surgery for esophageal cancer. Oncology Nursing Forum. 2013;**40**(3):E101-E107. DOI: 10.1188/13.ONF.E101-E107

[55] Greene CL, DeMeester SR, Worrell SG, et al. Alimentary satisfaction, gastrointestinal symptoms, and quality of life 10 or more years after esophagectomy with gastric pull-up. Journal of Thoracic and Cardiovascular Surgery. 2014;**147**(3):909-914. DOI: 10.1016/j.jtcvs.2013.11.004

[56] Mak RH, Mamon HJ, Ryan DP, et al. Toxicity and outcomes after chemoradiation for esophageal cancer in patients age 75 or older. Diseases of the Esophagus. 2010;**23**(4):316-323. DOI: 10.1111/j.1442-2050.2009.01014.x

[57] Sonti G, Ilyin SE, Plata-Salaman CR. Anorexia induced by cytokine interactions at pathophysiological concentrations. American Journal of Physiology. 1996;**270**(6 Pt 2):R1394-R402

[58] Zhou X, Wang JL, Lu J, et al. Reversal of cancer cachexia and muscle wasting by ActRIIB antagonism leads to prolonged survival. Cell. 2010;**142**(4):531-543. DOI: 10.1016/j.cell.2010.07.011

[59] Johns N, Stephens NA, Fearon KC. Muscle wasting in cancer. The International Journal of Biochemistry & Cell Biology. 2013;**45**(10):2215-2229. DOI: 10.1016/j.biocel.2013.05.032

[60] Mendes MC, Pimentel GD, Costa FO, Carvalheira JB. Molecular and neuroendocrine mechanisms of cancer cachexia. Journal of Endocrinology. 2015;**226**(3):R29-R43. DOI: 10.1530/JOE-15-0170

[61] Wu J, Huang C, Xiao H, et al. Weight loss and resting energy expenditure in male patients with newly diagnosed esophageal cancer. Nutrition. 2013;**29**(11-12):1310-1314. DOI: 10.1016/j.nut.2013.04.010

[62] Becker Veronese CB, Guerra LT, Souza Grigolleti S, et al. Basal energy expenditure measured by indirect calorimetry in patients with squamous cell carcinoma of the esophagus. Nutricion Hospitalaria. 2013;**28**(1):142-147. DOI: 10.3305/nh.2013.28.1.6152

[63] Cao DX, Wu GH, Zhang B, et al. Resting energy expenditure and body composition in patients with newly detected cancer. Clinical Nutrition. 2010;**29**(1):72-77. DOI: 10.1016/j.clnu.2009.07.001

[64] Dempsey DT, Feurer ID, Knox LS, et al. Energy expenditure in malnourished gastrointestinal cancer patients. Cancer. 1984;**53**(6):1265-1273

[65] Okamoto H, Sasaki M, Johtatsu T, et al. Resting energy expenditure and nutritional status in patients undergoing transthoracic esophagectomy for esophageal cancer. Journal of Clinical Biochemistry and Nutrition. 2011;**49**(3):169-173. DOI: 10.3164/jcbn.11-13

[66] Kobayashi K, Koyama Y, Kosugi S, et al. Is early enteral nutrition better for postoperative course in esophageal cancer patients? Nutrients. 2013;**5**(9):3461-3469. DOI: 10.3390/nu5093461

[67] Demeyer I, Bataillie K, Baute L. Long-term sedation in the ICU: Enteral versus parenteral feeding. Clinical Intensive Care. 1994;**5**(5 Suppl):13-16

[68] Takesue T, Takeuchi H, Ogura M, et al. A prospective randomized trial of enteral nutrition after thoracoscopic esophagectomy for esophageal cancer. Annals of Surgical Oncology. 2015;**22**(Suppl 3):S802-S809. DOI: 10.1245/s10434-015-4767-x

[69] Rajabi Mashhadi MT, Bagheri R, Ghayour-Mobarhan M, et al. Early postoperative enteral versus parenteral feeding after esophageal cancer surgery. Iranian Journal of Otorhinolaryngology. 2015;**27**(82):331-336

[70] Peng J, Cai J, Niu ZX, Chen LQ. Early enteral nutrition compared with parenteral nutrition for esophageal cancer patients after esophagectomy: A meta-analysis. Diseases of the Esophagus. 2016;**29**(4):333-341. DOI: 10.1111/dote.12337

[71] Lidder P, Flanagan D, Fleming S, et al. Combining enteral with parenteral nutrition to improve postoperative glucose control. British Journal of Nutrition. 2010;**103**(11):1635-1641. DOI: 10.1017/S0007114509993631

[72] Wu W, Zhong M, Zhu DM, et al. Effect of early Full-Calorie nutrition support following esophagectomy: A randomized controlled trial. Journal of Parenteral and Enteral Nutrition. 2016. pii: 0148607116651509. [Epub ahead of print]

[73] McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). Journal of Parenteral and Enteral Nutrition. 2016;**40**(2):159-211. DOI: 10.1177/0148607115621863

[74] Wang G, Chen H, Liu J, et al. A comparison of postoperative early enteral nutrition with delayed enteral nutrition in patients with esophageal cancer. Nutrients. 2015;**7**(6):4308-4317. DOI: 10.3390/nu7064308

[75] Weijs TJ, Berkelmans GH, Nieuwenhuijzen GA, et al. Routes for early enteral nutrition after esophagectomy. A systematic review. Clinical Nutrition. 2015;**34**(1):1-6. DOI: 10.1016/j.clnu.2014.07.011

[76] Fujita T, Daiko H, Nishimura M. Early enteral nutrition reduces the rate of life-threatening complications after thoracic esophagectomy in patients with esophageal cancer. European Surgical Research. 2012;**48**(2):79-84. DOI: 10.1159/000336574

[77] Manba N, Koyama Y, Kosugi S, et al. Is early enteral nutrition initiated within 24 hours better for the postoperative course in esophageal cancer surgery? Journal of Clinical Medicine Research. 2014;**6**(1):53-58. DOI: 10.4021/jocmr1665w

[78] Langelotz C, Spies C, Müller JM, Schwenk W. "Fast-track"-rehabilitation in surgery, a multimodal concept. Acta Chirurgica Belgica. 2005;**105**:555-559

[79] Arends J, Bachmann P, Baracos V, et al. ESPEN guidelines on nutrition in cancer patients. Clinical Nutrition. 2017; **36**(1):11-48. DOI: 10.1016/j.clnu.2016.07.015

[80] Gustafsson UO and Ljungqvist O. Perioperative nutritional management in digestive tract surgery. Current Opinion in Clinical Nutrition and Metabolic Care. 2011;**14**(5):504-509. DOI: 10.1097/MCO.0b013e3283499ae1

[81] Markar SR, Karthikesalingam A, Low DE. Enhanced recovery pathways lead to an improvement in postoperative outcomes following esophagectomy: systematic review and pooled analysis. Diseases of the Esophagus. 2015;**28**(5):468-475. DOI: 10.1111/dote.12214

[82] Chen L, Sun L, Lang Y, et al. Fast-track surgery improves postoperative clinical recovery and cellular and humoral immunity after esophagectomy for esophageal cancer. BMC Cancer. 2016;**16**:449. DOI: 10.1186/s12885-016-2506-8

[83] Wang JY, Hong X, Chen GH, et al. Clinical application of the fast track surgery model based on preoperative nutritional risk screening in patients with esophageal cancer. Asia Pacific Journal of Clinical Nutrition. 2015;**24**(2):206-211. DOI: 10.6133/apjcn.2015.24.2.18

[84] Mabvuure NT, Roman A, Khan OA. Enteral immunonutrition versus standard enteral nutrition for patients undergoing oesophagogastric resection for cancer. International Journal of Surgery. 2013;**11**(2):122-127. DOI: 10.1016/j.ijsu.2012.12.012

[85] Kubota K, Kuroda J, Yoshida M, et al. Preoperative oral supplementation support in patients with esophageal cancer. The Journal of Nutrition Health and Aging. 2014;**18**(4):437-440. DOI: 10.1007/s12603-014-0018-2

[86] Wong CS, Aly EH. The effects of enteral immunonutrition in upper gastrointestinal surgery: A systematic review and meta-analysis. International Journal of Surgery. 2016;**29**:137-150. DOI: 10.1016/j.ijsu.2016.03.043

[87] dos Reis AM, Kabke GB, Fruchtenicht AVG, et al. Cost-effectiveness of perioperative immunonutrition in gastrointestinal oncologic surgery: A systematic review. Arquivos Brasileiros de Cirurgia Digestiva. 2016;**29**(2):121-125. DOI: 10.1590/0102-6720201600020014

[88] Tanaka K, Yano M, Motoori M, et al. Impact of perioperative administration of synbiotics in patients with esophageal cancer undergoing esophagectomy: A prospective randomized controlled trial. Surgery. 2012;**152**(5):832-842. DOI: 10.1016/j.surg.2012.02.021

[89] Yokoyama Y, Nishigaki E, Abe T, et al. Randomized clinical trial of the effect of perioperative synbiotics versus no synbiotics on bacterial translocation after oesophagectomy. British Journal of Surgery. 2014;**101**(3):189-199. DOI: 10.1002/bjs.9385

[90] Han-Geurts IJ, Hop WC, Verhoef C, et al. Randomized clinical trial comparing feeding jejunostomy with nasoduodenal tube placement in patients undergoing oesophagectomy. British Journal of Surgery. 2007;**94**(1):31-35. Doi: 10.1002/bjs.5283

[91] Wani ML, Ahangar AG, Lone GN, et al. Feeding jejunostomy: does the benefit overweight the risk (a retrospective study from a single centre). International Journal of Surgery. 2010;**8**(5):387-390. DOI: 10.1016/j.ijsu.2010.05.009

[92] Elshaer M, Gravante G, White J, et al. Routes of early enteral nutrition following oesophagectomy. Annals of the Royal College of Surgeons of England. 2016;**98**(7):461-467. DOI: 10.1308/rcsann.2016.0198

[93] Abdelgadir MA, Mahadi SE, Nasr AO, Ahmed ME. Role of jejunostomy feeding catheter as a model for nutritional support. International Journal of Surgery. 2010;**8**(6):439-443. DOI: 10.1016/j.ijsu.2010.05.006

[94] Torres Júnior LG, de Vasconcellos Santos FA, Correia MI. Randomized clinical trial: Nasoenteric tube or jejunostomy as a route for nutrition after major upper gastrointestinal operations. World Journal of Surgery. 2014;**38**(9):2241-2246. DOI: 10.1007/s00268-014-2589-9

[95] Weimann A, Braga M, Harsanyi L, et al. ESPEN Guidelines on Enteral Nutrition: Surgery including organ transplantation. Clinical Nutrition. 2006;**25**(2):224-244. DOI: 10.1016/j.clnu.2006.01.015

[96] Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. New England Journal of Medicine. 2006;**355**(1):11-20. DOI: 10.1056/NEJMoa055531

[97] Ychou M, Boige V, Pignon JP, et al. Perioperative chemotherapy compared with surgery alone for resectable gastroesophageal adenocarcinoma: An FNCLCC and FFCD multicenter phase III trial. Journal of Clinical Oncology. 2011;**29**(13):1715-1721. DOI: 10.1200/JCO.2010.33.0597

[98] Sjoquist KM, Burmeister BH, Smithers BM, et al. Survival after neoadjuvant chemotherapy or chemoradiotherapy for resectable oesophageal carcinoma: an updated meta-analysis. Lancet Oncology. 2011;**12**(7):681-692. DOI: 10.1016/S1470-2045(11)70142-5

[99] Reisinger KW, Bosmans JW, Uittenbogaart M, et al. Loss of skeletal muscle mass during neoadjuvant chemoradiotherapy predicts postoperative mortality in esophageal cancer surgery. Annals of Surgical Oncology. 2015;**22**(13):4445-4452. DOI: 10.1245/s10434-015-4558-4

[100] Jiang N, Zhao JZ, Chen XC, et al. Clinical determinants of weight loss in patients with esophageal carcinoma during radiotherapy: A prospective longitudinal view. Asian Pacific Journal of Cancer Prevention. 2014;**15**(5):1943-1948

[101] Hardman WE. (n-3) fatty acids and cancer therapy. Journal of Nutrition. 2004;**134**(12): 3427S-3430S

[102] Fietkau R, Lewitzki V, Kuhnt T, et al. A disease-specific enteral nutrition formula improves nutritional status and functional performance in patients with head and neck and esophageal cancer undergoing chemoradiotherapy: results of a randomized, controlled, multicenter trial. Cancer. 2013;**119**(18):3343-3353. DOI: 10.1002/cncr.28197

[103] Vasson MP, Talvas J, Perche O, et al. Immunonutrition improves functional capacities in head and neck and esophageal cancer patients undergoing radiochemotherapy: A randomized clinical trial. Clinical Nutrition. 2014;**33**(2):204-210. DOI: 10.1016/j.clnu.2013.06.008

[104] Sunpaweravong S, Puttawibul P, Ruangsin S, et al. Randomized study of antiinflammatory and immune-modulatory effects of enteral immunonutrition during concurrent chemoradiotherapy for esophageal cancer. Nutrition and Cancer. 2014;**66**(1):1-5. DOI: 10.1080/01635581.2014.847473

[105] Talvas J, Garrait G, Goncalves-Mendes N, et al. Immunonutrition stimulates immune functions and antioxidant defense capacities of leukocytes in radiochemotherapy-treated head & neck and esophageal cancer patients: A double-blind randomized clinical trial. Clinical Nutrition. 2015;**34**(5):810-817. DOI: 10.1016/j.clnu.2014.12.002

[106] Miyata H, Yano M, Yasuda T, et al. Randomized study of the clinical effects of ω-3 fatty acid-containing enteral nutrition support during neoadjuvant chemotherapy on chemotherapy-related toxicity in patients with esophageal cancer. Nutrition. 2017;**33**:204-210. DOI: 10.1016/j.nut.2016.07.004

[107] Motoori M, Yano M, Miyata H, et al. Randomized study of the effect of synbiotics during neoadjuvant chemotherapy on adverse events in esophageal cancer patients. Clinical Nutrition. 2017; **36**(1):93-99. DOI: 10.1016/j.clnu.2015.11.008

[108] van Vliet MJ, Harmsen HJ, de Bont ES, Tissing WJ. The role of intestinal microbiota in the development and severity of chemotherapy-induced mucositis. PLoS Pathogens. 2010;**6**(5):e1000879. DOI: 10.1371/journal.ppat.1000879

[109] Bowen JM, Stringer AM, Gibson RJ, et al. VSL#3 probiotic treatment reduces chemotherapy-induced diarrhea and weight loss. Cancer Biology & Therapy. 2007;**6**(9):1449e54

[110] Xu Y-J, Cheng JC-H, Lee J-M, et al. A Walk-and-Eat intervention improves outcomes for patients with esophageal cancer undergoing neoadjuvant chemoradiotherapy. Oncologist. 2015;**20**(10):1216-1222. DOI: 10.1634/theoncologist.2015-0178

[111] Cong M-H, Li S-L, Cheng G-W, et al. An interdisciplinary nutrition support team improves clinical and hospitalized outcomes of esophageal cancer patients with concurrent chemoradiotherapy. Chinese Medical Journal (England). 2015;**128**(22):3003-3007. DOI: 10.4103/0366-6999.168963

[112] Jones CM, Griffiths EA. Should oesophageal stents be used before neo-adjuvant therapy to treat dysphagia in patients awaiting oesophagectomy? Best evidence topic (BET). International Journal of Surgery. 2014;**12**(11):1172-1180. DOI: 10.1016/j.ijsu.2014.09.008

[113] Spaander MC, Baron TH, Siersema PD, et al. Esophageal stenting for benign and malignant disease: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy. 2016;**48**(10):939-948. DOI: 10.1055/s-0042-114210

[114] Gray RT, O'donnell ME, Scott RD, et al. Impact of nutritional factors on survival in patients with inoperable oesophageal cancer undergoing self-expanding metal stent insertion. European Journal of Gastroenterology & Hepatology. 2011;**23**(6):455-460. DOI: 10.1097/MEG.0b013e3283469761

[115] Dai Y, Li C, Xie Y, et al. Interventions for dysphagia in oesophageal cancer. The Cochrane Database of Systematic Reviews. 2014;(10):CD005048. DOI: 10.1002/14651858.CD005048.pub4

[116] Grilo A, Santos CA, Fonseca J. Percutaneous endoscopic gastrostomy for nutritional palliation of upper esophageal cancer unsuitable foresophageal stenting. Arquivos de Gastroenterologia. 2012;**49**(3):227-231

[117] Yang C, Lin H, Hsieh T, Chang W. Palliative enteral feeding for patients with malignant esophageal obstruction: A retrospective study. BMC Palliative Care. 2015;**14**:58. DOI: 10.1186/s12904-015-0056-5