Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v30i1.3103

Significance Of Dietary Factors In Occurrence, Prevention And Treatment Of Esophageal Carcinoma

Abeer Asif[1,2], Shaifa Saleem[3], Ayesha Abdul Qadir Memon[4], Muhammad Mustafa[1], Arif Mahmood[5,6], Ghulam Rasool Bhurgri[7], Fahad Jibran Siyal[8], Muhammad Osama[4,9], Calvin R. Wei[10]*

[1]KAM School of Life Science, Forman Christian College University (FCCU), Lahore, Pakistan
[2]Department of Biology & Biotechnology, Worcester Polytechnic Institute, 100 Institute Rd, Worcester, MA 01609, USA
[3]School of Biochemistry and Biotechnology, University of the Punjab, Lahore, Pakistan
[4]Department of Pharmacy Practice, University of Karachi, Karachi, Pakistan
[5]Center for Medical Genetics and Hunan Key Laboratory of Medical Genetics, School of Life Sciences, Central South University, Changsha 410078, China
[6]Institute of Molecular Precision Medicine, Xiangya Hospital, Central South University, Changsha 410008, China
[7]Department of Pharmacology & Therapeutics, Indus Medical College, University of Modern Science, Tando Muhammad Khan, Sindh, Pakistan.
[8]Department of Pharmacology, Chandka Medical College, Shaheed Mohtarma Benazir Bhutto Medical University, Larkana, Sindh, Pakistan.
[9]Department of Pharmacology, University of Karachi, Karachi, Pakistan.
[10]Department of Research and Development, Shing Huei Group, Taipei, Taiwan.

***Corresponding Author:** - Calvin R. Wei
*Department of Research and Development, Shing Huei Group, Taipei, Taiwan,
E-mail:- wei.calvin@shinghueigroup.com

Abstract:
Esophageal cancer (EC) is a relatively rare cancer but highly fatal cancer due to delayed diagnosis and its malignant aggressive nature. Chemotherapy, radiotherapy, and esophagectomy are the main treatments for EC. However, recently, another complementary treatment has emerged in EC care: nutrition therapy.
Nutrition therapy utilizes diet and supplements to ensure that patients have enough nutrition to undergo treatment with minimal side-effects and long-term consequences by increasing treatment efficacy, vulnerability of EC cells, and reducing recurrence. The purpose of this study is to identify various EC-causing factors, pre- and post-operative circumstances & dietary habits that influence their development, along with the clinical steps that can be taken to improve EC care through nutrition therapy. We also emphasize the role of various nutritional components and supplements in EC prevention, cancer treatment efficacy, and rates of overall survival (OS) and recurrence.We found that several substances, including 5-fluorouracil, beta-carotene, and moringa, have anti-tumor properties, whereas vitamin C, and zinc also have the ability to boost the efficacy of treatment. Supplemental nutrition, such as glutamine, zinc, and omega-3 fatty acids, also decreased toxicity and stopped muscle deterioration after initial therapy.
On the other hand, we found that alcohol, smoking, red meat, excessive hot beverages, and self-

diagnosing supplements like B12 can all lead to increased risk of developing EC. Hence, individualized nutrition can minimize side effects, preserve muscle mass, and avert malnutrition.

Keywords: esophageal cancer; nutritional supplement; dietary factors

1. Introduction

With approximately 550,000 patients worldwide, esophageal cancer has become the eighth most common and the sixth deadliest cancer (1). With its malignant nature, most patients have an estimated survival rate of between 15 to 25%.Both esophageal adenocarcinoma and esophageal squamous cell carcinoma account for 90% of esophageal cancers (EC). The less frequent of the two globally, except in the US, esophageal adenocarcinoma (EA), mostly develops in distal areas(2). However, a decrease in Squamous cell carcinoma has recently been observed with an increase in esophageal adenocarcinoma in the US (3). EA commonly affect whites, while SCC's is often associated with African Americans (3). Although EC makes up for 1% of the total cancers in the US, it is much more common in other Asian countries like China, Iran, southern Africa, and India (4).

While SCC's are engendered as a result of lifestyle-related factors-smoking, alcohol, genetics, poor oral hygiene and obesity- EA's are often reported to follow up after a long-term history of acid reflux along with obesity (5, 6). Men also had a much higher rate of esophageal cancer when compared to women (1).However, tobacco is a factor regardless of the type of esophageal cancer because of the carcinogens and nitrosamines it contains(7). Recently, however, there's been an increasing focus on the role of food and prevention/treatment of cancer.For instance, a prospective clinical study (n=136) revealed that green tea extract supplements reduced the risk of colorectal cancer (8). Additionally, another cohort study (n=77,126) found that β-carotene supplementation increased the incidence of lung cancer by 18% (9). Therefore, supplementation and diet can play a cardinal role in determining a person's health throughout their life.

Similarly, food can play a significant part in the treatment experience even after diagnosis. A systematic review concluded that aloe vera mouthwash helped reduce oral mucositis in head and neck cancer patients that may arise due to radiation (10). This is also observed in a cell study that found white button mushroom extract to be a potential chemopreventive and therapeutic agent. They found that it mainly helps against prostate cancer cells as it decreases levels of prostate-specific antigens and hinders tumor growth (11). Additionally, a prospective clinical study (N=18) found that supplements that promote protein synthesis—β-hydroxy-β-methyl butyrate, arginine, and glutamine—helped reverse cachexia observed in cancer patients whose disease had advanced significantly (12).However, the role played by diet and nutrition continues beyond this. In fact, analysis shows that various foods and supplements may positively or negatively affect the efficacy of cancer treatment and overall survival rates of patients. They may have a positive effect, as seen in a phase 2 trial (n=60) where they observed that β-Blockade in combination with propranolol administered before operation helped reduce various metastasis biomarkers in breast cancer patients (13). In some studies, it was observed that triple-negative breast cancer cells were less likely to migrate through the ROS/JNK pathway when carotenoid lutein supplementation was present(14, 15). Similarly, a retrospective clinical study (n=22) found that a ketogenic diet in combination with chemotherapy and hyperthermia and hyperbaric oxygen therapy improved survival rates in patients with stage III–IV gastric adenocarcinoma (16). Supplements may also increase efficacy as a cervical cancer cell study observed that genistein, from soy, enhances cisplatin-based chemotherapy by inhibiting NF-κB and Akt/mTOR pathways(17).Diet and supplements may also cause adverse effects as explored in a clinical trial (n=1,134) which revealed that vitamin B12 and iron usage before and during chemotherapy was linked to poorer disease-free survival and increased recurrence in breast cancer patients (18). Therefore, diet and supplement intake have different effects based on the type of cancer and other accumulative factors. Here, we explore the available data to ascertain the effect of diet on esophageal cancer risk, treatment, and overall survival rates (OS), also summarized in *Table*

1. We also highlight the types of ECs, the factors that lead to their development, and recommend perioperative approaches as summarized in *Figure 1*.

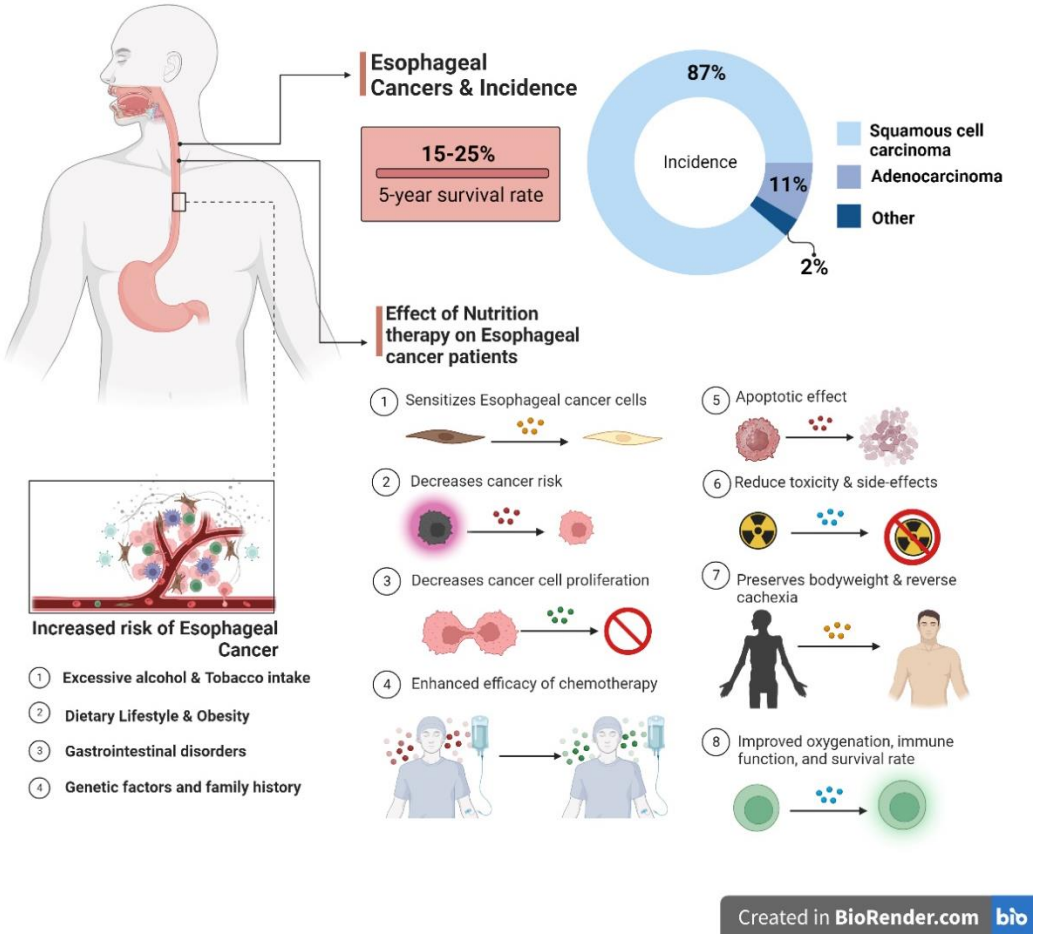

Figure 1: An overview of Esophageal cancers, incidence, risk factors, and effect of nutrition therapy.

2. Prevalence and incidence rates:

2.1. Incidence

The occurrence of esophageal cancer is diverse in different areas and populations worldwide. According to a report from 2018, around 5,70,000 human beings were diagnosed with esophageal cancer, which was 3.2% of all diagnosed cancers (19).

According to a rough estimate ESCC and EAC constitutes 87% and 11% of all esophageal cancers worldwide (20). The prevalence rate for both genders rises with increasing age. Esophageal cancer affects elder people largely, as 60% of esophageal cancer cases are seen in people over 65, and 12% of esophageal cancer cases were observed before age 55 (19, 21).

2.2. Mortality

Globally, the esophageal cancer frequency and deaths of all cancers are 3.2% and 5.3% respectively. In 2018, around 5,08,000 human beings (3,57,000 men & 1,51,000 women) expired due to esophageal cancer universally. The overall risk of mortality due to esophageal cancer for males and females is 1.00% and 0.36%, respectively (19, 22). Esophageal cancer leads to almost 16,000 deaths annually in the United States (19).

2.3. Trend

Differing epidemiologic trends are seen in esophageal cancer in different geographical regions. According to an estimate, the United States is predicted to have 15,000 new EAC cases annually by 2030 (23). The prevalence rate of esophageal cancer is increasing in Africa with the maximum disease

occurrence in East Africa (24).

3. Diagnosis

Managing esophageal cancer is complex due to challenges in identifying high-risk patients and the generally poor prognosis. Most cases are diagnosed at an advanced stage after symptoms like dysphagia, making early detection rare. Only one in eight cases are found at an early stage (T1).Common symptoms include dysphagia (50% reduction in esophagus diameter), vomiting, weight loss, and gastrointestinal bleeding (25).

During gastroscopy, high-resolution white-light endoscopy detects mucosal irregularities. If erosions, ulcers, strictures, or metaplasia are found, the origin must be determined as nonneoplastic or neoplastic. Dysplastic signs include color changes, fine granulation (orange peel effect), and small elevations and troughs in the Barrett layer (25). A prospective study investigating early neoplasia diagnosis in Barrett's esophagus during routine endoscopy yielded three significant findings: First, early tumors in short-segment Barrett's esophagus are primarily detected during initial endoscopy, not surveillance. Second, nearly 40% of early neoplasia remain unseen during endoscopy, necessitating four-quadrant biopsies for detection. Third, the detection rate of neoplasia is notably influenced by the macroscopic tumor type (26)

4. Risk factors and major causes of esophageal cancer

4.1. Tobacco smoking and alcohol addiction.

The use of tobacco and alcohol is observed to be a strong predictor of ESCC, despite some differences in the relative impact across different geographic regions (27-30). In normal tissue, smoking and drinking together can cause the formation of cancer. Tobacco use has been highlighted by the International Agency for Research on Cancer as one of the major causes of EC (esophageal cancer) and is a risk factor for ESCC (esophageal squamous cell carcinoma) and EAC (esophageal adenocarcinoma) globally (31, 32). The risk of ESCC was significantly greater among smokers than non-smokers, according to a meta-analysis (33). Like ESCC, cigarette use can increase the risk of EAC; however this link is not as significant. Smokers were almost two times as likely to get EAC. However, compared to current smokers, the risk of EAC did not reduce among smokers after quitting smoking (33-35). Excessive consumption of alcohol has been linked to increased risk of EC. Over 70% of ESCC patients in America had a history of alcohol use. According to studies, alcohol use contributed to 24,000 deaths due to ESCC worldwide in 2004.(36, 37). Compared to wine or beer, spirits may have an increased risk of cancer. Individual variations in alcohol sensitivity and tolerance may also be a factor. For instance, according to research, changes in the alcohol dehydrogenase gene can lower the risk of developing lung and gastrointestinal cancer. (38, 39)

4.2. Gastrointestinal disorders

Gastric atrophy and upper gastrointestinal malignancies have been linked in several studies. In a study, it was shown that individuals with gastric atrophy may have a two- to three-fold greater risk of esophageal squamous cell carcinoma (OSCC) and gastric cardia adenocarcinoma (GCA), but a likely decreased risk of OAC (oesophageal adenocarcinoma) (40). The role of gastroesophageal reflux disorder (GERD) in EAC carcinogenesis has been thoroughly researched. According to a study, a history of esophageal reflux, hiatal hernia, esophagitis/esophageal ulcer, and trouble swallowing was related with a high risk of EAC (41). Another meta-analysis including five different studies showed that frequent GERD symptoms are substantially linked to esophageal adenocarcinoma (42).

4.3. Obesity

Another known risk factor for EAC is obesity. A study indicated that even in adults with normal BMI, abdominal obesity was linked to an increased risk of EAC, whereas overall obesity was linked to a greater risk of EAC and gastric cardia adenocarcinoma (43). High BMI or increased waist

circumference appears to have a dose-dependent relationship with the risk of EAC (44, 45). Research found that BMI is closely related to the chance of developing EAC in both men and women, those with and without GERD symptoms. Comparing those with BMI less than 25 to those with BMI > 40, the chance of getting EAC is doubled for those with a BMI > 40, regardless of GERD symptoms (46)

4.4. Genetic factors and family history

ESCC and other malignancies are both influenced by epigenetic changes in the form of altered DNA methylation, histone modifications, and loss of genomic imprinting (44). More than 83% of ESCC have TP53 mutations. ESCC include overexpression of EGFR (found in up to 76% of cases) and CCND1 (46% of cases). EAC has been linked to CCNE1 amplification (19% of the cases), cyclin E amplification (17% of the cases), and MGST1 mutations (44, 47). Fanconi anemia (FA), an autosomal recessive disorder associated with genetic abnormalities, has been linked to increased risk of esophageal cancer due to their potential of becoming solid tumors (48).Esophageal cancer risk has been linked to a family history of various malignancies, including lung, prostate, breast, cervical, oral, and pharyngeal cancers. EAC has also been related to a family history of hiatal hernias (49-51)

4.5. Dietary factors

A study has found that drinking shallow well and surface water, an irregular diet, intake of corn, corn flour, pickled food, fried food, and hot food were all linked to an elevated risk of esophageal precancerous lesions (EPL) (52). Another research suggests eating pickled vegetables can double the risk of developing esophageal cancer (53). Most studies revealed an elevated risk of EC linked with greater drinking temperatures of tea and coffee; however, there was minimal evidence for a connection between the volume of consumption and EC risk. More than half of the research on other hot meals and drinks found that consuming them at a higher temperature significantly raised the risk of EC. Overall, the data is quite convincing that drinking hot beverages increases EC risk (54).If consumed excessively like red meat, increasing the risk of EA (55).

Likewise, consumption of scorching drinks and beverages can induce thermal injury and increase an individual's risk of EC as reported in meta-analysis studies (N=5,050) (56, 57). However, consuming green tea, as demonstrated in a population-based, case-control study in Shanghai can have a protective effect against EC for people who aren't smokers and alcohol drinkers (58, 59). On the other hand, smoking, opium consumption, alcohol intake, hookah & cigarettes, and nass chewing can all increase one's risk of ESCC (34, 60). Interestingly, even a low socioeconomic status increases the risk of developing EC (34). Similarly, inadequate vitamins and minerals can increase one's chance of EC. This was demonstrated in a pilot study where decreased Vitamin C, and E intake was linked to the development of EC (61). Similarly, a province in China with high EC rates was significantly deficient in Vitamin B2 (62)

5. Nutritional factors to decrease esophageal cancer risk:

According to research, several dietary factors are associated with EC. One study shows that increasing the diet of fruits and vegetables may reduce the occurrence of these cancers (36). The antioxidant properties of fruits and vegetables contribute to the protective effects by lowering oxidative stress and inflammation. Some studies have suggested that the nutrients folate and vitamin C, in these foods, lower the risk of esophageal cancer (63, 64).

A population-based study (N=38,790) highlighted that simply increasing fruit and vegetable consumption, specifically cruciferous vegetables, by 100g/day was enough to induce an 11% decrease in ESCC (65). This was further reinforced by a 32-study meta-analysis (N=10,037) (66). Similarly, a prospective study (N=490,802) identified that consumption of apples, peaches, nectarines, plums, pears, strawberries, and citrus fruits offered protective effects against ESCC, while spinach intake helped prevent EAC (67).

Interestingly, citrus fruit consumption may seem to have a negative effect in preventing EC. However, a meta-analysis study finds that, on the contrary, citrus fruits play a protective role (68). In fact, a 100 g/day increase in citrus fruits can significantly decrease EC risk (69). Furthermore, a meta-analysis (N=5730) identified that comparing individuals with the highest citrus fruit consumption with the lowest consumers had a 50% reduction in the overall risk of pharyngeal and oral cavity cancers (70). Notably, it was also found that most citrus fruits help prevent ESCC, but do not significantly contribute to EAC (71).

5.1 Supplements

Like foods, supplementation can also have conclusive or complementary effects on the risk and progression of EC. For instance, a meta-analysis study (N=1,958) and mouse model found that increased consumption of various carotenoids like beta-cryptoxanthin, β-carotene, lycopene, lutein, alpha-carotene, zeaxanthin, as well as alvocidib (flavonoid alkaloid) reduced the risk of EC (72, 73). While beta-carotene reported defense against EA, lycopene, Alpha-carotene, and beta-cryptoxanthin protected against ESCC. Similarly, an increased intake of zinc and iron also lowers risk. 5mg/day of zinc supplementation is linked to a 15% reduction in the risk of EC (74). Consequently, studies show that supplementation of Vitamin B2, C, E, A, β-carotene, and selenium have significant protective effects against EC development alongside decreased mortality rates (75, 76). However, believing that all supplements can have a positive effect can be detrimental. Without appropriate nutritional counseling, consuming supplements that are not the ideal fit for an individual can be counterproductive. For instance, a Meta-analysis shows that while Vitamin B2, B6, and B9 have a protective effect against EC development, Vitamin B12 can actually increase the risk of EC (77).

6. Malnutrition and its impacts on esophageal cancer

6.1. Mechanism of malnutrition

Dysphagia is a frequent biological cause of malnutrition, and dietary modifications often accompany it to avoid foods that aggravate symptoms and result in insufficient calorie intake. Dysphagia, anorexia, reflux, and early satiety are the most common adverse effects of the surgical intervention, frequently resulting in deficits in macronutrients and micronutrients (78-80). Malnutrition is exacerbated in individuals who are receiving radiotherapy and chemotherapy together. Mucositis, esophagitis, throat pain, are typical side effects of radiation(81). Pro-inflammatory chemicals secreted by growing tumors boost cachexia by stimulating anorexia and muscular atrophy. Furthermore, tumors release activin and the proteolysis-inducing factor, which encourage the breakdown of skeletal muscles (82, 83)

6.2. Weight loss

Chemotherapy and radiation impact nutritional status by encouraging muscle atrophy and weight loss. The percentage of patients needing nutritional care rose from 56 to 75% during induction chemotherapy, and malnutrition manifested in 83.8% of patients following the completion of radiation (84, 85). Esophageal cancer causes weight loss in addition to the effects of treatments like radiation and chemotherapy (86)

6.3. Nutritional assessment

Clinicians employ various nutritional assessment methods to evaluate the nutritional status and needs of esophageal cancer patients. An established measure of malnutrition is the percentage of weight loss over a specified duration, where a weight loss exceeding 5% in the past month or 10% within 3-6 months indicates significant malnutrition (87). Plasma proteins, including albumin, are frequently employed as nutritional indicators. However, due to its extended half-life (14-20 days), albumin is unsuitable for detecting slight changes in nutritional status and has a sluggish response to dietary interventions. Additionally, albumin levels may be affected by acute phase responses, making it an unreliable indicator of malnutrition (88). A retrospective study found a significant correlation between a positive response to chemoradiotherapy and weight loss of less than 10%, as well as a BMI

greater than 18 kg/m2. Furthermore, having a BMI greater than 18 kg/m2 was shown to be a predictor of survival, as indicated by both univariate and multivariate analyses (89)

7. Treatment strategies

7.1 Chemotherapy & Radiotherapy

Their role in cancer therapy is so critical that they may alter the treatment's efficacy. For instance, Vitamin C enhanced the anti-tumor activity of 5-Fu and cisplatin chemotherapy by sensitizing cancer cells to drug activated apoptosis and prevented movement of AP-1 and NF-κB (90, 91).
In another example, a double-blind, randomized study found that when zinc was supplemented with EC treatments, it helped improved survival rates even in patients with stages 3 or 4 of EC (92, 93)**.** Additionally, low-doses of flavopiridol; based on rohitukine, a chromone alkaloid; helped improve EC cell's response to radiation (94, 95). Likewise, supplements can also induce synergistic effects, as in the case of β-carotene and 1,25-dihydroxy vitamin D3 which inhibit cell growth and increase apoptosis in EC cells(96)

7.2. Surgical intervention:

Surgical interventions remain the primary choice for early-stage cancer treatment. Ablation methods, such as laser therapy, photodynamic therapy (PDT), radiofrequency ablation, argon plasma ablation (APC), and cryoablation, are employed to manage BE (Barrett's esophagus) lesions. (97-102). For lesions confined to the mucosal layer (T1a) or limited to the epithelium and lamina propria, effective treatments consist of endoscopic mucosal resection (EMR) for smaller tumors and endoscopic submucosal dissection (ESD) for lesions of various sizes. To ensure the most suitable treatment plan, endoscopic ultrasound (EUS) is used to accurately assess the extent of infiltration (103).

Esophagectomy is the most effective treatment for patients without adjacent organ invasion or distant metastasis. Surgical methods are selected based on tumor size and location, with open esophagectomy and minimally invasive esophagectomy being two common approaches. For thoracic esophageal cancer, the three most prevalent techniques are the transhiatal approach, Ivor Lewis esophagectomy (right thoracotomy and laparotomy), and McKeown technique (right thoracotomy followed by laparotomy and neck incision with cervical anastomosis). It's worth noting that some studies indicate significantly higher survival rates in patients undergoing whole-piece esophagectomy compared to transhiatal esophagectomy. Therefore, whole-piece esophagectomy is considered superior when dealing with tumors in the lower esophagus or the cardia (104) (105) (106). The surgical approach for neck esophageal cancer differs significantly from that used for chest esophageal cancer. Neck esophageal cancer requires extensive lumpectomy, involving the removal of the hypopharynx, esophagus, larynx, thyroid gland, parathyroid gland, cervical lymph nodes, and often a permanent tracheotomy (107). Presently, a preferable treatment involves reconstructing the esophagus using portions of the intestines or stomach (108).

Minimally invasive esophagectomy comprises various surgical techniques aimed at reducing surgical trauma. These techniques include thoracoscopic/laparoscopic esophagectomy (TLE), thoracoscopy/ laparotomy, mediastinoscopy/laparoscopy, mediastinoscopy/laparotomy, and robot-assisted minimally invasive surgery (RAMIE). With continuous advancements in endoscopic equipment and technology, minimally invasive esophagectomy has become more widespread. Studies like TIME (109) and MIRO (110) indicate that there is no significant difference in the R0 resection rate, number of lymphadenectomy, and 3- and 5-year survival rates between patients treated with minimally invasive esophagectomy and open esophagectomy ($P>0.05$). These findings suggest that both minimally invasive esophagectomy and open esophagectomy are equally effective in providing radical treatment for tumors.

8. Preoperative and post-operative scenarios

8.1. Preoperative Nutrition in Esophageal Cancer

For esophageal cancer patients, nutrition optimization and care are fundamental elements for better treatment, good quality of life, and prolonged survival. It serves as a key for improved, complete, and quick recovery after esophagectomy (111). Optimal preoperative and peri-operative nutrition is associated with lowered risk of post-operative problems, including both infectious as well as non-infectious problems (112). Furthermore, perioperative management includes the preoperative, intra-operative, and post-operative phases. Herein, we will discuss the coordination between nutrition and preoperative and post-operative stages of esophageal cancer in detail.

8.2. Preoperative Nutrition in Esophageal Cancer

Targeting modifiable pre-surgical risk factors is an effective approach for amending post-operative results (113). Among many risk factors, herein, we focus on improving the patient's nutritional status. In preoperative esophageal cancer patients, the previous history and current nutritional status should be evaluated before starting the treatment and before changing the diet of the patient. It will help in ensuring optimal nutrition of the patient before surgery. However, this type of management and nutritional therapies are challenging yet under discussion and requires more scientific research (111). Herein, we will focus on the recent insights related to nutrition and esophageal cancer surgery.

8.3. Preoperative nutritional therapy

Its key purpose is to stop or treat primary malnutrition by regular diagnosis to lower the treatment-related complications and alleviate the quality of life (114). Optimal nutrition aims to help to avoid loss of muscle mass, improve immune response and inflammation, provision of micro and macronutrients in adequate amounts, maintain glucose levels, lower the hypermetabolic response to surgery, and give the strength for speedy and full recovery (115, 116). Many nutritional supplements help in improvement by modulating anabolism (115-117). Preoperative nutritional therapy needs to be started and completed for a different number of days in patients according to their nutritional status. Patients having a history of mildly malnutritional status need 7-10 days of therapy, while patients with highly malnourished status need nutritional therapy for at least 10-14 days along with resistance exercise (118). If a patient has low physical strength, then 4-5 weeks of multimodal therapy with diet and exercise can help because their combined effect leads to muscle protein formation (118, 119). Still, more data is needed for finding out the best suitable duration of preoperative nutritional help in patients with malnutritional history (116, 120). Also, the limited findings for energy requirement, macro and micronutrients for cancer and surgical patients are limited. So, further research is required (118, 121). Some unique and potent targets for pre-optimization of nutritional status have currently been investigated, they are discussed below:

8.3.1 Immunonutrition

Some of the nutrients including omega-3 fatty acids, arginine, and nucleotides, are thought to be beneficial for the immune system, encourage protein synthesis, help respond better to surgical stress, and decrease post-surgical complications (122).

The European Society for Clinical Nutrition and Metabolism (ESPEN) suggests malnourished patients not use the immunonutrition in the preoperative phase but use it in the intra- or at least post-surgical phase (118). Yet, there needs to be more confidence in this guideline(122).

8.3.2 Alcohol intervention

Alcohol drinking is another risk factor for patients leading to post-surgical health problems (123-126). Increased alcohol drinking, i.e., more than two drinks per day or more than 28 g ethyl alcohol, leads to decreased capability of the immune system, elevated stress response through hormones, decelerated wound healing, and lowered heart functioning (124-128), all of these collectively slow down the post-surgical recovery. However, more findings are required to explain the suitable time, concentration, and interval for stopping alcohol consumption (125). Alcohol sobriety for a minimum

of 4 weeks before esophagectomy looks better in a better recovery agenda (129). In addition to only alcohol drinking, some other factors, including malnutrition and smoking, show the harmful effect on post-surgical morbidity rates (113).

8.3.3 Preoperative fasting and carbohydrate treatment

Previous research shows that fasting at least 6 hours for solid foods and 2 hours for clear liquids does not enhance any risk of aspiration (130). Furthermore, extended fasting reduces energy stores in the body (i.e., glycogen, skeletal tissue, adipose) and worsens the surgical stress response, which is further linked to catabolism, protein muscle loss, hyperglycemia, insulin resistance, and delayed healing (116, 118, 131-133). In this framework, preoperational (2 to 3 hours before surgery) intake of an oral carbohydrate solution is well-thought-out as an extra intervention to enhance energy storage and to lower post-surgical insulin resistance (116, 134, 135), and is these days suggested as a regular practice in improved healing after surgery (118, 120, 129). Almost 400 mL of a high-dose (12.5%) carbohydrate solution is suggested (133, 134). These pre-surgical fasting strategies, together with the usage of preoperative carbohydrate liquids, can be used before the esophageal cancer surgery, excluding the patients with critical dysphagia or some other obstructive indications, because these people may have an intensified risk of aspiration (129, 136). Future studies should be projected upon evaluating body composition, observing the loss of muscle mass, and finalizing protein, energy, and micronutrient needs in patients of esophageal cancer to improve nutritional status.

8.3.4 Vitamin D deficiency and preoperative anemia - novel targets

Some other compounds or conditions, in addition to those mentioned earlier, have also been found to affect the pre-optimization of diet for the control of esophageal cancer. They are novel targets for upcoming studies and investigations; up till now, there is limited data found about them, so their routine use is not recommended. They include vitamin D deficiency and preoperative anemia.

Critically low level of vitamin D is considered a risk factor for causing acute lung injury (ALI) and the more serious acute respiratory distress syndrome (ARDS) (137, 138). The patients who have inadequate critical levels of vitamin D (i.e., blood plasma 25(OH) D3 less than 20 nmol/l) showed a higher risk (37.5%) of pre-surgical lung injury as compared to other pre-surgical esophagectomy patients who have vitamin D levels more than 20 nmol/l. The latter showed a 15% risk (138).

Another condition is preoperative anemia. It is generally observed in esophageal cancer patients. It is a potential leading factor for perioperative blood exchange. So, it ultimately increases illness, deaths, and expenses (139-141). Therefore, the recognition, diagnosis, and appropriate cure of anemia are very necessary and fundamental for preoperative management in esophagectomy patients (139). Before surgery, iron therapy is advised for iron-deficient anemic patients (136). However, from patients undergoing esophagectomy, limited data shows that erythropoietin during neoadjuvant therapy enhances the hemoglobin (Hb) level and possible survival (142, 143).

Preoperative nutritional approaches for optimization of esophageal cancer patients

- Evaluate the nutritional status of the patient regularly, during neoadjuvant therapy and before surgery.
- Make diagnostic evaluations for finding out malnutritional status: weight fluctuations, body mass index (BMI), body composition (i.e., skeletal muscle mass), dietary consumption, physical activity, and inflammation in the body.
- Check basal metabolic rate (BMR) in patients having abnormal body composition, and/or weight, BMI, and/or elevated levels of swelling.
- Before the occurrence of metabolic problems, start the nutritional support for the patient.
- Motivate the patients to combine the protein-based supplements/diet with physical activity because of their synergetic effect.

- Ask the patient for alcohol abstinence four weeks before surgery.
- Prevent long-standing fasting before surgery: 6 hours for a solid diet and 2 hours for clear liquids, and carbohydrate drinks up to 2 hours.
- Malnourished patients should be discouraged from using immune nutrition.
- Before esophagectomy, individualized advice is required on nutritional goals and targets. It encourages the patients to maintain nutrition (111).

8.4. Post-operative Nutrition in Esophageal Cancer

An exceptional short-term and long-term focus is required for post-operative nutrition because esophagectomy is an invasive procedure, leading to an everlasting anatomical alteration (144). In esophagectomy patients, poor post-surgical oral intake of food adversely affected the nutritional status as well as the whole prognosis of patients. So, it is essential to have the proper oral food intake after surgery for esophageal cancer patients (145).

After the esophagectomy, the enteral mode of nutrition is preferred for starting the diet due to its advantages over parenteral nutrition, including less life-threatening problems and short time stay in the hospital (146-148). In contrast, only two nonrandomized studies deduced that initial oral feeding is practicable, harmless, and does not enhance complications (149, 150), as well as is a way of the shorter period of hospital stay (149), as compared to non-oral ways and tube feeding, during the first week. However, a randomized controlled trial on the welfare and possibility of initial oral nourishment is in progress (151).

Additionally, malabsorption can occur along with improper and reduced intake of food, in post-operational long-term nutritional conditions. Malabsorption is assumed to lead to a complex as well as multifactorial etiology, including bile acid malabsorption (BAM), exocrine pancreatic insufficiency (EPI), and small intestinal bacterial overgrowth (SIBO). After vagal denervation, exocrine pancreatic insufficiency may arise as a consequence of the loss of endogenous neuroendocrine signals that arouse the secretion of digestive enzymes by the pancreas and may be modified with pancreatic enzyme replacement therapy (PERT) (152, 153).

9. Nutritional intervention for prevention and treatment

Recent research reveals that dietary intake can act as a cardinal component of esophageal cancer therapy. It is so essential that in cases of low nutritional status pre-operation, patients may be linked to a higher tumor recurrence and worse survival rates (154, 155). A double-blinded controlled trial (N=53) found that when the standard enteral nutrition was replaced with an eicosapentaenoic acid, a type of omega-3 fatty acid-rich supplement, it allowed patients to sustain body mass after esophagectomy (156, 157)**.**

Similarly, different H-components can have varying effects. For instance, in a cell study, researchers found that moringa oleifera extract increased DNA fragmentation, lipid peroxidation, and induction of apoptosis to have an accumulated antiproliferative effect on esophageal cancer cells (158). Simultaneously, the synergistic effects of 5-fluorouracil and β-carotene with therapy had anti-tumor effects in both in vivo and invitro (159).

9.1. Side Effects & Survival

Nutritional Management can improve the nutritional standing of EC patients and help reduce the severity and side effects of radiation by reducing depressive symptoms, skin reactions and improving quality of life (160). An example of this would be glutamine supplementation which can protect the immune system and prevent protein degeneration in patients (161).

Supplements like omega-3 Fatty acid-containing diets, can help reduce chemotherapy toxicity, maintain body weight, and improve oxygen levels, all in extreme esophagectomy operations of EC (157, 162). In addition, other micronutrients like zinc can also help reduce excessive oral mucositis experienced in EC patients during treatment (163). Therefore, the effects of nutrition and

supplementation are a gold mine of opportunity, allowing not only significant improvements in preoperative and post-operative conditions but also in the treatment itself.

9.2 Nutrition Therapy in the Clinical Setting

In a clinical setting, the belief in nutritional therapy is starting to gain momentum. As demonstrated in clinical studies, patients who underwent a complete nutritional intervention during their chemotherapy treatment reported significant changes in albumin, proteins with improved nutritional status (160). In fact, studies report that when complimented with nutrition, patients had reduced toxicity, depression, skin issues, myelosuppression, fewer complications post-treatment, reduced in-patient related costs, less severe radiation esophagitis, and may be discharged much earlier in comparison to the control group (160, 164). Additionally, another clinical study (N=81) showed that even patients who were administered synbiotics benefited when coupled with enteral nutrition by experiencing reduced toxicity and symptoms like diarrhea (165). Similarly, it was found that treatments that included supplements like omega-3 fatty acids, selenium, Vitamin E, β-carotenoid, ONS were able to not only increase patient's OS, reduce mortality, and preserve weight, but also help improve post-operative nitrogen balance after surgery (166-168).

A focus on perioperative nutrition will not only let us alter the long-term course of a patient's cancer treatment, but also allow patients to have an economical, effective support to their regular treatment.

Context	Type	Name	Effect	Reference
Risk	Food	**Apples**	Decrease Risk of ESCC	**(67)**
Risk	Food	**Peaches**	Decrease Risk of ESCC	**(67)**
Risk	Food	**Nectarines**	Decrease Risk of ESCC	**(67)**
Risk	Food	**Plums**	Decrease Risk of ESCC	**(67)**
Risk	Food	**Pears**	Decrease Risk of ESCC	**(67)**
Risk	Food	**Strawberries**	Decrease Risk of ESCC	**(67)**
Risk	Food	**Citrus fruits**	Decrease Risk of EC	**(68)**
Risk	Food	**Spinach**	Decrease Risk of EAC	**(67)**
Risk	Food	**Red Meat**	Excessive consumption: Increase Risk of EAC	**(55)**
Risk	Food	Corn	Increase Risk of EC	(52)
Risk	Food	Cornflour	Increase Risk of EC	(52)
Risk	Food	Pickled food	Increase Risk of EC	(52)
Risk	Food	Fried food	Increase Risk of EC	(52)
Risk	Food	**Scorching Drinks**	Increase Risk of EC	(54) **(56, 57)**
Risk	Food	**Green Tea**	Decrease Risk of EC	**(58, 59)**
Risk	-	Smoking/Hookah	Increase Risk of ESCC	**(34, 60)**
Risk	-	Opium	Increase Risk of ESCC	**(34, 60)**
Risk	-	Alcohol	Increase Risk of ESCC	**(34, 60)**
Risk	Supplement	Beta-cryptoxanthin	Decrease Risk of ESCC	(72)
Side-Effects	Supplement	Arginine	Help reverse cachexia	(12).
Risk	Supplement	β-carotene	Decrease Risk of EAC	(72)
Risk	Supplement	Lycopene	Decrease Risk of ESCC	(72)
Risk	Supplement	Lutein	Decrease Risk of EC	(72)
Risk	Supplement	Alpha-carotene	Decrease Risk of ESCC	(72)
Risk	Supplement	Alvocidib	Decrease Risk of EC	(73)
Risk	Supplement	Zeaxanthin	Decrease Risk of EC	(72)
Risk | Side-Effects	Supplement	Zinc	Decrease Risk of EC| Improves Survival Rates| Reduce Excessive Oral Mucositis	**(74) (92, 93)** (163)

Risk	Supplement	Iron	Decrease Risk of EC| Deficiency affects survival rates	(136)
Risk	Supplement	Vitamin A	Decrease Risk of EC	**(75, 76)**
Risk	Supplement	Vitamin B2	Decrease Risk of EC	**(75, 76)**
Risk| Anti-Cancer	Supplement	Vitamin C	Decrease Risk of EC| Enhances chemotherapy efficacy and sensitizes cancer cells	**(75, 76)**
Side-Effects	Supplement	Vitamin D	Help prevent lung injury	(137, 138)
Risk	Supplement	Vitamin E	Decrease Risk of EC	**(75, 76)**
Risk	Supplement	Selenium	Decrease Risk of EC	**(75, 76)**
Risk	Supplement	Vitamin B12	Increase Risk of EC	**(77)**
Side-Effects	Supplement	Omega-3 fatty acid	Help sustain body mass| Reduce therapy toxicity, maintain bodyweight, immune system, and improve oxygenation.	(156, 157) (157, 162) (122)
Anti-cancer Effect	Supplement	Moringa oleifera	Antiproliferative Effect	**(158)**
Anti-cancer Effect	Supplement	5-fluorouracil + β-carotene	Synergistic Anti-tumor effect	**(159)**
Anti-cancer Effect	Supplement	β-carotene + 1,25-dihydroxyvitamin D3	Synergistic Effect: inhibit cell growth and increase apoptosis	Wang SK (96)
Side-Effects	Supplement	Glutamine	Protect Immune System and Prevent Protein Degradation.	(12)
Side-Effects	Supplement	β-hydroxy-β-methyl butyrate	Help reverse cachexia	(12)
Side-Effects	Supplement	Eicosapentaenoic acid	Preserve Body mass post-surgery	**(156, 157)**
Side-Effects	Supplement	Carbohydrate Solution	Preserve Body mass post-surgery	(129, 136)

Table 1: A summary of various foods and supplements and their interaction with esophageal Cancer. The data is divided into 1) Risk: The component increases or decreases risk of Esophageal Cancer (EC), 2) Anti-cancer Effects: The component helps fight off the cancer, and 3) Side-Effects: The component helps combat a side-effect of EC therapy.

10. Conclusion

To summarize, we find that nutrition therapy can have far-reaching effects in preventing esophageal cancer and improving treatment efficacy and survival rates. For instance, fruits, cruciferous vegetables, green tea, β-carotene, zinc, iron, selenium, and various vitamins-A, B2, C, E- can help lower cancer risk. Additionally, excessive hot drinks, alcohol, smoking, red meat consumption or self-diagnosing supplements like B12 can increase an individual's risk of developing EC.

We find that personalized nutrition can significantly help EC patients during their treatment by ameliorating therapy side effects, maintaining muscle mass, and preventing malnutrition. In addition, we find that 5-fluorouracil, 1,25-dihydroxy vitamin D3, β-carotene, and moringa can have significant anti-tumor effects. Additionally, Vitamin C, Zinc, or derivative compounds, like flavopiridol, can help treatment efficacy by increasing the sensitivity of cancerous cells. Nutritional components like glutamine, zinc, and omega-3 fatty acid supplementation can also help after primary treatment by reducing toxicity, preventing mucositis and skin irritation, and helping prevent muscle degradation. Therefore, we encourage authorities to actively integrate nutrition in perioperative stages and create

awareness amongst patients about their overall benefits.

The data demonstrates the need for a standard set of guidelines that should be used due to their economical nature and immense benefits. With these guidelines, cancer treatment could be furthered, and the overall experience of cancer care immensely enhanced. We also encourage future explorations on the link between nutrition, EC, and socioeconomic status.

Caption: Figure 2: An overview of Esophageal cancers, incidence, risk factors, and effect of nutrition therapy.

Table 1: A summary of various foods and supplements and their interaction with esophageal Cancer. The data is divided into 1) Risk: The component increases or decreases risk of Esophageal Cancer (EC), 2) Anti-cancer Effects: The component helps fight off the cancer, and 3) Side-Effects: The component helps combat a side-effect of EC therapy.

Supplementary Materials: None

References

1. Then EO, Lopez M, Saleem S, Gayam V, Sunkara T, Culliford A, et al. Esophageal Cancer: An Updated Surveillance Epidemiology and End Results Database Analysis. World journal of oncology. 2020;11(2):55-64.
2. Pennathur A, Gibson MK, Jobe BA, Luketich JD. Oesophageal carcinoma. The Lancet. 2013;381(9864):400-12.
3. Huang J, Koulaouzidis A, Marlicz W, Lok V, Chu C, Ngai CH, et al. Global Burden, Risk Factors, and Trends of Esophageal Cancer: An Analysis of Cancer Registries from 48 Countries. 2021;13(1):141.
4. Society AC. Key Statistics for Esophageal Cancer 2023 [Available from: https://www.cancer.org/cancer/esophagus-cancer/about/key-statistics.html.
5. Xie S-H, Lagergren J. Risk factors for oesophageal cancer. Best Practice & Research Clinical Gastroenterology. 2018;36-37:3-8.
6. Abnet CC, Arnold M, Wei W-Q. Epidemiology of Esophageal Squamous Cell Carcinoma. Gastroenterology. 2018;154(2):360-73.
7. Pournaghi S-J, Hojjat SK, Barazandeh Noveyri F, Tavakkoli Ghouchani H, Ahmadi A, Hamedi A, et al. Tobacco consumption, opium use, alcohol drinking and the risk of esophageal cancer in North Khorasan, Iran. Journal of Substance Use. 2019;24(1):105-9.
8. Shimizu M, Fukutomi Y, Ninomiya M, Nagura K, Kato T, Araki H, et al. Green Tea Extracts for the Prevention of Metachronous Colorectal Adenomas: A Pilot Study. Cancer Epidemiology, Biomarkers & Prevention. 2008;17(11):3020-5.
9. Satia JA, Littman A, Slatore CG, Galanko JA, White E. Long-term Use of β-Carotene, Retinol, Lycopene, and Lutein Supplements and Lung Cancer Risk: Results From the VITamins And Lifestyle (VITAL) Study. American Journal of Epidemiology. 2009;169(7):815-28.
10. Ahmadi AJCjoim. Potential prevention: Aloe vera mouthwash may reduce radiation-induced oral mucositis in head and neck cancer patients. 2012;18(8):635.
11. Wang X, Ha D, Mori H, Chen S. White button mushroom (Agaricus bisporus) disrupts androgen receptor signaling in human prostate cancer cells and patient-derived xenograft. The Journal of Nutritional Biochemistry. 2021;89:108580.
12. May PE, Barber A, D'Olimpio JT, Hourihane A, Abumrad NN. Reversal of cancer-related wasting using oral supplementation with a combination of β-hydroxy-β-methylbutyrate, arginine, and glutamine. The American Journal of Surgery. 2002;183(4):471-9.
13. Hiller JG, Cole SW, Crone EM, Byrne DJ, Shackleford DM, Pang J-MB, et al. Preoperative β-Blockade with Propranolol Reduces Biomarkers of Metastasis in Breast Cancer: A Phase II Randomized Trial. Clinical Cancer Research. 2020;26(8):1803-11.

14. Vuoso DC, D'Angelo S, Ferraro R, Caserta S, Guido S, Cammarota M, et al. Annurca apple polyphenol extract promotes mesenchymal-to-epithelial transition and inhibits migration in triple-negative breast cancer cells through ROS/JNK signaling. 2020;10(1):1-17.
15. Gong X, Smith JR, Swanson HM, Rubin LPJM. Carotenoid lutein selectively inhibits breast cancer cell growth and potentiates the effect of chemotherapeutic agents through ROS-mediated mechanisms. 2018;23(4):905.
16. İyikesici MSJNJoCP. Survival outcomes of metabolically supported chemotherapy combined with ketogenic diet, hyperthermia, and hyperbaric oxygen therapy in advanced gastric cancer. 2020;23(5):734-40.
17. Sahin K, Tuzcu M, Basak N, Caglayan B, Kilic U, Sahin F, et al. Sensitization of cervical cancer cells to cisplatin by genistein: the role of NF B and Akt/mTOR signaling pathways. 2012;2012.
18. Ambrosone CB, Zirpoli GR, Hutson AD, McCann WE, McCann SE, Barlow WE, et al. Dietary supplement use during chemotherapy and survival outcomes of patients with breast cancer enrolled in a cooperative group clinical trial (SWOG S0221). Journal of Clinical Oncology. 2020;38(8):804.
19. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2018;68(6):394-424.
20. Arnold M, Soerjomataram I, Ferlay J, Forman D. Global incidence of oesophageal cancer by histological subtype in 2012. Gut. 2015;64(3):381-7.
21. Montgomery E, Basman F, Brennan P, Malekzadeh R. Oesophageal cancer. World cancer report. 2014;15:528-43.
22. Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, et al. Global cancer observatory: cancer today. Lyon, France: international agency for research on cancer. 2018;3(20):2019.
23. Arnold M, Laversanne M, Brown LM, Devesa SS, Bray F. Predicting the future burden of esophageal cancer by histological subtype: international trends in incidence up to 2030. Official journal of the American College of Gastroenterology| ACG. 2017;112(8):1247-55.
24. Asombang AW, Chishinga N, Nkhoma A, Chipaila J, Nsokolo B, Manda-Mapalo M, et al. Systematic review and meta-analysis of esophageal cancer in Africa: epidemiology, risk factors, management and outcomes. World journal of gastroenterology. 2019;25(31):4512.
25. Meves V, Behrens A, Pohl JJV. Diagnostics and early diagnosis of esophageal cancer. 2015;31(5):315-8.
26. Behrens A, Pech O, Wuthnow E, Manner H, Pohl J, May A, et al. [Detection of early neoplasia in Barrett's oesophagus: focus attention on index endoscopy in short-segment-Barrett's oesophagus with random biopsies]. Zeitschrift fur Gastroenterologie. 2015;53(6):568-72.
27. Abnet CC, Arnold M, Wei WQ. Epidemiology of Esophageal Squamous Cell Carcinoma. Gastroenterology. 2018;154(2):360-73.
28. Pandeya N, Williams G, Green AC, Webb PM, Whiteman DC. Alcohol consumption and the risks of adenocarcinoma and squamous cell carcinoma of the esophagus. Gastroenterology. 2009;136(4):1215-24, e1-2.
29. Islami F, Fedirko V, Tramacere I, Bagnardi V, Jenab M, Scotti L, et al. Alcohol drinking and esophageal squamous cell carcinoma with focus on light-drinkers and never-smokers: a systematic review and meta-analysis. International journal of cancer. 2011;129(10):2473-84.
30. Freedman ND, Abnet CC, Caporaso NE, Fraumeni JF, Jr., Murphy G, Hartge P, et al. Impact of changing US cigarette smoking patterns on incident cancer: risks of 20 smoking-related cancers among the women and men of the NIH-AARP cohort. International journal of epidemiology. 2016;45(3):846-56.
31. IARC. List of classifications by cancer sites with sufficient or limited evidence in humans, IARC Monographs 2022 [Available from: https://monographs.iarc.who.int/wp-content/uploads/2019/07/Classifications_by_cancer_site.pdf.
32. Prabhu A, Obi KO, Rubenstein JH. The synergistic effects of alcohol and tobacco consumption on the risk of esophageal squamous cell carcinoma: a meta-analysis. The American journal of

gastroenterology. 2014;109(6):822-7.
33. Wang QL, Xie SH, Li WT, Lagergren J. Smoking Cessation and Risk of Esophageal Cancer by Histological Type: Systematic Review and Meta-analysis. Journal of the National Cancer Institute. 2017;109(12).
34. Kamangar F, Chow WH, Abnet CC, Dawsey SM. Environmental causes of esophageal cancer. Gastroenterology clinics of North America. 2009;38(1):27-57, vii.
35. Gammon MD, Schoenberg JB, Ahsan H, Risch HA, Vaughan TL, Chow WH, et al. Tobacco, alcohol, and socioeconomic status and adenocarcinomas of the esophagus and gastric cardia. Journal of the National Cancer Institute. 1997;89(17):1277-84.
36. Engel LS, Chow WH, Vaughan TL, Gammon MD, Risch HA, Stanford JL, et al. Population attributable risks of esophageal and gastric cancers. Journal of the National Cancer Institute. 2003;95(18):1404-13.
37. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, et al. Light alcohol drinking and cancer: a meta-analysis. Annals of oncology : official journal of the European Society for Medical Oncology. 2013;24(2):301-8.
38. Hashibe M, McKay JD, Curado MP, Oliveira JC, Koifman S, Koifman R, et al. Multiple ADH genes are associated with upper aerodigestive cancers. Nature genetics. 2008;40(6):707-9.
39. Druesne-Pecollo N, Tehard B, Mallet Y, Gerber M, Norat T, Hercberg S, et al. Alcohol and genetic polymorphisms: effect on risk of alcohol-related cancer. The Lancet Oncology. 2009;10(2):173-80.
40. Islami F, Sheikhattari P, Ren JS, Kamangar F. Gastric atrophy and risk of oesophageal cancer and gastric cardia adenocarcinoma--a systematic review and meta-analysis. Annals of oncology : official journal of the European Society for Medical Oncology. 2011;22(4):754-60.
41. Chow WH, Finkle WD, McLaughlin JK, Frankl H, Ziel HK, Fraumeni JF, Jr. The relation of gastroesophageal reflux disease and its treatment to adenocarcinomas of the esophagus and gastric cardia. Jama. 1995;274(6):474-7.
42. Rubenstein JH, Taylor JB. Meta-analysis: the association of oesophageal adenocarcinoma with symptoms of gastro-oesophageal reflux. Alimentary pharmacology & therapeutics. 2010;32(10):1222-7.
43. O'Doherty MG, Freedman ND, Hollenbeck AR, Schatzkin A, Abnet CC. A prospective cohort study of obesity and risk of oesophageal and gastric adenocarcinoma in the NIH-AARP Diet and Health Study. Gut. 2012;61(9):1261-8.
44. Huang FL, Yu SJ. Esophageal cancer: Risk factors, genetic association, and treatment. Asian journal of surgery. 2018;41(3):210-5.
45. Steffen A, Schulze MB, Pischon T, Dietrich T, Molina E, Chirlaque MD, et al. Anthropometry and esophageal cancer risk in the European prospective investigation into cancer and nutrition. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 2009;18(7):2079-89.
46. Hoyo C, Cook MB, Kamangar F, Freedman ND, Whiteman DC, Bernstein L, et al. Body mass index in relation to oesophageal and oesophagogastric junction adenocarcinomas: a pooled analysis from the International BEACON Consortium. International journal of epidemiology. 2012;41(6):1706-18.
47. Buas MF, He Q, Johnson LG, Onstad L, Levine DM, Thrift AP, et al. Germline variation in inflammation-related pathways and risk of Barrett's oesophagus and oesophageal adenocarcinoma. Gut. 2017;66(10):1739-47.
48. Rosenberg PS, Greene MH, Alter BP. Cancer incidence in persons with Fanconi anemia. Blood. 2003;101(3):822-6.
49. Dhillon PK, Farrow DC, Vaughan TL, Chow WH, Risch HA, Gammon MD, et al. Family history of cancer and risk of esophageal and gastric cancers in the United States. International journal of cancer. 2001;93(1):148-52.
50. Jiang X, Tseng CC, Bernstein L, Wu AH. Family history of cancer and gastroesophageal

disorders and risk of esophageal and gastric adenocarcinomas: a case-control study. BMC cancer. 2014;14:60.
51. Turati F, Negri E, La Vecchia C. Family history and the risk of cancer: genetic factors influencing multiple cancer sites. Expert review of anticancer therapy. 2014;14(1):1-4.
52. Pan D, Su M, Zhang T, Miao C, Fu L, Yang L, et al. A Distinct Epidemiologic Pattern of Precancerous Lesions of Esophageal Squamous Cell Carcinoma in a High-risk Area of Huai'an, Jiangsu Province, China. Cancer prevention research (Philadelphia, Pa). 2019;12(7):449-62.
53. Islami F, Ren JS, Taylor PR, Kamangar F. Pickled vegetables and the risk of oesophageal cancer: a meta-analysis. British journal of cancer. 2009;101(9):1641-7.
54. Islami F, Boffetta P, Ren JS, Pedoeim L, Khatib D, Kamangar F. High-temperature beverages and foods and esophageal cancer risk--a systematic review. International journal of cancer. 2009;125(3):491-524.
55. Zhu H-C, Yang X, Xu L-P, Zhao L-J, Tao G-Z, Zhang C, et al. Meat Consumption Is Associated with Esophageal Cancer Risk in a Meat- and Cancer-Histological-Type Dependent Manner. Digestive Diseases and Sciences. 2014;59(3):664-73.
56. Castellsagué X, Muñoz N, De Stefani E, Victora CG, Castelletto R, Rolón PA. Influence of mate drinking, hot beverages and diet on esophageal cancer risk in south america. International Journal of Cancer. 2000;88(4):658-64.
57. Luo H, Ge H. Hot Tea Consumption and Esophageal Cancer Risk: A Meta-Analysis of Observational Studies. Front Nutr. 2022;9:831567.
58. Zheng P, Zheng HM, Deng XM, Zhang YD. Green tea consumption and risk of esophageal cancer: a meta-analysis of epidemiologic studies. BMC Gastroenterol. 2012;12:165.
59. Gao YT, McLaughlin JK, Blot WJ, Ji BT, Dai Q, Fraumeni JF, Jr. Reduced risk of esophageal cancer associated with green tea consumption. J Natl Cancer Inst. 1994;86(11):855-8.
60. Cronin-Fenton D. A burning question: does hot green tea drinking increase the risk of esophageal squamous cell carcinoma? Clinical Epidemiology. 2018;10:1321-3.
61. Bollschweiler E, Wolfgarten E, Nowroth T, Rosendahl U, Mönig SP, Hölscher AH. Vitamin intake and risk of subtypes of esophageal cancer in Germany. Journal of Cancer Research and Clinical Oncology. 2002;128(10):575-80.
62. Li J, Zou X, Wang H, Tao D, Qiao Y, Gu Y, et al. Effect of riboflavin-fortified-salt intervention on esophageal preancerous lesions among population with high risk in Yanting County. Zhongguo Zhongliu Fangzhi Zazhi. 2009;16:325-8.
63. Zhao Y, Guo C, Hu H, Zheng L, Ma J, Jiang L, et al. Folate intake, serum folate levels and esophageal cancer risk: an overall and dose-response meta-analysis. Oncotarget. 2017;8(6):10458-69.
64. Bo Y, Lu Y, Zhao Y, Zhao E, Yuan L, Lu W, et al. Association between dietary vitamin C intake and risk of esophageal cancer: A dose-response meta-analysis. International journal of cancer. 2016;138(8):1843-50.
65. Yamaji T, Inoue M, Sasazuki S, Iwasaki M, Kurahashi N, Shimazu T, et al. & Japan Public Health, Center-based Prospective Study Group.(2008). Fruit and vegetable consumption and squamous cell carcinoma of the esophagus in Japan: the JPHC study. Int J Cancer.123(8):1935-40.
66. Liu J, Wang J, Leng Y, Lv C. Intake of fruit and vegetables and risk of esophageal squamous cell carcinoma: A meta-analysis of observational studies. International Journal of Cancer. 2013;133(2):473-85.
67. Freedman ND, Park Y, Subar AF, Hollenbeck AR, Leitzmann MF, Schatzkin A, et al. Fruit and vegetable intake and esophageal cancer in a large prospective cohort study. International Journal of Cancer. 2007;121(12):2753-60.
68. Wang A, Zhu C, Fu L, Wan X, Yang X, Zhang H, et al. Citrus Fruit Intake Substantially Reduces the Risk of Esophageal Cancer: A Meta-Analysis of Epidemiologic Studies. Medicine (Baltimore). 2015;94(39):e1390.
69. Vingeliene S, Chan DSM, Aune D, Vieira AR, Polemiti E, Stevens C, et al. An update of the

WCRF/AICR systematic literature review on esophageal and gastric cancers and citrus fruits intake. Cancer Causes & Control. 2016;27(7):837-51.
70. Zhao W, Liu L, Xu S. Intakes of citrus fruit and risk of esophageal cancer: A meta-analysis. Medicine (Baltimore). 2018;97(13):e0018.
71. Cirmi S, Navarra M, Woodside JV, Cantwell MM. Citrus fruits intake and oral cancer risk: A systematic review and meta-analysis. Pharmacological Research. 2018;133:187-94.
72. Ge XX, Xing MY, Yu LF, Shen P. Carotenoid intake and esophageal cancer risk: a meta-analysis. Asian Pac J Cancer Prev. 2013;14(3):1911-8.
73. Sato S, Kajiyama Y, Sugano M, Iwanuma Y, Sonoue H, Matsumoto T, et al. Alvocidib (Flavopiridol) suppresses tumor growth in SCID mice with human esophageal cancer xenografts without inducing apoptosis. Surg Oncol. 2006;15(2):107-13.
74. Ma J, Li Q, Fang X, Chen L, Qiang Y, Wang J, et al. Increased total iron and zinc intake and lower heme iron intake reduce the risk of esophageal cancer: A dose-response meta-analysis. Nutrition Research. 2018;59:16-28.
75. Taylor PR, Li B, Dawsey SM, Li J-Y, Yang CS, Guo W, et al. Prevention of Esophageal Cancer: The Nutrition Intervention Trials in Linxian, China1. Cancer Research. 1994;54(7_Supplement):2029s-31s.
76. Li K, Zhang B. The association of dietary β-carotene and vitamin A intake on the risk of esophageal cancer: a meta-analysis. Rev Esp Enferm Dig. 2020;112(8):620-6.
77. Ma JL, Zhao Y, Guo CY, Hu HT, Zheng L, Zhao EJ, et al. Dietary vitamin B intake and the risk of esophageal cancer: a meta-analysis. Cancer Manag Res. 2018;10:5395-410.
78. Aghajanzadeh M, Safarpour F, Koohsari MR, Ghanaei FM, Bodaghi SM, Tozandehgani H. Functional outcome of gastrointestinal tract and quality of life after esophageal reconstruction of esophagus cancer. Saudi journal of gastroenterology : official journal of the Saudi Gastroenterology Association. 2009;15(1):24-8.
79. Ginex P, Thom B, Jingeleski M, Vincent A, Plourde G, Rizk N, et al. Patterns of symptoms following surgery for esophageal cancer. Oncology nursing forum. 2013;40(3):E101-7.
80. Greene CL, DeMeester SR, Worrell SG, Oh DS, Hagen JA, DeMeester TR. Alimentary satisfaction, gastrointestinal symptoms, and quality of life 10 or more years after esophagectomy with gastric pull-up. The Journal of thoracic and cardiovascular surgery. 2014;147(3):909-14.
81. Mak RH, Mamon HJ, Ryan DP, Miyamoto DT, Ancukiewicz M, Kobayashi WK, et al. Toxicity and outcomes after chemoradiation for esophageal cancer in patients age 75 or older. Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus. 2010;23(4):316-23.
82. Zhou X, Wang JL, Lu J, Song Y, Kwak KS, Jiao Q, et al. Reversal of cancer cachexia and muscle wasting by ActRIIB antagonism leads to prolonged survival. Cell. 2010;142(4):531-43.
83. Johns N, Stephens NA, Fearon KC. Muscle wasting in cancer. The international journal of biochemistry & cell biology. 2013;45(10):2215-29.
84. Cox S, Powell C, Carter B, Hurt C, Mukherjee S, Crosby TD. Role of nutritional status and intervention in oesophageal cancer treated with definitive chemoradiotherapy: outcomes from SCOPE1. British journal of cancer. 2016;115(2):172-7.
85. Pan P, Tao G, Sun X. Subjective global assessment and prealbumin levels of esophageal cancer patients undergoing concurrent chemoradiotherapy. Nutricion hospitalaria. 2015;31(5):2167-73.
86. Deans DA, Tan BH, Wigmore SJ, Ross JA, de Beaux AC, Paterson-Brown S, 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):63-9.
87. Nitenberg G, Raynard B. Nutritional support of the cancer patient: issues and dilemmas. Critical reviews in oncology/hematology. 2000;34(3):137-68.
88. Care NCCfA. Nutrition support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition. 2006.
89. Di Fiore F, Lecleire S, Pop D, Rigal O, Hamidou H, Paillot B, 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. The American journal of gastroenterology. 2007;102(11):2557-63.
90. Abdel-Latif MMM, Babar M, Kelleher D, Reynolds JV. A pilot study of the impact of Vitamin C supplementation with neoadjuvant chemoradiation on regulators of inflammation and carcinogenesis in esophageal cancer patients. Journal of Cancer Research and Therapeutics. 2019;15(1):185-91.
91. Abdel-latif MMM, Raouf AA, Sabra K, Kelleher D, Reynolds JV. Vitamin C Enhances Chemosensitization of Esophageal Cancer Cells in Vitro. Journal of Chemotherapy. 2005;17(5):539-49.
92. Lin L-C, Que J, Lin K-L, Leung HW-C, Lu C-L, Chang C-H. Effects of Zinc Supplementation on Clinical Outcomes in Patients Receiving Radiotherapy for Head and Neck Cancers: A Double-Blinded Randomized Study. International Journal of Radiation Oncology*Biology*Physics. 2008;70(2):368-73.
93. Lin Y-S, Lin L-C, Lin S-W. Effects of zinc supplementation on the survival of patients who received concomitant chemotherapy and radiotherapy for advanced nasopharyngeal carcinoma: Follow-up of a double-blind randomized study with subgroup analysis. The Laryngoscope. 2009;119(7):1348-52.
94. Sato S, Kajiyama Y, Sugano M, Iwanuma Y, Tsurumaru M. Flavopiridol as a radio-sensitizer for esophageal cancer cell lines. Diseases of the Esophagus. 2004;17(4):338-44.
95. Schrump DS, Matthews W, Chen GA, Mixon A, Altorki NK. Flavopiridol mediates cell cycle arrest and apoptosis in esophageal cancer cells. Clinical Cancer Research. 1998;4(11):2885-90.
96. Wang SK YL, Wang TT, Huang GL, Yang LG, Sun GJ. Inhibition of Proliferation and Induction of Apoptosis by the Combination of β-carotene and 1,25-dihydroxyvitamin D3 in Human Esophageal Cancer EC9706 Cells. Asian Pacific Journal of Cancer Prevention. 2012;13(12):6327-32.
97. Agostinis P, Berg K, Cengel KA, Foster TH, Girotti AW, Gollnick SO, et al. Photodynamic therapy of cancer: an update. CA: a cancer journal for clinicians. 2011;61(4):250-81.
98. Smith MS, Cash B, Konda V, Trindade AJ, Gordon S, DeMeester S, et al. Volumetric laser endomicroscopy and its application to Barrett's esophagus: results from a 1,000 patient registry. Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus. 2019;32(9).
99. Wu H, Minamide T, Yano T. Role of photodynamic therapy in the treatment of esophageal cancer. Digestive endoscopy : official journal of the Japan Gastroenterological Endoscopy Society. 2019;31(5):508-16.
100. Pohl H, Sonnenberg A, Strobel S, Eckardt A, Rösch T. Endoscopic versus surgical therapy for early cancer in Barrett's esophagus: a decision analysis. Gastrointestinal endoscopy. 2009;70(4):623-31.
101. Pech O. Hybrid Argon Plasma Coagulation in Patients With Barrett Esophagus. Gastroenterology & hepatology. 2017;13(10):610-2.
102. Thota PN, Arora Z, Dumot JA, Falk G, Benjamin T, Goldblum J, et al. Cryotherapy and Radiofrequency Ablation for Eradication of Barrett's Esophagus with Dysplasia or Intramucosal Cancer. Digestive diseases and sciences. 2018;63(5):1311-9.
103. Ajani JA, D'Amico TA, Bentrem DJ, Chao J, Corvera C, Das P, et al. Esophageal and Esophagogastric Junction Cancers, Version 2.2019, NCCN Clinical Practice Guidelines in Oncology. Journal of the National Comprehensive Cancer Network : JNCCN. 2019;17(7):855-83.
104. Wright CD. Esophageal cancer surgery in 2005. Minerva chirurgica. 2005;60(6):431-44.
105. Rentz J, Bull D, Harpole D, Bailey S, Neumayer L, Pappas T, et al. Transthoracic versus transhiatal esophagectomy: a prospective study of 945 patients. The Journal of thoracic and cardiovascular surgery. 2003;125(5):1114-20.
106. Hagen JA, Peters JH, DeMeester TR. Superiority of extended en bloc esophagogastrectomy for carcinoma of the lower esophagus and cardia. The Journal of thoracic and cardiovascular surgery.

1993;106(5):850-8; discussion 8-9.
107. Peracchia A, Bonavina L, Botturi M, Pagani M, Via A, Saino G. Current status of surgery for carcinoma of the hypopharynx and cervical esophagus. Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus. 2001;14(2):95-7.
108. Miyata H, Yamasaki M, Takahashi T, Kurokawa Y, Nakajima K, Takiguchi S, et al. Larynx-preserving limited resection and free jejunal graft for carcinoma of the cervical esophagus. World journal of surgery. 2013;37(3):551-7.
109. Mariette C, Markar SR, Dabakuyo-Yonli TS, Meunier B, Pezet D, Collet D, et al. Hybrid Minimally Invasive Esophagectomy for Esophageal Cancer. The New England journal of medicine. 2019;380(2):152-62.
110. Straatman J, van der Wielen N, Cuesta MA, Daams F, Roig Garcia J, Bonavina L, et al. Minimally Invasive Versus Open Esophageal Resection: Three-year Follow-up of the Previously Reported Randomized Controlled Trial: the TIME Trial. Annals of surgery. 2017;266(2):232-6.
111. Steenhagen E. Preoperative nutritional optimization of esophageal cancer patients. Journal of thoracic disease. 2019;11(Suppl 5):S645.
112. Zhang B, Najarali Z, Ruo L, Alhusaini A, Solis N, Valencia M, et al. Effect of perioperative nutritional supplementation on postoperative complications—systematic review and meta-analysis. Journal of Gastrointestinal Surgery. 2019;23(8):1682-93.
113. Mantziari S, Hübner M, Demartines N, Schäfer M. Impact of preoperative risk factors on morbidity after esophagectomy: is there room for improvement? World journal of surgery. 2014;38(11):2882-90.
114. Anandavadivelan P, Lagergren P. Cachexia in patients with oesophageal cancer. Nature reviews Clinical oncology. 2016;13(3):185-98.
115. Evans DC, Martindale RG, Kiraly LN, Jones CM. Nutrition optimization prior to surgery. Nutrition in Clinical Practice. 2014;29(1):10-21.
116. Gillis C, Carli F. Promoting perioperative metabolic and nutritional care. Anesthesiology. 2015;123(6):1455-72.
117. Baracos VE, Martin L, Korc M, Guttridge DC, Fearon KC. Cancer-associated cachexia. Nature reviews Disease primers. 2018;4(1):1-18.
118. Weimann A, Braga M, Carli F, Higashiguchi T, Hübner M, Klek S, et al. ESPEN guideline: clinical nutrition in surgery. Clinical nutrition. 2017;36(3):623-50.
119. Vigano A, Kasvis P, Di Tomasso J, Gillis C, Kilgour R, Carli F. Pearls of optimizing nutrition and physical performance of older adults undergoing cancer therapy. Journal of geriatric oncology. 2017;8(6):428-36.
120. Wischmeyer PE, Carli F, Evans DC, Guilbert S, Kozar R, Pryor A, et al. American society for enhanced recovery and perioperative quality initiative joint consensus statement on nutrition screening and therapy within a surgical enhanced recovery pathway. Anesthesia & Analgesia. 2018;126(6):1883-95.
121. Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, et al. ESPEN guidelines on nutrition in cancer patients. Clinical nutrition. 2017;36(1):11-48.
122. Sandrucci S, Beets G, Braga M, Dejong K, Demartines N. Perioperative nutrition and enhanced recovery after surgery in gastrointestinal cancer patients. A position paper by the ESSO task force in collaboration with the ERAS society (ERAS coalition). European Journal of Surgical Oncology. 2018;44(4):509-14.
123. Yu Z, Li S, Liu D, Liu L, He J, Huang Y, et al. Society for Translational Medicine Expert Consensus on the prevention and treatment of postoperative pulmonary infection in esophageal cancer patients. Journal of thoracic disease. 2018;10(2):1050.
124. Eliasen M, Grønkjær M, Skov-Ettrup LS, Mikkelsen SS, Becker U, Tolstrup JS, et al. Preoperative alcohol consumption and postoperative complications: a systematic review and meta-analysis. Annals of surgery. 2013;258(6):930-42.
125. Oppedal K, Møller AM, Pedersen B, Tønnesen H. Preoperative alcohol cessation prior to elective surgery. Cochrane Database of Systematic Reviews. 2012(7).

126. Rubinsky AD, Bishop MJ, Maynard C, Henderson WG, Hawn MT, Harris AH, et al. Postoperative risks associated with alcohol screening depend on documented drinking at the time of surgery. Drug and Alcohol Dependence. 2013;132(3):521-7.
127. Tønnesen H, Nielsen P, Lauritzen J, Møller A. Smoking and alcohol intervention before surgery: evidence for best practice. British journal of anaesthesia. 2009;102(3):297-306.
128. Lauridsen SV, Thomsen T, Kaldan G, Lydom LN, Tønnesen H. Smoking and alcohol cessation intervention in relation to radical cystectomy: a qualitative study of cancer patients' experiences. BMC cancer. 2017;17(1):1-9.
129. Low DE, Allum W, De Manzoni G, Ferri L, Immanuel A, Kuppusamy M, et al. Guidelines for perioperative care in esophagectomy: enhanced recovery after surgery (ERAS®) society recommendations. World journal of surgery. 2019;43(2):299-330.
130. Brady MC, Kinn S, Stuart P, Ness V. Preoperative fasting for adults to prevent perioperative complications. Cochrane database of systematic reviews. 2003(4).
131. Sarin A, Chen Ll, Wick EC. Enhanced recovery after surgery—preoperative fasting and glucose loading—a review. Journal of surgical oncology. 2017;116(5):578-82.
132. Ljungqvist O. ERAS—enhanced recovery after surgery: moving evidence-based perioperative care to practice. Journal of Parenteral and Enteral Nutrition. 2014;38(5):559-66.
133. Nygren J, Thorell A, Ljungqvist O. Preoperative oral carbohydrate therapy. Current opinion in anaesthesiology. 2015;28(3):364-9.
134. Amer M, Smith M, Herbison G, Plank L, McCall J. Network meta-analysis of the effect of preoperative carbohydrate loading on recovery after elective surgery. Journal of British Surgery. 2017;104(3):187-97.
135. Torgersen Z, Balters M. Perioperative nutrition. Surgical Clinics. 2015;95(2):255-67.
136. Findlay JM, Gillies RS, Millo J, Sgromo B, Marshall RE, Maynard ND. Enhanced recovery for esophagectomy: a systematic review and evidence-based guidelines. Annals of surgery. 2014;259(3):413-31.
137. Parekh D, Dancer RC, Lax S, Cooper MS, Martineau AR, Fraser WD, et al. Vitamin D to prevent acute lung injury following oesophagectomy (VINDALOO): study protocol for a randomised placebo controlled trial. Trials. 2013;14(1):1-7.
138. Dancer RC, Parekh D, Lax S, D'Souza V, Zheng S, Bassford CR, et al. Vitamin D deficiency contributes directly to the acute respiratory distress syndrome (ARDS). Thorax. 2015;70(7):617-24.
139. Muñoz M, Gómez-Ramírez S, Kozek-Langeneker S, Shander A, Richards T, Pavía J, et al. 'Fit to fly': overcoming barriers to preoperative haemoglobin optimization in surgical patients. British Journal of Anaesthesia. 2015;115(1):15-24.
140. Ayantunde AA, Ng MY, Pal S, Welch NT, Parsons SL. Analysis of blood transfusion predictors in patients undergoing elective oesophagectomy for cancer. BMC surgery. 2008;8(1):1-7.
141. Melis M, McLoughlin JM, Dean EM, Siegel EM, Weber JM, Shah N, et al. Correlations between neoadjuvant treatment, anemia, and perioperative complications in patients undergoing esophagectomy for cancer. Journal of Surgical Research. 2009;153(1):114-20.
142. Abbrederis K, Bassermann F, Schuhmacher C, Voelter V, Busch R, Roethling N, et al. Erythropoietin-alfa during neoadjuvant chemotherapy for locally advanced esophagogastric adenocarcinoma. The Annals of thoracic surgery. 2006;82(1):293-7.
143. Rades D, Tribius S, Yekebas EF, Bahrehmand R, Wildfang I, Kilic E, et al. Epoetin alfa improves survival after chemoradiation for stage III esophageal cancer: final results of a prospective observational study. International Journal of Radiation Oncology* Biology* Physics. 2006;65(2):459-65.
144. Steenhagen E, van Vulpen JK, van Hillegersberg R, May AM, Siersema PD. Nutrition in peri-operative esophageal cancer management. Expert review of gastroenterology & hepatology. 2017;11(7):663-72.
145. Okada G, Momoki C, Habu D, Kambara C, Fujii T, Matsuda Y, et al. Effect of postoperative oral intake on prognosis for esophageal cancer. Nutrients. 2019;11(6):1338.

146. Barlow R, Price P, Reid TD, Hunt S, Clark GW, Havard TJ, et al. Prospective multicentre randomised controlled trial of early enteral nutrition for patients undergoing major upper gastrointestinal surgical resection. Clinical Nutrition. 2011;30(5):560-6.
147. 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.
148. Xiao-Bo Y, Qiang L, Xiong Q, Zheng R, Jian Z, Jian-Hua Z, et al. Efficacy of early postoperative enteral nutrition in supporting patients after esophagectomy. Minerva chirurgica. 2014;69(1):37-46.
149. Sun H-b, Liu X-b, Zhang R-x, Wang Z-f, Qin J-j, Yan M, et al. Early oral feeding following thoracolaparoscopic oesophagectomy for oesophageal cancer. European Journal of Cardio-Thoracic Surgery. 2015;47(2):227-33.
150. Weijs TJ, Berkelmans GH, Nieuwenhuijzen GA, Dolmans AC, Kouwenhoven EA, Rosman C, et al. Immediate postoperative oral nutrition following esophagectomy: a multicenter clinical trial. The Annals of thoracic surgery. 2016;102(4):1141-8.
151. Berkelmans GH, Wilts BJ, Kouwenhoven EA, Kumagai K, Nilsson M, Weijs TJ, et al. Nutritional route in oesophageal resection trial II (NUTRIENT II): study protocol for a multicentre open-label randomised controlled trial. BMJ open. 2016;6(8):e011979.
152. Heneghan HM, Zaborowski A, Fanning M, McHugh A, Doyle S, Moore J, et al. Prospective study of malabsorption and malnutrition after esophageal and gastric cancer surgery. Annals of surgery. 2015;262(5):803-8.
153. Huddy J, Macharg F, Lawn A, Preston S. Exocrine pancreatic insufficiency following esophagectomy. Diseases of the Esophagus. 2013;26(6):594-7.
154. Nakatani M, Migita K, Matsumoto S, Wakatsuki K, Ito M, Nakade H, et al. Prognostic Significance of the Prognostic Nutritional Index in Patients with Recurrent Esophageal Squamous Cell Carcinoma. Nutrition and Cancer. 2018;70(3):467-73.
155. Hao J, Chen C, Wan F, Zhu Y, Jin H, Zhou J, et al. Prognostic Value of Pre-Treatment Prognostic Nutritional Index in Esophageal Cancer: A Systematic Review and Meta-Analysis. Front Oncol [Internet]. 2020 2020; 10:[797 p.]. Available from:
http://europepmc.org/abstract/MED/32626652
https://doi.org/10.3389/fonc.2020.00797
https://europepmc.org/articles/PMC7311778
https://europepmc.org/articles/PMC7311778?pdf=render.
156. Sultan J, Griffin SM, Di Franco F, Kirby JA, Shenton BK, Seal CJ, et al. Randomized clinical trial of omega-3 fatty acid-supplemented enteral nutrition versus standard enteral nutrition in patients undergoing oesophagogastric cancer surgery. British Journal of Surgery. 2012;99(3):346-55.
157. Ryan AM, Reynolds JV, Healy L, Byrne M, Moore J, Brannelly N, et al. Enteral Nutrition Enriched With Eicosapentaenoic Acid (EPA) Preserves Lean Body Mass Following Esophageal Cancer Surgery: Results of a Double-Blinded Randomized Controlled Trial. Annals of Surgery. 2009;249(3):355-63.
158. Tiloke C, Phulukdaree A, Chuturgoon AA. The Antiproliferative Effect of Moringa oleifera Crude Aqueous Leaf Extract on Human Esophageal Cancer Cells. J Med Food. 2016;19(4):398-403.
159. Zhang Y, Zhu X, Huang T, Chen L, Liu Y, Li Q, et al. β-Carotene synergistically enhances the anti-tumor effect of 5-fluorouracil on esophageal squamous cell carcinoma in vivo and in vitro. Toxicology Letters. 2016;261:49-58.
160. Qiu Y, You J, Wang K, Cao Y, Hu Y, Zhang H, et al. Effect of whole-course nutrition management on patients with esophageal cancer undergoing concurrent chemoradiotherapy: A randomized control trial. Nutrition. 2020;69:110558.
161. Yoshida S, Kaibara A, Ishibashi N, Shirouzu K. Glutamine supplementation in cancer patients. Nutrition. 2001;17(9):766-8.

162. Matsuda Y, Habu D, Lee S, Kishida S, Osugi H. Enteral Diet Enriched with ω-3 Fatty Acid Improves Oxygenation After Thoracic Esophagectomy for Cancer: A Randomized Controlled Trial. World Journal of Surgery. 2017;41(6):1584-94.
163. Chaitanya NCSK, Shugufta K, Suvarna C, Bhopal T, Mekala S, Ponnuru H, et al. A Meta-Analysis on the Efficacy of Zinc in Oral Mucositis during Cancer Chemo and/or Radiotherapy—An Evidence-Based Approach. Journal of Nutritional Science and Vitaminology. 2019;65(2):184-91.
164. Wang SA, Li F, Zhu J, Chen X, Ren W, Gao B. Multidisciplinary nutritional management improves nutritional and hospitalized outcomes of patients with esophageal cancer undergoing chemoradiotherapy: A randomized control trial. Medicine (Baltimore). 2023;102(12):e33335.
165. Motoori M, Sugimura K, Tanaka K, Shiraishi O, Kimura Y, Miyata H, et al. Comparison of synbiotics combined with enteral nutrition and prophylactic antibiotics as supportive care in patients with esophageal cancer undergoing neoadjuvant chemotherapy: A multicenter randomized study. Clin Nutr. 2022;41(5):1112-21.
166. Long H, Yang H, Lin Y, Situ D, Liu W. Fish oil-supplemented parenteral nutrition in patients following esophageal cancer surgery: effect on inflammation and immune function. Nutr Cancer. 2013;65(1):71-5.
167. Yang L, Gao J, Zhou Y, Tao Z, He J, Yang J, et al. Effect of Oral Nutritional Supplements on Patients with Esophageal Cancer During Radiotherapy. Cancer Biother Radiopharm. 2023;38(2):89-94.
168. Yamashita K, Yamasaki M, Miyazaki Y, Matsuura N, Tanaka K, Makino T, et al. Protein-enhanced feeds after esophagectomy for esophageal cancer attenuate postoperative catabolism: a prospective observational study. Surg Today. 2022;52(4):624-32.