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PREHABILITATION INCLUDING PHYSICAL ACTIVITY AND INTEGRATED NUTRITIONAL-PSYCHOLOGICAL CARE IN THE PERIOPERATIVE MANAGEMENT OF ESOPHAGEAL CANCER

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ABSTRACT

Context: The aim of this study is to demonstrate that prehabilitation encompassing nutritional assessment, optimization of nutritional support, structured exercise, and psychological intervention significantly influences patients' recovery to their preoperative functional status. Moreover, in individuals presenting with poorer baseline condition, prehabilitation may contribute to functional improvement and reduce the risk of postoperative complications.
Methods: We conducted a review of the current literature on surgical prehabilitation for esophageal cancer, focusing on studies indexed in PubMed that examine preoperative interventions implemented prior to esophagectomy to improve patients' preoperative condition and enhance postoperative recovery.
Results: Available evidence from the literature indicates a beneficial effect of prehabilitation on postoperative functional capacity and the rate of patients' return to activities of daily living. At the same time, evidence regarding its impact on short- and long-term clinical outcomes remains limited, which underscores the need for further well-designed studies incorporating a broader range of variables.
Conclusions: The findings suggest that multimodal preoperative interventions, including physical activity, nutritional support, and anxiety reduction strategies, may serve as a valuable adjunct to enhanced recovery after surgery programs and facilitate a faster return of patients to basic activities of daily living.

KEYWORDS

Prehabilitation, Esophageal Cancer, Surgery, Nutrition, Physical Activity

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Introduction

According to the GLOBOCAN 2022 report, esophageal cancer ranks 11th in terms of the frequency of all cancers, while in the EU, according to ECIS 2022 statistics, it ranks 20th. Histologically, esophageal cancer can be classified into squamous cell carcinoma (SCC), which accounts for approximately 90% of diagnoses and develops in the proximal two-thirds of the esophagus, and adenocarcinoma (AC), which accounts for about 10% and is located in the distal esophagus [1,2].

Esophageal cancer is considered one of the most aggressive malignancies. In 2020, more than 0.6 million new cases and approximately 0.54 million deaths were reported worldwide [2]. According to ECIS statistics, the disease is four times more common in men. In the same year, the global incidence rate was 6.3 per 100,000 population [2].

Risk factors predisposing to esophageal cancer can be further categorized according to histological subtype. Factors characteristic of squamous cell carcinoma (SCC) include: (1) alcohol consumption, (2) caustic injury or chemical damage to the esophagus, (3) Plummer–Vinson syndrome, (4) esophageal achalasia, (5) a diet low in fruits and vegetables, (6) consumption of very hot foods and beverages, (7) low socioeconomic status, (8) vitamin deficiencies, (9) a history of malignancies of the oral cavity, pharynx, or larynx, (10) Howell–Evans syndrome, and (11) human papillomavirus (HPV) infection.

Risk factors specific to adenocarcinoma (AC) include: (1) obesity, (2) gastroesophageal reflux disease, and (3) Barrett's esophagus.

Factors common to both histological types include: (1) cigarette smoking and (2) a history of mediastinal radiotherapy [1,2].

Based on data from GLOBOCAN 2020, the estimated numbers of esophageal cancer cases and deaths for the years 2030 and 2040 were calculated by multiplying the incidence and mortality rates from 2020 by the projected global population for 2030 and 2040. It is projected that in 2030 there will be 739,666 new cases and 723,466 deaths due to esophageal cancer, while in 2040 the global burden is expected to reach 987,723

new cases and 914,304 deaths. These figures represent increases of 31.4% and 33.0% in 2030, and 63.5% and 68.0% in 2040, respectively, compared with 2020 [2].

Taken together, these data indicate that esophageal cancer remains a significant global health problem, with a slowly but steadily increasing burden worldwide.

Nutritional Disorders

Malnutrition represents a significant clinical problem not only in esophageal cancer but across a wide spectrum of oncological diseases. However, in esophageal cancer, one of the predominant symptoms and major contributing factors to nutritional deterioration is dysphagia, defined as difficulty swallowing. Progressive dysphagia leads to reduced oral intake, with patients consuming increasingly smaller portions of food. This, in turn, results in unintended weight loss, which may subsequently progress to malnutrition, sarcopenia, and cancer cachexia.

Loss of appetite secondary to dysphagia or odynophagia further exacerbates nutritional decline and may adversely affect treatment outcomes. As malnutrition progresses, patients frequently experience generalized weakness, persistent fatigue, and progressive loss of skeletal muscle mass [1].

According to available data, weight loss exceeding 10% during the course of esophageal cancer treatment is associated with nearly a threefold increase in 1-year mortality risk, independent of tumor stage, age, and treatment modality [3].

For this reason, all oncological patients—not only those with esophageal cancer—should undergo systematic assessment for malnutrition and metabolic disturbances. Failure to recognize nutritional impairment is associated with prolonged hospitalization, increased susceptibility to infections, higher rates of postoperative complications, and ultimately increased mortality [9].

To address these concerns, various screening tools and indices have been developed to facilitate early detection of nutritional risk. The most commonly used parameter is body mass index (BMI), which reflects overall body mass in relation to height and allows identification of underweight, malnutrition, and obesity. However, patients with normal or even elevated BMI may still be malnourished; therefore, BMI should not be used as the sole assessment tool [12].

One of the most widely applied instruments is the Subjective Global Assessment (SGA). This tool begins with a structured clinical interview collecting data on sex, age, height, recent weight changes (particularly within the previous six months and two weeks), dietary intake, alterations in food consumption (quantity, type, appetite), gastrointestinal symptoms (e.g., nausea, vomiting), and functional capacity [11,12].

The second stage involves a focused physical examination assessing subcutaneous fat loss (e.g., over the triceps and chest), muscle wasting (deltoid and quadriceps muscles), and the presence of ascites or peripheral edema (ankles, sacral region)[11].

Finally, patients are classified into one of three categories:

A – well nourished (stable or increasing body weight, no signs of malnutrition);

B – moderately malnourished (5–10% weight loss, mild physical findings);

C – severely malnourished (>10% weight loss with marked muscle and fat depletion)[11].

According to the European Society for Clinical Nutrition and Metabolism (ESPEN), a patient may be considered malnourished and eligible for nutritional intervention if at least one of the following criteria is met: weight loss exceeding 10–15% within the previous six months; BMI < 18.5 kg/m²; SGA Grade C classification; or preoperative serum albumin < 30 g/L in the absence of renal or hepatic dysfunction [31].

Another widely used screening tool is the SARC-F questionnaire, designed to identify individuals at risk of sarcopenia-related adverse outcomes [9]. It evaluates strength, assistance in walking, rising from a chair, climbing stairs, and history of falls.

Sarcopenia is characterized by progressive and generalized loss of skeletal muscle mass, strength, and function. It may result from aging, systemic diseases such as malnutrition, advanced organ failure, chronic inflammatory conditions, and malignancy [15]. A substantial proportion of patients with esophageal cancer are elderly and frequently present with preexisting sarcopenia and/or malnutrition prior to treatment initiation [15].

Postoperatively, sarcopenia may contribute to serious complications, including sarcopenic dysphagia, which in turn may predispose patients to pulmonary complications such as pneumonia, with reported incidence rates ranging from 9% to 71% [15]. Although the causal relationship between sarcopenia and dysphagia has not been fully established, their coexistence in the postoperative period is well documented. Preventive strategies include preoperative nutritional optimization combined with swallowing rehabilitation exercises, such as pursed-lip breathing, cervical range-of-motion exercises, shoulder stretching, mandibular opening

exercises, tongue strengthening, and submental muscle training. These exercises may not directly improve swallowing mechanics but can reduce food residue and aspiration risk [15]. The chin-tuck maneuver has also been described as an effective swallowing technique that protects the airway by improving laryngeal positioning and facilitating safer bolus transit through the esophagus [15].

Another significant nutritional disorder is malnutrition resulting from inadequate intake or impaired absorption of nutrients, leading to alterations in body composition and body cell mass, and consequently impairing both physical and cognitive function [9,10]. The Mini Nutritional Assessment Short Form (MNA-SF) is recommended, particularly for screening older adults at risk of malnutrition [9].

The most severe form of nutritional impairment is cachexia, a systemic syndrome associated with chronic heart failure, acquired immunodeficiency syndrome, chronic inflammatory conditions, and malignancy. According to criteria proposed by the European Association for Palliative Care (EAPC), cachexia may be diagnosed in the presence of: (1) weight loss ≥ 5% within six months; (2) weight loss > 2% within six months in patients with BMI < 20 kg/m²; or (3) weight loss > 2% accompanied by reduced appendicular lean mass (ALM) [11].

These conditions may overlap; for instance, sarcopenia and cachexia can coexist in the same patient. Although muscle wasting appears in both entities, their underlying pathophysiological mechanisms differ [13]. In clinical practice, however, differential diagnosis may be challenging, as there is no clear demarcation between these conditions [14].

In addition to screening tools and questionnaires, laboratory investigations play a crucial role in nutritional assessment. Routine evaluation should include complete blood count, lipid profile, liver function tests, coagulation parameters, electrolytes (Na, K, Ca, Mg, Fe), vitamin levels, acute-phase proteins, urea, urinalysis, and particularly total protein and serum albumin levels [12].

Screening assessment of these parameters should constitute a fundamental component of the initial evaluation and ongoing monitoring of older oncological patients. Nevertheless, the aforementioned tools do not provide an absolute diagnosis of nutritional status, as sarcopenia, malnutrition, and cachexia may coexist and overlap, complicating clinical interpretation.

The preoperative period

The preoperative period provides an opportunity to optimize patients' overall condition prior to surgery. One of the primary objectives is the optimization of nutritional status. In addition, the treatment of anemia, smoking cessation, and physiotherapy constitute important components of preoperative management [1].

Evidence from the literature indicates that weight loss exceeding 10% is associated with increased 90-day postoperative mortality [4]. However, despite a body weight loss of ≥10% from baseline prior to surgery, no significant association has been demonstrated with severe postoperative complications or length of hospital stay. With regard to mortality alone, early nutritional support during neoadjuvant treatment or prior to surgery is recommended, as it has been shown to contribute to the maintenance of preoperative body weight, attenuation of further weight loss, and preservation of body weight in the postoperative period. Therefore, early nutritional assessment and dietary intervention are strongly advised [4]. The benefits of preoperative nutritional support tend to become apparent at later stages of postoperative recovery, primarily through reduced postoperative weight loss [4].

Immunonutrition extends beyond basic nutritional supplementation by actively modulating the immune and inflammatory responses of the organism [16]. In a meta-analysis conducted by Cao et al., including 15 studies and 1,864 patients, the effects of immunonutrition in patients scheduled for esophagectomy were evaluated in comparison with standard preoperative nutrition. Immunonutrition formulations included arginine (which enhances T-lymphocyte function and nitric oxide production, thereby strengthening immune responses), omega-3 fatty acids (which reduce inflammation by inhibiting cytokine activity mediated via the NF-κB pathway), and ribonucleic acids (RNA) [7,16]. The final analysis demonstrated a reduced incidence of postoperative infectious complications following esophagectomy, as well as a shortening of hospital stay by approximately two days [7].

In another study, Kitagawa et al. compared preoperative immunonutrition with a standard diet. The authors reported a reduction in postoperative infectious complications and lower levels of immune response markers, although no significant effect on mortality was observed [17].

Overall, available evidence suggests that combinations of immunonutritional components may beneficially modulate inflammatory and immune responses, providing greater advantages than standard nutrition alone; however, confirmation in larger-scale studies is still required.

Patients undergoing chemotherapy face additional challenges, including mucositis, diarrhea, and loss of appetite, which may impair nutrient absorption and hinder the maintenance of adequate nutritional status. Several studies have attempted to address this issue through the use of elemental diets composed of pre-digested amino acids, which are more readily absorbed even in the presence of impaired gastrointestinal function [16].

In a study by Katada et al., patients receiving an elemental diet demonstrated a significantly lower incidence of diarrhea and better maintenance of caloric intake. Nevertheless, the principal limitation of this study was the short duration of follow-up [18].

Prehabilitation

Prehabilitation refers to the process of preparing patients for surgical intervention by improving physical fitness through aerobic training, resistance exercises, and, in some cases, respiratory exercises. The literature commonly distinguishes between unimodal prehabilitation, focused exclusively on exercise, and multimodal prehabilitation, which additionally incorporates nutritional support and psychological interventions [5,19].

These measures aim to reduce perioperative stress and, most importantly, to improve physical capacity and decrease the risk of complications and functional decline, which are particularly frequent in patients with esophageal cancer due both to the invasiveness of the procedure itself and to poor baseline functional status [5,19].

Given the relatively short preoperative period, the implementation of the most intensive feasible training program would theoretically be optimal; however, not all patients are able to tolerate such an approach. Therefore, individualized exercise programs should be tailored to each patient and adapted to the limited preoperative timeframe to avoid both underdosing and overdosing of exercise, as well as premature discontinuation of training [19].

In a study by Reijneveld et al., a structured physical training program lasting six to eight weeks was implemented under the supervision of a physiotherapist in a primary care setting. The recommended protocol included three training sessions per week, consisting of two supervised sessions and one home-based session. The program incorporated both resistance and aerobic exercises. Resistance training intensity was guided by the Borg Rating of Perceived Exertion scale, whereas aerobic training intensity was determined based on the results of the Steep Ramp Test (SRT) [19].

In addition to scheduled training sessions, participants were advised to engage in moderate physical activity for at least 30 minutes per day, five days per week, both during chemoradiotherapy and throughout the training program [19]. One of the objective outcome measures was the 6-minute walk test (6MWT), which demonstrated a significantly greater walking distance compared with the standard care group [23,24].

Observational data reported by An et al. indicate a reduction in both pneumonia and pulmonary complications among patients undergoing prehabilitation compared with control groups [20,21]. Furthermore, other studies have demonstrated a shorter length of hospital stay [20,21], as well as reduced hospitalization duration among patients who developed postoperative complications [25]. Improvements in immune function were also observed, potentially contributing to enhanced postoperative recovery through a reduced risk of nosocomial infections [20,21].

In a study by Mizusawa et al., the effects of preoperative inspiratory muscle training (IMT) on diaphragmatic motion following esophagectomy were evaluated. The authors demonstrated that IMT resulted in preservation or improvement of diaphragmatic mobility and was associated with more favorable respiratory parameters compared with patients who did not receive IMT. Inspiratory muscle training appears to be particularly beneficial in patients undergoing major thoracic surgery, after which respiratory function may be compromised [22].

The nutritional component of prehabilitation was addressed by Casey et al., who derived data for their narrative review from the National Oesophagogastric Nutrition Audit (NONA), a nationwide electronic survey distributed to centers treating esophageal and gastric cancer in the United Kingdom and Ireland. The authors concluded that assessment of body composition based solely on body mass index (BMI) and body weight is insufficient, while advanced methods for evaluating muscle mass, muscle function, and overall body composition remain rarely available despite their substantial potential impact on clinical management. According to the survey, 72% of centers had no access to body composition analysis, with only 8% relying on computed tomography scans performed primarily for research purposes. Electrical bioimpedance analysis (BIA) was used by 14% of centers, while dual-energy X-ray absorptiometry (DEXA) was available in only 6% [3].

Importantly, 90% of respondents agreed that access to body composition assessment would positively influence clinical outcomes, highlighting a significant discrepancy between clinical needs and healthcare system capabilities in most countries [3].

Based on the above evidence, it can be inferred that prehabilitation programs incorporating individualized physical activity and nutritional interventions demonstrate potential for improving prognosis during subsequent stages of treatment.

Psychological factors, including anxiety and depression related to surgery, play a significant role in postoperative pain control, length of hospitalization, and patient adherence to exercise programs. Numerous studies indicate that prehabilitation contributes to improvements in quality of life and reductions in anxiety, depression, pain intensity, and fatigue [34]. Consequently, patient motivation and engagement in prescribed exercises are of fundamental importance [23]. Positive effects have been observed in settings involving multidisciplinary outpatient clinics, as well as through telephone-based support, where patients were supervised by surgeons, oncologists, specialized nurses, and psychologists [3].

Nevertheless, data regarding the impact of these interventions on long-term survival and postoperative recovery trajectories remain limited, underscoring the need for large-scale, multicenter studies involving more extensive patient populations [16].

Intraoperative period during esophagectomy

Esophageal resection currently represents the cornerstone of treatment for locally advanced esophageal cancer without distant metastases. The addition of perioperative chemotherapy or neoadjuvant chemoradiotherapy to surgical management has been shown to improve oncological outcomes and increase the likelihood of long-term survival [26].

Advances in surgical technology have led to significant progress in esophagectomy techniques, evolving from highly invasive approaches involving thoracotomy and laparotomy to video-assisted thoracoscopy combined with laparoscopy, now referred to as minimally invasive esophagectomy (MIE). The use of minimally invasive techniques has been associated with reduced surgical trauma, thereby lowering the risk of severe wound-healing complications, pulmonary complications, postoperative pain, and excessive metabolic demands related to postoperative catabolism and increased energy expenditure [27,28]. Importantly, the length of hospital stay, risk of anastomotic leakage, and mortality rates are comparable to those observed after open esophagectomy [27], with further reductions in hospitalization duration achievable as surgical expertise improves.

In a study by Weijs et al., conducted in a cohort of 50 patients from three tertiary referral centers undergoing MIE, the median caloric intake on postoperative day five reached only approximately 58% of estimated energy requirements among patients receiving early oral feeding. This finding indicates that the majority of patients were unable to meet their full energy demands through oral intake alone [28]. Consequently, 38% of patients required additional nutritional support via enteral or parenteral routes, primarily due to postoperative complications or insufficient caloric coverage (<50% of requirements) [28].

Energy requirements following esophagectomy are substantially higher than in the preoperative state, largely due to pronounced postoperative catabolism and an intensified stress response associated with extensive surgical trauma [29,30]. Indirect calorimetry has been identified as one of the most accurate methods for estimating caloric needs, demonstrating that energy expenditure peaks within the first seven postoperative days at approximately 27 kcal/kg/day. In the presence of major complications or heightened metabolic stress, requirements may increase to as much as 33 kcal/kg/day. After postoperative day seven, energy expenditure gradually normalizes, approaching preoperative levels by approximately day fourteen [29,30].

Alongside increased energy demands, protein requirements are also elevated due to enhanced protein catabolism induced by surgery and systemic inflammation. According to recommendations from the ESPEN, hospitalized patients undergoing major surgical procedures should receive at least 1.2–1.5 g of protein/kg body weight/day to facilitate the restoration of lean body mass [31]. ESPEN further emphasizes the importance of monitoring and preventing a negative nitrogen balance, which commonly develops in the context of malignancy and perioperative stress and is associated with impaired wound healing, tissue regeneration, and immune function [31].

Postoperative nutrition is therefore a critical component of treatment, with the mode of delivery being of particular importance. ESPEN recommends a multimodal, stepwise approach, beginning with the least invasive method, namely early oral feeding [31]. If oral intake fails to meet nutritional requirements, oral nutritional supplements should be introduced. In cases where this approach remains insufficient and

gastrointestinal function is preserved, enteral nutrition should be initiated. Parenteral nutrition is reserved as a last resort when enteral feeding is not feasible or contraindicated [31].

The choice between enteral and parenteral nutrition remains clinically challenging. In a meta-analysis by Abouarab et al., including six studies and a total of 276 patients, enteral nutrition (EN) was associated with a lower incidence of overall and pulmonary complications, as well as a shorter length of hospital stay, compared with parenteral nutrition (PN). EN was also linked to smaller increases in serum bilirubin and C-reactive protein levels, suggesting a more favorable impact on hepatic function and immune response. Conversely, PN was associated with a smaller decline in serum albumin levels, potentially indicating more effective coverage of nutritional needs. No significant differences in mortality were observed between the two nutritional strategies [8].

Additional benefits in terms of reduced hospitalization duration and lower infection risk have been demonstrated with low-carbohydrate enteral diets. Terayama et al., in the ENLICHE study involving non-diabetic patients, showed that improved postoperative glycemic stability highlights the growing importance of precision metabolic nutrition, extending beyond caloric supplementation alone [32].

Similarly, Long et al. evaluated postoperative parenteral nutrition enriched with fish oil in patients undergoing esophagectomy and reported reductions in circulating pro-inflammatory cytokines, including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), along with moderate improvements in immune cell activity [33].

In line with ESPEN recommendations, nutritional strategies should follow an escalation-based approach, prioritizing the least invasive methods associated with the lowest complication risk.

As demonstrated in the literature, appropriate postoperative nutrition constitutes an indispensable component of comprehensive treatment, with its impact on both short- and long-term postoperative outcomes highlighted by Davies et al.

Conclusions

Esophageal cancer, as well as other malignancies, represents a serious disease entity whose management is complex and requires close collaboration not only among physicians, but also psychologists, nurses, physiotherapists, and, critically, the patient themselves. Patients with oesophagogastric malignancies are particularly vulnerable to malnutrition and loss of skeletal muscle mass. Therefore, comprehensive assessment of nutritional status and muscle function should constitute an integral component of therapeutic management in oncology patients, especially in older populations, in whom the risk of malnutrition, cachexia, and sarcopenia is substantially increased. The early use of validated screening tools enables the identification of patients at risk and the timely implementation of appropriate interventions, which is crucial for improving clinical outcomes. Despite the lack of full consensus regarding diagnostic criteria and thresholds for malnutrition, cachexia, and sarcopenia, current evidence indicates that available diagnostic tools allow for their effective identification and management in clinical practice [3,9].

Accumulating scientific evidence confirms that nutritional interventions—including patient education, enteral and parenteral nutrition, immunonutrition, and prehabilitation programs—should be regarded as active therapeutic strategies capable of modulating metabolic and immune responses and improving tolerance to oncological treatment. In particular, in the management of patients with esophageal cancer, the role of nutrition has undergone a substantial redefinition, evolving from a purely supportive measure to one of the key, evidence-based components of comprehensive therapeutic care, yielding measurable benefits in both treatment outcomes and patient quality of life [16].

At the same time, the heterogeneity of available studies, methodological variability, and the limited number of large, prospective clinical trials continue to hinder the development of uniform and universally applicable nutritional care protocols. Consequently, future research should focus on well-designed, multicenter clinical trials incorporating metabolic, inflammatory, and molecular markers, thereby facilitating the development of personalized nutritional care strategies. The effective implementation of such an approach requires close collaboration within multidisciplinary teams and full integration of current clinical guidelines, ensuring that nutrition becomes a consistent and proactive element of holistic oncological care [8,16].

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