Nutritional Support Techniques

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Gastrointestinal cancers represent a major cause of morbidity and mortality worldwide. A significant issue regarding the therapeutic management of these patients consists of metabolic disturbances and malnutrition. Nutritional deficiencies have a negative impact on both the death rates of these patients and the results of surgical or oncological treatments. Thus, current guidelines recommend the inclusion of a nutritional profile in the therapeutic management of patients with gastrointestinal cancers. The development of digestive endoscopy techniques has led to the possibility of ensuring the enteral nutrition of cancer patients without oral feeding through minimally invasive techniques and the avoidance of surgeries, which involve more risks. The enteral nutrition modalities consist of endoscopy-guided nasoenteric tube (ENET), percutaneous endoscopic gastrostomy (PEG), percutaneous endoscopic gastrostomy with jejunal tube extension (PEG-J), direct percutaneous endoscopic jejunostomy (DPEJ) or endoscopic ultrasound (EUS)-guided gastroenterostomy.

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1. Introduction

Digestive cancers are a major public health problem worldwide and one of the most significant causes of morbidity and mortality [1]. Two important challenges of the therapeutic management of patients with digestive cancer are metabolic impairment and malnutrition. Among the cancers that can lead to the patient's inability to ingest oral food are esophageal cancer, gastric cancer, and cancers causing gastric outlet obstruction (GOO)—pancreatic cancer, hepatobiliary neoplasia, or duodenal tumors. According to GLOBOCAN statistics from 2020, gastric cancer was the fifth most common malignancy in both sexes, with 1,089,103 cases (5.6% of all malignancy cases). Similarly, esophageal cancer ranked eighth, amounting to 604,100 cases (3.1% of all malignancy cases) [2]. As far as mortality is concerned, the same source reported gastric cancer as being the fourth leading cause of death, with 768,793 deaths reported (7.7% of all malignancy deaths), while esophageal cancer represented the sixth leading cause of death, with 544,076 deaths (5.5% of all malignancy deaths) [2]. In Romania, 3970 new cases of gastric cancer and 824 new cases of esophageal cancer were reported in both sexes in 2020, ranking seventh and 23rd, respectively [3]. Furthermore, 3246 deaths from gastric cancer and 716 from esophageal cancer were reported in Romania in 2020 [3]. The latest global statistics show that pancreatic cancer ranked 11th in the ranking of newly diagnosed cases of cancer in 2020 (495,773 new cases in 2020) and seventh in the ranking of cancer deaths (466,003 in 2020) [2]. In the same rankings, liver cancers ranked sixth (905,667 new cases in 2020) and third

(830,180 deaths in 2020), respectively [2]. For gastric and esophageal cancers, Romania is in the category of countries with moderate risk (the incidence rate for gastric cancer is 9.4 cases/100,000 inhabitants; the incidence rate for esophageal cancer is 2.3 cases/100,000 inhabitants), and for pancreatic cancer it is in the category of countries with higher risk (the incidence rate for pancreatic cancer is 7.7 cases/100,000 inhabitants) [2]. One possible explanation may be related to the increased prevalence of some risk factors for these malignancies, such as alcohol consumption and smoking, but also the reduced level of physical activity, with implications on body weight [4]. Lower incidence rates have been reported for biliary cancers and small bowel cancers [2].

Both the tumoral growth and the therapies applied for these malignancies usually determine metabolic impairments or malnutrition, with a great impact on morbidity and mortality [5]. The European Society for Clinical Nutrition and Metabolism (ESPEN) defines malnutrition as the result of reduced nutrient intake or absorption, with consequences on body composition. Currently, the following criteria are needed to establish the diagnosis of malnutrition:

- A body mass index (BMI) < 18.5 kg/m^2,
- Unintentional weight loss, associated either with low BMI or with a low fat free mass index [6].

The main underlying causes of malnutrition among cancer patients include the following:

- Obstruction of the digestive tract, with dysphagia and recurrent vomiting,
- Side effects of medical and surgical treatments that hinder adequate nutritional intake (nausea, anorexia, swallowing dysfunction, mucositis, etc.),
- Metabolic changes secondary to the systemic inflammatory response associated with neoplastic disorders [7][8][9].

Upper gastrointestinal obstruction, usually secondary to digestive cancers, represents one of the major causes of malnutrition [5]. Malignancies that induce intolerance to oral ingestion include head and neck cancer, esophageal cancer, gastric cancer, and all cancers causing gastric outlet obstruction (GOO)—pancreatic cancer, hepatobiliary neoplasia, or duodenal tumors [10][11][12][13]. Hebuterne et al. evaluated the nutritional status of 1903 cancer patients in different stages of evolution (local cancer in 25% of patients, regional cancer in 31% and metastatic cancer in 44% of patients) [14]. The prevalence of malnutrition showed variations based on the location of the tumor: pancreas, 66.7%; esophagus and stomach, 60.2%; head and neck, 48.9% [14].

Weight loss is found in almost 40–80% of cancer patients [15]. It is currently estimated that 10–20% of cancer deaths are determined by malnutrition [16]. Besides, malnutrition has been proven to have a negative impact on the results of surgical treatments, tolerance to chemotherapy, and risk of infection [7][8][9]. Hence, there is a bidirectional relationship: on one hand, cancer increases the risk of malnutrition, and on the other hand malnutrition increases the risk of treatment side effects, with unfavorable consequences in terms of morbidity and mortality [16][17].

Strong evidence supports that a nutritional profile should be included in the diagnostic and therapeutic management of cancer patients from the moment the neoplastic disease is identified [18]. Thus, to detect nutritional disorders at an early stage, ESPEN recommends:

- A regular assessment of the nutritional intake, BMI and changes that occurred in body weight since the diagnosis of cancer [18].
- In patients who present abnormalities in the screening evaluation, it is recommended to proceed with the evaluation of some parameters such as a quantitative evaluation of nutritional intake, an objective evaluation of muscle mass, physical performance, and symptoms secondary to nutritional disorders, and the degree of systemic inflammation [18].
- The energy intake required for cancer patients should be similar to that of healthy subjects (25–30 kcal/kg/day) [18][19].
- Protein intake required for cancer patients: 1–1.5 g/kg/day [18].
- The intake of vitamins and minerals in cancer patients should be similar to that of healthy subjects. ESPEN does not encourage the use of high doses of micronutrients in the absence of specific deficiencies [18][20][21].
- In cancer patients who present weight loss with insulin resistance, not only it is recommended to increase the energy intake, but also to reduce the glycemic load of the diet, by increasing the ratio between energy resulting from fats/energy resulting from carbohydrates [18][22].
- In cancer patients who suffer from malnutrition without any swallowing disorder, nutritional counselling, treatment of symptoms that prevent oral intake, and oral nutritional supplements are recommended [18][23].
- It is recommended to maintain or even increase the level of physical activity to support muscle mass and metabolic pattern [18][24].
- In cancer patients, ESPEN recommends corticosteroids for 1–3 weeks, or progestins as pharmaceutical agents that may lead to an increased appetite [18][25][26].
- In cancer patients whose nutritional status does not improve despite oral nutritional interventions, enteral nutrition is recommended. If enteral nutrition is insufficient or not feasible, parenteral nutrition (PN) is recommended [18].

Nevertheless, the specialized literature revealed heterogeneous data regarding the impact of oral nutritional interventions on cancer morbidity and mortality. In a meta-analysis that included 1414 cancer patients, Baldwin et al. highlighted the effectiveness of oral nutritional interventions on improving the nutritional status and quality of life [27]. However, the nutritional interventions investigated by these authors did not influence the mortality risk [27]. A

limitation of this meta-analysis is represented by the heterogeneity of the evaluated studies, with a negative impact on the magnitude of the results [27]. Another study published in 2021 showed an improvement of in-hospital mortality among cancer patients who received nutritional support, in contrast with cancer patients who did not receive nutritional support (14.4% vs. 16.9%) [28]. Meanwhile, the same study showed evidence for a lack of improvement of the re-hospitalization rate in the study group that received nutritional support [28]. Among the limitations of this study were the possible misclassification due to the use of the International Classification of Diseases (ICD10) codes and the underreporting of forms of cancer, as well as cases of malnutrition [28]. In addition, the types of enteral nutrition used were not well described [28].

To prevent the complications associated with malnutrition, it is necessary to provide nutritional support through enteral or parenteral nutrition to patients who cannot have an adequate oral intake [29]. By parenteral nutrition, the supply of nutrients is provided intravenously, while enteral nutrition allows the supply of nutrients directly into the digestive tract [29]. Comparing the two forms of nutrition (enteral/parenteral), the literature supports the greater benefits of enteral nutrition due to a lower risk of infection and lower costs [30][31]. In addition, enteral nutrition could decrease intestinal bacterial translocation and could promote intestinal defense mechanisms [32][33]. Amano et al. tracked the survival rates in three groups of patients: patients with cancer and enteral nutrition, patients with cancer and parenteral nutrition, and patients with cancer without artificial nutrition [34]. This study demonstrated the benefits of both enteral and parenteral nutrition, reflected by the median survival period [34]. Thus, patients with enteral nutrition had an average survival period of 43 days, patients with parenteral nutrition, 33 days, and patients without artificial nutrition, 15 days [34]. Hence, nutritional therapy with enteral nutrients is preferred in patients with an accessible gastrointestinal system [29]. When short-term enteral nutrient is needed, nasal/oral enteral tube feeding is recommended [29]. In patients with long-term or permanent enteral nutrition, however, feeding is preferred by means of a percutaneous enterostomy performed endoscopically, by radiological access or surgery [35].

Nevertheless, the development of digestive endoscopy has allowed the emergence of several enteral access techniques (see **Table 1**) [29]. In comparison with surgery, endoscopic enteral access techniques are less invasive, allow faster recovery of patients, and involve lower costs [36].

Table 1. Endoscopic techniques for enteral access.

Endoscopic Techniques for Enteral Access
1. Endoscopy-guided nasoenteric tube (ENET)
2. Percutaneous endoscopic gastrostomy (PEG)
3. Percutaneous endoscopic gastrostomy with jejunal tube extension (PEG-J)
4. Direct percutaneous endoscopic jejunostomy (DPEJ)

Endoscopic Techniques for Enteral Access
5. Endoscopic ultrasound (EUS)-guided gastroenterostomy

Another endoscopic method that ensures adequate nutritional intake in cancer patients is represented by endoscopic stenting [36][37]. The placement of esophageal stents in patients with advanced local cancer leads to improved dysphagia during neoadjuvant therapy [37]. Furthermore, esophageal, or enteral stents could be used as palliative therapy. Complications that might occur include stent migration [37]. It should be mentioned, however, that this migration might also indicate the tumor response to neoadjuvant therapy [37].

2. Nutritional Support Techniques for Digestive Cancer Patients

Nutritional support techniques for cancer patients without oral feeding can be divided into three categories:

- Tube feeding.
- Endoscopic stents.
- Gastrojejunostomy [15].

Nasogastric and Nasojejunal Tubes

Nasogastric and nasojejunal tubes allow the passage of the food bowl at the post-pyloric gastric level through flexible tubes inserted through the nostrils up to the level of the stomach or small intestine [18]. Nasogastric tubes (NGT) can be made of different materials (polyurethane, polyvinyl chloride, silicone) and may have different lumen diameters. In terms of the material, NGTs made of silicone polyurethane are usually preferred since they are more flexible and, consequently, less traumatic. Smaller diameter tubes are more comfortable for patients, but larger tube sizes enable easier administration of food formula and medications [18]. Nasojejunal tubes (NJT) are more flexible, smaller in diameter, and variable in length [18].

In most cases, the introduction of an NGT can be carried out safely using a blind technique. In patients with partial obstructive lesions or large hiatal hernias, NGT/NJT is recommended under endoscopic or fluoroscopic guidance [18]. While routine radiological confirmation of enteral tube position is commonly recommended for NJT, in the case of an NGT, radiological confirmation of the tube position might be considered only if insertion has been difficult or there is a doubt about the intragastric position of the tube [38][39].

An NGT is recommended for short periods of time (three to six weeks) because of the associated discomfort and potential complications, such as clogging, dislocation, irritation, ulceration and bleeding, and pulmonary aspiration [40][41]. ESPEN suggests the possibility of using NGTs with a smaller diameter and for longer periods of time, especially when the options of percutaneous endoscopic gastrostomy or radiologically inserted gastrostomy are not feasible [41]. If obstructive tumors are located proximal to the heart, an NGT could be considered as a first-line

technique to avoid a delay in nutritional support [40]. One study that included 1866 patients, identified esophageal and cricopharyngeal cancer (81%) among the most common indications for NGT placement [42]. Immediate complications occurred in 3% of patients, three of them presenting with perforation (one peritoneal, one pericardial, one pleural perforation) and one of them died later [42].

An NJT should be used in patients with obstructive tumors located distal to the stomach, in patients who have had a gastrectomy, or in those who do not tolerate gastric feeding because of recurrent aspiration, severe gastroesophageal reflux, gastroparesis, or gastric outlet obstruction (GOO) [43]. Shastri et al. identified gastric cancer (59%), followed by pancreatic cancer, as the most common indications of NJT placement. An NJT was the safest procedure with low complication rates, because, in every single case, an NJT was introduced under fluoroscopic guidance [42]. Contraindications for an NJT, as well as for NGT placement, include basal skull fracture and facial fracture [18].

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