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Gastro-oesophageal cancer related malnutrition: a challenge case to manage

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ABSTRACT

Gastro-esophageal cancer is a very common malignant tumours arising from the digestive tract. Hypoalbuminemia and weight loss often result from malnourishment. Malnourished patients have a higher incidence of mortality and morbidity causing prolonged hospital stay. To discuss the incidence and effects of Gastro-esophageal cancer related malnutrition and demonstrate different methods to solve this problem. The current review revealed that malnutrition increases the risk of complications and duration of stay in hospital and ICU in GIT cancer patients, as such, accounts for burden on ICU budget.

***Keywords*:** Gastro, esophageal cancer Hypoalbuminemia, ICU, major cancer surgery, SOFA score

1. INTRODUCTION

Cancer is an aggressive disease that directly destroys the region of origin and can metastasize and spread to other sites, causing multiple complications and progressive loss of organ function. The growth of the cancer may be initially slow or rapidly affecting nutritional

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status [1]. Gastro-esophageal cancer is a common malignant tumor of the GIT, and surgical treatment remains the first-line of treatment [2].

Although esophageal cancer is still rare in Western countries, it consider fatal in the vast majority of cases. In the United States, an approximately 17000 new cases were diagnosed in 2015, of them 15000 cases were died from the disease [3].

The esophagus extends anatomically from the crico-pharyngeal sphincter to the gastro esophageal (GE) junction and divided into three parts; the cervical, upper- to mid-thoracic, and thoracic portions. This is important, because choice of treatment approaches may vary according to the anatomical site of the cancer. It may not be possible to determine the site of origin if the cancer involves the GE junction itself. Despite all advances in treatment modalities and prevention, cancer remains one of the most debilitating diseases nowadays, and considers the second leading cause of death in USA [4].

Malnutrition and weight loss are common complication in GIT cancer patients and may be the first symptom to diagnose the presence of the cancer. And before starting treatment, patients may experience significant metabolic and physiological changes with increased requirement of macro- and micronutrients [5].

2. SCOOP OF THE PROBLEM

Prevalence of malnutrition is significantly vary with type of tumor, site, and extension, as well as treatment modalities. And the prevalence ranges between 15% and 80%. Also the reported in-hospital prevalence of malnourished patients on admission ranges up to 50%according to some literatures [6]. Malnutrition may affect negatively the surgical decision to respect the tumor or not, which is the main curative line of management of GIT cancer. Malnutrition and weight loss can increase the risk of postoperative complications, such as delayed wound healing, dehiscence of anastomosis line, and mortality [7].

The World Health Organization (WHO) classifies malnutrition as a great single risk factor that affects the public health [8]. This led to increasing evidence during recent years of importance of nutritional screening and therapy as adjuncts to modern surgical care because up to 42% of patients are at risk of malnutrition preoperatively [9].

Medical management of cancer patients means, administration of cytotoxic agents and/or radiation therapy. These modalities can eradicate or decrease tumor size, but usually have several serious side effects that cause weakness the patient, by decreasing appetite or causing nausea and vomiting, fatigue, and asthenia. When malnutrition happened, it is very important to decrease cytotoxic agent's dose and to modify the radiation regimen up to cessation of treatment and this cause reduction in the time of remission and decreasing overall survival rates to radio/chemotherapy [10-11].

In addition, malnutrition impairs immune system and red decreases the body’s defense against infectious microorganisms. So, malnutrition considered a poor prognostic factor and, as such, should be detected early and treated as early as possible [12].

Malnutrition affects the outcome of treatment for cancer (chemotherapy, radiation, and surgery) due to changes in metabolism and pharmacokinetics. Moreover, malnutrition is responsible for changes in drug absorption, protein binding, hepatic metabolism, and renal clearance of drugs metabolites [13]. All these changes may significantly increase the incidence of drug toxicity such as etoposide, cisplatinum, paclitaxel, and irinotecan metabolites [14].

Malnutrition causes depletion of nicotinamide adenine dinucleotide phosphate reserves so decreases the oxidative metabolism of the liver performed by cytochrome P-450 isoenzymes. Other metabolic pathways also impaired, thus prolonging drug half-life. The effect of malnutrition on renal function is less clear, but measurements of inulin clearance in malnourished children showed a reduced glomerular filtration rate (GFR) [15].

3. POSSIBLE MECHANISMS OF MALNUTRITION IN GIT TUMORS

Malnutrition is more frequent in gastrointestinal (GI), head and neck and lung and it is associated with a poor prognosis. The underlying etiology of malnutrition is multifactorial and includes abnormalities in GI function due to tumor-related mechanisms or treatment lines in addition to tumor-induced metabolic abnormalities [16].

A) Tumor-related mechanisms

Many nutritional troubles originate from effects of the tumor locally. Tumors in the gastrointestinal tract cause GIT obstruction, decrease digestion, nausea, vomiting and/or decrease absorption. Also changes in normal metabolism of carbohydrates, protein, and/or fats [16]. Malnutrition which occurred before surgery is due to decreased oral intake, tumour related cachexia, decreaded absorption due to local effects of CIT tumors. Moreover, low socioeconomic status, as in elderly and handicapped patients, represents an important risk factor [17]. The neoplastic growth causes mechanical obstruction to the way of the food in the digestive tract, causing dysphagia and decrease swallowing (as in head-neck, esophageal cancer, or mediastinic masses), also early satiety and abdominal pain caused by intestinal occlusion (small and large intestine) [18]. Furthermore, GIT tumors affect organ function, for example, diarrhea in pancreatic and biliary cancer due to lack of digestive enzymes. The presence of visceral pain during eating and digestion is another important factor that causes limitation of oral intake [19]. Moreover, after surgical removal of GIT tumors, many changes affect the processes of digestion causing, dumping syndrome (in gastric surgery), early satiety or diarrhea (in pancreatic and colonic resection). Each condition of these requires specific dietetic regimens for ideal nutritional rehabilitation [20].

B) Chemotherapy and radiation therapy related mechanisms

Finally, anticancer treatments (chemotherapy and radiation therapy) can cause anorexia, early satiety, nausea, vomiting, oral and intestinal mucositis with dysphagia, diarrhea, hemorroids, anal fissures, and modifications in smell and taste senses. All these symptoms may affect food choices and contribute to inadequate meal intake and reduced quality of life. In some cases, co-administered medications, taken to control symptoms or to treat adverse effects associated with anticancer treatments, can produce their own adverse events [21].

C) Surgical therapy related malnutrion

Laryngectomy, pharyngolaryngectomy, esophagectomy. Di-gestive tract surgery can interfere with nutrition by effects on swallowing and gastrointestinal motility, or more often by malabsorption [22]. The most common complications after oral cancer surgery are alterations in swallowing and mastication that may continue for up to a year after treatment in up to 50%

of the patients. Three years after surgery, 42% of laryngectomy and 50% of pharyngolaryngectomy patients experienced long-term dysphagia leading to nutritional deficits and requiring a modification of their diet or tube feeding. Chronic xerostomia, that also impairs swallowing, can occur in patients up to 5-years after treatment [23]. In neurogenic dysphagia, there are different levels of severity so, it is possible to distinguish two different types of diets, one for liquids and one for patients with pharyngeal problems concerning the bolus formation. [24]

Dysphagia, heartburn, hoaresness, reflux, abnormal gastric emptying, dumping syndrome (diarrhoea, abdominal cramps, nausea, dizziness, diaphoresis), increased stool frequency are frequently reported after esophagectomy; 80–90% of the patients experience early satiety, about 75% suffer from post-prandial dumping syndrome, 50–60% have reflux of food/fluid and absence of hunger in the first postoperative year. Weight loss is common after esophagectomy, and the majority of patients are unable to return to their preoperative weight [25].

Gastrectomy. Total gastrectomy has a profound effect on nutritional status, including weight loss, malabsorption, mal-digestion, shortened intestinal transit time and bacterial over-growth. This surgical intervention, by reducing the reservoir into which patients can eat and by altering the physiology of digestion produces malnutrition in approximately 80% of the patients [3]. Diarrhoea usually occurs within 1–2 h after eating, and is probably partly caused by vagotomy, lack of gastric hormones, and defective fat absorption due to pancreatic insufficiency [26].

Factors increasing malabsorption include defective stimulation of biliary and pancreatic secretions by ingested food by-passing the duodenum, and inadequate mixing of biliary and pancreatic secretions with food. Malabsorption of dietary fat has been proposed as a major contributor to weight loss. Malabsorption of aminoacids has also been reported, resulting in a state of persistent proteolysis for long periods after surgery [3]. Loss of gastric and duodenal absorptive surface causes malabsorption of iron, vitamin B12, calcium, fat and carotene; stasis in the afferent loop can lead to bacterial overgrowth and abnormalities in bile salt metabolism [27].

Pancreaticoduodenectomy. The degree of pancreatic func-tion impairment is related to the extent of parenchyma resection and the functional state of the residual pancreas. Accordingly with what was just previously mentioned, another contributing factor for malnutrition is disease progression. One year after curative resection, the malnutrition status is main-tained as well as many gastrointestinal symptoms [28].

After a follow-up longer at least one year, more than 50% of the patients submitted to pancreaticoduodenectomy have been reported to develop a pancreatic exocrine insufficiency. Pancreatic exocrine insufficiency is caused by a loss of enzymatic activity in the intestinal lumen, in particular lipase, with consequent malabsorption of fat, protein, starch, and fat-soluble vitamins, such as A, D E. [29]

Therapy is based on the oral administration of pancreatic enzymes aiming at providing the duodenal lumen with sufficient active lipase at the time of gastric emptying of nutrients .Foods containing long chain triglycerides (LCT) may be replaced by the recruitment of medium chain triglycerides (MCT) that are more rapidly hydrolyzed and absorbed. MCT should be given in four daily doses of about 15 mL, while higher doses are not recommended for the possible induction of diarrhea; there can be loss of endocrine function too, and when glucose is not well controlled, there will be weight loss [30].

4. PRIORITY OF NUTRITION IN PATIENTS WITH CANCER

Nutrition plays major (but not always fully understood) roles in many aspects of cancer development and treatment [31]. Malnutrition is a common problem in cancer patients that has been recognized as an important component of adverse outcomes, including increased morbidity and mortality and decreased quality of life. Weight loss has been identified as an indicator of poor prognosis in cancer patients. It has been shown that at the time of diagnosis, 80% of patients with upper gastrointestinal cancer and 60% of patients with lung cancer have already experienced a significant weight loss, [32]

Generally defined as at least a 10% loss of body weight in 6 months' time [33].Good nutrition practices can help cancer patients maintain weight and the body's nutrition stores, offering relief from nutrition impact symptoms and improving quality of life . Poor nutrition practices, which can lead to undernutrition, can contribute to the incidence and severity of treatment side effects and increase the risk of infection, thereby reducing chances for survival [34].

Nutrition impact symptoms are those symptoms that impede oral intake. They include, but are not limited to, anorexia, nausea, vomiting, diarrhea, constipation, stomatitis, mucositis, dysphagia, alterations in taste and smell, pain, depression, and anxiety [35].

Early recognition and detection of risk for malnutrition through nutrition screening followed by comprehensive assessments is increasingly recognized as imperative in the development of standards of quality of care in oncology practices. Undesirable weight gain may be an effect of chemotherapy treatment for early-stage cancers, possibly resulting from decreases in resting metabolism .Consequently; the eating practices of individuals diagnosed with cancer should be assessed throughout the continuum of care to reflect the changing goals of nutritional therapy [36]

5. NUTRITION OPTIONS IN PATIENTS WITH GIT CANCER

Nutrients are **macromolecules** (fat, proteins, lipid and water), **micro molecules** (vitamins, minerals, electrolytes and trace elements) and more important components of immune-modulating artificial nutrition as:

- Glutamine
- Arginine
- N-acetyl cysteine (as a cysteine precursor)
- Branched chain amino acids
- Nucleotides
- Long-chain n-3 fatty acids
- Antioxidant vitamins
- Trace elements
- Taurine

Immunomodulatory substance interfere with 3 basic areas of the immune responses directly or indirectly;

a) The mucosal barrier function

b) The cellular defence function and
c) The local or systemic inflammatory response [37].

Nutrition support is an important therapeutic intervention for improving outcomes in hospitalized patients. Nutrition support has evolved substantially over the past 20 years, from a primarily supportive strategy to an active therapeutic intervention. Understanding of nutrient effects upon disease processes has led to the development of specialized nutritional formulas. One class of these formulas are called immune modulating diets, or immunomodulating diets (IMDs) [38].

6. DISCUSSION

An impressive number of studies have demonstrated that perioperative arginine/omega-3 immunonutrition in patients with esophageal, gastric, colonic and head and neck cancer patients improves short-term outcomes, such as local wound complications, fistula rates, and length of hospital stay [39].

Immunonutrition contain pharmacologic doses of nutrients including arginine (Arg), ω-3 polyunsaturated fatty acids (ω-3 PUFA), glutamine (Glu) and ribonucleic acid (RNA). All are proved to enhance immune function in vitro and animal experiments. Some clinical trials has been reported to affect the risk of postoperative infection and length of hospital stay in patients underwent operation. But the outcome of these studies is inconsistent and new sufficient clinical evidences is absent for gastrointestinal surgery [40].

Glutathione plays a pivotal role as it acts directly as an antioxidant and maintains other components of defence in a reduced state. It has more specific effect on the function of lymphocytes via the thioredoxin system [41].

Parenteral nutrition has been in use since the 1960s. Total parenteral nutrition (TPN) involves providing all of patient's nutritional needs intravenously and is lifesaving in clinical settings in which adequate enteral based delivery of such nutrition is not possible. It has been one of the most promising modalities of nutrition in neonates, older pediatric patients, and adults with lost or impaired gut function. TPN infusion therapy has grown enormously over the last few decades. There are tens of thousands of patients worldwide permanently dependent on parenteral nutrition (PN) for survival. TPN, a major therapeutic advance in the modern medical era, stil provides ample opportunity for continued exploration [42-44].

In addition to a more recent study conducted by Thieme et al., 2013 to investigate methods of evaluation of the nutritional status that better correlate with postoperative complications and the length of hospital stay in patients submitted to gastrointestinal or abdominal wall surgeries. They reported that the immunologic status, analysed by total lymphocytes count was not correlated to postoperative outcomes, suggesting that this is not an adequate parameter to predict postoperative complications [45].

Chandrasinghe et al. 2013, showed a significant association between a low preoperative serum albumin of less than 35 g/ L, with a reduction in overall survival for patients undergoing surgery for rectal cancer. They concluded that albumin can be used as a cost effective and a sensitive marker to predict survival in rectal cancer compared to other available inflammatory markers [46]. According to Campos et al., 2008, several factors affect post-surgical wound healing such as protein malnutrition that can adversely affect wound healing. Collagen is the

most abundant protein in human body and provides strength, integrity and structure. Besides protein, wound healing is stimulated by an adequate amount of energy, vitamins A, C, E and B complex, zinc, cooper, and selenium. Malnutrition influence in wound healing quality and duration and serum proteins, such as albumin, are important to this process [47].

7. CONCLUSION

In conclusion, the current review revealed that malnutrition increases the risk of complications and length of stay in hospital in GIT cancer patients, as such, accounts for high proportion of ICU budget. We believe that the current review give reasons for raising attention about using serum albumin level nutritional status as a simple and low-cost prognostic tool to predict outcome and consequently, decreasing the incidence of complications GIT cancer patients.

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