

Stomach cancer mortality still represents a significant proportion of all cancer deaths. The majority of patients with advanced cancer experience cancer anorexia-cachexia syndrome with weight loss, reduced appetite, fatigue, and weakness. Neoplastic cachexia is a very common clinical manifestation of upper gastrointestinal (GI) tract cancer and is generally assumed to be secondary to the mechanical effects of the tumor on the upper digestive tract. The main reasons are obstruction to swallowing, early satiety, nausea and vomiting. Another reason for weight loss is the co-existence of systemic inflammation. Nutritional treatment in the group of patients with gastric cancer is still used too rarely and the knowledge about it is still very limited. Nutritional support should be given for patients both in the pre- and postoperative period. Nutrition should also be used in palliative treatment in patients with unresectable stomach cancer. The main principles of nutritional support and its influence are presented in this publication.

Key words: stomach cancer, cancer cachexia, enteral nutrition (EN), parenteral nutrition (PN).

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The role of dietary nutrition in stomach cancer

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Rates of incidence of stomach cancer have declined globally (10–20% per decade), from being the most common cancer in 1980 to around the fourth most frequent today. Stomach cancer mortality still represents a significant proportion of all cancer deaths [1]. The majority of patients with advanced cancer experience weight loss, reduced appetite, fatigue, and weakness. Chronic nausea and early satiety may also occur. This constellation of symptoms is known as the cancer anorexia-cachexia syndrome. Together with cancer pain, cancer anorexia-cachexia syndrome has been identified as one of the two most frequent and devastating problems affecting individuals with advanced malignancies. Neoplastic cachexia is a very common clinical manifestation of upper gastrointestinal (GI) tract cancer and is generally assumed to be secondary to the mechanical effects of the tumor on the upper digestive tract. The main reasons are obstruction to swallowing, early satiety, nausea and vomiting. Another reason for weight loss is the co-existence of systemic inflammation. Up to 50% of patients with cancer have an acute-phase protein response at the time of diagnosis, including patients with upper GI malignancy [2]. It explains the cachexia phenomenon in patients with cancer not involving the GI tract, such as non-small cell lung cancer [3]. Recognition that systemic inflammation plays a role in nutritional depletion may inform the development of appropriate therapeutic strategies to ameliorate weight loss, making patients more tolerant of cancer-modifying treatments such as chemotherapy [4].

Nutritional treatment is still used too rarely and the knowledge about it is still very limited. Cachexia in advanced cancer patients still means for doctors in too many cases that “there is nothing to do”. A major problem of patients with cancer cachexia and their families is “lack of response from health care professionals” in relation to cancer cachexia management. This finding illuminated the fact that patients and their family members wanted three things from healthcare professionals. They wanted their profound weight loss acknowledged, they wanted information about it and why it was happening, and they wanted interventions to deal with it [5]. The main principles of nutritional support and its influence will be presented in this publication.

Clinical implications of cachexia in stomach cancer

Cachexia in stomach cancer, as well as in other malignancies, has been indicated as an important prognostic factor for cancer patients [6]. Not only did weight loss predict overall survival, but it also indicated a trend towards lower chemotherapy response rates [7]. Cachexia is associated with symptoms such as fatigue, weakness, and poor physical performance, and thus leads to a lower self-rated quality of life. The main factors related to self-rated quality of life scores are weight loss (30%) and nutritional intake 20% commonly 50% [8]. Patients who continue to lose weight while receiving palliative chemotherapy have reduced global quality of life and performance scores when compared

to those whose weight loss stabilizes [9]. In cachexic cancer patients pain, depression, and fatigue constitute an identifiable symptom cluster associated with reduced physical functioning [10].

The stoppage of weight loss also has important clinical consequence for operated patients. Perioperative nutrition could effectively reduce the incidence of postoperative complications in moderately and severely malnourished gastrointestinal cancer patients. In one study there was a twofold reduction in complications ($p = 0.012$) and a threefold reduction in deaths ($p = 0.003$) in patients with perioperative nutrition. The most dramatic decrease was noted in major septic complications (14.9% vs. 27.9%, $p = 0.011$) such as pneumonia and wound infection [11]. The conclusion from another study is the suggestion that malnutrition immediately after surgery may play a significant role in the development of wound complications [12].

Nutritional treatment

In cachectic patients with gastric cancer nutrition should be an important and obligatory part of complex treatment. The nutritional support should be given for patients both in the pre- and postoperative period. Nutrition should also be used in palliative treatment in patients with unresectable stomach cancer. The knowledge about nutritional support in this group of patients is still not satisfactory for patients or medical staff. This is likely to lead to inconsistent, and perhaps inadequate, care of patients with palliative care needs [13]. In the choice between parenteral nutrition (PN) and enteral nutrition (EN) it is necessary to consider the pros and cons of both methods. Parenteral nutrition has the advantage of fast provision and easy administration of optimal nutrition once the central venous access is established, but in hospitalized patients there is an increased risk of septic complications related to immune dysfunction after PN. Enteral nutrition can maintain structural and functional integrity of the GI tract and is not associated with increased infectious complications [11]. The benefits from EN, in possible cases, are confirmed by other studies. Tube feeding, in which it is not important whether the patients have appetites, can reduce the risk of malnutrition and weight loss, and improve tolerance of chemotherapy [14].

Undernutrition is frequently seen in patients suffering from gastric cancer. Perioperative nutritional support may have an influence on reduction of surgical complications. It was reported that pre- and postoperative total PN can decrease morbidity and mortality of stomach cancer patients [15].

Maintaining adequate nutrient intake during active treatment can be challenging for cancer patients. Nausea, anorexia, and changes in taste and smell contribute to poor nutrition. Smaller, more frequent meals and nutrient-dense liquid supplements may improve nutrient intake [16]. It is necessary to accept that home parenteral nutrition can always be considered and can be an option to improve the quality of life of these patients because of the stay at home and feeling safer and more comfortable with family members [17]. A fine line exists between offering food to a patient and forcing a patient to eat; often, conflict arises as a result. Contributors to that conflict are reduced dietary intake by the

patient and the reaction to food refusal by the family, which frequently leads to patients eating to please. Enteral or parenteral nutrition can give the opportunity for the families to take an active part in the effective care for this patient population [18, 19]. This fact, as well as psychosocial support for cancer anorexia, can have benefit for both patients and their family members [20].

Home enteral and parenteral nutrition

Almost 50% of all patients undergoing resection of gastric cancer were found to develop post-operative taste deficit. This deficit may persist 1 year after gastrectomy or longer. There are also other agents such as proinflammatory cytokines, neuropeptides, chemotherapeutic agents and radiotherapy which lead to adverse changes in taste. Appetite deficit, aversions to dietary items and cancer-related depression additionally worsen patients' nutritional state.

They are four steps of nutritional support: oral dietary therapy, enteral nutrition, parenteral nutrition and improving appetite pharmacotherapy.

Oral dietary therapy after gastrectomy is based on frequent small meals with limitation of simple carbohydrates to prevent patients from experiencing symptoms of dumping syndrome.

Home EN is a therapy for the prevention and treatment of undernutrition associated with stomach cancer when oral intake is not sufficient to meet nutritional requirements. Placement of stomach or intestinal feeding tubes may allow optimal nutritional support to be provided to patients with stomach cancer, when obstruction and dysphagia are reported. This kind of treatment is safer, cheaper, and much more physiological than parenteral nutrition. That is why it is recommended in malnourished patients who are unable to swallow nutrients sufficiently with stomach cancer, with a functional lower gastrointestinal tract. There are several formulas designed for EN. Since 1990 immuno-modulating formulas for cancer patients have been developed. They consist of nutrients such as omega-3-fatty acids, glutamine, arginine, and polyribonucleotides. Several studies evaluating the immuno-modulating effect on patients of these formulas have been performed so far. Unfortunately the given analysis proves a decreased number of infectious complications but cancer patient survival was not improved. In many cases of stomach cancer home EN is necessary and recommended. Home EN is safe, with a low rate of complications related to EN.

In the late stage of stomach cancer, when tumor spread to the peritoneum and small bowel makes absorption insufficient, patients cannot meet their nutritional requirements by enteral intake. Parenteral nutrition can improve several nutrition parameters. This kind of treatment is recommended mostly to patients receiving radio-chemotherapy, but its use as palliative treatment is limited. Parenteral nutrition generally is not recommended for patients with advanced cancer disease and short life expectancy. There are specific goals of PN such as preventing and treating patients for malnutrition. This treatment will improve patients' quality of life, controlling some adverse effects of anti-tumor therapies. As it was proven, total parenteral nutrition provided in stomach cancer patients in selected cases is a safe and

lifesaving procedure preventing and treating cancer cachexia, enhancing compliance with anti-tumor treatments.

Nutritional supplementation and pharmacological support

The impact of several drugs with a potential influence on patients' nutritional status has been examined. They are hormones (ghrelin, insulin-like growth factor I, melatonin), cytokine inhibitors (monoclonal antibodies anti-TNF, pentoxifylline, eicosapentaenoic acid), appetite stimulators (anabolic steroids, megestrol acetate), antidepressants, and anti-emetics.

Supplementation with large amounts of vitamins and minerals during cancer treatment theoretically could reduce the effectiveness of chemotherapy or radiation therapy by enhancing repair of cellular oxidative damage to cancer cells. The American Cancer Society recommends limiting intake of antioxidant vitamins to tolerable upper limits of the Institute of Medicine Dietary Reference Intakes during chemotherapy or radiotherapy. Particular attention should be paid to food safety when cancer patients may be immunosuppressed [14]. The potential benefit in stoppage of cachexia can be achieved using fish oil or omega-3 fatty acid supplementation. In stomach cancer cachexia no highly effective therapy has been found. Megestrol (Megace) may improve appetite, calorie intake, sense of well-being, and weight gain in cancer patients, but taking it does not result in increased muscle mass or improvement in performance status [21]. The optimal dose has not been defined. Corticosteroids may improve appetite and the feeling of well-being; however, the effect is short-lived [22]. Dexamethasone, having the least mineralocorticoid effect, is preferred, and a single morning dose may prevent associated insomnia. Thalidomide (Thalomid) can show attenuation of loss of weight and muscle mass, but it still lacks recommendation [23]. Parenteral nutrition and EN, alone or used in combination, are still the most effective methods in perioperative and palliative treatment of cachectic stomach cancer patients.

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