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Review

Disease specific substrates in cancer cachexia – Reality and anticipation

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ABSTRACT

In recent years, the concept of nutrition in patients with tumour diseases has been changing very significantly. The article discusses the pathogenesis of tumour cachexia and sarcopenia, which have been intensively studied, particularly in the last ten years. The possibilities and modern approaches in nutritional support in oncology are reviewed with a special emphasis on the group of elderly patients. Also, a detailed list of the most frequently used pharmaconutrients in oncology is presented. The recommendations for nutritional care of elderly oncological patients are given and discussed.

1. Background

In recent years, the concept of nutrition in patients with tumour diseases has been very significantly changed both in terms of extended theoretical knowledge in this field and from the standpoint of practical use of nutritional support.[1,2] This change stems from both a more profound understanding of the mechanisms and clinical consequences of tumour cachexia and the practical availability of new nutritional preparations based on the principles of nutritional pharmacology. Great progress has been made also in the specification of indications for nutritional support in patients with different types of malignant tumours, as well as in the indications based on the stage of development of the disease.

Although in many cases the convincing arguments are based on the principles of evidence-based medicine (EBM), which confirm that nutritional support improves both morbidity and mortality,[3] it is often the case that an improvement in the quality of life is of greater importance than the length of a patient's survival. One of the main principles is to maintain the state of nutrition and particularly to decelerate the development of sarcopenia, because from the viewpoint of medical ethics, grave cachexia, with its associated shattering feeling of exhaustion, belongs to the same category of nociceptive stimuli as suffocation, death by thirst, and visceral or somatic pain. From this aspect, the perspective of an experienced clinician is one of the most important factors in deciding when and by what means nutritional support of the oncological patient is to be started.

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Unfortunately, even amongst oncologists there still exist outdated opinions that nutritional support does not significantly contribute to the therapeutic arsenal of care for oncological patients, and even that it can be harmful. This outdated approach stems from the lack of understanding of appropriate procedures of nutritional support in oncology, and also from the lack of knowledge of the latest methods and possibilities of pharmaconutrition (nutritional pharmacology) and the possibilities of organ-specific nutrition.

Nutritional support, in particular organ-specific nutrition aimed at the gut function maintenance regimen, is of major importance also for the maintenance of the intestinal barrier in patients treated with chemotherapy or actinotherapy. The collapse of the intestinal barrier in the course of treatment of the oncological patient usually has detrimental consequences for the progress of the disease as well as its whole prognosis. Translocation of endotoxin and possible subsequent translocation of living microorganisms to the blood circulation system can be a lethal mechanism which can determine the fate of the patient even in the case of an otherwise quite good prognosis based on intensive therapy of the tumour. Neglect of care for the intestinal barrier by providing precisely managed nutritional support using organ-specific preparations always creates great risk for the patient. The course and consequences of translocation of endotoxin from the intestinal lumen and eventually living organisms into the mesenteric lymphatic nodes and the blood circulation system may not show dramatic symptoms in the first stage, particularly in immunosuppressed patients and patients undergoing intensive chemotherapy.[4,5]

Metabolic stress (hypermetabolism, protein catabolism with development of SIRS and non-perforative sepsis from the intestinal tract) often takes place in a very latent manner, and is a frequently overlooked mechanism which prematurely kills the patient with tumour disease. In addition, the complex of changes consequent to damage of the intestinal barrier in the oncological patient is potentiated by any surgical intervention in the abdominal cavity, which is usually associated with hypoperfusion of the mesenteric bed, subsequent reperfusion of the intestine and nutritional deficit.

Progressive deterioration of the nutritional status is a typical manifestation of tumour disease, and the frequently present anorexia connected with a limited intake of food results in profound metabolic changes: increased proteolysis and lipolysis, decreased sensitivity to insulin, hypoalbuminemia connected with disorders in the balance of minerals, swellings and marked sarcopenia with a functional limitation of muscle activity. A decrease in musculature, which in intensified tumour catabolism amounts to hundreds of grams of muscle mass a day, weakening of the respiratory muscles, and immunosuppression due to hunger markedly participate in the syndrome of tumour cachexia and the resulting complications, such as pulmonary infections. These changes result in the premature death of patients who are otherwise curable from the oncological aspect and have favourable prognoses.

Another consequence of tumour cachexia is increased chemo- and radiotoxicity, which often causes interruption of planned oncological treatment, and probably significantly contributes to higher mortality.[6–9] Of great importance for a favourable result for oncological therapy is an early provision of nutritional support to oncological patients before full development or even commencement of refractory tumour cachexia. This is evidenced in numerous papers based on the latest and very exact studies.[10–13] These latest papers clearly demonstrate that nutritional support is one of the important factors which improve tolerance to aggressive oncological treatment, improve the quality of life and decrease mortality. The precondition is that nutritional support is based on correct indication, is not started late in the advanced or terminal state, and also, especially, is based on the use of new preparations which make use of nutritional pharmacology and specific nutrients in pharmacological doses, with proper and appropriate technique of administration (enteral nutrition, parenteral nutrition, combined and transient type of nutrition). There are great prospects in oncology for the application of anaplerotic nutritional substrates.

2. Pathogenesis of tumour cachexia

Pathogenesis of tumour cachexia has been intensively studied particularly in the last ten years. According to the latest knowledge, a pivotal role in the pathogenesis of tumour cachexia is played by the inflammatory reaction, with its extraordinarily rapid drawing on the energy of fat stores and devastation of muscles. The inflammatory reaction is systemic in nature, with interaction between the tumour and the host organism. An example is sensitivity to insulin and the circulating levels of cholesterol, which are under the regulation of the central nervous system and governed by humoral agents. From this aspect, food intake is controlled from the area of the hypothalamus and nucleus arcuatus, where orexigenic and anorexigenic neurons are located. A group of neurons in the nucleus arcuatus controls the production of polypeptides – pro-opiomelanocortins – which are subsequently cleft into active hormones, melanocortins. Among them, the alpha-melanocyte stimulating hormone mediates the anorexigenic response by the route of melanocortins MC_4. Functional integration of neuropeptide Y and pro-opiomelanocortin is closely connected with food intake. This mechanism is also supported by demonstrations that neuropeptide Y participates in the expression of “agouti-related protein”, which is the natural antagonist of the melanocortin receptor MC_4.[14] In the presence of a proliferating tumour the physiological balance between neuropeptide Y and pro-opiomelanocortin is changed and the nucleus arcuatus is adjusted for anorexigenic action, which is sensitive to the signals connected with the metabolic situation in the peripheral tissues. These signals include also an increase in proinflammatory cytokines produced by the growing tumour tissue, and the reaction of the surrounding tissue to this proliferation. The hypothalamus is informed about the presence of the tumour growing in the periphery even in the situation when the tumour size amounts to a few millimetres.[7] Demonstrations for this phenomenon are based on the knowledge that information on the inflammatory reaction originating from the action of the growing tumour is relayed by the vagus afferent routes to the hypothalamus, which generates a stress response by activation of pro-opiomelanocortin neurons and inhibition of neuropeptide Y neurons.

Table 1 – Occurrence of malnutrition and increased rest energy expense (REE).

Type and localization of the tumour	Degree of malnutrition	REE > 110% norms
Gastric carcinoma	83%	45%
Small-cell lung carcinoma	60%	100%
Bronchogenic lung carcinoma	66%	100%
Breast carcinoma	36%	?
Large intestine carcinoma	54%	30%
Rectal carcinoma	40%	30%
Esophageal carcinoma	79%	?
Sarcoma	39–66%	100%
Pancreatic carcinoma	83%	?
Other solid carcinomas	63%	75%

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The reaction to the acute inflammatory response is characterized by the total picture of the disease, which includes loss of weight, anorexia, as well as anti-inflammatory reactions caused by vagal mechanisms. This picture also includes the reaction to suppress the inflammation and the related immune response. In several recent years, new data have appeared which elucidate the role of the hypothalamus in the energy balance. The strong relationship between the hypothalamus and total energy balance of the organism both in the physiological and pathological situations, in particular in relation to body weight, includes also a neuroregulatory component.[15–18]

3. Sarcopenia and tumour cachexia

As suggested by its name, sarcopenia is characterized by a loss of the muscle mass, which is physiological in the course of ageing, but becomes a pathological phenomenon in some clinical conditions such as grave catabolism and tumour cachexia in oncological patients, in acute conditions connected with infection (sepsis), after serious operations, and in polytrauma. At present, the loss of muscle mass can be relatively well quantified by means of dual x-ray absorptiometry (DEXA), computer tomography, bioimpedance, biochemical methods, and most simply, by anthropometric methods. The development of sarcopenia is connected with a significant decrease in muscle strength and long-term muscle performance. In serious pathological sarcopenia, these functional manifestations are associated with a feeling of extraordinary fatigue, even up to an inability to secure the basal vital actions. Besides this marked exhaustion, the development of sarcopenia is inevitably connected also with a marked risk of injuries and falls, and respiratory infections associated with the weakening of the respiratory muscles and hypoventilation. The relationship between the causes of sarcopenia and an increase in morbidity and mortality is shown in Fig. 1.[19]

4. Malnutrition and frequent clinical problems in oncological patients

Longitudinal statistics from different research centres demonstrate that tumour cachexia represents the main complicating problem in oncological patients, at least in terms of prevalence. In some oncological patients, the decrease in body weight is one of the most frequent symptoms, reaching up to 66% in the course of the oncological disease. A decrease in body weight of more than 10% of the pre-disease weight occurs in 45% of adult oncological patients.[20] The occurrence of malnutrition is presented in Table 1. A survey of the most frequent mechanisms and clinical consequences is shown in Tables 2 and 3.

Malnutrition in oncological patients is the most frequent cause of postoperative complications in this category. A protracted decrease in energy supply and protein availability in food results in the deterioration of cellular and organ functions. This leads to markedly increased morbidity and

Table 2 – Comparison of metabolism and nutrition in starving and tumour disease.

Category	Starving	Tumour disease
Absence of appetite	Yes	Yes
Weight	↓	↓
Rest energy expense	↓	↑
Blood glucose	↓	±
Blood lactate	±	↑
Serum insulin	↓	±
Plasma glucagon	↑	±
Total plasma amino acids	↓	↓
Excretion of nitrogen in urine	↓	±
Glucose tolerance	↓	↓
Whole-body glucose turnover	↓	↑
Recycling of whole-body glucose (%)	↑	±
Recycling of whole-body glucose degree	±	↑
Whole-body protein turnover	↓	±
Whole-body protein synthesis	↓	±
Whole-body protein catabolism	±	Unknown
Gluconeogenesis from alanine	↑	↑
Plasma alanine		↓
Release of alanine from muscle	↑	↓
Release of glutamine		±
Intake of BCAA		↑

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↑, significant increase; ↓, significant decrease; ±, no change or without significant changes; BCAA amino acids with a branched chain.

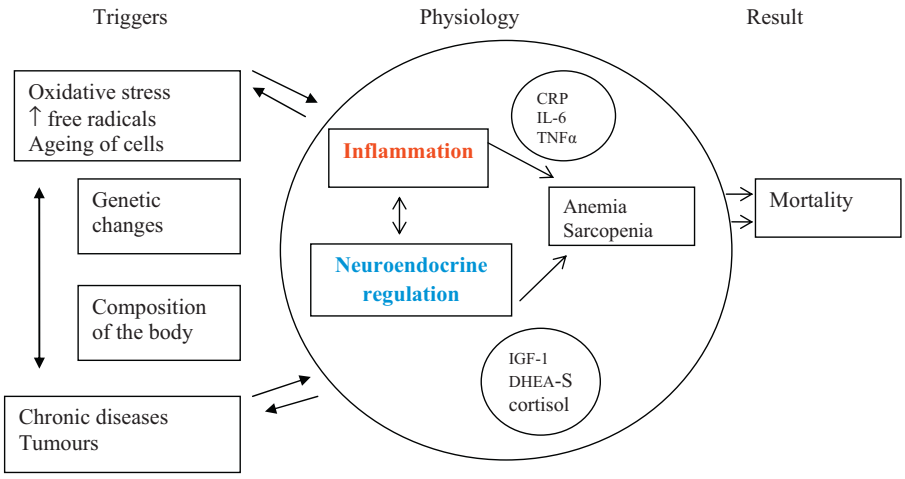

Fig. 1 – Relationship between the causes of sarcopenia and mortality.

mortality, as well as diminished response to chemotherapy.[27] An increase in postoperative complications accompanies particularly a decrease in body weight greater than 15%. This value is also characteristic of the development of immunosuppression and increased frequency of infectious complications, with their consequences for increased morbidity and mortality in oncological patients.

There is a close relationship between malnutrition and wound healing. Degraded wound healing is particularly evident during rapid development of protein-energy malnutrition, which closely correlates with a decrease in non-fat body mass, particularly a decrease below 10%. A number of studies have demonstrated a relationship between wound healing and a decrease in serum albumin, low transferrin levels (less than 1.5 g/l), or lymphopenia.[21] Another principal index which characterizes degraded healing is decreased content of hydroxyproline in the healing tissue.

Subclinical deficits of some vitamins and trace elements (vitamin C, zinc, selenium) are the principal bioindicators of degraded healing. An important role is played also by a deficit of some essential as well as non-essential amino acids such as lysine, arginine, hydroxyproline and glutamine.

5. Possibilities and modern approaches in nutritional support in oncology

Nutritional support serves as a means for the preservation of an acceptable quality of life, fewer complications from the oncological disease, and an improvement in the

Table 3 – Deteriorated physiological functions in malnutrition.

Principal damage	Mechanism	Clinical consequences
Shifts in body fluids	Swelling ECW expansion, ↑ interstitial fluid in lungs	Disorder in wound healing, increased distribution space for medicaments
Muscle strength	↑ fatigability Changes in contraction and relaxation	Respiratory infection
Healing	↓ colloid osmotic pressure ↓ OH-proline deposition	Dehiscence of sutures
Immunity insufficiency	↓ CD4, CD8 lymphocytes ↓ cytokines secretion ↓ DHR ↓ blastic transformation ↓ bactericidal capacity of neutrophils ↓ migration of lymphocytes, damage of function of neutrophils ↓ adhesion and chemo taxis	Infection complications
Hypothermia		Mortality on hospitalization

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conditions for chemo- and radiotherapy. In most cases, nutritional support requires the use of special preparations based on nutritional pharmacological formulae. According to the recommendations of the European Society for Parenteral and Enteral Nutrition (ESPEN), the use of conventional application of parenteral or enteral nutrition or prolonged delay before commencement of specialized nutritional support intended for oncological patients can be considered a failure of proper care for the patient. In countries with developed healthcare systems, non-provision of nutritional support to the oncological patient is considered to be an act of neglect. On the other hand, it is necessary that the indication for nutritional support is correct not only in its own right, but also from the standpoint of individual selection of preparations and dosage. As has already been mentioned, indication criteria must be taken into consideration:

(1) type of tumour and the stage of development of the disease;
(2) age, sex and weight of the patient, and the resulting proper dose of nutrients and energy, and the content of substrates with nutritional pharmacological effect;
(3) all contraindications related to the syndrome of "overfeeding", the possibilities of specific organ support, and the suitable route of administration (complete or supplementary parenteral nutrition, peripheral or central type of parenteral nutrition, puncture gastrojejunostomy, nasojejunal tube, or sipping).

The determination of nutritional support must be calculated precisely, and not just administered to the patient by estimate; as a minimum, the MUST system (malnutrition universal screening tool) must be employed.[29] In unstable patients with a less favourable reaction to the commencement of nutritional support, the most suitable thing is, of course, regular measurement of energy consumption and utilization of individual energy substrates by means of indirect energometry.[29,30]

As far as the route of administrations is concerned, in the first stage the most suitable one is sipping, and in the case of considerable loss of appetite and vomiting it is the administration of pharmacologically prepared enteral nutrition via a nasojejunal tube (the requirement of administration of liquid nutrition behind the Treitz ligament should always be respected to eliminate the risk of dilation of the abdomen, vomiting, or aspiration). In the overwhelming number of cases, proper dilution and administration of preparations behind the Treitz ligament will achieve successful dispensing of energy and a sufficient variety of amino acids to the catabolic patient with chronic type of tumour cachexia; this will improve his/her reaction to pharmacotherapy and actinotherapy.[7] The decision is very sensitive in situations where the patient will undergo surgery in the future, or where the patient has reached an enhanced degree of malnutrition. In the latter case, there is a risk that total parenteral nutrition administered into the central vein may lead to the development of infectious complications, in particular the development of catheter sepsis, which in this type of patient can have fatal consequences. For this reason, a well considered decision about the type and composition of the administered artificial nutrition is the principal precondition of its success and safe use. In most studies reporting unsatisfactory outcomes of artificial nutrition in oncological patients, a more profound analysis reveals a whole series of errors and ignorance in the use of the method. In these cases, artificial nutrition, in particular that administered in the form of parenteral nutrition or puncture gastrojejunostomy, becomes a treatment which endangers the patient, rather than a benefit. These opinions have also been formulated in the recent meta-analyses of the European Society for Parenteral and Enteral Nutrition (ESPEN). The decision algorithm for the administration of artificial nutrition to oncological patients is presented in Fig. 2.

Table 4 – Specific pharmacological effect of amino acids.

Substrate	Effect
Arginine	Stimulation of immunity Formation of NO Thymotropic effect, antineoplastic effect
Glutamine	Maintenance of intestinal barrier (toxins, starving, radiation) Substrate for cell division (mucosa, bone marrow)
BCAA + arginine	Support and synthesis of proteins in muscle and anabolism of host

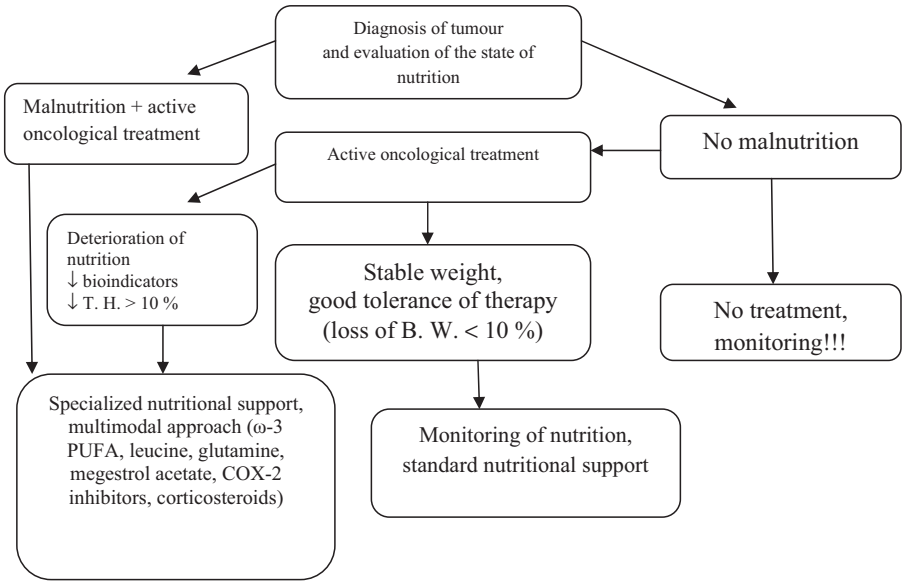
6. Possible pharmaconutrition in artificial nutrition in oncological patients

Amino acids – a list of the most frequently used pharmaconutrients in oncology is presented in Table 4.

Glutamine is undoubtedly one of the most frequently used pharmaconutrients due to its favourable and efficient effect in immunity modulation and it's securing of positive nitrogen balance. It is also a nutrient which has been demonstrated to ensure the integrity of the intestinal mucosa and thus the functionality of the intestinal barrier (Fig. 3). This effect of glutamine is of extraordinary importance, particularly in the course of chemotherapy.[5]

Arginine is a nonessential amino acid, which, however, under load, is not synthesized in sufficient amount to the endogenous metabolic pool, and which therefore must be supplemented as a potentially essential nutrient. Enteral nutrition enriched with arginine, RNA and omega-3 fatty acids is at present at the centre of attention from the standpoint of artificial nutrition of oncological patients. These enrichments aim to boost the mechanisms of immunomodulations and suppress growth of the tumour, and thus improve morbidity and mortality in oncological patients. In other supplements, these types of specific nutritions are enriched with vitamin D, E, C, selenium and coenzyme Q.

Leucine is a hydrophobic neutral branched amino acid with the properties of a branched amino acid, and is necessary for the synthesis of proteins. At the same time, leucine is an important source of energy, in particular for muscles. Oxidation of leucine, as in other branched amino acids, requires thiamine, riboflavin, pyridoxine, niacin, biotin, pantothenate, ubiquinone, magnesium, and iron. An important property of



Abbreviations: ***B. W.*** *– body weight,* ***PUFA*** *– polyunsaturated fatty acids*

Fig. 2 – Procedure of nutritional support in oncology.

leucine is its capacity to provide energy even under critical condition, when glucose intolerance has developed and glucose is oxidized with difficulty. It is also capable of replacing fatty acids as a source of energy, if under critical condition and hypoxia oxidation of fatty acids is blocked. Leucine is also an important precursor in cholesterol synthesis, thus playing an important role in the regeneration and reparation of tissues. Insufficiency of leucine in the muscles decreases the production of cholesterol, which is necessary for the building of the membranes of muscle cells. For this reason and by means of this mechanism leucine very markedly influences the intensity of sarcopenia[31]. Leucine gives rise to an important metabolite beta-hydroxy-beta-methyl-butyrate (HMB), a marked regulator in the anabolism of muscle tissue. Although hydroxymethylbutyrate does not have such a marked effect on the synthesis of proteins in the muscle and on the suppression of sarcopenia as does leucine, this metabolite is indispensable for the immune functions and for the regeneration of damaged cells in all tissues of the human organism, including those damaged by toxic medicaments and those required for the maintenance of the structural and functional ability of the muscle tissue (Fig. 4). In the muscle tissue, HMB acts by the mechanism of stabilization of the sarcolemma, and in addition it suppresses proteolysis of muscle proteins. Since maintenance of muscle tissue is dependent primarily on the synthesis of cholesterol and other isoprenoids de novo, use is made of HMB as a precursor in their synthesis, in particular in situations of increased metabolic requirement. At present, supplementation with HMB is recommended in the amount of 3 grams a day in three divided doses.[22]

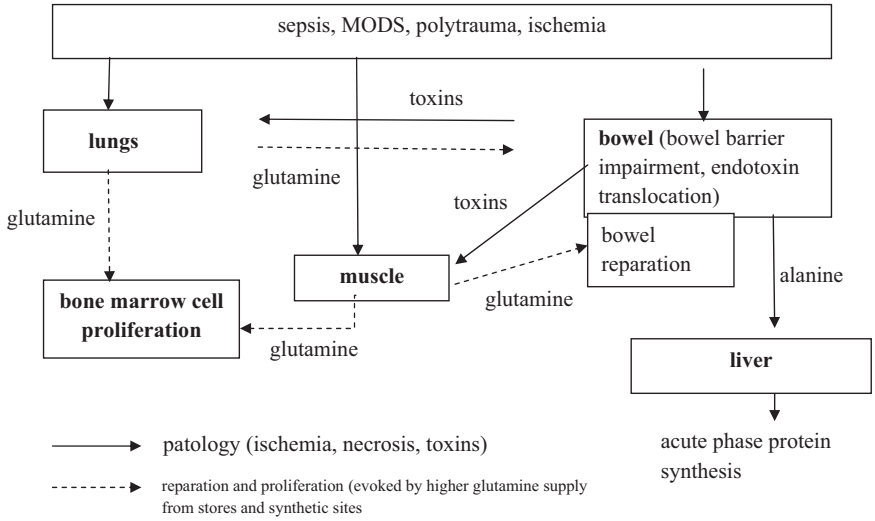


Fig. 3 – Role of glutamine in the critical condition.

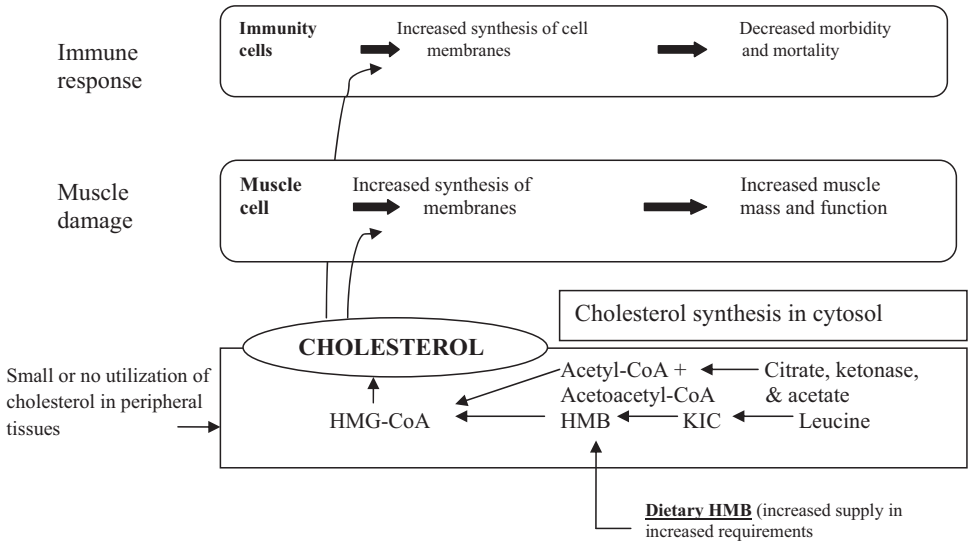


Fig. 4 – Effect of leucine and HMB on suppression of sarcopenia.

7. Pleiomorphous effect of polyunsaturated omega-3 fatty acids in pharmaconutrition in oncological patients

Polyene omega-3 and omega-6 fatty acids are indispensable fatty acids, which are not produced in the human body. In addition, the 'western type' diet contains a low amount of omega-3 fatty acids, so that the ratio omega-6 PUFA/omega-3 PUFA is usually increased above the optimal value. The human organism obtains the majority of the required amount of omega-3 fatty acids from fat contained in fish and from alpha-linolenic acid, contained in some plants and plant fruits (nuts). Contemporary clinical studies demonstrate that an increased supply of omega-3 fatty acids is capable of stabilizing body weight in patients suffering from the manifestations of tumour cachexia. For this effect, however, the usually recommended doses of omega-3 fatty acids are insufficient, and pharmacological doses must be consumed, corresponding to 5–10 g of omega-3 fatty acids daily. The above-mentioned studies employed higher metabolites of linolenic acid, namely eicosapentaenoic and docosahexaenoic acids. The preparations intended for the treatment of tumour cachexia currently available on the market contain mostly a mixture of EPA and DHA.[23,24]

Especially favourable effects have been observed with the use of n-3 PUFA in oncological patients after extensive abdominal surgery, where there appears to be a decreased occurrence of infectious complications, and the immune response of the patient is improved. Studies aimed at the effect of simultaneous therapy with anthracyclines in breast carcinoma demonstrate that after higher doses of omega-3 fatty acids the progression of the tumour is decelerated, toxicity of the anthracyclines is decreased, and mortality is improved.[25] The potential mechanism by which omega-3 fatty acids modulate the response to the tumour and improve tumour cachexia is presented in Fig. 5. The total effect is multifactorial, but one of the important mechanisms which explains the favourable effect of omega-3 fatty acids in tumour cachexia is the suppression of the inflammatory reaction. There exist papers which demonstrate that the suppression of tumour cachexia by the action of omega-3 fatty acids is closely connected with the presence of the markers of inflammatory reaction.[26]

8. Conclusions and recommendations

Recommendations of the European Society for Parenteral and Enteral Nutrition (ESPEN) for oncological and transplanted patients:

- Avoid prolonged preoperative fasting.
- Ensure a return to the normal dietary regimen after the surgery as soon as possible.
- Without the manifestations of malnutrition commence enteral nutrition in patients, where it is evident that they will not receive food normally for a period longer than 7 days, if an operation follows (it holds true also in the cases when the patient receives less than 60% of the recommended dose for a period longer than 10 days).
- It is recommended to postpone elective surgical intervention for the purpose of preoperative enteral nutrition in the oncological patient, if there is a marked nutrition risk defined by the presence of at least one of the following three criteria:

(1) A decrease in body weight greater than 15% in 6 months.
(2) BMI lower than 18.5 kg/m^2.
(3) Serum albumin lower than 30 g/l.

For patients in nutrition risk, the nasojejunal tube is to be introduced within 24 hour after surgery (recommendation degree A).

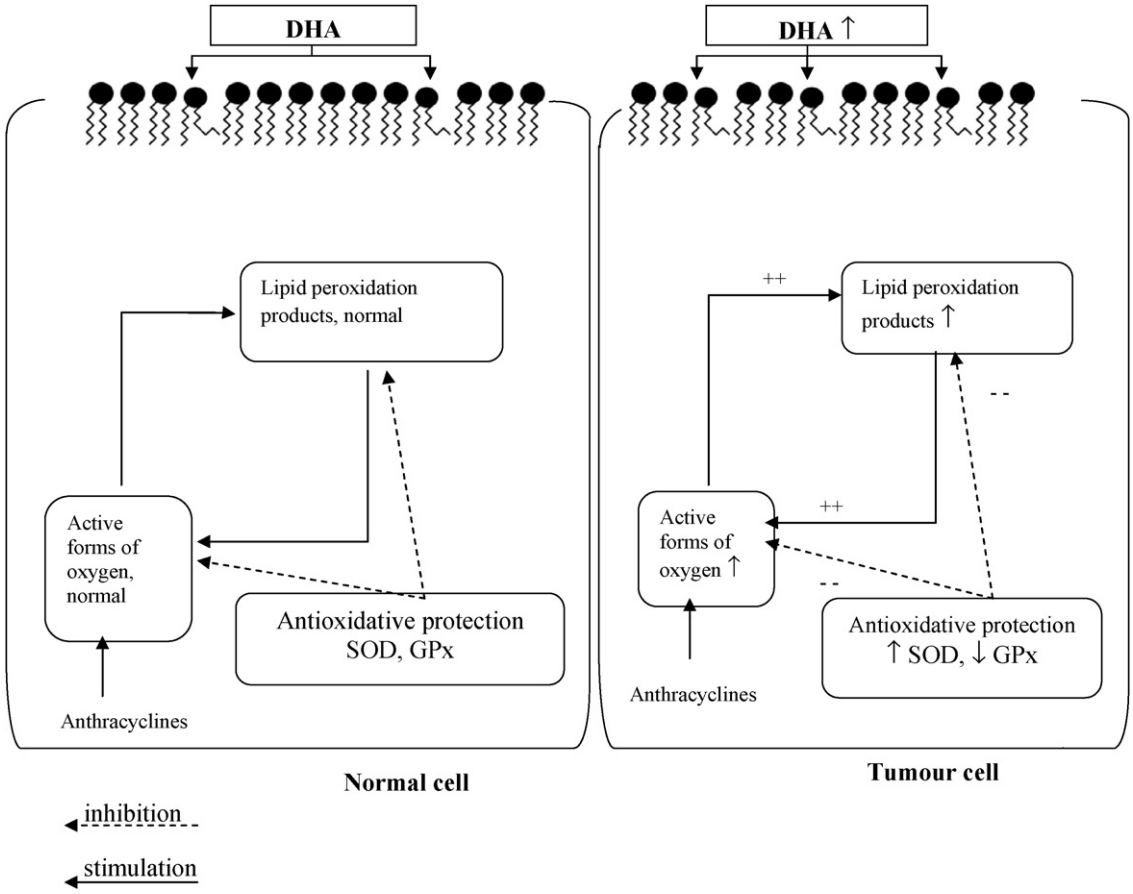


Fig. 5 – Role of omega-3 fatty acids on the metabolism of the normal and tumour cell.

- Commence nutritional support via a thin tube with a low flow (10–20 ml/hr particularly in expected worse tolerance of nutrition).
- Use enteral nutrition with specific substrates (arginine, omega-3 fatty acids and nucleotides) perioperatively irrespective of nutrition risk in the following patients: major surgery in an oncological disease in the area of the neck, head (laryngectomy, pharyngectomy); in the case of a major surgery of oncological character (esophagectomy, gastrectomy, pancreatoduodenectomy).

Frequently, patients exposed to major gastrointestinal surgery receive, simultaneously with enteral nutrition, large volumes of crystalloids intravenously during and after the surgery. A large liquid load can result in distension and an increase in body weight of several kilograms. This phenomenon can be the main cause of postoperative ileus and decelerated emptying of the stomach, and that is why the tube must be preferably introduced into the first loop of the jejunum. It prevents dilation of the stomach and the risk of gastric content aspiration.

Disproportionately low intake of energy in oncological patients for a period longer than 14 days is connected with high mortality. Enteral nutrition support using a tube is thus indicated also in patients without manifest signs of malnutrition, if such a prolonged period of insufficient food intake is expected.[27]

Conclusions from the guidelines of the European Society for Parenteral and Enteral Nutrition (ESPEN) in nonsurgical oncological patients [28,29]:

- Parenteral nutrition is not recommended when the nutritional condition of the oncological patient is good and the food intake is not disturbed and is not expected to be so in the future.
- Perioperative parenteral nutrition is strictly recommended in malnutrition patients, where the food intake is disturbed and enteral nutrition cannot be used. The benefits greatly exceed the risks.
- Routine parenteral nutrition, however, is not recommended as a standard in well-nourished patients during nonsurgical oncological treatment and in normal food intake, *which must be monitored quantitatively*.
- Parenteral nutrition is recommended in patients with untreatable malignant disease, if there is a rapid loss of body weight and a markedly decreased intake of nutrients orally or via a tube (supplementary parenteral nutrition).

Recommendations according to the ESPEN guidelines:

- In hematooncological patients, parenteral nutrition is to be reserved only for cases of grave mucositis, ileus, intractable vomiting (recommendation degree A).

- An addition of glutamine to nutrition is suitable (recommendation degree B).
- Total supply of energy per day in oncological patients is best measured by means of indirect energometry, but it is possible to use the recommendation of 20–25 kcal/kg of body weight per day in bedridden patients and 25–30 kcal/kg of body weight per day for walking patients.
- According to preliminary meta-analyses, in patients in the course of chemotherapy and actinotherapy it is suitable to use specific pharmaconutrition preparations.
- The therapeutic contribution of parenteral nutrition in oncological patients of a nonsurgical character is as follows: prevention and treatment of malnutrition (or tumour cachexia); improvement of the tolerance of oncological therapy; suppression of undesirable effects of oncological therapy; improvement of the quality of life.[7]
- Hematooncological patients are less endangered by infectious complications and impairment of the intestinal barrier with the use of parenteral nutrition supplemented with glutamine (recommendation degree B). Although the optimal dose of glutamine in hematooncological patients has not yet been exactly determined, according to the available studies a dose of approximately 0.6 g glutamine per kg of body weight a day is recommended.

Use of pharmaconutrition with arginine, omega-3 fatty acids, nucleotides and glutamine is indicated in the following situations[27]:

- Tumours in the region of the head and neck even in good nutritional condition (recommendation degree A).
- Extensive abdominal surgery – oesophagus, gastrectomy, duodenopancreatectomy (recommendation degree A).
- Presence of malnutrition in the perioperative period.

Nutrition support is indicated in all oncological patients suffering from marked malnutrition prior to major surgery, for a period of at least 10–14 days prior to the surgery, even if the surgery has to be postponed (recommendation degree A). The criterion of malnutrition in this case is:

- Decrease in body weight > 10–15% within 6 months.
- BMI < 18.5 kg/m^2.
- Serum albumin < 30 g/l (in absence of liver or renal dysfunction).

Although there is a high probability that nutrients are used also for the nutrition of the tumour tissue, the risk of increased morbidity and mortality resulting from tumour cachexia prevails over the clinical risk of the tumour's using the nutrition substrates for stimulation of its growth.

Conflict of interest

None declared.

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