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CAUSES OF MALNUTRITION AND CACHEXIA IN CANCER PATIENTS, AS WELL AS THEIR THERAPEUTIC IMPLICATIONS

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ABSTRACT:

Background: Tumour cachexia represents the most severe form of malnutrition in cancer patients and is responsible for nearly one-third of cancer-related deaths, either directly or indirectly. Malnutrition in cancer patients arises from factors related to the tumour itself, the patient's condition, or the treatment received.

Methods: This study reviews the primary mechanisms contributing to malnutrition in cancer patients, particularly in the context of different treatment modalities such as chemotherapy, radiation therapy, and surgery. The physiological impact of malnutrition, its implications on patient outcomes, and associated healthcare costs are also examined.

Results: Malnutrition in cancer patients occurs through four essential pathways:

- **Inadequate nutrition and energy consumption** – due to reduced appetite or difficulty in eating.
- **Modifications to nutrient absorption and digestion** – caused by tumour-related metabolic alterations.
- **Increased nutritional requirements** – resulting from the body's inflammatory response to cancer.
- **Changes in nutrient metabolism** – leading to muscle wasting and weight loss.

The consequences of malnutrition include loss of muscle mass and strength, reduced functional status, impaired quality of life, and greater dependence on caregivers. It also hampers the body's natural healing processes, increasing the risk of surgical complications such as infections and wound dehiscence. Additionally, malnutrition contributes to prolonged hospital stays, raising

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overall treatment costs. Severe weight loss is strongly correlated with lower survival rates in cancer patients.

Conclusion: Malnutrition is a critical concern in cancer care, significantly impacting patient health, treatment outcomes, and healthcare expenditures. Early intervention and nutritional support strategies are essential to mitigate its effects and improve patient prognosis.

KEYWORDS: quality of life, cancer, hunger, Cachexia due to cancer.

INTRODUCTION:

Because of its high morbidity and mortality, significant impact on the patient's and his family's quality of life, and frequency, cancer is one of the diseases with the highest potential for harm to health. The incidence of cancer in Spain is estimated to be 291 women and 321 men per 100,000 people. This number is predicted to rise by 35–45% in the following years. Still, mortality rates will decline primarily due to improved oncological and supportive care, including nutritional support. Nutrition and cancer are related in two ways: on the one hand, a poor diet can lead to a higher incidence of certain tumours (about 35–45% of tumours in men and up to 61% of tumours in women are related to diet); on the other hand, cancer and its treatments can cause malnutrition, which develops in 45–85% of cancer patients during the disease (Gaafer & Zimmers, 2021).

In a time when obesity is a worldwide epidemic, being overweight itself is now considered a risk factor for developing some forms of cancer, such as those of the breast, prostate, and endometrial, and it also raises the risk of dying from certain malignancies (liver, pancreas, etc.). If adults maintained a body mass index of less than 25.5 kg/m2, the 90,000 cancer deaths that occur in the USA each year may be prevented. Tumour cachexia is the highest manifestation of malnutrition in cancer patients and accounts for one-third of cancer patients' deaths, either directly or indirectly. The syndrome known as tumour cachexia, which the author will go into further detail about later in this research, is typified by severe weight loss, anorexia, and asthenia, ultimately culminating in malnourishment as a result of reduced food intake or anorexia. Due to a hypermetabolic condition that causes the tumour and host to compete for nutrients, which causes the patient to lose weight more quickly (Ni & Zhang, 2020).

Malnutrition prevalence among cancer patients

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Despite the high frequency of malnutrition among cancer patients, there is very little research that discusses the prevalence or incidence of malnutrition during cancer. The first is a reference work, despite criticism for excluding patients with head and neck cancers, who are among the patients in whom malnutrition is most common. (Hunis et al.) studied weight loss in over 3,000 cancer patients, dividing them into three groups based on the frequency of weight loss (Table I). According to (Nourissat et al., 2008) research, nutritional symptoms were examined in 645 cancer patients attending outpatient clinics (table II).

Table I: Frequency of weight loss by type of tumour in cancer patients

Loss of weight throughout the last six months (%)					
Tumor	**Patient No.**	**1-5%**	**5-10%**	**> 10%**	**Total**
Sarcomas	189	21%	11%	7%	39%
Gastric Ca.	317	31%	21%	33%	85%
Ca. Lung non-micro.	590	25%	21%	15%	61%
Ca. Lung micro.	437	23%	20%	14%	57%
Ca. Mom	289	22%	8%	6%	36%
Ca. Prostate	78	28%	18%	10%	56%
Ca. Colon	307	26%	14%	14%	54%
high-grade NHL	310	20%	13%	15%	48%
Non-lymphoblastic L. Ag.	129	27%	8%	4%	39%
Ca. Pancreas	110	29%	28%	26%	83%
low-grade NHL	291	14%	8%	10%	10%

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Based on these statistics, we may determine that more than 51% of patients had some form of nutritional issue at the time of diagnosis, and more than 76% had lost weight. In contrast to breast or haematological neoplasms and sarcomas, which are less common and less severe in cases of weight loss, malnutrition is more common in cases of pancreatic and stomach cancer. In our nation, the NUPAC study evaluated the nutritional health of 782 hospitalized patients receiving home/outpatient care in 2018–2019. The study focused on patients with locally advanced or metastatic cancer. The primary test, the Patient-Generated Subjective Global Assessment (ESR-PG), revealed that 42.30% of patients had anorexia, 53% had severe malnutrition or were at risk of developing it, and possibly most importantly, 83.7% of patients with advanced cancer needed nutritional intervention (Fu et al., 2022).

Table II: Nutritional Symptoms in Cancer Outpatients reasons for malnourishment in cancer patients

Nutritional symptoms in cancer patients	Patients with disseminated disease	All patients
Intake decrease	61%	61%
Anorexia	54%	54%
Overweight	14%	14%
Normal weight	37%	37%
Underweight	49%	49%
Weightloss:		
- Any %	74%	74%
– < 5%	15%	15%
– 5-10%	22%	22%
– 10-20%	26%	26%
– > 20%	11%	11%

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When discussing the causes of malnutrition in cancer patients, three areas must be covered, which we can name as follows: The first section discusses the fundamental mechanisms of malnutrition in cancer; the second section discusses tumour cachexia in particular; and the third section summarises the various causes of malnutrition that are related to the tumour, the patient, or the treatments. Table III illustrates the complexity of malnutrition in cancer and the fact that a patient may have almost all of the causes present in them. We'll primarily refer to the third portion (Bauer et al., 2002).

Fundamental processes by which malnutrition manifests in cancer

There are four primary pathways by which malnutrition in cancer patients can manifest itself:

- Inadequate nutrition and energy consumption.
- Modifications to nutrition absorption and digestion.
- A rise in requirements.
- Changes in the metabolism of nutrients.

Cachexia due to cancer:

The complex syndrome in question has the potential to contribute to nearly 25% of cancer-related deaths directly. It is typified by several symptoms, including anorexia, early satiety, rapid deterioration of general condition (pale and rough skin, hair loss, emaciated face), immunological changes (higher susceptibility to infections), and metabolic changes (anaemia, oedema, vitamin deficiency, hydro electrolyte alterations). Patients eat less food while maintaining their eating preferences. Cachexia is thought to affect 20–51% of cancer patients, and 65-81% of patients reach the terminal stages of the illness. In addition to raising morbidity and mortality, cachexia also manifestly lowers the quality of life for cancer patients and increases healthcare costs (fig. 1).

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Table III lists the several causes of malnutrition in cancer, which we will discuss (Evans et al., 2008).

Table III: Cancer patients' causes of malnutrition alterations in the digestive system brought on by tumours

From the tumour itself:	Alterations of the digestive system. Metabolic alterations. Production of catechizing substances.
Related to the patient:	Anorexia and cancer cachexia. Psychological factors.
Produced by oncological treatments:	Surgery. Radiotherapy. Chemotherapy.

Cancer anywhere in the digestive tract can cause mechanical or functional alterations that affect a patient's diet. Head and neck tumours are among the most common tumours in the more proximal parts that cause malnutrition, both because of changes in chewing, salivation, or swallowing and because of the discomfort that is often associated with them. Malnutrition in the oesophagus tract is primarily caused by dysphagia. Anorexia, early satiety, or restriction of gastric transit are associated with gastric tumours. The most noticeable clinical sign in the farther reaches of the digestive tract is the onset of occlusive or subocclusive symptoms, malabsorption, and poor digesting. The author has already provided commentary on the metabolic alterations brought on by the tumour and the release of chemicals that cause cachexia (Argilés et al., 2014).

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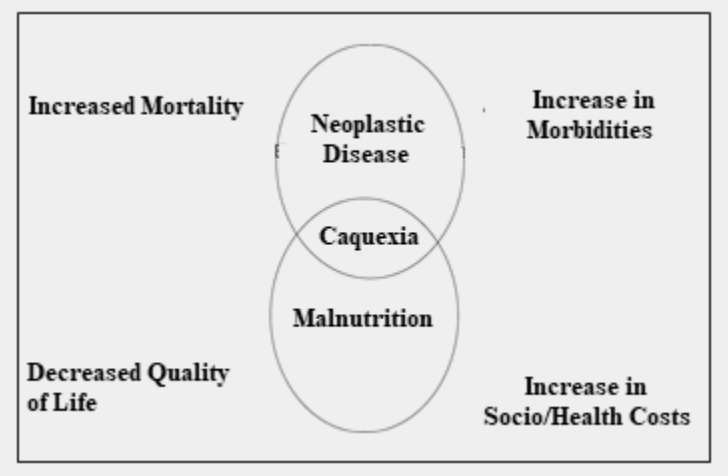

Figure 1: The relationships and effects of tumour cachexia and malnutrition.

The two leading causes of malnutrition in patients are anorexia and tumour cachexia. Anorexia is a complex disorder that affects many cancer patients. It is nearly the standard in advanced tumours, with rates as high as 71%. Pain, drugs, cancer therapies, and psychological changes can exacerbate anorexia. In many situations, anorexia will persist even after these reasons are treated. Psychological changes: The psychological effects of receiving a cancer diagnosis and the distress associated with undergoing various therapies can significantly affect cancer patients (Fearon et al., 2013). Several psycho-social elements that can result in a significant change in diet must be considered:

- People with cancer frequently experience depression, worry, and dread, which can exacerbate anorexia.
- The anxiety associated with managing several cancer treatments may exacerbate the patient's anorexia.
- Living alone and unable to cook or prepare meals because of physical changes results in less intake and a gradual decline in nutrition. One of the best social activities is dining; social isolation is exacerbated by hesitation and food aversion. All of this significantly impacts social interaction and, eventually, life satisfaction.

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Causes of malnutrition related to cancer treatments: cancer treatments, in all their forms, can cause malnutrition. This is particularly true when cancer is being treated with a variety of therapies, such as radiation, chemotherapy, and surgery (Vanhoutte et al., 2016).

Oncological Surgery:

Surgical procedures for cancer can be either soothing or curative. Still, they always result in significant metabolic stress and a heightened requirement for nutrients and energy, particularly in the case of curative procedures. In addition, a substantial number of patients have surgery when already malnourished, a fact that undoubtedly raises the risk of complications. During any surgery, a patient's typical food intake may be compromised by pain, anorexia, asthenia, gastroparesis, and paralytic ileus (caused by the anaesthesia and the surgery itself). These side effects are common in patients with more energy than usual—requirements for protein. Every digestive system surgery is unique; malnutrition can result from various post-surgical alterations. Surgery for large-scale resections of head and neck tumours, plastic surgery that can permanently change the way one chews and swallows, and resections of the small intestine, colon, rectum, pancreas, liver, and biliary system are all included (table IV) (Argilés & López-Soriano, 1999).

Table IV: Modifications of gastrointestinal oncology surgery leading to malnourishment

Surgery	Alterations
Liver/Biliary Surgery	Hyperglycemia. Encephalopathy. Alterations Hydroelectrolytic. Fat malabsorption. Fat-soluble Vit Deficiency, Ca.
Pancreatic Surgery	Fat and protein malabsorption. Fat-soluble Vit, Ca, Mg. Steatorrhea. Secondary hyperglycemia/diabetes.

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Head and neck surgery	Severe chewing-swallowing disorders. Xerostomia. Motor/mechanical dysphagia.
esophageal surgery	Swallowing disorders: reflux, fullness, satiety early. Dysphagia. Esophagogastric strictures.
Colon/Rectal Resections	Diarrhea. Hydroelectrolyte Alterations. Vit B12, Ca, Mg, Na, K malabsorption.

Oncological radiation therapy's impact on nutritional status depends on the tumour's location, extent, dosage, and fractionation. Additionally, side effects will vary depending on the patient's previous treatments, such as chemotherapy or treatments given in addition to radiation therapy. Generally speaking, the effects start to show up in the first two weeks of RT and reach their peak after two-thirds of the dose has been given. Cancer Patients' Causes of Malnutrition of the entire dosage typically don't go away until 2-4.5 weeks following the conclusion of therapy. Specific symptoms (such as xerostomia and taste and smell abnormalities) may take months or never (Obeagu & Obeagu, 2024b).

The most common side effects of radiation therapy for head and neck tumours include oropharyngeal mucositis, dysphagia, odynophagia, xerostomia, hypo- and dysgeusia, and altered or lost smell. The following are possible long-term effects: ulcers, xerostomia (caused by salivary gland fibrosis), taste loss, dental cavities, trismus (caused by muscle fibrosis), and osteoradionecrosis of the jaw (Obeagu & Obeagu, 2024a).

The acute effects of radiation therapy on the abdomen or pelvis (stomach, pancreas, colon, rectum, cervix, uterus, prostate) vary depending on the location of the irradiated lesion. These effects include diarrhoea, malabsorption, "choleretic" enteropathy, the irritative effect of non-reabsorbed bile salts, hydroelectrolyte changes, and cystitis. When left untreated, it can also result in subocclusive symptoms, ulcers, strictures, fistulas, diarrhoea, malabsorption, and enterocolitis. Effects of chemotherapy: the kind of medication used, the treatment plan (mono or polychemotherapy), the dosage, duration, and concurrent therapies, as well as the individual

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patient's predisposition based on their prior clinical and nutritional status, all influence the onset and severity of symptoms (Tan & Tan, 2022).

Cytostatics are the most hazardous chemotherapeutic drugs because they impact neoplastic and non-neoplastic cells, including bone marrow, digestive tract, and hair follicles, by acting systemically on rapidly reproducing cells. A multitude of adverse effects (Table V) may impact the patient's nutritional status, including but not limited to nausea, vomiting, anorexia, taste alterations, mucositis, and severe enteritis, which may present as oedema and mucosal ulceration resulting in malabsorption and diarrhoea that may be violent, severe, and bloody (Lyon et al., 2020).

Table V: Chemotherapy Side Effects

Anorexia.
Acute enteritis: ➔ Malabsorption and diarrhoea.
Oropharyngeal and esophageal mucositis ➔ Lower intake.
Nausea and vomiting: ➔ Lower intake.
Changes in taste and smell:
Decreases the threshold for bitter and salty flavours.
Increases the threshold for sweet flavours.
The metallic taste frequently appears.
Constipation: ➔ Increased by antiemetic and analgesic treatment.

More than 70% of patients experience nausea and vomiting as side effects of chemotherapy, making them the most prevalent side effects. They result in weight loss, electrolyte imbalances, decreased oral intake, and general weakness. Mucositis often has a brief duration. Severe pain may result, and oral intake may be difficult or impossible. Likewise, it has also been

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shown that there are modifications in body composition brought on by the effects of chemotherapy (Herschbach et al., 2020).

Malnutrition's effects on cancer

Cancer patients who are malnourished have a loss of strength and muscle mass, which has a significant impact on their functional state. It also lowers their quality of life and increases their reliance on carers or family members for care existence. As a result of increasing weight loss, the patient experiences asthenia and inactivity, which worsen the condition's functional capability by causing muscle atrophy. Breathing function deteriorates due to atrophy in the diaphragm and other breathing muscles. Similarly, cardiac changes show up as a reduction in myocardial mass, modifications to myofibrils, problems with electrical conduction, and a decline in function with a lower cardiac output (Cecerska-Heryć et al., 2021).

These patients' immunocompetence is also impacted by protein-energy malnutrition, primarily through cellular immunity and an increased risk of infectious complications, which are a significant cause of morbidity in this patient population. Moreover, malnutrition hinders the body's natural healing processes and raises the possibility of surgical problems, including suture dehiscence. Treatment expenditures are exacerbated by circumstances that increase hospital stays, such as those following surgery or infectious infections (Yilmaz et al., 2020).

DISCUSSION:

Malnutrition's effects on how well cancer treatments work

Additionally, a worse tolerance to chemotherapy and radiation therapy, as well as a worse response to them, are linked to malnutrition. Variations in how patients react to chemotherapy could be explained by the fact that malnourished people have slower tumour cell kinetics, which lessens their susceptibility to chemotherapeutic drugs. However, inadequate tolerance to therapies is impeded by hunger, making them more harmful. Medications cannot bind to them adequately

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due to decreased circulating proteins, which modifies the medications' half-live durations and pharmacokinetic properties (Sehouli et al., 2021).

Moreover, decreased glomerular filtration and oxidative metabolism may result in cytostatics acting less effectively and more hazardous. By improving the nutritional status of the patients, as in the case of malnourished colon cancer patients who received parenteral nutrition before surgery, we can say that there is a complementarity between nutritional treatment and oncological treatments, even though there is still debate regarding a potential increase in overall survival brought on by nutritional support (Zhang et al., 2021).

Undernourishment and life quality

The four main components of quality of life, physical, functional, emotional, and social well-being, characterize it and should be evaluated appropriately. Malnutrition impacts quality of life because it weakens muscles and leads to a feeling of weakness and asthenia. It also has an impact on mental health since it can create or worsen depressive symptoms. Losing weight due to cancer alters one's perception of one's physique, which makes depressive and powerless feelings even worse. More recently, Ravasco's group has shown that the worsening of nutritional status is the second most crucial factor in determining the quality of life, second only to the tumour's stage; hence, the percentage influence on the patient's quality of life was 30% (Gebremedhin et al., 2021).

Malnutrition's effects on cancer are the tumour's location, 30% of lost weight, 20% of intake, 10% of chemotherapy, 6% of surgery, 3% of the illness's length, and 1% of the tumour's stage. In actuality, malnutrition worsens the quality of life by raising the risk of complications, reducing the time free from symptoms, and shortening the time spent in a hospital. The vital tone usually improves, and the sense of weakness usually goes away shortly after beginning an appropriate nutritional intake, all of which help the patient feel better overall. The patient's initial condition, the kind and location of the tumour, and the course of the illness will all influence how helpful nutritional support is for quality of life (Mancuso et al., 2022).

CONCLUSION:

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Ultimately, it's important to remember how hunger affects mortality because significant weight loss is linked to a decreased chance of survival. The main factor contributing to morbidity and death in advanced cancer patients is weight loss. The American Cancer Society and the National Cancer Institute claim that malnutrition is still a significant issue for children with cancer and that it accounts for the death of one in three adult cancer patients. However, this relationship is less evident in the pediatric population. Cancer, but it doesn't impact survival.

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