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SPECIAL ARTICLE

Peculiarities of the obese patient with cancer: a national consensus statement by the Spanish Society for the Study of Obesity and the Spanish Society of Medical Oncology

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Abstract The relationship between obesity and cancer is clear and is present at all times during course of the disease. The importance of obesity in increasing the risk of developing cancer is well known, and some of the most prevalent tumours (breast, colorectal, and prostate) are directly related to this risk increase. However, there is less information available on the role that obesity plays when the patient has already been diagnosed with cancer. Certain data demonstrate that in some types of cancer, obese patients tolerate the treatments more poorly. Obesity is also known to have an impact on the prognosis, favouring lower survival rates or the appearance of secondary tumours. In this consensus statement, we will analyse the scientific evidence on the role that obesity plays in patients already diagnosed with cancer, and the available data on how obesity control can improve the quality of daily life for the cancer patient.

Keywords Cancer · Comorbidity · Morbid obesity · Mortality · Neoplasm recurrence · Obesity · Risk assessment · Survival rate

Introduction

From a public health perspective, obesity is known as the "tobacco of the 21st century". This association has been strengthened by the healthcare, social, and economic

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impacts of obesity. In Spain, 23% of the adult population are obese, placing our country among those with the highest incidence in the world [1].

The relationship between obesity and cancer is becoming more evident, and attention is being drawn to evaluating obesity in relation to cancer patients. The question is not simply how to evaluate obesity, but how to structure a more holistic approach to evaluating nutritional status in the context of the cancer patient's signs, both at baseline and throughout the disease course and subsequent treatment follow-ups.

Furthermore, a less known but well-documented aspect is the impact of obesity on the patient's tolerance to surgical, radiation, or systemic cancer treatments. When the toxicity of the treatments increases, this can cause further complications and occasionally can require discontinuation or dose reduction. In some tumours, this translates to a reduction in treatment efficacy.

The breakthroughs in cancer prevention and cancer treatments result in more long-surviving patients. It is extremely important for these patients to control obesity, because an obese patient with cancer has a higher probability of suffering metabolic comorbidities, developing secondary tumours or to have cancer relapses.

The Spanish Society for the Study of Obesity (SEEDO) and the Spanish Society of Medical Oncology (SEOM) developed a previous document that reviewed the most important aspects of obesity in relation to cancer prevention [2]. In this article, we will address the relationship between obesity and cancer in patients who have already been diagnosed with cancer. Our aim is that this consensus document will broaden the knowledge of this crucial relationship, and emphasise the need to work from a multidisciplinary perspective to control it.

Identifying obesity in the cancer patient

There are several ways to measure body composition and adiposity. A few of the most inexpensive, immediate, and non-invasive techniques are to measure weight, height, body mass index (BMI), and waist perimeter. Other safe and simple techniques to measure body fat that are used in clinical practice, although with important limitations, are the skinfold test, mainly the tricipital skinfold, because it is best related to total body fat, and Bioelectrical Impedance Analysis (BIA), which assesses the two main compartments of fat-free mass and fat mass, and is based on the ability of the human body to conduct electricity.

Dual-energy X-ray absorptiometry (DEXA), computerised tomography (CT), and magnetic resonance imaging (MRI) are the standard techniques to assess local distributions of fat, especially in obesity. However, their use in routine clinical practice is limited, due to their high cost, technical complexity, and radiation exposure in the case of CT, and at present, they are primarily research tools [3, 4].

The first step in identifying obese patients in an oncological context is to systematically include weight and height in physical exams, and also to calculate the BMI by dividing the weight in kilograms by the square of the height in meters (kg/m^2). A BMI of 25 or greater is considered overweight, and above 30 indicates obesity. Obtaining the BMI value also helps to raise awareness when obesity is present, both for physicians and patients [2].

Essentially, obesity is defined as an excess in body fat, which means to exceed the normal range of 12–20% of body weight in men and 20–30% in women [4]. The distribution of fat is crucial in assessing the risk of comorbidities. Thus, abdominal obesity is related to metabolic and cardiovascular alterations, as well as to the development of some cancer types. Measurement of the waist circumference (at the midpoint between the lower edge of the rib and the iliac crest) is strongly associated with abdominal fat. A waist measurement greater than 88 cm for women and 102 cm for men is considered central obesity, although the limits are different for Asian and Sub-Saharan populations, as well as for Central and South American ethnicities [3, 4].

Although this is usually the first time that a patient receives information regarding the strong link between obesity and cancer, it can also be a good motivator to adopt healthy changes in the cancer patient's lifestyle and eating habits [2].

The impact of obesity on cancer patients

Among the multiple comorbidities that cancer patients may present, obesity can have the highest impact on the patient's prognosis. Thus, in 2014, the American Society of Clinical Oncology (ASCO) published an article stating its position on this matter [5]. This article highlights the higher cancer incidence among the obese (and otherwise healthy) population, the increased risk of recurrence and cancer-related death in obese patients, and risk of developing secondary tumours and decreases in treatment efficacy, as well as a higher incidence of discontinuing cancer therapy [5–8].

A lower participation rate of obese patients in early detection programs has also been observed, and this factor likewise influences their prognosis. The main reasons cited for this low participation are: technical difficulties in physical exams, inadequate equipment, and the patient's refusal or rejection of the examinations, especially in breast and cervical cancer screening in women [9–11].

On the therapeutic strategy

In obese patients, cancer staging and performing imaging tests or endoscopic studies can be more difficult, which adversely affects the planning of a proper therapeutic treatment plan [12, 13].

Surgery

Obese patients have a higher rate of surgery-associated complications, which explain the higher associated mortality rates. The technical difficulties that attend certain surgical interventions could contribute to higher local recurrences [14]. In addition, an increase in post-surgery complications can have an impact on the subsequent adjuvant treatment, increasing the time to treatment administration, and even preventing it in some cases. Table 1 shows the main surgery-associated complications [14–18].

Radiotherapy

Although the influence of obesity on the efficacy of radiotherapy is controversial, there are technical limitations that interfere with obese patient management. Radiation treatment planning requires more attention to prevent systematic errors, especially for daily reproducibility of the treatment. Such errors can cause improper irradiation of the tumour and adjacent organs, leading to worse results and increased mortality in obese patients [12, 19, 20]. These post-surgical complications can affect the later use of adjuvant radiotherapy and, consequently, exacerbate patient survival [21]. As a result, some authors suggest brachytherapy and intraoperative irradiation as feasible alternatives to external beam irradiation for obese patients [22].

Hormone therapy

Obesity is linked to high-risk rates for breast and prostate cancer. Both cancers are highly sensitive to hormone treatments. At the same time, overweight and obesity are linked to a higher risk of recurrence and breast cancer death [7], although there are to date no conclusive studies of prostate cancer patients [23].

Table 1 Complications linked to surgery in obese patients with cancer

1. Thrombotic events (RR 1.5)
2. Slower wound healing
3. Increased surgery time
4. Prolonged hospital stays
5. Infectious complications
6. Glycaemic, cardiac decompensation, etc

In women, obesity and the presence of higher amounts of adipose tissue can promote higher levels of circulating oestrogens, which are derived by androgen conversion via the aromatase enzyme. However, patients with breast cancer and obesity who receive treatment with aromatase inhibitors (i.e., letrozole and anastrozole) have lower plasma oestrogen levels than at the start of treatment. Even then, those levels are twice as high as in normal weight patients who are receiving the same treatment [24].

Two studies in postmenopausal patients with hormone receptor-positive breast cancer have shown an association between higher BMI and reduced efficacy of treatment with anastrozole or aminoglutethimide vs. tamoxifen [25, 26]. In the "Arimidex, Tamoxifen Alone or in Combination (ATAC)" study, patients who received anastrozole treatment and had a high BMI (>35 kg/m^2) at the start of study had a higher probability of recurrence than those with a low BMI (<23 kg/m^2), both at a local and metastatic level [hazard ratio (HR) 1.39; confidence interval (CI) 95% 1.06–1.82 and HR 1.46; CI 95% 1.07–1.61, respectively] [25]. The authors concluded that anastrozole treatment in obese patients can be ineffective in fully inhibiting the aromatase enzyme. In the "Austrian Breast and Colorectal Cancer Study Group-6 (ABCSG-6)", overweight women who received treatment with tamoxifen and aminoglutethimide had worse progression free and global survival rates (HR 1.78; CI 95% 1.12–2.83 and HR 2.28; CI 95% 1.16–4.51, respectively) than women with normal weight at the start of study. However, no differences in the results based on the BMI were observed for those patients who only received tamoxifen [26].

The ABCSG-12 study compared treatment with anastrozole and tamoxifen in premenopausal patients treated with goserelin for ovarian suppression [27]. In overweight patients who received anastrozole, a higher risk of recurrence and worse overall survival rates were observed compared to patients with normal weight (HR 1.53; CI 95% 1.01–2.31 and HR 1.93; CI 95% 1.04–3.58, respectively) [27]. The results for all these studies suggest that hormone receptor-positive breast cancer patients with obesity or overweight received less benefit from treatment with aromatase inhibitors than do patients with normal weight.

In patients diagnosed with prostate cancer, obesity is related to a higher biochemical recurrence rate and higher specific mortality [28]. Anti-androgen therapy can be ineffective in obese patients, because incomplete suppression of testosterone secretion in these patients results in inadequate castration. This could be due to smaller drug concentrations in the target tissue, because the overall distribution area is larger [29]. A retrospective study published in 2011 showed that patients with prostate cancer and obesity who had received androgen deprivation therapy after radiotherapy presented a higher risk of metastasis and prostate cancer

mortality (HR 3.58; CI 95% 0.77–16.65; and HR 8.21; CI 95% 0.97–69.72, respectively) [30]. Although there are several hypotheses about the exact relationship between obesity and the evolution and prognosis in prostate cancer (lower testosterone levels, although more aggressive tumours…), there is yet no solid evidence and, especially, no reliable studies on human tissue.

Chemotherapy and targeted therapies

In oncology, the body composition measurement most frequently used to calculate chemotherapy doses is the body surface area, initially proposed by Pinkel in 1958 for the paediatric population [31].

In daily clinical practice, many oncologists limit the chemotherapy dosage to a maximum body surface area of 2.0 m^2 from concerns over higher toxicity and overdose risk [32]. However, several authors have documented that obese patients can tolerate full doses [33]. In light of this controversy, ASCO published clinical practice guidelines based on a systematic review of the literature between 1996 and 2010. This document showed that up to 40% of obese patients receive limited doses, despite the fact that full-weight-based cytotoxic chemotherapy doses are recommended to treat these cancer patients, mainly if the treatment objective is healing [34]. No evidence has been found for increased short- and long-term toxicity in obese patients who received full-weight-based doses. It should be noted that this recommendation applies only to chemotherapy and not to molecular-targeted therapies.

At present, there are few available data on the targeted therapy dosage for obese patients. Regarding monoclonal antibodies, there is no unified dosage regime for cancer patients in general: many of these agents are dosed according to body weight, others according to body surface area, and still others at fixed doses. For tyrosine-kinase (TKI) and mTOR inhibitors, doses are fixed (e.g., mg/day), and not adjusted according to body weight or body surface area. There are no clinical guidelines that address dosage for monoclonal antibodies, biologic therapies, TKI, or any other molecular-targeted therapy.

On the follow-up of the patient

The concept of cancer survival refers to all cancer-related physical, psychosocial, and economic problems, beyond the diagnosis and treatment phases. It includes everything related to the ability to obtain medical care, follow-up, care for the late effects of the treatment, second cancers, and the patient's quality of life [35]. The third in the classical stages of cancer survivorship, permanent survival, extends beyond remission and can be identified as the stage of cancer healing [36]. At this stage, not only do the secondary effects (prolonged or late) of the received treatments become more important, but there is also a higher risk of experiencing health issues, such as heart failure, osteoporosis, arterial hypertension, endocrinopathies, cognitive alterations, and obesity.

In the studies conducted among several groups of adult survivors of high-incidence tumours (breast, prostate, or gynaecological cancers), it was observed that up to two-thirds of the cured patients are overweight or obese, while less than 30% of the patients comply with the physical activity guidelines [37]. The broader-based and more reliable studies are those conducted in populations of patients who survived cancers during childhood and youth. In such an extensive cohort, practically, every patient has a chronic comorbidity by 45 years of age and a seven-fold higher risk of dying due to cardiovascular disease than general population. With its high prevalence, obesity plays a dominant role in this scenario. An extended analysis concludes that persons who survived cancers during childhood and youth have double the risk of being overweight and obese than do members of the same-age control population. Among the factors related to this high prevalence are changes in the diet, lack of regular exercise, and weight gain during the treatment phase of the cancer [38, 39].

Weight control through diet and exercise is very important for patients who have survived cancer, because this will have a considerable impact on the reduction of recurrences, second cancers, and cancer-related deaths. Furthermore, obesity prevention reduces cardiovascular and metabolic events [40]. Most studies of the relationship between obesity and the risk of recurrences or secondary cancers in the follow-up of cancer survivors have been conducted on high-incidence solid tumours. Obesity has been related to a worse prognosis in triple-negative breast cancer patients receiving neoadjuvant treatment [41]. Although axillary nodal involvement is the only prognosis-related clinical factor that exhibits significance in a multivariate analysis, obesity and menopausal status are promising prognosis factors. In a study conducted on 6295 women with oestrogen-receptor-positive breast cancer, a series of factors related to healthy habits were followed for 5 years: change in weight, BMI, physical activity, and alcohol and cigarette consumption. A weight increase greater than 10% and obesity have been linked to an increase in the late recurrence risk of breast cancer [HR 1.24; (95% CI 1.0–1.5)] [42].

Obesity has also been linked to survival in patients diagnosed with colorectal cancer [43]. Of 634 patients who were monitored until disease progression or death, type II obesity was linked to death risk, but not so clearly to progression-free survival. In stage I–III patients who were younger than 50 years of age, the presence of obesity increases the death risk two-to-five times [43]. Obesity has

also been linked to worse survival and worse quality of life in patients diagnosed with endometrial cancer. In a literature review that analysed over 4000 references to studies of endometrial cancer survivors, it was observed that an increase in physical activity and controlling obesity led to a better quality of life and healthy habits for these patients [44]. A similar study linked BMI, physical activity, and quality of life in patients who survived ovarian cancer, and recommended measures to promote physical activity and weight control [45].

There are many publications that emphasise the role of the oncologist in the patient's health education. The transition from being a cancer patient to being a survivor is the best opportunity to educate regarding lifestyle changes that might help to reduce the risk of recurrence and other diseases, as well as to improve quality and quantity of life [5]. It is essential to continue the research in this field to better understand how diet and weight control can affect cancer survivors, to establish biomarkers and basic research paradigms, and to emphasise the importance of the patient's learning about healthy life habits [46].

Managing obesity in the cancer patient

Dietary pattern during and after the treatment of cancer patients

From a nutritional perspective, obesity is a highly prevalent chronic metabolic problem that poses a true intervention challenge in cancer patients. There are three critical points of interest concerning dietary pattern interventions.

Dietary pattern to prevent the development of cancer

Tackling obesity to reduce cancer development must become a priority, together with reducing smoking and other risk factors [2]. At this prevention stage, the intervention should be planned as an alteration of habits that leads to weight loss that is sustained more than 5–10% in time [47].

A healthy diet is encouraged, always prioritising foodstuffs of vegetable origin. To maintain a healthy weight, excesses are discouraged; red and processed meat consumption should be limited; at least two and a half portions of fruit and vegetables should be consumed every day; whole grain cereals should be chosen over refined products; and alcohol consumption should be restricted. All this should be combined with physical exercise and lifestyle measures ("Appendix 1") [48, 49]. Apart from these general guidelines, there are specific dietary measures for different tumours, such as limiting exposure to aflatoxin in food or not having food or drinks that are too hot [50].

Dietary pattern during cancer treatment

After a malignant disease has been diagnosed, during the specific therapeutic plan of the disease (surgery, chemotherapy, and/or radiotherapy), the nutritional intervention should be focused on maintaining lean mass, as this is one of the most important factors for the patient's functionality and quality of life ("Appendix 2"). Weight loss in patients who are receiving treatment has been associated with an increase in the risk of malnutrition and associated consequences [51].

During treatment, the diet must cover the patients' protein-caloric needs and be adapted to their stress situation on an ongoing basis. An approximate estimate of the necessary caloric intake would be 25–30 kcal and 1.2–1.5 g of protein for each kg in weight as adapted for calculation. Obesity-specific formulas can also be used. Under these circumstances, the diet should be adapted to maintain said protein intake with dairy foods, fish, eggs, legumes, and meat. "Empty" calories, such as those in fat, should be limited, especially saturated fats and refined sugars [5]. Diet adaptation should be individual, according to the symptoms associated with the active treatment, such as dry mouth, nausea, diarrhoea, weight loss, or gain [52].

Lean mass control can be performed by measuring lean fat with impedancemetry or other anthropometric measurements. In addition, muscle function can be measured by dynamometry or a walk test. In this respect, keeping up with a physical activity program is the only safe way to maintain lean mass during cancer treatment.

Dietary pattern after treatment

The patients who have overcome the disease are at a higher risk of obesity, especially "sarcopenic obesity", and the metabolic complications associated with poor nutritional habits and inactivity. That is the reason why long-term obesity treatment is so important [37].

At present, there are study data from assessment of the impact of weight loss on cancer patients, especially breast cancer, through behavioural strategies aimed at calorie restriction and increasing physical activity [44, 53, 54]. Calorie restriction, increased physical activity, and behavioural orientation constitute the basis for weight control, and should be recommended as the main strategies for losing weight [55].

A highly practical approach is necessary, one that includes BMI assessment and structured weight loss recommendations. In some cases, referral to specialised services may be necessary for some patients. In this way, they will receive the necessary nutritional attention and be included in cancer rehabilitation programs aimed at obesity prevention or reduction through changing dietary habits and healthy exercising ("Appendix 3").

Lifestyle interventions are not a routine part of cancer care [46]. The achievement of persistent weight loss is not clearly established in practical clinical interventions for the diet, physical activity, and weight control in cancer survivors [56]. There are various resources on the internet for health professionals and patients that describe nutritional intervention during and after cancer treatment ("Appendix 4").

Physical activity during and after the treatment of cancer patients

Although there are several studies that evidence the beneficial effect of physical activity on recurrence and survivorship of some cancers, as well as on the improvement of general physical status, psychological well-being, quality of life, body composition, self-esteem, muscle mass, and strength, there are no published studies that assess physical activity as part of the weight loss treatment in obese patients who are cancer survivors and that address the long-term effects on obesity-related comorbidities [57].

Women with breast cancer who practice regular physical activity show a reduction in specific mortality of 30% and a recurrence of 50% [58]. In lymphedema patients, exercising the upper limbs seems to reduce its incidence and severity [59]. In patients who have survived colon cancer, the published studies show a reduction in specific mortality and a cancer recurrence of around 50%. However, less than 30% of the patients in this category do exercises [37]. The ongoing CHALLENGE study evaluates the long-term effects of physical exercise on colorectal cancer [60]. Although data are scarce, prostate cancer patients who participated in a physical exercise programme that consisted of walking 90 min per week achieved a mortality reduction up to 46% over sedentary patients [61].

Exercise helps cancer survivors to cope with physical and psychological challenges. The American College Sports Medicine (ACSM) [5] and ASCO [62] guidelines explicitly recommend cancer patients to:

1. avoid inactivity;
2. follow the physical activity recommendations for the general population, if health status and physical fitness allows it (150 min of moderate activity or 75 min of vigorous activity weekly). It is also advisable to do strength exercises twice weekly to enhance muscular mass;
3. engage in prescribed exercises, taking into account that there are peculiarities that can limit some patients, such as the surgery or radiotherapy undergone, or the risk of infections due to immunosuppression (e.g., requiring avoidance of public gyms). Survivors with bone metastases must change the way they practice exercise to reduce impacts and intensity and thus avoid fractures.

Pharmacological treatment during and after treatment

Since treatment with orlistat (Xenical®) for obese patients was approved in Spain in 1998, no other treatment was marketed until 2015 when the European Medicines Agency (EMA) approved two new treatments: liraglutide (Saxenda®) and a combination of bupropion (360 mg) with naltrexone (16 or 32 mg) (Mysimba®) (Table 2). However, there are more medicines available in the United States, including lorcaserin and the extended-release formulation of the phentermine/topiramate combination [63]. No clinical trials have yet been conducted to assess the efficacy and safety of these drugs to treat obese patients with cancer, but is seems logical to imagine a result similar to that achieved in patients without cancer.

Liraglutide, an agonist of glucagon-like peptide-1 (arGLP-1) receptor, is known as an approved treatment for type 2 diabetes mellitus (DM2), with a maximum dose of 1.8 mg daily and subcutaneous administration. Weight losses at 3.0 mg doses range from 5.7 to 8.0% of the initial weight, and gastrointestinal symptoms (nausea and vomiting) are the best known adverse effects, especially during the first weeks of treatment. The naltrexone/bupropion combination is administered orally and can decrease the initial body weight by 5.4–8.1%. The most frequent adverse effects with this combination are headache, dry mouth, nausea, and dizziness, and they occur at the start of treatment.

The use of arGLP-1 in patients with DM2 has been compromised from the start by the appearance of pancreatic cancer and medullary carcinoma of the thyroid. However, it has been noted that the concentration of GLP-1 receptors in human pancreatic tumoural tissue is significantly less than in the surrounding healthy tissue. They are also usually absent in those tumours with longer diameters, lymphatic metastasis, and clinically associated with a worse prognosis [64]. There are no studies of arGLP-1 treatment in humans that support a stimulating effect on the calcitonin levels or on the development of C-cell hyperplasia [65]. In fact, a research study has shown that activation of glucagon-like peptide-1 receptor has an antitumour effect on human pancreatic cancer cells, mainly by inhibiting the PI3K/AKT pathway [64]. Despite this, it seems logical to avoid this drug family for obesity treatment in patients with a history of medullary thyroid carcinoma or multiple endocrine neoplasia type 2.

Medication for obesity in cancer patients should follow the same guidelines as for people without a history of cancer [63]. This includes escalation of the available doses for each drug and an initial follow-up after the first month of treatment, thereafter being quarterly. Likewise, suspension of treatment is recommended if, after 3 months, the patient did not lose more than 5% of the initial weight.

Table 2 Medicines approved by the European Medicine Agency (EMA) for the mid- and long-term obesity treatment

	Pancreatic lipase inhibitors	Combination of opioid antagonists/antidepressants	Human GLP-1 receptor agonists
Marketed in Spain	Yes	Intended for the first half of 2017	Yes
Generic name	Orlistat 60 mg and 120 mg	Naltrexone/bupropion 8 mg/90 mg	Liraglutide 6 mg/ml
Formulation	Capsule	Tablet	Prefilled pen
Brand name	Alli® (60 mg) Xenical® (120 mg)	Mysimba®	Saxenda®
Doses and frequency in adults	60 mg or 120 mg t.i.d. after or during a low-fat meal	Dose escalation: 2 tablets b.i.d. for a total dose of 32 mg naltrexone/360 mg bupropion	Maintenance dose: 3 mg q.d.
Average of weight loss compared to placebo	2.5 kg (60 mg) 3.4 kg (120 mg)	2.0–4.1 kg (32 mg/360 mg)	5.8–5.9 kg
Common side effects (incidence >5%)	Abdominal pain, abdominal discomfort, rectal vs. faecal urgency, malabsorption of fat soluble vitamins (A, D, E, K), nausea, vomiting, constipation, headaches, drug interactions (e.g. cyclosporine, levothyroxine sodium or anticonvulsants), potentiation of the effects of warfarin	Nausea, vomiting, constipation, headaches	Nausea, vomiting, diarrhoea, constipation, headaches
Serious adverse effects	Hepatic failure and oxalate nephropathy	Depression, development of a maniac phase	Pancreatitis; contraindicated with a personal or family history of MTC (for development of hyperplasia and C-cell carcinoma in rodents), MEN2, acute renal failure (associated with persistent vomiting)

b.i.d. twice daily, *MTC* medullar thyroid carcinoma, *MEN2* multiple endocrine neoplasia type 2, *q.d.* once daily, *t.i.d.* three times a day

Bariatric surgery

There is no reason to reject bariatric surgery for an obese patient with no cancer history when his/her medical team considers that the patient is disease free. Doubts surface when the patient has an active cancer process, or has had it immediately before treatment. There are no studies available that address this problem, but some practical experiences have been reported.

In 2009, Gagné et al. conducted a retrospective study that described 36 patients with a previous history of cancer who underwent bariatric surgery: two patients who were diagnosed with cancer during the pre-operative assessment, and another two whose cancers were discovered during the surgery (a renal carcinoma and a low-grade lymphoma) [66]. During follow-up, two patients were diagnosed with a relapse of the original neoplastic process (a renal cell carcinoma and a melanoma), while the third had a new cancer that was unrelated to the primary. The study concluded that bariatric surgery does not seem to be contraindicated in patients with a cancer history.

Despite the weight loss caused by the catabolic processes in cancer patients, bariatric surgery can be considered a preliminary step that facilitates a more efficient, subsequent therapeutic approach. The use of vertical sleeve gastrectomy has been reported in four patients who had both morbid obesity and a neoplastic process (a carcinoid tumour of the small intestine, two hypernephromas, and a prostate cancer) as a step preliminary to definitive surgery treatment, with no post-surgery short-term morbidity [67].

In 2015, Kim et al. performed a metabolic surgery on 30 patients with DM2, a BMI of less than 35 kg/m^2, and a previous history of radical gastrectomy for a gastric cancer [68]. The patients underwent a Roux-en-Y gastrojejunostomy, and not only there was a significant improvement of the BMI at 12 months, but also remission of the DM2 in 30% of the patients and metabolic improvement in 20%.

Finally, the role of bariatric surgery should be noted when tackling obesity caused by surgery for a craniopharyngioma. The treatment for this cancer type, usually located in the hypothalamic hypophyseal region, causes the appearance of "hypothalamic obesity" in half of all patients. In a review of 21 cases with different surgical approaches (8 vertical sleeve gastrectomies, 6 Roux-en-Y gastric bypasses, 6 gastric bands, and a biliopancreatic

diversion), relatively low weight reduction was observed at 12 months (15.1 kg average) [69].

In conclusion, a previous cancer history must not be considered an absolute contraindication for bariatric surgery. In fact, it can sometimes be a useful tool to provide more effective cancer therapy for patients with morbid obesity.

Psychosocial support

More than half of European patients diagnosed with cancer survive 5 years or longer after their primary diagnosis [70]. The cohort studies show that, when compared to patients with no history of cancer, these patients have higher anxiety levels that can be expressed as normal feelings of vulnerability or sadness, or as extreme symptoms of distress, fatalism, hopelessness, panic, refusal, or avoidance [71].

There are many narrative reviews of this topic, as opposed to systematic reviews and meta-analysis. The International Psycho-Oncology Society (IPOS) has proposed several guidelines to improve integrated care for cancer patients, their families, and caregivers while at the same time searching for solid evidence-based arguments to support its position [72]. This society declares that (i) quality care for the cancer patient should integrate psychosocial aspects into routine care and that (ii) the anxiety should be measured as a sixth vital sign, after temperature, blood pressure, pulse, respiratory rate, and pain. This view is also supported by the National Comprehensive Cancer Network (NCCN), and other scientific societies.

Reviews of the literature on the effectiveness and benefits of psychosocial interventions in cancer patients suggest weaker evidence than previously thought. The more thorough the review, the lower the probability of concluding that psychosocial interventions are effective [73].

The literature review conducted by Villoria et al. concluded that the cases analysed showed favourable results regarding the improvement of the patients' emotional, physical, functional status, as well as their quality of life [74]. However, the methodological limitations and, at times, conflicting results warrant caution when drawing conclusions about whether or not psychological intervention in cancer is effective, and the benefits of its application.

The importance of several aspects, such as encouraging the patient-physician relationship, providing clear and adequate information, offering support, and trying to improve the emotional, physical, and functional status of patients, has been highlighted during all phases (diagnostic, treatment, disease free/survivorship stage, and relapse/terminal disease phase). This would help to reduce uncertainty, facilitate decision making, and improve adjustment to the disease. Above all, though, it would improve the patient's quality of life. The review stresses the need to design psychological interventions that are tailored to the patient's needs and that reflect the characteristics of each phase of the disease [74].

In its report on psychosocial intervention for cancer patients, the Institute of Health Carlos III draws the same conclusions, stressing the importance of a customised intervention for each patient throughout the cancer process to achieve the best efficacy [75].

The importance of multidisciplinarity when managing obese patients with cancer

A multidisciplinary approach is needed to manage obesity in cancer patients. This is not just a catch phrase, but a reality. It is obvious that the central axis of cancer patient care is the oncologist. This implies something as simple as identifying obesity as a possible medical problem for these patients. Nevertheless, advice about the need to change lifestyle habits will be more convincing if it comes from the oncologist, a specialist who has played a crucial role during the course of the disease.

The nursing staff in oncology departments, who know the patients and are adequately trained and motivated, can likewise play a very important role and provide a few basic rules on how to change one's lifestyle with the aim of losing weight. This nursing task could be coordinated with the primary care physician in programs designed and agreed to by both levels of care.

The endocrinologist, together with the dietician and nutritionist, is the specialist who is most qualified to treat obesity specifically. Considering the present infrastructure of most endocrinology departments, there are obvious challenges in assuming direct responsibility for the care of all patients who have various degrees of obesity and cancer. According to the underlying oncologic disease, the nutritional status, the degree of obesity, the food intake capacity, and the integrity of the digestive tract, the complexity of the nutritional intervention can require participation by the endocrinologist and nutritionists.

Psychologic support for this problem can be very useful. It is advisable to agree the roles jointly in each centre for each one of the functions and to optimise the attention focused on the crucial problem of obesity in cancer patients (Fig. 1).

Conclusions

The oncologist must inform the patient about the relationship between obesity and several types of cancer, and also remind him/her about the importance of losing

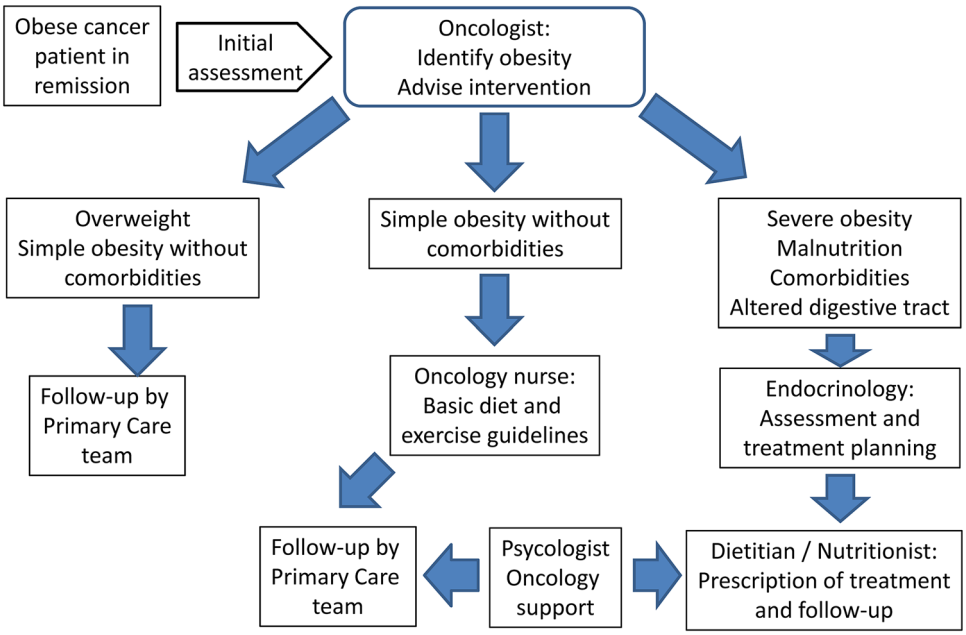

Fig. 1 Multidisciplinary approach to the obese patient with cancer

weight, because obesity is also associated with a high risk of cancer-related recurrences and mortality. Furthermore, obesity interferes with the effectiveness of systemic treatments play a role in treatment morbidity and increase the risk of secondary tumours. Obesity is one of the comorbidities with the highest impact on the prognosis. Obese patients have a higher rate of surgery-associated complications. For the most frequent types of cancer, obesity is correlated with a higher biochemical recurrence rate and a higher specific mortality. Controlling concomitant health problems, such as obesity, is very important for prolonged survival after remission, the healing phase of cancer. Dietary intervention and physical activity are very important for patients who are cancer survivors, because this will have a considerable impact on reducing recurrences, second cancers, and cancer-related deaths. The transition from being a cancer patient to a cancer survivor is the best opportunity to educate regarding lifestyle changes that might help to reduce the risk of recurrence, associated diseases, and improve the patient's quality of life.

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Compliances with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest that could inappropriately affect this work.

Ethical statement The study has been performed in accordance with the ethical standards of the Declaration of Helsinki and its later amendments. This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

Appendix 1: Dietary pattern for cancer prevention

A healthy lifestyle based on a balanced and diversified diet and regular physical exercise, as well as avoiding toxic substances, reduces significantly the risk of cancer. Learning how to eat in a healthy and balanced way means regaining health. All foods provide different types of nutrients. Some studies have shown that the Mediterranean dietary pattern is effective to prevent some tumours.

Key Points:

- Choose a variety of foods in such quantities that help to maintain a healthy weight.
- Eat fruits and vegetables 3–5 times a day.
- Choose legumes, whole wheat, and unrefined cereals.
- Eat fish and lean meats. Limit consumption of processed and red meat.
- If you drink alcohol, limit consumption. Women should not exceed one drink per day and two for men.
- Fats of animal origin should be limited. Consume 3–5 tablespoons of extra virgin olive oil per day, preferably raw or cooked at low temperatures.

General recommendations: Establish an adequate balance among the three major groups of macronutrients (50–60% carbohydrates, 15–20% proteins, and 20–30% fats).

The carbohydrates found in fruits and vegetables provide the vitamins and minerals that are essential for proper body function. These should be complemented with legumes

(lentils, peas, beans, chickpeas, etc) and wholegrain cereals (brown rice, wholemeal flour, and wholemeal bread).

Proteins are nutrients that are mainly structural. They can be of animal origin (fish, lean meats, such as poultry breast and thigh, loin of pork, leg of lamb, sirloin steak, etc, dairy products and eggs) or vegetal (legumes, soy, cereals, etc). Dairy products are essential as mixed foods.

Fats are structural and energetic nutrients. It is important to distinguish between less healthy (saturated) and healthy (unsaturated) fats, such as extra virgin olive oil, nuts, or blue fish. Food should be cooked lightly, such as by boiling or steaming, and fried foods should be avoided.

It is essential to maintain proper hydration, regular meals, and to complement these nutritional guidelines with daily physical exercise.

Example of a plate of food:

Appendix 2: Dietary pattern during cancer treatment

An optimal, healthy, and balanced diet contributes to better tolerance of cancer treatments and improved quality of life. Cancer patients have different nutritional needs, and their eating habits can be altered by several factors. This can lead to cases of malnutrition, by excess or deficiency.

With an adequate diet prior to starting treatment, the patient will build up the nutritional reserves needed to maintain energy and reduce side effects. The importance of diet and hydration during treatment should not be overlooked.

Key Points:

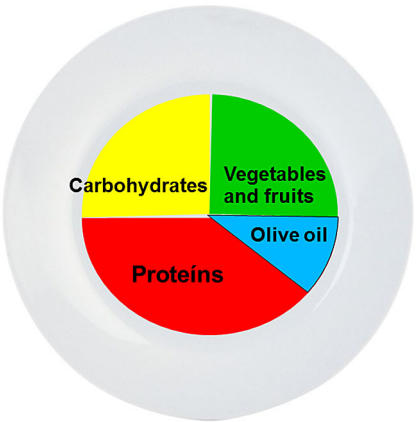
- Follow the Mediterranean diet standard, without avoiding your favourite meals.
- Organise daily intake into 5–6 meals, according to a timetable of your choosing, and keep in mind that meals should not be more than 2–3 h apart, if possible.
- Plan the energy-protein enrichment of your diet by adding dairy products (such as milk powder or grated cheese), eggs (cut up in salads, with soups or vegetables, beaten into mashed potatoes, soups, creams, gravies, and milk shakes), and meat or fish (in salads, gravies, fillings for omelettes, casseroles, and stews).
- Try to maintain an intake of five vegetable servings (fruits and vegetables) per day. Remember that these are low-energy foods, so they cannot be a substitute for other sources of carbohydrates, such as potatoes, pasta, or rice.
- Use simple cooking techniques, such as baking or steaming, and adapt them to your needs throughout the day (crushed, easy to chew, nutritionally enriched with proteins, and/or healthy fats, etc).
- If you cannot tolerate solid food, you can prepare milk shakes, juices, creams, soups, etc, and nutritionally enrich these with proteins and/or healthy fats (egg whites, grated cheese, or extra virgin olive oil).

General recommendations: A more personalised balance of the three major groups of macronutrients should be established by increasing protein consumption up to 1–1.5 g/day (40–50% carbohydrates, 20–25% proteins, and 20–30% fats).

Carbohydrates are an essential source of energy, but proteins are nutrients that are fundamentally structural. Consumption of fish and poultry should be increased, and red meat should be avoided. Choose smaller portions with high nutritional content, and enrich meals with proteins and/or healthy fats that are easy to digest.

Moderate physical activity complements all of these guidelines, as well as drinking two litres of liquid a day, preferably water. If you experience weight loss, digestive symptoms, severe anorexia, nausea, or vomiting, please consult your physician.

Example of a plate of food:



Appendix 3: Dietary pattern after cancer treatment

Patients who have survived cancer have special nutritional needs due to the risk of late secondary effects, such as obesity, cardiovascular diseases, and metabolic syndrome. Certain healthy diet and physical activity habits can also reduce the risk of cancer recurrence for cancer survivors. Obesity and its comorbidities are one of the most important treatable factors. A healthy diet and lifestyle are habits that can improve quality of life for cancer survivors.

Nutritional plans have been centred on diets with low calorie content, low-fat content, low carbohydrate content, and a Mediterranean pattern. At present, there is not enough data to endorse one type of diet over others. Following cancer treatment, it is advisable to consider a global rehabilitation of your habits and lifestyle directed at improving the quality of life.

Key Points:

- The foundation of your eating habits should be vegetable foods with a wide variety of fruits and vegetables.
- Eat foods that are low in fat, salt, and rapidly absorbed sugars.
- Avoid toxic substances, such as alcohol or cigarettes.
- Control your weight. In case of obesity, reduce and maintain a healthy weight.
- Engage in physical activity for 30 min most days of the week.
- Stress control is a key factor.
- Make the time to consider these guidelines and start making changes to acquire a healthier lifestyle.

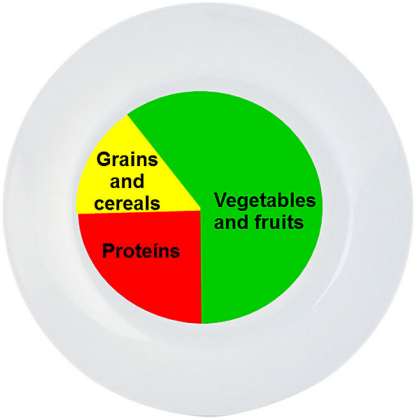
General recommendations: A balanced diet adjusted for actual energy expenditure should be established to avoid weight gain. At this point, it is important to limit high-energy food, such as fats and carbohydrates (40–50% carbohydrates, 15–20% proteins, and 20–30% fats).

The way to control weight is to consume carbohydrates from vegetables and fruits, and reduce the quantity of other foods with a higher energy density, such as bread, potatoes, pasta, or rice. At the same time, consume low-fat protein sources, such as fish and lean meat, low-fat dairy products, or egg whites.

Low lean mass together with an increase in fat mass (sarcopenic obesity) is a common occurrence following cancer treatment, so it is essential to engage in moderate physical activity to control and maintain long-term weight loss.

Following a healthy and balanced diet will help you to recover from the treatment effects and to enjoy a better quality of life. In the long term, it will be necessary to re-apply all the basic concepts and guidelines of the dietary pattern for the Mediterranean diet, adding the need to control total calories in the diet to control excess bodyweight.

Example of a plate of food:



Appendix 4: Online resources for healthcare professionals and patients

Online Resources For Healthcare Professionals

American Cancer Society (ACS) Guidelines

http://www.cancer.org/healthy/eathealthygetactive/acsguidelinesonnutritionphysicalactivityforcancerprevention

http://onlinelibrary.wiley.com/doi/10.3322/caac.21142/full

Clinical guidelines to identify, assess and treat overweight and obesity in adults from the National Heart, Lung, and Blood Institute (NHLBI)

http://www.nhlbi.nih.gov/guidelines/obesity/prctgd_c.pdf

Strategies for prevention of obesity from the Center for Disease Control and Prevention (CDC)

http://www.cdc.gov/obesity/resources/recommendations.html#Obesity http://www.cdc.gov/obesity/childhood/solutions.html

Online resources for patients

http://www.choosemyplate.gov/en-espanol.html

http://www.niddk.nih.gov/health-information/informacion-de-la-salud/control-de-peso/para-adultos/Pages/como-mejorar-su-salud-consejos-para-adultos.aspx

http://www.nhlbi.nih.gov/files/docs/public/heart/parent_curr.pdf

http://www.cancer.org/healthy/eathealthygetactive/acsguidelinesonnutritionphysicalactivityforcancerprevention/acs-guidelines-on-nutrition-and-physical-activity-for-cancer-prevention-intro

American Institute for Cancer Research

http://www.aicr.org

Seattle Cancer Care Alliance. Food Safety Guidelines

http://www.seattlecca.org/food-safety-guidelines.cfm

US Food and Drug Administration. Overview of Dietary Supplements

http://www.fda.gov/Food/ResourcesForYou/Consumers/ucm109760.htm

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