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Epidemiological Data on the Nutritional Status of Cancer Patients Receiving Treatment with Concomitant Chemoradiotherapy, Radiotherapy or Sequential Chemoradiotherapy to the Abdominopelvic Area

Aurora Serralde-Zúñiga[1§], Denisse Castro-Eguiluz[2§], José Luis Aguilar-Ponce[3], Angélica Andrea Peña-Ruiz[3], Jorge Víctor Castro-Gutiérrez[3], Samuel Rivera-Rivera[4], Carlos Aranda-Flores[5], Verónica Casique-Pérez[3,6], Silvia Eugenia Alarcón-Barrios[3], Jaime de la Garza-Salazar[3], Miriam Sánchez-López[3] and Alfonso Dueñas-González[7*]

[1]Department of Nutrition, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City; [2]Consejo Nacional de Ciencia y Tecnología (CONACyT) - Department of Clinical Research, Instituto Nacional de Cancerología, Mexico City; [3]Departments of Internal Medicine, Nutrition and Clinical Research, Instituto Nacional de Cancerología, Mexico City; [4]Sociedad Mexicana de Oncología A.C., Mexico City; [5]Consejo Mexicano de Oncología, A.C., Mexico City; [6]Department of Nutrition, Facultad de Ciencias de la Salud, Universidad Autónoma de Tlaxcala, Tlaxcala, Tlax , Mexico; [7]Instituto de Investigaciones Biomédicas UNAM-Instituto Nacional de Cancerología, Mexico City, Mexico.

ABSTRACT

Cancer patients are particularly susceptible to undernourishment so associated weight loss is frequent. Approximately 15% of patients lose >10% of their usual body weight, 40-80% become undernourished, and about 20% die as a result. Well-nourished patients have a higher survival rate when compared with patients at risk of undernourishment (19.9 vs. 3.7 months); hence, nutritional intervention is pivotal. Undernourishment negatively influences the patient's prognosis, and its prevalence depends on the tumor type and location, disease stage, treatment, and the applied nutritional evaluation tool. During abdominopelvic radiotherapy, up to 90% of patients experience symptoms of varying severity; weight loss during radiotherapy is an early indicator of nutritional deterioration, and he the use of radiation is associated with a higher likelihood of undernourishment. In patients with gynecological malignancies, 12.5-54% are malnourished before receiving oncological treatment, worsening after treatment in 35.8-82% of cases. There is also deterioration of the nutritional status in patients with colorectal cancer once pelvic radiotherapy is initiated, whereby 50% of cases are malnourished at the beginning of treatment, and 66 7% are so when it ends. Although there are notable differences in the impact of radiotherapy on weight according to the radiated region, 88% patients receiving abdominal radiotherapy were found to lose weight compared to 38% of patients whose treatment was limited to the pelvis. (REV INVES CLIN. 2018;70:117-20)

Key words: Epidemiology. Pelvic cancer. Radiotherapy. Chemotherapy. Nutritional status. Gastrointestinal toxicity.

Corresponding author:
*Alfonso Dueñas-González
Subdirección de Investigación Clínica
Instituto Nacional de Cancerología
Av. San Fernando, No. 22
Col. Sección XVI, Del. Tlalpan
C.P. 14080, Ciudad de México, México
E-mail: alfonso_duenasg@yahoo.com

[§]These authors contributed equally to this work.

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INTRODUCTION

Cancer patients are particularly susceptible to undernourishment and its consequent decrease in the fat and muscle compartments. It results from the adverse effects derived from the tumor or the cancer treatment, be it chemotherapy, radiotherapy, both, or surgery. All cancer treatments may compromise food intake, digestion, and nutrient absorption, hence aggravating the nutritional status of the patient. Undernourishment negatively affects the patient's prognosis as it impacts disease progression, diminishes the response to cancer treatment, worsens the patient's quality of life, increases the hospital stay, and decreases the survival rate. All these factors contribute to an increase in health-care expenses[1]. In these patients, weight loss is frequent whereby approximately 15% of cancer patients lose >10% of their usual body weight[2], 40-80% become undernourished[3], and about 20% die as a result[4]. The prevalence of weight loss depends on the type of tumor and its location, disease stage, treatment, and the applied nutritional evaluation tool. Nutritional intervention is important because well-nourished patients evaluated by the subjective global assessment (SGA) tool, have a higher survival rate when compared with patients at risk of undernourishment or that have some degree of undernourishment (19.9 months in well-nourished patients, SGA A, compared to 3.7 months in patients at risk of undernourishment, SGA B, or patients with undernourishment, SGA C)[5].

Nutritional conditions classified as malnutrition, overweight, or obesity have different implications, and all carry a bad prognosis in cancer patients. Greater histological aggressiveness has been described in overweight and obese patients with prostate cancer and those with breast cancer. Furthermore, undernourishment has been associated with histological aggressiveness in patients with lung, colorectal, head and neck, stomach and esophagus cancers[6]. A cohort study described the body mass index (BMI) of 404 patients with cervical cancer: malnourished patients (BMI <18.5 kg/m^2) with cervical cancer at stages IB1/IB2 had a decreased overall survival (hazard ratios = 2.37; 95% confidence intervals [CI], 1.28-4.38; p < 0-01)[7]. The 5-year overall survival rate was 33% for a BMI <18.5 kg/m^2, 60% for a BMI between 18.5 kg/m^2 and 24.9 kg/m^2, and 68% for a BMI >24.9 kg/m^2. A BMI <18.5 kg/m^2 was associated with an increased risk of Grade 3 or 4 complications when compared with a BMI >24.9 kg/m^2.

Depletion of muscular mass is more relevant than BMI in the nutritional diagnosis because it is associated with poor function and has an impact on morbidity and mortality, thus decreasing survival[6,8,9]. Bioelectrical impedance analysis is a technique that evaluates changes in body composition and nutritional status. Phase angle measurement, derived from bioelectrical impedance, reflects the relative contribution of fluid and cell membranes from the body whereby a smaller phase angle suggests cell death and a reduction in cellular integrity, and a greater phase angle reflects a higher amount of intact cell membranes. Phase angle measurement is a prognostic marker in diverse diseases and one of the most sensitive markers of undernourishment. In colorectal cancer patients (n = 52), a phase angle >5.57° was significantly associated with a better survival rate (median survival of 40.4 months), compared to smaller phase angles (median survival of 8.6 months)[10].

EPIDEMIOLOGICAL DATA

The type of gynecological tumor has an influence on the nutritional status, increasing the patients' risk of developing malnutrition. In a Korean study, malnutrition was found in 47.9% of cervical cancer patients, in 52.8% of ovarian cancer patients, and in 60% of endometrial cancer cases[11]. Considering the disease stage, 48% of patients in Stage I, 42.9% of patients in Stage II, 65% of patients in Stage III, and 55.6% of patients in Stage IV were undernourished. Malnutrition was more prevalent in patients who received chemotherapy than in patients not treated with chemotherapy within the previous 6 months. Depression and loss of appetite are significant predictive factors of malnutrition (odds ratio [OR] = 1.087, p = 0.01, and OR = 0.749, p = 0.002, respectively) in gynecological cancer patients[11]. Level of evidence B.

The tool used to assess nutritional status determines the prevalence of malnutrition. A cross-sectional study that analyzed 66 patients with colorectal cancer demonstrated that when using anthropometric markers, 7.6% of patients were undernourished according to their BMI, 53% were undernourished according to the tricipital skinfold, and 36.4% according

to the SGA[12]. Therefore, it is advisable to perform a complete nutritional assessment using objective and subjective tools[12] and to supply documented evidence of the deterioration in the patient's nutritional status with different nutritional assessment tools[13]. Level of evidence B.

Radiotherapy is a cornerstone of cancer treatment. It is applied to the abdominal or pelvic regions for gynecological, urological, and lower gastrointestinal cancer treatment, as a single therapy or in combination with surgery or chemotherapy. It is used to treat thousands of patients every year. During fractionated pelvic radiotherapy, administered daily for 5-7 weeks, up to 90% of patients experience symptoms of variable severity due to the proximity of the gastrointestinal tract to the pelvic organs. The symptoms experienced during treatment include changes in bowel habits in 94% of patients, loose stools in 80%, frequency in 74%, difficulty passing gas in 65%, pain in 60%, distress in 48%, tenesmus in 44%, restrictions in daily activity in 40%, urgency in 39%, and fecal incontinence in 37%[14]. In 5-10% of patients, serious chronic complications may develop, such as obstruction due to progressive fibrosis, fistulae, and vascular sclerosis[15]. Other less severe bowel symptoms appear in 6-78% of patients, which, nevertheless, compromise their quality of life. These may include urgency, frequency, fecal incontinence, diarrhea, steatorrhea, tenesmus, pain, constipation, and weight loss. The severity of acute bowel toxicity may predetermine the degree of chronic bowel changes. Therefore, early intervention to prevent or reduce acute toxicity may be worthwhile in the long term[15]. Level of evidence B.

Several studies have evaluated the impact of radiotherapy on the patients' nutritional status[15,16]. Previous or current radiotherapy has been significantly associated with undernourishment (OR= 1.53; 95% CI 1.21-1.92)[16.] Level of evidence B.

There are important differences in the impact of radiotherapy, depending on the irradiated area. In a study of patients who received abdominal radiotherapy, 88% experienced important weight loss, losing an average of 3.4 kg, in comparison to patients receiving pelvic radiotherapy, of whom 38% lost an average of 2.4 kg[17]; other authors have reported an average weight loss of 4.4 kg (p = 0.06)[18]. Level of evidence B. Furthermore, it has been demonstrated that patients with cervical cancer have vitamin deficiencies, even before they begin cancer treatment. In particular, significantly decreased levels of plasma folate, Vitamin A, and Vitamin C have been reported[19]. Level of evidence B.

Using several nutritional markers, malnutrition has been documented in women with cervical cancer more frequently than in patients with other gynecological tumors (p = 0.02)[20]. According to the patient-generated SGA, 66% of cervical cancer patients are either at nutritional risk or malnourished even before receiving cancer treatment[21,22]. Indeed, the prevalence of malnutrition in cervical cancer patients covers a wide range, varying from 4% in Stage I to 60% in Stage IV[23]. Weight loss in these patients goes in hand with a low nutrient intake, which has been reflected in altered levels of plasma phospholipids[24]. Other authors have described that 31.6% of patients with cervical cancer are at severe risk of malnutrition, as assessed by nutritional risk screening[25]. Weight loss is greater in patients receiving radiotherapy (−3.6 ± 5.6 kg, in relation to the previous 6 months), compared to untreated patients (+0.2 ± 2.2 kg), mainly as a result of gastrointestinal symptoms such as constipation, anorexia, nausea, vomiting, and diarrhea25, aside from the decreased caloric and protein intake. Undernourishment is frequently caused by a reduced dietary intake. In 31 rectal cancer patients, dietary intake decreased by 15% at 5 weeks after radiotherapy, associated to a temporary weight loss of 1 kg[26]. Another study has described this nutritional decline in patients with colon cancer: when initiating pelvic radiotherapy, 50% of patients were undernourishment, while 66.7% were undernourishment by the end of treatment ($p < 0.05$)[27]. The authors did not record a significant reduction in energy and protein intake, but a reduction in serum zinc levels was described (95.9 µg/dl-78 µ g/dl)[27]. Level of evidence B.

Using bioelectrical impedance, abnormalities in the phase angle have been described (−0.23° ± 0.37) in association with the severe weight loss (>5% of usual weight) observed in 19% of patients in the month following pelvic radiotherapy (−1.26 kg ± 2.09 kg)[28]. Moreover, once radiotherapy is concluded, patients may persist with gastrointestinal symptoms (30%-66%) depending on the type of cancer and irradiated area, and patients describe them as detrimental to their quality of life[29-31]. Level of evidence B.

CONCLUSIONS

Several observational studies have documented the negative impact of oncological treatment on the nutritional status of patients, whether treatment is based on radiotherapy, chemotherapy or both. Unfortunately, due to the heterogeneity of the patients included in these studies, the type of tumor, clinical stage, nutritional assessment, or treatment, it was not always possible to draw conclusive interpretations of the results. Even so, it is clear that cervical cancer patients are at high risk of developing undernourishment, and radiotherapy treatment further increases this condition.

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