

# NUTRIENT RECOMMENDATIONS FOR CANCER PATIENTS TREATED WITH PELVIC RADIOTHERAPY, WITH OR WITHOUT COMORBIDITIES

DENISSE CASTRO-EGUILUZ<sup>1\*</sup>, JOSÉ ANTONIO LEYVA-ISLAS<sup>2</sup>, JULISSA LUVIAN-MORALES<sup>3,4</sup>, VIRGINIA MARTÍNEZ-ROQUE<sup>3</sup>, MIRIAM SÁNCHEZ-LÓPEZ<sup>3</sup>, GUADALUPE TREJO-DURÁN<sup>3</sup>, ROBERTO JIMÉNEZ-LIMA<sup>3,4</sup> AND FANNY JOCELYN LEYVA-RENDÓN<sup>5</sup>

<sup>1</sup>Consejo Nacional de Ciencia y Tecnología (CONACyT) - Department of Clinical Research, Instituto Nacional de Cancerología, Mexico City; <sup>2</sup>Nutritional and Metabolic Support, ISSSTE Hospital Regional Lic. Adolfo López Mateos, Mexico City; <sup>3</sup>Departments of Clinical Research, Nutrition, Gynecology, and Radiotherapy, Instituto Nacional de Cancerología, Mexico City; <sup>4</sup>Postgraduate Unit, Universidad Nacional Autónoma de México, Mexico City; <sup>5</sup>Department of Clinical Nutrition, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico.

## ABSTRACT

Radiotherapy is one of the main treatment options used in pelvic cancers. Ionizing radiation induces damage to surrounding tissues, resulting in disruption of normal physiological functions and symptoms such as diarrhea, tenesmus, incontinence, and rectal bleeding, which can all significantly alter the patient's quality of life. These patients are at increased risk of developing protein-calorie malnutrition and micronutrient deficiencies. Therefore, designing a proper nutritional intervention plan, with an optimal proportion of protein, fat, and carbohydrates, is required to reduce or even reverse the patients' poor nutritional status, increase their tolerance and response to oncology treatment, decrease the rate of complications and improve their quality of life. The aim of this review was to establish a nutritional plan that includes recommendations on macronutrient proportions and micronutrient intake in patients receiving pelvic radiotherapy. The following nutritional plan has been recommended in the literature: Energy: 28-31 kcal/kg/day, using the Harris-Benedict formula adjusted for body weight in obese patients; protein: 20-30%; fat: 30-40%; and carbohydrates: 40-50%. The maintenance of adequate levels of Vitamin D, Vitamin E, Vitamin A, calcium, magnesium, thiamin, riboflavin, and niacin must be emphasized. Physical activity must also be increased to maintain muscle mass. Nutrient requirements must be established in an integral manner, considering the patient's age, nutritional status, and the presence of comorbidities. Unnecessary dietary restrictions should be avoided to ensure an adequate nutritional status. (REV INVES CLIN. 2018;70:130-5)

**Key words:** Pelvic cancer. Radiotherapy. Chemotherapy. Comorbidity. Obesity. Type 2 diabetes. Hypertension. Renal insufficiency. Elderly. Nutrient recommendations.

### Corresponding author:

\*Denisse Castro-Eguiluz  
Consejo Nacional de Ciencia y Tecnología  
Av. de los Insurgentes Sur, 1582  
Col. Crédito Constructor, Del. Benito Juárez  
C.P. 03940, Ciudad de México, México  
E-mail: [angeldenisse@gmail.com](mailto:angeldenisse@gmail.com)

Received for publication: 02-03-2018  
Accepted for publication: 03-05-2018  
doi: 10.24875/RIC.18002526

## INTRODUCTION

As a result of radiotherapy treatment of pelvic tumors, healthy tissues may become compromised by radiation, including the intestinal tract, urinary tract, bone, sexual organs, and skin. A frequent problem is the development of bowel symptoms that may lead to a decrease in food intake, diarrhea and malabsorption, thereby affecting the patients' nutritional status and quality of life. During pelvic radiotherapy treatment, weight loss is an early indicator of a decline in nutritional status. In a period of 6 weeks, approximately 50 Gy of radiation to the pelvic area is associated with a 10% weight loss in 59% of patients<sup>1</sup>. However, when cancer patients receive individualized nutritional advice, their nutritional status is not as compromised as in patients who only receive general recommendations<sup>1,2</sup>.

It is important to avoid unnecessary dietary restrictions in patients receiving this treatment modality, to ensure an adequate intake of energy, protein, fat, carbohydrates, vitamins, and minerals, and to avoid weight loss and malnutrition. When establishing nutritional recommendations for this group of patients, the patient's age, nutritional status, disease stage, treatment, and comorbidities such as obesity, diabetes, hypertension, and renal insufficiency should be considered.

## MACRO AND MICRONUTRIENT RECOMMENDATIONS FOR PATIENTS WITHOUT COMORBIDITIES

### Macronutrients

The impact of the nutritional intervention was assessed in a randomized clinical trial, using nutrition counseling following the American Dietetic Association (ADA) medical nutrition therapy protocol for radiation oncology, specifically for patients treated with pelvic radiotherapy<sup>3</sup>. According to this protocol, the recommended energy intake for these patients is 28-31 kcal/kg/day and 1.1-1.3 g/kg/day of protein. This intervention was proven to be beneficial to the nutritional status of patients, whereby they lost 400 g, compared to the control group who only received a general nutrition talk and booklet, and lost an average

of 4.7 kg. In addition, by the 8<sup>th</sup> week of treatment, 18 patients in the intervention group had an adequate nutritional status, as determined by PG-SGA A, compared with 11 patients in the control group ( $p = 0.02$ )<sup>3</sup>. Level of evidence A, strength of recommendation 1.

In the case that a patient develops post-radiotherapy enteritis and in accordance with the ESPEN guidelines, the recommended energy intake is 25-35 kcal/kg/day, considering the catabolic or anabolic conditions of the patient and the disease stage<sup>4</sup>. The previously referred ADA protocol recommends a protein intake of 1.1-1.3 g/kg/day<sup>3</sup>. In case of acute enteritis, protein intake may be increased up to 1.5 g/kg/day<sup>4</sup>.

In a controlled trial to evaluate the efficacy of a low or modified fat diet for the prevention of gastrointestinal toxicity, patients with pelvic tumors due to receive radical radiotherapy were randomized to a low-fat (20% total energy from long-chain triglycerides), modified-fat (20% from long-chain triglycerides and 20% from medium-chain triglycerides), or normal-fat diet (40% total energy from long-chain triglycerides)<sup>5</sup>. Gastrointestinal toxicity, assessed with the Inflammatory Bowel Disease Questionnaire-Bowel score, was not significantly different between groups. However, full compliance with the fat content prescription was only 9% in the normal-fat diet group, compared to 93% in the low-fat diet group, and this may have confounded the results. There is no evidence to support a low-fat diet during pelvic radiotherapy; fat recommendation for these patients is 30-40% of the total energy intake, although emphasizing that a higher proportion should be obtained from monounsaturated fatty acids. Level of evidence B, strength of recommendation 2.

Fat restriction (40 g fat per day) may be considered only when fatty acid malabsorption is present<sup>6</sup>. Level of evidence B, strength of recommendation 1. Furthermore, pancreatic enzyme supplements may be used if patients present pancreatic insufficiency or bile binders if the patient presents bile salt malabsorption, to facilitate fat digestion and absorption in patients with steatorrhea<sup>7</sup>.

The optimal proportion of carbohydrates and fat in cancer patients has yet to be determined but may be inferred from the following observations. In some

Table 1. Recommended daily intake of vitamins and minerals, and theoretical recommendations for critically ill patients<sup>11</sup>

Micronutrients	Recommended daily intake	Critically ill patients
Vitamin A	700-900 µg	3 mg
Vitamin B1	1.5 mg	100 mg
Vitamin B6	2 mg	100-300 mg
Vitamin B12	2.4 µg	5-10 µg
Biotin	30 µg	30 µg
Vitamin C	75-90 mg + 35 mg in smokers	2000-3000 mg
Vitamin D	5-15 µg	45-100 µg
Vitamin E	15 mg	1000 mg
Copper	900 µg	10 mg
Selenium	55-75 µg	300-500 µg
Zinc	8-11 mg	40 mg

cancer patients, insulin resistance and altered glucose uptake and utilization in muscle have been demonstrated<sup>4</sup>. However, fat oxidation is normal or even increased, suggesting that a higher proportion of fat over carbohydrates is beneficial. Most of the recommendations for patients with cancer anorexia are focused on increasing energy intake, and this is more easily accomplished using fat as the main energy source. Hence, when considering the protein intake that must be ensured in these patients, the recommendation for carbohydrates is 40-50% of the total energy intake<sup>4</sup>. Level of evidence B, strength of recommendation 1.

## Micronutrients

Vitamin and mineral deficiencies in cancer patients depend on their nutritional status, and the complications derived from the disease and its treatment. In a prospective study of rectal cancer patients who received radiotherapy, a temporary decrease in vitamin and mineral intake was observed<sup>8</sup>. At the end of radiotherapy, the intakes of calcium, magnesium, retinol equivalents, thiamin, riboflavin, and niacin were reduced; whereas the intakes of vitamins C, D,  $\alpha$ -tocopherol, and iron, were unchanged. At treatment completion, fiber, calcium, iron, and Vitamins D and E were below the Dietary Reference Intake (DRI), while magnesium, thiamin, riboflavin, and niacin were in the lower limit but within the DRI. Absorption of fat-soluble vitamins may be decreased if steatorrhea is present, so supplementation of these vitamins is advised if this is the case<sup>8</sup>. Level of evidence B, strength of recommendation 1.

A prospective observational study demonstrated that Vitamin D deficiency is associated with an increase in the severity of radiation-induced acute proctitis (odds ratio = 3.07,  $p = 0.013$ )<sup>9</sup>. Even though there is no evidence that proctitis may be prevented with Vitamin D supplementation, established recommendations must be considered to fulfill daily Vitamin D requirements, judging in each individual case whether the patient is exposed to sunlight or not, to activate the Vitamin D precursor in the skin. Level of evidence B, strength of recommendation 1.

A clinical trial demonstrated that supplementation with 400 mg/day of Vitamin E decreased peripheral neurotoxicity caused by cisplatin treatment, with a relative risk = 0.14 (95% confidence interval [CI], 0.2-1;  $p < 0.05$ )<sup>10</sup>. Therefore, Vitamin E supplementation should be administered to patients receiving cisplatin-based chemotherapy. Level of evidence A, strength of recommendation 1.

To the best of our knowledge, there are no established recommendations of vitamin and mineral intake for cancer patients who receive pelvic radiation therapy. Hence, the recommended daily intake of vitamins and minerals proposed by the National Academy of Sciences is a useful and safe measure in the absence of specific nutrient deficiencies<sup>4</sup>. However, the presence of reduced food intake and hypercatabolism is consistently acknowledged in cancer-associated malnutrition; hence, in severely malnourished patients, daily requirements for micronutrients may be taken from recommendations for critically ill patients (Table 1)<sup>4,11</sup>.

## NUTRIENT RECOMMENDATIONS FOR PATIENTS WITH COMORBIDITIES

### Obesity

Obesity is a risk factor for the development of cancer and mortality. It is estimated that 20% of cancer cases are related to obesity, and obese cancer patients have a worse prognosis<sup>12</sup>. Women with morbid obesity (body mass index  $\geq 35$ ) and cervical cancer were proven to have a higher risk of death (hazard ratio = 1.26, 95% CI, 1.1-1.45) when compared to women with cervical cancer and a normal weight<sup>13</sup>. Excess body fat plays a role in cancer recurrence and patient survival. In addition, overweight and obese women need to undergo a greater and more aggressive radiation protocol. Delivery of external radiotherapy is complicated in obese patients since it is associated with an increased risk of preparation errors and requires a larger margin. In the particular case of cervical cancer, the use of high-energy radiation to the middle pelvis without overdosing peripheral healthy tissues represents a technical challenge. For these reasons, it is of utmost importance to implement an adequate nutritional treatment for obese patients with cervical cancer<sup>12,13</sup>. Level of evidence B, strength of recommendation 1. The nutritional approach to obese patients with cancer must be individualized, starting with recommendations focused on lifestyle changes, an increase in physical activity and changes in eating habits. To calculate the energy requirements of obese patients, the Harris-Benedict formula is recommended, using the patient's adjusted body weight to obtain a moderate energy requirement and thus promote gradual weight loss<sup>14</sup>. The adjusted body weight is calculated using the following formula:

Adjusted body weight = Ideal weight + (50% [Current weight – Ideal weight])

Level of evidence B, strength of recommendation 1.

It is important to maintain a balanced macronutrient distribution. To preserve the patient's muscle mass, protein intake must be at least 1 g/kg/day, or the protein proportion must be increased to 20-30% of the total energy intake. The recommended proportion of carbohydrates is 40-50% total energy intake, and the recommended proportion of fat is 30-40%. Fiber intake must be considered according to individual

tolerance, but a greater proportion of soluble fiber than insoluble fiber is highly recommended. Concerning physical activity in cancer patients, it is associated with maintenance or significant improvements in aerobic capacity, muscle strength, health-related quality of life, self-esteem, and with reduction in fatigue and anxiety<sup>15</sup>. Clinical trials have provided evidence that physical activity is well-tolerated and safe at different stages of cancer<sup>16</sup>. The American College of Sports Medicine (ACSM) guidelines recommend an increase in physical activity, at least 3 times per week, for a total of 75-150 min of low to moderate intensity exercise per week<sup>17</sup>. Level of evidence B, strength of recommendation 1.

### Type 2 diabetes mellitus

To manage the cancer patient with diabetes that receives pelvic radiotherapy, recommendations have not been determined. Albeit, in patients with insulin resistance, glucose metabolism is impaired; however, utilization of fat is normal thus suggesting a benefit for a higher fat proportion<sup>4</sup>. Energy recommendations may be determined with the Harris-Benedict formula using the patient's current weight – if adequate –, or the adjusted weight if the patient is obese. According to the Canadian Diabetes Association, the recommended nutrient proportion is: 40-50% total energy from carbohydrates; 15-20% total energy from protein (or 1-1.5 g/kg/day), taking into account the patient's renal function, and 30-40% total energy from fat, with a greater proportion of monounsaturated fatty acids. Consumption of a variety of unprocessed, nutrient-dense foods is emphasized<sup>18</sup>. Level of evidence A, strength of recommendation 1.

The optimal proportion of carbohydrates, protein, and fat in cancer patients with pre-diabetes has not been determined but may be derived from intervention studies in the general pre-diabetic population. A randomized clinical trial, in pre-diabetic patients, demonstrated that a high protein diet (30% protein, 30% fat, and 40% carbohydrate), compared to a high carbohydrate diet (15% protein, 30% fat, and 55% carbohydrate), leads to remission of pre-diabetes to normal glucose tolerance in 100% of subjects<sup>19</sup>. The high-protein diet group exhibited significant improvement in insulin sensitivity ( $p = 0.001$ ), cardiovascular risk factors ( $p = 0.04$ ), inflammatory cytokine levels ( $p = 0.001$ ), oxidative stress markers ( $p = 0.001$ ),

and an increased percentage of lean body mass ( $p = 0.001$ ), and compared to patients on the high-carbohydrate diet at 6 months. These findings suggest that pre-diabetic cancer patients could benefit from a high-protein diet. Level of evidence A, strength of recommendation 1.

## Hypertension

In cancer patients with high blood pressure that receives pelvic radiation therapy, there is no evidence on useful dietary interventions. However, energy requirements may be estimated using the Harris-Benedict formula, with adjusted weight if the patient is obese, or the current weight if the patient has a normal body weight. The same macronutrient proportion as described above may be recommended (20-30% protein, 30-40% fat, and 40-50% carbohydrates)<sup>14</sup>. Level of evidence B, strength of recommendation 2.

The dietary approaches to stop hypertension (DASH) diet are a program recommended for patients with hypertension<sup>20</sup>. This diet recommends an increased intake of fruits and vegetables, low-fat dairy, fish, poultry, nuts and seeds, and a decreased intake of red meats; thus favoring an increase in dietary fiber, potassium, magnesium and calcium, and minerals that modulate blood pressure through different mechanisms. With this diet, potassium intake may reach 4700 mg/day, magnesium may reach 500 mg/day, and calcium 1240 mg/day. Level of evidence B, strength of recommendation 1. Although there is no evidence supporting a benefit from this dietary approach in cancer patients with hypertension that receive pelvic radiotherapy, the DASH diet may be considered safe for cancer patients during chemo- and radiation therapy.

Sodium restriction must be enforced depending on blood pressure readings; an intake < 3000 mg/day is recommended. It is important to consider that sodium restriction changes food flavor and palatability, which may be counterproductive in patients with anorexia and taste alterations. The lipid profile in the diet of these patients must also be monitored whereby cholesterol intake must not exceed 200 mg/day and the intake of monounsaturated fatty acids must be increased, which can be easily accomplished with the DASH diet<sup>20</sup>. Level of evidence B, strength of recommendation 1.

## Renal insufficiency

No evidence was found concerning dietary interventions in cancer patients with renal insufficiency that receives pelvic radiation. Authors consider that a nutritional approach similar to the one used routinely for patients with renal insufficiency may be utilized for cancer patients as well. In patients with chronic renal failure that is not on replacement therapy and with a glomerular filtration rate (GFR) < 25 ml/min, a protein intake of 0.6 g/kg/day, including 2/3 of high biological value protein, is recommended. In patients with a GFR ranging between 25 and 70 ml/min, the recommended protein intake is 0.6 g/kg/day, including 2/3 of high biological value protein. In patients with a GFR > 70 ml/min, protein intake can oscillate between 0.8 and 1 g/kg/day. In all cases, the recommended energy intake should consider the patient's age: in patients 60 years of age and older, it is 30 kcal/kg/day, and in patients younger than 60, it is 35 kcal/kg/day<sup>21</sup>. Level of evidence B, strength of recommendation 2.

Protein recommendation for clinically stable patients on hemodialysis is 1.2-1.4 g/kg/day. In patients on peritoneal dialysis, the same recommendation applies. In both cases, it is important to monitor that 60% protein is of high biological value. Another significant aspect to consider in patients on peritoneal dialysis is glucose absorption from the dialysis fluid since it alone can provide 25-30% total energy. If the patient is in acute renal failure, basal energy requirements may be estimated with the Harris-Benedict formula, multiplied by a factor of 1.3; the protein requirement is 0.5-1 g/kg/day, and an adequate intake of essential amino acids must be monitored<sup>22</sup>. Level of evidence B, strength of recommendation 2.

## Geriatric patients without comorbidities

To the best of our knowledge, there is no evidence of dietary interventions that could benefit elderly cancer patients who receive pelvic radiation therapy. Even so, energy requirements in this population may be determined with the Harris-Benedict formula, multiplied by the activity factor. Protein recommendations for the elderly are 0.9-1.1 g/kg/day, 30-35% fat, and 45-55% carbohydrates<sup>23</sup>. Level of evidence B, strength of recommendation 1.



Table 2. Recommended daily intake of vitamins and minerals in the elderly according to the World Health Organization<sup>23</sup>

Vitamins	Minerals
Vitamin A: 600-700 µg/day	Calcium: 800-1200 mg/day
Vitamin B12: 2.5 µg/day	Chromium: 50 µg/day
Vitamin C: 60-100 mg/day	Folate: 400 µg/day
Vitamin D: 10-15 µg/day	Iron: 10 mg/day
Vitamin E: 100-400 mg/day	Magnesium 225-280 mg/day
Vitamin K: 60-90 µg/day	Selenium: 50-70 µg/day
Riboflavin: 1.1-1.3 mg/day	

Vitamin and mineral requirements for geriatric patients are described in table 2.

## CONCLUSIONS

Nutrient requirements for patients undergoing pelvic radiotherapy must be established in an integral manner, considering the age of the patient, the nutritional status and the presence of comorbidities and complications derived from the disease and its treatment. It is of utmost importance to avoid unnecessary dietary restrictions to ensure that the patient sustains an adequate nutritional status.

## REFERENCES

1. Ravasco P, Monteiro-Grillo I, Vidal PM, Camilo ME. Dietary counseling improves patient outcomes: a prospective, randomized, controlled trial in colorectal cancer patients undergoing radiotherapy. *J Clin Oncol*. 2005;23:1431-8.
2. Poulsen GM, Pedersen LL, Østerlind K, Bæksgaard L, Andersen JR. Randomized trial of the effects of individual nutritional counseling in cancer patients. *Clin Nutr*. 2014;33:749-53.

3. Isenring EA, Bauer JD, Capra S. Nutrition support using the american dietetic association medical nutrition therapy protocol for radiation oncology patients improves dietary intake compared with standard practice. *J Am Diet Assoc*. 2007;107:404-12.
4. Arends J, Bachmann P, Baracos V, et al. ESPEN guidelines on nutrition in cancer patients. *Clin Nutr*. 2017;36:11-48.
5. Wedlake LJ, McGough C, Shaw C, et al. Clinical trial: efficacy of a low or modified fat diet for the prevention of gastrointestinal toxicity in patients receiving radiotherapy treatment for pelvic malignancies. *J Hum Nutr Diet*. 2012;25:247-59.
6. Bosaeus I, Andersson H, Nyström C. Effect of a low-fat diet on bile salt excretion and diarrhoea in the gastrointestinal radiation syndrome. *Acta Radiol Oncol Radiat Phys Biol*. 1979;18:460-4.
7. Andreyev J. Gastrointestinal complications of pelvic radiotherapy: are they of any importance? *Gut*. 2005;54:1051-4.
8. Guren MG, Tobiassen LB, Trygg KU, Drevon CA, Dueland S. Dietary intake and nutritional indicators are transiently compromised during radiotherapy for rectal cancer. *Eur J Clin Nutr*. 2006;60:113-9.
9. Ghorbanzadeh-Moghaddam A, Gholamrezaei A, Hemati S. Vitamin D deficiency is associated with the severity of radiation-induced proctitis in cancer patients. *Int J Radiat Oncol Biol Phys*. 2015;92:613-8.
10. Pace A, Giannarelli D, Galiè E, et al. Vitamin E neuroprotection for cisplatin neuropathy: a randomized, placebo-controlled trial. *Neurology*. 2010;74:762-6.
11. de Baptista GA, Melo CM. Cáncer- Vitaminas- minerales: relación compleja. *Arch Latinoam Nutr*. 2014;64:220-30.
12. Boeing H. Obesity and cancer—the update 2013. *Best Pract Res Clin Endocrinol Metab*. 2013;27:219-27.
13. Benedetto C, Salvagno F, Canuto EM, Gennarelli G. Obesity and female malignancies. *Best Pract Res Clin Obstet Gynaecol*. 2015;29:528-540.
14. Barak N, Wall-Alonso E, Sitrin MD. Evaluation of stress factors and body weight adjustments currently used to estimate energy expenditure in hospitalized patients. *JPEN J Parenter Enteral Nutr*. 2002;26:231-8.
15. Alves CR, da Cunha TF, da Paixão NA, Brum PC. Aerobic exercise training as therapy for cardiac and cancer cachexia. *Life Sci*. 2015;125:9-14.
16. Jones LW, Alfano CM. Exercise-oncology research: Past, present, and future. *Acta Oncol*. 2013;52:195-215.
17. Thompson PD, Arena R, Riebe D, Pescatello LS, American College of Sports Medicine. ACSM's new preparticipation health screening recommendations from ACSM's guidelines for exercise testing and prescription, ninth edition. *Curr Sports Med Rep*. 2013;12:215-7.
18. Evert AB, Boucher JL, Cypress M, et al. Nutrition therapy recommendations for the management of adults with diabetes. *Diabetes Care*. 2014;37 Suppl 1:S120-43.
19. Stentz FB, Brewer A, Wan J, et al. Remission of pre-diabetes to normal glucose tolerance in obese adults with high protein versus high carbohydrate diet: randomized control trial. *BMJ Open Diabetes Res Care*. 2016;4:e000258.
20. Svetkey LP, Trial RC. Effects of dietary patterns on blood pressure. *Arch Intern Med*. 1999;159:285.
21. Toigo G, Aparicio M, Attman P-O, et al. Expert working Group report on nutrition in adult patients with renal insufficiency (Part 2 of 2). *Clin Nutr*. 2000;19:281-91.
22. Toigo G, Aparicio M, Attman PO, Cano N. Expert working Group report on nutrition in adult patients with renal insufficiency (part 1 of 2). *Clin Nutr*. 2000;19:197-207.
23. WHO. Keep Fit for Life. Meeting the Nutritional Needs of Older Persons. Marketing and Dissemination, World Health Organization, Geneva, Switzerland. WHO Library Cat Data; 2002. p. 119.