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Detection of risk factors that influence weight loss in patients undergoing radiotherapy

Jon Cacicedo[a,*], *Francisco Casquero*[a], *Lorea Martinez-Indart*[b], *Olga del Hoyo*[a], *Alfonso Gómez de Iturriaga*[a], *Irma Muruzabal*[a], *Claudia Carvajal*[a], *Elsira Bóveda*[a], *Blanca Ruiz*[a], *Armando Loayza*[a], *Begoña Usategui*[a], *Aurora Lasso*[a], *Eduardo Hortelano*[a], *Pedro Bilbao*[a]

[a] *Department of Radiation Oncology, Cruces University Hospital, Baracaldo, Vizcaya, Spain*
[b] *Department of Statistics and Epidemiology, Cruces University Hospital, Baracaldo, Vizcaya, Spain*

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ABSTRACT

Aim: To identify risk factors that influence weight loss in patients receiving radiotherapy.
Background: It is a well-known fact that cancer patients can be affected by malnutrition at the onset of the disease and during treatment due to the toxicity. Pretreatment weight loss alone does not predict those who will need nutritional supplementation. Instead, a variety of nutritional and tumor related factors needs to be taken into account.
Material and methods: A retrospective study was conducted on 129 patients with different tumor locations. Weight loss was evaluated during radiotherapy and one month after treatment. The impact of age, ECOG, chemotherapy, pretreatment weight loss, tumor location, previous surgery and TNM were analyzed. We aimed to identify a high-risk group of patients before starting treatment.
Results: The average net weight loss during radiotherapy and one month after treatment for this group of patients was 0.68 kg and 1.6 kg, respectively. Median weight loss during radiotherapy was 2.6 kg for head and neck (HN) patients and 0.27 kg for other tumor sites ($p = 0.028$). Median weight loss one month after radiotherapy was 3.7 kg for HN patients and 1.1 kg for the rest of the patients ($p = 0.034$). The median weight loss one month after treatment was 3.2 kg for patients receiving chemotherapy and 0.5 kg for those patients who did not receive chemotherapy ($p < 0.001$). A regression analysis determined that HN tumor location and the use of chemotherapy were independent risk factors.
Conclusions: Nutritional status must be monitored and managed before, during and after treatment. A variety of nutritional and tumor-related factors must be considered. According to our results, head and neck tumors and the use of chemotherapy are the only two factors considered statistically significant. Because patients continue to lose weight after treatment, we recommend close surveillance after radiotherapy.

* *Corresponding author at*: Department of Radiation Oncology, Cruces University Hospital, c/Plaza de Cruces s/n 48903, Baracaldo, Vizcaya, Spain. Tel.: +34 946006232; fax: +34 946006627.
E-mail address: jon.cacicedofernandezbobadilla@osakidetza.net (J. Cacicedo).
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1. Background

Patients receiving radiotherapy and chemotherapy often have a compromised nutritional status preceding and during treatment due to irradiation of large areas of mucous membranes and salivary glands. Toxicities such as nausea, vomiting, diarrhea, anorexia or dysphagia can negatively affect the nutritional status by decreasing food intake and/or absorption of nutrients.[1,2] Considering the widespread prevalence of malnutrition, prompt identification is required, followed by an appropriate, effective treatment.

Weight loss during treatment not only increases the risk of adverse outcomes but also may interrupt the treatment, which compromises tumor control.[3,4] Therefore, dietetic intervention should be considered in the treatment plan, especially for head and neck (HN) patients.[5–7] In short, a high number of patients with cancer are affected by malnutrition; the occurrence of certain symptoms leads to an inadequate food intake. Patients who have malnutrition can be managed with a variety of oral dietary approaches including dietary modification, counseling by a dietician and/or oral nutritional supplements (ONS).[8]

2. Aim

The aim of this study was to assess the previous nutritional status of a cohort of 129 consecutive patients, to describe the characteristics of these patients before receiving treatment, and to detect which risk-factors may influence weight loss during radiotherapy.

3. Materials and methods

The medical records of 129 consecutive patients were retrospectively reviewed (July 2010 to December 2010). Ethical approval was obtained for this study from the Cruces University Hospital. We described our population, evaluated weight loss (during radiotherapy and one month after treatment) and analyzed any nutritional or disease related factors that might influence weight loss during radiotherapy. In deciding which factors were important, we concentrated on those associated with malnutrition, including pretreatment weight loss, tumor site and stage, age, influence of chemotherapy, previous surgery and performance status.

3.1. *Nutritional considerations*

Patients received individualized dietary counseling based on regular foods. All patients were encouraged to eat their normal diet ad libitum and were given nutritional counseling that included recommendations of a full liquid, puréed, or soft diets using common household foods when appropriate. Dietary recommendations were adjusted to control associated symptomatologies caused by tumor or treatment toxicity. No routine nutritional supplements were employed.

3.2. *Nutritional assessment*

At the first clinical visit, the medical staff registered the following information: patient's age, gender, cancer location, TNM stage, surgery prior to radiotherapy, chemotherapy protocol. All patients also had a nutritional assessment at their first clinic visit. Baseline body weight was defined as that measured at the time of initial consultation, and a physician assessed the patient's performance status at baseline using the ECOG (Eastern Cooperative Oncology Group) scale. Nutritional assessment (body weight and dietetic counseling) was performed at pretreatment and weekly during radiation therapy. Self-reported weight loss within the six months preceding enrollment in the study was recorded from the first clinical visit.

All patients were treated 5 days per week with continuous-course, once-daily radiation therapy. The patients' body weight was obtained, and nutritional counseling was provided at least once weekly during the course of radiation therapy. Patients were typically seen 4 weeks after radiation therapy was completed. At this time, body weight was obtained and compared with baseline weight. A blood count, including serum albumin, was obtained at pretreatment and at the end of radiotherapy.

All patients were considered eligible, regardless of whether the proposed radiotherapy was primary, adjuvant to surgery, combined with chemotherapy or of palliative intent.

In summary, this study aims to describe the nutritional status of a cohort of patients before starting treatment and to evaluate changes in their nutritional status (body weight) throughout radiotherapy. In our opinion, there are factors that may influence weight loss during radiotherapy. For patients undergoing radiotherapy, tumor location or type of antineoplasic treatment should be considered as a risk for malnutrition. Our aim is to identify a high-risk group of patients before starting treatment.

3.3. *Statistical analysis*

Continuous variables are expressed using a mean and standard deviation. Categorical variables are described as numbers and percentages.

Student's *t*-test and Mann–Whitney *U*-test were used to compare the following variables: weight loss during radiotherapy, weight loss one month after radiotherapy with previous surgery, TNM, chemotherapy, serum albumin level, ECOG and tumor location.

Student's *t*-test or Mann–Whitney *U*-test was performed depending on the distribution of the variable.

A univariate and multivariate linear regression model was developed to determine which variables were associated with weight loss.

Statistical significance was set for a p value less than .05.

Data were analyzed using statistical Package for the Social Sciences (SPSS, version 19.0).

4. Results

4.1. *Patient characteristics*

The results of 129 consecutive patients were retrospectively reviewed.

Table 1 – Distribution of tumor location.

	N	%
Head and neck	24	18.8
Brain	3	2.3
Rectum	13	10.2
Histiocytoma	1	0.8
Lymphoma	1	0.8
Breast	29	22.7
Prostate	20	15.6
Lung	21	16.4
Sarcoma	1	0.8
Gynecological	13	10.2
Bladder	2	1.6
Unknown	1	0.8
Total	129	100

N = number of patients and % = percentage.

Table 2 – Descriptive statistics.

	N	$\tilde{X}$	±SD
Age	124	62.15	11.48
Baseline weight (kg)	129	73.32	14.39
Height (cm)	125	163	8
Weight loss (%)	117	1.75	3.82
Serum albumin baseline level	120	4.26	0.34
Weight week 1	126	73.62	14.29
Weight week 2	127	73.32	14.34
Weight week 3	126	73.30	14.40
Weight week 4	121	72.85	14.38
Weight week 5	111	73.28	14.13
Weight week 6	64	73.52	12.50
Weight week 7	30	76.23	13.28
Weight week 8	11	79.45	13.57
Serum albumin level after radiotherapy	123	4.18	0.43
Weight loss (kg) six months preceding treatment	117	1.25	2.74
Weight loss one month after radiotherapy	127	1.60	3.85
Weight loss during radiotherapy	129	0.68	3.01

$\tilde{X}$ = mean, N = number of patients, and SD = standard deviation.

Of the 129 patients, 61.24% ($n = 79$) were male, and 38.75% ($n = 50$) were female, with a mean age of 62 years (range 29–87). The distribution of tumor location and descriptive statistics are shown in Tables 1 and 2, respectively. No prophylactic nasogastric tube or gastrostomy was placed in any patient.

4.2. *Pretreatment weight loss*

Pretreatment weight loss was evaluated globally and according to different tumor locations to assess its effect on weight loss during radiotherapy and one month after treatment (Tables 3 and 4). The influence of pretreatment weight loss greater than 5% was evaluated (Table 5). There was no statistically significant difference between patients that lost more than 5% of their weight or less than 5% of their weight before radiotherapy and the median weight lost during radiotherapy or one month after treatment.

Table 3 – Pretreatment weight loss.

Pretreatment WL	N	%
No loss	89	77.6
<5%	11	9.5
5–10%	9	7.8
>10%	7	6.0
Total	116	100

N = number of patients, WL = weight loss, and % = percentage.

Table 4 – Pretreatment weight loss related to tumor location.

Tumor location	Pretreatment WL	N	%
Head and neck	No loss	14	63.6
	<5%	4	18.2
	5–10%	3	13.6
	>10%	1	4.5
	Total	22	100
Brain	No loss	3	100
Rectum	No loss	7	53.8
	<5%	3	23.1
	>10%	3	23.1
	Total	13	100
Sarcoma	No loss	1	100
Hystiocitoma	Unknown	1	100
Lymphoma	No loss	1	100
Breast	No loss	23	85.2
	<5%	2	7.4
	5–10%	1	3.7
	>10%	1	3.7
	Total	27	100
Prostate	No loss	17	100
Lung	No loss	10	62.5
	<5%	1	6.3
	5–10%	2	12.5
	>10%	3	18.8
	Total	16	100
Gynecological	No loss	11	84.6
	>10%	2	15.4
	Total	13	100
Bladder	No loss	1	50
	<5%	1	50
	Total	2	100

N = number of patients, WL = weight loss, and % = percentage.

Table 5 – Median weight loss during radiotherapy and one month after treatment related to pretreatment weight loss.

	Weight loss (%)	MWL (kg)
MWL during radiotherapy	<5	0.6782
	≥5	0.8750
MWL one month after treatment	<5	1.7040
	≥5	1.1250

MWL = median weight loss, < = less than, and ≥ = equal or more than).

4.3. *Weight loss during and after treatment*

Patient weights at the start and end of treatment were used to calculate body weight loss during radiotherapy. Weight loss was evaluated weekly during radiotherapy and one month after treatment. A total of 49.6% of patients lost weight throughout radiotherapy, with a median weight loss during treatment of 2.85 kg (SD ± 2.72). This weight loss corresponds to a 3.63% (SD ± 3.01) net reduction from their baseline weight. One month after treatment, 63% of patients lost weight with a median weight loss of 3.47 kg (SD ± 3.62), which corresponds to a 4.42% (SD ± 3.90) net reduction from their baseline weight. Overall, the average net weight loss for this group of 129 patients from the first to last day of radiation therapy (during treatment) and one month after treatment in this study was 0.68 kg and 1.6 kg, respectively.

4.4. *Previous surgery*

The influence of previous surgery on weight loss was analyzed. Weight loss during radiotherapy was 0.6 kg (SD ± 2.75) for patients that underwent surgery before radiotherapy and 1.13 kg (SD ± 3.43) for patients that did not undergo surgery before radiation treatment. This difference was not statistically significant.

4.5. *Age*

There were 55 patients (45.1%) older than 65 years and 67 (54.9%) patients younger than 65 years. Median weight loss during radiotherapy in patients over 65 years old was 1.98 kg (SD ± 3.90), whereas patients below 65 lost 1.29 kg (SD ± 3.70). We did not find significant differences in weight loss during treatment or one month after treatment according to age.

4.6. *ECOG*

In respect to performance status, 86 patients were classified as ECOG 0 (73.5%) and 31 as ECOG 1 (26.5%). Median weight loss during radiation therapy for patients with ECOG 0 was 0.3 kg (SD ± 2.71), whereas median weight loss for patients with ECOG 1 was of 1.8 kg (SD ± 3.77), ($p = 0.011$). Median weight loss one month after treatment was 1.16 kg (SD ± 3.67) for patients categorized as ECOG 0 and 3.02 kg (SD ± 4.22) for patients with ECOG 1, ($p = 0.016$).

4.7. *Tumor location*

The influence of tumor location was analyzed by comparing median weight loss during radiotherapy between HN patients and other tumor sites. Median weight loss during radiotherapy was 2.64 kg (SD ± 4.75) for HN patients and 0.27 kg (SD ± 2.24) for all other patients ($p = 0.028$). The median weight loss one month after radiotherapy was 3.72 kg (SD ± 5.46) for HN patients and 1.1 kg (SD ± 3.19) for other tumor sites ($p = 0.034$). A similar comparison was made between patients with lung cancer and other tumor sites. Median weight loss during radiotherapy was 1.04 kg (SD ± 3.01) for lung cancer patients and 0.65 kg (SD ± 3.01) for all others. Median weight loss one month after treatment was 2.9 kg (SD ± 5.38) for lung cancer patients and 1.3 kg (SD ± 3.43) for patients with other tumor sites. These differences were not statistically significant. There were small clinical differences in weight loss between patients with colorectal cancer and other cancer types, but no statistically significant differences were found.

Table 6 – Chemotherapy according to tumor location.

Tumor location	QT	N	%
Head and neck	No	13	59.1
	Yes	9	40.9
	Total	22	100.0
Brain	Yes	3	100.0
Colo-rectum	No	1	8.3
	Yes	11	91.7
	Total	12	100.0
Hystiocitoma	Yes	1	100.0
Lymphoma	Yes	1	100.0
Breast	No	12	52.2
	Yes	11	47.8
	Total	23	100.0
Prostate	No	17	100.0
Lung	No	5	29.4
	Yes	12	70.6
	Total	17	100
Sarcomas	No	1	100
Gynecological	No	4	30.8
	Yes	9	69.2
	Total	13	100
Bladder	Yes	1	100

N = number of patients, QT = chemotherapy, and % = percentage.

4.8. *TNM*

Forty-eight patients (37.2%) were classified as stage I and II, and 47 patients (36.4%) had locally advanced disease (stages III and IV). Weight loss during radiotherapy was 0.4 kg (SD ± 2.35) for stages I and II patients and 1.5 kg (SD ± 3.79) for stages III and IV ($p = 0.22$). Weight loss one month after treatment was 0.9 kg (SD ± 2.72) and 2.6 kg (SD ± 4.93) for stages I–II and II–IV, respectively ($p = 0.20$).

4.9. *Chemotherapy*

A total of 58 (51.3%) patients received chemotherapy (concomitant scheme in 30.1%) and 53 (48.6%) did not. The use of chemotherapy according to tumor location is described in Table 6. Median weight loss during treatment was 1.8 kg (SD ± 3.32) for patients who received chemotherapy and 0.02 kg (SD ± 2.56) for patients that did not ($p < 0.001$).

The median weight loss one month after treatment was 3.2 kg (SD ± 4.30) for patients who received chemotherapy and 0.5 kg (SD ± 3.03) for patients that did not ($p < 0.001$).

Weight loss in patients receiving chemotherapy according to tumor location is shown in Table 7.

Table 7 – Weight loss in patients receiving chemotherapy according to tumor location.

Tumor location	WL (kg)	N	Median WL (kg)	SD
Head and neck	WL during radiotherapy	9	6.13	2.95
	WL one month after	9	7.63	2.60
Brain	WL during radiotherapy	3	0.86	2.40
	WL one month after	3	1.83	2.81
Colo-rectum	WL during radiotherapy	11	0.89	2.92
	WL one month after	10	1.85	3.67
Hystiocitoma	WL during radiotherapy	1	−2.10	
	WL one month after	1	0.20	
Lymphoma	WL during radiotherapy	1	−3.10	
	WL one month after	1	−3.30	
Breast	WL during radiotherapy	11	0.07	1.03
	WL one month after		0.92	1.52
Lung	WL during radiotherapy	12	1.70	3.84
	WL one month after	12	4.68	6.36
Gynecological	WL during radiotherapy	9	2.11	1.98
	WL one month after	8	2.38	1.47
Bladder	WL during radiotherapy	1	3.70	
	WL one month after	1	4.20	

WL = weight loss in kg and SD = standard deviation.

4.10. *Albumin*

Median serum albumin levels for pretreatment and posttreatment were 4.27 g/dl and 4.18 g/dl, respectively. These values were compared, but no statistically significant differences were found.

The significant factors identified on univariate analysis were HN tumor location, ECOG and the use of chemotherapy. When multivariate analysis was performed, only chemotherapy and HN area were considered independent risk factors. There were no other factors considered statistically significant.

5. Discussion

It is a well-known fact that cancer patients can be affected by malnutrition at the onset of the disease and during treatment due to the toxicity. Pretreatment weight loss alone does not predict those who will need nutritional supplementation. Instead, a variety of nutritional and tumor related factors needs to be taken into account. For example, in HN cancer patients, radiotherapy can have a compounding effect on nutritional status.[9]

Understanding this relationship, we aimed to identify those factors that may have influenced the patients' weight loss during radiation therapy.

Malnutrition in oncology patients has an impact on clinical evolution and therapeutic adherence.[10] Ravasco et al. extensively studied the effectiveness of nutritional counseling and found an improvement in the quality of life in HN cancer patients when receiving counseling instead of supplements without any advice.[11] Ravasco et al. also demonstrated that dietary counseling improves outcomes in colorectal cancer patients undergoing radiotherapy. Nutritional counseling was shown to be as effective as high energy and high protein ONS during radiotherapy.[12] Therefore, general dietary recommendations for specific cancers and recommendations according to therapy type are always given in our nutritional protocol for symptom control in this patient population (anorexia, nausea, dysphagia, mucositis, etc.). In general, we recommend a balanced and healthy diet according to their symptoms to help the patient achieve adequate intake.

HN patients clearly lost more weight (at least three times more) during radiotherapy and one month after treatment as compared to other pathologies. Therefore, this evidence further emphasizes the role of cancer location in nutrition, as previously reported.[13–15] No statistically significant differences were found for other tumor locations. This finding is particularly relevant because HN cancer patients have additional nutritional deficits. The anatomical location of the tumor itself may cause dysphagia, and radiation therapy causes mucosal reactions that may further limit oral intake.

Mangar et al. found that an advanced tumor stage could be used to identify patients at high risk of malnutrition during radiation therapy.[9] However, weight change had no significant association with advanced stage in our study. Approximately 60% of patients had no available TNM classification; thus, a definitive conclusion cannot be reached due to the small number of patients with an available classification.

In recent years, the role of malnutrition as a predictor of cancer survival has received considerable attention. A serum albumin level provides an estimate of visceral protein function. A depressed serum albumin has been associated with a greater incidence of morbidity and mortality in hospitalized patients. Several studies report similar findings.[2,16,17] Recently, Gupta and Lis performed a systematic review to identify epidemiologic studies of the relationship between serum albumin and cancer survival. This review concluded that pretreatment serum albumin levels provide useful prognostic information for cancer[18]; therefore, maintaining an acceptable serum albumin level is desirable. However, we did not find a significant decrease in median serum albumin level between pretreatment and posttreatment in this study. This result might be explained by the low median weight loss during treatment.

There is a lack of evidence-based data regarding toxicity in the elderly patients, especially in the field of radiation therapy.[19] In the present study, surprisingly, weight loss showed no significant association with age. Other authors have reported the opposite.[9] In our study, the percentage of patients over 65 years was 45.1%. The influence of increasing age on weight loss was analyzed, but age was not found to be an influential factor in weight loss.

Patients receiving chemotherapy had a significant weight loss during treatment and an increased weight loss one month after treatment when compared to patients that did not receive chemotherapy. Because of this finding, we consider chemotherapy to be a major risk factor for weight loss. It is noteworthy that the use of chemo-radiotherapy may increase the severity of mucosal reactions, nausea and vomiting; thus, contributing to the increased weight loss of patients undergoing radiotherapy.[9] The radiosensitization effect of chemotherapy leads to increased acute toxicities that prevent effective oral feeding. Ineffective oral feeding leads to severe weight loss in a significant number of patients.

The influence of surgery previous to radiation therapy in weight loss was analyzed, and there was a trend in weight loss during radiation therapy for patients that underwent previous surgery; however, this difference was not found statistically significant.

It has been published previously that low performance status can be used in a predictive manner to identify patients at high risk of malnutrition during radiation therapy.[9] In general, these differences have been found by comparing ECOG score 0–1 vs. ECOG 2–3. However, we could not identify low ECOG scores (>2) as a risk factor. This result occurred because 100% of patients had an ECOG score of 0–1. Otherwise, there was a clinical difference in weight loss during radiotherapy and one month after treatment between patients categorized as ECOG 1 vs. ECOG 0. This difference was found significant in univariate analysis but not in multivariate analysis.

This study provides a description of the baseline nutritional status of patients before starting radiochemotherapy and the influence of parameters such as age, pretreatment weight loss, chemotherapy, prior surgery, TNM, and cancer location on the trends of weight loss during treatment. Tumors in the head and neck area and the use of chemotherapy were the only two risk factors considered statistically significant in this study. Patient outcomes may be optimized if nutritional status is adequately monitored and managed before and during treatment. Because patients continue to lose weight after treatment, patients should be watched closely after completing radiotherapy.

6. Conclusions

A nutritional assessment is essential prior to radiation therapy. Decisions about the treatment of disease-related malnutrition should be guided by evidence where possible. Nutritional status and risk factors, such as tumor location (especially head and neck) and the use of chemotherapy, should be evaluated because these factors can influence weight loss during radiotherapy even if patients do not present with weight loss at pretreatment evaluation.

Conflict of interest

None of the authors has any financial or relationship conflicts of interest in presenting this paper.

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