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ORIGINAL RESEARCH

Influence of chemoradiotherapy on nutritional status, functional capacity, quality of life and toxicity of treatment for patients with cervical cancer

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Abstract

Aim: Assess the influence of chemoradiotherapy on the nutritional status, functional capacity and quality of life (QoL), associating these indicators at baseline with toxicity and interruption of oncologic treatment in women with cervical cancer.

Methods: Prospective cohort study performed on 49 women diagnosed with cervical cancer, who underwent treatment between August 2015 and January 2016. For data collection, two appointments were conducted by the lead researcher: the first occurred the day before the first chemotherapy session (T0) and the other at the end of chemotherapy session (T1). Nutritional status was measured by anthropometry (weight, height, mid-upper arm circumference and triceps skinfold thickness) and computed tomography (skeletal muscle index—SMI), functional capacity by handgrip strength (HGS) and Karnofsky Performance Status (KPS), and application of QoL questionnaire (EORTC QLQ-C30).

Results: The average age was 45 ± 13.8 years and 81.6% of the women were diagnosed in stages II and III. There was significant reduction in HGS, KPS and QoL between T0 and T1, in addition to a significant QoL reduction according to worsening nutritional status. The interruption of chemotherapy was significantly associated with the variables of nutritional status assessed at baseline. Women who interrupted treatment due to acute toxicity also had a significant lower median SMI than those who concluded the treatment and 83% of these patients presented cachexia.

Conclusions: Chemoradiotherapy treatment in patients with cervical cancer had changed negative nutritional parameters, function capacity and QoL, and poor nutritional status at baseline was associated with chemotherapy interruption.

Key words: cervical cancer, chemoradiotherapy, functional capacity, nutritional status, quality of life.

Introduction

Cervical cancer represents the fourth most common neoplasia in the female population and one of the main causes of death among women worldwide.[1] Most instances of cervical cancer occur in developing countries,[1] with close to 50% diagnosed in an advanced stage.[2] Chemoradiotherapy is the most frequent treatment used for this type of cancer, being chosen for patients that had a tumour size exceeding 4 cm, when they are not indicated for surgery.[3]

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Cisplatin is the most effective cytotoxic agent against cervical cancer.[4] The administration in combination with 25 fractions of daily pelvic radiotherapy is suggested as the first line of treatment for patients with locally advanced cervical cancer (stage II through stage IVa—local metastasis—according to the staging system of the International Federation of Gynaecology and Obstetrics).[3]

Chemotherapy enhances the effects of radiotherapy and provides greater efficiency against tumour cells; however, the combined use of these oncologic therapies attacks both neoplastic cells and normal cells, increasing the risk of toxicity.[5] An elevated incidence of toxicity is described in chemoradiotherapy, with hematologic[6,7] and gastrointestinal toxicity being the most commonly found in these cases.[8,9] The presence of symptoms having a nutritional impact, such as nausea, vomiting and anorexia, can reduce nutritional intake and accelerate muscle loss[10,11] which results in impaired muscle function.[12] This depletion may be reflected in different functional tests, such as hand grip

Nutrition & Dietetics

strength (HGS), a good indicator of nutrition status and clinical outcome.[13,14]

The adverse effects provoked by antineoplastic therapy may aggravate pre-existing alterations of the nutritional status (NS), creating a vicious cycle. Therefore, degradation of the NS can result in a greater chance of toxicity due to the combined oncologic treatments[15] and bring about other adverse consequences, such as a diminished response and tolerance of the treatment, and reduced quality of life (QoL).[16] The NS has been described as a strong predictor of QoL in gynaecological cancer patients.[17] On the other hand, the QoL has also been used for assessing the tolerance to oncologic treatment, and it is essential for measurement of the side effects of chemotherapy.[18]

Despite the limited literature, an increased frequency of malnutrition has been shown in patients with cervical cancer, especially among women diagnosed in an advanced stage (4–60% between the stages I and IV, respectively).[19–21] However, the extent of oncological treatment impacts on nutritional status, QoL and functional capacity remain unknown. Therefore, the present study has two aims: to assess the influence of chemoradiotherapy on the nutritional status, functional capacity, and QoL in women with cervical cancer; and to evaluate if the patient's baseline characteristics are related to chemotherapy toxicity and interruption of the oncologic treatment.

Methods

The present study is a prospective cohort, observational study, performed on women diagnosed with cervical cancer, registered in the National Institute of Cancer, Jose Alencar Gomes da Silva, who were proposed to undergo chemoradiotherapy. Inclusion criteria were all patients over 20 years old, who had never undergone prior treatment, had their diagnosis confirmed via a histopathology report and underwent treatment between August 2015 and January 2016. Patients with HIV virus, kidney disease under dialysis treatment, with oedema and/or ascites, as well as those with pacemaker or stent, were excluded, because these conditions influence nutritional status and/or the bioelectrical impedance measures.

Enrolment of the patients occurred during the pre-cancer treatment group counselling, which aims to provide group counselling before cancer treatment. All patients presenting nutritional risk or malnutrition are referred for an individual appointment with a registered dietitian. The eligible patients were instructed on the project and signed an informed consent term. The present study was approved by the Research Ethical Committee of the Brazilian National Cancer Institute—CEP/INCA under number 1.150.108/2015 and followed the Guidelines for Reporting Observational Studies (Strengthening the Reporting of Observational Studies in Epidemiology Statement—STROBE).[22]

Chemoradiotherapy treatment in the Brazilian National Institute of Cancer consisted of a weekly dose of cisplatin as the only type of chemotherapy, with a combination of daily doses of external-beam radiotherapy (25 fractions). All patients who met the inclusion criteria were invited to participate in the present study, of which only three women refused and five were subjected to exclusive radiotherapy because of poor performance status contraindicated for chemotherapy. Patients who did not complete the proposed treatment were not included in the post-treatment evaluation.

During the study period, 49 women diagnosed with cervical cancer and receiving chemoradiotherapy treatment were enrolled. Of this group, 10 patients did not conclude treatment due to elevated toxicity from chemotherapy, 1 patient interrupted her treatment due to being diagnosed with pulmonary metastasis and 4 other patients abandoned treatment by their own choice. Therefore, the number of patients that concluded the proposed treatment and underwent the evaluation at T1 was 34.

For data collection, two appointments were conducted by the lead researcher: the first one occurred the day before the first chemotherapy session (T0) and the second at the end of the last chemotherapy session (T1), roughly 35 days after T0. The research interview included personal data (age, ethnicity, marital status); clinical history (histological type, stage, comorbidities) and data related to the oncologic treatment (type of chemotherapy, number of sessions, duration of treatment, and clinical intercurrences)—obtained from medical records; nutritional status (anthropometric measures and body composition assessment); QoL and functional capacity assessments. All notes and assessments were performed by the same trained researcher.

At T0 and T1, the following anthropometric measurements were performed: weight, height, mid-upper arm circumference (MUAC) and triceps skinfold thickness (TSF). The patients were asked whether they had unintentional weight loss during the past 6 months. Calculation of the mid-arm muscle circumference (MUAMC) and corrected mid-upper arm muscle area (cMUAMA) was obtained using the MUAC and TSF values, by means of specific formulas, and classified according to Frisancho.[23] The body mass index (BMI) was calculated using the actual weight and height (assessed in T0 and T1), and classified according to criteria of the World Health Organisation.[24] The usual body weight was obtained from patient's reports. Likewise, the percentage weight loss (%WL) between T0 and T1 was obtained using the following formula: Usual body weight –current body weight × 100/usual body weight.

Cancer cachexia was diagnosed following the International Consensus of Cachexia that classifies cachexia into three stages: pre-cachexia, cachexia and refractory cachexia.[25] Pre-cachexia is defined as unintentional weight loss of up to 5% in 6 months with the presence of anorexia. Cachexia is defined as greater than 5% weight loss during 6 months, or the combination of weight loss >2% with a BMI less than 20 kg/m^2. In refractory cachexia, patients do not present any response to antineoplastic therapy, with a limited functional capacity and life expectation of less than 3 months.[25] The usual 6-month weight, referred by the patient, was used to calculate the percentage weight loss for cachexia diagnosis.

Skeletal muscle mass was assessed exclusively at T0, for patients who underwent computerised tomography (CT) up to 20 days before the first chemotherapy session. The CT assessment at T1 was not possible because this exam is not routinely performed after chemoradiotherapy. The skeletal muscle content for the diagnosis of sarcopenia was determined via analysis of a cross-sectional image of the third lumbar vertebrae (L3). The images were analysed using the software SliceOmatic 5.0 (Tomovision, Canada), allowing for specific demarcation of the skeletal musculature, expressed in Hounsfield Units (HU) in the range from –29 to +15.[26] All images were analysed by a single trained researcher.

The skeletal muscle index (SMI), that corresponds to the area of muscle tissue obtained from the image of the L3, normalised to height and expressed in cm^2/m^2, was used for sarcopenia classification, according to the cut-off established for women (≤38.9 cm^2/m^2).[27]

Functional capacity was assessed according to HGS using a dynamometer device (Jamar [Bolingbrook, IL, USA]), following the recommendations of the Brazilian Society of Hand Therapists.[28] The patient was asked to squeeze the dynamometer with as much strength as possible and the result was registered in kilograms (kg). Before beginning, a pre-test was performed to familiarise the patient with the device. The test consisted of two measurements; performed with the patient's dominant hand, with a 1-minute pause between each, and averages were used for analysis.

Furthermore, the Karnofsky performance scale (KPS) was applied by the same trained researcher and used for classifying the patients according to the degree of their functional disabilities, representing a general measurement of the independence of the individual to care for themselves and conduct their daily activities. The scale ranges between 0 and 100, where the higher the value obtained, the better the performance of daily functions.[29]

QoL assessment was performed using the questionnaire EORTC QLQ-C30, from the European Organisation of Research and Treatment of Cancer (EORTC), validated for the Brazilian population.[30] The EORTC QLQ-C30 comprises 30 items, divided into three parts. The first part addresses questions related to cognitive, functional, emotional, social and physical performance. The second part reports the individual's perception concerning overall health. In these two parts, a higher score indicated good development of daily capacities. The last part presents the scale of symptoms and a higher score obtained in this section of the questionnaire represents worsened symptoms. A summary score of the QoL is also obtained by the sum of the questionnaire's scales.

For the evaluation of toxicity from radiotherapy and chemotherapy treatment, a specific questionnaire of the National Cancer Institute Common Toxicity Criteria for adverse events version 4.0 was used.[31] The questionnaire determines the intensity of the symptoms presented, with a score ranging from 0 to 5. Interruptions or delay in chemotherapy treatment due to severe toxicity were classified as dose-limiting toxicity (DLT), according to institution protocol.

DLT variables were considered as follows: (i) gastrointestinal disorders—uncontrollable vomiting and diarrhoea with haemodynamic repercussions; (ii) haematologic disorders—febrile neutropenia requiring hospitalisation, thrombocytopenia (<50.000/mm^3), or haemoglobin concentrations <6.5 g/dL; (iii) renal disorders—creatinine clearance <40 mL/min or patient requiring dialysis.

Statistical analysis was performed using version 22.0 of the SPSS statistical package for Windows (Chicago, IL, USA). Adherence to a normal curve was tested evaluate the symmetry of the distribution curve of the variables. A non-normal distribution of the variables was identified, except for age. Data were expressed as median (range) for numeric variables, and percentage for qualitative variables.

The difference between proportions was tested using the χ^2 test or Fisher's exact test. The differences between the medians were assessed by the non-parametric Mann–Whitney (independent variables) or Wilcoxon tests (related variables) for two groups, and the ANOVA Kruskal–Wallis test for more than two groups. For all analysis, a P value of <0.05 was considered statistically significant.

Results

At baseline (n = 49), the average age of the study population was 45 ± 13.8 years, and 16.3% (8/49) were over 65 years. The majority of patients were single (25/49) and 38.8% (19/49) were housewives. Regarding race, 44.9% were pardo (mixed races), 42.9% white and 12.2% black. Almost 60% (29/49) of the women did not present associated comorbidities and arterial hypertension was the most prevalent comorbidity (14/49; 28.6%).

Concerning cancer stage, 18.4% of the women were diagnosed with stage I, 55.1% with stage II and 26.5% with stage III. The most prevalent histological type was squamous cell carcinoma (85.7%), followed by adenocarcinoma (14.3%). Regarding the oncologic treatment, the median total treatment duration of patients who completed the treatment (n = 34) was 32 days (range: 26–47), and the average number of chemotherapy and radiotherapy sessions were 5 (range: 4–6) and 22 (range: 19–27), respectively. All patients received cisplatin as the only type of chemotherapy.

Table 1 shows the parameters used for the nutritional assessment, functional capacity and QoL questionnaire (EORTC QLQ-C30) separated into its specific scales, before and after treatment with chemoradiotherapy, among patients who concluded the oncologic treatment. There was a significant reduction in weight, BMI, handgrip strength and KPS between T0 and T1. Of the total population, 41.2% was diagnosed with pre-cachexia and cachexia at T0 and an increase in the frequency of pre-cachexia was observed after chemoradiotherapy (8.8–17.6%), although it was non-significant.

In relation to BMI classification before treatment, most of the patients had excess weight (overweight and obese).

Table 1 Nutritional assessment, functional capacity and quality of life questionnaire (EORTC QLQ-C30), separated into its specific scales, before and after treatment of women with cervical cancer who completed chemoradiotherapy

	Results (n = 34)		
Variables	*T0*	*T1*	P *value*
Weight (kg)[(a)]	67.60 (44.5–100.2)	65.86 (37.2–98.0)	**0.003**
BMI (kg/m^2)[(a)]	27.19 (19.26–43.56)	26.40 (16.10–41.78)	**0.002**
BMI classification[(b)]			
Underweight	0 (0)	4 (11.8)	**<0.001**
Healthy	11 (32.4)	10 (29.4)	
Overweight	23 (67.6)	20 (58.8)	
TSF (mm)[(a)]	25.0 (8–50)	25.5 (6–48)	0.936
MUAC (cm)[(a)]	29.8 (22–44)	30.0 (19.5–41.5)	0.687
MUAMC (cm)[(a)]	22.58 (17.88–31.71)	21.98 (17.51–27.52)	0.374
cMUAMA (cm^2)[(a)]	34.09 (18.96–73.55)	31.99 (17.91–53.81)	0.437
Cachexia stage[(b)]			0.767
No cachexia	20 (58.8)	17 (50.0)	
Pre-cachexia	3 (8.8)	6 (17.6)	
Cachexia	11 (32.4)	11 (32.4)	
HGS[(a)]	24.25 (10–32.5)	22.0 (12.5–33)	**0.050**
KPS (%)[(a)]	90 (60–100)	80 (60–100)	**0.001**
Summary score of QoL[(a)]	80.60 (27.56–100)	72.07 (30.13–97.78)	**0.004**
Global health status[(c)]	81.62 (17.26)	82.11 (20.43)	0.727
Physical function[(c)]	78.24 (19.72)	69.41 (24.73)	**0.037**
Role performance[(c)]	72.55 (34.30)	53.92 (37.17)	**0.047**
Emotional function[(c)]	57.11 (30.09)	62.25 (33.41)	0.334
Cognitive function[(c)]	83.82 (25.45)	79.41 (29.60)	0.384
Social function[(c)]	78.92 (32.39)	54.90 (38.82)	**0.001**
Total functional scale[(c)]	71.10 (18.97)	64.84 (19.42)	**0.041**
Fatigue [(c)]	27.78 (26.84)	37.91 (30.72)	0.132
Nausea and vomiting[(c)]	13.40 (22.06)	27.94 (26.50)	**0.001**
Pain[(c)]	34.31 (31.50)	23.53 (32.08)	0.141
Dyspnoea[(c)]	10.78 (25.59)	10.78 (21.27)	0.963
Insomnia[(c)]	31.37 (38.44)	26.47 (38.30)	0.430
Appetite loss[(c)]	12.74 (24.64)	27.45 (37.13)	**0.048**
Constipation[(c)]	27.45 (40.59)	18.63 (35.95)	0.196
Diarrhoea[(c)]	1.96 (7.96)	40.20 (39.17)	**0.001**
Financial difficulties[(c)]	46.08 (41.86)	44.15 (44.15)	0.170
Total symptom scale[(c)]	23.68 (17.32)	28.81 (17.21)	0.103

Values in bold present statistical significance ($P < 0.05$).
cMUAMA = corrected mid-upper arm muscle area; HGS = handgrip strength; KPS = Karnofsky performance scale; MUAC = mid-upper arm circumference; MUAMC = mid-arm muscle circumference; TSF = triceps skinfold thickness.
Summary score of QoL = (Physical Functioning+ Role Functioning+ Social Functioning+ Emotional Functioning+ Cognitive Functioning +100-Fatigue+100-Pain+100-Nausea_Vomiting+100-Dyspnoea+100-Sleeping Disturbances+100-Appetite Loss+100-Constipation+100-Diarrhoea)/13.
[(a)] Median (minimum – maximum), Mann–Whitney test.
[(b)] Absolute number (%), McNemar–Bowker test.
[(c)] Mean (SD), Wilcoxon test.

However, a significant increase in the frequency of underweight individuals (BMI <18.5 kg/m^2) was observed after the completion of chemoradiotherapy (0% vs 11.8%), as well as a reduction in frequency of those presenting healthy and excess body weight. No statistical difference was observed between T0 and T1 for the other anthropometric parameters (MUAC, TSF, MUAMC and cMUAMA) (Table 1).

When compared to the parameters assessed by the QoL questionnaire between T0 and T1, there was a significant reduction in physical capacity, role performance, social function and total functional scale. On the scale of symptoms, a significant increase was observed for the symptoms of nausea and vomiting, appetite loss and diarrhoea (Table 1).

Regarding the summary score of QoL, a significant reduction was found after the chemoradiotherapy treatment. At both evaluation times (T0 and T1), there was a significant reduction in the summary score according to the NS. Patients with pre-cachexia and cachexia had lower

Table 2 Summary score of quality of life obtained by the EORTC QLQ-C30 before and after chemoradiotherapy according to nutritional status

		Summary score of QoL (EORTC QLQ-C30)			
Nutritional status variables		*T0 Median (min–max)*	P *value**	*T1 median (min–max)*	P *value**
Percentage weight loss	5%	81.32 (50.81–100)	**0.012**	74.19 (38.72–97.78)	**0.048**
	≥5%	66.92 (27.56–93.08)		66.03 (30.13–90.51)	
Cachexia diagnosis	No cachexia	81.85 (50.81–100)	**0.018**	76.92 (38.72–97.78)	**0.035**
	Pre-cachexia	74.50 (57.52–87.39)		72.93 (56.50–90.51)	
	Cachexia	66.92 (27.56–93.08)		63.50 (30.13–76.50)	

Values in bold present statistical significance ($P < 0.05$).
*Mann–Whitney test.

scores, reflecting the influence of NS on the individual's perception of health (Table 2).

Concerning the oncologic treatment, 20.4% (n = 10) of the 49 patients enrolled in the present study discontinued chemotherapy due to severe toxicity, with the main causes being gastrointestinal (37.5%), hematologic (25%) and renal toxicity (25%). The interruption of radiotherapy occurred in only 8.2% of the patients in the present study. Even when chemotherapy was interrupted due to severe toxicity, radiotherapy was maintained as the exclusive treatment.

The interruption of chemotherapy was significantly associated with the variables of NS assessed at T0 (%WL, cachexia and sarcopenia). Age over 65 years, comorbidities and the stage of cancer showed no statistical difference, as well as the summary score of QoL and the performance status (KPS) (Table 3). Women that interrupted treatment due to acute toxicity from chemotherapy also had a significantly lower median SMI than those who concluded the treatment. It is important to note that roughly 83% of the patients that suspended their chemotherapy presented cachexia and %WL greater than 5%.

According to the Common Criteria of Toxicity (CCT), there was an incidence of symptoms related to chemoradiotherapy toxicity in 94% of the patients of the present study, and approximately 79% reported at least one symptom with severity greater than grade II. The most frequent symptoms were nausea (75.8%), fatigue (66.7%), diarrhoea

Table 3 Association of clinical variables, nutritional status and quality of life with chemotherapy interruption

		Chemotherapy interruption (n = 49)		
Variables		*No*	*Yes*	P *value*
Age (n, %)	<65 years	32 (86.5)	9 (75.0)	0.350*
	>65 years	5 (13.5)	3 (25.0)	
Comorbidities (n, %)	No	16 (59.3)	13 (59.1)	0.450*
	Yes	11 (40.7)	9 (40.9)	
Cancer stage (n, %)	Stage I	7 (18.9)	2 (16.7)	
	Stage II	21 (56.8)	6 (50.0)	0.828*
	Stage III	9 (24.3)	4 (33.3)	
KPS	Mean (SD)	87.30 (9.02)	82.73 (11.91)	0.309**
Percentage weight loss[(a)] (n, %)	<5% in 6 months	25 (69.4)	2 (16.7)	**0.001***
	>5% in 6 months	11 (30.6)	10 (83.3)	
Cachexia (n, %)	No cachexia	23 (62.2)	1 (8.3)	
	Pre-cachexia	3 (8.1)	1 (8.3)	**0.003***
	Cachexia	11 (29.7)	10 (83.3)	
Sarcopenia[(b),(c)] (n, %)	No sarcopenia	28 (96.6)	6 (66.7)	**0.011***
	Sarcopenia	1 (3.4)	3 (33.3)	
SMI (cm^2/m^2)	Mean (SD)	47.11 (6.83)	40.22 (9.59)	**0.024****
Summary score of QoL	Mean (SD)	77.94 (14.23)	66.74 (19.88)	0.099**

Values in bold present statistical significance ($P < 0.05$).
KPS = Karnofsky performance scale; SMI = skeletal muscle index.
Summary score of QoL = (Physical Functioning+ Role Functioning+ Social Functioning+ Emotional Functioning+ Cognitive Functioning +100-Fatigue+100-Pain+100-Nausea_Vomiting+100-Dyspnoea+100-Sleeping Disturbances+100-Appetite Loss+100-Constipation+100-Diarrhoea)/13.
*χ^2 test; ** Mann–Whitney test.
[(a)] Total number equal to 48 patients because one patient was unable to report the usual weight.
[(b)] Total number equal to 38 patients who had CT available at T0.
[(c)] Muscle area analysis in the image of the cross-section of the third lumbar (L3), and sarcopenia with SMI ≤ 38.9 cm^2/m^2.

(60.6%), xerostomia (60.6%), dysgeusia (48.5%), pain (42.4%), constipation (27.3%) and vomiting (24.2%). The tested variables in Table 1 (age exceeding 65 years, comorbidities, stage, KPS, %WL, sarcopenia and cachexia diagnosis) did not associate with the number or severity of symptoms outlined in the CCT ($P > 0.05$).

Discussion

There are few studies that describe the nutritional status of patients with gynaecological cancer. In the present study, the nutritional status of patients with cervical cancer was obtained via different methods of nutritional assessment. According to the BMI, 61.8% of the patients were overweight, a lower prevalence than reported (78.5%) in a study performed with cervical cancer patients eligible for surgical treatment,[32] probably due to difference in the cancer stage.

Tartari *et al.,* in a study with cancer patients of different tumour sites undergoing chemotherapy, also observed a high prevalence of excess weight according to BMI, especially in patients with gynaecologic tumours.[33] However, the present study found a significant reduction in body weight and BMI, in addition to an increase in the frequency of underweight individuals after chemoradiotherapy treatment.

In the present study, despite of the low frequency of underweight individuals diagnosed by the BMI, roughly 33% of the patients had cachexia and/or weight loss greater than 5% before chemoradiotherapy. Other authors also reported a pre-treatment weight loss ranging from 26% to 40% among patients with gynaecological cancer.[34,35] Weight loss and anorexia, present in cancer cachexia, can provoke a limitation in the doses of chemoradiotherapy, in addition to higher chances of treatment toxicity.[15] It has been suggested that the %WL seems to be a better parameter than BMI in cancer patients undergoing chemotherapy[36] and a good prognostic factor of QoL irrespective of the type of cancer.[37]

Despite the wide use of anthropometric parameters for determination of the NS, the BMI has a limited value, because it is not capable of distinguishing the different body compartments.[38] The relevance of the quantification of muscle mass in cancer patients submitted to chemotherapy has increased in recent years due to the correlation between skeletal muscle content and the occurrence of toxicity that can determine a dose reduction or chemotherapy interruption.[39,40]

According to the QoL parameters assessed in the questionnaire, a significant reduction in physical capacity, social function, total scale function and the QoL summary score after treatment was observed. Osann *et al*.,[41] also showed that the application of radiotherapy associated with chemotherapy in patients with cervical cancer leads to a worsening of the QoL. However, the perception of patients concerning their overall health before and after chemoradiotherapy is considered to be satisfactory when compared with the reference values of the EORTC for women with different cancer types and stages[42] (Summary score of the present study: 77.94 ± 14.75 and 69.76 ± 15.55, before and after treatment respectively; Reference of EORTC: 59.3 ± 24.9).

The QoL summary score in the study population showed a positive association between NS at T0 and T1, with a significant reduction according to worsening of the NS. Data of the present study corroborate with recent literature, which has shown lower QoL scores among cancer patients presenting weight loss or malnutrition.[11,17,43] Malnutrition is now considered an independent factor for the deterioration of QoL,[44] and a recent systematic review concluded that poor NS is significantly associated with the QoL reduction in cancer patients, independently of the tumour site.[37]

The present study, found DLT in roughly 80% of the sample. The gastrointestinal toxicities such as nausea and diarrhoea were the most common, corroborating with other studies that report an elevated incidence of toxicity in gynaecologic tumours,[8,9] in addition to the association between severity and decline of the NS.[10] The gastrointestinal symptoms can negatively impact the NS reducing of nutrient intake and accelerating muscular degradation, with worsened physical capacity and consequent QoL.[11,37]

When analysing the variables related to cancer treatment interruption, one can observe that only those related to the NS presented a statistically significant association (diagnosis of cachexia and %WL). In addition, women that interrupted treatment had a median SMI significantly lower than those that did not interrupt treatment. Recognising the factors that can contribute to the reduction of toxicity risks is of utmost importance, and our results suggest that the NS before treatment should be taken into consideration by considering the body weight and %WL[45] and, whenever possible, body composition evaluation.[36] The lack of studies assessing the influence of chemoradiotherapy on NS and QoL of cervical cancer patients makes the present study an important contribution to the identification of variables related to unfavourable outcomes to cancer treatment for this group.

Some limitations of the present study should be pointed out. The small sample size limited a detailed statistical analysis, especially the analysis between different groups according to their NS. The inclusion of all cervical cancer patients who underwent chemoradiation therapy resulted in a sample with distinct stages of the disease, which may interfere with the different outcomes of oncologic therapy.

In addition, data on dietary intake were not collected, making it impossible to associate food intake with NS. A long-term follow up would be beneficial for a better understanding of the relationship between NS and chemoradiation therapy outcomes. Moreover, it was not possible to perform the CT scan after treatment to assess changes in the NS. In the clinical setting, body composition can be easily assessed using electrical bioimpedance; however, this technique has low accuracy in cancer patients, especially in advanced stage of the disease.[46]

In accordance with our results, the combination of chemotherapy and radiotherapy for cervical cancer treatment caused a significant reduction in weight and an increase in the frequency of malnutrition. In addition, a significant

impairment in functional capacity and QoL were observed after the cancer therapy. The QoL summary score also demonstrated a significant reduction according to worsening of nutritional status. The vast majority of patients who interrupted chemotherapy treatment presented pre-cachexia/cachexia, as well as a significant pre-treatment weight loss.

The present study indicates the need to perform further studies on this target population, evaluating multimodal strategies, such as nutritional, physical activity and pharmacological interventions, in order to prevent or reduce treatment complications and consequently the optimisation of chemoradiotherapy. Moreover, determining and registering the risk factors for interrupting antineoplastic therapy should be considered prior to treatment.

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Conflict of interest

The authors have no conflicts of interest to declare.

Authorship

MAA conducted the experimental and clinical work, data collection, data analysis and interpretation, prepared and revised the manuscript. MRG conducted the experimental and clinical work, data collection, prepared and revised the manuscript. GVC conceived and coordinated the study, conducted statistical analysis, prepared and revised the manuscript. The authors certify that the enclosed manuscript is original. All authors agree with the manuscript and declare that the content has not been published elsewhere.

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