ORIGINAL ARTICLE

RISK FACTORS ASSOCIATED WITH ACUTE RADIODERMATITIS AMONG CANCER PATIENTS

Carolina Machado Eisenhut[1], Milena Schneiders[2], Rafael de Lima Carmo[3]

Jacira Batista de Oliveira[4], Ana Cláudia Mesquita Garcia[5]

Érica de Brito Pitilin[6], Paula Elaine Diniz dos Reis[7]

Vander Monteiro da Conceição[8]

Highlights: (1) Identification of relevant clinical risk factors for acute radiodermatitis; (2) Correlation between overweight and greater vulnerability to skin toxicity from radiotherapy; (3) Evidence of the impact of smoking on the severity of skin reactions.

How to cite:

Eisenhut CM, Schneiders M, Carmo R de L, de Oliveira JB, Garcia ACM, Pitilin É de B. et al. Fatores de risco associados a radiodermatite aguda entre pacientes oncológicos. Rev. Contexto&Saúde. 2025;25(50):e15836

[1] Federal University of Fronteira Sul – UFFS. Chapecó/SC, Brazil. https://orcid.org/0000-0003-0964-7620

[2] Federal University of Alfenas – UNIFAL. Alfenas/MG, Brazil. https://orcid.org/0000-0002-7471-7886

[3] Federal University of Fronteira Sul – UFFS. Chapecó/SC, Brazil. https://orcid.org/0000-0003-3196-2598

[4] West Regional Hospital - Oncology Department. Chapecó/SC, Brazil. https://orcid.org/0000-0002-3863-3917

[5] Federal University of Alfenas– UNIFAL. Alfenas/MG, Brazil.https://orcid.org/0000-0001-9793-7905

[6] Federal University of Fronteira Sul – UFFS. Chapecó/SC, Brazil. https://orcid.org/0000-0003-3950-2633

[7] University of Brasilia – UnB. Brasília/DF, Brazil. https://orcid.org/0000-0002-9782-3366

[8] Federal University of Fronteira Sul – UFFS. Chapecó/SC, Brasil. https://orcid.org/0000-0003-0972-0795

RISK FACTORS ASSOCIATED WITH ACUTE RADIODERMATITISAMONG CANCER PATIENTS

ABSTRACT

Aim: Cutaneous radiotoxicity occurs due to damage caused by the generation of free-radicals and reactive oxygen species in fast-dividing cells in the basal layer and dermis. Exposure to radiation also leads to impairment of the barrier function of the epidermis. The aim is therefore to carry out a global assessment of cancer patients undergoing external RT, exploring other patient-related factors that may be associated with the occurrence of radiodermatitis after this treatment. The aim is therefore to identify the risk factors associated with acute radiodermatitis in cancer patients. **Method:** This is a cross-sectional study, of the survey type, carried out in accordance with the Checklist Strengthening the Reporting of Observational Studies in Epidemiology.**Result:** It was identified that patients on continuous medication for the treatment of other comorbidities have a 2.3-fold increase in the chance of radiodermatitis. Another relevant finding in this investigation was that being overweight increased the chance of this outcome by 4.7 times. Smoking, in turn, is a factor associated with severe skin reactions, as chronic exposure to tobacco hinders the skin's healing process and causes changes in the physiology of systems, including the skin. **Conclusion:** Finally, the risk factors identified should be part of the clinical assessment of patients who will undergo or are undergoing radiotherapy for cancer treatment.

Keywords: Radiotherapy; Oncology; Risk Factors; Skin; Radiodermatitis.

INTRODUCTION

Malignant tumors have become major diseases that significantly compromise human health and life. According to estimates by the International Agency for Research on Cancer, a total of 19.3 million new cases of cancer and 10 million deaths were expected by the year 2020[1], which confirms the fatality potential of malignant neoplasms.

Radiotherapy (RT) is one of the main modalities for cancer treatment, used exclusively or in combination with other therapies. Its function is to destroy or slow down tumor growth using ionizing radiation[2]. The sophistication of this treatment has increased markedly over the last two decades, since the delimitation of the irradiation field and the preservation of normal tissue have been improved[3].

For certain tumors, RT represents the first line of treatment, and it is estimated that around half of all patients diagnosed with cancer will be irradiated at some point during the

course of the disease[4]. There are different methods of delivering ionizing radiation, the best known being external radiotherapy or teletherapy, brachytherapy and radioisotope therapy[5-6]. All patients receiving external RT are at risk of skin reactions[7], and it is estimated that up to 95% of them develop moderate to severe skin reactions, called radiodermatitis[8].

Radiotoxicity of the skin occurs due to damage caused by the generation of free radicals and reactive oxygen species in rapidly dividing cells in the basal layer and dermis. Exposure to radiation also leads to impairment of the barrier function of the epidermis and unlike other mechanical or chemical damage to the skin, radiation-induced damage is repetitive and accumulates over the course of treatment[9]. Acute radiodermatitis can present with mild to intense erythema, dry peeling, wet peeling and, in more severe cases, ulceration, hemorrhage and tissue necrosis[10].

It is also important to note that radiodermatitis has a negative impact on the patient's functional capacity and, depending on its severity, can jeopardize the continuity of treatment, compromising local control of the disease and the survival rate, as well as the patient's quality of life[11].

Despite increasing therapeutic precision, normal tissues are still inevitably exposed, i.e. vulnerable to the development of different adverse reactions[10]. The occurrence and severity of radiodermatitis are related to the accumulated dose of ionizing radiation over time, the irradiated site, the planning technique and the dose distribution[12]. Some studies also point out that the severity of radiodermatitis may be associated with factors related to the patient themselves, such as nutritional status, exposure to the sun, smoking, among others[9,13], but these studies are generally conducted with small samples and specific to a particular irradiated area.

Patients often have multiple comorbidities and use multiple medications, which can interfere with the effects of radiotherapy. Notably, the symptoms that occur during and after radiotherapy are not necessarily caused by the radiation, the mechanisms behind a symptom can be diverse and require different treatments, highlighting the importance of differential diagnosis[14].

Therefore, this study aims to make a global assessment of cancer patients undergoing external RT, exploring other patient-related factors that may be associated with the occurrence

of radiodermatitis after this treatment. The aim is therefore to identify the risk factors associated with acute radiodermatitis in cancer patients.

Recognizing how risk factors can be associated with the occurrence of radiodermatitis in oncology patients helps health professionals to assess patients who are going to undergo external RT more thoroughly and, consequently, to provide quality health care with a view to preventing such problems. Furthermore, knowledge of risk factors can help to draw up recommendations and standardize protocols for the prevention and treatment of radiodermatitis.

METHOD

StudyType

This is a cross-sectional, survey-type study, carried out in accordance with the Checklist Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)[15].

Time and Place of Study

The research was carried out in a radiotherapy outpatient clinic of a reference hospital in cancer treatment in the southern region of Brazil, from March to September 2021.

Population and Sample of Study

The population of the study consisted of cancer patients undergoing external RT, either in isolation or combined with another oncological treatment modality.

To calculate the sample, we considered the number of patients treated at the radiotherapy outpatient clinic in the last three months prior to data collection, December 2020 to February 2021. During this period, the health service treated 273 patients for external RT. The formula used for sample calculation was as follows: sample size = z2.p(1 - p)/e2 /1+ (z2.p(1 - p) / e2.N), where "N" is the population size, "e" is the margin of error (percentage in decimal format), and "z" is the z score. In this study, the authors used a 95% confidence level (z score = 1.96) and a 5% sampling error rate. Therefore, the estimated sample for this investigation was 160 patients, to this value was added the 20% percentile related to possible

refusals and losses of participants during data collection, so the sample size established was 192 individuals. The sample calculation was carried out using the SurveyMonkey® (https://pt.surveymonkey.com/mp/sample-size-calculator/).

Eligibility Criteria

The eligibility criteria were: adult patients, regardless of gender, with preserved cognitive functions (assessed by questions such as: name, address, age and date of birth) with RT completed in less than 30 days, in clinical conditions that allowed participation in this study. Patients with incomplete medical records and/or data were excluded.

Instruments

Sociodemographic and clinical characterization: the following variables were collected: gender, age group, schooling, skin color, marital status, monthly income, family history of cancer, use of medication to treat radiodermatitis, type of neoplasm, presence of metastasis, presence of allergies, use of tobacco, use of continuous medication (for the treatment of comorbidities and not radiodermatitis), previous chronic disease, number of applications, surface irradiated, exposure to the sun, time of exposure, treatment carried out, nutritional status, healthy diet, previous lesion in the irradiated area.

RTOG Acute Radiation Morbidity Scoring Criteria: used the indicator for irradiation dermatitis (radiodermatitis) from the instrument developed by Cox, Stetz and Pajak16 and translated into Brazilian Portuguese by Saad et al.[17]. The condition of the skin is classified into five grades: Grade 0, represents skin with no reaction; Grade 1, mild erythema, desquamation, epilation, reduced sweating; Grade 2, moderate erythema, shiny, exudative dermatitis in plaques, confined to the fold and moderate edema; Grade 3, exudative dermatitis beyond the skin folds, intense edema; and Grade 4, ulceration, hemorrhage, necrosis[16]. This instrument is freely accessible according to the Radiation Therapy Oncology Group (RTOG).

Data Collection

Before starting data collection, a pilot test was carried out with 30 participants in order to test the suitability of the study's data collection procedure. These participants were included in the study as the data collection procedures were not adjusted.

RISK FACTORS ASSOCIATED WITH ACUTE

RADIODERMATITISAMONG CANCER PATIENTS

Data collection took place between March and September 2021. Participants were approached in the waiting room of the radiotherapy outpatient clinic, and 198 individuals were eligible. Considering that there were two refusals, the final sample consisted of 196 patients undergoing external RT. Data was collected up to 30 days after the end of the last RT session, by applying the instruments mentioned above (interview), followed by skin assessment (direct observation by the researchers). Interviews lasted an average of 15 minutes. Data such as the type of cancer, number of external RT applications, history of adverse reactions to treatment, presence of metastases and whether the patient had undergone combined treatment or RT alone up to the time of collection were obtained from the participants' medical records. Data collection took place in a private room at the outpatient clinic where the study was carried out.

Data Analisis

The data collected was tabulated and evaluated by pairs to correct any typing errors and then stored and analyzed using the Statistical Package for the Social Sciences (SPSS) version 20.0. A hierarchical approach and conditional logistic regression were used, with the regression coefficients representing the logarithms of the odds ratios. Three hierarchical levels were considered for the analysis, represented by the determinants at the distal (gender; age; family history of cancer; use of sunscreen; medication to treat radiodermatitis; type of neoplasm; presence of metastasis), intermediate (use of tobacco; use of continuous medication; previous chronic illness; number of applications) and proximal (irradiated surface; exposure to the sun; time spent in the sun without protection; treatment carried out; nutritional status; healthy diet; previous lesion in the irradiated area; presence of allergies) levels. The multivariate regression analysis was conducted according to the plan proposed in the hierarchical approach for assessing the causality of radiodermatitis. Forward logistic regression was used for each block of variables. The set of variables at one level was analyzed independently of those at the other levels. The adjustments of the variables of subsequent levels were integrated when statistically significant, following the same order adopted for the other levels.The variables were kept in the final model when the adjustments were adequate. The modeling process consisted of the selected variables. The variables that proved to be statistically significant at a 20% level (p< 0.20) in the univariate analysis were selected for the

final logistic model. The crude and adjusted odds ratios were presented with their respective 95% confidence intervals. A significance level of p<0.05 was used for these inferential statistical tests.

Ethics Aspects

The study was approved by the Human Research Ethics Committee, under ethical opinion number 4.559.007, and CAAE: 42990320.4.0000.0116 of 25/02/2021. After being informed about the aim and procedures of the study, those patients who agreed to take part gave their written consent by signing the Free and Informed Consent Form in two copies.

RESULTS

The sociodemographic variables and the occurrence of radiodermatitis and their respective degrees of evaluation are shown in Table 1. It should be noted that all 196 participants underwent conventional external RT.

**RISK FACTORS ASSOCIATED WITH ACUTE
RADIODERMATITISAMONG CANCER PATIENTS**

Table 1. Sociodemographic and clinical characterization of the participants. Chapecó, Brazil, 2021.

Variable		n =196	%
Gender			
	Female	106	54,1
	Male	90	45,9
Age group			
	18 to 59 years	94	48,0
	> 60 years	102	52,0
EducationLevel			
	Illiterate	7	3,6
	Incompleteprimaryeducation	62	31,6
	Complete primaryeducation	77	39,3
	High schoolincomplete	6	3,1
	Completed high school	23	11,7
	Incompleteuniversitydegree	7	3,6
	Completeduniversitydegree	14	7,1
Skin Color			
	White	186	94,9
	Yellow	4	2,0
	Brown	4	2,0
	Black	2	1,0
Marital status			
	Married	120	61,2
	Divorced	18	9,2
	Stableunion	15	7,7
	Widowed	29	14,8
	Single	14	7,1
Rent (mw*)			
	Lessthan 1	23	11,7
	1 to 2	52	26,5
	2 to 3	88	44,9
	3 to 5	20	10,2
	More than 5	13	6,6
Radiodermatitis			
	Yes	109	55,6
	No	87	44,4
Grade			
	Grade 0	87	43,9
	Grade 1	79	40,3
	Grade 2	21	11,2
	Grade 3	9	4,6

*mw = minimum wage (value: R$1.320, US$275,41).

The demographic and health characteristics associated with radiodermatitis according to the univariate analyses of the variables at the distal hierarchical level are shown in Table 2. Female gender, age under 59 and the presence of metastases were associated with the occurrence of the outcome in this block.

Table 2. Demographic and health characteristics associated with radiodermatitis according to the results of univariate analysis of the distal level. Chapecó, Brazil, 2021.

Variables	Radiodermatitis		Total	OR raw$_{(IC\ 95\%)}$	p-value
	Sim	Não	n (%)		
	n (%)	n (%)			
Gender					0,095
Female	64 (32,7)	42 (21,4)	106 (54,1)	0,65 (0,37 – 1,15)	
Male	45 (23,0)	45 (23,0)	90 (45,9)	1	
Age					0,036
Until 59years	59 (30,1)	35 (17,9)	94 (48,0)	1	
60 yearsor more	50 (25,5)	52 (26,5)	102 (52,0)	1,75 (1,99 – 3,10)	
Family historyofcancer					0,488
Yes	74 (37,8)	58 (29,6)	132 (67,3)	1,05 (0,58 – 1,92)	
No	35 (17,9)	29 (14,8)	64 (32,7)	1	
Use ofsunscreen					0,281
Yes	52 (26,5)	37 (18,9)	89 (45,4)	1	
No	57 (29,1)	50 (25,5)	107 (54,6)	1,23 (0,69 – 2,17)	
Medicationtotreatradiodermatitis					0,395
Yes	107 (54,6)	84 (42,9)	191 (97,4)	1	
No	2 (1,0)	3 (1,5)	5 (2,6)	1,91 (0,31 – 11,69)	
Typeofneoplasm					0,361
Solid	105 (53,6)	82 (41,8)	187 (95,4)	1,60 (0,41 – 6,15)	
Non-solid	4 (2,0)	5 (2.6)	9 (4,6)	1	
Metastasis					0,104
Yes	12 (6,1)	16 (8,2)	28 (14,3)	0,54 (0,24 – 1,23)	
No	97 (49,5)	71 (36,2)	168 (85,7)	1	

OR = Oddisratio.

Table 3 shows the univariate analyses of the variables at the intermediate hierarchical level. The results showed that tobacco use and the use of continuous medication were

associated with the occurrence of radiodermatitis.

Table 3. Behavioral characteristics and health history associated with radiodermatitis according to the results of univariate analyses at the intermediate level. Chapecó, Brazil, 2021.

Variable	Radiodermatitis		Total	OR raw$_{(IC\ 95\%)}$	p-value
	Sim	Não	n (%)		
	n (%)	n (%)			
Use oftabacco					0,050
Yes	36 (18,4)	19 (9,7)	55 (28,1)	1,76 (1,92- 3,36)	
No	73 (37,2)	68 (34,7)	141 (71,9)	1	
Use ofcontinuousmedication					0,152
Yes	77 (39,3)	68 (34,7)	145 (74,0)	0,67 (0,34 – 1,29)	
No	32 (16,3)	19 (9,7)	51 (26,0)	1	
Previouschronicillness					0,237
Yes	70 (35,7)	61 (31,1)	131 (66,8)	0,76 (0,41 – 1,39)	
No	39 (19,9)	26 (13,3)	65(33,2)	1	
Numberofapplications					0,340
Until 15 sessions	31 (15,8)	28 (14,3)	59 (30,1)	1	
16 or more	78 (39,8)	59 (30,1)	137 (69,9)	0,83 (0,45- 1,54)	

OR = Oddisratio.

The univariate analyses of the variables at the proximal hierarchical level are shown in Table 4. The irradiated surface in an area of folds, constant humidity and friction, combined treatment, previous injury to the irradiated area and the presence of allergies were associated with the risk of radiodermatitis. On the other hand, shorter sun exposure times (10 to 59 minutes) and adequate nutritional status were protective factors.

Table 4. Characteristics associated with radiodermatitis according to the results of univariate analysis of the proximal level. Chapecó, Brazil, 2021.

Variables	Radiodermatitis		Total	OR raw(IC 95%)	p-value
	Sim	Não	n (%)		
	n (%)	n (%)			
Irradiated surface					**0,002**
Area of folds, humidity and constant friction	70 (35,7)	37 (18,9)	107 (54,6)	2,42 (1,36 – 4,32)	
Unfolded area with little moisture and no friction	39 (19,9)	50 (25,5)	89 (45,4)	1	
Exposuretothesun					**0,000**
Yes	34 (17,3)	6 (3,1)	40 (20,4)	6,12 (2,43-15,40)	
No	75 (38,3)	81 (41,3)	156 (79,6)	1	
Unprotected exposure to the sun					**0,026**
Between 10 and 59 min	98 (50,0)	85 (43,4)	183 (93,4)	1	
Higherthan60 min	11 (5,6)	2 (1,0)	13 (6,6)	0,21 (0,04 – 0,97)	
Treatmentcarried out					**0,032**
Exclusive radiotherapy	28 (14,3)	34 (17,3)	62 (31,6)	1,53 (1,29 – 1,99)	
Combinedtreatment	81 (41,3)	53 (27,0)	134 (68,4)	1	
Nutritional status					**0,000**
Adequate BMI	35 (17,9)	56 (28,6)	91 (46,4)	1	
Overweight BMI	74 (37,8)	31 (15,8)	105 (53,6)	0,26 (0,14 – 0,47)	
Healthynutrition					0,433
Yes	102 (52,0)	80 (40,8)	182 (92,9)	1	
No	7 (3,6)	7 (3,6)	14 (7,1)	1,25 (0,43 – 3,78)	
Previous injury to the irradiated area					**0,015**
Yes	33 (16,8)	14 (7,1)	47 (24,0)	2,26 (1,12 – 4,57)	
No	76 (38,8)	73 (37,2)	149 (76,0)	1	
Presenceofallergies					**0,037**
Yes	21 (10,7)	8 (4,1)	29 (14,8)	2,35 (1,98 – 5,62)	
No	88 (44,9)	79 (40,3)	167 (85,2)	1	

OR = Oddisratio.

The final result of the hierarchical multivariate analysis is shown in Table 5. After adjustment in the final model, the use of continuous medication was 2.30 times more likely to cause radiodermatitis and being overweight was 4.78 times more likely to cause the outcome.

Minimal exposure to the sun and an irradiated surface without folds, with little humidity and without friction were protective factors for radiodermatitis.

Table 5. Final hierarchical explanatory model of the factors associated with the occurrence of radiodermatitis. Chapecó, Brazil, 2021.

Model	OR raw	OR adjusted	IC 95% (OR adjusted)
Intermediatelevel			
Use ofcontinuousmedication	0,67	2,30	1,04 – 5,08
Proximal level**			
No sunexposure	6,12	0,14	0,04 – 0,42
Overweight	0,26	4,78	2,35 – 9,71
Irradiated surface without folds, low humidity and no friction	2,42	0,31	0,15 – 0,64

**adjusted by the variables of the same level and by the variables of the intermediate and distal levels.

DISCUSSION

For contextualization purposes, it is important to mention that in the local radiotherapy service in this study, external radiotherapy is carried out using a linear accelerator, mostly using the 2D method, although the 3D method is already available in the service. In this sense, it is important to note that radiotherapy equipment using cobalt as a source is six times more likely to develop severe radiodermatitis when compared to patients treated with a linear accelerator[18]. With regard to the 2D method, researchers have stated that this method also increases the risk of developing severe radiodermatitis sixfold compared to patients treated with the Intensity-modulated radiation therapy (IMRT) or Volumetric Modulated Arc Therapy (VMAT) methods[18]. It is therefore valid to consider that the participants in this investigation are more susceptible to developing the most severe form of radiodermatitis.

RISK FACTORS ASSOCIATED WITH ACUTE
RADIODERMATITISAMONG CANCER PATIENTS

It was also found that patients taking continuous medication to treat other comorbidities had a 2.3-fold increase in the chance of radiodermatitis. Although there is a limitation regarding stratification by type of drug used by the participants, many drugs (for example, antibiotics, barbiturates, sulphonamides) can cause rash, urticaria and some can simply increase skin photosensitivity, such as: tetracycline, ketoprofen, methotrexate, hydrochlorothiazide and promethazine[19]. In another study[20], the author identified an association between the continuous use of statins and breast radiodermatitis, with a fourfold increase in the chance of radiodermatitis in grades II and IV. In the same study, hypothyroidism was a risk factor for the development of radiodermatitis in the early supraclavicular region.

With regard to tobacco consumption, it was possible to identify it as a factor associated with severe skin reactions, as chronic exposure to tobacco hinders the skin's healing process and causes changes in the physiology of systems, including the skin. Among the patients evaluated in the study by Vieira et al.[13], all those who reported current tobacco use or had stopped using tobacco in the last six months had developed erythema, which is one of the initial signs of radiodermatitis.

Another result of this study was that minimal exposure to the sun was a protective factor for radiodermatitis. Physiologically, the scientific literature describes[28] that exposure to ultraviolet radiation sensitizes the skin, a factor that increases the risk of phototoxicity and photoallergy; therefore, if this exposure is associated with the use of medication and radiotherapy, the chance of radiodermatitis increases.

In a study of patients diagnosed with breast cancer who underwent radiotherapy[13], acute radiodermatitis was more common in those who used hormone therapy concomitantly with radiotherapy, with erythema in the axillary and frontal regions, and dry scaling in the frontal region, which reinforces the evidence that oral hormone therapy is a factor associated with a greater chance of developing acute radiodermatitis.

Another relevant finding in this study was that being overweight increased the chance of the outcome by 4.7 times. Thus, the influence of obesity on the effectiveness of radiotherapy is discussed. For example, in a retrospective Canadian study, external beam radiotherapy was administered to treat localized prostate cancer in a population with a high body mass index (BMI). In this population, BMI remained a significant predictor of

biochemical relapse[21]. However, in another study carried out in Iraq with women with breast cancer, higher BMI was not observed as a predictor of increased radiodermatitis[22].

Overweight patients undergoing treatment for cervical cancer also have increased treatment-related toxicities compared to normal weight patients[23]. Higher BMI is associated with poorer quality of life in cancer patients treated with RT before, during and after treatment, reflected in worse symptoms, impaired function and interference in key aspects of life[24]. In addition, high BMI was predictive of an increase in skin problems in the results of a study carried out in Argentina [25].

In women who irradiate the breast area, in addition to BMI, it is also important to consider the volume of the breasts, which favors the occurrence of skin folds and local humidity, which increases the chance of radiodermatitis, especially in the inframammary fold region[13]. In the study by Vieira et al.[13], 71.15% of the women had a BMI greater than [25,] classified as obese or overweight. There was a higher incidence of erythema in the axillary region and inframammary fold, dry desquamation in the axillary region and wet desquamation in the axillary region and inframammary fold in overweight patients, as well as a higher incidence of degrees of radiodermatitis in patients with large breasts.

On the other hand, in a study carried out in the United States[26], there was no significant association between favorable treatment parameters (PSA, Gleason score, TNM stage, margins, age) and BMI in terms of relapse in patients after prostatectomy followed by biochemical relapse and salvage radiotherapy, but obesity was associated with a higher relapse rate in the multifactorial analysis.

It is worth noting that high BMI and, consequently, overweight facilitate the presence of skin folds in the treatment area, and this factor is associated with intensified skin reactions, since the appositional skin has areas that are in contact with others, resulting in excess moisture, heat and friction[9,27], which allows us to understand that the irradiated surface without folds, little moisture and no friction, was a protective factor for the radiodermatitis outcome.

Limitations

The study's limitations include the assessment of the participant's nutritional status only by confirming a healthy eating habit based solely on self-report, and the lack of

stratification of continuous medication for the treatment of other comorbidities (such as statins). Although these limitations affect the strength of the evidence produced, they do not reduce the clinical importance of the findings, which can serve as a basis for further research.

Contributions

The evidence from this research will enable health professionals to pay attention to the risk factors associated with radiodermatitis and refine their clinical assessment during the follow-up of cancer patients undergoing external RT. At the same time, the scientific community will have evidence to support its investigations and provide a deeper understanding of the behavior of the associated clinical variables.

CONCLUSIONS

When the participants in this study are referred for external radiotherapy, they are already at risk of developing radiodermatitis, given that the 2D method is the most commonly used in this therapy. That said, the sample found that being on continuous medication for the treatment of other non-cancer health problems was related to the outcome of radiodermatitis. Despite the limitations in terms of stratification of the medications in use, it is clear that a detailed anamnesis by health professionals in relation to this factor is important. Another characteristic associated with the occurrence of radiodermatitis was being overweight, so proper nutritional guidance and monitoring for cancer patients with a high BMI should be considered, above all because of its correlation with poorer quality of life indices and an increase in areas with folds. Similarly, tobacco consumption was another related factor, which requires appropriate professional guidance regarding its consumption, as well as its effects on other systems of the human body. Finally, the shorter time spent in the sun appears to be a protective effect for the outcome under study, so this, as well as the other risk factors identified, should be part of the clinical assessment of patients who will undergo or are undergoing radiotherapy for cancer treatment.

RISK FACTORS ASSOCIATED WITH ACUTE

RADIODERMATITISAMONG CANCER PATIENTS

REFERENCES

1. Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: A Cancer Journal for Clinicians, 71(3), 209–249.https://doi.org/10.3322/caac.21660

2. Lu, Z., Zheng, X., Ding, C., Zou, Z., Liang, Y., Zhou, Y., & Li, X. (2022). Deciphering the Biological Effects of Radiotherapy in Cancer Cells. Biomolecules, 12(9), 1167.https://doi.org/10.3390/biom12091167

3. Coleman, C. N., Eke, I., Makinde, A. Y., Chopra, S., Demaria, S., Formenti, S. C., Martello, S., Bylicky, M., Mitchell, J. B., &Aryankalayil, M. J. (2020). Radiation-induced Adaptive Response: New Potential for Cancer Treatment. Clinical Cancer Research, 26(22), 5781–5790.https://doi.org/10.1158/1078-0432.ccr-20-0572

4. Zaffaroni, M., Vincini, M. G., Corrao, G., Marvaso, G., Pepa, M., Viglietto, G., Amodio, N., &Jereczek-Fossa, B. A. (2022). Unraveling Mitochondrial Determinants of Tumor Response to Radiation Therapy. International Journal of Molecular Sciences, 23(19), 11343.https://doi.org/10.3390/ijms231911343

5.Chandra, R. A., Keane, F. K., Voncken, F. E. M., & Thomas, C. R. (2021). Contemporary radiotherapy: present and future. The Lancet, 398(10295), 171–184. doi:10.1016/s0140-6736(21)00233-6

6. Gourgou, S., & Azria, D. (2022). Essais cliniques enOncologieRadiothérapie: réflexionméthodologique. Cancer/Radiothérapie.https://doi.org/10.1016/j.canrad.2022.06.002

7. Backler, C., Bruce, S., Suarez, L., & Ginex, P. (2020). Radiodermatitis: Clinical Summary of the ONS Guidelines™ for Cancer Treatment–Related Radiodermatitis. Clinical Journal of Oncology Nursing, 24(6), 681–684.https://doi.org/10.1188/20.cjon.681-684

8. Rosenthal, A., Israilevich, R., & Moy, R. (2019). Management of acute radiation dermatitis: A review of the literature and proposal for treatment algorithm. Journal of the American Academy of Dermatology, 81(2), 558–567.https://doi.org/10.1016/j.jaad.2019.02.047

9. Winter, S. F., Vaios, E. J., Shih, H. A., Grassberger, C., Parsons, M. W., Gardner, M. M., Ehret, F., Kaul, D., Boehmerle, W., Endres, M., & Dietrich, J. (2023). Mitigating Radiotoxicity in the Central Nervous System: Role of Proton Therapy. Curr. Treat. Options in Oncol. 24, 1524–1549. https://doi.org/10.1007/s11864-023-01131-x

10. Yang, X., Ren, H., Guo, X., Hu, C., & Fu, J. (2020). Radiation-induced skin injury: pathogenesis, treatment, and management. Aging.https://doi.org/10.18632/aging.103932

11. Fuzissaki, M. A., Paiva, C. E., Oliveira, M. A., Canto, P. P. L., & Maia, Y. C. P. (2019). The Impact of Radiodermatitis on Breast Cancer Patients' Quality of Life During

Radiotherapy: A Prospective Cohort Study. Journal of Pain and Symptom Management. 58(1), 92-99. https://doi.org/10.1016/j.jpainsymman.2019.03.017

12. AHN, S., SUNG, K., KIM, H. J., CHOI, Y. E., LEE, Y. K., KIM, J. S., LEE, S. K., & ROH, J.-Y. (2019). Reducing Radiation Dermatitis Using a Film-forming Silicone Gel During Breast Radiotherapy: A Pilot Randomized-controlled Trial. *In Vivo*, *34*(1), 413–422. https://doi.org/10.21873/invivo.11790

13. Vieira LAC, Menêses AG, Bontempo PSG, Simino GPR, Ferreira EB, Guerra ENS, Reis PED. Incidence of radiodermatitis in breast cancer patients during hypofractionated radiotherapy. RevEscEnferm USP. 2022;56:e20220173. https://doi.org/10.1590/1980-220X-REEUSP-2022-0173en

14. De ruysscher*et al.*Radiotherapy toxicity. *Nature Reviews Disease Primers*, v. 5, n. 1, 21 fev. 2019. Disponível em: https://doi.org/10.1038/s41572-019-0064-5. Acesso em: 8 maio 2023.

15. Malta M, Cardoso LO, Bastos FI, Magnanini MMF, Silva CMFP da. Iniciativa STROBE: subsídios para a comunicação de estudos observacionais. Rev Saúde Pública [Internet]. 2010Jun;44(3):559–65. Available from: https://doi.org/10.1590/S0034-89102010000300021

16. Cox, J. D., Stetz, J., & Pajak, T. F. (1995). Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European organization for research and treatment of cancer (EORTC). International Journal of Radiation Oncology*Biology*Physics, 31(5), 1341–1346.https://doi.org/10.1016/0360-3016(95)00060-c

17. SAAD, E.D *et al*. Critérios comuns de toxicidade do Instituto Nacional de Câncer dos Estados Unidos. Revista Brasileira de Cancerologia, São Paulo, v. 48, n. 1, p. 63- 96, mar. 2002.

18. Cardozo AS, Simões FV, Santos VO, Portela LF, Silva RC. Radiodermatite severa e fatores de risco associados em pacientes com câncer de cabeça e pescoço. TextoContextoEnferm 2020; 29: e20180343.

19. McNees, P. (2006). Skin and Wound Assessment and Care in Oncology. *Seminars in Oncology Nursing*, *22*(3), 130–143. https://doi.org/10.1016/j.soncn.2006.04.003

20. Cavalcante LG. Fatores de risco para desenvolvimento de radiodermite em mulheres com câncer de mama. [dissertação]. Botucatu: Programa de Pós-graduação em Enfermagem, Universidade Estadual Paulista; 2019.

21. Palma, D., Pickles, T., &Tyldesley, S. (2007). Obesity as a predictor of biochemical recurrence and survival after radiation therapy for prostate cancer. *BJU International*, *100*(2), 315–319. https://doi.org/10.1111/j.1464-410x.2007.06897.x

RISK FACTORS ASSOCIATED WITH ACUTE

RADIODERMATITISAMONG CANCER PATIENTS

22. Adil, A. Noaimi, N. Dawood, A., & Dalia S. Noaimi. (2023). The frequency of acute radiodermatitis and associated risk factors among patients with breast cancer treated by radiotherapy. Journal of Pakistan Association of Dermatologists, 33(2), 629–636.

23. Ross, K. H., Gogineni, K., Subhedar, P. D., Lin, J. Y., &McCullough, L. E. (2019). Obesity and cancer treatment efficacy: Existing challenges and opportunities. *Cancer*, *125*(10), 1588–1592. https://doi.org/10.1002/cncr.31976

24. Fang, P., Tan, K. S., Troxel, A. B., Rengan, R., Freedman, G., & Lin, L. L. (2013). High body mass index is associated with worse quality of life in breast cancer patients receiving radiotherapy. *Breast Cancer Research and Treatment*, *141*(1), 125–133. https://doi.org/10.1007/s10549-013-2663-2

25. Córdoba, E. E., Lacunza, E., &Güerci, A. M. (2021). Clinical factors affecting the determination of radiotherapy-induced skin toxicity in breast cancer. Radiation oncology journal, 39(4), 315–323. https://doi.org/10.3857/roj.2020.00395

26. King, C. R., Spiotto, M. T., & Kapp, D. S. (2009). Obesity and Risk of Biochemical Failure for Patients Receiving Salvage Radiotherapy After Prostatectomy. *International Journal of Radiation Oncology*Biology*Physics*, *73*(4), 1017–1022. https://doi.org/10.1016/j.ijrobp.2008.05.041

27. Bernier, J., Bonner, J., Vermorken, J. B., Bensadoun, R. J., Dummer, R., Giralt, J., Kornek, G., Hartley, A., Mesia, R., Robert, C., Segaert, S., & Ang, K. K. (2008). Consensus guidelines for the management of radiation dermatitis and coexisting acne-like rash in patients receiving radiotherapy plus EGFR inhibitors for the treatment of squamous cell carcinoma of the head and neck. *Annals of Oncology*, *19*(1), 142–149. https://doi.org/10.1093/annonc/mdm400

28. Sibaud V. Anticancer treatments and photosensitivity. J Eur Acad Dermatol Venereol. 2022 Jun;36 Suppl 6(Suppl 6):51-58. doi: 10.1111/jdv.18200.

RISK FACTORS ASSOCIATED WITH ACUTE

RADIODERMATITISAMONG CANCER PATIENTS

Authors' contributions	
Carolina Machado Eisenhut:	Conceptualization; Investigation; Project administration; Writing–original draft.
Milena Schneiders:	Visualization; Writing–original draft; Writing–review & editing.
Rafael de Lima Carmo:	Visualization; Writing–original draft; Writing–review & editing.
Jacira Batista de Oliveira:	Visualization; Writing–original draft; Writing–review & editing.
Ana Cláudia Mesquita Garcia:	Visualization; Writing–review & editing.
Érica de Brito Pitilin:	Data curation; Formal analysis; Visualization.
Paula Elaine Diniz dos Reis:	Supervision; Formal analysis; Visualization.
Vander Monteiro da Conceição:	Conceptualization; Datacuration; Formal analysis; Investigation; Methodology; Supervision.
All the authors approved the final version of the text.	
Conflict of interest:	There is no conflict of interest.
Financing:	No financing.
Corresponding author:	Vander Monteiro da Conceição Federal University of Fronteira Sul – UFFS SC-484, Km 02 - Fronteira Sul, Chapecó/SC, Brazil. CEP 89815-899 vander.conceicao@uffs.edu.br
Editor-in-chief:	Adriane Cristina Bernat Kolankiewicz. Ph.D