

Original Article

Skin Toxicities and Practices of Patients Receiving Radiotherapy

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Correspondence: Duzgun Gonul, RN, PhD of Internal Medicine Nursing, Health Sciences University, Tepecik Training and Research Hospital, Palliative Care Department, Yenisehir/ Konak. Izmir, Turkey e-mail: gonulgurbuz84@hotmail.com**Abstract****Background:** The identification of skin toxicities due to radiotherapy in cancer patients is important in planning strategies to eliminate or reduce the severity of potential skin reactions.**Objective:** The aim of this study was to determine the frequency of skin toxicity in patients receiving radiotherapy and to determine the evidence-based practices of patients in dealing with skin toxicity.**Methods:** The study sample consisted of 84 patients treated between December 2016 and May 2017 in the Department of Radiation Oncology at a university hospital. Skin toxicity was categorized using the Classification of Skin Reactions Associated with Radiation Therapy Form, which was developed by the Radiation Therapy Oncology Group (RTOG). Data were analyzed using the SPSS 25.0 program. One-way analysis of variance was used to compare quantitative variables; chi-square test was used for categorical variables. A $p < 0.05$ was considered statistically significant.**Results:** Of the patients who had received radiotherapy, 70.2% ($n = 59$) had an acute skin reaction, RTOG Grade-1 skin reactions being the most frequent (44%, $n = 37$). The degree of RTOG skin toxicity was found to increase as the RT dose increased. Evidence-based applications such as aloe vera (8.3%, $n = 7$), using high-factor sunscreen for sun exposure (16.7%, $n = 14$), and moisturizing the skin (32.1%, $n = 27$) were not frequent. The evidence-based practice score of the Grade-1 group (17.00 ± 2.53) was higher than that of the Grade-0 group (12.6 ± 5.44) or Grade 2 and above (14.32 ± 4.25).**Conclusion:** The findings of this study showed that skin toxicity is quite prevalent among RT patients. Randomized clinical trials are required to propose solutions to this problem. Additionally, these findings support the importance of the patient training for the prevention of skin toxicities and the necessity of taking precautions after the RT treatment.**Keywords:** radiodermatitis, evidence-based practice, skin care**Introduction**

New methods are continuously being added to the treatment of cancer patients. Current treatment methods for cancer are chemotherapy (CT), radiotherapy (RT), surgery, and immunotherapy (IT). These methods are used alone or in

combination depending on characteristics of the patients diagnosed with cancer and their disease status. In general, primary (therapeutic), combined (with other treatment methods), adjuvant (supplementary) and palliative (supportive) treatments are used in 50-70% of patients with cancer at any stage of their disease

(Singh et al., 2016; Miller et al., 2016; Deng and Cassileth, 2008).

The purpose of RT is to destroy cancer cells; however, healthy cells within the treatment area are also affected. Radiation damage to the normal tissue depends on the extent and location of the treatment area, total and daily dose administered, age and general condition of the patient, and quality of treatment. It is possible to minimize the side effects with the selection of the appropriate device, proper planning, and careful follow-up during the treatment (Atalar and Ozyar, 2010). One of the most common side effects of radiation is acute skin reaction ranging from mild erythema to moist desquamation and sometimes ulceration. All patients receiving external RT have the potential to develop a reaction at the treatment area. Salvo and Olsen et al reported that 85-87% of patients receiving RT had moderate to severe skin reactions (Salvo et al. 2010; Olsen et al. 2001). In a study by Hornsby et al., moist desquamation categorized as grade 3 was reported in 10-15% of the groups that developed side effects (Hornsby et al. 2004). Skin reactions to radiation are not "burns". These reactions occur as a result of the damage to the skin's basal cell layer, and the fundamental reason is the imbalance between the normal production of cells in this layer and the destruction of the cells on the skin surface (Trueman, 2013). It is essential to minimize the damage as much as possible by ensuring that the applied intervention is based on best practice and evidence-based guidelines (Porock and Kristjanson, 1999).

Providing care for cancer patients requires multidisciplinary teamwork. Radiotherapy and oncology nurse is an important and complementary healthcare professional in this teamwork. The overall goal of the radiotherapy nurse is to ensure that the patient and their family continue to function at the highest level during the course of the disease and to improve their quality of life. Nurses aim to control the symptoms of acute and late side effects with evidence-based nursing practices (Kav, 2000).

Biological response to radiation can be categorized acute, subacute and late reactions. Early reactions caused by RT occur in the first 3 months of the treatment. Subacute reactions may develop 3 to 6 months after RT, and late reactions may occur 6 months and years after. In RT, the symptoms are mostly in the area of

radiation treatment, and the severity of symptoms increases when RT is co-administered with CT (Bostanoglu, 2014). Few studies exist in the literature concerning how frequently the patients use evidence-based applications against skin reactions caused by RT. In a study by Deng et al., *Aloe vera* and calendula were reported to prevent allergic reactions (Deng et al, 2004). Ghasemi et al. reported that 1% atorvastatin applied as a topical gel to breast cancer patients reduced skin toxicity caused by radiotherapy (Ghasemi et al, 2018). In a study investigating the use of topical steroids, Bostrom et al. reported that physician-evaluated erythema level was significantly reduced in patients using topical steroids compared to those using placebo (Bostrom et al, 2001). In one study, D'Haese et al. indicated that the use of evidence-based practices should be increased in order to reduce the use of conventional and inappropriate methods (D'Haese et al, 2010).

Aim

The aim of this study was to determine the prevalence of skin toxicity in patients receiving RT and patients' use of evidence-based applications to prevent skin toxicity. For this purpose, the following questions were asked:

1. What is the prevalence of skin toxicity in patients receiving RT, and how is the degree of toxicity distributed?
2. To what extent do patients receiving RT use evidence-based practices to counteract skin toxicities?

Methods

Research design and setting: This study had a descriptive cross-sectional design and was conducted in the Department of Radiation Oncology at a university hospital between December 2016 and May 2017. Study reporting was completed according to the guidelines in the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement [10]. Necessary approval for the study was obtained from the Ethics Committee for Clinical Research at Ege University. The patients were informed about the objectives of the study and about how the data would be handled, and they were asked to provide written consent for the study.

Patient selection: The study population consisted of all patients who received RT in the

Department of Radiation Oncology at a university hospital. The study sample included patients who agreed to participate and met the inclusion criteria. The patients who were over 18 years of age, had the capacity to communicate verbally, received at least 5 sessions of RT (as the side effects emerge after at least 5 cycles), and

volunteered to participate were included. The study sample was selected through random sampling (convenience sampling), one of the non-probability sampling techniques. The study included 84 patients (11 patients were excluded as they were under 18 years of age) (Figure 1).

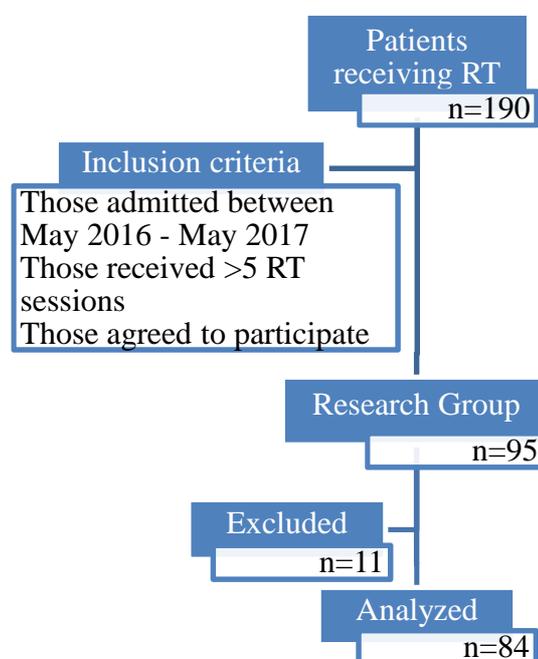


Figure 1.The study flowchart.

Variables: Skin reactions categorized according to the Radiation Therapy Oncology Group (RTOG) classification (Grade 1 / Grade 2 / Grade 3 / Grade 4) were dependent variables. Independent variables were patients' gender (male / female), age (18-38 / 39-59 / 60-80 / >80 years of age), educational status (not literate / literate / primary school / secondary school / high school / university), marital status (married / unmarried / divorced-widow-separated), having a chronic illness (yes / no), work environment (indoor / outdoor), smoking (yes / no), alcohol use (yes / no), cancer type (breast / lung / head and neck / stomach / other), evidence-based applications, and the RT dose and frequency.

Data were obtained through face-to-face interviews, which were done after RT in the waiting room and lasted for about 10 minutes.

Sociodemographic data were collected using the Patient Identification Form, which was created by the researchers based on the literature. The side effects associated with RT were evaluated using the Radiation Therapy-Related Skin Reactions Classification Form developed by RTOG (Bostanoglu, 2014).

The Patient Identification Form included a list of questions probing personal and health-related characteristics of the patients and evidence-based practices employed by the patients.

The RTOG Form is one of the most commonly used scoring systems for the standardization and reporting of early and late effects of radiation. In this form, skin reactions associated with RT treatment are classified using toxicity criteria developed by the RTOG. The RTOG classification grades skin reactions zero to four

as well as acute or late reactions. In acute reactions, Grade 1 indicates mild rash, tenderness, heat increase, and itching on the skin while Grade 4 indicates ulceration, bleeding, and necrosis. Here, grading is done by evaluating the patient's skin.

Quantitative variables: Each patient was scored for applying each of the 24 evidence-based practices for protection from skin toxicity; they were scored “1” for correct application or “0” for incorrect application to give a total evidence-based practice (EBP) score ranging from 0 to 24. A higher ABP score indicated that the patient employs more evidence-based practices.

Statistical methods: The data were analyzed with SPSS 25.0 program (SPSS Inc., Chicago, USA) and presented as a number, percentage, mean, and standard deviation. Chi-square (Fisher's exact test) was used for the comparison of the categorical data (i.e., sociodemographic and clinical characteristics) in terms of the RTOG classification. Mean EBP scores of the RTOG skin toxicity groups were compared using one-way analysis of variance (ANOVA) and post hoc Tukey HSD (honestly significant difference) procedure. The statistical significance level was set at $p < 0.05$.

Results

A total of 84 patients were included in data analysis. Of these, 57.1% were male, 44% were in age group 60-80 year, and 86.9% were married, 70.2% were unemployed; of those who were employed, 78.6% worked indoors. It was found that 72.6% of the patients did not smoke and 90.5% did not consume alcohol. The sociodemographic characteristics of the patients were given in Table 1. It was found that 33.3% ($n = 28$) of the patients had lung cancer, 77.4% ($n = 65$) received only RT, 54.8% had no chronic disease other than cancer, 71.4% had ($n = 60$) received RT at a dose of 2 Gy, 38.1% ($n = 32$) received 12-21 RT sessions, and 42.9% ($n = 36$) received RT in the breast area (Table 2). It was found that sources of information about RT were healthcare personnel for 57.1% ($n = 48$), the internet for 3.6% ($n = 3$), or the other sources for 2.4% ($n = 2$) of the patients. The most common three practices against skin toxicities were “avoiding lotions” (86.9%; $n = 73$), “preference of cotton or soft-contact-surface clothing” (86.9%; $n = 73$), and “avoiding skin-tight underwear” (83.3%; $n = 70$). The least common

three practices were “*Aloe vera* application to the treatment area” (8.3%, $n = 7$), “using high-factor sunscreens” (16.7%, $n = 14$), and “moisturizing skin” (32.1%, $n = 27$) (Table 3).

Acute skin reaction developed in 70.2% ($n = 59$) of the patients who received RT with RTOG Grade 1 being the most frequent (44%; $n = 37$) (Figure 2).

The proportion of RTOG Grade 2 among the patients over 60 years of age (37.5%; $n = 15$) was higher than those under the age of 60 (15.9%; $n = 7$) ($\chi^2 = 2.33$; $p = 0.036$). The RTOG grade of the skin toxicity was increased as the RT dose increased ($\chi^2 = 9.36$; $p = 0.01$). The proportion of RTOG Grade 1 skin toxicity or above was significantly higher among patients receiving RT (72.3%; $n = 47$) or RT+CT (78.6%; $n = 11$) than those receiving CT+IT (20.0%; $n = 1$) ($\chi^2 = 5.73$; $p = 0.05$). While Grade 1 skin toxicity was more common among patients with breast / head-neck cancer (68.0%; $n = 17$) and rectum / prostate cancer (66.7%; $n = 6$), Grade 2 skin toxicity was more common among patients with lung cancer (31.3%; $n = 10$) ($\chi^2 = 17.63$; $p = 0.005$). No significant relationship was found between skin toxicity and gender, marital status, occupation, education, source of health-related information, work environment, smoking, alcohol use, accompanying non-cancer diseases, and number of RT sessions ($p > 0.05$). Table 4 shows the comparison of sociodemographic and clinical subgroups of patients with regard to the RTOG-grade skin toxicities.

One-way ANOVA indicated a significant difference between the mean ABP scores of the patients with different RTOG skin toxicities ($F = 9.28$; $p = 0.000$) (Figure 3). Post hoc Tukey HSD analysis demonstrated that the mean ABP score of the patients with Grade 1 skin toxicity (17.00 ± 2.53) was significantly higher than those of the patients with Grade 0 (12.6 ± 5.44) or Grade 2 and above (14.32 ± 4.25) ($p < 0.01$; Figure 3).

Discussion

Radiodermatitis (RD) is an important side effect of direct exposure to radiation during cancer treatment. A meta-analysis study has reported that RD concerns about 95% of all cancer patients receiving radiation therapy (Von Elm et al, 2007). Salvo et al. and Olsen et al. reported moderate to severe skin reactions in 85-87% of RT patients (Salvo et al. 2010; Olsen et al. 2001).

Table 1. Sociodemographic characteristics of patients.

Characteristics		(n)	%
Gender	Female	36	42.9
	Male	48	57.1
Age group (year)	18-38	10	11.9
	39-59	34	40.5
	60-80	37	44.0
	> 80	3	3.6
Marital status	Married	73	86.9
	Single	6	7.1
	Divorced/Widowed	5	6.0
Occupation	Public sector	2	2.4
	Private sector	9	10.7
	Self-employed	14	16.7
	Unemployed	59	70.2
Education	Illiterate	8	9.5
	Literate	8	9.5
	Elementary	39	46.4
	Secondary	11	13.1
	High school	12	14.3
	University	6	7.2
Social security	Has	84	100.0
	Has not	0	0.0
Work environment	Indoors	68	81.0
	Outdoors	16	19.0
Smoking	Yes	23	27.4
	No	61	72.6
Alcohol consumption	Yes	5	6.0
	No	79	94.0

Table 2. Disease characteristics of patients.

Characteristic		(n)	%
Cancer type	Breast	12	14.3
	Lung	28	33.3
	Head and neck	13	15.5
	Stomach	4	4.8
	Colon	3	3.6
	Prostate	6	7.1
	Other	18	21.4
Treatment type	Radiotherapy (RT)	65	77.4
	Chemotherapy (CT)	2	2.4
	Immunotherapy	3	3.6
	Hormone therapy	0	0.0
	CT-RT	14	16.7
Non-cancer comorbidity	HT	26	31.0
	DM	9	10.7
	HT-DM	3	3.6
	None	46	54.8
RT area	Head	21	25.0
	Neck	6	7.1
	Breast	36	42.9
	Abdomen	5	6.0
	Pelvis	16	19.0
RT method	External	84	100.0
	Internal	0	0.0

	150 cGy	2	2.4
	180 cGy	16	19.0
RT dose (cGy)	200 cGy	60	71.4
	220 cGy	2	2.4
	250 cGy	4	4.8
Number of RT sessions	2-11	30	35.7
	12-21	32	38.1
	22-32	22	26.2

RT: Radiotherapy, CT: Chemotherapy, HT: Hypertension, DM: Diabetes mellitus, cGy: Centigray

Table 3. Evidence-based practices of patients for the protection from skin toxicity related to RT

Practice	Yes		No	
	(n)	%	(n)	%
I don't use lotion	73	86.9	11	13.1
I prefer clothes made of cotton or those with a soft contact surface	73	86.9	11	13.1
I don't use skin-tight underwear	70	83.3	14	16.7
I pay attention to an adequate and balanced diet	70	83.3	14	16.7
I don't use baby powder	69	82.1	15	17.9
I don't use plasters or other products that will stick to my skin in the treatment area	69	82.1	15	17.9
I don't wear clothes that compress the treatment area	68	81	16	19
I keep the irritated skin surface clean and dry	64	76.2	20	23.8
I don't use perfume	63	75	21	25
I don't use perfumed soap	63	75	21	25
I don't rub the treatment area as it can irritate the skin	62	73.8	22	26.2
I avoid long-term application of hot or cold	61	72.6	23	27.4
I don't use makeup	59	70.2	25	29.8
I use soft towels for drying	57	67.9	27	32.1
I use non-irritating deodorant	57	67.9	27	32.1
I use protective clothing (hat, scarf, etc.) against sunlight	48	57.1	36	42.9
I do not refrain from washing my skin and my body	43	51.2	41	48.8
I bathe with warm water	42	50	42	50
I use prescribed topical steroids	37	44	47	56
I avoid using razors to shave body hair, I use electrical devices	32	38.1	52	61.9
I avoid swimming as chlorinated water can cause skin irritation	31	36.9	53	63.1
I moisturize my skin	27	32.1	57	67.9
I use high-factor sunscreens for sun exposure	14	16.7	70	83.3
I apply <i>Aloe vera</i> to the area of treatment	7	8.3	77	91.7

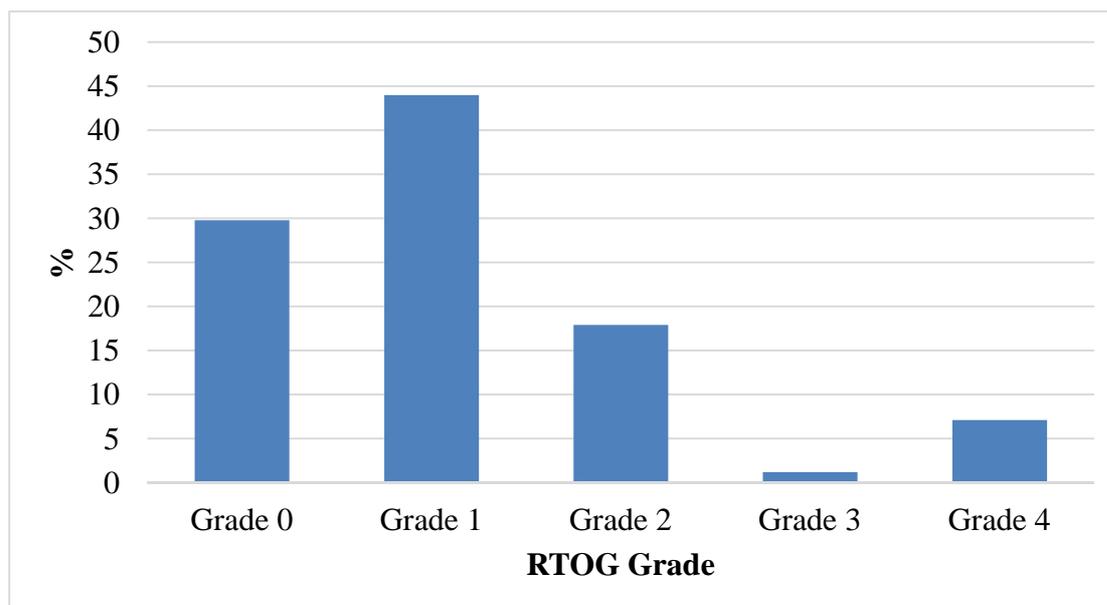


Figure 2. Distribution of acute skin reactions according to the RTOG categories.

Table 4. Comparison of the patients insociodemographic and clinical subgroups in terms of RTOG-grade skin toxicities.

Characteristic		Grade 0		Grade 1		≥Grade 2		χ^2	P
		n	%	n	%	n	%		
Gender	Female	8	22.2	19	52.8	9	25.0	2.33	0.312
	Male	17	35.4	18	37.5	13	27.1		
Age group (year)	<60	11	25.0	26	59.1	7	15.9	9.18	0.010
	≥60	14	35.0	11	27.5	15	37.5		
Marital status	Married	21	28.8	34	46.6	18	24.7	5.29	0.214*
	Single	1	16.7	3	50.0	2	33.3		
	Divorced/Widowed	3	60.0	0	0.0	2	40.0		
Occupation	Public sector	0	0.0	2	100.0	0	0.0	3.24	0.834*
	Private sector	2	22.2	4	44.4	3	33.3		
	Self-employed	6	42.9	5	35.7	3	21.4		
	Unemployed	17	28.8	26	44.1	16	27.1		
Education	Illiterate /Literate	3	18.8	7	43.8	6	37.5	3.20	0.531*
	Elementary	18	36.0	20	40.0	12	24.0		
	High school or above	4	22.2	10	55.6	4	22.2		
Medical knowledge	Healthcare personnel	10	20.8	25	52.1	13	27.1	7.64	0.078
	Other	3	60.0	0	0.0	2	40.0		
	None	12	38.7	12	38.7	7	22.6		
Work environment	Indoor	18	26.5	31	45.6	19	27.9	1.80	0.408*
	Outdoor	7	43.8	6	37.5	3	18.8		
Smoking	Yes	8	34.8	6	26.1	9	39.1	4.61	0.100
	No	17	27.9	31	50.8	13	21.3		
Alcohol consumption	Yes	1	20.0	1	20.0	3	60.0	2.75	0.167*
	Do	24	30.4	36	45.6	19	24.1		

Non-cancer disease	Yes	14	36.8	13	34.2	11	28.9	2.89	0.235
	No	11	23.9	24	52.2	11	23.9		
RT dose (cGy)	≤180 cGy	8	44.4	6	33.3	4	22.2	9.36	0.036
	200 cGy	15	25.0	31	51.7	14	23.3		
	≥220 cGy	2	33.3	0	0.0	4	66.7		
Number of RT sessions	2-11	12	41.4	11	37.9	6	20.7	5.16	0.276
	12-21	10	31.3	15	46.9	7	21.9		
	22-32	3	13.6	11	50.0	8	36.4		
Cancer type	Breast/Head-neck	4	16.0	17	68.0	4	16.0	17.63	0.005*
	Lung/Stomach	16	50.0	6	18.8	10	31.3		
	Colon/Prostate	1	11.1	6	66.7	2	22.2		
	Other	4	22.2	8	44.4	6	33.3		
Treatment	Radiotherapy	18	27.7	28	43.1	19	29.2	7.98	0.063*
	CT/IT	4	80.0	0	0.0	1	20.0		
	CT-RT	3	21.4	9	64.3	2	14.3		

*Fisher's exact test RT: Radiotherapy, CT: Chemotherapy, IT: Immunotherapy, cGy: Centigray

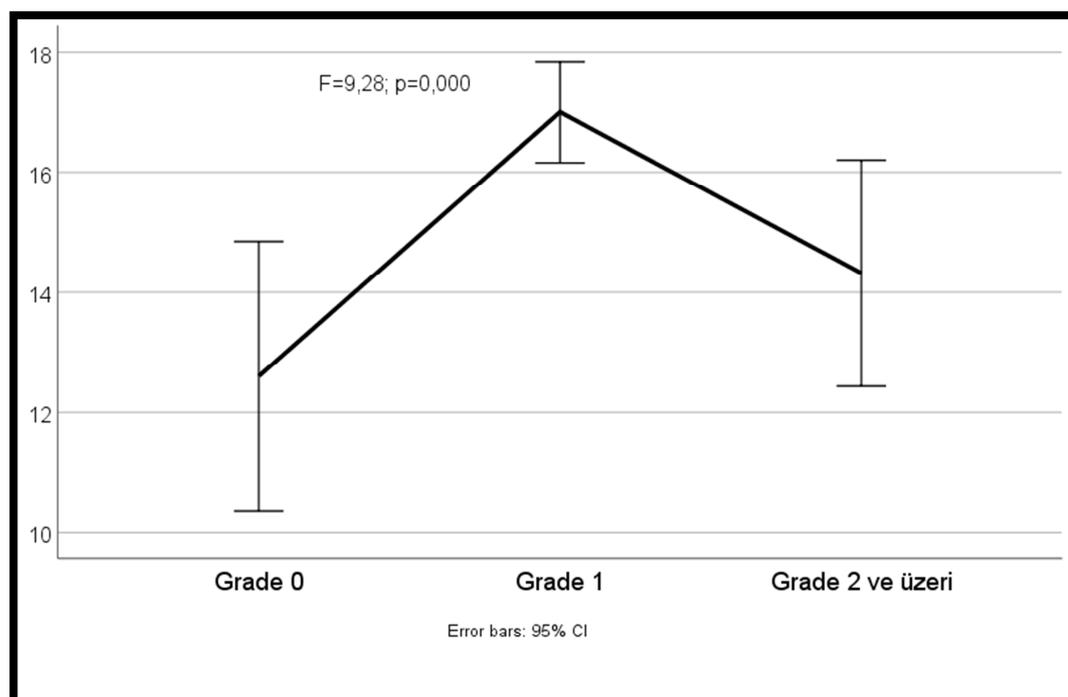


Figure 3. Mean ABP scores of patients in the RTOG categories.

Our study found somewhat lower rates of acute skin toxicity (70%) among the patients receiving RT 8.3% of which had skin toxicities of Grade 3 or above. Hornsby et al., reported that 10 to 15% of patients receiving RT developed moist desquamation (Grade 3)(Hornsby et al, 2004). In recent years, the use of modern equipment such as intensity-modulated radiation therapy (IMRT)

has reduced the dose intensity on the skin and the severity of acute RD for many patients. However, skin toxicity continues to be a problem for patients. While RD may improve eventually, desquamation in the skin causes pain and reduced quality of life. Regular assessment of skin care and early diagnosis and treatment of skin reactions are often recommended to improve

patient comfort, quality of life, and clinical outcomes (Cox et al, 1995; Chan et al, 2014; Bensadoun et al, 2013; Boldeston et al 2006; McQuestion, 2011).

Factors affecting the severity of skin reaction include both treatment-related factors and individual or patient-related factors. These risk factors were listed by McQuestion as skin care, concurrent CT, IT, or targeted therapies, drugs, comorbid diseases such as diabetes or renal failure, advanced age, prolonged nutritional status, chronic sun exposure, smoking, and environmental conditions (McQuestion, 2011). Bernier et al. reported that combining RT and systemic therapy might exacerbate cutaneous reactions, which may result in severe xerosis, inflammation, skin thinning, and necrosis of the upper dermis and epidermis (Bernier et al, 2008). Bostanoglu has reported that the symptoms in the RT treatment were mostly in the area of radiation exposure and the severity of symptoms increased when co-administered with CT (Bostanoglu, 2014). Similarly, skin toxicity was more severe in patients older than 60 years of age and in those receiving simultaneous CT in our study. In contrast, diabetes and smoking were not associated with the development of skin toxicity in our study, which suggests that randomized controlled clinical trials should be performed.

The skin is affected more negatively in the breast, perineum, and head and neck, regions, which are the target tissues of radiotherapy in related cancers (DeSantis et al, 2014). Similarly, slightly toxic skin reactions were observed in the breast, head-neck, rectum, and perineum regions whereas skin toxicity was more severe in lung and gastric cancers in our study.

Karabacak et al. reported that RT-related reactions were observed in areas under pressure, such as the back of the ear, gluteal region, under breast, axilla, neck, rectal region, and bony protrusions; they also pointed out that the severity of symptoms increased with increasing radiation doses (Karabacak et al, 2014). Similarly, the severity of skin toxicity was found to increase with increasing RT doses in our study.

A review by Bensadoun et al. focused on a preventive and supportive skin care approach that helps patients undergoing oncology treatment and their caregivers choose the most suitable products for daily skin care. The skin's barrier function can be maintained and the

severity of the symptoms can be controlled by using appropriate skin care products (Bensadoun et al, 2013).

There is a limited amount of prospective randomized data on the use of topical or other pharmacological or supportive care agents for the prevention and treatment of RD. In general, findings on the clinical value of topical agents and wound dressings that prevent or reduce the effects of RD and help patients are inconsistent. For this reason, it is difficult to establish robust evidence-based clinical practice guidelines for skin care in patients receiving RT. However, the 24 items that were used in our study for the calculation of the EBP score were established based on the literature (Leventhal and Young, 2017; Hegedus et al 2017; Roy et al, 2001). The higher average score in the group with Grade 1 skin toxicity suggests that patients initially do not follow the recommendations and change their behavior after they had observed signs of toxicity.

Patient training should include instructions about cleaning the treatment area only with warm water and drying the area by pressing a soft towel gently without irritation. The patient should be advised to avoid using soap, deodorant, talc powder, perfume, make-up, strong-scented lotions, or ointments on the treatment area as they may exacerbate skin irritation. They should be reminded that soap should not be used unless necessary and mild soaps (synthetic detergents: syndet or soap-free soap) should be preferred when necessary. They should be recommended wearing loose clothing made of cotton and warned against wearing tight clothing on the treatment area. They should also be reminded that the treatment area must be protected from heat sources such as hot water thermophore and electric blanket, sun, wind, and cold. Wearing protective clothing (hats, scarves, etc.) for this purpose should be recommended.

Limitations

The fact that this study was carried out in the department of radiation oncology at a single center (a university hospital) and included the patients who received external RT due to the lack of internal RT patients in the period of study at this center constitutes a significant limitation.

Conclusion

Skin toxicity was quite prevalent in patients receiving RT. There is a need for novel, more successful approaches where skin reactions and

other side effects in cancer patients are reduced. It is very important for the nurses to follow up and inform the patients in a timely manner in order to prevent skin reactions due to RT. Nursing care and timely implementation of nursing interventions may delay or prevent the side effects and improve the quality of life and comfort of the patient during the treatment process. The treatment area should be evaluated daily for erythema, pain, dryness or moist skin rash; it should be noted that patient education is an important part of health care.

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