DOI: 10.24938/kutfd.1310521 Kırıkkale Üniversitesi Tıp Fakültesi Dergisi 2023;25(2):273-278
Original Article *Özgün Araştırma*

EVALUATION OF SKIN SIDE EFFECTS OF RADIATION THERAPY IN ABDOMINAL AND PELVIC REGIONS: A CLINICAL ASSESSMENT

Abdominal ve Pelvik Bölgelerde Radyoterapinin Cilt Yan Etkilerinin İncelenmesi: Klinik Bir Değerlendirme

Rahşan HABİBOĞLU[1] Fevziye İlknur KAYALI[1] İrem SARICANBAZ[1]

[1] *Radiation Oncology Clinic, Ankara Bilkent City Hospital, ANKARA ,TÜRKİYE*

ABSTRACT

Objective: This study aimed to evaluate the skin side effects of abdominal and pelvic radiation therapy. Radiation therapy is widely used in the treatment of various cancers, but it can cause significant skin changes as a side effect. These effects are classified into acute, subacute, or chronic stages depending on their timing and severity.

Material and Methods: We examined 60 patients who underwent radiation therapy between 2016 and 2018 and obtained their information from treatment records. Sixteen patients received palliative radiation therapy, while 44 patients received curative radiation therapy. Pelvic radiation therapy was administered to 41 patients, and abdominal radiation therapy was performed on 19 patients. The end point of the study was assesing skin reactions.The grading of radiation dermatitis was evaluated by using the Radiation Therapy Oncology Group / European Organization for Research and Treatment of Cancer criteria.

Results: 75% of the study population was male and 25% female. The ages of the patients ranged from 29 to 82, with a median age of 56**.** The grade 1 side effect rate among patients who experienced side effects was calculated as 82.75% (24 patients), while the grade 2 side effect rate was calculated as 17.24% (5 patients). These side effects were generally mild to moderate and did not significantly differ based on patient age or gender. However, patients receiving concurrent chemotherapy showed an increased frequency of skin side effects ($p<0.001$). Therefore, it is crucial to monitor and manage skin side effects associated with abdominal and pelvic radiation therapy.

Conclusion: In conclusion, skin side effects in patients undergoing abdominal and pelvic radiation therapy are typically mild to moderate, regardless of age or gender. However, the frequency of these side effects is higher in patients receiving concurrent chemotherapy. This study highlights the importance of closely monitoring and developing effective management strategies for skin side effects in patients undergoing radiation therapy. Further comprehensive research is needed to improve the management of skin side effects related to abdominal and pelvic radiation therapy.

Keywords: *Skin side effects, abdominal radiation therapy, pelvic radiation therapy, radiotherapy, radiodermatitis*

ÖZ

Amaç: Bu çalışmanın amacı, abdominal ve pelvik radyoterapinin cilt yan etkilerini değerlendirmektir. Radyoterapi, çeşitli kanserlerin tedavisinde yaygın olarak kullanılan bir yöntem olmasına rağmen, ciltte önemli değişikliklere neden olabilir. Bu etkiler, zamanlama ve şiddete bağlı olarak akut, subakut veya kronik aşamalar olarak sınıflandırılır.

Gereç ve Yöntemler: Çalışmamızda, 2016-2018 yılları arasında radyoterapi alan 60 hasta incelenmiş ve hastaların bilgileri tedavi kayıtlarından elde edilmiştir. Hastaların 16'sı palyatif, 44'ü ise küratif radyoterapi almıştır. Pelvik radyoterapi 41 hastaya, abdominal radyoterapi ise 19 hastaya uygulanmıştır. Çalışmanın amacı cilt reaksiyonlarının değerlendirilmesiydi. Radyasyon dermatitinin derecesi "Radiation Therapy Oncology Group / European Organization for Research and Treatment of Cancer" kriterleri kullanılarak değerlendirildi.

Bulgular: Çalışma popülasyonunun %75'i erkek ve %25'i kadındır. Hastaların yaşları 29 ila 82 arasında değişmekte olup, ortanca yaş 56 'dır. Yan etki yaşayan hastalarda 1. derece yan etki oranı %82.75 (24 hasta), 2. derece yan etki oranı ise %17.24 (5 hasta) olarak saptandı. Abdominal ve pelvik radyoterapi alan hastalarda cilt yan etkileri sıklıkla gözlenmiştir. Bu yan etkiler genellikle hafif ila orta şiddetli olup, hastaların yaş veya cinsiyetine bağlı olarak önemli farklılıklar göstermemektedir. Ancak, eşzamanlı kemoterapi alan hastalarda cilt yan etkilerinin sıklığı artmaktadır ($p<0.001$). Bu nedenle, abdominal ve pelvik radyoterapi ile ilişkili cilt yan etkilerinin yakından takip edilmesi ve yönetilmesi önemlidir.

Sonuç: Sonuç olarak, abdominal ve pelvik radyoterapi alan hastalarda cilt yan etkileri genellikle hafif ila orta şiddetlidir ve yaş veya cinsiyete bağlı olarak önemli farklılıklar göstermez. Ancak, eşzamanlı kemoterapi alan hastalarda cilt yan etkilerinin sıklığı artmaktadır. Bu çalışma, radyoterapi alan hastalarda cilt yan etkilerinin yakından takip edilmesi ve etkili yönetim stratejilerinin geliştirilmesinin önemini vurgulamaktadır.

Anahtar Kelimeler: *Cilt yan etkileri, abdominal radyoterapi, pelvik radyoterapi, radyoterapi, radyodermit*

Correspondence / Yazışma Adresi: **Dr. Fevziye İlknur KAYALI**
Radiation Oncology Clinic, Ankara Bilkent City Hospital, ANKARA ,TÜRKİYE
Phone / Tel: +905398447558 **E-mail** / E-posta: ilknurkayali@yahoo.com
Received / Geliş Tarihi: 06.06.2023 **Accepted** / Kabul Tarihi: 23.07.2023

KÜ Tıp Fak Derg 2023;25(2):273-278
Doi: 10.24938/kutfd.1310521

INTRODUCTION

Radiation therapy plays a crucial role in the management of diverse malignancies. Nevertheless, the emergence of radiation-induced skin changes represents a notable adverse effect associated with this treatment modality (1). The impact of radiation therapy on the skin exhibits substantial variations in terms of severity, temporal pattern, and prognosis. When these changes manifest, they are typically categorized into acute, subacute, or chronic phases (1,2).

Established guidelines provide well-defined tolerance doses for normal pelvic structures and organs during radiation therapy. The primary objective of these guidelines is to optimize the therapeutic ratio (3). Despite meticulous adherence to treatment protocols, the proximity of healthy tissues to the radiation field may still result in treatment-related toxicity, thereby detrimentally affecting patients' quality of life (4,5).

During pelvic radiotherapy, the irradiated skin region may exhibit an array of reactions, including erythema, burning sensation, pruritus, and increased sensitivity (1). These reactions typically manifest within the initial week of treatment and may intensify over the course of therapy. The severity of skin reactions is contingent upon factors such as the radiation dosage, duration of treatment, and inherent characteristics of the individual's skin (2). While some individuals may experience mild skin reactions, others may encounter more pronounced manifestations. Risk factors for acute radiation dermatitis is given in Table 1.

The classification of these reactions is typically performed according to the rigorous criteria set forth by the Radiation Therapy Oncology Group (RTOG), the European Organization for Research and Treatment of Cancer (EORTC), and common toxicity criteria (6). The aim of this study is to determine the incidence, severity, and frequency of acute skin side effects in patients undergoing radiotherapy to the abdomen and pelvic region.

Table 1: Risk factors for acute radiation dermatits (5).

Patient related factors	Extrinsic factors
Age (Advanced)	Total radiation dose
Gender (Female)	Type of radiation
Smoking	Concurrent chemotherapy
Nutritional status (obesity)	Fractionation schedule
Co-morbidities (diabetes mellitus, connective tissue disease)	Quality of radiation beam
Atopy	Drugs (Antibiotics - Anti-tuberculosis medications)
Radiosensitivity disorders (Ataxia telangiectasia Xeroderma pigmentosa)	
Immun Status	

MATERIALS AND METHODS

This retrospective study was conducted at our clinics between 2016 and 2018 to investigate the effects of abdominopelvic radiotherapy on a cohort of 60 patients. Patient information was obtained from their treatment records, ensuring accurate and reliable data collection. The study adhered to the ethical principles outlined in the Declaration of Helsinki and received approval from the institutional ethical committee (E-1-23-3518). The ethics committee approval of the study was obtained from the Ankara Bilkent City Hospital (E-1-23-3518). The end point of the study was assesing skin reactions.

The study population comprised of 45 male patients (75%) and 15 female patients (25%), with an age range of 29 to 82 years (median age: 56). Out of the total study population, 16 individuals (26.6%) underwent palliative radiotherapy, while 44 patients (73.3%) received curative radiotherapy. Pelvic radiotherapy was administered to 41 patients (68.3%), and 19 patients (31.6%) underwent abdominal radiotherapy.

Radiotherapy doses were administered as follows: 180 cGy per fraction in 36 patients, 200 cGy per fraction in 11 patients, 300 cGy per fraction in 8 patients, and 400 cGy per fraction in 5 patients. The selection of treatment regimens was based on individual patient characteristics and the therapeutic objectives.

A subset of the patients received concurrent chemotherapy. Among the 60 patients, 28 did not receive concurrent chemotherapy. For those who did,

KÜ Tıp Fak Derg 2023;25(2):273-278
Doi: 10.24938/kutfd.1310521

two patients were treated with 5-fluorouracil (5FU) every three weeks, 21 patients received 5FU infusion, one patient received UFT (tegafur-uracil), two patients received FUFA (folinic acid, 5FU, and leucovorin) every three weeks, and six patients received weekly FUFA treatment.

The grading of radiation dermatitis was performed by the patient's physician at the initiation, as well as weekly throughout the treatment course, and at the completion of therapy by using the RTOG/EORTC criteria, which provide a standardized system for assessing and classifying acute skin reactions.

Statistical analysis was conducted using SPSS version 23.0. Descriptive statistics, including frequencies and percentages, were employed to summarize qualitative variables. The chi-square test was utilized to analyze the association between different factors, with a significance level set at $p<0.05$.

The study was designed and executed with meticulous attention to scientific rigor and confidence to ensure the validity and reliability of the data. This allowed for a comprehensive evaluation of the observed effects of abdominopelvic radiotherapy on the patient cohort, enabling meaningful conclusions to be drawn.

RESULTS

Abdomen and pelvic regions were examined for skin side effects in a retrospective study conducted on 60 patients who received radiotherapy. When considering the entire population, skin side effects were detected in 29 out of 60 patients (48.3%). In the overall population, grade 1 side effects were present in 24 patients (40%), while grade 2 side effects were present in 5 patients (8.3%). The grade 1 side effect rate among patients who experienced side effects was calculated as 82.75% (24 patients), while the grade 2 side effect rate was calculated as 17.24% (5 patients). The Table 2 presents patient characteristics and distribution percentages of patients experiencing Grade 1 side effects and the Table 3 presents patient characteristics and distribution percentages of patients experiencing Grade 2 side effects.

Table 2: Characteristics and treatments of 24 patients with grade 1 side effects

Patients' Characteristics	N	%
Gender		
Male	19	79
Female	5	21
Cancer Type		
Bladder cancer	2	8
Stomach cancer	8	33
Rectal cancer	13	54
Bone metastasis	1	4
Radiation Therapy Site		
Pelvic region	16	67
Abdominal region	8	33
Radiation Therapy Doses		
3000 cGy	1	4
4500 cGy	8	33
5000 cGy	1	4
5040 cGy	12	50
6600 cGy	2	8
Chemotherapy		
Concurrent chemotherapy	20	83
No chemotherapy	4	17
Chemotherapy Types		
UFT	1	4
Weekly FUFA	5	21
3-Weekly 5FU	2	8
5FU infusion	12	50

UFT: Tegafur-uracil, FU: 5-fluorouracil, FUFA: Folinic acid, 5-fluorouracil, and leucovorin

When comparing female and male patients, skin reactions were observed in 5 out of 15 female patients (33.3%) and in 22 out of 45 male patients (48%). There was no statistically significant difference in skin side effects between female and male patients in terms of gender ($p=0.587$).

In terms of age, when comparing the groups below and above the median age of 56, no statistically significant difference was found in terms of side effects ($p=0.779$). Similarly, when comparing the abdomen and pelvic regions in terms of radiation therapy, no statistically significant difference was found in terms of side effects ($p=0.281$). Distribution of patients experiencing skin side effects based on the radiotherapy areas is summarized in the Table 4.

KÜ Tıp Fak Derg 2023;25(2):273-278
Doi: 10.24938/kutfd.1310521

Table 3: Patient characteristics and distribution percentages of patients experiencing grade 2 side effects

Patient Characteristics	N	%
Gender		
Male	4	80
Female	1	20
Cancer type		
Rectal cancer	5	100
Radiation Therapy Area		
Pelvic region	5	100
Radiation Therapy Doses		
5040 cGy	5	100
Chemotherapy		
Concurrent chemotherapy	4	80
No chemotherapy	1	20
Chemotherapy Types		
Weekly FUFA	1	20
5FU infusion	3	60
No chemotherapy	1	20

FU: 5-fluorouracil, FUFA: Folinic acid, 5-fluorouracil, and leucovorin

Table 4: Distribution of patients experiencing skin side effects based on the radiation therapy areas

Radiation Therapy Area	Pelvic Region	Abdominal Region	Total
Bladder cancer	2	0	2
Stomach cancer	0	8	8
Rectal cancer	13	0	13
Bone metastasis	1	0	1
Total	16	8	24

However, statistically significant results were obtained among patients who received concurrent chemotherapy ($p<0.001$). The distribution of patients experiencing skin side effects based on the radiotherapy dose, concurrent chemotherapy, chemotherapy type, and grade is summarized in the Table 5 and 6. Furthermore, there was a statistically significant relationship between the total doses administered and the occurrence of side effects among the groups ($p<0.001$).

Table 5: Distribution of patients experiencing grade1 skin side effects based on the radiotherapy dose, concurrent chemotherapy and chemotherapy type

Radiation Therapy Dose (cGy)	Concurrent Chemotherapy	Chemotherapy Type	Skin Side Effect	Grade 1
3000	0	UFT	1	
4500	0	Weekly FUFA	5	
5000	0	3-weekly 5FU	2	
5040	4	5FU Infusion	12	
6600	0			
Total				20

UFT: Tegafur-uracil, FU: 5-fluorouracil, FUFA :folinic acid, 5-fluorouracil, and leucovorin

Table 6: Distribution of patients experiencing grade 2 skin side effects based on the radiotherapy dose, concurrent chemotherapy and chemotherapy type

Radiation Therapy Dose (cGy)	Concurrent Chemotherapy	Chemotherapy Type	Skin Side Effect
5040	1	5FU Infusion	3
5040	2	Weekly FUFA	1
Total	3		4

DISCUSSION

In this retrospective study, the occurrence and severity of skin side effects in the abdomen and pelvic regions were evaluated in 60 patients who underwent radiotherapy. The results showed that grade 1 skin side effects were observed in 24 patients, indicating mild reactions, while grade 2 side effects were observed in 5 patients, indicating more moderate reactions.

The association between patient age and the occurrence of skin side effects has been the subject of several studies, yielding diverse findings. In a study conducted by Mehreen et al., involving 96 patients undergoing

KÜ Tıp Fak Derg 2023;25(2):273-278
Doi: 10.24938/kutfd.1310521

radiotherapy for rectal cancer, advanced age was identified as a contributing factor to an increased incidence of grade 1 skin side effects, although no significant association was observed with grade 2 side effects (7). Conversely, another study demonstrated a positive correlation between age and the severity of skin reactions, suggesting that as age advanced, the grade of skin reactions also escalated (2). However, it is noteworthy to highlight that our study specifically observed grade 1 and grade 2 skin side effects, with no instances of higher-grade reactions being recorded. Moreover, contrasting these findings, another study reported that age did not constitute a risk factor for skin side effects (8). It is plausible that advanced age may augment the risk of skin reactions due to the presence of comorbidities. Nevertheless, our study, when stratified by the median age, did not reveal a significant influence of age on skin side effects.

In the publication by Navyashree Suresha et al., the female gender was reported as a risk factor for acute reactions (5). However, similar to our study, the majority of the conducted studies did not find a statistically significant association between gender and being a risk factor (2,7).

In our study, we did not find a statistically significant difference in skin reactions between the abdominal and pelvic regions when considering radiation exposure. Specifically, studies investigating the skin side effects of breast radiotherapy have suggested an increased likelihood of side effects with larger breast size (3,4). This association is primarily related to the size of the breast rather than the localization of the radiation field. While different levels of side effects may be observed when examining internal organ toxicities, it is logical to find no significant difference in terms of skin reactions between the abdominal and pelvic regions .

In a comprehensive study assessing the impact of intensity-modulated radiotherapy (IMRT) or volumetric-modulated arc therapy (VMAT) on skin side effects, compelling evidence has emerged regarding the pivotal role of dose-volume parameters (9). Similarly, an investigation focusing on dose-related effects has underscored the correlation between cumulative radiation dose surpassing specific threshold values and the manifestation of skin side effects (10). Furthermore, the localized nature of dermatitis within the radiation therapy field, its delayed onset following irradiation initiation, and the subsequent exacerbation of its severity with escalating dose levels all serve as tangible indications of its direct association with radiation dosage (11). Importantly, our own study's findings further corroborated these observations by revealing a statistically significant relationship between the total administered doses and the occurrence of skin side effects across the various groups.

In a study comparing concurrent chemoradiotherapy (CCRT) with radiotherapy alone (RT) in patients with nasopharyngeal cancer, it has been demonstrated that the addition of chemotherapy has a positive impact on overall survival and disease-free survival. However, it has also been shown to have an adverse effect on the incidence and severity of radiodermatitis (12). Our study's findings align with these observations, as we obtained statistically significant results indicating a higher occurrence of radiodermatitis and its severity among patients who received concurrent chemotherapy.

In conclusion, skin side effects in patients undergoing abdominal and pelvic radiation therapy are typically mild to moderate, regardless of age or gender. However, the frequency of these side effects is higher in patients receiving concurrent chemotherapy. This study highlights the importance of closely monitoring and developing effective management strategies for skin side effects in patients undergoing radiation therapy. Further comprehensive research is needed to improve the management of skin side effects related to abdominal and pelvic radiation therapy.

The limitations of our study can be listed as follows: retrospective design, incomplete information regarding medication use or comorbidities of the patients, and relatively small sample size.

Conflict of Interest: The author have indicated no conflicts of interest regarding the content of this article.

Support and Acknowledgment: No financial support was received from any institution or person.

Researchers' Contribution Rate Statement: Concept/Design: FİK, RH ; Analysis/Interpretation: RH, İS, FİK ; Data Collection: RH, İS, FİK; Writer: RH, İS, FİK; Critical Review: RH, İS, FİK ; Approver: RH, İS, FİK

Ethics Committee Approval: The ethics committee approval of the study was obtained from the Ankara Bilkent City Hospital (E-1-23-3518).

REFERENCES

1. Bray FN, Simmons BJ, Wolfson AH, Nouri K. Acute and chronic cutaneous reactions to ıonizing radiation therapy. Dermatol Ther (Heidelb). 2016;6(2):185-206.
2. Ryan JL. Ionizing radiation: The good, the bad, and the ugly. J Invest Dermatol. 2012;132(3 Pt 2):985-93.
3. Gay HA, Barthold HJ, O'Meara E, Bosch WR, El Naqa I, Al-Lozi R, et al. Pelvic normal tissue contouring guidelines for radiation therapy: A Radiation Therapy Oncology Group consensus panel atlas. Int J Radiat Oncol Biol Phys. 2012;83(3):e353-62.
4. Purdy JA. Dose to normal tissues outside the radiation therapy patient's treated volume: A review of different radiation therapy techniques. Health Phys. 2008;95(5):666-76.
5. Suresha N, Dandekeri S. A clinico-epidemiological study on radiation induced dermatitis of head and neck malignancy patients at a teritiary care centre in south India. IP Indian J Clin Exp Dermatol. 2019;5(4):327-31
6. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys. 1995;31(5):1341-6.
7. Mehreen S, Bashir A, Qadri MHA, Ahmad A. Frequency and severity of acute perineal skin reactions in rectal cancer patients at completion of preoperative pelvic radiotherapy. Pakistan Journal of Medical & Health Sciences. 2023;17(2):192-4.
8. Parker JJ, Rademaker A, Donnelly ED, Choi JN. Risk factors for the development of acute radiation dermatitis in breast cancer patients. int J Radiat Oncol Biol Phys. 2017;99 E40-1.
9. Kawamura M, Yoshimura M, Asada H, Nakamura M, Matsuo Y, Mizowaki T. A scoring system predicting acute radiation dermatitis in patients with head and neck cancer treated with intensity-modulated radiotherapy. Radiat Oncol. 2019;14(1):14.
10. Hegedus F, Mathew LM, Schwartz RA. Radiation dermatitis: An overview. Int J Dermatol. 2017;56(9):909-14.
11. Bernier J, Bonner J, Vermorken JB, Bensadoun RJ, Dummer R, Giralt J, et al. 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. Ann Oncol. 2008;19(1):142-9.
12. He Y, Guo T, Guan H, Wang J, Sun Y, Peng X. Concurrent chemoradiotherapy versus radiotherapy alone for locoregionally advanced nasopharyngeal carcinoma in the era of intensity-modulated radiotherapy: A meta-analysis. Cancer Manag Res. 2018;10:1419-28.