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Research

Bone Health Following Pelvic Radiotherapy: Incidence of Pelvic Insufficiency Fractures and Evaluation of Prognostic Factors

Pelvik Radyoterapi Sonrası Kemik Sağlığı: Pelvik Yetmezlik Fraktürlerinin Sıklığı ve Prognostik Faktörlerin Analizi

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ABSTRACT

Objective: Pelvic radiotherapy (RT) can reduce bone strength, leading to pelvic insufficiency fractures (PIFs). This study evaluates the incidence of PIFs and associated risk factors among patients undergoing pelvic RT.

Methods: The study included cervical and endometrial cancer patients without pre-existing PIFs who received 3D-conformal RT (45-50.4 Gy). Trabecular bone Hounsfield unit (HU) values in the 4th lumbar vertebra and sacrum were measured on planning computed tomography (CT) scans using a 1-cm region of interest. The diagnosis of PIF was confirmed on follow-up magnetic resonance imaging evaluated by experienced radiologists. Statistical analyses were performed using IBM SPSS Statistics® 25, including the Mann-Whitney U test, multivariate logistic regression, and receiver operating characteristic (ROC) analysis ($p<0.05$).

Results: A total of 128 patients (69 with cervical cancer and 59 with endometrial cancer) were included; the median age was 68 years. The PIF incidence was 35.2% (n=45), with a median time to diagnosis of 19 months. Most PIFs (76.2%) occurred in the sacrum. Pain was present in 53.3% of cases; symptomatic patients received one or more of the following: non-steroidal anti-inflammatory drugs, vitamin E, pentoxifylline, or vertebroplasty. PIFs were significantly associated with low sacral HU ($p=0.012$), cervical cancer diagnosis ($p=0.033$), and concurrent chemotherapy ($p=0.023$). ROC analysis identified a sacral HU cut-off of ≤-8 ($p=0.011$; area under the curve=0.634). In multivariate logistic regression, sacral HU (≤-8) was the only independent risk factor for PIF (odds ratio: 3.04; 95% confidence interval: 1.36-6.83; $p=0.007$).

Conclusion: A simple bone mineral density assessment method can predict PIF risk. In patients receiving pelvic RT, a diagnosis of cervical cancer, concurrent chemotherapy, and low sacral HU values increase the risk of fracture. Early identification of high-risk patients and timely preventive measures may improve clinical outcomes.

Keywords: Pelvic insufficiency fractures, radiotherapy, bone mineral density, Hounsfield unit, osteoporosis

ÖZ

Amaç: Pelvik radyoterapi (RT), kemik dayanıklılığını azaltarak pelvik yetmezlik fraktürlerine (PIF) yol açabilir. Bu çalışmada, pelvik RT uygulanan hastalarda PIF sıklığı ve ilişkili risk faktörleri değerlendirilmiştir.

Gereç ve Yöntem: Çalışmaya, tedavi öncesi PIF olmayan, 3D-konformal RT (45-50,4 Gy) almış serviks ve endometrium kanserli hastalar dahil edilmiştir. Planlama bilgisayarlı tomografilerinde 4. lomber vertebra ve sakrum bölgesinin trabeküler kemik Hounsfield ünitesi (HU) değerleri 1 cm çapında ilgi bölgesi kullanılarak ölçülmüştür. Yetmezlik fraktürü tanısı, takip manyetik rezonans görüntülemeleri ile deneyimli radyologlar tarafından konulmuştur. İstatistiksel analizler IBM SPSS Statistics® 25 kullanılarak Mann-Whitney U testi, çok değişkenli lojistik regresyon ve alıcı işlem karakteristiği eğrisi (ROC) analizi ile yapılmıştır ($p<0,05$).

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ÖZ

Bulgular: Toplam 128 hasta (69 serviks kanseri, 59 endometrium kanseri) dahil edilmiş olup medyan yaş 68'dir. PIF insidansı %35,2 (n=45) olup medyan tanı süresi 19 aydır. PIF'lerin %76,2'si sakrumda görülmüştür. Hastaların %53,3'ünde ağrı mevcut olup, semptomatik hastalara non-steroid anti-enflamatuvar ilaçlar, E vitamini, pentoksifilin veya vertebroplasti uygulanmıştır. PIF gelişimi, düşük sakrum HU (p=0,012), serviks kanseri tanısı (p=0,033) ve eş zamanlı kemoterapi (p=0,023) ile anlamlı ilişkili bulunmuştur. ROC analizinde, sakrum HU için cut-off ≤-8 olarak belirlenmiştir (p=0,011, eğri altındaki alan=0,634). Çok değişkenli lojistik regresyonda, sakrum HU (≤-8) PIF için tek bağımsız risk faktörü olarak bulunmuştur (olasılık oranı: 3,04; %95 güven aralığı: 1,36-6,83; p=0,007).

Sonuç: Basit bir kemik mineral yoğunluğu değerlendirme yöntemiyle PIF riski öngörülebilir. Pelvik RT alan hastalarda serviks kanseri tanısı, eş zamanlı kemoterapi ve düşük sakrum HU değerleri fraktür riskini artırmaktadır. Yüksek riskli hastaların erken tespiti ve zamanında önlem alınması, klinik sürece katkı sağlayabilir.

Anahtar Kelimeler: Pelvik yetmezlik fraktürleri, radyoterapi, kemik mineral yoğunluğu, Hounsfield ünitesi, risk faktörleri

INTRODUCTION

Radiotherapy (RT) is essential for gynecological cancers, playing a key role in tumor control and organ preservation. However, the impact of pelvic RT on bone health and the associated risk of RT-induced bone damage remain underexplored. Pelvic insufficiency fractures (PIFs) are a common complication of pelvic RT, occurring in one in five patients (1).

Radiation-induced bone damage primarily results from the cytotoxic effects of ionizing radiation on osteoblasts and osteoclasts and from vascular injury in irradiated areas (2,3). These changes lead to a decrease in bone mineral density (BMD) and formation of weakened areas within the bone matrix, significantly increasing fracture risk, even with minimal trauma or during routine activities. The incidence of PIFs reported in the literature varies widely, from 9.7% to 89% (1,4-8). Moreover, recent series report higher detection rates than in the past, likely due to stricter follow-up and increased use of imaging techniques (6). Despite advancements in RT techniques that minimize radiation exposure to healthy tissues, such as intensity-modulated RT (IMRT) and volumetric-modulated arc therapy, the incidence of PIFs remains high, particularly in post-menopausal women and patients with predisposing risk factors such as low body mass index (BMI) or osteoporosis (9-11). Furthermore, systemic therapies, particularly chemotherapy administered concurrently with RT, can exacerbate bone weakening, further increasing fracture risk. Additionally, differentiating PIFs from metastatic bone lesions is crucial for proper treatment planning and management. Therefore, a multidisciplinary approach is essential to develop preventive strategies for PIFs.

This study aims to determine the frequency of PIFs in patients with endometrial and cervical cancer who have undergone pelvic RT, to investigate the relationship between CT-derived Hounsfield unit (HU) values and PIF occurrence, and to examine the prognostic factors influencing this condition.

METHODS

Patient Selection

Our study included patients who were diagnosed at our center between 2020 and 2024 and underwent pelvic RT and intracavitary high-dose-rate brachytherapy for cervical or endometrial cancer. Eligible patients had no history of PIF prior to treatment, had an Eastern Cooperative Oncology Group performance status of 0 or 1, were aged 18 years or older, and had a minimum follow-up of four months. Patients with a prior cancer diagnosis or a history of RT were excluded from the study. Ethical approval was obtained from the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (approval no: 2023-24-33, date: 18.12.2023). Written informed consent was obtained and was available in the patient files.

Staging and Treatment Planning

Staging and treatment decisions were established through multidisciplinary tumor board discussions. Patients were staged using contrast-enhanced pelvic magnetic resonance imaging (MRI), thoraco-abdominal computed tomography, and positron emission tomography-computed tomography (PET-CT) when necessary. Diagnosis was based on tumor biopsy, with lymph node biopsy and final pathology performed when indicated. Staging was performed according to the 8th edition (2018) of the American Joint Committee on Cancer TNM staging system (12).

Patients were immobilized supine, with arms raised, on a lung board with knee support, and with a full bladder. Contrast-enhanced CT scans were obtained from the carina to the upper femur at 3 mm slices. The images were transferred to the Monaco 5.11 treatment planning system (TPS; Elekta AB PUBL, Stockholm, Sweden). The clinical target volume (CTV), the planned target volume (PTV), and the organs at risk (OARs)—rectum, sigmoid colon, femoral heads, bowel, bladder, and kidneys—were contoured by a radiation oncologist. All patients underwent three-dimensional

conformal RT (3D-CRT). Total prescribed doses were 45-50.4 Gy (1.8-2 Gy per fraction per day) for PTV-pelvis, and 54-56 Gy (1.8 Gy per fraction per day) for metastatic lymph node PTV, delivered 6- and 18-MV-X beams. QUANTEC dose constraints were used for OAR dose tolerances (13). Plans required 95% of the PTV to be covered by the prescribed dose, with <2 cc receiving >107% of the isodose. Intracavitary brachytherapy planning was performed using CT imaging and the Gamma Med Plus iX® v 15.1 TPS (Varian Medical Systems) prior to each fraction. The treatment aimed to deliver 90% of the prescription dose to at least 90% of the high-risk CTV (HR-CTV). The OAR limits were 70 Gy for the rectum and sigmoid colon and 90 Gy for the bladder (14).

Bone Density Measurement

Bone density was measured on CT simulation images. A 1 cm region of interest (ROI) was defined to measure the mean trabecular bone density of the 4th lumbar (L4) vertebra in HU (15). Additionally, two 1 cm ROIs were placed in the trabecular bone of the right and left sacrum (Figures 1 and 2). Bone density values below 100 HU were classified as indicating osteoporosis (16-18).

Follow-up and Detection of Pelvic Insufficiency Fracture

The patients were followed with MRI and/or PET-CT scans every 3 months during the first 2 years, every 6 months until year 5, and annually thereafter. Insufficiency fractures, evaluated on follow-up MRI by experienced radiologists, were characterized by low-signal (hypointense) changes on time T1-weighted images and high-signal (hyperintense) changes with surrounding edema on T2-weighted images.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics® version 25 (IBM Corp, Armonk, NY, USA). The distributions of the variables were assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Patient characteristics were summarized using descriptive statistics. The chi-square test was used to compare qualitative variables and to evaluate the factors influencing PIFs. The Mann-Whitney U test was applied to compare quantitative variables between groups defined by a two-category qualitative variable. The effectiveness of HU values as cut-off points for insufficiency fractures was analyzed using receiver operating characteristic (ROC) analysis. Multivariate logistic regression analysis was performed. A p-value <0.05 was considered statistically significant.

RESULTS

The study included 128 patients, of whom 69 had cervical cancer and 59 had endometrial cancer. The median age was 68 years (range: 36-85 years). Post-menopausal women comprised 77.3% (n=99) of the cohort, while premenopausal women comprised 22.7% (n=29). The median BMI was 29.1

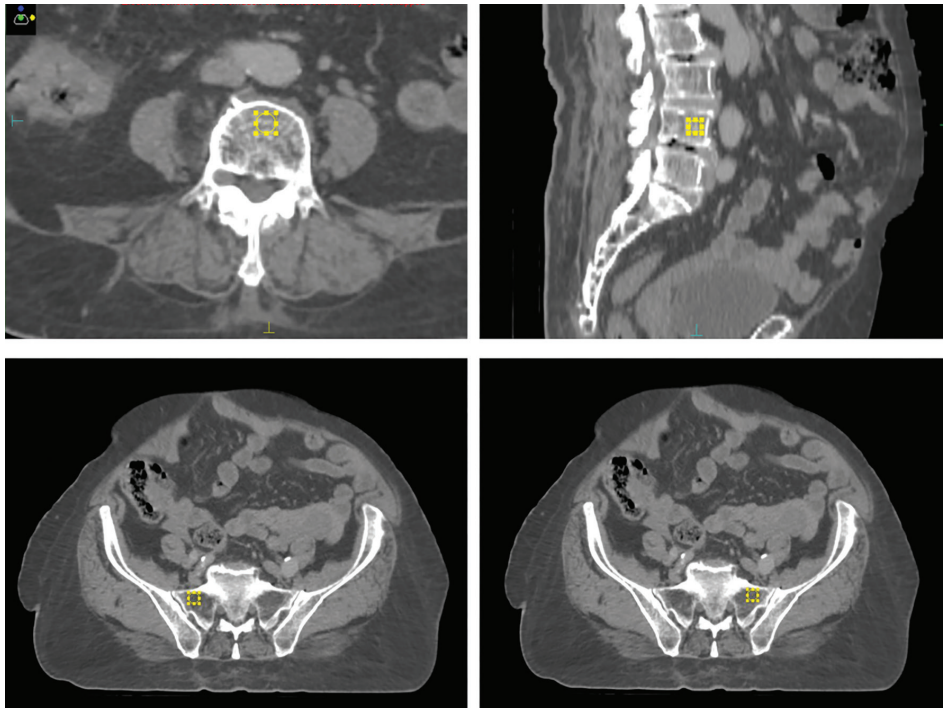

Figure 1. Measurement of bone density in Hounsfield units over bilateral sacral ala and L4 trabecular bone
L4: 4th lumbar vertebra

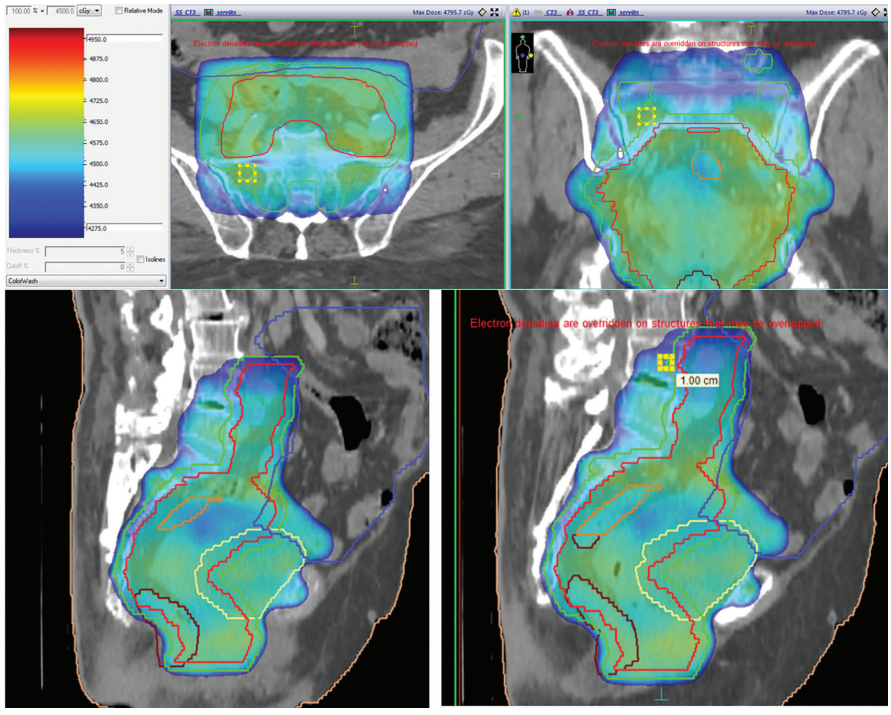

Figure 2. Radiotherapy plan views and ROI's for BMD measurements
ROI: Region of interest, BMD: Bone mineral density

(16.8-42) for cervical cancer patients and 30.8 (18-52.5) for uterine cancer patients (p=0.184). The median BMI for the entire group was 33.3 (range: 16.8-52.5). Comorbidities were present in 51.6% (n=66) of patients. The most common comorbidities included hypertension (16.4%; n=21), diabetes (9.4%; n=12), cardiovascular diseases (7.8%; n=10), and chronic obstructive pulmonary disease/asthma (8.6%; n=11).

Among cervical cancer patients, 5.8% (n=4) underwent pelvic MRI, 2.9% (n=2) had PET-CT, while the majority (91.3%; n=63) underwent both imaging modalities. The most common histologic subtypes were squamous cell carcinoma in cervical cancer (89.9%; n=62) and endometrioid adenocarcinoma in uterine cancer (84.7%; n=50). Among patients with cervical cancer, 13.0% (n=9) were stage 1, 15.9% (n=11) were stage 2, 40.6% (n=28) were stage 3, and 30.4% (n=21) were stage 4. Among patients with uterine cancer, 50.8% (n=30) were stage 1, 22% (n=13) were stage 2, 25.4% (n=15) were stage 3, and 1.7% (n=1) were stage 4. Total doses of 45-50.4 Gy (1.8-2 Gy per fraction) for PTV-pelvis and 54-56 Gy (1.8 Gy per fraction) for metastatic lymph node PTV were delivered using 3D-CRT. The median HR-CTV D90 was 89.1 Gy (range, 69-107 Gy) for cervical cancer patients and 75.5 Gy (range, 68.3-97.2 Gy) for uterine cancer patients.

Chemotherapy was administered concurrently with RT in 92.8% (n=64) of cervical cancer patients. Among patients with uterine cancer, 52.5% (n=31) received chemotherapy; only 1.7% (n=1) received it concurrently, and 50.8% (n=30) underwent adjuvant or neoadjuvant therapy. Overall, 7.2% (n=5) of cervical cancer patients and 47.5% (n=28) of uterine cancer patients did not receive chemotherapy. The median L4-HU value was 119 (range -9 to 306), while the median sacrum HU value was 19 (range -130 to 168). Using 100 HU as the osteoporosis threshold (16-18), 66.7% (n=46) of cervical cancer patients and 55.9% of uterine cancer patients had HU-L4 values exceeding this threshold, with no significant difference between the groups (p=0.213). For HU-sacrum values, no significant difference in osteoporosis risk was found between the two groups (p=0.133). In the total population, osteoporotic changes were detected in 38.3% of patients in the L4 region, while 61.7% had no osteoporosis. However, in the sacral region, osteoporosis was significantly more common: 90.6% of patients were below the 100 HU threshold, indicating a high risk of osteoporosis. Descriptive data are presented in Table 1.

The median follow-up time was 29 months (range, 9-79 months). The median time from RT completion to PIF detection was 19 months (range, 2-49 months), and the overall incidence of PIF was 35.2% (n=45) (Figure 3). For PIF diagnosis, MRI alone was used in 82.2% (n=37) of cases, while MRI+PET-CT was used in 17.8% (n=8). The median standardized uptake value (SUV) of PIF was 4.0 (2.7-5.9).

Table 1. Baseline characteristics for endometrial and cervical cancer groups

	Cervical cancer, n (%)	Uterine cancer, n (%)	p	
Age	57 (36-85)	65 (39-85)	-3.025*	0.002
BMI	29.1 (16.8-42)	30.86 (18-52.58)	-1.328*	0.184
Menopausal status				
Pre-menopausal	24 (34.8)	5 (8.5)	12.562**	<0.001
Post-menopausal	45 (65.2)	54 (91.5)		
Comorbidity				
Absent	25 (36.2)	34 (57.6)	5.859**	0.015
Present	44 (63.8)	25 (42.4)		
Chemotherapy (yes/no)				
No	5 (7.2)	28 (47.5)	26.876**	<0.001
Yes	64 (92.8)	31 (52.5)		
Chemotherapy type				
Concurrent with RT	64 (92.8)	1 (1.7)	109.512**	<0.001
Other (adjuvant/neoadjuvant/no chemotherapy)	5 (7.2)	58 (98.3)		
HU-L4-osteoporosis-100 HU				
Absent	46 (66.7)	33 (55.9)	1.551**	0.213
Present	23 (33.3)	26 (44.1)		
HU-sacrum-osteoporosis-100 HU				
Absent	4 (5.8)	8 (13.6)	2.256**	0.133
Present	65 (94.2)	51 (86.4)		

*: Mann-Whitney U test, **: Chi-square test, BMI: Body mass index, HU: Hounsfield unit, L4: 4th lumbar vertebra, RT: Radiotherapy

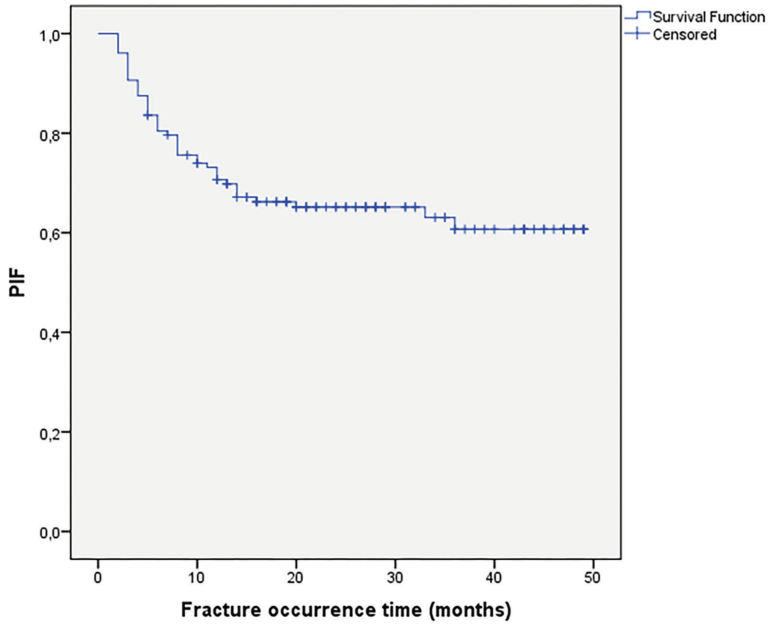

Figure 3. Follow-up duration (months) and incidence of PIF
PIF: Pelvic insufficiency fracture

Table 2. Evaluation of prognostic factors affecting pelvic insufficiency fractures

	PIF status		Chi-square	p
	Absent, n (%)	Present, n (%)		
Age group				
<65 years	47 (68.1)	22 (31.9)	0.703	0.402
≥65 years	36 (61.0)	23 (39.0)		
Disease				
Cervical cancer	39 (56.5)	30 (43.5)	4.548	0.033*
Uterine cancer	44 (74.6)	15 (25.4)		
Menopausal status				
Pre-menopausal	17 (58.6)	12 (41.4)	0.637	0.425
Post-menopausal	66 (66.7)	33 (33.3)		
BMI	29.1 (16.8-42)	30.86 (18-52.58)	-0.806	0.420
BMI group				
Normal and overweight	24 (60)	16 (40)	0.487	0.485
Obese	27 (67.5)	13 (32.5)		
Comorbidity				
Absent	40 (67.8)	19 (32.2)	0.419	0.518
Present	43 (62.3)	26 (37.7)		
Chemotherapy (yes/no)				
No	23 (69.7)	10 (30.3)	0.459	0.498
Yes	60 (63.2)	35 (36.8)		
Chemotherapy type				
Concurrent with RT	36 (55.4)	29 (44.6)	5.183	0.023*
Other (adjuvant/neoadjuvant/no chemotherapy)	47 (74.6)	16 (25.4)		
HU-L4	146 (-4-306)	105 (-9-222)	-0.200	0.842
HU-Sacrum	31.5 (-130-168)	6 (-103-162)	-2.498	0.012*

PIF: Pelvic insufficiency fracture, BMI: Body mass index, RT: Radiotherapy, HU: Hounsfield unit, L4: 4th lumbar vertebra, *: P significant

The most common fracture site was the sacrum (76.2%; n=32), followed by the pubis (14.3%; n=6), the sacroiliac region (7.1%; n=3), the lumbar spine (7.1%; n=3), and the iliac region (2.4%; n=1). Among patients diagnosed with PIF, 53.3% (n=24) experienced pain, while 46.7% (n=21) were asymptomatic. In 23 symptomatic patients, treatment included non-steroidal anti-inflammatory drugs, vitamin E, and pentoxifylline; vertebroplasty was performed in one patient.

Age, cancer type, menopausal status, BMI, presence of comorbidities, and HU-L4 and HU-sacrum values were analyzed as potential factors influencing PIFs. The analyses revealed significant differences associated with low HU-sacrum values (p=0.012), cervical cancer type (p=0.033), and receipt of CRT (p=0.023) (Table 2). In the ROC analysis for HU-sacrum values, the area under the curve was 0.634 (95% CI: 0.545-0.718). The cut-off value was determined to be ≤-8 and was statistically significant (p=0.011). For this cut-off value, sensitivity was 48.89%, and specificity was 78.31% (Figure 4). In the multivariate logistic regression analysis, sacral HU (≤-8 vs. >-8) was identified as an independent risk factor for PIF (OR: 3.04; 95% CI: 1.36-6.83; p=0.007). Patients in the low HU category had an approximately threefold higher risk of developing PIF. In contrast, chemotherapy type (p=0.407) and diagnosis (p=0.908) were not statistically significant independent predictors (Table 3).

DISCUSSION

PIF fractures were previously considered a rare complication of pelvic RT; however, with the widespread use of advanced imaging techniques, they are now more frequently detected. In older studies, the incidence of PIFs was reported as 5-10% (19,20), whereas modern studies have reported rates as high as 20-40% (1,5). The routine use of MRI has played a crucial role in this increase by revealing asymptomatic fractures (21). However, studies on PIF incidence show wide

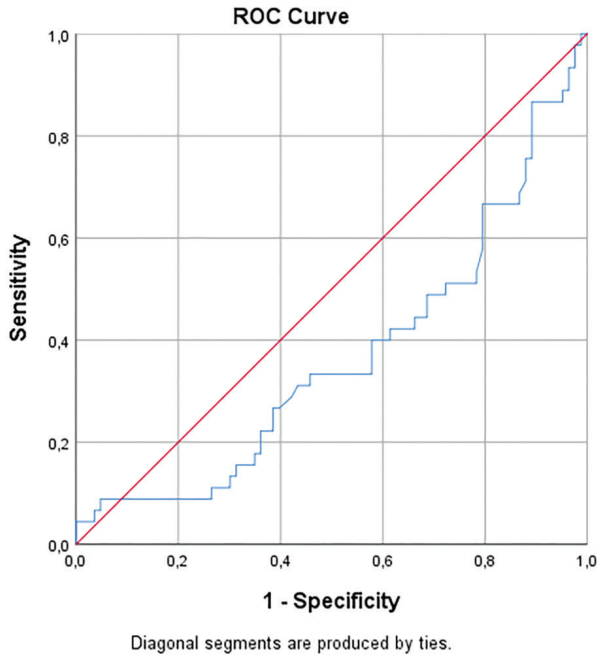

Figure 4. ROC analysis for HU-sacrum values
ROC: Receiver operating characteristic, HU: Hounsfield unit

Table 3. Multivariate logistic regression analysis for predictors of pelvic insufficiency fractures

Variable	B	S.E.	Wald	df	p-value	OR [Exp (B)]	95% CI (lower-upper)
Chemotherapy type	0.758	0.915	0.687	1	0.407	2.134	0.355-12.822
Diagnosis	-0.108	0.930	0.013	1	0.908	0.898	0.145-5.555
Sacrum HU* (≤-8 vs. >-8)	1.112	0.412	7.274	1	0.007	3.042	1.355-6.827

HU: Hounsfield unit, S.E.: Standard error, OR: Odds ratio, CI: Confidence interval, *: Sacrum HU cut-off value (≤-8) was determined using receiver operating characteristic analysis

variation, and there is no standardized risk assessment model currently available. In our study, we analyzed factors influencing PIF development after pelvic RT in 128 patients and evaluated the role of HU values obtained from CT images in predicting PIF risk.

The effects of RT on bone are dose-dependent. Pathophysiological studies suggest that osteoblast function begins to deteriorate at radiation doses of approximately 30 Gy, with cell death evident at approximately 50 Gy (22). Although advanced RT techniques have the potential to reduce radiation exposure to bone, Rijpma-Jacobs et al. (8) found that these techniques may not provide adequate protection in areas subject to high mechanical load, particularly in the sacrum. In a study of 27 anal cancer patients, the incidence of PIF was 50%, despite the use of rotational RT techniques in all cases (7). Similarly, Duranson et al. (1) reported a 5-year cumulative incidence of PIF of 22% among patients with cervical cancer treated with IMRT. In our clinic, 3D-CRT was used for all patients, and PIF occurred in 35.2% of cases. Although we could not evaluate pelvic-bone dose-volume parameters because the standard RT technique was used for all patients, several relevant studies have addressed this topic. For instance, Kronborg et al. (7) demonstrated that dose-volume parameters such as V30 Gy and V40 Gy for sacral bones were effective predictors of PIF risk. Ramlov et al. (23) reported that reducing the sacral D50% dose from 40 Gy to 35 Gy could decrease PIF incidence from 45% to 22%. A study by Mori et al. (24) examined the effects of carbon ion RT on PIF risk and investigated the relationship between dose and linear energy transfer (LETd) parameters. Their findings indicated that the D50% relative biological effectiveness-weighted dose to the sacrum was an important risk factor for PIF, whereas LETd and physical dose parameters were not significant predictors of PIF. Similarly, Huang et al. (25) found that BMD loss due to RT was reduced by 43% in patients who underwent pelvic bone marrow-sparing IMRT (PBMS-IMRT), compared with a 53% reduction in the control group.

PBMS-IMRT showed potential to reduce PIF incidence by 5% through minimizing BMD loss by 10%. In patients with low BMD, advanced RT techniques such as PBMS-IMRT may serve as a preventive strategy. Nevertheless, some studies have not found a significant correlation between RT dose parameters and PIF incidence (1,6). The current literature provides only limited evidence regarding the impact of modern RT techniques on PIF risk; our findings based on 3D-CRT highlight the need for caution in generalizing these results. While preliminary data (e.g., PBMS-IMRT) suggest potential dosimetric advantages and a possible reduction in the risk of PIF, larger comparative studies across cancer types and populations are required to determine whether these benefits translate into clinically meaningful improvements in practice.

The prognostic significance of advanced age, post-menopausal status, and low lumbar and sacral BMD in the development of PIFs has been well established in numerous studies (1,2,5,6,8). In our study, osteoporosis status was assessed based on HU values. Among patients with PIF, 90.6% had a sacral HU value <100, reinforcing the strong association between BMD loss after RT and PIF development. Similarly, Duranson et al. (1) demonstrated that BMD measurements from planning CT scans were strong predictors of PIF development, with lower sacral BMD values significantly increasing PIF risk ($p<0.001$). In our cohort, the statistically significant HU cut-off value (≤-8) was determined through a ROC analysis focusing exclusively on trabecular bone in the sacral region. Although low sacral BMD values are associated with increased PIF risk, the cut-off value may be specific to our population and measurement method and may vary across CT protocols and patient populations. Our findings indicate that sacral HU ≤-8 may be an independent risk factor for PIF, conferring approximately a threefold increase in risk. In contrast, chemotherapy type and diagnosis were not significant predictors. These results highlight the potential of HU-based sacral bone density assessment as a practical and clinically relevant parameter for early risk stratification in patients undergoing pelvic RT.

Patients receiving pelvic RT face a greater risk of PIF than non-irradiated counterparts. An analysis of Surveillance, Epidemiology, and End Results Program data from 6,428 patients aged 65 and older, including patients with anal canal, cervical, and rectal cancers, revealed that fracture incidence was significantly higher among patients who underwent pelvic RT. Specifically, in a cohort of 1,605 cervical cancer patients, the five-year fracture rate was 5.9% in the non-RT group compared to 8.2% in the RT group (26). Moreover, Huang et al. (25) demonstrated that systemic bone density loss can occur after RT, even in areas outside the radiation field. Similarly, Haque and Hossen (27) reported that bone loss following RT is not limited to the irradiated sites but may also have systemic effects on the entire skeletal system. This suggests that radiation-induced PIFs may result not only from localized BMD loss but also from systemic osteoporotic processes, emphasizing the need for bone-protective measures in high-risk patients.

The ROI technique used to determine HU values in our study focused exclusively on trabecular bone density. Therefore, direct comparisons with studies such as Huang et al. (25), which evaluated both cortical and trabecular density through contoured whole-bone assessments, may not be appropriate. PIF incidence rates in the literature range widely, from 1.7% to 89% (1,4-6,11,20,26-28). One of the highest reported rates comes from Mir et al. (5), who performed post-RT MRI examinations on 266 patients and detected PIFs in 37.4% of patients. The prevalence of PIF in our study was 35.2%, which is among the highest reported in the literature. This high incidence may be attributed to the high baseline prevalence of osteoporosis in our patient population. The prevalence of osteoporosis in Turkish women aged 50 years and older has been reported as 30-50%, which is higher than the 20-40% observed in European and U.S. populations (29,30). This could explain the higher PIF incidence (35.2%) in our study compared with those reported in the literature, where rates ranged from 9.7% (6) to 22% (1).

Huang et al. (25) reported that BMD loss following pelvic RT peaked within the first month of treatment and subsequently stabilized. Similarly, Rijpma-Jacobs et al. (8) reported that the mean time to PIF diagnosis was 17 months, with most fractures occurring within the first year. In Mir et al.'s (5) study, where the median follow-up was 12 months, 93% of fractures were detected within the first year. In our study, the median time from RT completion to PIF diagnosis was 19 months; however, 80% of fractures occurred within the first year, a discrepancy that warrants verification. Although some studies have reported earlier onset (6.5 months) (6), our findings align with the 11.5-19-month median latency period reported in other studies (1,3,7,8,28). The sacral bone and sacroiliac joints are the most common PIF locations, as documented in multiple studies, including ours (1,3,5-8,23). The lateral sacral wings are major weight-bearing structures, making them the most frequently affected sites. In our study, 82.2% of PIFs were detected by MRI. Although MRI remains the primary diagnostic modality, PET-CT has also demonstrated high sensitivity in detecting PIFs. PET-CT findings typically reveal diffuse or linear metabolic activity along the sacroiliac joint (21). In our study, the SUV for

PIFs in patients undergoing PET-CT was 4 (2.7-5.9), which is consistent with the SUV range of 1.7-5.9 reported in the literature (21,31). These findings suggest that PET-CT can serve as a complementary diagnostic tool for PIF detection. Another important consideration is the underdiagnosis of insufficiency fractures and their potential misidentification as metastatic lesions. Rijpma-Jacobs et al. (8) reported that in a cohort of 300 rectal cancer patients, only 12 PIFs were initially diagnosed, but this number increased to 32 upon detailed imaging review. This finding underscores the importance of systematic imaging to ensure early and accurate diagnosis of PIF.

Management of PIFs should be individualized according to the patient's condition and symptom severity. However, most cases can be effectively managed with conservative treatment without requiring hospitalization. Pain management is a critical component of the care of symptomatic patients, in which anti-inflammatory drugs can be used alongside analgesics for effective relief. In our study, 53% of patients reported pain, similar to the 56% reported Rijpma-Jacobs et al.'s (8) series, while other studies reported prevalences as high as 70% and 86% (7,25,31). A meta-analysis by Sapienza et al. (3), which included 3,929 patients, reported that 61% of the 504 PIF cases were symptomatic. In cases of bone fractures, surgical interventions such as vertebroplasty may be necessary. In Rijpma-Jacobs et al.'s (8) study, hyperbaric oxygen therapy was administered to only one patient. Another important consideration is that even asymptomatic patients should receive bone-strengthening interventions to improve BMD and prevent future fractures. Post-menopausal patients or those with low BMD may require a multidisciplinary approach, including prophylactic treatments (e.g., bisphosphonates or denosumab) and lifestyle modifications. Additionally, optimizing RT planning with bone-sparing techniques for high-risk patients and reducing sacral dose exposure may help lower fracture risk.

In routine clinical practice, pelvic bone density is not incorporated into RT planning, despite its strong association with PIF risk. Given the marked variability in osteoporosis prevalence across populations and the wide range of PIF incidences reported in the literature, there is a need for simple, standardized tools for risk stratification. HU-based BMD assessment derived from planning CT scans represents such a tool, as it is cost-free and readily accessible. Our findings, demonstrating a strong correlation between low sacral HU values and PIF risk, support its potential clinical utility. Nevertheless, before this parameter can be routinely adopted into RT planning workflows, its predictive value should be validated in larger cohorts.

Study Limitations

Our study has some limitations. The exclusive use of 3D-CRT limits the generalizability of our findings to centers utilizing advanced RT techniques. Additionally, our study used HU values from planning CT images as a surrogate for BMD, employing 100 HU as a reference threshold based on data from the Turkish population (18). Various HU cut-off values have been proposed in the literature for predicting osteoporosis across different populations. Further standardization of HU measurements and their integration into routine RT planning protocols are necessary to enhance their clinical applicability.

CONCLUSION

Our study demonstrates that PIF can be predicted using a simple BMD density assessment. In patients receiving pelvic RT, particularly those with cervical cancer, concurrent chemotherapy and low sacral HU values were identified as significant risk factors for fractures. Early identification of high-risk patients and timely preventive measures may significantly improve clinical outcomes.

ETHICS

Ethics Committee Approval: Ethical approval was obtained from the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (approval no: 2023-24-33, date: 18.12.2023).

Informed Consent: Written informed consent was obtained and was available in the patient files.

FOOTNOTES

Authorship Contributions

Surgical and Medical Practices: M.K.B., S.A., E.H., E.K.U., Concept: M.K.B., S.A., E.H., E.K.U., Design: M.K.B., S.A., E.H., Data Collection or Processing: M.K.B., S.A., O.Ö., F.B.G., B.H., B.G.T., Analysis or Interpretation: M.K.B., K.N.B., E.K.U., Literature Search: M.K.B., S.A., O.Ö., F.B.G., B.H., B.G.T., Writing: M.K.B., S.A., E.H., K.N.B., E.K.U.

Conflict of Interest: Esengül Koçak Uzel Prof. MD is a Editorial Member in Medical Journal of Bakırköy. She had no involvement in the peer-review of this article and had no access to information regarding its peer-review. The other authors declared no conflict of interest.

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REFERENCES

1. Duranson A, Thevenet V, Guyon F, Babin G, Lebreton C, Renaud T, et al. Pelvic insufficiency fractures after intensity modulated radiation therapy combined with chemotherapy for cervix carcinoma: incidence and impact of bone mineral density. Clin Transl Radiat Oncol. 2023;41:100650.
2. Ikushima H, Osaki K, Furutani S, Yamashita K, Kishida Y, Kudoh T, et al. Pelvic bone complications following radiation therapy of gynecologic malignancies: clinical evaluation of radiation-induced pelvic insufficiency fractures. Gynecol Oncol. 2006;103:1100-4.
3. Sapienza LG, Salcedo MP, Ning MS, Jhingran A, Klopp AH, Calsavara VF, et al. Pelvic insufficiency fractures after external beam radiation therapy for gynecologic cancers: a meta-analysis and meta-regression of 3929 patients. Int J Radiat Oncol Biol Phys. 2020;106:475-84.
4. Blomlie V, Rofstad EK, Talle K, Sundfør K, Winderen M, Lien HH. Incidence of radiation-induced insufficiency fractures of the female pelvis: evaluation with MR imaging. AJR Am J Roentgenol. 1996;167:1205-10.
5. Mir R, Dragan AD, Mistry HB, Tsang YM, Padhani AR, Hoskin P. Sacral insufficiency fracture following pelvic radiotherapy in gynaecological malignancies: development of a predictive model. Clin Oncol (R Coll Radiol). 2021;33:e101-9.
6. Kurrumeli D, Oechsner M, Weidenbächer B, Brambs C, Löffler M, Combs SE, et al. An easy way to determine bone mineral density and predict pelvic insufficiency fractures in patients treated with radiotherapy for cervical cancer. Strahlenther Onkol. 2021;197:487-93.
7. Kronborg CJ, Pedersen BG, Klemmensen J, Lefévre AC, Wind KL, Spindler KG. Pelvic insufficiency fractures and bone pain after radiation therapy for anal cancer: relation to pelvic bone dose-volume parameters. Adv Radiat Oncol. 2022;8:101110.
8. Rijpma-Jacobs L, van der Vlies E, Meek DB, Bollen TL, Siersema PD, Weusten BLAM, et al. Pelvic insufficiency fractures and pelvic bone metastases after neoadjuvant (chemo)radiotherapy for rectal cancer. Acta Oncol. 2023;62:1295-300.
9. Schmeler KM, Jhingran A, Iyer RB, Sun CC, Eifel PJ, Soliman PT, et al. Pelvic fractures after radiotherapy for cervical cancer: implications for survivors. Cancer. 2010;116:625-30.
10. Oh D, Huh SJ. Insufficiency fracture after radiation therapy. Radiat Oncol J. 2014;32:213-20.
11. Bazire L, Xu H, Foy JP, Amessis M, Malhaire C, Cao K, et al. Pelvic insufficiency fracture (PIF) incidence in patients treated with intensity-modulated radiation therapy (IMRT) for gynaecological or anal cancer: single-institution experience and review of the literature. Br J Radiol. 2017;90:20160885.
12. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, et al. The eighth edition AJCC cancer staging manual: continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin. 2017;67:93-9.
13. Marks LB, Yorke ED, Jackson A, Ten Haken RK, Constine LS, Eisbruch A, et al. Use of normal tissue complication probability models in the clinic. Int J Radiat Oncol Biol Phys. 2010;76(3 Suppl):S10-9.
14. Dimopoulos JC, Petrow P, Tanderup K, Petric P, Berger D, Kirisits C, et al. Recommendations from gynaecological (GYN) GEC-ESTRO working group (IV): basic principles and parameters for MR imaging within the frame of image based adaptive cervix cancer brachytherapy. Radiother Oncol. 2012;103:113-22.
15. Schwaiger BJ, Gersing AS, Baum T, Noël PB, Zimmer C, Bauer JS. Bone mineral density values derived from routine lumbar spine multidetector row CT predict osteoporotic vertebral fractures and screw loosening. AJNR Am J Neuroradiol. 2014;35:1628-33.
16. Pickhardt PJ, Pooler BD, Lauder T, del Rio AM, Bruce RJ, Binkley N. Opportunistic screening for osteoporosis using abdominal computed tomography scans obtained for other indications. Ann Intern Med. 2013;158:588-95.
17. Berger-Groch J, Thiesen DM, Ntalos D, Grossterlinden LG, Hesse E, Fensky F, et al. Determination of bone density in patients with sacral fractures via CT scan. Orthop Traumatol Surg Res. 2018;104:1037-41.
18. Cansu A, Atasoy D, Eyüboğlu I, Karkucak M. Diagnostic efficacy of routine contrast-enhanced abdominal CT for the assessment of osteoporosis in the Turkish population. Turk J Med Sci. 2020;50:110-6.
19. Huh SJ, Kim B, Kang MK, Lee JE, Lim DH, Park W, et al. Pelvic insufficiency fracture after pelvic irradiation in uterine cervix cancer. Gynecol Oncol. 2002;86:264-8.
20. Feltl D, Vosmik M, Jirásek M, Stáhalová V, Kubes J. Symptomatic osteoradionecrosis of pelvic bones in patients with gynecological malignancies-result of a long-term follow-up. Int J Gynecol Cancer. 2006;16:478-83.
21. Ji Y, Shao C, Cui Y, Shi D, Su N, Wang Y, et al. Sacral insufficiency fracture after radiotherapy for cervical cancer: appearance and dynamic changes on 18F-fluorodeoxyglucose positron emission tomography/computed tomography. Contrast Media Mol Imaging. 2021;2021:5863530.
22. Oh D, Huh SJ, Nam H, Park W, Han Y, Lim DH, et al. Pelvic insufficiency fracture after pelvic radiotherapy for cervical cancer: analysis of risk factors. Int J Radiat Oncol Biol Phys. 2008;70:1183-8.
23. Ramlov A, Pedersen EM, Røhl L, Worm E, Fokdal L, Lindegaard JC, et al. Risk factors for pelvic insufficiency fractures in locally advanced cervical cancer following intensity modulated radiation therapy. Int J Radiat Oncol Biol Phys. 2017;97:1032-9.
24. Mori Y, Okonogi N, Matsumoto S, Furuichi W, Fukahori M, Miyasaka Y, et al. Effects of dose and dose-averaged linear energy transfer on pelvic insufficiency fractures after carbon-ion radiotherapy for uterine carcinoma. Radiother Oncol. 2022;177:33-9.
25. Huang J, Gao J, Zhang F, Gu F, Ding S, Yang Q, et al. Pelvic bone marrow sparing intensity modulated radiation therapy reduces the bone mineral density loss of patients with cervical cancer. Int J Radiat Oncol Biol Phys. 2025;121:107-17.
26. Baxter NN, Habermann EB, Tepper JE, Durham SB, Virnig BA. Risk of pelvic fractures in older women following pelvic irradiation. JAMA. 2005;294:2587-93.
27. Haque M, Hossen MS. Insights into pelvic insufficiency fracture following pelvic radiotherapy for cervical cancer: a comparative review. BMC Womens Health. 2024;24:306.
28. Chan S, Rowbottom L, McDonald R, David E, Chung H, Yee A, et al. Pelvic insufficiency fractures in women following radiation treatment: a case series. Ann Palliat Med. 2016;5:233-7.
29. Wright NC, Looker AC, Saag KG, Curtis JR, Delzell ES, Randall S, et al. The recent prevalence of osteoporosis and low bone mass in the United States based on bone mineral density at the femoral neck or lumbar spine. J Bone Miner Res. 2014;29:2520-6.
30. Kanis JA, Norton N, Harvey NC, Jacobson T, Johansson H, Lorentzon M, et al. SCOPE 2021: a new scorecard for osteoporosis in Europe. Arch Osteoporos. 2021;16:82.
31. Park SH, Kim JC, Lee JE, Park IK. Pelvic insufficiency fracture after radiotherapy in patients with cervical cancer in the era of PET/CT. Radiat Oncol J. 2011;29:269-76.