Original Article

Associations between breast radiation dermatitis and post-mastectomy pain syndrome in patients with breast cancer: A multicenter retrospective study

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ABSTRACT

Objective: This study explores the relationship between breast radiation dermatitis (BRD) and post-mastectomy pain syndrome (PMPS) among patients with breast cancer. Both BRD and PMPS significantly impact quality of life, yet their correlation and risk factors require further investigation.
Methods: We conducted a multicenter retrospective analysis of 784 patients with breast cancer who underwent postoperative radiotherapy between 2017 and 2023. Clinical data on BRD and PMPS were collected through patient questionnaires and hospital records, examining risk factors and evaluating the prevalence of PMPS among those with BRD.
Results: BRD affected 81.25% of patients, with higher incidence among older and obese individuals. PMPS was observed in 23.4% of the BRD group versus 13.6% in non-BRD patients (P=0.009). Early BRD onset during radiotherapy (P=0.004) and larger dermatitis areas (P=0.000) were strongly associated with increased PMPS risk.
Conclusions: This study highlights the significant relationship between BRD and PMPS, underscoring the need for early interventions to manage BRD and reduce chronic pain risk. Tailored care strategies could improve outcomes for high-risk patients.

Introduction

With the increasing incidence of breast cancer, it has now become the most common malignant tumor among women worldwide.[1] The therapeutic approaches for breast cancer are complex and multifaceted.[2,3] Surgical intervention remains the primary treatment modality for patients with Stage I, Stage II, and certain Stage III breast cancers.[4,5] Postoperative patients often require adjuvant therapies, including radiotherapy, chemotherapy, targeted therapy, or endocrine therapy.[6] Breast cancer is associated with a significant risk of metastasis or recurrence. Consequently, adjuvant radiotherapy is frequently employed post-surgery, targeting areas such as the breast, supraclavicular region, and axillary lymph nodes.[7] This approach aims to mitigate the likelihood

of local recurrence and distant metastasis, thereby enhancing the overall survival rates of patients.

Breast radiation dermatitis (BRD) is a dermatological reaction that occurs during or following radiotherapy for breast cancer.[8,9] It is a prevalent side effect among patients undergoing radiation treatment. The primary etiology of BRD is the direct DNA damage inflicted on skin cells by ionizing radiation, as well as the resultant inflammatory response within the skin's microenvironment.[10] Radiation disrupts cellular integrity, prompting the release of inflammatory mediators, which further exacerbate cellular injury and manifest as dermatological symptoms.[11] The clinical presentation of BRD can range from mild to severe, encompassing: 1) Erythema (characterized by mild swelling and redness); 2) Dryness and desquamation; 3) Pruritus; 4) Eczematous changes or

vesiculation; 5) In extreme cases, necrosis or ulceration of the skin may occur. The management of BRD typically involves a combination of preventive strategies, meticulous skin care, and symptomatic treatment.[12–14] Preventive measures may include the application of topical skin protectants and the modulation of radiation dose distribution to minimize damage to surrounding healthy tissue.[15] For established dermatitis, therapeutic interventions may consist of moist dressings, topical corticosteroids, and analgesics to alleviate symptoms and promote healing.[16,17]

Post-mastectomy pain syndrome (PMPS) is a form of chronic pain that manifests primarily as dull, dragging, numb, shooting, or stabbing sensations following breast cancer surgery.[18] It is one of the potential complications that may arise postoperatively, persisting for several months to years. Several factors are associated with the incidence of PMPS, including age, radiotherapy, and the type of surgical procedure.[19–22] Among these, radiotherapy is a significant risk factor, with breast cancer patients undergoing radiotherapy being more susceptible to postoperative pain symptoms. Patients who undergo breast-conserving surgery or mastectomy and are at high risk of recurrence often require adjuvant radiotherapy. The extent of radiotherapy is determined by the surgical scope and the severity of the disease. Radiotherapy can induce neuropathic pain, contributing to the development of PMPS.[19]

Over the past 30 years, the prognosis for malignant breast tumors has significantly improved, with an increasing number of individuals undergoing breast radiotherapy and achieving long-term survival.[23,24] However, research on the correlation between BRD and PMPS is still lacking. Additionally, knowledge regarding the prevention and treatment of BRD and PMPS has not been widely disseminated. The primary aim of this study is to explore the high-risk factors for BRD. More importantly, it seeks to investigate the relationship between BRD and PMPS in breast cancer patients, providing critical guidance for the prevention and treatment of high-risk patients.

Methods

Study population

This study is a multicenter retrospective analysis involving patients who underwent breast cancer surgery followed by postoperative radiotherapy between 2017 and 2023. The participating institutions include the Cancer Hospital of the Chinese Academy of Medical Sciences, Xuanwu Hospital of Capital Medical University, Henan Provincial People's Hospital, and Yichang Central People's Hospital. The inclusion criteria for the study included: 1) female breast cancer patients; 2) patients who underwent surgical treatment followed by postoperative breast radiotherapy; 3) patients who fully understood and voluntarily participated in the study. The exclusion criteria included: 1) male patients; 2) patients who received neoadjuvant chemotherapy; 3) patients who had distant metastasis at the time of diagnosis. All study protocols were reviewed and approved by the Ethics Committee of the Cancer Hospital of the Chinese Academy of Medical Sciences (IRB No. NCC2907). Written informed consent was obtained from each participating patient.

Clinical baseline data

Patient characteristics were collected from medical records, including age, body mass index (BMI), ethnicity, age at menarche, type of breast surgery, type of axillary surgery, marital status, medical history, smoking history and menstrual status. The types of breast surgery encompassed breast-conserving surgery, total mastectomy, and breast reconstruction with implants. Therapy Marital status was categorized as unmarried, married, or other. Medical history included hypertension, diabetes, heart disease, smoking or other conditions. Menstrual status was classified as postmenopausal or regular menstruation. All patients were treated with 3-dimensional adjuvant whole breast conventional radio therapy. The

radiotherapy methods include hypofractionated radiotherapy (49.5 Gy/15 f) and conventional fractionated radiotherapy (50 Gy/25 f). The tumor bed boost radiotherapy is administered as either 6 Gy in 3 fractions or 10 Gy in 5 fractions.

Questionnaire design

The questionnaires used in the study included assessments of BRD following radiotherapy and persistent pain following breast surgery.

The assessment of BRD comprised: 1) Onset Time: During radiotherapy, after the completion of radiotherapy; 2) Affected Area Size: $S \leq 2$ cm^2, 2 cm$^2 < S \leq 5$ cm^2, and $S \geq 5$ cm^2; 3) Severity of Dermatitis: Grade 1 (Mild): Slight erythema and/or pruritus. Grade 2 (Moderate): Pronounced erythema and swelling, possibly accompanied by pain, causing discomfort. Grade 3 (Severe): Dry desquamation or mild moist desquamation. Grade 4: Severe eczematous desquamation covering a large area, significantly impacting the patient's quality of life. Grade 5: Presence of ulcers, bleeding, or necrosis;[9,25] 4) Treatment: No treatment, corticosteroid treatment, other antimicrobial dressing treatments.

The assessment of persistent pain following breast surgery primarily included: 1) Type of Pain: Severe pain such as stabbing pain, electric shock-like pain, swelling pain, and numbness of the skin in the surgical area; 2) Location of Pain: Breast area, ipsilateral axilla, ipsilateral upper arm, and other areas such as back pain and headaches; 3) Pain Intensity: Evaluated using the Numeric Rating Scale (NRS) ranging from 0 to 10, where 0 represents no pain and 10 represents the worst imaginable pain; 4) Pain Management: Whether the pain was treated with analgesics, acupuncture, or nerve block.

Questionnaire distribution and collection

The survey was conducted by trained professionals who guided patients in completing the questionnaires. Patients in this study were interviewed via telephone or the internet to ascertain whether they had experienced BRD or PMPS. If patients reported symptoms of BRD or postoperative pain and consented to participate in the study, the questionnaire was sent to them online. For patients who did not respond within two weeks, we made follow-up contact. If necessary, the questionnaire was reissued, or patients were asked to complete it via telephone.

Data analysis

Statistical analysis was performed using IBM SPSS 20.0 for Windows (IBM SPSS, Armonk, NY). Histograms and Q–Q plots were utilized to assess the normality of the data. All values are presented as the number of patients, percentages, and 95% confidence intervals (95% CI) for normally distributed data, and as medians within interquartile ranges for non-normally distributed data. Parametric unpaired t-tests were used to analyze normally distributed data, while non-parametric Mann–Whitney U tests were employed for non-normally distributed data. Using logistic regression analysis or random forest models to identify and interpret the risk factors for BRD in breast cancer treatment. A *P*-value of 0.05 was considered statistically significant. Since the publication of the protocol, there have been no changes in methods or trial outcomes.

Results

Analysis of clinical information of radiotherapy patients

This study followed a total of 2100 patients from the Cancer Hospital of the Chinese Academy of Medical Sciences, Xuanwu Hospital of Capital Medical University, Henan Provincial People's Hospital, and Yichang Central People's Hospital. Among them, 784 patients underwent breast cancer surgery and received radiation therapy postoperatively, and they agreed to participate in this study. Of these, 637 patients (81.25%) were

diagnosed with BRD during or after radiotherapy and were classified into the BRD group, while 147 patients (18.75%) did not develop BRD and were classified into the HP group.

The average age of the 784 patients was 50.27 ± 10.91 years. Patients in the HP group (mean age 48.10 ± 10.74) were younger than those in the BRD group (mean age 50.77 ± 10.90) ($P = 0.008 < 0.05$, Table 1). The mean age at menarche was 13.75 ± 1.71 years, and the mean BMI was $24.42 \pm 2.49 \, kg/m^2$. No significant differences were found in the age at menarche and BMI between the BRD and HP groups ($P > 0.05$, Table 1). According to the World Health Organization's definition, a $BMI > 30 \, kg/m^2$ is categorized as obese. In the BRD group, 168 patients (26.4%) had a BMI exceeding $30 \, kg/m^2$, compared to only 26 patients (17.7%) in the HP group, showing a statistically significant difference between the two groups ($P = 0.028 < 0.05$, Table 1). A total of 295 patients (37.6%) underwent breast-conserving surgery, 462 patients (58.9%) underwent total mastectomy, and 27 patients (3.4%) underwent breast reconstruction. In the BRD group, 239 patients (37.5%) had breast-conserving surgery, 374 patients (58.7%) underwent total mastectomy, and 24 patients (3.8%) underwent breast reconstruction. In the HP group, 56 patients (38.1%) had breast-conserving surgery, 88 patients (59.9%) underwent total mastectomy, and 3 patients (2.0%) underwent breast reconstruction. There were no significant differences between the two groups regarding the type of surgery ($P > 0.05$, Table 1). In the BRD group, 292 patients received conventional fractionated radiotherapy (CRT), while 345 patients received hypofractionated radiotherapy (HFRT). In the HP group, 58 patients received CRT, and 89 patients received HFRT. There was no statistically significant difference between the two groups ($P > 0.05$, Table 1). In the BRD group, 363 patients received boost

radiation to the tumor bed, while in the HP group, 75 patients received boost radiation to the tumor bed ($P > 0.05$, Table 1). There was no statistically significant difference between the two groups. In the BRD group, 363 patients received boost radiation to the tumor bed, compared to 75 in the HP group, with no statistically significant difference between the groups. Similarly, there were no significant differences between the BRD and HP groups in terms of ethnicity, hypertension, diabetes, heart disease, menstrual status, and smoking status ($P > 0.05$, Table 1). Concerning PMPS, 149 patients (23.4%) in the dermatitis group exhibited PMPS symptoms, while 488 patients (76.6%) did not. In the healthy group, 20 patients (13.6%) exhibited PMPS symptoms, while 127 patients (86.4%) did not, indicating a significant difference between the two groups ($P = 0.009 < 0.05$, Table 1).

Logistic regression model and random forest models

In this analysis, we initially used a logistic regression model to assess the risk factors for BRD group or HP group. The results from the logistic regression model identified "Age" and "BMI" as significant influencing factors (Fig. 1), with the model achieving a predictive accuracy of 81.38% and an area under the curve (AUC) of 0.63 (Fig. 2). Although the model was capable of identifying features significantly associated with the target variable, its discriminative power was relatively limited, with an AUC indicating moderate performance. To further enhance model performance, a random forest model was employed. The random forest model improves predictive accuracy and robustness by integrating multiple decision trees. The results showed that the predictive accuracy of the random forest model significantly increased to 91.58%, and the AUC

Table 1
Clinical information of 784 patients undergoing breast surgery and radiotherapy.

	BRD group ($n = 637$)	HP group ($n = 147$)	Total ($n = 784$)	P
Age (years, Mean $\pm$ SD)	50.77 ± 10.90	48.10 ± 10.74	50.27 ± 10.91	0.008
Menarche (years, Mean $\pm$ SD)	13.75 ± 1.71	13.88 ± 1.73	13.77 ± 1.72	0.407
Body weight				
BMI (kg/m^2, Mean $\pm$ SD)	24.32 ± 2.44	24.84 ± 2.67	24.42 ± 2.49	0.221
BMI $> 30 \, kg/m^2$	168 (26.4)	26 (17.7)	194 (24.7)	0.028
BMI $\leq 30 \, kg/m^2$	469 (73.6)	121 (75.3)	590 (75.3)	
Type of operation				0.581
Breast-conserving	239 (37.5)	56 (38.1)	295 (37.6)	
Mastectomy	374 (58.7)	88 (59.9)	462 (58.9)	
Breast-reconstruction	24 (3.8)	3 (2.0)	27 (3.4)	
Ethnic group				0.252
Han	590 (92.6)	132 (89.8)	722 (92.1)	
Others	47 (7.4)	15 (10.2)	62 (7.9)	
Hypertension				0.671
Yes	86 (14.0)	18 (12.2)	104 (13.3)	
No	548 (86.0)	129 (87.8)	677 (86.7)	
Diabetes				0.980
Yes	35 (5.5)	8 (5.4)	43 (5.5)	
No	602 (94.5)	139 (94.6)	741 (94.5)	
Heart disease				0.342
Yes	10 (1.6)	4 (2.7)	14 (1.8)	
No	627 (98.4)	143 (97.3)	770 (98.2)	
Menstrual status				0.991
Normal	321 (50.4)	74 (50.3)	395 (50.4)	
Menopause	316 (49.6)	73 (49.7)	389 (49.6)	
Smoking history				0.149
Yes	24 (3.8)	10 (6.8)	34 (4.3)	
No	613 (96.2)	137 (93.2)	750 (95.7)	
Type of radiation				0.190
HFRT	345 (54.2)	89 (60.5)	434 (55.4)	
CRT	292 (45.8)	58 (39.5)	350 (44.6)	
Tumor bed boost radiotherapy				0.092
Yes	363 (57.0)	75 (51.0)	438 (58.6)	
No	274 (43.0)	72 (49.0)	346 (41.4)	
PMPS				
Yes	149 (23.4)	20 (13.6)	169 (21.6)	0.009
No	488 (76.6)	127 (86.4)	615 (78.4)	

BRD group, Breast radiation dermatitis group; HP group, Healthy patient group; BMI, Body mass index; HFRT, Hypofractionated radiation therapy; CRT, Conventional fractionated radiation therapy; PMPS, Post-mastectomy pain syndrome.
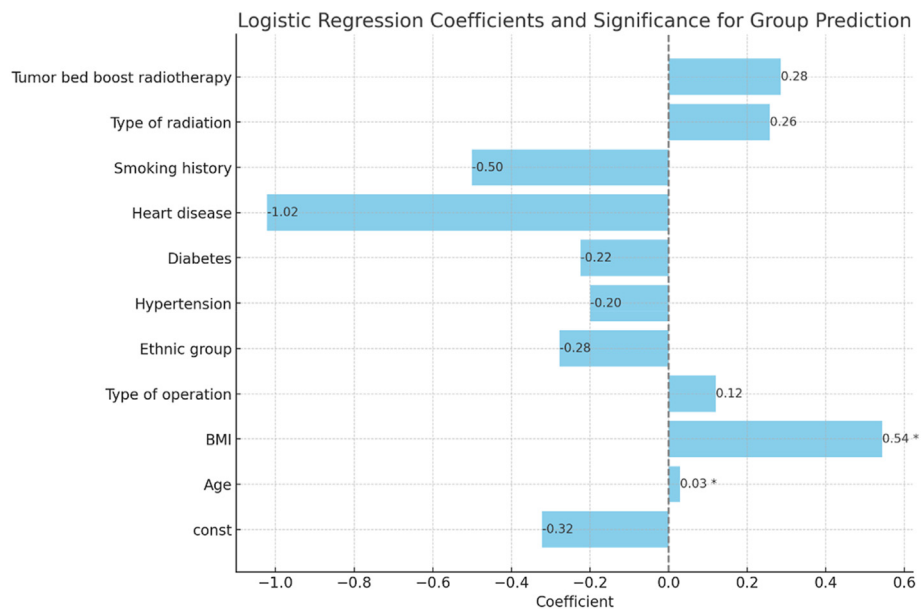
Logistic Regression Coefficients and Significance for Group Prediction

Fig. 1. Displays the regression coefficients and their significance for each variable. Each bar represents a variable in the model, with the length of the bar indicating the regression coefficient of that variable. Bars marked with an asterisk (*) indicate that the variable is statistically significant ($P < 0.05$). BMI, Body mass index.
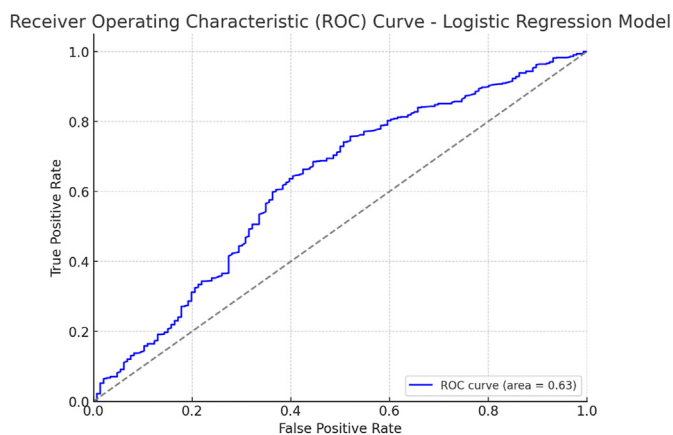

Fig. 2. The area under the curve (AUC) of the logistic regression model is 0.63.

Fig. 3. The area under the curve (AUC) of the random forest model is 0.97.

also substantially rose to 0.97 (Fig. 3). This demonstrates that the random forest model performs exceptionally well in distinguishing between the dermatitis and control groups.

Information on patients with BRD

Further analysis was conducted on the 637 patients who developed BRD, categorizing them into two groups based on the presence of PMPS. Among these, 149 patients were in the PMPS group, while 488 patients were in the non-PMPS group.

Based on the timing of BRD onset, 108 patients (72.5%) in the PMPS group developed dermatitis during radiotherapy, while 41 patients (27.5%) developed it after the completion of radiotherapy. In contrast, 290 patients (59.4%) in the non-PMPS group developed dermatitis during radiotherapy, and 198 patients (40.6%) developed it after radiotherapy, indicating a statistically significant difference between the two groups ($P = 0.004 < 0.05$, Table 2). In the PMPS group, 27 patients (18.1%) had a dermatitis area less than 2 cm^2, 64 patients (43.0%) had an area between 2 cm^2 and 5 cm^2, and 58 patients (38.9%) had an area greater than 5 cm^2. In the non-PMPS group, 220 patients (45.1%) had a dermatitis area less than 2 cm^2, 178 patients (36.5%) had an area between 2 cm^2 and 5 cm^2, and 90
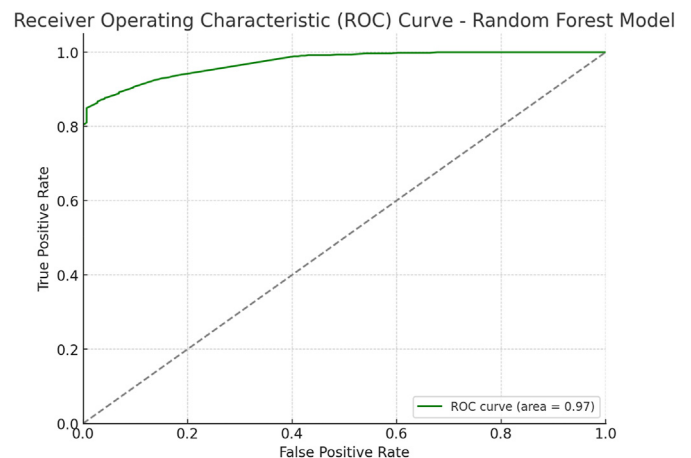
patients (18.4%) had an area greater than 5 cm^2. There was a statistically significant difference in dermatitis area between the two groups ($P = 0.000 < 0.05$, Table 2). There were no statistically significant differences between the PMPS and non-PMPS groups concerning the severity of dermatitis and the treatments administered ($P > 0.05$, Table 2).

Information of patients in the PMPS group

A further analysis was conducted on the 149 patients who received radiotherapy and exhibited symptoms of PMPS. The average NRS pain score was 3.44 ± 2.05, with a median score of 3.00. Among these patients, 89 (59.7%) experienced stabbing pain, 128 (85.9%) experienced electric shock-like pain, 52 (34.9%) experienced swelling pain, and 14 (9.4%) experienced numbness. Regarding the location of pain, 105 patients (70.5%) reported pain in the breast area, 77 patients (51.7%) reported pain in the axillary region, 53 patients (35.6%) reported pain in the upper arm, and 24 patients (16.1%) reported pain in other areas. In terms of pain management, 127 patients (85.2%) used analgesics, 34 patients (22.8%) received acupuncture treatment, and 12 patients (8.1%) underwent local nerve block therapy.

Table 2
Dermatitis information on 637 patients with radiotherapy dermatitis.

	PMPS group (*n* = 149)	Non-PMPS group (*n* = 488)	Total (*n* = 637)	*P*
Time of onset of dermatitis				0.004
During radiotherapy	108 (72.5)	290 (59.4)	398 (62.5)	
After radiotherapy	41 (27.5)	198 (40.6)	239 (37.5)	
Area of dermatitis				0.000
S ≤ 2 cm^2	27 (18.1)	220 (45.1)	247 (38.8)	
2 cm^2<S ≤ 5 cm^2	64 (43.0)	178 (36.5)	242 (38.0)	
S > 5 cm^2	58 (38.9)	90 (18.4)	148 (23.2)	
Degree of dermatitis				0.386
Degree 1	93 (62.4)	334 (68.4)	427 (67.0)	
Degree 2	47 (31.5)	120 (24.6)	167 (26.2)	
Degree 3	7 (4.7)	24 (4.9)	31 (4.9)	
Degree 4	2 (1.3)	10 (2.0)	12 (1.9)	
Degree 5	0	0	0	
Dermatitis treatment				0.236
Untreated	12 (8.1)	35 (7.2)	47 (7.4)	
Corticosteroid therapy	101 (67.8)	364 (74.6)	465 (73.0)	
Dressing treatment	36 (24.2)	89 (18.2)	125 (19.6)	

PMPS, Post-mastectomy pain syndrome.

Discussion

Risk factors for BRD

This study successfully collected data from 2100 patients across four hospitals in China, including 784 patients who underwent breast cancer surgery followed by radiotherapy. These four hospitals represent the levels of breast cancer surgery and radiotherapy available at national, provincial, and municipal hospitals in China. Among the 784 patients, 637 developed radiation dermatitis during their treatment, resulting in an incidence rate of approximately 81.25% for post-mastectomy BRD, consistent with the incidence rates reported in previous studies.[26–28] Research has indicated that radiotherapy is a significant risk factor for the development of PMPS.[19] In this study, 149 patients exhibited PMPS symptoms, indicating that the probability of developing chronic postoperative pain among patients who received radiotherapy is approximately 19.01%, which is slightly higher than the overall incidence of chronic postoperative pain among breast cancer patients.

In this study, age emerged as a significant factor influencing the incidence of BRD following breast cancer radiotherapy. With advancing age, the content of collagen and elastin in the skin diminishes, rendering the skin more fragile and less elastic.[29,30] This increased fragility makes the skin of elderly patients more susceptible to radiation-induced damage. Additionally, older skin tends to be thinner, particularly in the epidermal and dermal layers, which reduces its protective capacity against radiation and elevates the risk of BRD.[31] The regenerative capacity of skin cells also declines with age, leading to slower repair of damage. Consequently, during radiotherapy, the damaged skin of elderly patients struggles to recover quickly, resulting in more severe and prolonged dermatitis symptoms. Moreover, poor blood circulation in the skin of older individuals affects the supply of nutrients and oxygen, further impeding the healing process.[32] As the immune system's functionality declines with age, the activity of immune cells decreases.[33] This weakened immune response makes it more challenging for elderly patients to effectively control inflammation induced by radiotherapy, leading to more severe BRD. Older adults are also more prone to chronic low-grade inflammation, which can exacerbate acute inflammatory responses during radiotherapy and worsen dermatitis symptoms.[34] Additionally, the elderly population typically suffers from multiple chronic conditions, such as diabetes and cardiovascular diseases.[35] These comorbidities impair the skin's repair capacity and overall health, thereby increasing both the incidence and severity of BRD.

Similarly, this study identifies obesity (high BMI) as a significant risk factor for acute BRD following breast cancer radiotherapy. In obese patients, the subcutaneous fat layer is thicker, leading to uneven distribution

of radiation in the skin and subcutaneous tissues. This increased thickness results in greater scattering and reflection of radiation during penetration, thereby increasing the localized radiation dose and the risk of skin damage. Obesity may also impair the skin's barrier function, reducing its protective capability.[36] The lower water content in adipose tissue can lead to dryness and cracking of the skin, further heightening the risk of BRD. Additionally, obesity is associated with a state of chronic low-grade inflammation, wherein a substantial number of macrophages and other immune cells in adipose tissue release inflammatory mediators such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6).[37] This chronic inflammatory state makes the skin more susceptible to radiation-induced damage and exacerbates the inflammatory response in BRD. Furthermore, obese patients tend to have more skin folds, which are prone to accumulating sweat and bacteria, increasing the risk of infection. During radiotherapy, these skin folds are more susceptible to friction and pressure, leading to barrier damage and the onset of BRD.

Relationship between BRD and PMPS

Among the 637 patients with BRD, 149 patients developed PMPS, accounting for 23.4%. This percentage is higher than the 13.6% observed in the healthy group,[19] indicating a statistically significant difference and suggesting that patients with BRD are more likely to develop PMPS. Further analysis divided the 637 BRD patients into two groups based on the presence or absence of PMPS: the PMPS group and the non-PMPS group. Statistical comparisons revealed that approximately 72% of patients in the PMPS group developed BRD during radiotherapy, whereas only 59% of patients in the non-PMPS group experienced BRD during this period. This finding suggests that the onset of BRD occurred earlier in the PMPS group compared to the non-PMPS group. Additionally, the study found that about 38% of patients in the PMPS group had BRD areas greater than 5 cm^2, significantly higher than the non-PMPS group. This indicates that a larger BRD area is associated with an increased likelihood of developing PMPS.

BRD may contribute to or exacerbate PMPS through several mechanisms: 1) Direct Tissue Damage: BRD induces damage to the skin and subcutaneous tissues, extending beyond the epidermal layer to deeper structures, including nerve endings.[38] Persistent inflammation and tissue injury may lead to the development of chronic pain; 2) Neuro-inflammation: Radiotherapy triggers localized neuroinflammatory responses, releasing inflammatory mediators such as cytokines and chemokines, including TNF-α, IL-1, and IL-6.[39] These mediators can activate or sensitize nociceptive nerve endings, resulting in prolonged and chronic pain; 3) Fibrosis: A long-term complication of radiotherapy is tissue fibrosis. Fibrosis not only affects skin elasticity and structure but also exerts pressure on or stretches nerve fibers, leading to chronic

pain.[40,41] Postoperative radiotherapy may cause fibrosis around the breast tissues, contributing to chronic pain; 4) Vascular Damage: Radiotherapy-induced vascular injury results in inadequate local blood supply, tissue hypoxia, and poor nutrient delivery.[41] This exacerbates tissue damage and inflammatory responses, potentially causing persistent pain; 5) Sensory Nerve Remodeling: Localized tissue damage and inflammatory responses from BRD and surgery can lead to sensory nerve remodeling.[42] This remodeling may result in sensory abnormalities, such as hyperalgesia (severe pain from mild stimuli) or allodynia (pain from non-painful stimuli); 6) Psychological Factors: Chronic pain is not solely a physiological issue but also a psychological one.[43,44] The discomfort and distress caused by BRD can increase patient stress and anxiety, which can intensify pain perception and contribute to the worsening of chronic pain.

Treatment of radiotherapy dermatitis and treatment of PMPS

In our survey, all patients undergoing radiotherapy received appropriate preventive measures for BRD. These measures included keeping the radiotherapy area dry and clean, regularly using non-irritating moisturizers to protect the skin barrier, and avoiding products containing alcohol or fragrances.[45,46] If patients developed BRD during radiotherapy, they were actively treated with topical corticosteroid creams and other antimicrobial dressings. However, no specific treatment protocol has been established for PMPS, and there has generally been a lack of patient education regarding pain prevention related to radiotherapy. For patients experiencing PMPS, acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs) are typically used to manage pain, but the administration of these analgesics is often irregular.[47]

The treatment strategies for BRD and PMPS in breast cancer patients share several commonalities and interrelated aspects. The primary goals of both treatment plans are to alleviate patient pain and improve quality of life. Both BRD and pmps involve inflammatory responses and the healing of skin and nerve damage, thus anti-inflammatory treatments and promoting recovery are key strategies for managing both conditions. Topical corticosteroids, such as hydrocortisone cream, are effective in reducing inflammation and itching associated with BRD and can also mitigate postoperative inflammatory responses. Topical application of lidocaine gel or patches can provide localized pain relief for both BRD and chronic postoperative pain. Systemically, nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen are commonly used to manage inflammation and pain caused by BRD, as well as PMPS. For moderate to severe pain, opioids such as morphine and oxycodone are employed. Although primarily used for PMPS, these opioids can also be utilized in cases of severe pain resulting from BRD. Moreover, cognitive-behavioral therapy (CBT) has been shown to be effective for all types of chronic pain, especially in patients experiencing anxiety and depression. By altering patients' perceptions and behaviors related to pain, CBT helps them better manage chronic pain and can also reduce the psychological stress and anxiety associated with BRD during radiotherapy.

In conclusion, the treatment of BRD and PMPS should involve a multidisciplinary team approach, encompassing specialties such as oncology, dermatology, pain management, and psychology. This collaborative effort can provide comprehensive care and support, thereby optimizing treatment outcomes and improving the quality of life for patients. By thoroughly considering each patient's specific circumstances, individualized treatment plans can be developed to concurrently manage BRD and PMPS. For instance, the severity of dermatitis and the characteristics of the pain should guide the selection of appropriate pharmacological and non-pharmacological treatments. This tailored approach ensures that both BRD and chronic pain are effectively addressed, enhancing overall patient care.

Limitations

Due to the retrospective nature of this study, there is a possibility of inaccuracies in details such as the timing of the occurrence of radiation dermatitis and the size of the affected areas due to recall bias from patients. Incomplete medical records for some patients resulted in unrecorded chronic toxicities such as fibrosis, lymphedema, and telangiectasia. These are the limitations of this study. It is hoped that in future research, observational study methods can be used to more comprehensively explore the relationship between BRD and PMPS.

Conclusions

This multicenter study primarily focused on investigating BRD and PMPS in breast cancer patients, encompassing a total of 784 participants. Through analysis of the clinical data of these patients, the study found that elderly and obese patients are more prone to developing BRD. Furthermore, there is a correlation between BRD and PMPS. The findings suggest that if dermatitis occurs during radiotherapy or if the affected area exceeds 5 cm^2, greater attention should be paid to the prevention and management of PMPS. The treatment strategies for BRD and PMPS share certain similarities and commonalities. A multidisciplinary team approach and personalized treatment plans can provide more comprehensive care and support, thereby optimizing treatment outcomes and improving the quality of life for patients.

CRediT authorship contribution statement

Yingpeng Ren: Conceptualization, Methodology, Data curation, Writing - Original draft preparation. **Shuguang Zhang:** Data curation, Writing - Original draft preparation. **Xiaoli Geng:** Visualization, Investigation. **Qingheng Yang:** Visualization, Investigation. **Liquan Ouyang:** Visualization, Investigation. **Ye Zhao:** Software, Validation. **Jing Zhao:** Software, Validation. **Hua Kang:** Writing - Reviewing and Editing. **Jing Wang:** Writing - Reviewing and Editing. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Ethics statement

This study was approved by the Ethics Committee of the Cancer Hospital of the Chinese Academy of Medical Sciences (IRB No. NCC2907). All participants provided written informed consent.

Funding

Declaration of competing interest

The authors declare no conflict of interest.

Data availability statement

Readers who require the data from this study can contact the authors or the corresponding author via email, and we will provide the relevant data.

Declaration of generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

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