Construction and validation analysis of a risk factor and risk prediction model for radiation dermatitis in patients undergoing postoperative radiotherapy for early stage breast cancer

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ABSTRACT

Background: Building a risk prediction model, validating it, and researching the risk variables for radiation dermatitis in patients receiving post-operative radiotherapy for early breast cancer. Materials and Methods: A total of 326 patients with early-stage breast cancer who underwent postoperative radiotherapy in hospital between August 2020 and August 2023 were selected and divided into 198 in the modeling group and 128 in the validation group; and the modeling group was divided into an occurrence group and a non-occurrence group according to whether they had radiation dermatitis. Logistic regression was used to investigate the risk factors for the development of dermatitis, and the predictive effect of the model was tested by the receiver operating characteristic curve (ROC). Results: Combined diabetes, conventional split radiotherapy, compensatory membrane application, and albumin <40g/L were independent risk factors for radiation dermatitis (P < 0.05); the area under the curve (AUC) was 0.821 and 0.908 in the modeling and validation groups, respectively, P < 0.001, with goodness-of-fit test (Hosmer-Leme-show, H-L) validity. Conclusion: Clinically, it is important to consider the risk factors of radiation dermatitis among patients who receive postoperative radiotherapy for early-stage breast cancer. Utilizing a risk prediction model, doctors can identify and evaluate patients' risk levels, aiding in the timely implementation of preventive measures.

INTRODUCTION

One of the most common malignancies in women is breast cancer (BC). Global data survey (1) shows that the incidence rate of BC can reach 11.7% in 2020, and it shows a trend of increasing year by year. Domestic data shows (2) that the incidence of cancer in female patients can reach 16%, threatening women's health and lives. Surgery with adjuvant radiotherapy and chemotherapy is currently an important means of treating BC. Cancer lesions are removed through surgery and the cancer cells are completely killed through the adjuvant means of radiotherapy and chemotherapy, thus enhancing the cancer recovery rate. While treatment maximizes control of the disease, radiotherapy treatment is administered to increase the incidence of adverse effects during treatment. Both conventional 2D fractionated and 3D Intensity modulated radiation therapy (IMRT) are commonly used in clinical radiotherapy treatment. Studies have shown (3) that both types of radiotherapy are equally effective in treating the disease, but IMRT radiotherapy treatment is associated with fewer adverse effects radiotherapy, including conventional significantly lower incidence of radiation dermatitis (RD). Based on an established Chinese database and

the requirements of the research, this study developed a dependable, impartial, accurate, and practical database intended to assist patients with RD following early surgical interventions in BC. The primary content of the database includes patient information. One of the more frequent adverse responses to radiation for BC is RD. In patients receiving radiation for BC, the incidence of RD can range from 37.5 to 95%, per a survey (4,5). Although most patients are only mild and timely symptomatic treatment can significantly improve skin damage without affecting the implementation of treatment, there are still some patients at high risk of RD, leading to interruption of treatment and recurrence of the disease. According to Gradishar et al. (6), oedema, pigmentation, and erythematous changes in the peri-mammary skin occur during the first two to three weeks of radiotherapy treatment for early breast cancer. These symptoms worsen over time as the radiation dose increases and may result in plasma exudate or crusting. Based on an established Chinese database and research requirements, this study devised a database with essential features of dependability, impartiality, accuracy, and practicality, aimed at supporting patients with RD after early BC surgical interventions. The primary database content comprises patient information. As demonstrated by

Li et al. (7), nutritional index scores were predictive of skin sensitivity following radiation therapy, and poor nutrition during patient treatment not only hampered healing but also increased the severity of acute radiation dermatitis. There are few prior radiation dermatitis studies on following radiotherapy for early breast cancer. With the goal of providing a reference value for disease assessment and reducing or preventing the occurrence of radiation dermatitis, the current study used multi-factor logistic regression and subject work curves to analyze independent risk factors for the development of radiation dermatitis developing a risk prediction model. In this study, risk factors for the development of RD were analyzed in 326 patients receiving postoperative irradiation for early-stage BC. A risk prediction model was created, and its predictive efficacy was assessed and verified.

MATERIALS AND METHODS

Study subjects

The clinical data of 326 patients with BC in early-stage who were diagnosed with surgery and postoperative radiotherapy at our hospital from August 2020 to August 2023 were selected for this study. The study was approved and agreed by the institutional ethics committee, ethics committee number (No. 2023MSXM103).

Inclusion and exclusion criteria

Inclusion criteria:(A) pathological tissue biopsy confirmed the diagnosis of BC in accordance with the 2019 Chinese Anti-Cancer Association Guidelines and Norms for the Diagnosis and Treatment of BC ⁽⁵⁾; (B) all were treated with radiotherapy after surgery performed at our hospital; (C) all had unilateral tumor onset; (D) clinical history was complete; (E) patients had normal reading, writing, cognitive and mental status.

Exclusion criteria:(A) dermatitis had already appeared in the affected limb before radiotherapy treatment; (B) history of previous trauma to the chest or upper limb or history of radiotherapy; (C) metastasis of axillary lymph nodes had already appeared in the tumor lesion; (D) adverse effects of radiotherapy were more severe and poorly tolerated; (E) combination of liver, kidney, and lung disease, as well as other malignant tumors such stomach, liver, and lung cancer. A literature search was used to identify predictors of RD after radiation for early BC, and expert judgment was integrated. 16 model variables were included in the pre-test, which was used to determine the prevalence of RD in a sample of patients with early BC who received post-operative radiation at a rate of 28.13 percent. Using the formula for the logistic sample calculation: sample size = number of influencing factors x (5 \sim 10) times, a total sample size of 80~160 was obtained.

Considering a 10% missed visit rate and expanding the study sample size according to the actual situation, a total of 326 sample cases were finally selected. The modeling grouping was carried out in a ratio of 6:4, with 198 cases being the modeling group and 128 cases being the validation group. The modeling group was divided into 58 cases (29.29%) in the occurrence group according to whether the patients had RD or not, with patients aged 36-55 years, mean age (46.85 ± 7.68); Body Mass Index (BMI): 13 cases <18.5kg/m2, 18 cases 18.5-23.9kg/ m2, 27 cases > 24kg/m2. There were 140 cases (70.71%) in the non-occurrence group, with patients aged 34-53 years, mean age (46.54 ± 6.37) years; BMI: 58 cases < 18.5kg/m2, 44 cases 18.5-23.9kg/ m2, 38 cases > 24 kg/m2.

Diagnostic assessment methods for each indicator

The diagnosis and assessment of radiation dermatitis necessitates a thorough evaluation of various indicators to determine its severity and treatment options. The study employed the skin reaction grading system developed by the Radiation Therapy Oncology Group (RTOG) and laboratory examinations as diagnostic evaluation methods. The RTOG system classified radiation dermatitis into grades ranging from 0 to 4. These grades were assessed based on the degree of erythema, edema, erosion, and other symptoms by two radiotherapy practitioners. Grade 0 suggests no symptoms, while grade 1 indicates mild symptoms, such as dry peeling with local dark red skin. Moderate symptoms, involving edema, congestion or erosion, are attributed to grade 2, while severe symptoms like skin infection and ulceration are associated with

Laboratory tests can aid in the diagnosis and assessment of radiation dermatitis, alongside clinical observations. One significant marker to evaluate the severity of the condition is the white blood cell count (WBC). WBC levels can be elevated in patients with radiation dermatitis due to skin inflammation. Venous blood was obtained from patients and analyzed using a tube method to determine WBC count. By monitoring changes in the WBC count, the severity of radiation dermatitis and associated condition changes were assessed. The normal range for WBC is (4.0~10.0) 109 L. Additionally, albumin (Alb) and hemoglobin (HGB) were examined as crucial indicators for assessing the severity of radiation dermatitis. The albumin level can be determined through venous blood collection after fasting using an automatic biochemical instrument. Its reference range is 40-55 g/L. Conversely, hemoglobin (HGB) levels were measured by a fully automated blood cell analyzer and assessed through colorimetric methodology. The reference range for HGB is 120-160 g/L for men and 110-150 g/L for women.

Research instruments

General information questionnaire: based on a self -made questionnaire on RD in patients with early who received postoperative radiotherapy, expert assessment, and consultation, including patient's age, body mass index, pathological type, combined diabetes, cancer stage, radiotherapy total radiotherapy dose, modality, combined chemotherapy, presence of postoperative complications, surgical treatment modality, axillary lymph node metastasis, Equivalent compensation (Manufacturer: body membrane Shenzhen Medical Tongchuang Technology Ltd.) Co., application, Alb, HGB, WBC count, etc.

Model construction

A risk prediction model was established with the weights of independent risk factors. Drawing on a mature database in China as a reference, and considering research needs, this study established a database with key features of reliability, objectivity, truthfulness, and operational adaptability for patients with RD following early BC surgery. Patient information formed the core data content of the database.

Data collection methods

The investigators were cooperated and assessed before the implementation of the survey. The assessment included collecting data, filling in the data and entering the data, and each participating medical staff was required to pass the assessment criteria. To learn more about the patients, the hospital's information system was inspected. After the data collection was completed, two people checked the data, and then the attending radiologist verified the data to assess whether the patients had RD to ensure the accuracy and authenticity of the data collection. The medical records of 382 patients with early BC treated with post-operative radiotherapy were finally collected.

Statistical data analysis

Statistical analysis was performed on the data using SPSS25.0. The count data were described using [number of cases (%)] and the $\chi 2$ test was performed between groups; Using [mean standard deviation (x s)], the measurement data was found to follow a normal distribution. A multi-factor logistic regression model was used to screen the independent factor risk indicators, and a risk assessment model was created with a *P value* of 0.05. The *t-test* for independent samples was run between groups. The ROC curve, as well as the Hosmer-Lemeshow test and area under the ROC curve, were used to determine the predictive scoring model's accuracy; the correlation between the occurrence of RD in the modeling and validation groups was tested by Pearson.

RESULTS

Single factor analysis of RD in patients undergoing postoperative radiotherapy

In accordance with table 1. By monitoring changes in the WBC count, the severity of radiation dermatitis and associated condition changes were assessed. The normal range for WBC is (4.0~10.0) 109 L. Additionally, albumin (Alb) and hemoglobin (HGB) were examined as crucial indicators for assessing the severity of radiation dermatitis. The albumin level can be determined through venous blood collection after fasting using an automatic biochemical instrument. Its reference range is 40-55 g/L. Conversely, hemoglobin (HGB) levels were measured by a fully automated blood cell analyzer and assessed through colorimetric methodology. The reference range for HGB is 120-160 g/L for men and 110-150 g/L for women.

Logistic multiple factor regression analysis of RD in patients undergoing postoperative radiotherapy

Variables with statistical significance (P < 0.05) in table 1 were used as independent variables and assigned using the numbers 0 and 1. The 0 in the assignment indicates that this factor is no occurrence factor, and 1 means that this factor is no occurrence factor. The assignments are detailed in table 2.

Radiation dermatitis incidence served as the dependent variable in the univariate analysis. The results of the logistic regression analysis revealed that combined diabetes had an odds ratio (OR) of 2.13, while conventional radiotherapy had an OR of 2.385. Alb (< 40g/L) had an OR of 2.002 and P-value of less than 0.05. In logistic regression, an OR of 1 indicates no effect of the factor on the occurrence of the disease, while an OR greater than 1 implies that the factor represents a risk factor. The odds ratios for diabetes mellitus, conventional segmented radiotherapy, equivalent compensation application, and Alb (< 40g/L) all exceeded 1, indicating that these four factors acted as independent risk factors radiation dermatitis in postoperative radiotherapy for early breast cancer. Table 3 shows these four factors in detail.

Predictive Scoring System for the Risk of RD in Patients Undergoing Postoperative Radiotherapy

The minimum for combined diabetes was 0.757, and the model was built using multifactor analysis of risk factor index weights to predict the occurrence of RD in individuals receiving radiation following early BC surgery. The β value of each risk factor in this model was divided by 0.757, and the results were obtained by rounding to obtain the risk weight assignments. The total score is 0-10. Using the combined radiotherapy modality (conventional radiotherapy) base score of 1, grade score of 2, and

total score of 2; the equivalent compensation body film application base score of 2, grade score of 2, and total score of 4; the Alb (g/L) base score of 2, grade score of 1, and total score of 2; and the combined diabetes base score of 1, grade score of 2, and total score of 2. For information, as shown in table 4.

Table 1. Univariate analysis of the occurrence of RD in patients undergoing radiotherapy after early BC('x ± s).

Project indicators Occurrence group(n=58) Non-occurrence group(n=140) χ²/t Age (years) 46.85±7.68 46.54±6.37 0.293 Body Mass Index (BMI)(kg/m²) <18.5 13 58 8.843 18.5~23.99 18 44 >24 27 38 8 Pathological type: invasive ductal carcinoma 18 52 0.670 Invasive lobular carcinoma 19 42 46 Combined diabetes: ves 34 43 13.43 Combined diabetes: No 24 97 4.951 Cancer stage (stage): I*II 21 75 4.951 III*IV 37 65 65 Radiotherapy modality: conventional segmentation 41 55 16.19 IMRT 17 85 5.188 Total radiotherapy dose (Gy): ≥40 36 62 62 Combination chemotherapy: No 21 76 5.364 Combined chemotherapy: No 21 76 76 Surgical treatment: Breast conservation </th <th></th> <th></th>		
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110~150 or 120~160 26 90		
WBC Count(×10⁹·L) 9.94±2.26 9.26±1.06 2.883	<10⁹·L) 9.94±2.26 9.26±1.06	0.00

Note: BMI: body mass index; Alb: albumin; HGB: haemoglobin; WBC: white blood cell count.

Table 2. Assignment of Patient's.

Projects	Assignment			
Body Mass Index (BMI)(kg/m²)	Raw data			
Combined diabetes	No=0;Yes=1			
Cancer stage (stage)	~ =0; ~ V=1			
Radiotherapy	IMRT=0;Traditional			
modalities	division=1			
Total radiotherapy measurement (Gy	<40=0;>40=1			
Combined chemotherapy	No=0;Yes=1			
Any post-operative complications	No=0;Yes=1			
Lymph node metastasis in the axilla	No=0;Yes=1			
equivalent compensation body membrane applications	No=0;Yes=1			
Alb(g/L)	40~55=0;<40=1			
	110~150 or			
HGB(g/L)	165~195=0;>150 or >195=1;<110 or <165=2			
EBV DNA values	<400=0;>400=1			
WBC Count(×109·L)	Raw data			

Note: Alb: albumin; HGB: haemoglobin; WBC: white blood cell count.

Table 3. Logistic Multiple Factor Regression Analysis of RD in Patients Undergoing Postoperative Radiotherapy for Early Stage BC

			Waldχ ² ν	OR	95%CI		P
Projects	β	SE		values	Lower limit	Upper limit	values
Constant term	-3.101	0.448	47.998	0.045	-	-	0.000
Combined diabetes	0.757	0.370	4.186	2.131	1.032	4.400	0.041
Radiotherapy modality (conventional segmentation)	0.869	0.373	5.425	2.385	1.148	4.956	0.020
equivalent compensation body membrane applications	1.159	0.380	9.279	3.186	1.512	6.715	0.002
Alb(<40g/L)	1.234	0.401	9.478	2.002	3.436	1.566	7.538

Note: Alb: albumin.

Table 4. Predictive scoring model for the risk of developing RD in patients undergoing radiotherapy after early BC surgery.

Factor indicators	Basic score	Grading	Total points
Combined diabetes: yes	1	2	2
Radiotherapy modality: conventional segmentation	1	2	2
equivalent compensation body membrane applications: yes	2	2	4
Alb(g/L)<40	2	1	2

Note: Alb: Albumin; Total score = Base score x Grade score.

Analysis of the effectiveness of a predictive risk model for the development of radiodermatitis

To test the practicality of the radiation dermatitis prediction risk model in postoperative radiotherapy for early breast cancer, it was tested in a clinical setting alongside the actual situation. The results of the ROC curve analysis showed that the AUC for the actual situation diagnosis was 0.907, with a sensitivity of 86.20% and specificity of 83.60%, P < 0.001, while the AUC for the model diagnosis was 0.821, with a sensitivity of 74.14% and specificity of 92.86%, P < 0.001. The value of the goodness of fit test for both diagnoses Hosmer-Leme-show was (χ2 = 4.562, P = 5.192), as detailed in figures 1 and 2. The specificity of the diagnostic prediction model surpassed that of the actual model by 9.26%, and yet the sensitivity was deficient by 8.06%, with an AUC 0.086 lower than the actual model. It indicates that the prediction model of radiation dermatitis is proficient in excluding non-radiation dermatitis patients but lacks the ability to accurately identify patients with radiation dermatitis. Furthermore, the AUC index is lower than that of the actual model, which suggests that the overall performance of the prediction model is slightly poorer. While the model has the capability to diagnose and predict the likelihood of radiation dermatitis to some extent, there remains scope for enhancement in its diagnosis of the condition.

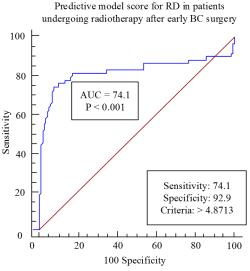


Figure 1. Model group ROC curve analysis.

Data from patients with RD from early BC radiotherapy were brought into a risk prediction scoring model to assess whether patients with different scores actually developed RD during treatment. The findings revealed that the incidence of RD ranged from 0% for 0 to 1, to 5.05% for 2, 7.68% for 3, 12.28% for 4, to 30.57% for 5, 41.27% for 6, to 54.18% for 7, to 74.38% for 9, and 100% for 10. The severity of RD was graded according to the findings, with a low risk score of 0 to 4 points, medium risk 5 to 7 points; high risk 8 to 10 points. The incidence of

RD was 6.06%, 21.72% and 57.58% in the low, intermediate and high risk modeling groups and 4.69%, 27.34% and 61.72% in the validation group respectively, which were analyzed by Pearson's test showing good correlation between the two groups (r = 0.548, 0.486, both P < 0.05), as detailed in figure 3. The incidence of radiation dermatitis was 1.37% higher in the low-risk modeling group than in the validation group and 6.38% higher than that of the validation group. Additionally, the incidence of high-risk modeling was 4.14% higher than that of the validation group. Based on these findings, it is evident that the model's predictions align with the actual occurrence of radiation dermatitis. The above suggests that the model can evaluate the patient's radiation dermatitis risk more precisely and anticipate the probable occurrence in the patient, consequently offering appropriate recommendations to the physician.

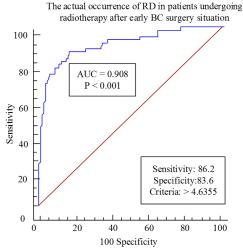


Figure 2. Validation group model ROC curve analysis.

Note: Vertical column is ROC curve sensitivity, horizontal column is ROC curve specificity; AUC indicates area under the curve, P indicates the presence of predictive value of the diagnosis; the trend of high and low curves reflects the diagnostic value of the curve; BC represents breast cancer; RD indicates radiation dermatitis.

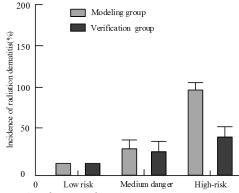


Figure 3. Classification of predictive scoring model levels and incidence of RD in the two groups.

Note: The incidence of radiation dermatitis is listed vertically in the modeling and validation groups.

DISCUSSION

In this study, the survey showed that in 198 patients with early breast cancer treated with postoperative radiotherapy, 50 (25.25) % had radiation dermatitis, the incidence was at a low to medium level. The cross-sectional study conducted by Leache et al. (7) revealed that the occurrence of reflex dermatitis in early-stage breast cancer patients was 31.2%, and that the dermatitis manifested in varying degrees of severity. The incidence of postoperative reflex dermatitis in early breast cancer is lower in this study compared to the study conducted by Leache et al. (7). This could be due to the younger age of the subjects in this study who had better body tissue and skin condition, along with the implementation of radiotherapy and effective preventive measures. Consequently, the incidence of radiation dermatitis was lower. The study results correlate with those suggested by Pagare et al. (8). Paja et al.'s (9) study demonstrated that patients with neck tumors could experience radiation-induced dermatitis with an incidence rate of up to 18.4%. However, the incidence of reflex dermatitis in cervical tumours is lower than in this study. This observation could be attributed to the fact that radiotherapy for breast cancer involves larger areas, whereas radiotherapy for cervical tumors typically affects only localized areas. The extent of breast cancer radiotherapy coverage is greater, leading to heightened exposure of the skin to increased doses over an extended period of time, thereby increasing the potential for skin damage. Further, the skin located in the breast vicinity is comparatively delicate and hence more vulnerable to the impact of radiation therapy. This causal analysis concurs with the findings of Pasalar and colleagues' study (10), which demonstrated the presence of small lesions in cases of early breast cancer, as well as relatively brief duration of radiation therapy and lower incidence of radiation dermatitis.

Contrary to the study's findings (95% CI: 1.032-4.400; p = 0.041), coupled diabetes was an independent risk factor for the development of radiodermatitis following radiation for early BC. Ben-David and colleagues (11) found that the incidence of radiation dermatitis was significantly higher in patients with early breast cancer and diabetes (28.16%) compared to those without diabetes (14.06%). The study provided evidence that radiation therapy causes vascular damage and inflammatory reactions in the skin, while diabetes may also cause vascular damage and microcirculation disorders that affect blood supply to the skin. Furthermore, impaired immune function also affects regulation and repair processes. In addition, chronic inflammatory reactions frequently accompany patients with diabetes. Radiation therapy induces an inflammatory response in the skin, which may become even more acute in the presence of diabetes. This interaction potentially contributes to the occurrence and heightened severity of radiodermatitis. The analysis of the causes is in line with Wang *et al.* ⁽¹²⁾ conclusion, which demonstrates that diabetes can lead to a metabolic disorder in the endocrine system. As a result, there is a reduction in the metabolic capacity of tissue cells, the immune function is adversely affected, and there is an increase in the occurrence of radiation dermatitis.

The findings of this study indicated that conventional fractionated radiotherapy (95% CI: 1.148-4.956; P = 0.020) was an independent risk factor for the development of RD following radiotherapy for early stage BC. The most often utilised radiotherapy for early stage breast cancer is traditional fractionated radiotherapy. IMRT radiation is gradually being employed in clinical practise due to advancements in medicine. The therapeutic efficacy of IMRT radiotherapy is comparable to that of conventional segmented treatment for early-stage breast cancer, as ascertained by a previous study (13). No substantial difference in therapeutic performance or disease recurrence was observed between the two approaches. However, IMRT offers increased precision in radiation dose delivery and superior control over dose distribution, thereby minimizing radiation exposure to surrounding healthy tissues and reducing the incidence of radiation-induced dermatitis. This cause analysis is also supported by the results of Boustani et al. (14) study, which showed that the increase in the radiotherapy dose, the size of the radiotherapy skin, and the length of the radiotherapy can all worsen the side effects on the skin around the radiotherapy site and increase the risk of developing radiation dermatitis.

The use of equivalent compensation body membranes was one of the independent risk factors for the development of RD following radiation for early BC, according to the study's findings (95% CI: 1.512 to 6.715; P = 0.002). Equivalent compensation of body membrane should be a protective way to reduce the risk of radiation dermatitis. Moore and colleagues (2015) found that compensating for the body's membrane can improve skin state affected by low doses of radiation resulting from building effects, and effectively manage micrometastatic lesions. However, inadequate individualization and incorrect use of the equivalent compensation body membrane, such as excessive application, can exacerbate local damage by thickening the equivalent compensation body membrane. Consequently, the adoption of radiotherapy treatment raises the occurrence of radiation dermatitis. This cause analysis is consistent with the findings of the (16) study by Liu X et al. Liu X et al. (16) demonstrated that although the compensating film can aid in better positioning the treatment in radiotherapy, the precise location of the position cannot be clarified in

multiple treatments, requiring multiple applications of the compensating film, which worsens the degree of local skin damage.

As a result of radiation for early BC, the study's findings indicated that Alb 40g/L was one of the independent risk factors for the development of RD (95% CI: 1.512-6.715; P = 0.002). After analysis,albumin is a crucial indicator of a patient's nutritional status and can provide insight into both their nutritional status and liver function. A low albumin level could indicate poor nutrition or abnormal liver function, often coinciding with a decreased immune function. This negative impact affects the metabolic state of skin tissue, thereby increasing skin sensitivity to radiation, which ultimately leads to radiation dermatitis. This cause analysis was also supported by the study of Hummell et al. (17). According to research by Hummell et al. (17), people who are malnourished are more likely to have dermatitis, allergies, rashes, and acne on their skin.

Data presented as tables 3 and 4 and figures 1 and 2, indicate that the risk prediction model is highly practical and has a strong discriminatory ability to assess the risk of RD in patients with early-stage postoperative radiotherapy for BC, and is suitable for screening for high-risk RD. The risk assessment model is capable of gathering substantial clinical data and relevant factors to holistically appraise the individual traits and health status of patients, ultimately resulting in the allocation of a corresponding risk score. This serves to facilitate a more comprehensive understanding of radiation levels dermatitis risk for both healthcare practitioners and patients, aiding implementation of appropriate preventive measures. Simultaneously, the risk prediction model has a potent identification capability. It can detect patients with a high risk of radiation dermatitis, effectively prevent and control the condition, offer bespoke treatment recommendations, and enhance patient recovery outcomes. At present, the risk prediction models have been well used in the clinical field. It was demonstrated by Ren et al. (18) that the risk model of pathogenic bacteria of pulmonary infection in late preterm infants has a high diagnostic value and can effectively explain the occurrence of pulmonary infection in order to guide clinical treatment, prevention, and control of disease. The clinical staff can use this scoring system to dynamically assess the risk of RD in early-stage postoperative radiotherapy for BC and take appropriate treatment and care measures based on the assessment results, potentially reducing the incidence of RD. This is because the predictive scoring system has a high discriminatory ability in assessing and differentiating patients' risk of developing RD.

CONCLUSION

Combined diabetes, conventional fractionated radiotherapy, application of compensation membrane, and albumin levels below 40g/L independently increase the risk of radiation dermatitis following early breast cancer surgery. The study additionally formulates a radiation dermatitis risk prediction model. This model evaluates and distinguishes risk levels according to patients' characteristics and related factors. In turn, doctors can receive appropriate treatment recommendations based on the model's findings.

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REFERENCES

- Herzog SK and Fuqua SAW (2022) ESR1 mutations and therapeutic resistance in metastatic breast cancer: progress and remaining challenges. Br J Cancer, 126(2):174-186.
- Irfandi R, Santi S, Raya I, et al. (2022) Study of new Zn(II)
 Prolinedithiocarbamate as a potential agent for breast cancer:
 Characterization and molecular docking. Journal of Molecular
 Structure, 1252:1-18.
- Pointreau Y, Moreau J, Vendrely V, et al. (2022) Quelapport de la modulation d'intensité pour la radiothérapie des cancers du rectum? Impact of IMRT for neoadjuvant rectal cancer? Cancer Radiother, 26(6-7):865-870.
- Bernhardt T, Kriesen S, Manda K, et al. (2022) Induction of Radiodermatitis in Nude Mouse Model Using Gamma Irradiator IBL 637. Skin Pharmacol Physiol, 35(4):224-234.
- Mirghani HO, Albalawi AF, Alanazi NM, et al. (2022) A systematic review on the role of topical corticosteroids for the management of radiation dermatitis. *Journal of Pharmaceutical Research Inter*national, Volume and page number???
- Gradishar WJ, Moran MS, Abraham J, et al. (2022) Breast Cancer, Version 3.2022, NCCN Clinical Practice Guidelines in Oncology. J Natl ComprCanc Netw, 20(6): 691-722.
- Li Y, Liu C, Luo X, et al. (2022) Controlling nutritional status score and prognostic nutrition index predict the outcome after severe traumatic brain injury. NutrNeurosci, 25(4): 690-697.
- Pagare PP, Rastegar A, AbdulmalikO, et al. (2022) Modulating hemoglobin allostery for treatment of sickle cell disease: current progress and intellectual property. Expert OpinTher Pat, 32(2): 115 -130.
- Paja M, Merlo I, Rodríguez-Soto J, et al. (2023) White blood cell count: a valuable tool for suspecting Cushing's syndrome. J Endocrinol Invest, 46(1): 141-149.
- 10. Pasalar M, Ahadi B, Mirzaei HR, et al. (2022) Comparing Dermolina -Henna cream with Mometasone cream in improving radiodermatitis among patients with breast cancer: A randomized active-

- control double-blind clinical trial. J Integr Complement Med, 28 (11): 895-903.
- Ben-David MA, Hoffer O, Kirshenabum D, et al. (2022) Thermal monitoring of tumor and tissue state during radiation therapy - A complex case of radiation recall. Crit Rev Biomed Eng, 48(2):125-131.
- 12. Wang F, Mao Y, Wang H, et al. (2022) Semaglutide and diabetic retinopathy risk in patients with type 2 diabetes mellitus: A meta-analysis of randomized controlled trials. Clin Drug Investig, 42(1):17
- Sehar U and Naseem ML (2022) How deep learning is empowering semantic segmentation: Traditional and deep learning techniques for semantic segmentation: A comparison. Multimed Tools Appl, 81(21):30519-30544.
- 14. Boustani J and Créhange G (2022) Escalade de dose dans les cancers de l'œsophage: revue de la littérature [Dose-escalated radio-

- therapy in esophageal cancer: A review of the literature]. *Cancer Radiother*, **26(6-7)**:884-889.
- Moore TD, Martin-Creuzburg D, Yampolsky LY (2023) Diet effects on longevity, heat tolerance, lipid peroxidation and mitochondrial membrane potential in Daphnia. *Oecologia*, 202(1): 151-163.
- 16. Liu X, Van Slyke AL, Pearson E,et al. (2022) Improving the efficiency of small animal 3D-printed compensator IMRT with beamlet intensity total variation regularization. Med Phys, 49(8): 5400-5408.
- Hummell AC and Cummings M (2022) Role of the nutrition-focused physical examination in identifying malnutrition and its effectiveness. Nutr Clin Pract, 37(1):41-49.
- 18. Ren W, Jiang J, Wang Y, et al. (2022) Analysis of pathogenic distribution and drug resistance of catheter-related blood stream infection in hemodialysis patients with vein tunneled cuffed catheter. European Journal of Inflammation, 19: 1-7.