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Review

Effectiveness of topical corticosteroids on the prevention of acute radiation dermatitis in patients with breast cancer: An updated systematic review and meta-analysis

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ABSTRACT

Objectives: To evaluate the effect of topical corticosteroids (TCS) in preventing acute radiation dermatitis in patients with breast cancer.
Methods: An updated systematic review and meta-analysis were conducted following the preferred reporting items for systematic reviews and meta-analyses. Randomized controlled trials (RCTs) in six English databases (PubMed, Web of Science, Scopus, CINAHL, Cochrane Library, Embase), three Chinese databases (Sinomed, China National Knowledge Infrastructure, Cqvip), and two clinical trial registration platforms (CHICTR, Clinicaltrials.gov) were systematically searched from inception to 1 February 2024.
Results: Thirteen RCTs were included, with 1172 patients in this updated review. Meta-analysis showed that TCS reduced the rate of moist desquamation (OR = 0.31; 95% CI = [0.22, 0.44]; $P < 0.01$), the incidence of Radiation Therapy Oncology Group ratings of grade 2 or higher (OR = 0.22; 95% CI = [0.14, 0.32]; $P < 0.01$), the incidence of Common Terminology Criteria for Adverse Events ratings of grade 2 or higher (OR = 0.56; 95% CI = [0.37, 0.84]; $P < 0.01$), the mean score of radiation dermatitis (SMD = −0.46; 95% CI = [−0.59, −0.34]; $P < 0.01$), skin erythema and hyperpigmentation readings, and improved subjective symptoms.
Conclusions: TCS can effectively prevent acute radiation dermatitis in patients with breast cancer.
Systematic review registration: Prospero (CRD42024507890).

Introduction

According to the American Cancer Society's 2022 statistics, breast cancer is the most common cancer in women, with 2.3 million new cases of breast cancer in 2022, accounting for 11.6% of the number of new cancer cases in 2022.[1] While radiotherapy plays an essential role in the comprehensive treatment of patients with breast cancer, Radiation dermatitis occurs in approximately 95% of radiotherapy patients, and acute radiation dermatitis is the most prevalent type of radiation dermatitis.[2,3] Topical corticosteroids are one of the recommended medications for preventing and treating radiation dermatitis in current clinical practice guidelines. Its anti-inflammatory effect is achieved by vasoconstriction, reduction of capillary permeability, and inhibition of leukocyte proliferation and migration.[4,5]

A systematic review summarizing the evidence for topical corticosteroids in combating acute radiation dermatitis in patients with breast cancer was published in 2017.[6] The systematic review showed that the use of topical corticosteroids reduced the incidence of moist desquamation (OR = 0.29; 95% CI = [0.19, 0.45]; $P < 0.01$) and the mean score of radiation dermatitis (SMD: −0.47, 95% CI: [−0.61, −0.33]; $P < 0.01$), and improved the quality of life in patients with breast cancer. However, it did not evaluate other relevant indicators, such as the incidence of Common Terminology Criteria for Adverse Events and Radiation Therapy Oncology Group ratings of grade 2 or higher. In addition, this systematic review included the use of topical corticosteroids with other medications. It failed to evaluate the effectiveness of topical corticosteroids separately in preventing acute radiation dermatitis, which somewhat biases the findings of this systematic review.

In recent years, a growing number of studies have further investigated the effectiveness of corticosteroids in preventing acute radiation dermatitis in patients with breast cancer. We needed to update the existing systematic review and meta-analysis to include previous and

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existing evidence on the effectiveness of corticosteroids in preventing acute radiation dermatitis in patients with breast cancer. Therefore, we conducted a new systematic review and meta-analysis that increased the number of included studies and added new outcome indicators to more comprehensively estimate the effectiveness of topical corticosteroids in preventing acute radiation dermatitis in patients with breast cancer.

Methods

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[7] and registered on Prospero (CRD42024507890).

Inclusion and exclusion criteria

Inclusion criteria

Studies that met the following criteria were included: (1) Population: Patients newly diagnosed with breast cancer and treated with radiotherapy to the chest wall, breast, and localized lymph node regions. (2) Intervention: Topical corticosteroids were administered to prevent acute radiodermatitis in patients with breast cancer. (3) Control groups that received the blank control, placebo, and other medications. (4) Outcomes: Primary outcomes: incidence of moist desquamation, the incidence of Radiation Therapy Oncology Group (RTOG) ratings of grade 2 or higher, the incidence of Common Terminology Criteria for Adverse Events (CTCAE) ratings of grade 2 or higher, the mean score of radiation dermatitis; Secondary outcomes: quality of life, skin erythema and hyperpigmentation readings, subjective symptoms. (5) Study: The research design was a randomized controlled trial (RCT).

Exclusion criteria

We excluded studies that (1) Published in languages other than English or Chinese. (2) No access to full text. (3) With a JADAD score below 3. (4) No data reported on any of the following four primary outcomes: the incidence of moist desquamation, the incidence of RTOG ratings of grade 2 or higher, the incidence of CTCAE ratings of grade 2 or higher, or the mean score of radiation dermatitis.

Search strategy

RCTs in six English databases (PubMed, Web of Science, Scopus, CINAHL, Cochrane Library, Embase), three Chinese databases (Sinomed, China National Knowledge Infrastructure, Cqvip), and two clinical trial registration platforms (CHICTR, Clinicaltrials.gov) were systematically searched from inception to 1 February 2024. The search strategies involved a combination of Medical Subject Headings (MeSH) terms and free text terms. Medical Subject Headings (MeSH) terms and free text terms used include: “Breast Neoplasms,” “Breast neoplasm*”, “Breast tumor*”, “Breast cancer*”, “Mammary cancer*”, “Malignan*”, “Radiodermatitis”, “Radiodermatitides”, “Radiation-Induced Dermatitis”, “Radiation Recall Dermatitis”, “Radiation Recall Dermatitides”, “Radiation Recall Reaction*”, “Steroids”, “Steroid*”, “Catatoxic steroid*”, “Corticosteroid*”. The detailed search strategy or search history is shown in Supplementary material 1.

Data extraction and screening

Importing searched studies into Endnote 20.6 software, two researchers (Zhang and Yang) were invited to cross-view the titles and abstracts of studies for initial screening, and two researchers (Zhang and Yang) then read the remaining studies according to the inclusion criteria.

When two researchers disagreed about the studies, the third researcher (Liu) was invited to participate in the discussion, and the third researcher decided to include the study if necessary.

For included studies, the Microsoft Excel software was used to extract data including the following: (1) General information (e.g., First author's name, Nationality, Publication year); (2) Characteristics of the population with breast cancer (e.g., Demographic characteristics, Sample size, Radiotherapy region); (3) Characteristics of intervention (e.g., Medication type, Length and Frequency of intervention); (4) Main Outcomes and Assessment Tools.

Risk of bias and evidence level assessment

Two reviewers (Zhang and Yang) judged the risk of bias with the Cochrane Collaboration's tool for risk of bias assessment.[8] The Joanna Briggs Institute (JBI) Levels of Evidence and Grades of Recommendation tool was employed to assess the quality of evidence. In the JBI evidence grading system, the evidence level is divided into five levels from high to low: level 1 to level 5.[9] Any discrepancy was resolved through discussion with a third researcher (Liu).

Methodological quality assessment

The modified JADAD scale was used to evaluate the quality of the included literature.[10] The total score was seven points, 1–3 points for low-quality literature, and 4–7 points for high-quality literature. Low-quality literature was excluded.

Data analysis

Relevant statistical analysis was conducted with Revman Manager 5.4 software and Stata 17.0 software. The pooled effect size was generated by calculating the SMD of the continuous variable and OR of the dichotomous variable. 95% CI expressed the pooled effect size.[11] The Higgins I^2 statistic and Q test were adopted to assess the heterogeneity. Sensitivity analysis was applied to explore the potential sources of heterogeneity and verify the stability of the statistical results when heterogeneity between studies was significant. Potential publication bias ($P < 0.05$ statistically significant) was assessed through the funnel plots and Egger's test.[12] Furthermore, Individual study results that could not be pooled in the meta-analysis were summarized qualitatively.

Publication bias

The funnel plot and Egger's test were applied to measure publication bias in the presence of a sufficient number of included studies ($n > 10$).[13] Publication bias was considered to exist if the funnel plot showed asymmetry and Egger's test showed a P-value of less than 0.05. Trim-and-fill analysis was implemented to assess further the potential impact of publication bias on the pooled effect size.

Results

Through computerized searches, 522 studies were retrieved. After the exclusion of duplicates, 386 studies remained. Following the inclusion and exclusion criteria, a preliminary screening of reading titles and abstracts was conducted, and 16 studies were retained. After further screening the full-text literature, 13 studies were finally included (Fig. 1).

Characteristics of the included studies and levels of evidence

The 13 studies included in this review were all in English, and the studies were from eight countries, including the United Kingdom, the United States, Iran, the Philippines, Austria, Sweden, Turkey, and India. A total of 1172 patients with breast cancer receiving radiotherapy were included in this review, with sample size ranging from 21 to 202 per study.

Topical corticosteroids used in the experimental group included Mometasone, Methylprednisolone, Betamethasone, Beclomethasone, and Hydrocortisone. The duration of the interventions lasted from 5 to 11 weeks. The characteristics of the included studies are shown in Table 1.

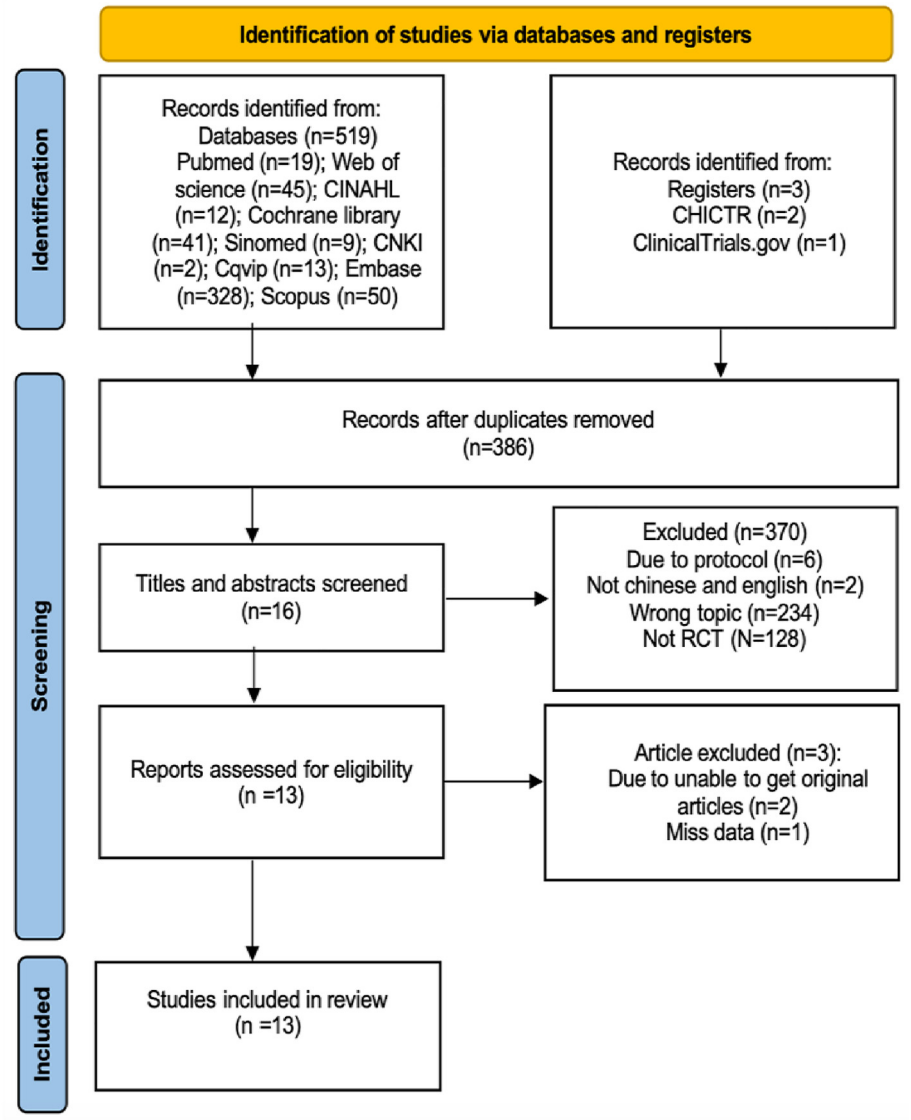

Fig. 1. PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

The JBI evidence grading system was applied to assess the level of evidence.[9] Overall, the level of evidence among the studies was relatively high (Level of Evidence Grade is Level 1). Table 2 details the level of evidence for the included studies.

Risk of bias

The assessment of risk of bias showed that all studies were at low to moderate risk of bias. The sources of risk of bias were mainly related to other bias, reporting bias, and measurement bias. Fig. 2 shows the results of the risk of bias assessment of the included studies.

Methodological quality assessment

The JADAD scores of all included studies were greater than 3, suggesting that the included studies were of high quality. Table 3 shows the results of the methodological quality assessment of the included studies.

Effects of topical corticosteroids on the incidence of moist desquamation

Eleven studies[14–24] assessed the effects of topical corticosteroids on the incidence of moist desquamation in patients with breast cancer who received radiotherapy, and there was no heterogeneity between these studies ($P = 0.93$, $I^2 = 0\%$). Therefore, the fixed-effects model was used to calculate the pooled effect size. The results showed that topical corticosteroids as the protective factor significantly reduced the incidence of moist desquamation compared to the control group ($n = 1074$; OR = 0.31; 95% CI = [0.22, 0.44]; $P < 0.01$) (Fig. 3A). In addition, more than 10 studies were included in the meta-analysis of the incidence of moist desquamation, so the funnel plot test and Egger's test were used to discriminate the presence of publication bias. The funnel plot and Egger's test found no publication bias in terms of the effects of topical corticosteroids on the incidence of moist desquamation ($P = 0.254 > 0.05$) (Fig. 3B).

Effects of topical corticosteroids on the mean score of radiation dermatitis

Twelve studies[14–18,20–26] assessed the effects of topical corticosteroids on the mean score of radiation dermatitis in patients with breast cancer treated with radiotherapy. The fixed-effects model was applied to calculate the pooled effect size since the heterogeneity among these studies was low ($P = 0.08$, $I^2 = 39\%$). The results showed that topical corticosteroids reduced the mean score of radiation dermatitis in patients with breast cancer compared with controls ($n = 1085$; SMD = −0.46;

Table 1
Characteristics of included studies.

Author (Year)	Nation	Simple *(n)*	Age (mean/range)	Radiotherapy region	Experimental arm	Control arm	Frequency of intervention	Period of intervention	Main outcomes	Assessment methods
BostroÈm et al. (2001)	Sweden	49	47–76	Breast	Mometasone	Emollient	Before 24 Gy, twice a week. After that, once daily.	9 weeks	MMF in combination with emollient cream treatment significantly decreased acute radiation dermatitis ($P = 0.003$) compared with emollient cream [alone.]	Spectrophotometer; Seven-point scale; VAS
Schmuth et al. (2002)	Austria	21	29–75	Breast and chest wall	Methylprednisolone	Dexpanthenol	Twice a day	8 weeks	MMF in combination with emollient cream treatment significantly decreased acute radiation dermatitis ($P = 0.003$) compared with emollient cream alone.	Clinical score; Evaporimeter; Skindex-16; SF-36
Farhan et al. (2003)	Iran	72	27–70	Breast and chest wall	Betamethasone	Placebo	Twice a day	6–7 weeks	Maximum severity of complaints stated by patients in terms of burning and pruritus had been lesser in betamethasone group ($P < 0.001$). No significant differences were observed between two groups in terms of pain intensity.	RTOG
Shukla et al. (2006)	India	60	28–60	Chest wall, Breast, Localized lymph node	Beclomethasone	No treatment	Twice a day	5 weeks	The difference in moist desquamation of the axillary skin in the two groups was statistically significant ($P = 0.0369$).	–
Omidvari et al. (2007)	Iran	51	34–66	Chest wall, Localized lymph node	Betamethasone	Petrolatum	Twice a day	7 weeks	Patients receiving betamethasone had less severe ARD than the other two groups throughout the course of the study, but this difference was significant only at the end of the third week ($P = 0.027$). No significant difference was observed between the petrolatum and control arms.	RTOG

(*continued on next page*)

Table 1 (*continued*)

Author (Year)	Nation	Simple *(n)*	Age (mean/range)	Radiotherapy region	Experimental arm	Control arm	Frequency of intervention	Period of intervention	Main outcomes	Assessment methods
Miller et al. (2011)	America	166	27–89	Chest wall, Localized lymph node	Mometasone	Placebo	Once daily	11 weeks	No difference in the mean maximum grade of radiation dermatitis by treatment arm (1.2 for MMF vs. 1.3 for placebo; $P = 0.18$). Common Terminology criteria for adverse events toxicity was greater in the placebo group ($P = 0.04$), primarily from pruritus.	CTCAE version 3.0; Skindex-16; Symptom experience diary; Skin toxicity assessment tool
Ulff et al. (2013)	Sweden	102	28–90	Chest wall, Breast, Localized lymph node	Betamethasone	Essex/Canoderm	Once daily	7 weeks	There was a statistically significant difference ($P = 0.05$) in skin reactions when assessed with RTOG in favour of the group treated with the potent steroid. Patient related symptoms did not difference between the treatment groups.	RTOG; Colorimeter & Corneometer; VAS; DLQI
Hindley et al. (2014)	UK	120	Experimental: 69 Control: 60	Chest wall, Breast	Mometasone	Diprobase	Once daily	5 weeks	Mean RTOG scores were significantly less for MF than for D ($P = 0.046$). Maximum RTOG and mean erythema scores were significantly less for MF than for D ($P = 0.018$ and $P = 0.012$, respectively).	RTOG; DLQI; HAD; Reflectance spectrophotometer
Meghrajani et al. (2016)	Philippine	50	(31–70) C: 51.78 E: 50.48	Chest wall, Localized lymph node	Hydrocortisone	Placebo	Twice a day	6 weeks	Its extent and severity were milder in the steroid group. Mean ARD scores were also lower in the steroid group (0.713 vs. 0.874, $P = 0.024$).	CTCAE version 3.0; VAS; DLQI
Ulff et al. (2017)	Sweden	202	27–97	Chest wall, Breast, Localized lymph node	Betamethasone	Moisturizer	Once daily	7 weeks	Patients receiving hypofraction RT developed less skin reactions than those treated with conventional RT. Treatment with a	RTOG; VAS

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Table 1 (*continued*)

Author (Year)	Nation	Simple *(n)*	Age (mean/range)	Radiotherapy region	Experimental arm	Control arm	Frequency of intervention	Period of intervention	Main outcomes	Assessment methods
									potent steroid resulted in clinically and statistically significantly less skin reactions ($P < 0.001$) regardless of RT schedule.	
Ho et al. (2018)	America	124	26–80	Breast and chest wall	Mometasone	Eucerin	Twice a day	7–7.5 weeks	The rate of moist desquamation was 54.8% in the entire cohort, with a significantly reduced incidence in the MF arm than in the E arm (43.8% vs 66.7%; $P = 0.012$). The MF arm had a lower incidence of maximum skin toxicities ($P = 0.036$).	CTCAE version 4.03; Skindex-16
Uysal et al. (2020)	Turkey	50	46	Breast	Betamethasone	Moisturizer	Once daily	–	Topical treatment with betamethasone cream resulted in clinically and statistically significantly less skin reactions compared to moisturizer ($P < 0.05$).	CTCAE version 5.0
Kianinia et al. (2021)	Iran	105	(28–81) 50.36	Chest wall, Breast, Localized lymph node	Mometasone/ Hydrocortisone	Moisturizing base cream	Once daily	5 weeks	No differences were observed among the groups concerning the incidence of the maximum ARD grade ($P = 0.2$).	CTCAE version 4.0

ARD, Acute Radiation Dermatitis; CTCAE version 3.0/4.0/4.03/5.0, Common Terminology Criteria for Adverse Events 3.0/4.0/4.03/5.0; D, Diprobase; DLQI, Dermatology Life Questionnaire Index; E, Eucerin; Gy, Gray; HAD, Hospital Anxiety and Depression Scale; MF, Mometasone Furoate; MMF, Mometasone Furoate; RT, Radiation Therapy; RTOG, Radiation Therapy Oncology Group; SF-36, 36-Item Short form health survey; VAS, Visual Analogue Scale; Skindex-16, Skindex scale.

Table 2
Evidence certainty of outcomes.

Number	Outcomes	Evidence certainty
1	Incidence of CTCAE ratings grade of 2 or higher	Level 1A
2	Incidence of RTOG ratings grade of 2 or higher	Level 1A
3	Incidence of moist desquamation	Level 1A
4	Mean acute radiation dermatitis score	Level 1A
5	Diary of symptom experience	Level 1C
6	Evaluation of the SF-36 quality of life scale	Level 1C
7	TPE & TPM scores	Level 1C
8	Erythema readings	Level 1C
9	HAD scores	Level 1C
10	Clinical scores	Level 1C
11	VAS scores	Level 1C
12	DLQI	Level 1C
13	SD-16 scores	Level 1C
14	Seven-point scale scores	Level 1C

CTCAE, Common Terminology Criteria for Adverse Events; DLQI, Dermatology Life Questionnaire Index; HAD, Hospital Anxiety and Depression Scale; RTOG, Radiation Therapy Oncology Group; SD-16, Skindex scale; SF-36, 36-Item Short form health survey; TPE, The total patient erythema index; TPM, The total patient melanin index; VAS, Visual Analogue Scale.

95% CI = [−0.59, −0.34]; $P < 0.01$) (Fig. 4A). Twelve studies were included in the meta-analysis of the mean score of radiation dermatitis. The funnel plot test and Egger's test were required to examine publication bias. The results of the funnel plot and Egger's test showed publication bias exists in terms of the effects of topical corticosteroids on the mean score of radiation dermatitis ($P < 0.01$) (Fig. 4B). The trim-and-fill analysis revealed that five additional studies would be necessary to influence the effects of topical corticosteroids on the mean score of radiation dermatitis (Supplementary material 2). However, these studies would not alter the differences between Experimental and Control.

Effects of topical corticosteroids on the incidence of CTCAE ratings of grade 2 or higher

Five studies[14,16,21,22,25] assessed the effects of topical corticosteroids on the incidence of CTCAE ratings of grade 2 or higher in patients with breast cancer treated with radiotherapy. There was no heterogeneity among these studies ($P = 0.36$, $I^2 = 8\%$).

The fixed-effects model was used to calculate the pooled effect size accordingly. The results showed that topical corticosteroids acted as the protective factor in reducing the incidence of CTCAE ratings of grade 2 or higher in patients with breast cancer who received radiotherapy, compared with the controls ($n = 495$; OR = 0.56; 95% CI = [0.37, 0.84]; $P < 0.01$) (Fig. 5).

Effects of topical corticosteroids on the incidence of RTOG ratings grade of 2 or higher

Five studies[15,18,20,23,24] evaluated the effects of topical corticosteroids on the incidence of RTOG ratings of grade 2 or higher in patients with breast cancer treated with radiotherapy. Heterogeneity was low ($P = 0.67$, $I^2 = 0\%$), and the pooled effect size was calculated through the fixed-effects model. The results showed that topical corticosteroids acted as the protective factor in reducing the incidence of RTOG ratings of 2 or higher compared to the controls ($n = 520$; OR = 0.22; 95% CI = [0.14, 0.32]; $P < 0.01$) (Fig. 6).

Effects of topical corticosteroids on the quality of life

Six studies[15,16,18,21,22,26] evaluated topical corticosteroids' effect on breast cancer patient's quality of life. However, none of the six studies provided the mean and standard deviation values necessary for the meta-analysis of quality of life. We contacted the authors, but no data were obtained. Therefore, a descriptive analysis was performed with available data from the six studies. Overall, most studies have confirmed that topical corticosteroids improve quality of life.

Quality of life in the six included studies was measured with the DLQI (Dermatologic Quality of Life Index) scale and the Skindex-16 scale. The DLQI scale consists of 10 items with a score range of 0–3 for each item and a total score range of 0–30. The Skindex-16 scale is a 16-item scale with a score range of 0–6 for each item and a total score range of 0–96. Higher scores on both scales indicate a poorer quality of life.[27]

In terms of DLQI scale scores, Meghrajani et al.[22] and Hindley et al.[15] found that patients in the steroid group had a higher quality of life. However, UIff et al.[18] found no significant difference in quality of life between the steroid group and the control group.

In terms of Skindex-16 scale scores, Miller et al.[16] and Schmuth et al.[26] found a trend toward improvement in quality of life in the steroid group. Interestingly, Ho et al.[21] concluded that there was no significant difference in quality of life between the steroid and the control group.

Effects of topical corticosteroids on skin erythema and hyperpigmentation readings

Four studies[15–18] have evaluated the effects of topical corticosteroids on skin erythema and hyperpigmentation readings in patients with breast cancer undergoing radiation therapy.

In terms of skin erythema readings, Hindley, Ulff, and BostroÈm[15,17,18] demonstrated in their studies that lower readings of skin erythema were observed in the experimental group.

In terms of hyperpigmentation readings, Miller et al.[16] found that the experimental group had lower hyperpigmentation readings compared to the control group. While BostroÈm et al.[17] found no significant difference in the total melanin index between the topical corticosteroids group and the control group.

Effects of topical corticosteroids on subjective symptoms (itching and pain)

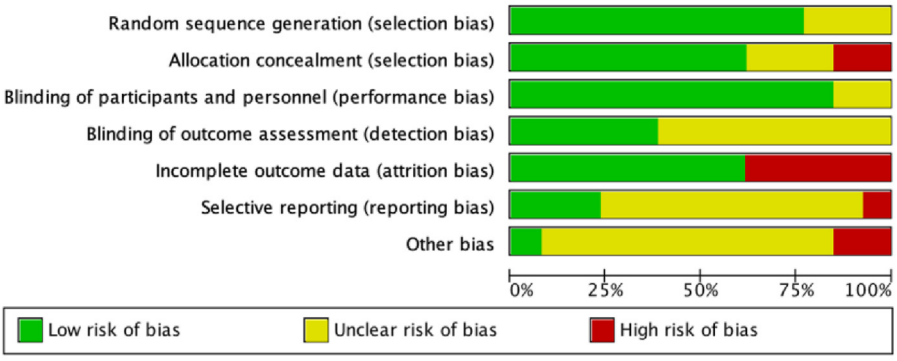
Due to insufficient data for meta-analysis, only descriptive analysis was performed. Seven studies[16–18,20–22,24] examined the effects of topical corticosteroids on subjective symptoms such as itching and pain in patients with breast cancer receiving radiotherapy.

Five of these studies[16,18,20,22,24] demonstrated that patients in the experimental group had less itching and burning than those in the control group. Differences between the two groups were statistically significant. In contrast, the remaining two studies[17,21] demonstrated no significant differences between the experimental and the control groups in reducing subjective symptoms such as itching and pain.

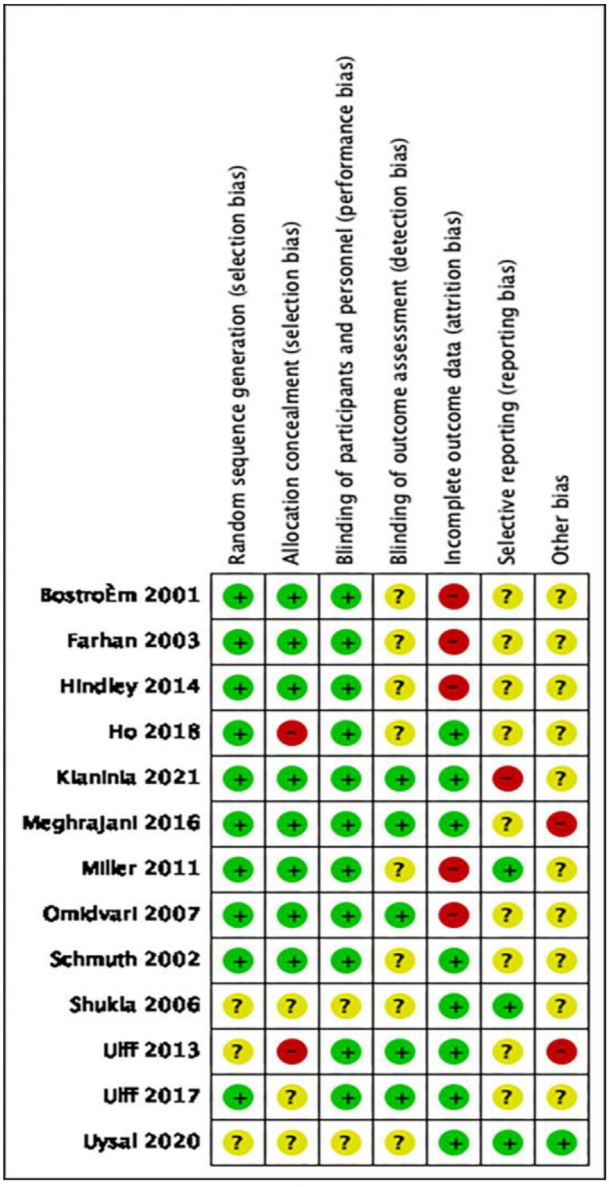
Discussion

This updated meta-analysis included 13 randomized controlled trials to determine the effects of topical corticosteroids on preventing acute radiation dermatitis in patients with breast cancer. Consistent with the previous study,[6] the results of this study suggest that topical corticosteroids can reduce the incidence of moist desquamation and the mean score of radiation dermatitis and enhance the quality of life in patients with breast cancer who received radiotherapy. However, publication bias was found in the effects of topical corticosteroids on the mean score of radiation dermatitis. The trim-and-fill analysis result showed that five additional studies were needed to maintain the stability of the pooled effect size. This phenomenon suggests that more high-quality studies are required to reduce publication bias in the future. Furthermore, this study demonstrated that topical corticosteroids reduced the incidence of CTCAE and RTOG ratings of grade 2 or higher and reduced skin erythema and hyperpigmentation readings in patients with breast cancer undergoing radiotherapy. This result is consistent with the study by Tam et al.[28]

Firstly, corticosteroids have anti-inflammatory effects through vasoconstriction, reduction of capillary permeability, and inhibition of



(a)



(b)

Fig. 2. (a) Risk of bias graph. (b) Risk of bias summary.

Table 3
Quality assessment of included studies (JADAD scale).

Authors (Year)	Randomized grouping	Randomized hiding	Blinding	Withdrawals and dropouts	Scores
BostroÈm et al. (2001)	2	2	2	1	7
Schmuth et al. (2002)	2	2	2	1	7
Farhan et al. (2003)	2	2	2	1	7
Shukla et al. (2006)	1	1	1	1	4
Omidvari et al. (2007)	2	2	2	1	7
Miller et al. (2011)	2	2	2	1	7
Ulff et al. (2013)	1	0	2	1	4
Hindley et al. (2014)	2	2	2	1	7
Meghrajani et al. (2016)	2	2	2	1	7
Sio et al. (2016)	2	2	1	1	6
Ulff et al. (2017)	2	1	2	1	6
Ho et al. (2018)	2	0	2	1	5
Uysal et al. (2020)	1	1	1	1	4
Kianinia et al. (2021)	2	2	2	1	7

leukocyte proliferation and migration.[4,5] The anti-inflammatory effect helped prevent and reduce skin inflammation symptoms in the treated area in patients with breast cancer undergoing radiotherapy and ultimately improved the quality of life. However, corticosteroids also have adverse effects on the skin and the body, such as glaucoma, Cushing's syndrome, hypertension, hirsutism, and hyperpigmentation.[29] The nurses should carefully observe the patient's skin and general condition while administering topical corticosteroids. Furthermore, nurses are responsible for explaining the precautions and proper use of topical corticosteroids to patients and their families to minimize the occurrence of adverse reactions.

Secondly, the topical corticosteroids used in the experimental group had moderate to high efficacy in the included studies. Previous studies have shown that the use of moderate-to-high-efficacy topical

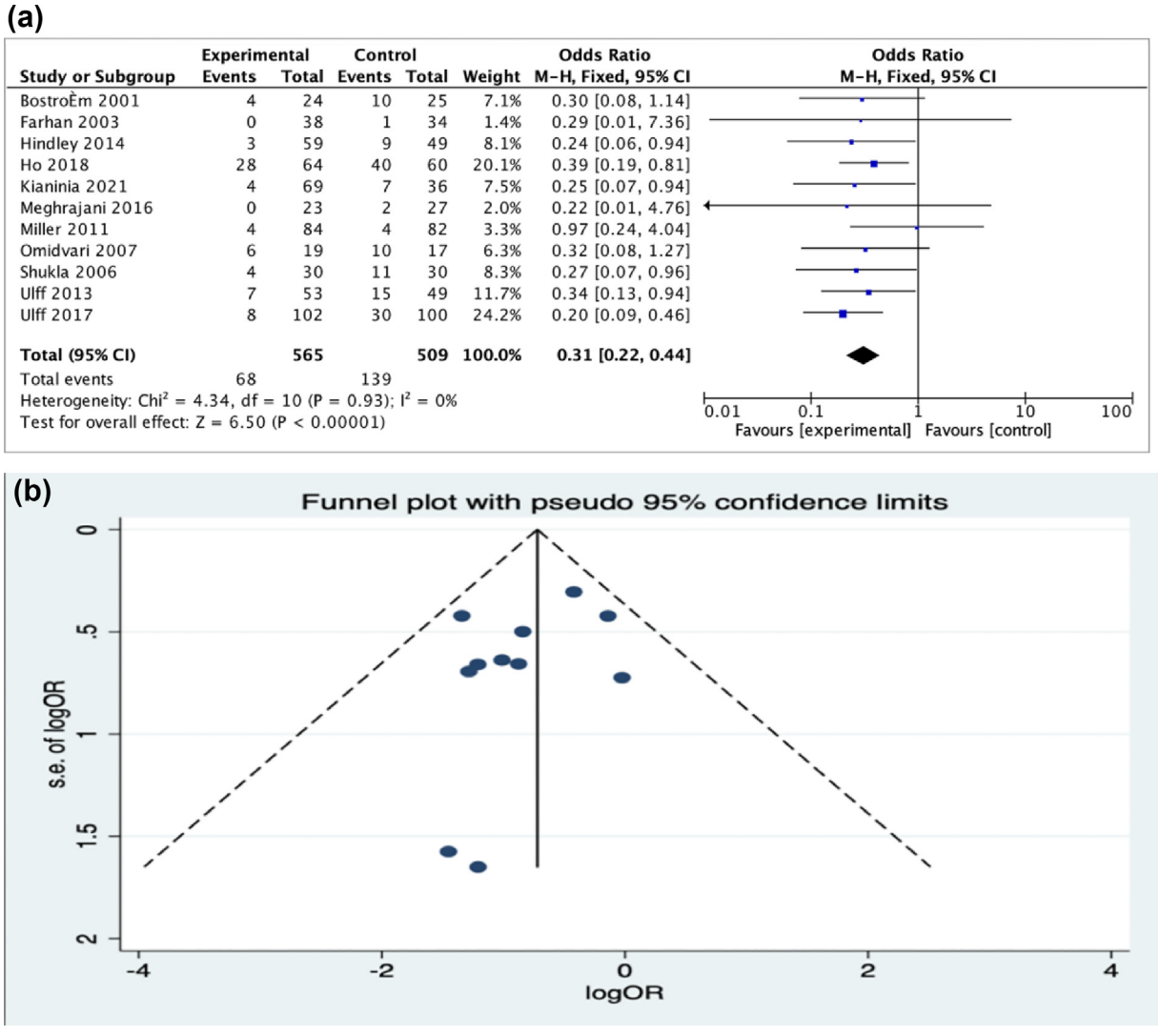


Fig. 3. (a) Incidence of moist desquamation. (b) The funnel plot of incidence of moist desquamation.

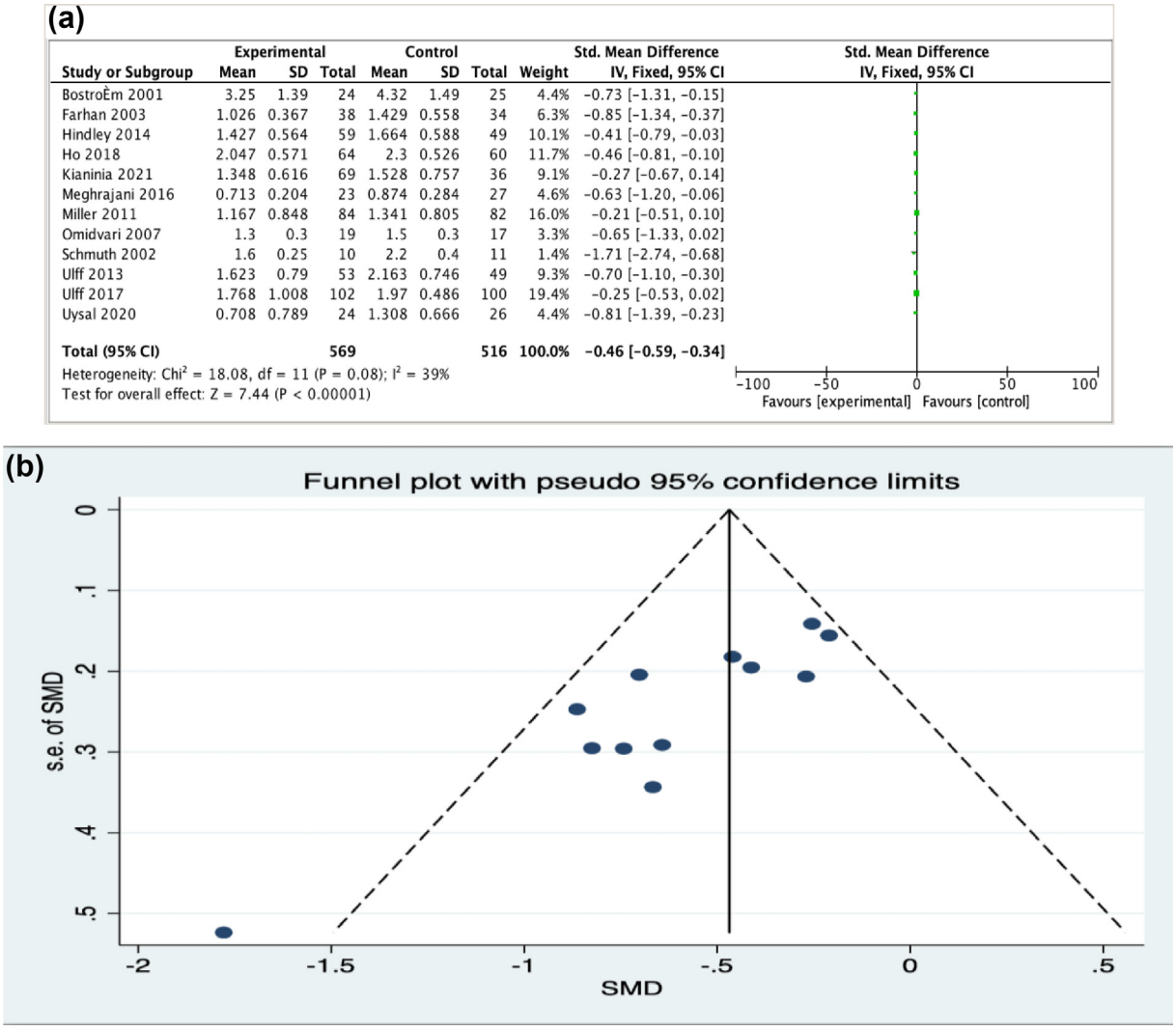


Fig. 4. (a) Mean acute radiation dermatitis score. (b) The funnel plot of mean acute radiodermatitis score.

corticosteroids should not exceed 12 weeks. Otherwise, the incidence of adverse reactions, such as hirsutism and fungal skin infections, could be increased.[29,30] Nurses should communicate with physicians and patients to manage the duration of administration to minimize the occurrence of adverse effects.

Thirdly, the primary dosage forms of topical corticosteroids used in the included studies were ointments, creams, and sprays. Each dosage form has its advantages and disadvantages.[31] Ointments of topical corticosteroids usually have fewer compounds added and are less irritating to the skin, making them suitable for patients with sensitive skin.

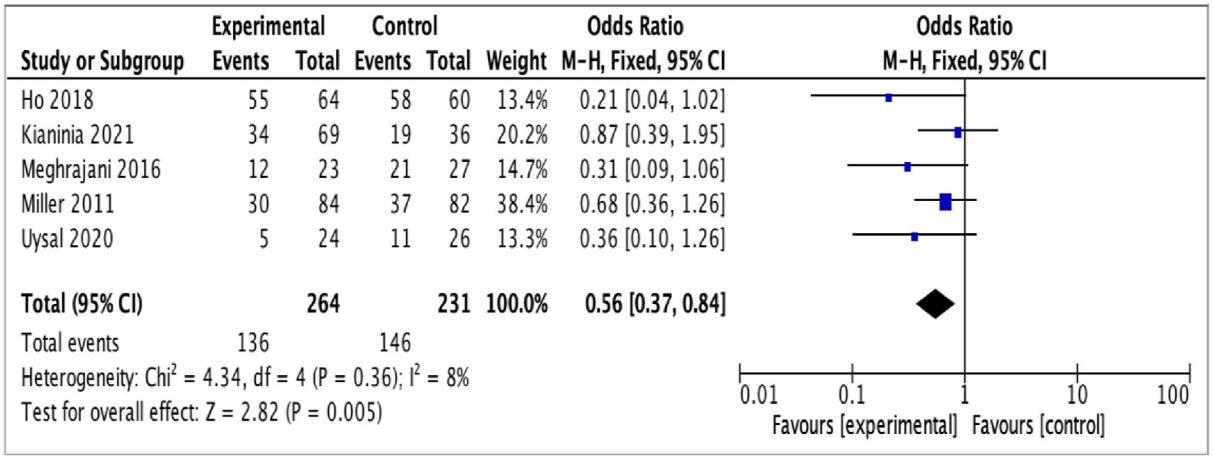


Fig. 5. Incidence of CTCAE ratings grade of 2 or higher. CTCAE, Common Terminology Criteria for Adverse Events.

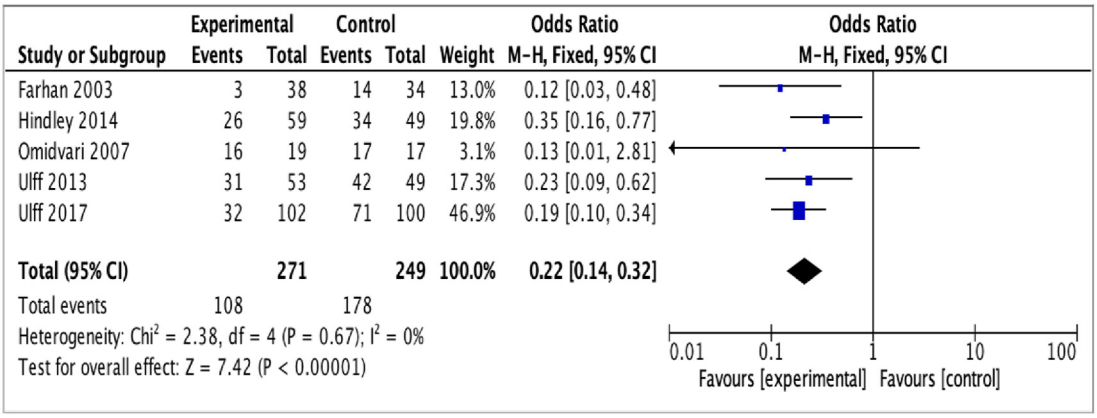


Fig. 6. Incidence of RTOG ratings grade of 2 or higher. RTOG, Radiation Therapy Oncology Group.

However, the added oils in ointments may cause subjective discomfort, such as stickiness and occlusive sensations, which may reduce the patient's willingness to use them or induce folliculitis. Sprays have a relatively high liquid content and are suitable for patients with dry skin and hairiness. However, alcohol in sprays may cause localized skin irritation or allergic reactions and increase the risk of acute inflammation of the patient's skin. Appropriate dosage forms of topical corticosteroids should be carefully selected for patients based on skin conditions and subjective preferences to improve treatment compliance and, ultimately, the effectiveness of the medication.

Finally, previous studies have revealed that corticosteroids are more effective when applied to the moist skin surface. Plastic films, bandages, or gloves are recommended to keep the skin moist and enhance the sealing and penetration of the drug.[29,32] Clinical nurses are encouraged to explore more practical techniques to enhance the efficacy of corticosteroids and improve the patient experience based on the characteristics of the corticosteroid formulation and the patient's skin condition.

Significance and limitations

This study is an updated systematic review. We updated the included studies based on the previous systematic review[6] according to the research progress and added the evaluation of three outcome indicators, namely, the incidence of CTCAE ratings grade 2 or higher, the incidence of RTOG ratings grade 2 or higher, and erythema and hyperpigmentation readings of the skin.

The results of this study contribute to a more comprehensive evaluation of the impact of topical corticosteroids on the prevention of acute radiation dermatitis in patients with breast cancer and provide references for clinical practitioners and researchers.

This study has some limitations. First of all, this study only included literature whose languages were Chinese or English, and some literature might have been excluded. Secondly, the sample sizes of some studies were so small that the risk of bias was moderate. Finally, the number of included studies in the meta-analysis for some of the outcome indicators (e.g., Incidence of CTCAE and RTOG ratings of 2 or higher) was limited (e.g., the number of included studies for incidence of CTCAE and RTOG ratings of 2 or higher was five).

Therefore, there has been no subgroup analysis according to the type of medications, and it is not determined which of the topical corticosteroids is more effective in preventing radiation dermatitis in patients with breast cancer. All of the above factors may limit the validity of the study's results.

Conclusions

This updated meta-analysis provided relevant evidence of topical corticosteroids' positive effects on preventing acute radiation dermatitis in patients with breast cancer. Due to the relatively small sample sizes of some of the included studies, more multi-center and high-quality randomized controlled trials with large sample sizes are needed to validate further topical corticosteroids' benefits in preventing acute radiation dermatitis in patients with breast cancer.

Ethics statement

Not required.

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CRediT authorship contribution statement

Weichao Liu: Conceptualization, Writing original draft, Formal analysis. **Liping Wang**: Writing – Conceptualization, Methodology, Review & Editing. **Chengang Hong**: Conceptualization, Methodology, Writing – Review & Editing. **Qianyu Zhang**: Formal analysis. **Jinghan Yang**: Formal analysis. 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.

Declaration of competing interest

The authors declare no conflict of interest.

Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

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

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

Supplementary data

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References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024 Apr 4. https://doi.org/10.3322/caac.21834.
2. Fan Yuanyuan, Lian Jianfeng. Progress of research on adjuvant radiotherapy for breast cancer. *Chin J Radiolog Health*. 2023;32(2):193–197 [In Chinese].
3. McQuestion M. Evidence-based skin care management in radiation therapy: clinical update. *Semin Oncol Nurs*. 2011;27(2):e1–e17. https://doi.org/10.1016/j.soncn.2011.02.009.
4. Wong RKS, Bensadoun R, Boers-Doets CB, et al. Clinical practice guidelines for the prevention and treatment of acute and late radiation reactions from the MASCC Skin Toxicity Study Group. *Support Care Cancer*. 2013;21(10):2933–2948. https://doi.org/10.1007/s00520-013-1896-2.
5. Liu Di, Zheng Zhewen, Zhang Shuyuan, et al. Research progress on skin toxicity related to radiotherapy of breast cancer. *China Med Herald*. 2021;18(9):39–42 [In Chinese].
6. Haruna F, Lipsett A, Marignol L. Topical management of acute radiation dermatitis in breast cancer patients: a systematic review and meta-analysis. *Anticancer Res*. 2017;37(10):5343–5353. https://doi.org/10.21873/anticanres.11960.
7. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Int J Surg*. 2021;88:105906. https://doi.org/10.1136/bmj.n71.
8. Higgins JPT, Altman DG, Gotzsche PC, et al. The cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928. https://doi.org/10.1136/bmj.d5928.
9. Joanna Briggs Institute Levels of Evidence and Grades of Recommendation Working Party. *Supporting Document for the Joanna Briggs Institute Levels of Evidence and Grades of Recommendation*. The Joanna Briggs Institute; 2014. https://joannabriggs.org/sites/default/files/2019-05/JBI%20Levels%20of%20Evidence%20Supporting%20Documents-v2.pdf. Accessed February 23, 2023, 2014.
10. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Contr Clin Trials*. 1996;17(1):1–12. https://doi.org/10.1016/0197-2456(95)00134-4.
11. Higgins JPT, Thomas J, Chandler J, et al., eds. *Cochrane Handbook for Systematic Reviews of Interventions*. 2nd ed. Chichester, UK: John Wiley & Sons; 2019.
12. Jones DR, Lau J, Carpenter J, Rücker G, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ*. 2011;343:d4002. https://doi.org/10.1136/bmj.d4002.
13. Shi L, Lin L. The trim-and-fill method for publication bias: practical guidelines and recommendations based on a large database of meta-analyses. *Medicine (Baltim)*. 2019;98(23):e15987. https://doi.org/10.1097/MD.0000000000015987.
14. Kianinia M, Roayaei M, Mahdavi H, et al. A double-blind randomized trial on the effectiveness of mometasone 0.1% cream and hydrocortisone 1% cream on the prevention of acute radiation dermatitis in breast cancer patients following breast conserving surgery. *Shiraz Univ Med Sci*. 2021;(3):406–414. https://doi.org/10.30476/mejc.2021.83528.1173.
15. Hindley A, Zain Z, Wood L, et al. Mometasone furoate cream reduces acute radiation dermatitis in patients receiving breast radiation therapy: results of a randomized trial. *Int J Radiat Oncol Biol Phys*. 2014;90(4):748–755. https://doi.org/10.1016/j.ijrobp.2014.06.033.
16. Miller RC, Schwartz DJ, Sloan JA, et al. Mometasone furoate effect on acute skin toxicity in breast cancer patients receiving radiotherapy: a phase III double-blind, randomized trial from the north central cancer treatment group N06C4. *Int J Radiat Oncol Biol Phys*. 2011;79(5):1460–1466. https://doi.org/10.1016/j.ijrobp.2010.01.031.
17. Bostrom A, Lindman H, Swartling C, et al. Potent corticosteroid cream (mometasone furoate) significantly reduces acute radiation dermatitis: results from a double-blind, randomized study. *Radiother Oncol*. 2001;59(3):257–265. https://doi.org/10.1016/s0167-8140(01)00327-9.
18. Ulff E, Maroti M, Serup J, et al. A potent steroid cream is superior to emollients in reducing acute radiation dermatitis in breast cancer patients treated with adjuvant radiotherapy. A randomised study of betamethasone versus two moisturizing creams. *Radiother Oncol*. 2013;108(2):287–292. https://doi.org/10.1016/j.radonc.2013.05.033.
19. Shukla P, Gairola M, Mohanti B, et al. Prophylactic beclomethasone spray to the skin during postoperative radiotherapy of carcinoma breast: a prospective randomized study. *Indian J Cancer*. 2006;43(4):180–184. https://doi.org/10.4103/0019-509x.29424.
20. Ulff E, Maroti M, Serup J, Nilsson M, Falkmer U. Prophylactic treatment with a potent corticosteroid cream ameliorates radiodermatitis, independent of radiation schedule: A randomized double blinded study. *Radiother Oncol*. 2017;122(1):50–53. https://doi.org/10.1016/j.radonc.2016.11.013.
21. Ho AY, Olm-Shipman M, Zhang Z, et al. A randomized trial of mometasone furoate 0.1% to reduce high-grade acute radiation dermatitis in breast cancer patients receiving postmastectomy radiation [published correction appears in Int J Radiat Oncol Biol Phys. 2018 Sep 1;102(1):231]. *Int J Radiat Oncol Biol Phys*. 2018;101(2):325–333. https://doi.org/10.1016/j.ijrobp.2018.02.006.
22. Meghrajani CF, Co HS, Arcillas JG, et al. A randomized, double-blind trial on the use of 1% hydrocortisone cream for the prevention of acute radiation dermatitis. *Expet Rev Clin Pharmacol*. 2016;9(3):483–491. https://doi.org/10.1586/17512433.2016.1126506.
23. Omidvari S, Saboori H, Mohammadianpanah M, et al. Topical betamethasone for prevention of radiation dermatitis. *Indian J Dermatol Venereol Leprol*. 2007;73(3):209. https://doi.org/10.4103/0378-6323.32755.
24. Farhan F, Kazemian A, Alagheband H, et al. Topical betamethasone for the prevention of acute radiation dermatitis in breast cancer patients. *Int J Radiat Res*. 2003;1(2):105–111. https://sid.ir/paper/286290/en.
25. Uysal B, Gamsız H, Dincoglan F, et al. Comparative evaluation of topical corticosteroid and moisturizer in the prevention of radiodermatitis in breast cancer radiotherapy. *Indian J Dermatol*. 2020;65(4):279–283. https://doi.org/10.4103/ijd.IJD_607_18.
26. Schmuth M, Wimmer MA, Hofer S, et al. Topical corticosteroid therapy for acute radiation dermatitis: a prospective, randomized, double-blind study. *Br J Dermatol*. 2002;146(6):983–991. https://doi.org/10.1046/j.1365-2133.2002.04751.x.
27. Wu XY, Song LJ, Han BJ, et al. An overview of assessment tools and methods for radiation dermatitis. *World Tradit Chin Med*. 2021;16(13):1942–1947 [In Chinese].
28. Tam S, Zhou G, Trombetta M, et al. Topical corticosteroids for the prevention of severe radiation dermatitis: a systematic review and meta-analysis. *Support Care Cancer*. 2023;31(7):382. https://doi.org/10.1007/s00520-023-07820-5.
29. Stacey SK, McEleney M. Topical corticosteroids: choice and application. *Am Fam Physician*. 2021;103(6):337–343.
30. Passi I, Salwan S, Kumar B. US-FDA approved drugs in 2020 and 2021: a review. *Mini Rev Med Chem*. 2023;23(12):1273–1297. https://doi.org/10.2174/1389557523666221208104530.
31. Mehta AB, Nadkarni NJ, Patil SP, et al. Topical corticosteroids in dermatology. *Indian J Dermatol Venereol Leprol*. 2016;82(4):371–378. https://doi.org/10.4103/0378-6323.178903.
32. Coloe J, Zirwas MJ. Allergens in corticosteroid vehicles. *Dermatitis*. 2008;19(1):38–42.