Original Study

Prospective Study of Breast Radiation Dermatitis

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Abstract

Radiation dermatitis is a common distressing side effect of breast radiotherapy. This study of 148 patients aimed to determine the trend of radiation dermatitis. Radiation dermatitis appears to peak at 2 weeks after radiotherapy; treatment factors such as technique or dosing regimen do not appear to have a substantial effect, but our study was limited by small sample size. Radiation dermatitis should continue to be followed closely, especially in the 2 weeks following RT.

Background: Despite clear benefits of radiotherapy (RT) for breast cancer, there are numerous side effects. Radiation dermatitis has a significant impact on quality of life and can result in treatment interruptions or cessation. The purpose of this study was to prospectively follow breast radiation dermatitis and determine trends including peak toxicity. **Patients and Methods:** Upon initiation of RT treatment, to assess skin reaction, each patient was seen weekly by the healthcare team, or contacted via telephone to assess patient-reported symptoms. Weekly progression of radiation dermatitis was assessed using the Common Terminology Criteria for Adverse Events (CTCAE), version 4.03. Patients were stratified for analysis of radiation dermatitis based on RT technique and dosage. **Results:** A total of 148 patients with 2 or more skin assessments were analyzed. The majority of patients received 2-field tangential RT (64.2%) with a dose of 5000 cGy in 25 fractions. Overall, patients experienced the most Grade 2 CTCAE toxicity (61.9%) 2 weeks after completion of RT; Grade 3 toxicity also peaked at this time (8.3%). Regardless of stratification by RT technique or by dosage of RT, Grade 2 and 3 toxicities consistently peaked at 1 or 2 weeks after RT. **Conclusions:** Breast radiation dermatitis appears to peak approximately 2 weeks after RT. Treatment factors such as technique or dosing regimen do not appear to have a substantial effect on radiation dermatitis, but our study was limited by small sample size. This study provides additional evidence that radiation dermatitis should continue to be followed closely, especially in the 2 weeks following RT.

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Introduction

Breast cancer is the most common type of malignancy in women, and is often managed by surgical excision of the tumor, followed by adjuvant radiotherapy (RT) intended to decrease the risk of locoregional recurrence and improve survival.[1-6] RT significantly decreases rates of recurrence and disease-related death in early breast cancer, as shown by several randomized trials.[4] Despite the benefits of RT, there are several acute and long-term side effects. One such side effect is a significant skin reaction, commonly referred to as radiation dermatitis, which is a distressing side effect for many patients undergoing this treatment.

Radiation dermatitis is a result of tissue damage caused by an accumulation of inflammation, cell necrosis, and cell death, as well as changes in endothelial cells,[7,8] which manifest in a variety of symptoms including erythema, edema, dry or moist desquamation, and pain ranging from mild to severe or debilitating.[1,9,10] Although tissue damage begins after the initial fraction of RT, symptoms of radiation dermatitis usually appear within 1 to 4 weeks of starting radiation, and remain or continue to increase for the duration of RT. Symptoms have been reported to heal approximately 2 to 4 weeks after RT has ended.[7,11] The symptoms of radiation dermatitis can have a significant impact on patient quality of life (QoL), and in serious cases, can result in treatment interruptions or cessation.[12] Patient factors such as smoking status[1] and larger breast size[13] can increase the risk of radiation dermatitis,[1] as can treatment factors such as use of bolus for RT[1] and use of chemotherapy.[14] Comfort measures such as analgesics and topical creams applied to the area

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are available to patients, but there is evidence to show that the severity of radiation dermatitis peaks 1 to 2 weeks after the last fraction of RT.[1,9,15] The purpose of this study was to prospectively follow radiation dermatitis owing to breast RT.

Patients and Methods

All patients who received adjuvant breast or chest wall RT at the Sunnybrook Odette Cancer Centre between December 2013 and November 2015 were eligible for the study. Patients were recruited by a member of their care team at the initial visit with their radiation oncologist. Only patients who had 2 or more reports of skin toxicity including the baseline assessment were included in the present analysis for greater continuity in data reporting, as several patients had incomplete data during treatment and follow-up. This study was a prospective cohort study of 148 patients examining the progression of radiation dermatitis after breast RT. Upon initiation of RT treatment, and as per standard clinical practice at our center, each patient was seen in a weekly review clinic by their radiation oncologist, nurse, or clinical research associate to assess skin reaction; for the purposes of the study, data were collected each week at this visit. Weekly visits/data collection continued until the last week of RT. Records of radiation dermatitis obtained after completion of RT were collected via telephone contact with the patient or in a follow-up visit with the treating radiation oncologist; patients who received a telephone call were asked to give self-reported symptoms to determine severity. Time to follow-up visit or telephone call was variable among patients. Weekly progression of radiation dermatitis was assessed until follow-up using a series of 6 scales: Common Terminology Criteria for Adverse Events (CTCAE) pain score, erythema, edema, patient-assessed pain, moist desquamation, and bleeding. Several of the 6 scales (erythema, edema, moist desquamation, and bleeding) corresponded to a specific grade on the CTCAE version 4.03 (v4.03) scale for radiation dermatitis (see Supplemental Table 1 in the online version).[16] Severity was recorded on a varying-point Likert scale for each of the 6 criteria; each numeric score corresponded to a description of the severity (see Supplemental Table 2 in the online version). Medications prescribed for radiation dermatitis were also recorded weekly. All information was collected on a web-based application, and an integrated biomatrix database system for breast cancer research used by our institution stored and organized the data. Informed consent was obtained from each patient, and the study was approved by the institutional research ethics board.

All patients on the study received adjuvant breast or chest wall RT. A variety of treatment positions were used, including lateral decubitus, supine, and prone as per the treating physician's preference. Several patients were treated with active breathing control. Patients received 3-dimensional conformal RT (3DCRT) in tangential fields (2-field), with or without the addition of nodal fields (3- or 4-field). Patients also received an additional dose (boost) to the tumor bed if clinically indicated. Tissue equivalent bolus was used on a selected group of patients at the discretion of the treating physician.

Patients were initially stratified into 6 groups to analyze skin reaction: 2-field with and without boost; 3-field with and without boost; and 4-field with and without boost. Patients were further stratified into subgroups depending on prescribed dose and the fractionation of schedule of RT, both of tangential fields and boost. Any potential subgroup that had a sample size of 5 patients or less was included in an "other" category.

Reports of radiation dermatitis were stratified by week following RT for the purposes of this study. If a patient had 2 reports within the same 7-day period, the worst score for each of the 6 scales between the 2 reports was used for the analysis.

Descriptive statistical analyses were conducted on demographic and RT treatment information to determine categorical proportions. To analyze the data and generate weekly scores for all subgroups in each of the aforementioned 6 scales assessing severity of skin reaction, Structured Query Language was used with its built-in statistical functions. To analyze the trend of radiation dermatitis according to the CTCAE v4.03, Grade 2 radiation dermatitis was defined as: erythema = 2, edema = 1, and moist desquamation = 2 as per the descriptors associated with each score (see Supplemental Table 2 in the online version) corresponding to CTCAE v4.03 grades (see Supplemental Table 1 in the online version); Grade 3 radiation dermatitis was defined as: moist desquamation = 3, and bleeding = 1. Descriptive statistical analyses were employed to determine median and range of radiation dermatitis severity, and progression to Grade 2 and Grade 3 radiation dermatitis by week was analyzed using proportions for the categorical values.

Results

A total of 148 patients were enrolled between March 2014 and July 2015. The median age was 61 years (range, 31-88 years). One hundred thirty-six (91.9%) patients were nonsmokers and 64 (43.2%) had received chemotherapy. The majority of patients had received lumpectomy (108; 73.0%) versus mastectomy (40; 27.0%) (Table 1).

Among 148 patients, 95 (64.2%) received 2-field tangential RT; other techniques included 3-field RT (9; 6.1%) and 4-field RT (44; 29.7%). The majority of patients were treated with 4256 cGy in 16 daily fractions (46; 31.1%), or 5000 cGy in 25 daily fractions (94; 63.5%). RT treatment details are reported in Table 2. One patient received a palliative course of RT (3000 Gy in 5 fractions); as this regimen was not adjuvant in intent, this patient was excluded from the analysis of radiation dermatitis progression. Forty-five (30.4%) patients received a boost dose of RT to the tumor bed, of which 17 (37.8%) had a simultaneous integrated boost; the rest (28; 62.2%) had a sequential boost. The most common treatment position was supine (120; 81.1%). A bolus was used for 20 (13.51%) patients.

Radiation Dermatitis Data

The median duration of RT among all patients was 5 weeks (range, 4-7 weeks). Each of the 148 patients had at least 2 documented appointments with their radiation oncologist during their RT treatment (median, 3; range, 2-7). Approximately one-half (50.7%) of patients had an additional 1 to 2 appointments after the last treatment date. Data was captured until week 10. Rates of data collection by week ranged from 0.7% (week 10) to 73.0% (week 2), with a median rate of 48.3%. The median worst skin reaction, combining data from all 6 scales, occurred at 6.25 weeks after first fraction of RT (Table 3).