Assessment of Cutaneous Toxicity in Patients Treated with Ultra-Hypofractionated Radiotherapy in the Right Breast at the Pernambuco Cancer Hospital, Brazil

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Abstract

Ultra-hypofractionated (UH) radiotherapy (RT) has emerged as a cost-effective and time-saving alternative for early breast cancer treatment and real-world evidence in public healthcare remains limited. **Objective:** To evaluate the degree of acute cutaneous toxicity in patients treated with UH RT (26 Gy in 5 fractions) for right-sided breast cancer (BC) in a Brazilian public hospital. **Methods:** A retrospective cross-sectional analytical study was conducted using medical records of 117 female patients treated between November 2021 and November 2023 at the Pernambuco Cancer Hospital. Eligible patients underwent adjuvant UH RT to the right breast. Skin toxicity was classified according to the Radiation Therapy Oncology Group (RTOG) scale. Statistical analysis included chi-square and Fisher's exact tests with a 5% significance threshold. **Results:** The mean age of patients was 59.9 years, with 80.3% over 50 years old and 51.3% having systemic arterial hypertension. Most tumors were invasive ductal carcinoma (76.1%) with luminal B (44.4%) and luminal A (37.6%) subtypes. Quadrantectomy was performed in 95.7%, with 38.5% receiving chemotherapy. Acute radiodermatitis was observed in 66.7% of patients: Grade 1 in 54.7%, Grade 2 in 9.4%, Grade 3 in only 2.6%, and no Grade 4 cases. A statistically significant association was found between hypertension and the presence of radiodermatitis (p=0.050), suggesting a potential link with underlying vascular changes or obesity, warranting further investigation. **Conclusion:** This study reinforces that UH RT is a safe and feasible treatment for right-sided BC, even in public hospitals lacking advanced RT technologies. These findings support the broader implementation of UH regimens in resource-limited settings to optimize treatment access and reduce patient burden.

Introduction

BC is a heterogeneous neoplasm with distinct biological subtypes and behaviors, requiring individualized treatment strategies. It is the second most common cancer worldwide and the most frequent in Brazil, with approximately 73,000 new cases estimated for 2023. Classical studies (NSABP-B04 and B06) confirmed the benefit of adjuvant RT, improving local control and reducing BC mortality. However, equipment limitations have motivated the development of shorter treatment regimens. Moderate hypofractionation (MH) demonstrated equivalence in local control and overall survival, reducing the number of sessions and improving cosmetic outcomes. Subsequently, ultra-hypofractionation (UH) was validated by studies such as FAST and FAST-Forward, which confirmed its oncologic safety and cosmetic equivalence using regimens of 26–28.5 Gy in 5 fractions, establishing it as a new standard for early-stage patients.

Radiodermatitis is the main cutaneous toxicity related to RT, caused by damage to keratinocytes and microvasculature. Its severity depends on dose, breast size, and technology used, and it is classified according to the Radiation Therapy Oncology Group (RTOG) scale. Studies have shown that the incidence of acute effects decreases with shorter regimens, from 78% with conventional fractionation to 47% with MH and 33% with UH.

Methods and Materials

This cross-sectional, quantitative, descriptive, and analytical study reviewed medical records of female BC patients treated with adjuvant UH RT to the right breast at the Pernambuco Cancer Hospital between November 2021 and November 2023. Descriptive and inferential statistical analyses were performed. Categorical variables were summarized as absolute and relative frequencies, while age was analyzed using mean, standard deviation, and median. Associations between categorical variables were tested using Pearson's chi-square or Fisher's exact test, with a 5% significance level. Data were entered into Microsoft Excel and analyzed using IBM SPSS version 27. Incomplete or conflicting records, illegible information, lack of histopathological confirmation, male patients, pregnant women, individuals under 18 years old, and those treated with conventional or moderately hypofractionated regimens were excluded. The study followed the Declaration of Helsinki and Resolution No. 466/2012 of the Brazilian National Health Council and was approved by the Research Ethics Committee of the Pernambuco Cancer Hospital (approval No. 6,862,724). Informed consent was waived due to the use of secondary anonymized data.

Results

From November 2021 to November 2023, a total of 117 patients with right-sided BC were treated with UH RT. The patients' ages ranged from 26 to 86 years, with a mean of 59.9 years (SD = 12.6) and a median of 61.0 years. Most patients (53.8%) were aged 50–69 years, followed by those ≥70 years (26.5%) and <49 years (19.7%). Arterial hypertension was present in 51.3% of patients, diabetes in 14.5%, and smoking in 2.6%. Regarding histological type, 76.1% had invasive ductal carcinoma, 5.1% ductal carcinoma in situ, 5.1% invasive papillary carcinoma, 4.3% lobular carcinoma, and 3.4% each had mucinous or intracystic papillary carcinoma. Tumor grades were distributed as follows: 60.7% grade 2, 21.4% grade 3, and 17.9% grade 1. Most frequent molecular subtypes were Luminal B (44.4%) and Luminal A (37.6%), followed by Luminal hybrid (6.0%), triple-negative (2.6%), and HER2-enriched (1.7%).

Chemotherapy was administered to 38.5% of patients, and 95.7% underwent quadrantectomy. Tumor size distribution was 60.7% T2, 27.4% T1, 8.5% in situ, and 3.4% T3. Among the 107 patients staged from T1 to T3, 94.4% were N0. The most common clinical stages were IIA (59%) and IA (25.6%). Additionally, 22.2% of patients received a radiotherapy boost.

Acute radiodermatitis occurred in 66.7% of patients, most of which were Grade 1 (54.7%), followed by Grade 2 (9.4%) and Grade 3 (2.8%), with no Grade 4 cases. A significant association ($p < 0.05$) was observed between systemic arterial hypertension and the occurrence of acute radiodermatitis, with higher rates among hypertensive patients (75.0% vs. 57.9%). No other significant associations ($p > 0.05$) were identified between the severity of radiodermatitis and other clinical variables (table 1)

	Acute Radiodermitis			
Variable	Yes (78)	No (39)	Total	p-Value
	n (%)	n (%)	n (%)	
Hypertension				p[1] = 0,050*
Yes	45 (75,0)	15 (25,0)	60 (100,0)	
No	33 (57,9)	24 (42,1)	57 (100,0)	
Diabetes				p[1] = 0,711
Yes	12 (70,6)	5 (29,4)	17 (100,0)	
No	66 (66,0)	34 (34,0)	100 (100,0)	
Smoking				p[2] = 1,000
Yes	2 (66,7)	1 (33,3)	3 (100,0)	
No	76 (66,7)	38 (33,3)	114 (100,0)	
Chemotherapy				p[1] = 0,687
Yes	31 (68,9)	14 (31,1)	45 (100,0)	
No	47 (65,3)	25 (34,7)	72 (100,0)	
Staging T				p[2] = 0,580
Tis	6 (60,0)	4 (40,0)	10 (100,0)	
T1	22 (68,8)	10 (31,3)	32 (100,0)	
T2	46 (64,8)	25 (35,2)	71 (100,0)	
T3	4 (100,0)	-	4 (100,0)	
Staging				p[2] = 0,934
TIS	6 (60,0)	4 (40,0)	10 (100,0)	
IA	20 (66,7)	10 (33,3)	30 (100,0)	
IIA	46 (66,7)	23 (33,3)	69 (100,0)	
IIB	6 (75,0)	2 (25,0)	8 (100,0)	
Surgery				p[2] = 0,664
Mastectomy	4 (80,0)	1 (20,0)	5 (100,0)	
Lumpectomy	74 (66,1)	38 (33,9)	112 (100,0)	
Boost				p[1] = 0,753
Yes	18 (69,2)	8 (30,8)	26 (100,0)	
No	60 (65,9)	31 (34,1)	91 (100,0)	

Table 1: Assessment of acute radiodermatitis according to comorbidities and clinical data

Discussion

In Brazil, most RT centers, both public and private, are concentrated in major cities, serving patients from rural areas who must travel long distances for treatment. This highlights the importance of shorter treatment regimens, which improve accessibility and efficiency. In public hospitals, linear accelerators often lack advanced technologies such as intensity-modulated radiotherapy (IMRT), directly influencing complication rates. The FAST-Forward trial demonstrated that adjuvant breast RT delivered in five fractions is safe, without increasing recurrence or acute toxicity. However, data from settings lacking advanced technology, particularly in Brazil, remain limited. The Radiotherapy Department at the Pernambuco Cancer Hospital (HCP) serves the public health system using a Varian Cx linear accelerator (6 MV) without IMRT. Treatment was restricted to right-sided cases because five-fraction planning for left-sided breasts exceeded cardiac dose limits due to the absence of IMRT or Deep Inspiration Breath Hold (DIBH). Over two years, 117 patients were treated with ultra-hypofractionation, followed for approximately six months to assess post-radiotherapy complications. Postmenopausal women, typically presenting with luminal subtypes and better prognosis, comprised 80.3% of the cohort, similar to FAST-Forward. Although the original trial included only invasive tumors, this regimen was also applied to in situ lesions, given no radiobiological reason for exclusion (5.1% ductal carcinoma in situ, 3.4% intracystic papillary). While 70% of tumors were T1 in FAST-Forward, 60.7% in this cohort were T2, likely reflecting limited early screening in Brazil's public healthcare system. Common risk factors include high BMI, smoking, large breast volume, and diabetes. Although previous meta-analyses found no link between hypertension and radiodermatitis, this study identified an association (75% vs. 57.6%; p<0.05). This may be related to obesity or vascular dysfunction, warranting further research. The incidence of acute radiodermatitis (66.7%) matched the FAST-Forward trial (62%), with most cases being mild (Grade 1). Limitations include its retrospective design, potential underreporting of complications, variable grading between physicians, and restriction to right-sided treatments due to technological constraints.

Conclusions

Ultra-hypofractionated radiotherapy for right-sided breast cancer is therefore a treatment regimen that can be safely implemented in hospitals lacking advanced technologies, with a limited risk of acute radiodermatitis. This approach optimizes treatment delivery, increases patient access, and reduces treatment burden and discomfort.

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