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Efficacy of Quad Shot Radiation therapy for symptom palliation in Advanced and Metastatic Breast Cancer

[1*]Dr. Aqsa Jadoon, [2] Salman Arif, [3] Sohaib, [4]Dr. Faryal, [5]Dr. Kanwal

Article Details

Dr. Aqsa Jadoon
Resident Radiation Oncology, CMH Rawalpindi. Corresponding Author Email ID: aqsa.jadoon45@gmail.com
Salman Arif
Consultant Radiation Oncology, CMH Rawalpindi. oncologist.salman@gmail.com
Sohaib
Consultant Radiation Oncology, CMH Lahore. sohaib63@hotmail.com
Dr. Faryal
Resident Radiation Oncology, CMH Rawalpindi. faryalsahi96@gmail.com
Dr. Kanwal
Resident Radiation Oncology, CMH Rawalpindi. drkanwalxhd@gmail.com

ABSTRACT

Background: Advanced and metastatic breast cancer often presents with debilitating symptoms such as pain and bleeding. Palliative radiotherapy aims to alleviate these symptoms. This quasi-experimental study compared the efficacy of Quad-shot radiation therapy (QS) to standard palliative radiotherapy (SOC) for symptom control in such patients. Methods: Conducted at the Combined Military Hospital, Rawalpindi, over six months, the study included 50 female patients with histopathologically confirmed invasive breast carcinoma, aged ≥18 years, with significant localized symptoms and ECOG PS 1-3. Patients were randomized into two groups: SOC (20 Gy in 5 fractions over one week) and QS (14.8 Gy in 4 fractions over two consecutive days, twice daily). Outcomes included pain relief (Numerical Rating Scale, NRS) and bleeding control (CTCAE criteria), assessed at baseline, one week, and three weeks post-treatment. Data were analyzed using paired t-tests, McNemar tests, or Wilcoxon signed-rank tests, with $p < 0.05$ considered statistically significant. Results: The median age was 48 years in the QS group and 50 years in the SOC group. Baseline NRS pain scores were 9.1 (QS) and 9.6 (SOC). Post-treatment, the QS group demonstrated a significantly greater reduction in pain (mean decrease: 3.7 vs. 2.1, $p = 0.05$). Bleeding episodes also decreased more in the QS group (mean change: 1.9 vs. 1.2 episodes, $p = 0.05$). Both regimens achieved effective symptom control, with QS showing superior outcomes in pain and bleeding resolution. Conclusion: Quad-shot radiotherapy is an effective and efficient alternative to standard palliative radiotherapy, offering superior symptom relief for pain and bleeding in patients with advanced or metastatic breast cancer. Further studies with larger sample sizes are warranted to validate these findings.

INTRODUCTION

Breast cancer is the most common global malignancy and the leading cause of cancer deaths [1]. Advanced breast cancer (ABC), which includes locally advanced and metastatic disease, poses a considerable clinical challenge due to its associated symptoms, poor prognosis, and limited treatment options. As the disease progresses, patients often experience distressing symptoms, including pain, bleeding, ulceration, and reduced quality of life, necessitating effective palliative interventions [2]. For patients with inoperable or advanced disease, curative treatment may not be an option, necessitating a focus on symptom control and improving the quality of life through palliative measures [3].

Palliative radiotherapy has emerged as a key modality in the management of symptomatic ABC. Radiotherapy offers effective relief of distressing symptoms by shrinking the tumor mass, controlling local disease, and providing relief from pain, bleeding, or ulcerative lesions [4]. Unlike curative therapy, the goal of palliative radiotherapy is not to eradicate the cancer but to improve the patient's well-being and minimize discomfort. It is often employed when surgical or systemic therapies are not feasible or when the disease is refractory to other treatments [5].

Studies have shown that radiotherapy can significantly reduce tumor size, control local symptoms, and enhance the quality of life in patients with symptomatic ABC [6]. Various regimens and techniques are available, and the optimal approach is typically tailored to the individual's condition, balancing efficacy with the need to minimize side effects. However, challenges remain in determining the ideal dose, fractionation schedules, and patient selection criteria to achieve the best possible outcomes [6].

Quad Shot radiation therapy, also known as "hypofractionated palliative radiotherapy," is a specific treatment protocol used primarily for patients with advanced or incurable cancers. This approach delivers radiation in a short period with fewer, larger doses, aiming to alleviate symptoms caused by the tumor quickly [7].A study by Kil et showed that all patients reported notably decreased symptoms at 2 to 3 weeks after quad shot therapy with an overall subjective palliative response rate of 100% [8].

This study aims to evaluate the efficacy of palliative radiation therapy in improving symptom control in patients with advanced breast cancer. By addressing the role of RT in alleviating the pain associated with symptomatic ABC, the findings will contribute to optimizing palliative care strategies and improving the holistic management of patients with advanced-stage disease.

METHODS

This quasi-experimental study was conducted to compare the efficacy of Quad-shot radiation therapy (RT) to a standard palliative RT regimen for symptom control in patients with advanced or metastatic breast cancer. The study was conducted at the Combined Military Hospital, Rawalpindi, over a period of 6 months following approval from the hospital's Ethical Review Committee (ERC).

The study included a total of 50 patients, divided into two groups of 25 each. Participants were recruited using a convenience non-probability sampling technique.

INCLUSION CRITERIA

1) Patients with Invasive breast carcinoma proven on histopathology
2) Only female patients aged 18 years or older
3) Patients with advanced and metastatic breast cancer, unfit for curative treatment, presenting with significant symptoms of localized breast pain and bleeding
4) ECOG PS 1-3

EXCLUSION CRITERIA

1) Pregnant females
2) Patients with collagen vascular disorder
3) Patients with autoimmune disorder
4) Patients who underwent curative RT previously
5) Sarcomas or histologies other than Invasive Breast carcinoma
5) ECOG PS 4-5

INTERVENTIONS

The study compared two palliative radiotherapy regimens:

1. **Standard Arm (Arm-1):** Patients received 20 Gy of radiotherapy in 5 fractions over one week.
2. **Experimental Arm (Arm-2, Quad-shot group):** Patients received 14.8 Gy of radiotherapy in 4 fractions, delivered twice daily with a minimum 6-hour interval between fractions over two consecutive days.

All radiotherapy was delivered using a 6 MV linear accelerator (LINAC) with three-dimensional conformal radiotherapy (3D-CRT) to limit radiation exposure to healthy tissues.

OUTCOME MEASURES

PRIMARY OUTCOME

- Symptom control, focusing on pain relief and bleeding cessation
- Pain was assessed using the Numerical Rating Scale (NRS), where 0 represented no pain and 10 represented maximum pain.
- Bleeding control was recorded as either complete or partial resolution of symptoms based on the CTCAE criteria.

A study proforma was developed to collect patient demographics, tumor characteristics, treatment details, baseline symptoms, and post-treatment outcomes (bleeding and pain). Data were collected by the principal investigator and cross-checked by a senior colleague to ensure accuracy and reduce bias. Patients were followed up at 1 week and 3 weeks after completing radiotherapy to assess symptom control.

Descriptive statistics were used to summarize patient demographics and treatment outcomes. Categorical variables, such as symptom control, were expressed as frequencies and percentages, while continuous variables, such as pain scores were presented as means with standard deviations or medians with interquartile ranges.

Differences in symptom relief between the two treatment groups were assessed using paired t-tests, McNemar tests, or Wilcoxon signed-rank tests, as appropriate. Statistical analysis was conducted using SPSS version 22, and a p-value of <0.05 was considered statistically significant.

RESULTS

A total of 50 patients were included in the study, with 25 patients receiving Quad-shot radiation therapy (QS) and 25 patients receiving the standard of care (SOC) which was 20 Gy of radiotherapy in 5 fractions. The median age of patients in the QS group was 48 years, while in the SOC group, the median age was 50 years.

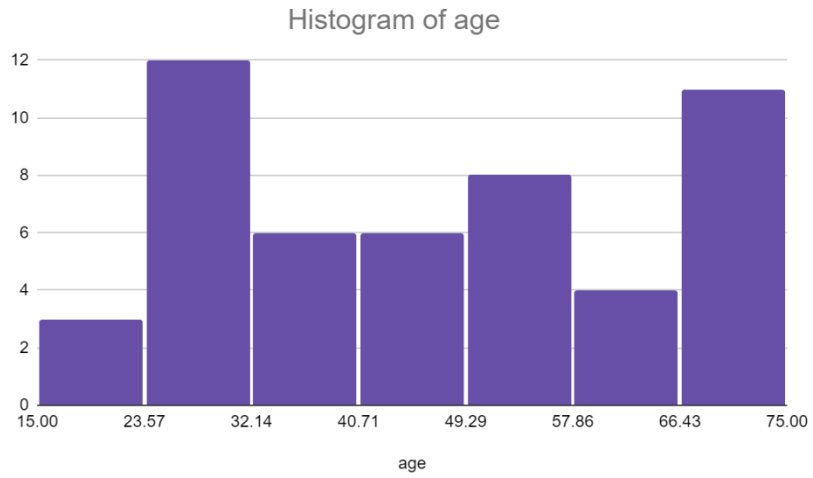

FIGURE 1: HISTOGRAM OF AGE

The mean baseline NRS score for pain in the QS group was 9.1 compared to 9.6 in the SOC group. After treatment, a significant reduction in VAS scores was observed in both groups; however, the QS group showed a greater mean decrease in points (3.7) compared to 2.1 points in the SOC group ($p = 0.05$).

At baseline, the frequency of bleeding episodes was similar in both groups, with the QS group having a mean of 2.1 episodes per week and the SOC group having 2.3 episodes per week. Post-treatment, the bleeding frequency decreased significantly in both groups, but the reduction was more pronounced in the QS group (mean change: 1.2 episodes) compared to the SOC group (mean change: 1.9 episodes) ($p = 0.05$).

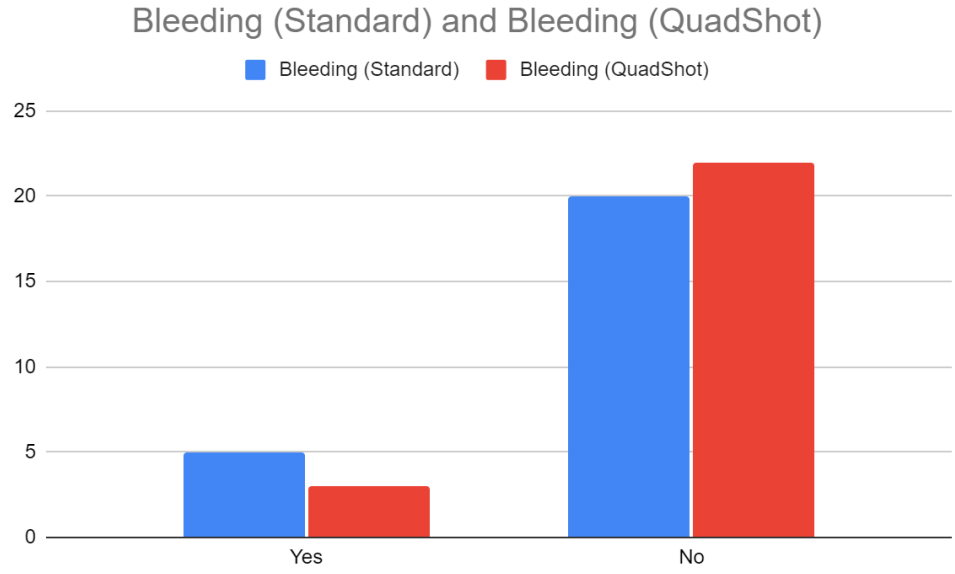

FIGURE 2: COMPARISON OF BLEEDING BETWEEN BOTH GROUPS

DISCUSSION

The Quad-shot (QS) radiation therapy regimen has been widely studied for its palliative use, particularly in cancers where curative treatment is not feasible. The QS regimen, typically consisting of 14.8 Gy delivered in four fractions over two days, has shown effectiveness in

advanced head and neck cancers. Studies report high symptom palliation rates (up to 100% in some cases) and manageable toxicity. A study of 21 patients showed an objective response in 85.7% of cases, with minimal side effects. The regimen is noted for significantly improving patients' quality of life by controlling symptoms such as pain, bleeding, and dysphagia [9]. QS therapy has also been explored in other cancers, including sarcomas and skin cancers, with promising results. A study on recurrent or metastatic sarcomas treated with proton QS therapy showed a subjective palliative response in 70% of cases [10]

The regimen is noted for significantly improving patients' quality of life by controlling symptoms such as pain, bleeding, and dysphagia. A study with 34 head and neck cancer patients found that 94% of patients achieved either tumor response or symptom relief after at least one cycle of QS therapy [11]

The present study shows a greater decrease in pain (VAS score reduction of 3.7) in the QS group compared to the SOC group (reduction of 2.1) after treatment. In a review of radiotherapy for symptomatic advanced breast cancer, radiotherapy effectively reduced pain in most patients, with 95% of patients experiencing symptomatic improvement [3]. This is consistent with the pain reduction seen in the QS group.

Both the QS and SOC groups showed a reduction in the frequency of bleeding episodes, but the QS group had a more significant reduction (mean change of 1.9 vs. 1.2 in the SOC group). In another study evaluating Quad-shot for advanced head and neck cancers, a significant improvement in bleeding control was reported in many patients, similar to the breast cancer study. Local symptom improvement, including control of bleeding, was a key outcome of Quad-shot regimens in the study by Finnegan et al [12].

A study by Lee et al retrospectively evaluated the effectiveness and safety of a five-fraction, high-conformal ultra-hypofractionated radiotherapy (RT) approach for treating primary tumors in 27 patients with metastatic breast cancer (MBC) who did not undergo surgery. Results showed that the treatment was well-tolerated, with only 15% experiencing mild, self-resolving skin toxicity. The best infield response rate was 82%, and the median time to objective response was 10.8 months post-RT. At a median follow-up of 18.3 months, the 2-year local control rate was 77%, though patients with fewer prior lines of systemic therapy had significantly better outcomes. The findings suggest that this RT approach offers promising local control with minimal toxicity, though further research is needed to refine its role and dosing in this patient population. Future research could refine our study by considering the abovementioned variables into account [13].

Despite adequate management using systematic chemotherapy, localized radiation can play a crucial role in alleviating symptoms in patients with symptomatic breast cancer [14-16]. With advancements in systemic therapies leading to improved overall survival (OS) in these patients, there is a growing interest in incorporating locoregional treatments like radiotherapy (RT). As a nonsurgical locoregional option, RT offers the advantages of minimizing disruptions to systemic therapy, enhancing convenience, and reducing morbidity. Consequently, palliative RT is particularly well-suited for these patients and is prioritized among breast-directed treatments for alleviating local symptoms[15-17] A study showed significant improvements in bleeding and offensive odor however a modest improvement in pain after using radiotherapy for symptom control [18].

While Quad-shot (QS) therapy has been extensively studied in other malignancies, our study contributes to the limited evidence regarding its efficacy in advanced or metastatic breast cancer, providing valuable insights into symptom palliation in this patient population. The study's small sample size (50 patients) limits the generalizability of findings and increases the

potential for type II error. Larger studies are needed to confirm these results. While symptom relief was measured, the broader impact of the treatments on patients' overall quality of life was not evaluated, which is a critical aspect of palliative care.

CONCLUSION: The results from our study are consistent with findings from the literature that suggest Quad-shot therapy is effective in managing pain and bleeding in advanced cancers, with some studies highlighting a significant improvement in symptom control and tolerability when compared to more conventional radiotherapy schedules.

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