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Research Article

Comparative Evaluation of Christie Versus Conventional Palliative Radiotherapy in Patients with Incurable Locally Advanced Head and Neck Squamous Cell Carcinoma: A Prospective Randomized Study.

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Abstract:

Background: Patients presenting with incurable locally advanced head and neck squamous cell carcinoma (LAHNSCC) frequently experience significant symptoms requiring effective palliation. Several hypofractionated radiotherapy regimens are used in clinical practice; however, no universally accepted standard schedule exists. This study was conducted to compare the clinical outcomes of two commonly used palliative radiotherapy schedules—Christie and conventional hypofractionated radiotherapy—in this patient population.

Objectives: To compare treatment response, toxicity profile, treatment tolerance, quality of life, and survival outcomes between Christie and conventional palliative radiotherapy regimens in patients with incurable locally advanced head and neck squamous cell carcinoma.

Methods: This prospective randomized study included **70 patients** with treatment-naïve, incurable LAHNSCC who were unsuitable for definitive therapy. Patients were randomized in a **1:1 ratio** into two treatment groups.

- **Arm A (Christie schedule):** 50 Gy delivered in 16 fractions over 3.1 weeks (3.125 Gy per fraction, five fractions per week).
- **Arm B (Conventional schedule):** 20 Gy delivered in 5 fractions (4 Gy per fraction) over one week, repeated after a three-week interval to achieve a total dose of 40 Gy in 10 fractions over 3.5 weeks.

Patients were evaluated before treatment, at completion of radiotherapy, and at one-month follow-up. Tumor response was assessed using WHO response criteria, while treatment-related toxicities were graded according to RTOG guidelines. Quality of life was evaluated using the University of Washington Quality of Life Questionnaire (UW-QOL, version 4).

Results: Treatment completion rates were **80% in the Christie arm and 72% in the conventional arm**. Partial tumor response was observed in **92.8% of patients receiving Christie radiotherapy and 96% of those treated with the conventional regimen**. Complete nodal response occurred more frequently in the Christie group (**85.7%**) compared with the conventional group (**76%**). Grade 3 mucositis was observed in **four patients in the Christie arm**, whereas no grade 3 mucositis occurred in the conventional arm. Significant improvement in performance status and quality-of-life scores was observed in both treatment groups. Median overall survival was **6 months in the Christie arm** compared with **3.5 months in the conventional arm**.

Conclusion: Both palliative radiotherapy regimens provided meaningful symptom relief and improvement in quality of life in patients with incurable LAHNSCC. However, the Christie schedule demonstrated improved locoregional control and longer overall survival

with manageable toxicity. These findings suggest that the Christie regimen may represent a preferable palliative radiotherapy option for appropriately selected patients.

Keywords: locally advanced head and neck cancer; squamous cell carcinoma; palliative radiotherapy; christie regimen; hypofractionation; conventional

Introduction

Head and neck cancers represent a significant global health burden and are among the most frequently diagnosed malignancies worldwide. According to recent global cancer estimates, cancers of the lip and oral cavity accounted for more than one million newly diagnosed cases in 2022. These malignancies constitute a major proportion of cancers in many developing nations, particularly in South Asia. In India, head and neck cancers rank among the most common cancers, with lip and oral cavity malignancies representing the second most frequently diagnosed cancer type. A considerable proportion of patients in India present with advanced disease at the time of diagnosis, often due to delayed healthcare access, socioeconomic limitations, and high prevalence of tobacco-related risk factors.

Management of locally advanced head and neck squamous cell carcinoma (LAHNSCC) generally requires a multidisciplinary approach involving surgery, radiotherapy, and systemic therapy. However, a substantial number of patients present with disease that is either unresectable or unsuitable for radical treatment. Advanced stage disease, extensive locoregional involvement, poor nutritional status, and compromised performance status frequently makes aggressive multimodality treatment impractical. In such circumstances, the primary goal of therapy shifts from cure to palliation, with emphasis on alleviating distressing symptoms and maintaining an acceptable quality of life.

Patients with incurable LAHNSCC often experience a range of debilitating symptoms including severe pain, dysphagia, ulceration, bleeding, foul odor, and functional impairment affecting speech and swallowing. These symptoms significantly compromise nutritional intake, physical activity, and psychosocial well-being. Therefore, effective palliative strategies are essential to reduce symptom burden and enhance patient comfort during the remaining course of the disease.

Radiotherapy plays a pivotal role in the palliative management of advanced head and neck cancer because it can provide rapid symptom relief, improve local disease control, and preserve organ function. In contrast to radical treatment schedules that require prolonged treatment duration, hypofractionated radiotherapy regimens are often preferred in the palliative setting. These schedules deliver larger doses per fraction over a shorter period, making them more convenient for patients with limited life expectancy and reduced tolerance to lengthy treatment courses.

Despite the widespread use of palliative radiotherapy in this clinical setting, there is no universally accepted standard dose-fractionation schedule. Various hypofractionated regimens have been proposed and evaluated, each attempting to achieve a balance between treatment efficacy, patient convenience, toxicity profile, and healthcare resource utilization. Among the commonly employed regimens, the Christie schedule and conventional hypofractionated radiotherapy are frequently used in clinical practice for symptom control in patients with incurable disease.

The Christie regimen delivers a moderately hypofractionated radiation dose over a relatively short treatment duration and has been reported to produce encouraging symptomatic improvement and tumor response. Conventional hypofractionated schedules, on the other hand, provide a simpler treatment approach and are often considered in patients with poor performance status or logistical limitations. However, data directly comparing the clinical outcomes of these regimens remain limited.

Considering the high burden of advanced head and neck cancer in resource-constrained settings and the need for effective yet practical palliative treatment strategies, further evaluation of different hypofractionated schedules is warranted. The present prospective randomized study was therefore undertaken to compare the **toxicity, treatment tolerance, tumor response, quality of life, and survival outcomes** associated with **Christie and conventional palliative radiotherapy regimens** in patients with **incurable locally advanced head and neck squamous cell carcinoma**.

Aim

To compare the efficacy and tolerability of the **Christie regimen and conventional palliative radiotherapy schedule** in patients with incurable locally advanced head and neck squamous cell carcinoma.

Objectives

To evaluate and compare **tumor response, treatment-related toxicities, changes in performance status, quality of life, and overall survival** between patients treated with the Christie regimen and those receiving conventional palliative radiotherapy.

Methodology

Study Design and Patient Selection

This **prospective randomized comparative study** was conducted in the Department of Radiation Oncology at **Sarojini Naidu Medical College, Agra**, between **March 2023 and March 2025**. The study included patients diagnosed with **locally advanced head and neck squamous cell carcinoma (LAHNSCC)** who were considered unsuitable for definitive curative treatment.

A total of **70 treatment-naïve patients** meeting the eligibility criteria were enrolled after obtaining written informed consent. Ethical approval for the study was obtained from the **Institutional Ethics Committee of SN Medical College, Agra**.

Patients were randomly assigned in a **1:1 ratio** into two treatment groups, with **35 patients in each arm**.

Eligibility Criteria

Patients were included if they had:

- Histologically confirmed **squamous cell carcinoma of the head and neck**

- **AJCC Stage IVA or IVB disease** not amenable to curative surgery or chemoradiotherapy
- **Karnofsky Performance Status (KPS) > 40**
- Adequate hematological, renal, and hepatic function parameters
- Age ≥18 years and willingness to provide informed consent

Patients were excluded if they had **distant metastasis, prior treatment for head and neck cancer, non-squamous histology, primary tumors of the thyroid, paranasal sinuses, salivary glands, nasal cavity, or nasopharynx, significant uncontrolled comorbidities, or pregnancy/lactation**.

Treatment Protocol

Patients were allocated using **simple randomization (draw of lots)** into the following treatment arms:

Arm A (Christie regimen):

Patients received **50 Gy in 16 fractions** over **3.1 weeks** (3.125 Gy per fraction, five fractions per week). Spinal cord sparing was performed after the **11th fraction through replanning**.

Arm B (Conventional hypofractionated regimen):

Patients received **20 Gy in 5 fractions** (4 Gy per fraction) over one week, followed by a repeat course after a three-week interval, resulting in a total dose of **40 Gy in 10 fractions** over 3.5 weeks. Spinal cord sparing was implemented during replanning for the **final fraction**.

Radiotherapy Technique

All patients underwent **treatment simulation** prior to radiotherapy. Treatment was delivered in the **supine position using parallel opposed lateral fields** encompassing the primary tumor and involved cervical lymph nodes. Radiation was delivered using a **Cobalt-60 teletherapy unit**, with dose prescribed to the **midplane at the central axis**.

Pretreatment Evaluation

Baseline assessment included **detailed clinical examination, Karnofsky performance status evaluation, complete blood counts, renal and liver function tests**, and radiological investigations including **chest X-ray, ultrasonography of the abdomen, and contrast-enhanced CT scan of the head and neck**. Tumor staging was performed according to the **AJCC 8th edition staging system**.

Treatment Assessment and Follow-Up

Patients were evaluated **daily during radiotherapy and weekly during treatment intervals**. Acute radiation toxicities were graded according to the **Radiation Therapy Oncology Group (RTOG) criteria**. Tumor and nodal responses were assessed using **WHO response criteria**.

Quality of life was assessed using the **University of Washington Quality of Life Questionnaire (UW-QOL, version 4)** at **baseline, at completion of treatment, and at one-month follow-up**.

Patients were followed for **at least six months or until death**, with clinical assessment at each visit to evaluate treatment response, symptom relief, and disease progression.

Statistical Analysis

Data analysis was performed using **SPSS version 28.0.1**. Categorical variables were compared using the **Chi-square test**, while changes in quality-of-life scores were analyzed using the **Wilcoxon signed-rank test**. Survival outcomes were estimated using the **Kaplan–Meier method**, and a **p-value <0.05** was considered statistically significant.

Results

A total of **70 patients** were enrolled in the study and randomized equally into two treatment arms (**35 patients each**). During treatment, **6 patients (17.1%) in the Christie arm** and **10 patients (28.5%) in the conventional arm** discontinued treatment prematurely. These patients were retained in the analysis according to the **intention-to-treat principle**.

The **median age** of patients was **50 years (range: 27–70)** in the Christie arm and **53 years (range: 22–73)** in the conventional arm. A male predominance was observed in both groups (**91.2% in the Christie arm and 71.4% in the conventional arm**).

Chewable tobacco use was the most common addiction, reported in **85.7% of patients in the Christie arm and 80% in the conventional arm**. The **oral cavity** was the most frequently involved primary site in both treatment groups. Most tumors were classified as **moderately differentiated squamous cell carcinoma**, and all patients belonged to **stage IV disease**, with a higher proportion of **stage IVA cases in the Christie arm** and **stage IVB in the conventional arm**.

Pain was the most common presenting complaint, followed by **dysphagia, cosmetic disfigurement, difficulty in chewing, and reduced physical and social activity**. Nasogastric tube feeding was required in approximately **47% of patients** during the course of treatment.

Table 1: Baseline Demographic and Clinical Characteristics.

Parameter	Arm A (Christie)	Arm B (Conventional)
Age (years)	Median 50 (Range 27–70)	Median 53 (Range 22–73)
Gender	Male: 31 (91.2%) Female: 4 (11.4%)	Male: 25 (71.4%) Female: 10 (28.6%)
Tobacco chewing	30 (85.7%)	28 (80%)
Smoking	27 (77.1%)	24 (68.6%)
Primary Site	Oral cavity: 21Oropharynx: 11Larynx: 3	Oral cavity: 27Oropharynx: 4Larynx: 4
Histology (MDSCC)	23 (65.7%)	22 (62.8%)
Stage IVA / IVB	23 (65.7%) / 12 (34.3%)	17 (48.6%) / 18 (51.4%)

Performance status was evaluated using the **Karnofsky Performance Scale (KPS)** before and after radiotherapy. Both treatment arms demonstrated **statistically significant improvement in KPS scores following treatment ($p < 0.0001$)**.

The mean KPS score increased from **53.45 ± 8.14 to 69.63 ± 6.49 in the Christie arm**, while in the conventional arm it improved from **50.8 ± 11.52 to 64.0 ± 9.57**. The magnitude of improvement was greater in patients treated with the **Christie regimen**.

Table 2: Karnofsky Performance Status (KPS) Before and After Radiotherapy.

Parameter	Arm A (Christie)	Arm B (Conventional)
Pre-RT Mean KPS	53.45 ± 8.14	50.8 ± 11.52
Post-RT Mean KPS	69.63 ± 6.49	64.0 ± 9.57
Improvement	Significant	Significant
p-value	<0.0001	<0.0001

The most frequently observed radiation-related toxicities were **mucositis and dermatitis**. Mucositis typically appeared after approximately **eight fractions of radiotherapy**.

Grade 3 mucositis was documented in **four patients in the Christie arm**, whereas **no cases of grade 3 mucositis were observed in the conventional arm**. No grade 3 dermatitis was reported in either treatment group. Approximately **20 patients required hospitalization for management of mucositis during treatment**.

At the **one-month follow-up**, no significant severe radiation-related toxicity was observed in either arm.

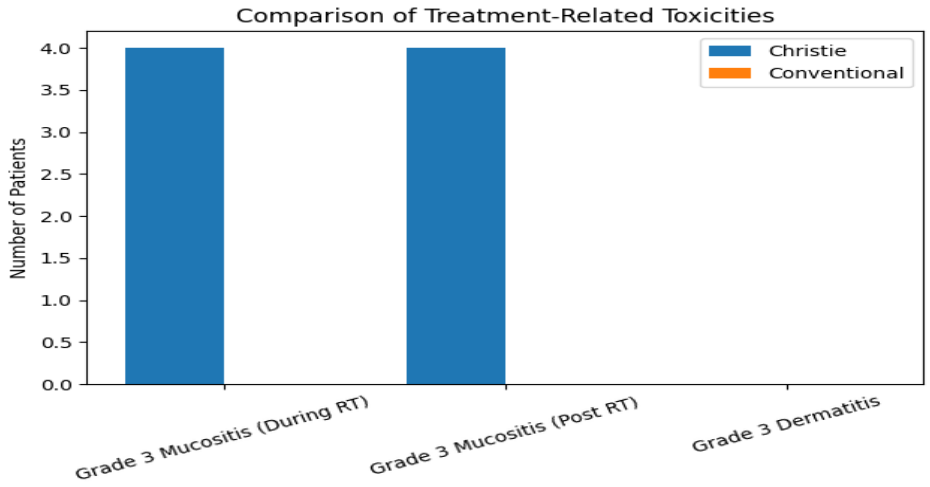

Figure 1: Toxicity comparison.

Tumor response was evaluated at completion of treatment using **WHO response criteria**.No patient in either arm achieved complete response at the primary tumor site. **Partial tumor response** was observed in **92.8% of patients in the Christie arm** and **96% of patients in the conventional arm**, while the remaining patients demonstrated **stable disease**. No cases of progressive disease were recorded during the initial response assessment.

With respect to nodal disease, **complete nodal response** was observed in **85.7% of patients receiving the Christie regimen** and **76% of those treated with the conventional schedule**. Partial nodal response was seen in the remaining patients.

Table 3: Objective Tumor and Nodal Response.

Response	Arm A (Christie)	Arm B (Conventional)
Tumor Response		
Partial response	26 (92.8%)	24 (96%)
Stable disease	2 (7.2%)	1 (4%)
Progressive disease	0	0
Nodal Response		
Complete response	24 (85.7%)	19 (76%)
Partial response	4 (14.3%)	6 (24%)

At the first follow-up visit, **27 patients in the Christie arm and 25 patients in the conventional arm** were available for evaluation. Two patients in the conventional arm and one patient in the Christie arm expired within the first month following radiotherapy.

After radiotherapy, **42 patients were able to tolerate palliative chemotherapy** due to improvement in their general condition. The most commonly administered regimen consisted of **weekly intramuscular methotrexate (50 mg) combined with oral gefitinib (250 mg daily)**. A small number of patients received **paclitaxel–carboplatin combination chemotherapy**, depending on their performance status and institutional treatment protocol.

Quality of life was assessed using the **UW-QOL questionnaire**. Significant improvement in **overall quality of life scores** was observed in both treatment groups (**$p < 0.001$**). The overall QOL score improved from **21.89 ± 12.45 to 71.48 ± 19.88 in the Christie arm**, and from **22.65 ± 12.98 to 68.64 ± 18.64 in the conventional arm**.Marked improvement was observed in domains including **pain, appearance, swallowing, chewing, speech, physical activity, mood, and anxiety**. However, **taste and saliva scores declined after treatment in both groups**, reflecting radiation-induced xerostomia and taste alteration. Symptomatic improvement, particularly in **pain relief**, was more pronounced in patients treated with the **Christie regimen.**

Table 4: Quality of Life (UW-QOL) Change After Radiotherapy.

Domain	Arm A (Christie)	Arm B (Conventional)
Pain	21.43 → 89.29	34.38 → 89.67
Appearance	38.39 → 78.57	37.50 → 77.08
Activity	38.39 → 71.43	42.71 → 66.67
Swallowing	23.57 → 56.07	38.71 → 72.46
Chewing	17.86 → 51.14	19.79 → 37.50
Mood	33.93 → 83.04	33.33 → 67.71
Overall QOL	21.89 → 71.48	22.65 → 68.64
p-value	<0.001	<0.001

Patients were followed for a **minimum duration of six months (range: 6–21 months)** or until death. The **median overall survival** was **6 months in the Christie arm** compared with **3.5 months in the conventional arm**. Kaplan–Meier survival analysis demonstrated **better survival outcomes in patients receiving the Christie schedule**.

Table 5: Median Overall Survival.

Treatment Arm	Median Survival (months)	95% CI
Christie (Arm A)	**6.0**	4.48 – 7.52
Conventional (Arm B)	**3.5**	1.35 – 4.65

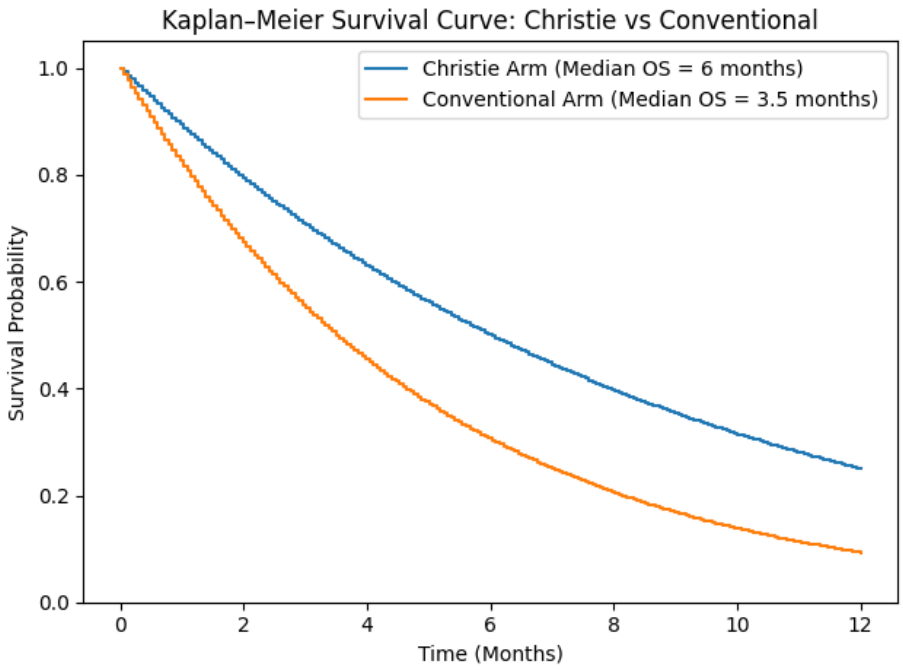

Figure 2: Statistically simulated survival curve.

Discussion

Advanced head and neck squamous cell carcinoma remain a major health concern in developing countries, where a large proportion of patients present with **locally advanced and unresectable disease**. In such situations, treatment is primarily palliative, with the goal of **relieving distressing symptoms and improving quality of life** rather than achieving cure. Hypofractionated radiotherapy schedules are therefore widely used because they provide **rapid symptom control with shorter treatment duration**, which is particularly beneficial for patients with limited life expectancy.

In the present study, two commonly used palliative radiotherapy regimens—the **Christie schedule and a conventional hypofractionated regimen**—were evaluated in patients with incurable locally advanced head and neck squamous cell carcinoma. Both regimens demonstrated **significant improvement in performance status following radiotherapy**, indicating effective symptom palliation. Improvement in Karnofsky Performance Status was greater in the Christie arm, suggesting better functional recovery. Similar improvements in performance status following palliative radiotherapy have been reported in previous studies evaluating hypofractionated schedules for advanced head and neck cancers.

Treatment-related toxicity in this study was generally manageable. **Mucositis was the most frequently observed adverse effect**, with a small proportion of patients in the Christie arm developing grade 3 mucositis. These findings are comparable to those reported by Soni A and colleagues, who observed higher rates of grade 3 mucositis in patients treated with the Christie regimen compared with other hypofractionated schedules. Likewise, A. Al-Mamgani et al., who originally described the Christie regimen, also reported significant mucosal toxicity, although it was considered acceptable in view of the clinical benefits achieved. In contrast, studies by B. K. Mohanti et al. and S. Das using the **40 Gy/10 fraction schedule** reported relatively lower rates of severe toxicity.

The tumor response observed in the present study was encouraging. A high proportion of patients in both arms achieved **partial tumor regression**, while nodal response was slightly better in the Christie arm. These findings are broadly consistent with earlier reports. For example, John Corry et al. demonstrated good objective response rates with hypofractionated palliative radiotherapy in advanced head and neck cancers. Similarly, studies by S. Ghoshal et al. and Ankur Mudgal et al. have reported favorable locoregional response following short-course palliative radiotherapy schedules.

Quality of life is a critical endpoint in patients receiving palliative treatment. In the present study, both treatment arms showed **significant improvement in overall quality-of-life scores**, particularly in domains related to **pain relief, swallowing, activity, and emotional well-being**. However, taste and salivary function declined following treatment, which is consistent with radiation-induced xerostomia reported in previous studies. Similar improvements in multiple quality-of-life domains have been described by Soni A et al. and S. Ghoshal et al., highlighting the role of palliative radiotherapy in reducing symptom burden in advanced head and neck cancer.

With regard to survival outcomes, the **median overall survival was higher in the Christie arm** compared with the conventional regimen in the present study. Although survival in such patients is generally limited, previous studies have reported variable survival outcomes with hypofractionated radiotherapy schedules. For instance, S. Das et al. reported a median survival of approximately **7 months**, while Ankur Mudgal et al. reported survival approaching **9 months** in selected patients receiving palliative radiotherapy.

Overall, the findings of this study suggest that both regimens are effective in providing symptomatic relief in patients with incurable disease. However, the **Christie schedule demonstrated comparatively better locoregional response, improvement in performance status, and longer survival**, although with slightly higher acute mucosal toxicity.

Nevertheless, the study has certain limitations, including **a relatively small sample size and limited follow-up duration**, which may affect the interpretation of long-term outcomes. Future **multicenter studies with larger patient populations and longer follow-up** would help establish the optimal palliative radiotherapy schedule for patients with advanced head and neck cancer.

Conclusion

Palliative radiotherapy plays a crucial role in the management of patients with **incurable locally advanced head and neck squamous cell carcinoma**, where the primary goal of treatment is symptom relief and improvement in quality of life. In the present study, both the **Christie regimen and the conventional hypofractionated schedule** demonstrated meaningful clinical benefit in terms of **symptom palliation, improvement in performance status, and enhancement of overall quality of life**.

Although both treatment approaches were effective, patients treated with the **Christie regimen showed comparatively better locoregional response, greater improvement in performance status, and longer median overall survival**. While a slightly higher incidence of acute mucosal toxicity was observed with this regimen, these adverse effects were **manageable with appropriate supportive care**.

Based on the findings of this study, the **Christie schedule appears to offer a favorable balance between treatment efficacy and tolerability**, making it a suitable palliative radiotherapy option for patients with incurable locally advanced head and neck cancer, particularly in **resource-limited healthcare settings**.

Further **large-scale multicenter studies with longer follow-up** are required to confirm these findings and to establish an optimal palliative radiotherapy schedule for this patient population.

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