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COMPARATIVE EVALUATION OF PAIN RELIEF IN METASTATIC LUNG CANCER USING TWO PALLIATIVE RADIOTHERAPY SCHEDULES: A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Purpose: Pain is one of the most disabling symptoms in metastatic lung cancer. Hypofractionated external beam radiotherapy (EBRT) is a widely used palliative modality, but the optimal schedule remains debated. This study compared two regimens—30 Gy in 10 fractions versus 20 Gy in 5 fractions—for pain palliation and opioid reduction.

Methods: In this prospective observational study, 96 patients with histologically confirmed metastatic lung carcinoma and moderate-to-severe chest pain were enrolled. Patients received either 30 Gy/10 fractions (Group A, n=48) or 20 Gy/5 fractions (Group B, n=48). Pain intensity was measured using the Brief Pain Inventory (BPI), and opioid use was calculated in morphine milligram equivalent (MME). Assessments were conducted at baseline, 1 month, 3 months, and 6 months after radiotherapy. Logistic regression identified predictors of pain palliation.

Results: Both regimens significantly reduced pain and opioid consumption. At 1 month, 71% of patients achieved partial or complete relief. At 3 and 6 months, ~30% maintained complete relief, with no significant difference between groups. Mean BPI scores declined from 7.9 at baseline to 3.3 at 1 month and remained improved at 6 months (4.2 in Group A, 4.3 in Group B). Opioid use fell from ~26 mg baseline to <5 mg at 6 months. Toxicities were limited to Grade I–II esophagitis, skin erythema, and fatigue. Logistic regression revealed no significant predictors of pain palliation ($p>0.05$). **Conclusions:** Both regimens offer equivalent, durable pain palliation with minimal toxicity. The shorter 20 Gy/5 regimen is preferable in advanced disease due to patient convenience and resource efficiency.

Keywords: Metastatic lung cancer, Palliative radiotherapy, Hypofractionation, Pain relief

Introduction

Lung cancer remains the leading cause of cancer-related mortality worldwide, accounting for an estimated 2.2 million new cases and 1.8 million deaths in 2020.[1] Despite advances in screening,

diagnostics, and systemic therapies, the majority of patients continue to present with advanced or metastatic disease, where the therapeutic focus shifts from curative intent to palliation of symptoms and maintenance of quality of life.[2,3]

Among the wide spectrum of symptoms encountered in advanced lung cancer, chest pain is particularly debilitating, with reported prevalence rates ranging from 20% to 60%.[4] Pain arises from multiple mechanisms, including pleural infiltration, chest wall invasion, rib metastasis, and perineural spread such as brachial plexus involvement in superior sulcus (Pancoast) tumors.[5] Conventional analgesics, including opioids, are frequently prescribed but may provide incomplete or short-lived relief and are associated with significant side effects such as constipation, drowsiness, and tolerance.[6] This underscores the importance of integrating effective local palliative strategies, such as radiotherapy, into the management of painful thoracic disease.

External beam radiotherapy (EBRT) has long been established as a highly effective modality for palliation of tumor-related chest pain and other local symptoms in lung cancer.[7] Short-course or hypofractionated radiotherapy regimens are commonly employed due to their convenience, lower resource requirements, and ability to minimize the treatment burden for patients with limited life expectancy.[8,9] Randomized controlled trials and meta-analyses have consistently demonstrated that shorter schedules provide pain relief equivalent to longer regimens, though differences may exist in terms of duration of response, retreatment rates, and toxicity.[10,11]

Two of the most widely used hypofractionated schedules are 30 Gy in 10 fractions over 2 weeks and 20 Gy in 5 fractions over 1 week. The former is often considered a standard regimen that balances efficacy with tolerability, while the latter is attractive for patients with poor performance status or limited prognosis due to its shorter overall treatment time and fewer hospital visits.[12,13] However, practice patterns vary globally, and the optimal schedule that maximizes pain control while minimizing treatment burden remains a matter of debate.[14]

This prospective observational study was therefore designed to directly compare these two regimens—30 Gy in 10 fractions versus 20 Gy in 5 fractions—in patients with metastatic lung carcinoma presenting with chest pain. The primary endpoints were pain relief, assessed using the Brief Pain Inventory (BPI), and changes in analgesic requirements, quantified by Morphine Milligram Equivalent (MME) scores. By addressing this clinically relevant question, the study aims to provide evidence that can guide optimal palliative radiotherapy scheduling for patients with advanced lung cancer.

Methods

Patients and Study Design

This prospective observational study was conducted in the Department of Radiotherapy, Burdwan Medical College & Hospital, from May 2021 to April 2022. A total of **96 patients** with histologically confirmed metastatic lung carcinoma and moderate-to-severe chest pain were enrolled. Institutional ethics approval and written informed consent were obtained from all participants.

Eligibility criteria: Patients aged ≥18 years with ECOG performance status 0–2, life expectancy >3 months, and baseline pain score ≥4 on the Brief Pain Inventory (BPI) were included. Exclusion criteria were prior thoracic radiotherapy, uncontrolled concurrent illness, or inability to comply with follow-up.

Treatment groups: Patients were assigned to one of two fractionation schedules:

- **Group A (n=48):** 30 Gy in 10 fractions over 2 weeks
- **Group B (n=48):** 20 Gy in 5 fractions over 1 week

Treatment was delivered using cobalt-60 teletherapy with parallel-opposed fields encompassing the symptomatic chest site.

Pain and Analgesic Assessment (BPI & MME Working Principle)

Pain measurement: Pain was assessed using the **Brief Pain Inventory (BPI)** severity scale. The BPI is a validated patient-reported questionnaire that measures both the **intensity of pain** (worst,

least, average, and current over the last 24 hours) and the **interference of pain** with general activity, mood, walking ability, normal work, relations with others, sleep, and enjoyment of life. Patients rated their pain on a **0–10 numeric scale** (0 = no pain, 10 = worst imaginable pain)[2].

Analgesic use: Concurrent analgesic consumption was recorded and converted into **oral morphine milligram equivalents (MME)** using standard conversion tables. This allowed direct comparison of opioid use across patients receiving different drugs and routes of administration.

Pain response definition: Following international consensus guidelines for palliative radiotherapy trials, responses were categorized as:

- **Complete response (CR):** BPI worst pain score = 0 with no increase in MME.
- **Partial response (PR):** Reduction in BPI worst pain score by ≥2 points without an increase in MME, or ≥25% reduction in MME without an increase in pain score.
- **No response/progression:** Increase in pain score by ≥2 or ≥25% increase in MME without improvement in pain score.

Follow-up and Evaluation

Pain (BPI) and opioid use (MME) were assessed at **baseline**, **1 month**, **3 months**, and **6 months** after completion of radiotherapy.

The **primary endpoint** was pain palliation (CR + PR) at follow-up. Secondary endpoints included changes in mean BPI score, mean MME consumption.

Results

Patient Characteristics

Ninety-six patients were enrolled. Baseline characteristics were similar between groups.

Table 1. Baseline characteristics

Characteristic	Group A (30 Gy/10)	Group B (20 Gy/5)	Total (%)
Mean age (years)	56.2	55.8	–
Male sex	43 (90%)	42 (88%)	85 (89%)
Female sex	5 (10%)	6 (12%)	11 (11%)
ECOG 0–1	35 (73%)	34 (71%)	69 (72%)
ECOG 2	13 (27%)	14 (29%)	27 (28%)
Smoking history	44 (92%)	43 (90%)	87 (91%)
Baseline pain score (mean)	7.9 ± 0.6	7.7 ± 0.7	–

Pain Response

Table 2. Pain response following radiotherapy

Time point	Complete response	Partial response	No response/progression
1 month	34%	37%	29%
3 months	31%	36%	33%
6 months	28%	34%	38%

(No significant difference between regimens, $p > 0.05$)

Pain Severity (BPI scores)

Table 3. Mean BPI pain severity scores

Time point	Group A (30 Gy/10)	Group B (20 Gy/5)
Baseline	7.9 ± 0.6	7.7 ± 0.7
1 month	3.3 ± 1.2	3.4 ± 1.1
3 months	3.7 ± 1.4	3.8 ± 1.5
6 months	4.2 ± 1.6	4.3 ± 1.7

Both regimens achieved significant pain reduction compared with baseline ($p < 0.001$).

Opioid Consumption

Table 4. Mean opioid use (MME)

Time point	Group A (30 Gy/10)	Group B (20 Gy/5)	p-value
Baseline	26.7 ± 8.8	26.3 ± 10.6	0.83
1 month	8.5 ± 6.3	8.2 ± 5.9	0.77
3 months	4.3 ± 5.1	4.7 ± 6.0	0.65
6 months	3.4 ± 4.9	4.3 ± 7.5	0.46

Opioid requirements declined significantly in both groups over time.

Predictors of Pain Palliation

Table 5. Logistic regression analysis

Variable	Odds Ratio (95% CI)	p-value
Age >60 years	1.08 (0.52–2.23)	0.82
Male sex	0.94 (0.41–2.17)	0.89
ECOG 2 vs 0–1	0.87 (0.40–1.92)	0.71
Smoker vs non	1.11 (0.42–2.91)	0.83
Baseline pain ≥8	1.20 (0.56–2.59)	0.61
RT schedule (20/5)	1.05 (0.49–2.23)	0.90

No independent predictors of pain palliation were identified.

A total of **96 patients** with metastatic lung carcinoma and moderate-to-severe chest pain were enrolled between May 2021 and April 2022. Of these, 48 patients received **30 Gy in 10 fractions** (Group A), while 48 received **20 Gy in 5 fractions** (Group B). Baseline characteristics were comparable between the two groups. The mean age was 56.2 years in Group A and 55.8 years in Group B. The overall cohort was predominantly male (89%), with a high prevalence of smoking history (91%). ECOG performance status was 0–1 in 72% and 2 in 28% of patients. Baseline mean BPI pain scores were **7.9 ± 0.6** in Group A and **7.7 ± 0.7** in Group B.

Pain Response

At **1 month** post-treatment, **71%** of patients achieved either complete or partial pain relief, with no significant difference between treatment arms. At **3 months**, 31% of patients maintained complete response and 36% partial response. By **6 months**, 28% retained complete relief and 34% partial relief, while 38% had no response or progression. Pain palliation was thus durable in a substantial proportion of patients, though the overall response declined over time.

Pain Severity (BPI Scores)

Mean BPI pain severity scores showed a marked reduction following radiotherapy in both groups.

- At **baseline**, scores were 7.9 ± 0.6 (Group A) and 7.7 ± 0.7 (Group B).
- At **1 month**, they declined to 3.3 ± 1.2 and 3.4 ± 1.1, respectively.
- At **3 months**, scores remained low at 3.7 ± 1.4 and 3.8 ± 1.5.
- At **6 months**, they slightly increased but remained improved compared with baseline, at 4.2 ± 1.6 and 4.3 ± 1.7.

Both schedules provided **statistically significant pain relief compared with baseline ($p < 0.001$)**, with no significant differences observed between groups.

Opioid Consumption (MME)

Baseline opioid use was comparable in both arms, averaging 26.7 ± 8.8 mg (Group A) and 26.3 ± 10.6 mg (Group B). Following treatment, opioid consumption declined significantly in both groups:

- At **1 month**, mean use fell to 8.5 ± 6.3 mg (Group A) and 8.2 ± 5.9 mg (Group B).

- At **3 months**, it further decreased to 4.3 ± 5.1 mg and 4.7 ± 6.0 mg, respectively.
- At **6 months**, mean consumption reached its lowest levels at 3.4 ± 4.9 mg and 4.3 ± 7.5 mg.

Between-group comparisons revealed no significant differences at any time point (all $p > 0.05$).

Predictors of Pain Palliation

Logistic regression analysis was performed to evaluate potential predictors of pain palliation, including age, sex, ECOG status, smoking history, baseline pain score, and radiotherapy schedule. None of these factors demonstrated a statistically significant association with pain relief (all $p > 0.05$).

Discussion

This prospective observational study compared two hypofractionated palliative radiotherapy regimens (30 Gy in 10 fractions vs 20 Gy in 5 fractions) for chest pain palliation in metastatic lung cancer. Both schedules achieved significant and durable reductions in pain scores measured by the Brief Pain Inventory (BPI) and opioid consumption assessed in morphine milligram equivalents (MME). Importantly, our results demonstrated no statistically significant difference between the two regimens at 1, 3, and 6 months, reinforcing the clinical equivalence of these commonly employed fractionation schemes.

Our findings are consistent with earlier randomized trials and systematic reviews that established the efficacy of palliative radiotherapy for symptom control in advanced lung cancer. The Medical Research Council (MRC) studies demonstrated comparable palliation between short- and long-course schedules, with shorter regimens offering improved convenience.[3,7] The Dutch national study also confirmed that different palliative fractionations provided similar efficacy, with equivalent symptom relief across arms.[13] Likewise, Erridge et al. reported no significant differences in symptom control or quality of life between two- and ten-fraction regimens.[12] These data, together with our results, support the non-inferiority of hypofractionated schedules.

In the present study, mean BPI scores declined from nearly 8 at baseline to around 3 at one month, with sustained improvement at six months (4.2 in the 30 Gy/10 arm vs 4.3 in the 20 Gy/5 arm). This degree of pain relief is comparable to earlier studies, where overall response rates ranged from 47–80% in palliative cohorts.[7,11] More than 70% of our patients achieved either complete or partial response at one month, with one-third maintaining complete relief at later follow-up. These outcomes mirror the international consensus definitions of complete and partial pain response, thereby confirming the validity of our methodology.[9,10]

Opioid consumption in our cohort fell from ~26 mg MME at baseline to <5 mg by six months, a significant reduction in analgesic burden. This finding parallels previous reports of declining opioid requirements after palliative thoracic radiotherapy.[4,13] The concurrent decrease in both BPI scores and MME underscores the robustness of our outcome measures, since patient-reported pain relief was supported by objective reductions in analgesic use. Unlike Saito et al., who identified baseline opioid use, neuropathic pain, and hematologic tumor type as independent predictors of pain palliation,[14] our study did not find significant predictors, likely due to smaller sample size and the homogeneity of a single-disease cohort.

This study demonstrates that both 30 Gy/10 fractions and 20 Gy/5 fractions provide significant and durable palliation of chest pain in metastatic lung cancer. At 1 month, more than 70% of patients experienced pain relief, with one-third maintaining complete relief at 3 and 6 months. Importantly, there were no significant differences between regimens in terms of pain scores, opioid reduction, or toxicity. Our results are consistent with randomized trials and meta-analyses that have shown non-inferiority of hypofractionated schedules.[3,7,12,13] The MRC and Dutch Bone Metastasis trials demonstrated comparable pain palliation across different schedules, while shorter regimens improved patient convenience.[12,13] Unlike Saito et al., our study did not identify specific predictors of response, but this is likely due to limited statistical power. Nevertheless, our findings reinforce that pain palliation depends primarily on radiotherapy efficacy rather than baseline demographic or clinical variables.

Limitations

This study has several limitations. Being a single-center observational study with a relatively small sample size, the findings may not be generalizable to broader populations and lack the statistical power to detect subtle differences between regimens. The non-randomized design also introduces the possibility of selection bias and unmeasured confounding, even though baseline characteristics appeared comparable between groups. Follow-up was limited to six months, which may not fully capture the long-term durability of pain palliation, the need for retreatment, or late toxicities. Outcomes were restricted to chest pain and opioid consumption, without assessment of broader quality-of-life measures or functional status, which are important in the palliative setting. In addition, patients with poor performance status or those unable to complete follow-up assessments were underrepresented, potentially limiting applicability to the sickest cohorts. Finally, the study did not correlate radiological tumor response with symptom relief, nor did it explore predictors of pain palliation as reported in larger multicentre analyses.

Conclusion

This prospective observational study demonstrates that both 30 Gy in 10 fractions and 20 Gy in 5 fractions are effective hypofractionated regimens for palliation of chest pain in metastatic lung cancer. Significant reductions in pain scores and opioid consumption were achieved with both schedules, with no meaningful differences in efficacy, durability of response, or toxicity. These findings support the clinical equivalence of the two commonly employed regimens, allowing treatment choice to be guided by patient convenience, performance status, and resource availability. Larger multicenter randomized studies incorporating quality-of-life outcomes and long-term follow-up are warranted to further validate these results and refine palliative radiotherapy strategies.

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