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EFFECTIVENESS OF PALLIATIVE HYPOFRACTIONATED RADIOTHERAPY 21GY IN 7 FX FOR SYMPTOMATIC HEPATOCELLULAR CARCINOMA AND LIVER METASTASIS

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ABSTRACT:
Objectives: To address the gap in evidence regarding the effectiveness of a short-course hypofractionated radiotherapy protocol (21 Gy in 7 fractions) in providing pain relief for patients with symptomatic HCC or liver metastases who are not candidates for curative therapies.
Materials and Methods: After CPSP and CMH Rawalpindi ethical approval, patients underwent CT simulation and received 21 Gy in 7 fractions using 6-MV LINAC-IMRT with image guidance. Pain was assessed by VAS at baseline, 1 and 3 months, with response defined as ≥2-point reduction without increased analgesic use. Clinical outcomes and supportive care were monitored, and data were analyzed using SPSS v25 with appropriate descriptive and paired statistical tests.
Results: Among 23 patients (mean age 42.3±9.63 years), 60.9% were male. Hepatocellular carcinoma was present in 69.6%, and most had moderate-to-severe pain. Mean VAS pain score decreased from 7.03±1.35 at baseline to 4.17±1.62 at 1 month and 3.25±1.83 at 3 months (p=0.00). Bleeding scores also significantly decreased from 5.15±1.48 to 2.45±1.27 and 2.04±1.23 at 1 and 3 months, respectively (p=0.00). Responders were 60.9% at 1 month and 47.8% at 3 months.
Conclusion: It was concluded that palliative hypofractionated radiotherapy (21 Gy in 7 fractions) significantly reduced pain and bleeding in patients with HCC and liver metastases at 1 and 3 months, supporting its feasibility and effectiveness for symptom relief in advanced hepatic malignancies.

KEYWORDS: Palliative Hypofractionated Radiotherapy, Hepatocellular Carcinoma, Liver Metastasis

INTRODUCTION:

Hepatocellular carcinoma (HCC), the most common primary liver cancer, has an age-standardized incidence rate of 22.4 in males and 7.2 in females per 100,000 in Eastern Asia, making it the sixth most common cause of cancer-related death worldwide, according to Globocan 2022 (1). Its incidence has increased globally over the past two decades and is expected to continue rising in some countries (2). Asia and Africa have the highest incidence, largely due to the high prevalence of chronic hepatitis B and C infections (3). Early detection may allow curative treatment through surgery or liver transplantation, while other therapies can relieve symptoms and prolong survival (4, 5). Patients with advanced cancers frequently have liver metastases (1, 6). Most patients have severe or incurable disease, thus curative treatments like resection, transplantation, or ablative therapy are only available in certain situations. In this situation, symptom-directed palliative techniques like radiotherapy (RT) are essential for enhancing patients' quality of life (7, 8).

For individuals with limited performance status , conventional radiation regimens may not be feasible since they usually use moderate doses over extended durations (9). A promising substitute is hypofractionated radiation, which administers larger doses per fraction across fewer sessions (10). The 21 Gy regimen administered in seven parts has demonstrated promise in striking a balance between toxicity, logistical viability, and symptom alleviation (11). However, there isn't much local evidence assessing its efficacy, especially in South Asian settings where patients frequently arrive late and have impaired liver function. The purpose of this study is to assess how well patients with advanced hepatocellular carcinoma or severe liver metastases from other cancers can manage their symptoms with the palliative radiation regimen 21Gy in 7Fx.

The finding will help optimize palliative care methods and enhance the overall management of patients with advanced-stage cancer by examining the impact of RT in reducing the pain associated with symptomatic HCC.

Objective: To address the gap in evidence regarding the effectiveness of a short-course hypofractionated radiotherapy protocol (21 Gy in 7 fractions) in providing pain relief for patients with symptomatic HCC or liver metastases who are not candidates for curative therapies.

MATERIALS AND METHODS:

Study Design: Single arm clinical trial

Study setting: Combined Military Hospital, Rawalpindi.

Duration of the study: The study was conducted from July 25 to Jan 2026.

Sampling Technique:

Non-probability Consecutive sampling.

Sample size: The sample size for this study was calculated using proportions of treatment response based on prior data (12), where a clinically significant improvement in hepatic pain—defined as a reduction of at least 2 points in the worst pain on the Visual Analogue Scale at 1 month. Assuming a two-sided alpha of 0.05 and a power of 80% to detect this difference, the minimum sample size required was estimated using the WHO sample size calculator. This yielded a sample size of 23 participants for this study with Laura A Dawson et al as my reference study.

Selection criteria:

Inclusion criteria:

- Adults aged 18 years or older with Hepatocellular carcinoma (with diagnosis based on biopsy or multi-phasic CT or MRI) or liver metastases (diagnosed on biopsy).
- Cancer unsuitable for or refractory to standard local, regional or systemic therapies.
- Patients with high burden of hepatic cancer (>50% of the liver, more than 10 lesions, locally advanced disease ->10cm or vascular invasion).
- Patients with Child-Pugh class A or B liver function.
- ECOG performance status ≤ 3.
- Score of at least 4 out of 10 for pain and discomfort on VAS.
- Patients with life expectancy of at least 3 months.

Exclusion criteria:

- Patients previously treated with hepatic radiotherapy or hepatic TACE.
- Patients with anticancer therapy in plan.
- Patients with Child-Pugh class C liver dysfunction, uncontrolled coagulopathy, or poor general condition (ECOG PS 04).

Methods: After approval of the study proposal by the College of Physicians and Surgeons Pakistan (CPSP) and the ethical committees of the CMH Rawalpindi. All patients underwent a planning CT simulation scan in the supine position, with the clinical target volume (CTV) encompassing the painful liver tumor, usually including the entire liver, and a planning target volume (PTV) margin of 10–25 mm determined according to respiratory-induced liver motion. Radiotherapy was delivered using a 6-MV LINAC with intensity-modulated radiotherapy (IMRT), with a total prescribed dose of 21 Gy in 7 fractions over 7 days and image-guided verification according to departmental protocol. Data collected included patient demographics, tumor characteristics, radiotherapy regimen, baseline pain, and post-treatment outcomes. The primary outcome was pain response, assessed using the 0–10 Visual Analogue Scale (VAS) at baseline, 1 month, and 3 months after treatment, with pain response defined as a reduction of ≥2 VAS points without an increase in analgesic use. Patients were followed clinically at 1 and 3 months, while supportive care and analgesic use were monitored and adjusted according to standard palliative care guidelines; repeat imaging was performed when clinically indicated. Patients who received at least 5 of the planned 7 fractions were included in the per-protocol analysis. Descriptive statistics were used to summarize patient characteristics and treatment outcomes, with categorical variables presented as frequencies and percentages and continuous variables presented as means with standard deviations or medians with interquartile ranges, as appropriate. Changes in pain relief, bleeding control, and quality of life were assessed using paired t-tests, McNemar's test, or the Wilcoxon signed-rank test, depending on the type and distribution of the variables. A structured study proforma was used to record patient and treatment-related information; data were collected by the researcher and independently checked by a senior colleague before entry to minimize errors and potential bias.

The SPSS version 25 was used to enter and analyze the gathered data.

RESULTS: A total of 23 patients were included in the study, with a mean age of 42.3±9.63 years. Among the participants, 14 (60.9%) were male and 9 (39.1%) were female. Regarding age distribution, 2 (8.7%) patients were aged 20–30 years, 8 (34.8%) were aged 31–40 years, 8 (34.8%) were aged 41–50 years, and 5 (21.7%) were aged >50 years. Hepatocellular carcinoma was the most common tumor type, observed in 16 (69.6%) patients, while 7 (30.4%) had metastatic liver tumors. At baseline, moderate pain was reported by 12 (52.2%) patients, severe pain by 9 (39.1%), and mild pain by 2 (8.7%) patients (Table 1).

Table 1: Baseline Demographic Characteristics (n=23)

Variables	
Age (Years)	42.3±9.63

Gender	
Male	14(60.9%)
Female	9(39.1%)
Age Groups	
20-30 years	2(8.7%)
31-40 years	8(34.8%)
41-50 years	8(34.8%)
>50 years	5(21.7%)
Tumor type	
Hepatocellular carcinoma	16(69.6%)
Metastatic liver tumor	7(30.4%)
Baseline pain severity	
Mild	2(8.7%)
Moderate	12(52.2%)
Severe	9(39.1%)

The mean VAS score was 7.03±1.35 at baseline, which decreased to 4.17±1.62 at 1 month and further decreased to 3.25±1.83 at 3 months following radiotherapy (Table 2).

Table 2: Mean VAS Pain Scores at Baseline, 1 Month, and 3 Months After Radiotherapy (n=23)

Variables	Mean VAS ± SD
Assessment time	
Baseline	7.03±1.35
1 month	4.17±1.62
3 months	3.25±1.83

At 1 month following radiotherapy, 14 (60.9%) patients were classified as responders, while 9 (39.1%) were non-responders. At 3 months, 11 (47.8%) patients remained responders, whereas 12 (52.2%) were classified as non-responders (Table 3).

Table 3: Pain Response at 1 Month and 3 Months Following Radiotherapy

Variables	1 month, n (%)	3 month, n (%)
Pain response		
Responders	14(60.9%)	11(47.8%)
Non Responders	9(39.1%)	12(52.2%)

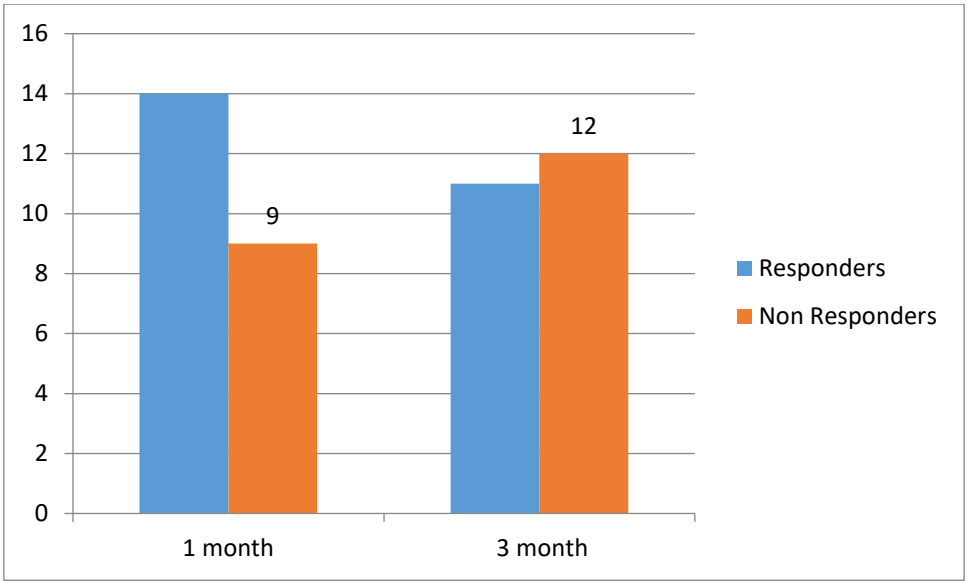


Fig 1: Pain Response at 1 Month and 3 Months Following Radiotherapy

The mean VAS pain score decreased from 7.03 ± 1.35 at baseline to 4.17 ± 1.62 at 1 month, with a mean reduction of 2.86 points (p=0.00). Similarly, the mean bleeding score decreased from 5.15 ± 1.48 at baseline to 2.45 ± 1.27 at 1 month, showing a mean reduction of 2.70 points (p=0.00). Overall, both pain and bleeding scores showed a statistically significant improvement after radiotherapy (Table 4).

Table 4: Comparison of Pain and Bleeding Control Before and After Radiotherapy

Variables	Baseline Mean ± SD	1 Month Mean ± SD	Mean Difference	p-value
Pain response	7.03 ± 1.35	4.17 ± 1.62	2.86	0.00
Bleeding score	5.15 ± 1.48	2.45 ± 1.27	2.70	0.00

The mean VAS pain score decreased from 7.03 ± 1.35 at baseline to 3.25 ± 1.83 at 3 months, showing a mean reduction of 3.78 points (p=0.00). Similarly, the mean bleeding score decreased from 5.15 ± 1.48 at baseline to 2.04 ± 1.23 at 3 months, with a mean reduction of 3.11 points (p=0.00). Overall, both pain and bleeding scores demonstrated statistically significant improvement at 3 months following radiotherapy (Table 5).

Table 5: Comparison of Outcomes at Baseline and 3 Months after Radiotherapy

Variables	Baseline Mean ± SD	3 Month Mean ± SD	Mean Difference	p-value
Pain response	7.03 ± 1.35	3.25 ± 1.83	3.78	0.00
Bleeding score	5.15 ± 1.48	2.04 ± 1.23	3.11	0.00

DISCUSSION:

The present study aim is to evaluate a palliative hypofractionated radiotherapy regimen (21 Gy in 7 fractions) for symptom relief in patients with symptomatic hepatocellular carcinoma (HCC) and liver metastases. Treatment yielded significant clinical improvements: mean VAS pain scores decreased from baseline 7.03±1.35 to 4.17±1.62 at one month and 3.25±1.83 at three months. Bleeding scores similarly fell from 5.15±1.48 to 2.45±1.27 and 2.04±1.23 over the same intervals. These findings indicate that this schedule is an effective option for symptom management in advanced hepatic malignancies. In the context of HCC, effective palliative care is especially important since patients with advanced disease often experience pain, discomfort in the abdomen, and other tumor-related symptoms. According to guidelines, depending on the patient demographic, the prevalence of pain in HCC might range from roughly 22% to 66.8%. However, changing medication metabolism can complicate pain management in patients with underlying liver impairment (13).

Patients showed a statistically significant reduction of 2.86 points in their VAS pain score at one month after therapy, and at three months, the cumulative drop was 3.78 points (p<0.001). These findings are consistent with the body of knowledge about palliative hepatic radiotherapy. Notably, 48% of patients with HCC or liver

metastases experienced significant symptom palliation at one month (n=41), with favorable overall treatment tolerability, according to Soliman et al.

At one month after palliative radiation, a follow-up study of 52 patients with symptomatic HCC showed a 51.9% total symptom response rate, with a roughly 50% response rate among patients with pain (median time to recurrence: 89 days). The new cohort's three-month sustained pain reduction further supports the proven effectiveness of palliative hepatic irradiation. The 21 Gy in 7 fractions regimen, which has been verified in larger liver metastasis cohorts with abdominal pain response rates of approximately 80% and a median response length of 13 weeks, is closely aligned with historical data. This dose fraction scheme, which is acknowledged by current consensus reviews as a standard schedule for whole-liver irradiation, shows repeatable symptom control in line with previous research. Nine patients (39.1%) did not exhibit a reaction after one month, whereas 14 patients (60.9%) were categorised as responders. Twelve patients (52.2%) did not respond after three months, while eleven individuals (47.8%) continued to do so. In the context of palliative care for advanced cancers, the drop in the percentage of responders with time is conceivable and could be explained by either restarted tumour progression or the short duration of palliative symptom management. Our finding aligns with another study findings by Yeung et al.(1) consistent with findings where, following palliative liver irradiation for HCC, symptom improvement was observed in approximately half of the patients after one month; the median duration of symptom control was roughly three months. The data presented here therefore show a similar temporal pattern: marked early symptom improvement, with the proportion of responders declining over time. This score decreased from 5.15 ± 1.48 to 2.45 ± 1.27 after one month and further to 2.04 ± 1.23 after three months, representing a reduction of 2.70 and 3.11 points, respectively. Both changes were statistically significant ($p < 0.001$).

The hemostatic efficacy of palliative radiotherapy is well recognized, with systematic reviews confirming its utility for tumor-related hemorrhage across diverse malignancies (14). Direct comparison with our bleeding outcomes requires cautious interpretation, given the heterogeneity of primary tumor types, fractionation schedules, and bleeding assessment scales in the published literature. Nevertheless, the statistically significant score reduction observed here demonstrates that this regimen provides meaningful hemostatic control alongside effective pain palliation in advanced hepatic disease.

The use of 21 Gy delivered in 7 fractions provides a balanced approach between achieving adequate local symptom control and preserving the remaining functional liver tissue (15). As the liver has a limited tolerance to radiation, dose escalation may be problematic, particularly in patients with extensive hepatic tumor burden. Previous studies of whole-liver irradiation have demonstrated that 21 Gy in 7 fractions is a feasible regimen in the palliative treatment setting (12). The current cohort comprised 16 patients (69.6%) with HCC and 7 (30.4%) with liver metastases a clinically relevant combination given that both primary and secondary hepatic malignancies frequently cause severe local symptoms. Combining these patient populations aligns with established literature; for example, Soliman et al.(7) evaluated 21 patients with HCC alongside 20 with liver metastases, observing a 48% symptom response rate at one month. Similarly, palliative irradiation limited to metastases has shown distinct benefit, such as a retrospective series of 73 patients

CONCLUSION:

It was concluded that Palliative hypofractionated radiotherapy (21 Gy in 7 fractions) provide significant symptomatic relief in patients with hepatocellular carcinoma and liver metastases. Statistically significant reductions in both pain and bleeding scores were observed at 1 and 3 months post-treatment, demonstrating durable symptom control and a high rate of sustained pain response. These findings confirm that a 21 Gy in 7-fraction regimen is a feasible, effective palliative approach for mitigating symptom burden in advanced hepatic malignancies. Larger, prospective studies with extended follow-up are recommended to validate these outcomes.

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