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Original Article

Role of Radiotherapy in Improving Quality of Life in Patients with Hepatocellular Carcinoma and Liver Metastasis

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) and liver metastases (LM) are often associated with significant symptoms such as pain and abdominal discomfort, impacting the quality of life (QoL) of affected patients. Current treatments vary in effectiveness and often leave a substantial unmet medical need in symptom management.

Objective: This study aimed to assess the efficacy of external radiation therapy (ERT) in alleviating symptoms and improving the QoL in patients with HCC and LM, focusing on those presenting primarily with pain or abdominal discomfort.

Methods: After institutional review board approval, patients with HCC or painful LM, not previously treated with tumor resection, radiofrequency ablation, or systemic therapy, were included. Eligible participants exhibited symptoms such as pain, nausea, and fatigue, and had a performance status of 0-2. A single fraction dose of ERT was administered, and symptom relief was evaluated using the Brief Pain Inventory (BPI) and QoL using the Functional Assessment of Cancer Therapy-Hepatobiliary (FACT-Hep) and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30). Completion rates of these questionnaires were tracked at baseline, one week, and one month post-treatment.

Results: Of the 43 patients enrolled (23 HCC, 20 LM), significant improvement in the FACT-G TOI was observed in 34% of patients at one month post-ERT. When focusing on those with pain or abdominal discomfort, 59% reported clinically significant symptom relief. However, QoL improvement was noted in only about one quarter of patients, with one third experiencing worsening QoL at one month. Questionnaire completion rates were high initially but decreased over time, reflecting the challenging nature of the patient population.

Conclusion: ERT demonstrated potential benefits in symptom relief, particularly for pain and abdominal discomfort in patients with HCC and LM. Nonetheless, the impact on overall QoL was mixed, highlighting the need for further research into optimizing therapeutic strategies for this patient group.

Keywords: Hepatocellular carcinoma, liver metastases, external radiation therapy, quality of life, symptom management, pain relief, abdominal discomfort, clinical oncology, palliative care.

INTRODUCTION

Radiotherapy has increasingly been recognized as a potentially valuable treatment option for hepatocellular carcinoma (HCC), a major liver malignancy and the third leading cause of cancer-related deaths worldwide (1). Despite its efficacy in local tumor control, with reported local control rates ranging from 71% to 86% at 2 years in selected patient populations treated with conformal radiotherapy (CRT) or stereotactic body radiation therapy (SBRT), its application remains limited due to the extent of liver involvement, poor underlying liver function, or the presence of extra-hepatic metastases (2). Current treatment protocols primarily include systemic therapy, trans-arterial chemo-embolization (TACE), or best supportive care. However, there is scant research on the utilization of external radiation therapy (ERT) for treating HCC and liver metastases, and it is not routinely recommended in several major clinical guidelines (3-5).

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The European Association for the Study of the Liver and the American Association for the Study of Liver Diseases have both suggested that ERT's role in HCC management is still under investigation, and existing studies do not support its routine use. Conversely, guidelines from the Asian Pacific Association for the Study of the Liver and the Korean Liver Cancer Society present a more favorable view. These guidelines suggest that SBRT and charged particle therapy can be reasonable options for patients who have failed other local therapies and also consider ERT as a viable option for symptomatic liver metastases in various clinical settings, particularly when patients exhibit a Child-Pugh class A or B liver function and the irradiated total liver volume receiving over 30 Gy remains under 60% (6, 7).

The reluctance to widely adopt ERT stems primarily from the lack of randomized clinical trials demonstrating its efficacy. Historical studies involving whole-liver radiation therapy, typically delivering doses ranging from 20 to 30 Gy, have indicated some benefits in symptom management and occasional tumor shrinkage. Nevertheless, these outcomes were often observed in patients who were also undergoing chemotherapy, and assessments did not rigorously evaluate patient-reported symptom control or quality of life (QoL). More recently, a specific study focused on the palliative effects of RT on liver metastases symptoms, using a regimen of 10 Gy in two fractions, reported a physician-observed symptom response rate of 54% at two weeks, although this was accompanied by significant toxicity in some cases (8, 9).

Despite these challenges, the potential of radiotherapy to improve QoL for patients with advanced HCC or liver metastases remains significant, urging the need for more comprehensive and methodologically sound research to better define its role in the treatment spectrum of liver cancers. Such evidence is crucial to guide clinical practice and refine existing treatment guidelines, potentially expanding the therapeutic options available to this patient population.

MATERIAL AND METHODS

After receiving approval from the institutional research ethics committee, a study was conducted to evaluate the effectiveness of radiotherapy in palliating symptoms and improving the quality of life for patients with hepatocellular carcinoma (HCC) and painful liver metastases (LM). The study adhered to the ethical principles outlined in the Declaration of Helsinki.

Patients eligible for inclusion were diagnosed with HCC or had painful liver metastases, had not undergone any previous tumor resection, radiofrequency ablation, or systemic therapy, and exhibited symptoms such as abdominal pain, body aches, nausea, or fatigue. They were required to have a performance status of 0-2 and fall within the Child-Pugh A or B classification. Exclusion criteria included hemoglobin levels below 8 g/dl, platelet counts under 50000 per microliter, classification as Child-Pugh C, or having received any systemic treatment or undergoing trans-arterial chemo-embolization (TACE) in the past month.

Prior to the radiation treatment, all patients were premedicated with intravenous granisetron 3 mg, esomeprazole 40 mg, and dexamethasone 4 mg. The planning target volume covered the entire liver, guided by ultrasound imaging. The prescribed radiation dose was 7 Gy delivered in one fraction using parallel opposed fields on a cobalt-60 machine, selected for its safety and convenience as a typical dose for palliative care.

For the assessment of symptomatic improvement and quality of life, the Modified Brief Pain Inventory (BPI) and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30), along with the Functional Assessment of Cancer Therapy-Hepatobiliary (FACT-Hep), were utilized. The BPI and these questionnaires were completed by patients or their attendants at baseline and one month post-treatment to measure pain intensity, interference, and various aspects of quality of life. The FACT-Hep included both the general cancer-specific quality of life indicators of the Functional Assessment of Cancer Therapy-General (FACT-G) and the hepatobiliary subscale (HBS). Adverse events were monitored and recorded according to the Common Toxicity Criteria for Adverse Events (CTCAE) version 5.0.

Data collection was systematically conducted, and all data were anonymized for analysis. The statistical analysis was performed using SPSS version 25. The primary endpoint was defined as the proportion of patients who achieved clinically significant improvements in their symptoms, specifically a reduction in BPI pain scores of 2 or more points, a change of 10 points in EORTC QLQ-C30 scores, at least 5 points in HBS, and changes of 6 and 8 points in FACT-G and FACT-Hep scores, respectively. The study sample consisted of 43 patients, with 23 diagnosed with HCC and 20 with LM.

This study design ensured a comprehensive evaluation of the radiotherapy's impact on the symptoms and quality of life for patients with advanced liver cancers, setting a foundation for future research and potential modifications in treatment guidelines.

RESULTS

In a recent study investigating the effects of radiotherapy on patients with hepatocellular carcinoma (HCC) and liver metastases (LM), a comprehensive analysis of symptom improvement and quality of life was conducted. The study's findings, summarized in several tables and figures, provide insights into the treatment's efficacy.

Patient characteristics, detailed in Table 1, illustrate the demographic and clinical profile of the participants. A total of 43 patients were enrolled, with 23 diagnosed with HCC and 20 with LM. The median age was 49 years, ranging from 29 to 76 years. The majority of patients were male (27 out of 43), and they presented with varying degrees of liver involvement and symptoms such as pain, abdominal discomfort, nausea, vomiting, and fatigue. Most patients were within the Child-Pugh A or B stage, indicative of less severe liver disease, and a roughly equal number had either no extra-hepatic disease or presented with it.

Table 1: Patient Characteristics

Characteristic	Total	Details
Tumor Type		
Hepatocellular carcinoma (HCC)	23	
Liver metastases (LM)	20	
Age (years)		
Median Age	49	
Range	29-76	
Gender		
Male	27	
Female	16	
ECOG Performance Status		
0	14	
1	15	
2	14	
Percentage of Liver Involved		
<25%	8	
25-50%	12	
50-75%	17	
>75%	6	
Presence of Extra-hepatic Disease		
Yes	21	
No	22	
Main Symptom		
Pain	28	
Abdominal Discomfort	8	
Nausea/Vomiting	3	
Fatigue	3	
Underlying Liver Disease		
Hepatitis B	19	
Hepatitis C	14	
Child-Pugh Stage		
A	29	
B	14	

Table 2: Completion Rates for BPI, FACT-Hep, and EORTC QLQ-C30 Questionnaires

Questionnaire	Follow-Up	Completion Rate (%)	HCC Patients	LM Patients
BPI	Baseline	97	96	90
	1 Week	64	60	68

	1 Month	76	84	67
FACT-Hep	Baseline	94	89	95
	1 Week	69	54	74
	1 Month	64	77	66
EORTC QLQ-C30	Baseline	86	74	90
	1 Week	66	58	68
	1 Month	57	49	61

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The completion rates for various quality of life and symptom assessment tools are reported in Table 2. At baseline, the completion rate for the Brief Pain Inventory (BPI) was notably high at 97%, with a slight decrease to 76% at the one-month follow-up. The Functional Assessment of Cancer Therapy-Hepatobiliary (FACT-Hep) and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30) also showed high initial completion rates, which generally decreased over time, reflecting challenges in sustained patient follow-up.

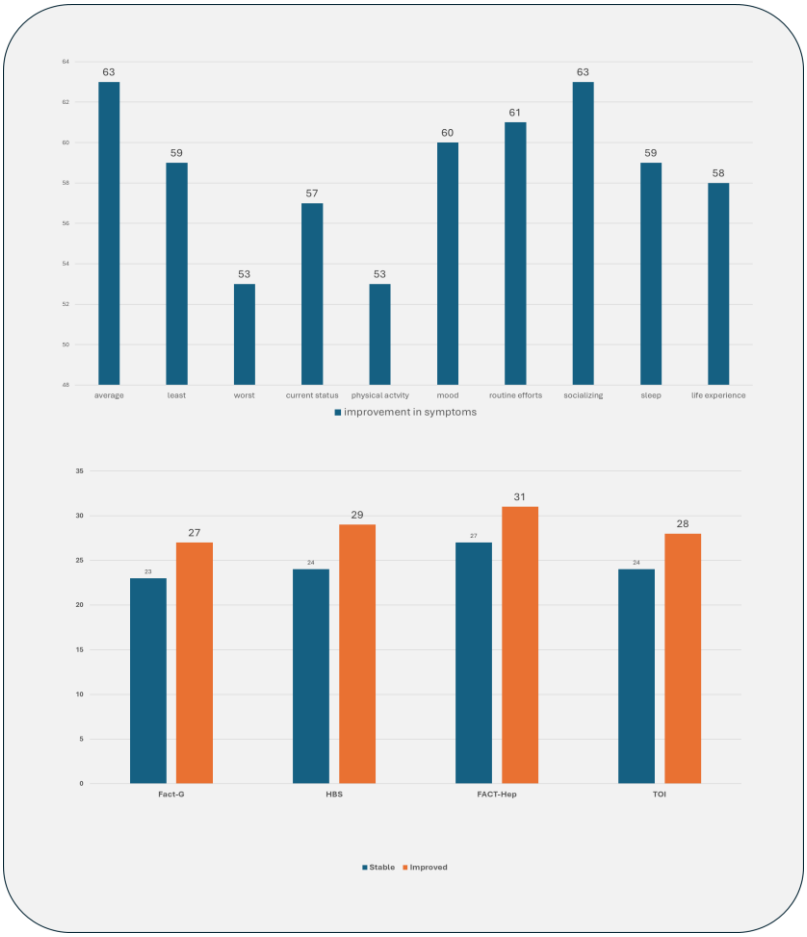

Figure 1, Figure 2 Study Characteristics, Symptoms Improvement

The results of the symptom improvement assessments (Figure 1) show that 63% of patients reported an average improvement across all symptoms. Socializing and mood improvements were particularly notable, each observed in 63% of patients, suggesting significant enhancements in these quality of life aspects post-treatment. Physical activity showed the least improvement, with 53% of patients noting betterment, highlighting areas where additional supportive care might be needed.

Quality of life assessments, as illustrated in Figure 2, show that improvements were more frequently reported than stable conditions across all measured domains. The Hepatobiliary Scale (HBS) and FACT-Hep tools showed that 27% and 29% of patients, respectively, reported improvements, compared to stability, which hovered around 24% and 27%. These findings suggest that radiotherapy may significantly enhance specific aspects of life quality in cancer patients.

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Furthermore, Figure 3 provides a detailed breakdown of the percentages of patients who experienced stable versus improved symptoms across various dimensions such as physical activity, emotional stability, and cognitive function. Notably, improvements in pain and nausea were reported by 29% and 26% of patients, respectively. This is particularly significant considering these symptoms are among the most challenging aspects of patient care in HCC and LM, reinforcing the potential of radiotherapy to alleviate substantial burdens in these patients.

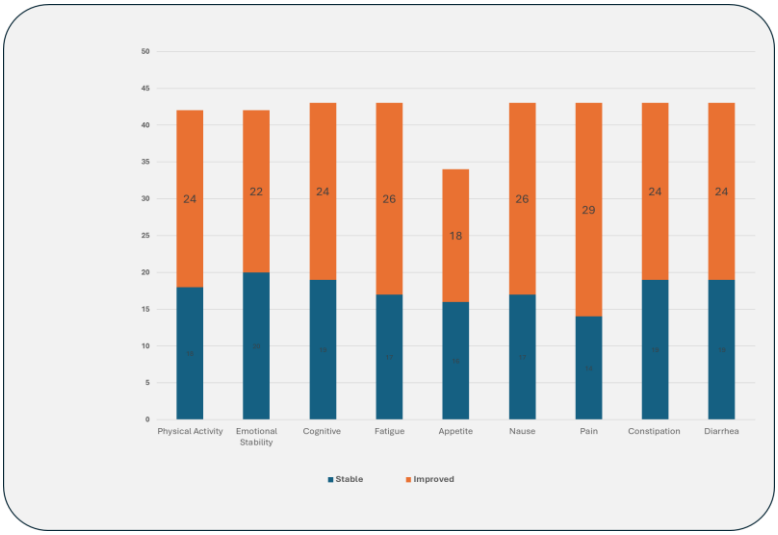

Figure 3 Number of patients vs Improvement Status

The aggregated data from this study underscore the potential of radiotherapy to markedly improve both the symptoms and overall quality of life for patients suffering from advanced liver cancers. The numerical improvements across various patient-reported outcomes highlight the therapy's efficacy and underscore the importance of continued research and patient monitoring in this field.

DISCUSSION

In the study conducted, external radiation therapy (ERT) was administered to patients with hepatocellular carcinoma (HCC) and liver metastases, resulting in a clinically significant improvement in Functional Assessment of Cancer Therapy-General Trial Outcome Index (FACT-G TOI) in 34% of patients after one month of treatment. The efficacy of ERT was particularly notable among patients whose primary symptoms were pain or abdominal discomfort, with 59% experiencing significant symptom improvement. This outcome suggests the potential utility of pain and abdominal discomfort as primary symptoms for inclusion criteria in future studies.

However, the improvement in quality of life (QoL) was modest, with approximately a quarter of the study cohort noting betterment, while around one third reported a worsening of QoL at the first-month mark. The decline in QoL post-treatment is consistent with findings from other studies involving advanced-stage HCC patients, where deteriorations were often associated with worse Child-Pugh scores, lower albumin levels, and higher bilirubin levels, indicating that treatment may exacerbate the already poor QoL in these patients (16).

Despite these challenges, the response rates for the study were relatively high, with completion rates for questionnaires being above 50% at the first month, although they declined to 44% subsequently. This decrease can be attributed to the poor life expectancy and the deteriorating health of the participants, a common issue in studies involving terminally ill patients (17-19).

The research was limited to a single fraction dose of radiotherapy, and about 40% of patients reported a reduction in symptoms such as pain or abdominal discomfort. However, the benefits were constrained by the overall poor prognosis and the advanced nature of the disease in the patient population, factors that may have diluted the observable benefits of the treatment (18, 19).

This study highlights several strengths, including the focus on a patient group with limited treatment options and the use of validated instruments to measure symptom relief and QoL. Nevertheless, the limitations are notable, primarily the small sample size and the short follow-up period, which restrict the generalizability and the depth of conclusions that can be drawn about the long-term benefits of ERT. Moreover, the study's observational nature and the lack of a control group limit the ability to attribute changes in symptoms and QoL directly to the treatment provided (20).

CONCLUSION

In conclusion, while ERT shows promise in symptom management, particularly for pain and abdominal discomfort in HCC and LM patients, the impact on overall QoL is less certain and often negative in the short term. Future studies should consider expanding the sample size and including a longer follow-up period to better understand the potential and limitations of ERT in this patient population. Additionally, the incorporation of a control group could provide a more robust framework for evaluating the true efficacy of the treatment. These recommendations aim to refine the approach in future trials, potentially leading to more targeted and effective treatment protocols for this challenging patient demographic.

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