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Radiotherapy outcomes in NAFLD patients supported by isocaloric low-carbohydrate high-protein diet and transient elastography monitoring

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ABSTRACT

Background: Radiotherapy-induced liver injury (RILI) is a significant complication in cancer treatment, particularly among patients with pre-existing non-alcoholic fatty liver disease (NAFLD). Non-invasive monitoring with transient elastography allows early detection of steatosis and fibrosis, while targeted nutritional support such as an isocaloric low-carbohydrate high-protein (LC-HP) diet may enhance hepatic resilience during therapy. ***Materials and Methods:*** One hundred adult NAFLD patients undergoing radiotherapy for solid tumors, mainly involving the gastrointestinal, hepatobiliary, gynecologic, and thoracic regions were prospectively enrolled in a 6-month LC-HP dietary intervention. Clinical assessments included anthropometry, biochemical markers, body composition, immune parameters, and transient elastography values [controlled attenuation parameter (CAP) and liver stiffness measurement (LSM)]. In these patients, part of the non-tumorous liver was located within the low- to moderate-dose region of the radiotherapy fields, as determined from the treatment planning data, resulting in partial hepatic irradiation. Radiotherapy data (cancer type, intent, field, and dose) were documented to contextualize hepatic exposure. ***Results:*** Despite concurrent radiotherapy, CAP and LSM values declined significantly ($P < 0.05$), indicating reductions in hepatic steatosis and fibrosis. BMI, waist circumference, and body fat percentage decreased, while skeletal muscle mass increased. Serum cholesterol and triglycerides decreased, prealbumin levels improved, and lymphocyte counts rose significantly ($P < 0.001$). These findings suggest that structured nutritional support can mitigate hepatic stress and preserve immune competence during radiotherapy. ***Conclusion:*** Integrating an isocaloric LC-HP diet with transient elastography monitoring improved hepatic, metabolic, and immune outcomes in NAFLD patients receiving radiotherapy.

INTRODUCTION

Radiotherapy remains a cornerstone of cancer treatment, but hepatic toxicity continues to pose a serious clinical challenge, particularly in patients with pre-existing liver vulnerability. Radiation-induced liver disease (RILD) is a dose-limiting complication characterized by hepatic dysfunction, fibrosis, and in severe cases, liver failure. Patients with underlying metabolic disorders such as non-alcoholic fatty liver disease (NAFLD) are especially at risk, as hepatic steatosis and fibrosis increase susceptibility to radiation-related injury and may compromise treatment tolerance and outcomes [1, 2]. Clinical and dosimetric studies have further demonstrated that the risk of classical and non-classical RILD increases with higher mean liver dose and larger irradiated liver volumes, particularly in patients with pre-existing chronic liver disease, underscoring the need for strategies that preserve hepatic reserve during radiotherapy [3, 4].

NAFLD has emerged as the most prevalent chronic liver disease worldwide, with a rising incidence parallel to obesity, insulin resistance, and metabolic syndrome [5, 6]. Epidemiological data suggest that approximately one quarter of the global adult population is affected, and NAFLD is strongly associated with type 2 diabetes, cardiovascular disease, and overall mortality, highlighting its importance as a systemic metabolic disorder in oncology patients [7]. While lifestyle modification remains the cornerstone of management, the optimal

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dietary approach remains controversial. Low-carbohydrate high-protein (LC-HP) diets have shown promise in improving body composition, lipid metabolism, and hepatic steatosis, but long-term efficacy and safety remain under investigation [8]. For oncology patients, such nutritional strategies may play a critical role in supportive care by enhancing hepatic resilience, maintaining nutritional status, and mitigating treatment-related complications.

Recent advances in imaging have provided new opportunities for precise monitoring of hepatic changes during therapy. Transient elastography, a rapid and reproducible ultrasound-based modality, enables simultaneous assessment of liver stiffness (reflecting fibrosis) and the controlled attenuation parameter (CAP, reflecting steatosis) [9, 10]. Multiple studies in NAFLD cohorts have validated transient elastography against histology and other elastography techniques, and it is increasingly incorporated into clinical practice and research protocols as a non-invasive tool for staging and longitudinal follow-up of fatty liver disease [11-13]. Unlike liver biopsy, elastography is non-invasive and suitable for serial monitoring, making it particularly valuable for patients undergoing radiotherapy who require close surveillance of liver health. Despite its potential, few studies have systematically explored the combined impact of dietary interventions and radiotherapy on hepatic outcomes using elastography.

Based on this background, the present study aimed to evaluate the efficacy of an isocaloric LC-HP diet in improving hepatic steatosis, fibrosis, body composition, and metabolic parameters in NAFLD patients undergoing radiotherapy, with transient elastography as the primary imaging tool. To our knowledge, no previous prospective study has specifically investigated an isocaloric LC-HP diet in NAFLD patients receiving radiotherapy while using transient elastography to serially monitor hepatic steatosis and fibrosis. By integrating nutritional support with non-invasive hepatic monitoring, this work seeks to provide evidence for strategies that may reduce radiation-related hepatic injury, support immune competence, and improve resilience during cancer treatment.

MATERIALS AND METHODS

Study subjects

Adult patients (≥18 years) with a confirmed diagnosis of non-alcoholic fatty liver disease (NAFLD) who were undergoing radiotherapy for cancer management at Youjiang Ethnic Medical College Affiliated Hospital were prospectively recruited. Eligible participants provided written informed consent. Exclusion criteria included alcoholic liver disease (ALD), hepatitis C virus genotype 3 infection, autoimmune hepatitis, secondary causes of fatty liver such as drug-induced steatosis (e.g., tamoxifen, glucocorticoids), hypothyroidism, Mauriac syndrome, severe systemic illness, or contraindications to radiotherapy. The study protocol was approved by the Ethics Committee of Youjiang Ethnic Medical College Affiliated Hospital and conducted in accordance with the principles of the Declaration of Helsinki.

Radiotherapy context

All participants were receiving external beam radiotherapy as part of oncologic treatment. Primary tumor sites included mainly gastrointestinal, hepatobiliary, gynecologic, breast, and thoracic malignancies, treated with conventional fractionated external beam radiotherapy delivered by a medical linear accelerator (e.g., Varian Clinac iX, Varian Medical Systems, Palo Alto, CA, USA) using 6–10 MV photon beams. Treatment planning was performed with a three-dimensional conformal or intensity-modulated radiotherapy technique on a commercial planning system (e.g., Eclipse, Varian Medical Systems, Palo Alto, CA, USA). Radiotherapy details - including primary cancer type, treatment intent (curative or palliative), radiation field, prescribed dose (Gy), and hepatic dose-volume parameters where available - were documented from medical records. For curative-intent treatments, the prescribed tumor dose typically ranged from 50 to 60 Gy in daily fractions of 1.8–2.0 Gy, whereas palliative regimens commonly delivered 30 Gy in 10 fractions of 3.0 Gy. For each patient, liver dose–volume parameters such as mean liver dose and the percentage of normal liver volume receiving ≥20 Gy (V20) and ≥30 Gy (V30) were extracted from the dose–volume histogram to characterize hepatic exposure. In most cases, a portion of the non-tumorous liver was included within the low- to moderate-dose region of the treatment fields, resulting in partial hepatic irradiation. These data were used to contextualize hepatic exposure and to evaluate the potential interaction between radiotherapy and nutritional intervention outcomes.

Intervention methods

At baseline, a structured survey was conducted to record dietary preferences, family history of fatty liver disease, and medication use. Educational leaflets were distributed to improve awareness of fatty liver and to enhance dietary compliance. Participants were then assigned an isocaloric low-carbohydrate high-protein (LC-HP) diet. Height and weight were measured by trained staff, and body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Ideal body weight was estimated as height (cm) minus 105, and waist circumference (WC) was measured according to standardized protocols. Daily caloric needs were calculated as ideal

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body weight (kg) multiplied by an energy coefficient [g/(kg·d)]. Protein intake was prescribed at more than 20% of total daily energy or 1.5 g/kg/day, not exceeding 30% of energy or 2.0 g/kg/day. To ensure compliance, protein supplementation was provided with isolated whey protein (Jingteng Medical Technology Co., Ltd., China), 20 g dissolved in warm water or milk once or twice daily, tailored to individualized nutritional assessment. The overall macronutrient distribution was 40–45% carbohydrate, 20–30% protein, and 20–30% fat.

Observation indicators

Assessments were performed at baseline and after 6 months of intervention. Anthropometric indices included BMI and WC. Biochemical analyses comprised total protein (TP), albumin (ALB), prealbumin (PA), iron (Fe), zinc (Zn), hemoglobin (Hb), blood urea nitrogen (BUN), creatinine (Cr), uric acid (UA), total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL). Body composition measurements included percentage of body fat, protein, and water, skeletal muscle content, and waist -to-hip ratio using a multi-frequency bioelectrical impedance analyzer (e.g., InBody 770, InBody Co., Ltd., Seoul, Korea). Liver imaging was conducted using transient elastography (FibroTouch transient elastography system, Hisky Medical Technologies, Beijing, China), performed by certified physicians to determine controlled attenuation parameter (CAP, dB/m) and liver stiffness measurement (LSM, kPa). Immune function was assessed through lymphocyte counts, given the known impact of radiotherapy on lymphopenia and treatment tolerance.

Statistical analysis

Data were analyzed using SPSS version 22.0 (IBM Corp., USA). Normally distributed variables were expressed as mean ± standard deviation (SD) and compared using paired t-tests or one-way ANOVA, as appropriate. Non-normally distributed variables were analyzed with the Mann–Whitney U test. Categorical variables were summarized as frequencies and percentages, with group differences assessed using the χ^2 test. A P-value < 0.05 was considered statistically significant.

RESULTS

Baseline characteristics

A total of 100 patients with NAFLD undergoing radiotherapy were enrolled. The mean age was 44.8 ± 12.5 years (range 22–68), including 57 males (57.0%) and 43 females (43.0%). Comorbidities included a family history of fatty liver in 35 patients (35.0%), type 2 diabetes in 31 (31.0%), and obesity in 24 (24.0%). Regarding medication use, 23 patients (23.0%) received hypoglycemic drugs (19 of whom used metformin), 16 (16.0%) were on lipid-lowering drugs (13 of whom used atorvastatin), and 26 (26.0%) were taking antihypertensive drugs (15 of whom used ARBs). Dietary habits revealed frequent intake of red meat in 54 patients (54.0%), sugary beverages in 39 (39.0%), and insufficient vegetable intake (<400 g/day) in 48 (48.0%). Primary tumor sites were mainly located in the gastrointestinal, hepatobiliary, gynecologic, breast, and thoracic regions, and most patients received conventional fractionated external-beam radiotherapy with curative intent, while a smaller proportion were treated with palliative regimens. In typical curative schedules, the prescribed tumor dose was around 50 –60 Gy in daily fractions of 1.8–2.0 Gy, whereas common palliative regimens delivered approximately 30 Gy in 10 fractions of 3.0 Gy, resulting in partial irradiation of the non-tumorous liver in the majority of cases. These baseline characteristics are consistent with typical NAFLD profiles in cancer patients, highlighting multiple metabolic risk factors for radiation-induced hepatic vulnerability (table 1).

Table 1. Baseline characteristics of the study population.

Indicator	Category/ value	Percentage (%)
Age (years)	44.8±12.5 (range 22-68)	–
Gender (Male/Female)	57/43	57.0/43.0
Family history of fatty liver	35	35.0
Type 2 diabetes	31	31.0
Obesity	24	24.0
Medication history		
Hypoglycemic drugs (Metformin: 19 cases)	23	23.0
Lipid-regulating drugs (Atorvastatin: 13 cases)	16	16.0
Antihypertensive drugs (ARBs: 15 cases)	26	26.0
Dietary preferences		
Red meat intake ≥5 times/week	54	54.0
Sugary drinks ≥3 times/week	39	39.0
Vegetable intake <400 g/day	48	48.0

Anthropometric outcomes

Compared with pre-radiotherapy baseline measurements, significant improvements were observed in anthropometric indices after six months of dietary intervention and completion of radiotherapy. Both BMI and waist circumference (WC) decreased significantly (P < 0.05). The reduction in BMI (mean change: –1.5 kg/m^2, P = 0.001) and WC (mean change: –4.2 cm, P = 0.002) indicated reduced abdominal adiposity, suggesting that the LC-HP diet was effective even under the metabolic stress of concurrent cancer treatment. Paired baseline and post-radiotherapy values for BMI and WC are summarized in table 2.

Metabolic outcomes

Blood lipid and biochemical markers also demonstrated significant improvements. Relative to pre-radiotherapy baseline, total cholesterol (TC) and triglycerides (TG) levels decreased significantly (P =

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0.012 and P = 0.003, respectively). Protein nutritional indices, including total protein (TP) and albumin (ALB), increased significantly (P = 0.016 and P = 0.049). Hemoglobin (Hb) and zinc (Zn) showed slight increases, though these were not statistically significant (P = 0.214 and P = 0.352). These findings indicate that the intervention improved systemic metabolism and preserved nutritional status during radiotherapy. Detailed pre- and post-radiotherapy values of metabolic indicators are presented in table 3.

Table 2. Anthropometric parameters before radiotherapy and 6 months after completion of radiotherapy and LC-HP dietary intervention (n = 100).

Parameter	Baseline (pre-radiotherapy) [mean ± SD]	6 months post-radiotherapy [mean ± SD]	Mean change	P-value
BMI (kg/m²)	28.5 ± 3.4	27.0 ± 3.2	−1.5	0.001
Waist circumference (cm)	96.2 ± 8.7	92.0 ± 8.5	−4.2	0.002

Table 3. Metabolic indicators before radiotherapy and 6 months after completion of radiotherapy and LC-HP dietary intervention (n = 100).

Parameter	Baseline (pre-radiotherapy) [mean ± SD]	6 months post-radiotherapy [mean ± SD]	Mean change	P-value
Total cholesterol (TC, mmol/L)	5.50 ± 0.90	5.10 ± 0.85	−0.40	0.012
Triglycerides (TG, mmol/L)	2.10 ± 0.80	1.70 ± 0.70	−0.40	0.003
Total protein (TP, g/L)	69.0 ± 5.5	71.5 ± 5.3	+2.5	0.016
Albumin (ALB, g/L)	40.0 ± 3.8	41.2 ± 3.6	+1.2	0.049
Hemoglobin (Hb, g/L)	132 ± 15	134 ± 14	+2	0.214
Zinc (Zn, μmol/L)	10.5 ± 1.8	10.8 ± 1.9	+0.3	0.352

Body composition

Analysis of body composition showed favorable changes following intervention. Compared with pre-radiotherapy baseline values, body fat percentage decreased significantly (P = 0.009), while skeletal muscle content and protein percentage increased significantly (P = 0.023 and P = 0.005, respectively). The water percentage also improved significantly (P = 0.034). These results suggest that the LC-HP diet helped maintain lean body mass and prevent sarcopenia, which is particularly important for patients undergoing radiotherapy. Corresponding pre- and post-radiotherapy body composition data are summarized in table 4.

Table 4. Body composition parameters before radiotherapy and 6 months after completion of radiotherapy and LC-HP dietary intervention (n = 100).

Parameter	Baseline (pre-radiotherapy) [mean ± SD]	6 months post-radiotherapy [mean ± SD]	Mean change	P-value
Body fat percentage (%)	33.0 ± 5.8	30.8 ± 5.5	−2.2	0.009
Skeletal muscle content (kg)	25.5 ± 4.2	26.3 ± 4.4	+0.8	0.023
Protein percentage (% body weight)	16.0 ± 1.1	16.5 ± 1.1	+0.5	0.005
Total body water (%)	48.2 ± 4.0	49.5 ± 4.1	+1.3	0.034

Liver elastography parameters

Transient elastography revealed marked improvements in hepatic parameters. Liver stiffness measurements (LSM) declined significantly compared with pre-radiotherapy baseline (P = 0.015), while CAP values, reflecting hepatic steatosis, also decreased (P = 0.003). These findings indicate that the LC-HP intervention mitigated progression of steatosis and fibrosis in patients at high risk of radiation-induced hepatic injury. Baseline and post-radiotherapy CAP and LSM values are shown in table 5.

Table 5. Liver elastography parameters (CAP and LSM) before radiotherapy and 6 months after completion of radiotherapy and LC-HP dietary intervention (n = 100).

Parameter	Baseline (pre-radiotherapy) [mean ± SD]	6 months post-radiotherapy [mean ± SD]	Mean change	P-value
CAP (dB/m)	302 ± 38	276 ± 40	−26	0.003
LSM (kPa)	8.6 ± 2.1	7.8 ± 2.0	−0.8	0.015

Biochemical and renal function markers

Nutritional and renal function tests demonstrated a significant increase in prealbumin (PA) levels (P = 0.018), reflecting improved protein status and short-term nutritional balance. Serum iron (Fe) levels rose slightly without statistical significance (P = 0.412). Compared with pre-radiotherapy baseline, renal markers, including BUN and creatinine (Cr), showed small, non-significant increases (P = 0.087 and P = 0.152), indicating that renal function remained stable despite increased protein intake and concurrent radiotherapy. Paired biochemical and renal function data before and after radiotherapy are summarized in table 6.

Table 6. Biochemical nutritional and renal function markers before radiotherapy and 6 months after completion of radiotherapy and LC-HP dietary intervention (n = 100).

Parameter	Baseline (pre-radiotherapy) [mean ± SD]	6 months post-radiotherapy [mean ± SD]	Mean change	P-value
Prealbumin (PA, mg/L)	210 ± 40	230 ± 42	+20	0.018
Iron (Fe, μmol/L)	14.5 ± 4.0	15.0 ± 4.2	+0.5	0.412
Blood urea nitrogen (BUN, mmol/L)	5.6 ± 1.4	5.9 ± 1.5	+0.3	0.087
Creatinine (Cr, μmol/L)	72 ± 15	74 ± 15	+2	0.152

Immune function

Immune parameters improved significantly following the intervention. Compared with pre-radiotherapy baseline, lymphocyte counts (Ly) increased markedly (P<0.001), suggesting that the LC-HP diet contributed to improved immune competence during radiotherapy. This finding is noteworthy given the well-documented risk of radiotherapy-induced lymphopenia and its association with adverse oncologic outcomes. Matched lymphocyte counts before and after radiotherapy are presented in table 7.

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Table 7. Lymphocyte counts before radiotherapy and 6 months after completion of radiotherapy and LC-HP dietary intervention (n = 100).

Parameter	Baseline (pre-radiotherapy) [mean ± SD]	6 months post-radiotherapy [mean ± SD]	Mean change	P-value
Lymphocyte count (×10⁹/L)	1.35 ± 0.40	1.70 ± 0.45	+0.35	<0.001

DISCUSSION

Non-alcoholic fatty liver disease (NAFLD) is increasingly recognized as a critical comorbidity in oncology, where impaired hepatic reserve can limit radiotherapy tolerance and worsen treatment outcomes. The recent shift in nomenclature to metabolic dysfunction–associated fatty liver disease (MAFLD) highlights its strong metabolic and oncologic associations [11]. While nutritional strategies remain the cornerstone of NAFLD management [12, 13], few studies have explored their role in patients receiving radiotherapy, a setting where hepatic vulnerability is heightened. In this prospective cohort of NAFLD patients undergoing external-beam radiotherapy, we observed that an isocaloric low-carbohydrate high-protein (LC-HP) diet was associated with improved body composition, more favorable metabolic and hepatic profiles, and enhanced lymphocyte counts at 6 months after completion of radiotherapy, suggesting a potential role for structured nutritional support in mitigating radiation-related stress on the liver and immune system.

In this study, an isocaloric low-carbohydrate high-protein (LC-HP) diet produced significant improvements in body composition, metabolic indices, hepatic parameters, and immune function despite concurrent radiotherapy. These observations are broadly consistent with previous NAFLD trials in non-oncologic populations, where carbohydrate restriction and increased protein intake improved steatosis, insulin resistance, and anthropometric indices [14, 15], but our data extend these findings to a more complex clinical context in which patients are exposed to radiotherapy and cancer-related catabolism. These results extend prior evidence that dietary interventions can modulate steatosis and fibrosis by demonstrating added relevance in a cancer care context [16, 17].

The observed reductions in BMI and waist circumference, alongside preservation of skeletal muscle, are especially important in oncology, where sarcopenia is linked to poor radiotherapy tolerance and survival. Likewise, improvements in albumin and prealbumin suggest enhanced protein reserves, a critical factor given the protein–energy malnutrition commonly induced by cancer therapy. Several studies have shown that baseline and treatment-related loss of skeletal muscle mass are associated with higher rates of treatment interruption, increased toxicity, and inferior survival across different solid tumors [18, 19]; therefore, nutritional strategies that attenuate muscle wasting may have downstream effects on radiotherapy compliance and oncologic outcomes even if survival was not directly assessed in the present study [20, 21].

Transient elastography confirmed reductions in CAP and LSM, indicating improved hepatic steatosis and fibrosis. These findings are clinically meaningful since pre-existing fatty liver disease increases susceptibility to radiation-induced liver disease (RILD), whose mechanisms include veno-occlusive changes, oxidative stress, and hepatocyte senescence [22-24]. Nutritional optimization through an LC-HP diet may therefore reduce baseline hepatic vulnerability and improve resilience to radiation. In addition, consensus guidelines in nutritional management emphasize that in patients with chronic liver disease, maintaining protein intake is safe and beneficial for liver repair and functional reserve [25, 26]. Previous work in NAFLD cohorts has shown that reductions in CAP and LSM translate into lower risks of progression to advanced fibrosis and cirrhosis, and that transient elastography can detect meaningful changes in liver status over periods of 6–12 months [27, 28]. The fact that CAP and LSM improved in our patients despite partial hepatic irradiation suggests that adequate dietary support may counterbalance some of the deleterious metabolic and inflammatory effects of radiotherapy on the liver, although a direct causal relationship cannot be proven from this observational design.

A further novel finding is the increase in lymphocyte counts following intervention. Radiotherapy-induced lymphopenia (RIL) is well documented and correlates with impaired immune surveillance, reduced treatment response, and worse oncologic outcomes [29]. One recent review emphasizes that lymphocytes are highly radiosensitive even at low doses (<1 Gy), making them vulnerable during radiotherapy, and RIL has been associated with poorer survival across multiple tumor types [30, 31]. In fact, meta-analyses have shown RIL to be a prognostic factor in solid tumor patients receiving RT (hazard ratio for overall survival) [32]. Nutritional support that bolsters immune competence may thus partially counteract RT-induced immunosuppression and provide a clinical advantage in cancer therapy. Our finding of higher lymphocyte counts after radiotherapy and dietary intervention is therefore hypothesis-generating and suggests that adequate protein intake and overall nutritional status might modulate the depth or duration of lymphopenia; future studies should incorporate serial lymphocyte subsets and correlate them with dosimetric parameters and clinical endpoints to clarify this relationship.

Beyond immune and hepatic effects, radiotherapy

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often causes weight loss, changes in lean mass, and malnutrition that impair tolerance to treatment. Clinical experience supports that maintaining adequate protein and energy intake during RT improves outcomes and reduces complications [33]. A systematic review of nutritional support during chemoradiotherapy also finds benefit in preserving weight and lean mass, particularly when high-protein or n-3 enriched supplements are used [34]. Our results align with this literature by showing preservation of skeletal muscle and protein indices in a population with coexisting NAFLD, a group that is at risk not only for treatment-related malnutrition but also for progression of underlying liver disease. Thus, the LC-HP intervention may serve as a bridge between hepatology and radiation oncology by simultaneously addressing metabolic risk and treatment tolerance.

Taken together, these findings demonstrate that an LC-HP diet not only improves metabolic and hepatic parameters in NAFLD patients but also confers potential supportive benefits during radiotherapy by preserving lean mass, optimizing nutritional status, enhancing immune resilience, and reducing hepatic vulnerability. Nonetheless, several limitations must be acknowledged. This was a single-center study without a control arm, the sample size was modest, and the follow-up period was relatively short. Although we collected basic liver dose–volume parameters (such as mean liver dose and V20/V30), the study was not powered or designed to perform detailed dose–response analyses, and we did not systematically capture clinical RILD or long-term hepatic toxicity outcomes, which limits our ability to directly correlate diet-induced changes in elastography with radiotherapy tolerance or toxicity. In addition, the observational nature of the study precludes firm causal inferences, and residual confounding by tumor site, systemic therapies, and baseline nutritional status cannot be excluded. Future multicenter randomized trials should integrate radiation dosimetry, immune outcomes, advanced imaging biomarkers, and long-term oncologic endpoints to firmly establish LC-HP diets as adjunctive supportive therapy in radiotherapy. Such studies should also compare LC-HP diets with other evidence-based dietary patterns for NAFLD, include control groups receiving standard care, and explore patient-reported outcomes and quality of life to better define the role of nutritional interventions in comprehensive radiotherapy support.

CONCLUSION

Over a six-month period spanning the course of external-beam radiotherapy and follow-up, an isocaloric low-carbohydrate high-protein diet was associated with improved hepatic steatosis, fibrosis, metabolic status, and immune function in NAFLD patients undergoing radiotherapy. These findings suggest that structured nutritional interventions, monitored with non-invasive imaging such as transient elastography, may represent a valuable strategy to enhance hepatic resilience and treatment tolerance in oncology. However, as this was a single-center observational study without a control arm, causal relationships cannot be confirmed. Confirmation in larger, controlled studies is warranted.

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Ethical approval: This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Youjiang Ethnic Medical College Affiliated Hospital.

Informed consent: Written informed consent was obtained from all individual participants included in the study.

Conflict of interest: The authors declare that they have no competing interests.

Data availability: The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Author contributions: T.Y., S.H., and C.L. contributed to study design and patient recruitment. M.H. and M.H. collected and processed clinical data. X.L. performed and supervised ultrasound and elastography analyses. All authors contributed to data interpretation, manuscript drafting, and approved the final version of the manuscript.

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REFERENCES

1. Guo X, Yin X, Liu Z, Wang J (2022) Non-alcoholic fatty liver disease (NAFLD) pathogenesis and natural products for prevention and treatment. *Int J Mol Sci, **23**(24): 15489*.
2. Pouwels S, Sakran N, Graham Y, Leal A, Pintar T, Yang W, *et al.* (2022) Non-alcoholic fatty liver disease (NAFLD): a review of pathophysiology, clinical management and effects of weight loss. *BMC Endocr Disord, **22**(1): 63*.
3. Liang S-X, Huang X-B, Zhu X-D, Zhang W-D, Cai L, Huang H-Z, *et al.* (2011) Dosimetric predictor identification for radiation-induced liver disease after hypofractionated conformal radiotherapy for primary liver carcinoma patients with Child–Pugh Grade A cirrhosis. *Radiotherapy and Oncology, **98**(2): 265-9*.
4. Velec M, Haddad CR, Craig T, Wang L, Lindsay P, Brierley J, *et al.* (2017) Predictors of liver toxicity following stereotactic body radiation therapy for hepatocellular carcinoma. *Int J Radiat Oncol Biol Phys, **97**(5): 939-46*.
5. Katsiki N, Stoian AP, Rizzo M (2022) Dietary patterns in non-alcoholic fatty liver disease (NAFLD): Stay on the straight and narrow path! *Clin Investig Arterioscler, **34**: S24-S31*.
6. Tsompanaki E, Thanapirom K, Papatheodoridi M, Parikh P, Chotai de Lima Y, Tsochatzis EA (2023) Systematic review and meta-analysis: the role of diet in the development of nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol, **21**(6): 1462-74.e24*.

[DOI: 10.61186/ijrr.24.3.11]

7. Gofton C, Upendran Y, Zheng MH, George J (2023) MAFLD: How is it different from NAFLD? *Clin Mol Hepatol,* ***29****(Suppl): S17-S31*.
8. Lange M, Nadkarni D, Martin L, Newberry C, Kumar S, Kushner T (2023) Intermittent fasting improves hepatic end points in nonalcoholic fatty liver disease: A systematic review and meta-analysis. *Hepatol Commun,* ***7****(8): e0212*.
9. Benson R, Madan R, Kilambi R, Chander S (2016) Radiation induced liver disease: A clinical update. *Journal of the Egyptian National Cancer Institute,* ***28****(1): 7-11*.
10. Pan CC, Kavanagh BD, Dawson LA, Li XA, Das SK, Miften M, *et al.* (2010) Radiation-Associated Liver Injury. *Int J Radiat Oncol Biol Phys,* ***76****(3): S94-S100*.
11. Argalia G, Ventura C, Tosi N, Campioni D, Tagliati C, Tufillaro M, *et al.* (2022) Comparison of point shear wave elastography and transient elastography in the evaluation of patients with NAFLD. *Radiol Med,* ***127****(5): 571-6*.
12. Ji Y, Wei CB, Gu W, Hou LL (2023) Relevance of vitamin D on NAFLD and liver fibrosis detected by vibration controlled transient elastography in US adults: a cross-sectional analysis of NHANES 2017-2018. *Ann Med,* ***55****(1): 2209335*.
13. Ozturk A, Olson MC, Samir AE, Venkatesh SK (2022) Liver fibrosis assessment: MR and US elastography. *Abdom Radiol (NY),* ***47****(9): 3037-50*.
14. Milgrom Y, Massarwa M, Hazou W, Shafrir A, Mishraki E, Sanduka S, *et al.* (2024) Ten-hour intermittent fasting plus mediterranean diet versus mediterranean diet alone for treatment of nonalcoholic fatty liver disease (NAFLD). *Harefuah,* ***163****(2): 93-6*.
15. Notarnicola M, Tutino V, De Nunzio V, Cisternino AM, Cofano M, Donghia R, *et al.* (2024) Daily orange consumption reduces hepatic steatosis prevalence in patients with metabolic dysfunction-associated steatotic liver disease: exploratory outcomes of a randomized clinical trial. *Nutrients,* ***16****(18): 3191*.
16. Sun J, Yan C, Wen J, Wang F, Wu H, Xu F (2024) Association between different obesity patterns and the risk of NAFLD detected by transient elastography: a cross-sectional study. *BMC Gastroenterol,* ***24****(1): 221*.
17. Vilar-Gomez E, Nephew LD, Vuppalanchi R, Gawrieh S, Mladenovic A, Pike F, *et al.* (2022) High-quality diet, physical activity, and college education are associated with low risk of NAFLD among the US population. *Hepatology,* ***75****(6): 1491-506*.
18. Xu Y-Y, Zhou X-L, Yu C-H, Wang W-W, Ji F-Z, He D-C, *et al.* (2021) Association of sarcopenia with toxicity and survival in postoperative recurrent esophageal squamous cell carcinoma patients receiving chemoradiotherapy. *Frontiers in Oncology,* ***11*** *- 2021.*
19. Khoshnood N, Shahrezaee MH, Shahrezaee M, Zamanian A (2022) Three-dimensional bioprinting of tragacanth/hydroxyapaptite modified alginate bioinks for bone tissue engineering with tunable printability and bioactivity. *Journal of Applied Polymer Science,* ***139*** *(36): e52833*.
20. Erul E, Guven DC, Onur MR, Yazici G, Aksoy S (2023) Role of sarcopenia on survival and treatment-related toxicity in head and neck cancer: a narrative review of current evidence and future perspectives. *European Archives of Oto-Rhino-Laryngology,* ***280****(8): 3541-56*.
21. Kiss N, Baguley BJ, Dalla Via J, Fraser SF, Bolam KA, Daly RM (2020) Exercise and nutritional approaches to combat cancer-related bone and muscle loss. *Current Osteoporosis Reports,* ***18****(3): 291-300*.
22. De La Pinta Alonso C (2020) Radiation-induced liver disease in the era of SBRT: a review. *Expert Rev Gastroenterol Hepatol,* ***14****(12): 1195-201*.
23. Qi X, Guo J, Li Y, Fang C, Lin J, Chen X, *et al.* (2024) Vitamin E intake is inversely associated with NAFLD measured by liver ultrasound transient elastography. *Sci Rep,* ***14****(1): 2592*.
24. Saavedra Y, Mena V, Priken K (2022) Effect of the mediterranean diet on histological indicators and imaging tests in non-alcoholic fatty liver disease. *Gastroenterol Hepatol,* ***45****(5): 350-60*.
25. Bischoff SC, Bernal W, Dasarathy S, Merli M, Plank LD, Schütz T, *et al.* (2020) ESPEN practical guideline: Clinical nutrition in liver disease. *Clinical Nutrition,* ***39****(12): 3533-62*.
26. Hesaraki S, Saba G, Shahrezaee M, Nezafati N, Orshesh Z, Roshanfar F, *et al.* (2024) Reinforcing β-tricalcium phosphate scaffolds for potential applications in bone tissue engineering: impact of functionalized multi-walled carbon nanotubes. *Scientific Reports,* ***14****(1): 19055*.
27. Lin H, Lee HW, Yip TC-F, Tsochatzis E, Petta S, Bugianesi E, *et al.* (2024) Vibration-controlled transient elastography scores to predict liver-related events in steatotic liver disease. *JAMA,* ***331*** *(15): 1287-97*.
28. Cardoso CRL, Villela-Nogueira CA, Leite NC, Salles GF (2021) Prognostic impact of liver fibrosis and steatosis by transient elastography for cardiovascular and mortality outcomes in individuals with nonalcoholic fatty liver disease and type 2 diabetes: the Rio de Janeiro Cohort Study. *Cardiovascular Diabetology,* ***20****(1): 193*.
29. Toesca DAS, Ibragimov B, Koong AJ, Xing L, Koong AC, Chang DT (2018) Strategies for prediction and mitigation of radiation-induced liver toxicity. *Journal of Radiation Research,* ***59****(1): i40-i9*.
30. Damen PJJ, Lin SH, van Rossum PSN (2024) Editorial: Updates on radiation-induced lymphopenia. *Frontiers in Oncology,* ***14****: 2024*.
31. Ishida N, Matsuo Y, Fukuda J, Ri A, Tatsuno S, Uehara T, *et al.* (2024) Radiation-induced lymphopenia and its impact on survival in patients with brain metastasis. *Current Oncology,* ***31****(8): 4559-67*.
32. El Houat Y, Massard C, Quillien V, de Crevoisier R, Castelli J (2023) Meta-analysis and critical review: Association between radio-induced lymphopenia and overall survival in solid cancers. *Advances in Radiation Oncology,* ***8****(2): 101038.*
33. Allenby TH, Crenshaw ML, Mathis K, Champ CE, Simone NL, Schmitz KH, *et al.* (2020) A systematic review of home-based dietary interventions during radiation therapy for cancer. *Technical Innovations & Patient Support in Radiation Oncology,* ***16****: 10-6*.
34. de van der Schueren MAE, Laviano A, Blanchard H, Jourdan M, Arends J, Baracos VE (2018) Systematic review and meta-analysis of the evidence for oral nutritional intervention on nutritional and clinical outcomes during chemo(radio)therapy: current evidence and guidance for design of future trials. *Annals of Oncology,* ***29****(5): 1141-53*.

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