

Physical activity and hepatocellular carcinoma: A narrative review

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ABSTRACT

Hepatocellular carcinoma (HCC), is one of the most common malignancies around the world, is on the rise and is associated with patient disability. Although HCC can be a devastating disease, regular early detection (surveillance) and diagnosis are the best chance of long-term survival. Cancer's typical consequences and side effects include liver failure, fatigue, loss of muscle mass, reduced muscle strength and functional endurance capacity, reduced flexibility and mobility, nutritional deficiencies, and pain. Rehabilitation is a comprehensive strategy to slow the progression of HCC and reduce functional deficits. Rehabilitation is aimed at patients in all stages of cancer and, as a treatment, provides an improvement in the patient's functional status and quality of life. The purpose of this commentary is to summarise the available information on the rehabilitation of hepatocellular carcinoma. Functional examination and exercise are the mainstays of rehabilitation treatment in HCC. HCC carcinoma and cancer treatment can lead to fragility and sarcopenia. One of the main options to influence sarcopenia and frailty is rehabilitation. Sarcopenia and frailty are two domains that have the potential to be intermediate for patients with personalised and evidence-based HCC rehabilitation. Rehabilitation in patients with HCC can be of significant benefit in improving the clinical condition of patients.

KEYWORDS: hepatocellular carcinoma; cancer rehabilitation; exercise; quality of life; sarcopenia; frailty; activities of daily living

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INTRODUCTION

Liver tumors are an increasing cause of morbidity and mortality of patients. Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide and the most common primary liver tumor [1–6]. It is the fifth most common cause of cancer and the second leading cause of death in men after lung cancer [7]

Recent advances in therapeutic modalities allocated through an updated BCLC (Barcelona Clinic Liver Cancer) flowchart, including liver transplantation, resection, ablation (eg, radiofrequency), transarterial chemoembolization, and modern chemotherapy, have significantly improved the prognosis of patients [8–10]. Although HCC can be a devastating disease, regular early detection (surveillance) and diagnosis are the best chance of long-term survival. A multidisciplinary approach is essential in the treatment of hepatocellular carcinoma. The risk factors for the development of hepatocellular carcinoma (HCC), are multifactorial and include age, with older individuals being at higher risk, sex, with men having a higher incidence, excessive alcohol consumption, smoking, and obesity. These risk factors contribute to the pathogenesis of HCC through various mechanisms, highlighting the importance of comprehensive lifestyle interventions and targeted screening programs to mitigate the burden of this deadly disease [11, 12]. However, liver cirrhosis remains the most significant risk factor with active replication of viral hepatitis B and C, alcoholic liver disease, and nonalcoholic fatty liver disease, the most frequent modulating factors [13–18].

Hepatic complications of HCC include signs of liver decompensation such as liver encephalopathy, portal vein thrombosis, ascites, variceal bleeding, and jaundice; pyogenic liver abscess and macrovascular invasion of the portal vein by tumor tissue can also occur [19–21]. The most common sites of extrahepatic metastasis are the lung, abdominal lymph nodes, bones, and adrenal glands [22, 23]. Patients may have various symptoms such as upper abdominal discomfort, weight loss, fever, anorexia, fatigue, or diarrhea. Rarely can unusual symptoms occur in HCC due to paraneoplastic syndromes such as hypoglycemia, erythrocytosis, hypercalcemia, or severe watery diarrhea. Physical examination may reveal symptoms of cirrhosis, including hepatomegaly, splenomegaly, ascites, jaundice, and encephalopathy, together with sarcopenia and altered functional status [24]. Rehabilitation of cancer patients is an integral component of their overall treatment. This multifaceted process encompasses various interventions and therapies aimed at improving the overall course of the disease and addressing the physical, emotional, and functional deficits caused by cancer and its treatments. It involves a collaborative effort among healthcare professionals, including

physicians, physiotherapists, occupational therapists, psychologists, and nutritionists, to tailor individualized rehabilitation plans that address the unique needs and challenges of each patient. Through a combination of exercise, physical therapy, psychosocial support, pain management, nutritional counseling, and education, rehabilitation endeavors to optimize functional independence, enhance quality of life, alleviate symptoms, and promote holistic well-being throughout the cancer survivorship journey.

There are several potential treatment-related side effects to the treatment of HCC. Surgery can cause pain, weakness, and fatigue [25, 26]. Medicines to prevent rejection of liver transplants can cause high blood pressure, hair loss or growth, and mood changes [27, 28]. Additionally, fatigue may be present. Rehabilitation is a potential option to alleviate treatment-related adverse events. Cancer rehabilitation focuses on reducing or eliminating side effects of cancer treatment and improving overall well-being and quality of life in cancer survivors [29–31].

Rehabilitation accelerates the patient's convalescence into a family or work environment. Dedicated to restoring functional status, rehabilitation is a

cornerstone of the prognosis and integration of the patient into society. This supportive cancer care is standardized for oncological diseases in patients in all stages of cancer [32, 33]. The survival rate of cancer patients is increasing and therefore public attitudes and awareness of the needs of cancer patients are evolving. Rehabilitation goals can be restorative, supportive, preventive, and palliative. Rehabilitation goals encompass a spectrum of aims, including restorative, supportive, preventive, and palliative objectives. Restorative goals focus on maximizing functional abilities, promoting recovery, and restoring independence in activities of daily living. Supportive goals aim to provide emotional, social, and practical assistance to help individuals cope with the physical and emotional challenges of cancer and its treatments. Preventive goals target minimizing the risk of complications. Palliative goals concentrate on improving quality of life and symptom management for individuals with advanced or incurable cancer, prioritizing comfort, dignity, and emotional well-being. By addressing these diverse goals, rehabilitation plays a crucial role in optimizing outcomes and enhancing the overall quality of life for cancer patients and survivors.

In addition to its general impact, HCC can influence the specific functional deficits of the affected patient of the affected patient, which often leads to a severe derangement of patient-reported outcomes, such as quality of life [34]. Typical symptoms are fatigue, loss of muscle mass, reduced muscle strength, reduced endurance, reduced functional capacity, reduced flexibility and mobility, nutritional deficits, pain, polyneuropathy, lymphedema, incontinence, sexual dysfunction, and cognitive deficits [35]

Therefore, the overall goals of rehabilitation are to improve the physical, cognitive, psychological, and social aspects of the quality of life of patient [36]. Rehabilitation therapies are associated with a significant effect on physical function, muscle strength, and psychosocial status [37]. Therefore, the potential rehabilitation benefits of hepatocellular carcinoma should not be underestimated. One of the main rehabilitation approaches in the prevention and treatment of HCC is exercise [38, 39]. Interest in the role of exercise in the primary prevention of cancer is increasing as evidence of its protective effects accumulates, most notably through the insulin resistance-tumor growth pathway [40]. There is strong evidence to suggest that adequate physical activity,

especially gait, is associated with a lower risk of hepatocellular carcinoma [41].

The purpose of this review article is to summarise the available information on the rehabilitation of hepatocellular carcinoma.

Sarcopenia and hepatocellular carcinoma

Sarcopenia is defined as the loss of skeletal muscle mass that occurs with aging [42], One of the main causes of sarcopenia may be chronic inflammation, as it affects the breakdown of muscle proteins and their synthesis through various signaling pathways [43]. Sarcopenia requires additional attention as a new and promising prognostic factor for various malignancies, including hepatocellular carcinoma [44, 45]. As evaluated by computed tomography, skeletal muscle volume deficit predicts a poor prognosis for all stages of cancer and in patients treated with sorafenib [46]. Sarcopenia and rapid depletion of skeletal muscles contribute to poorer survival in patients with liver cirrhosis [44, 45]. Furthermore, this condition is associated with poorer daily activities [47] and is a significant prognostic factor in patients after transarterial embolisation [48–50]. Decreased muscle mass at the level of sarcopenia is a negative predictive factor in patients with hepatocellular carcinoma [49, 50]. Sarcopenia was also identified as a risk factor [51].

A study by Kobayashi et al. [52] tested the effect of hepatocellular carcinoma surgery on sarcopenia and postoperative results. The cohort consisted of 241 patients who were retrospectively analysed. Intramuscular mass and psoas index tested the quality and quantity. Postoperative muscle quality depletion has been associated with a higher recurrence of hepatocellular carcinoma.

Several pathological conditions are associated with sarcopenia, including advanced organ failure, inflammatory diseases, malignancies, endocrine diseases, sedentary lifestyles, and malnutrition. In liver disease, the main mechanisms of sarcopenia can be considered: amino acid energy malnutrition, imbalance in protein synthesis and breakdown, and increased myostatin expression, which strongly suppresses skeletal muscle growth [53, 54]. Therefore, sarcopenia may be the result of various pathological conditions, such as impaired liver function reserve. However, the same factors that increase the progression of sarcopenia and worsen the patient's prognosis are unclear. Skeletal muscle atrophy is often observed in patients with chronic liver damage. The prevention of skeletal muscle atrophy is a critical issue for patient management. However, patients with liver damage usually rest in bed during

hospitalisation for treatment. Koya et al. [55] tested the effect of physical activity in patients with colorectal cancer. The group consisted of 54 patients who completed 20 minutes of exercise daily combined with stretching, strength training, balance exercises, and aerobic activities. Exercise was not associated with the Child-Pugh class. The intervention led to improved cardiac variability and distance according to the 6 min walking test. Branched-chain amino acids have led to the most significant arrest of muscle mass decline. Exercise effectiveness, branched chain amino acids, and exercise supplementation were effective due to improved trophic and muscle strength in patients with liver cirrhosis [56].

Primary methods of influencing sarcopenia include exercise and nutrition [57]. Exercise is vital to prevent sarcopenia [58]. Exercise-based has anti-inflammatory effects with the potential to reduce local cytokine expression and increase the expression of antiapoptotic factors, suggesting that exercise may prevent sarcopenia [59]. The correlation between SMI, visceral fat, and the prognosis of patients with hepatocellular carcinoma was tested by Yabusaki et al. [60, 61]. Sarcopenia was found in 89 of 195 patients and was significantly correlated with gender, low body mass index, low fat, and low serum albumin. Low SMI

values were shown to be an independent prognostic factor in patients with a body mass index greater than 22.

Functional assessment

Functional testing of a patient's condition plays a vital role in determining the physical fitness of patients with HCC [62, 63]. The functional examination of patients aims to comprehensively assess and evaluate the patient's physical, cognitive, and emotional abilities, with the overarching goal of understanding their functional capacity and limitations. This examination involves a systematic evaluation of various domains, including mobility, strength, balance, coordination, endurance, activities of daily living (ADLs), cognition, psychosocial functioning, and quality of life. By gaining insight into the patient's functional status, healthcare professionals can tailor personalized rehabilitation plans, set realistic goals, monitor progress, and implement targeted interventions to optimize functional outcomes and enhance overall well-being. A functional examination of the patient will help determine the physical condition of the patients. The worse physical condition of patients is associated with worse outcomes of hepatocellular carcinoma treatment [64–66].

Several test batteries are used to examine the physical function of patients.

Chair stand test

The chair stand test is a test that aims to test the strength and endurance of the legs in patients [63, 67]. The evaluation is based on the time a patient takes the test. The patient was in a sitting and standing chair five times during the test. A stopwatch and a standard height chair with a straight back are essential to perform the test. The patient sits with a straight and supported back, his arms crossed over his chest. The tested patient sits down five times as fast as possible and then rises. The best test result is the shortest possible time. The chair-stand test is a reliable metric to predict waiting for morbidity and mortality in patients with liver cirrhosis [68, 69].

Timed Up and go test

This test is used primarily in the elderly population [70, 71]. The timed up and go test is generally aimed at determining the physical condition of patients [72]. It was aimed at improving the functional ability of patients and determining the risk of falls [73]. A chair and a stopwatch are required for the test. The patient sits in a chair to perform the Timed up and go test correctly. The patient feet are placed at a location marked by a line. After the start signal, the patient climbs out of the chair

and walks 3 m. The examiner records the time the patient walked the specified distance and returned to the chair. A longer distance can be used as a test variation.

6. min walking test

One of the most commonly used tests to assess functional capacity is the 6-minute walk test [74–76]. The 6-min test is easy to apply and assesses exercise tolerance, the effectiveness of therapies and rehabilitation programmes, and the function of the cardiovascular and respiratory systems [74]. Initially, the 6 min test was used for patients with respiratory diseases. However, the test is now commonly used to assess functional performance in various diseases [77]. The test evaluates the distance travelled in 6 minutes in metres over flat terrain. During the test, the patient is instructed to walk at his own pace and cover the largest possible distance. If shortness of breath or leg pain occurs, patients may stop as needed.

Gripping force

Grip strength is an essential parameter for patients. Low grip strength is indirectly associated with mortality from cardiovascular disease, respiratory disease, chronic obstructive pulmonary disease, and all types of cancer [78]. A dynamometer can be used to

measure the gripping force. It is essential to measure grip strength bilaterally.

Frailty index

The frailty index is used to measure the health status of the elderly [79]. The frailty index serves as a proxy measure of ageing and vulnerability to poor outcomes and is defined as the proportion of functional deficits present in an individual. Older adults are at increased risk for falls, disability, hospitalisation, and death [80–83]. Symptoms include general weakness, exhaustion, slow gait, poor balance, decreased physical activity, cognitive impairment, and weight loss. These deficits include diseases, signs, symptoms, laboratory abnormalities, cognitive impairments, and disability in daily activities. Frailty is a significant factor in patients with hepatocellular carcinoma [84].

Liver frailty index

The liver frailty index, developed by Lai et al. [85], is calculated by examining grip strength, chair stand test, and balance test [86]. When the gripping force is applied, three examinations are performed. The result shows the average of three tests. The chair-stand test records the time required to stand and sit on a chair in five repetitions. The patient has crossed arms on his chest. In the balance test, the balance is recorded in three positions

(side-to-side, semi-tandem, and tandem). The results of the liver frailty index are associated with patient outcomes [86].

SF-36 Quality of Life Questionnaire

The quality of life questionnaire was created based on an adequate evaluation of therapy in medicine. The SF-36 questionnaire is a standardised format for assessing patients' quality of life of patients [87]. SF-36 contains 36 questions, the results of which are scored. This questionnaire addresses a set of general, coherent, and easy-to-apply questions on patient quality of life. In patients with hepatocellular carcinoma, it is an easy-to-apply form of objectification to record the effectiveness of therapy [88].

EuroQol-5D (EQ-5D)

Another option of examining the quality of life is the EuroQol-5D (EQ-5D) questionnaire, EQ-5D, used to measure quality of life. EQ-5D is a valid form of quality of life measurement [89, 90]. EQ-5D includes five aspects: mobility, self-care, daily activities, pain, discomfort, anxiety, and depression, and a visual analogue scale that assesses subjective perceived health on a scale from 0-100.

Functional Independence Measure (FIM)

Functional independence assessment is an assessment tool that contains 18 items that include evaluation of daily activities such as

eating, grooming, bathing, upper body dressing, lower body dressing, toilet use, bladder control, bowel motility, bed use, chair, wheelchair, toilets, baths, showers, ability to manage stairs, and cognitive components such as understanding, social interaction, problem solving, and memory [91].

Frailty and rehabilitation

Frailty is originally a geriatric syndrome of reduced functional reserve to cope with stressors; recently, it has been translated to hepatology [60, 61]. Frailty increases the risk of other syndromes and multiplies the adverse health consequences, especially in patients and the elderly [60]. Frailty syndrome is highly prevalent in elderly cancer patients [92]. Frailty is also associated with the length of hospital stay and a poor prognosis in HCC patients who have undergone liver transplantation [84]. Muscle mass decreases significantly during hospitalization and treatment of patients [93]. The essential treatment strategy is nutrition and exercise interventions. Exercise is the primary treatment for frailty and has improved physical fragility. Tsuchihashi et al. [94] tested the effectiveness of exercise in improving frailty in patients with HCC. There were 114 patients in the intervention group and 67 patients in the control group. The patients in

the intervention group exercised a combination of aerobic and strength training (20 - 40 min/day). Exercise has been associated with an improvement in the frailty index.

Activities of daily living and rehabilitation

In cancer patients, activities of daily living (ADL) are often impaired [95, 96]. The potential cause is associated with muscle atrophy and dysfunction [97]. The decreased ability to perform ADL activities is associated with a poor response to cancer treatment, mortality, and quality of life. Sarcopenia is often observed in patients with hepatocellular carcinoma, which contributes to a reduced ability to perform ADL. Muscle mass decreases significantly and ADLs are reduced in patients during hospitalisation. One of the main aspects of rehabilitation is the effective maintenance of muscle mass, physical function, and cognitive functions, leading to better ADL. Naratao et al. [96] tested the effectiveness of rehabilitation in patients with hepatocellular carcinoma in a study. The group consisted of 19 patients. After rehabilitation, there was an increase in the ability to perform ADL, an increase in the muscular strength of the knee extensors.

Exercise as medicine

Several forms of exercise can be effectively utilized to address physical function in patients with hepatocellular carcinoma (HCC). However, exercise interventions must be tailored to each patient's individual functional condition. This personalized approach ensures that the exercise regimen is appropriate and safe, taking into account factors such as disease severity, treatment status, comorbidities, and overall fitness level. Benefits of exercise may include improvements in physical strength, endurance, mobility, balance, and overall quality of life. Additionally, exercise can help mitigate treatment-related side effects such as fatigue, muscle weakness, joint stiffness, and cognitive impairment. By incorporating various types of exercise, such as aerobic training, resistance training, flexibility exercises, and balance training, healthcare professionals can develop comprehensive rehabilitation programs tailored to the specific needs and abilities of HCC patients. These programs aim to optimize physical function, promote functional independence, and enhance overall well-being throughout the cancer survivorship journey.[98]. Exercise interventions are known to alleviate or prevent the harmful effects of oncological disease and treatment.

Aerobic exercise

Aerobic exercise is one of the first supportive care approaches for cancer patients and cancer survivors [99, 100]. Aerobic exercise has been shown to positively affect physical performance [101] and quality of life of cancer patients [102] and is believed to affect immunological parameters positively. Primary forms of aerobic exercise include walking, cycling, or swimming. It is also possible to use a stationary bicycle or treadmill as an alternative. However, the intensity of exercise must be prescribed individually according to the patient's needs.

Strength training

Strength training uses resistance to stimulate muscle contraction [103] and is generally used in cancer patients [104]. This approach also improves joint mobility and increases muscle, tendon, and ligament strength. It is a safe, simple, and effective intervention to induce muscle hypertrophy, increase muscle strength, and improve the patient's functional ability. Strength training can be performed using simple exercises and tools that use resistance. It is essential to gradually increase the exercise load with respect to the state of health. Additionally, it is vital to maintain slow controlled movement during exercise.

Balance exercises

Balance exercises in rehabilitation play an essential role in fall prevention of falls [105, 106]. Balance exercises are integral components of rehabilitation programs, particularly in the context of fall prevention for patients undergoing treatment for conditions such as hepatocellular carcinoma (HCC). These exercises are designed to enhance postural control and stability, reducing the risk of falls and associated injuries. Central to balance training is the improvement of postural control, which involves the ability to maintain equilibrium and stability during static and dynamic activities. These exercises focus on strengthening core muscles, improving proprioception, and enhancing coordination between sensory systems such as vision, proprioception, and vestibular function [107–110].

One common approach in balance training involves the use of self-weight or balance pads that simulate unstable surfaces. By performing exercises on these surfaces, patients are challenged to engage their stabilizing muscles more effectively, thereby improving balance and proprioception. Examples of exercises include standing on one leg, performing squats, lunges, or other dynamic movements while maintaining balance on an unstable

surface. Integrating balance exercises into rehabilitation programs not only helps reduce the risk of falls but also promotes functional independence and confidence in daily activities. Moreover, these exercises can contribute to overall physical fitness and enhance the effectiveness of multidisciplinary rehabilitation interventions for patients with HCC and other oncological conditions.

Efficacy of exercise in the treatment of hepatocellular carcinoma

Exercise is one of the essential components in the treatment and rehabilitation of cancer patients [111]. Most cancer patients should start exercising as soon as possible under the supervision of a specialist physical therapist and physiatrist. This setting should be planned according to the risk factors and individual goals of the patient.

Kaibori et al. [112] evaluated the effectiveness of exercise in a study. The cohort consisted of 42 patients who underwent hepatectomy and were randomised into a group that exercised and underwent dietary changes and a control group that underwent only dietary changes. Weight and fat loss were observed in the exercise group. Fasting insulin levels improved significantly in the exercise group.

Exercise in patients with hepatocellular carcinoma usually involves aerobic exercise

and strength training [111]. Both forms of exercise are associated with improving the functional health of cancer patients. The benefit is also seen in improving physical health, mental health, quality of life, and, in some cancers, also survival. Most cancers can perform strength exercises without side effects to increase muscle strength. Exercise to improve sensorimotor functions is essential for patients with polyneuropathy and elderly patients.

Hashida et al. [113] evaluated the effectiveness of exercise-based rehabilitation in patients with hepatocellular carcinoma. The study focused on the prognosis of patients with hepatocellular carcinoma. The cohort consisted of 152 patients who underwent transcatheter arterial chemoembolization. Muscle mass was examined using the skeletal muscle index (SMI). Exercise-based rehabilitation in patients was associated with longer survival (median 552 vs. 424 days; $p = 0.0359$). Kaibori et al. [112] tested the association between preoperative examinations and results after hepatocellular carcinoma surgery. The group consisted of 61 patients who underwent surgery. The result was determined using maximal oxygen consumption (VO_2). The recurrence of hepatocellular carcinoma, the number of

deaths, liver failure, and complications in the form of cirrhosis were monitored after surgery. The better cardiovascular condition was associated with higher survival rates in patients who underwent hepatectomy.

Rehabilitation can be applied not only to hepatocellular carcinoma but also in haematoma patients. Koya et al. [114] tested exercises in patients with hepatoma who underwent transcatheter arterial chemoembolization. The cohort consisted of 209 patients randomised into an intervention group (n = 107) and a control group (n = 102). The patients in the intervention group had a significantly higher skeletal muscle index than the non-exercise group (p = 0.0029).

Prehabilitation

Rehabilitation methods also play an important role in the prehabilitation of patients. Prehabilitation is a treatment that focuses on preparing the patient before surgery [115, 116]. Prehabilitation is a continuous process of patient care. Prehabilitation includes exercise, psychological, and nutritional support [117, 118]. Prehabilitation represents a potentially effective strategy to improve the functional status and quality of life of patients. Prehabilitation offers a valuable opportunity to enhance the healthcare outcomes of patients diagnosed with hepatocellular

carcinoma (HCC). This proactive approach involves implementing interventions before cancer treatment, with the goal of optimizing patients' physical and psychological health, enhancing their functional capacity, and mitigating the potential adverse effects of treatment. In the context of HCC, prehabilitation strategies may include tailored exercise programs, nutritional counseling, smoking cessation support, stress reduction techniques, and education on coping strategies. These interventions aim to improve patients' overall fitness levels, strengthen their immune systems, and enhance their resilience to withstand the physical and emotional challenges associated with cancer diagnosis and treatment. By engaging in prehabilitation, patients with HCC may experience several benefits, including reduced postoperative complications, faster recovery times, improved tolerance to treatment modalities such as surgery, chemotherapy, or liver transplantation, and enhanced quality of life. Furthermore, prehabilitation empowers patients to actively participate in their own care, fostering a sense of control and confidence in managing their health. It also provides an opportunity for healthcare providers to identify and address potential risk factors or comorbidities that could impact

treatment outcomes. Overall, prehabilitation holds significant promise in optimizing the healthcare of patients with hepatocellular carcinoma, offering a proactive and holistic approach to cancer care that prioritizes patient well-being and treatment success. The most popular protocol in prehabilitation is enhanced recovery after surgery (ERAS).

Enhanced recovery after surgery (ERAS)

ERAS is multimodal perioperative care, the main objective is to achieve early recovery in patients undergoing major surgery [119–122]. ERAS is comprehensive in scope and covers all areas of the patient's path through the surgical process. Regardless of surgical specialisation, all ERAS protocols have the same goals: preoperative patient optimisation, reduction of perioperative stress, maintenance of postoperative physiological function, and accelerated postoperative recovery time [123]. The ERAS protocol includes a multidisciplinary team of clinicians, nurses, physiotherapists, psychologists, social workers, and dieticians. Multidisciplinary efforts focus on the preoperative, intraoperative, and postoperative phases of care.

The concept of faster recovery after surgery (ERAS) is widely used in surgery. ERAS refers to the application of various effective methods to reduce surgical stress and complications

during the preoperative, intraoperative, and postoperative periods. It usually includes preoperative education, improved methods of anaesthesia and analgesia, and preoperative and postoperative rehabilitation. ERAS can alleviate the physiological and psychological trauma of patients, reducing the stress response and complications during the perioperative period. Recently, the randomised study of He et al. [124] aimed to compare the effectiveness of the ERAS protocol in terms of days of hospitalisation and quality of life in patients with hepatocellular carcinoma. There was a reduction in hospitalisation days in the ERAS group ($p = 0.04$) and quality of life in the ERAS group. Furthermore, the study did not show differences in blood loss, several open surgeries, mortality, and complications associated with the operation. The efficacy of the ERAS protocol in liver surgery was verified in an analysis by Rouxel et al. [125]. A total of 4 randomised studies ($n = 542$) were included. There was a reduction in hospitalisation days in the ERAS group. A reduction in complications was identified in two of the four studies. Furthermore, Ratti et al. [126] verified the efficacy of the ERAS protocol in patients with hepatocellular carcinoma in a study. The group consisted of 208 patients with

hepatocellular carcinoma after resection surgery. Laparoscopic surgery was associated with lower blood loss and postoperative morbidity. Treatment with ERAS led to lower blood loss and reduced postoperative morbidity in patients who were unable to be candidates for a minimally invasive approach. Finally, Fujio et al. [127] also verified the efficacy of the ERAS protocol in patients with hepatocellular carcinoma in a study. According to Fujio et al., the ERAS protocol is a convenient and safe method that leads to faster recovery. In patients who underwent

the ERAS protocol, a shorter hospital stay was recorded during both laparoscopic surgery and open hepatectomy.

CONCLUSION

Comprehensive rehabilitation in patients with HCC is an integral part of modern multidisciplinary treatment. Functional examination and exercise are essential components of rehabilitation treatment. Exercise is associated with an improvement in functional status, quality of life, and survival of patients.

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