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Review

Exercise-Based Interventions Combined with Branched-Chain Amino Acid Supplementation for the Prevention and Management of Sarcopenia in Liver Cirrhosis: A Scoping Review

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Abstract: Sarcopenia is a common and clinically relevant complication of liver cirrhosis, associated with impaired physical function, reduced quality of life (QOL) , and increased morbidity and mortality. Various nutritional and exercise strategies, including branched-chain amino acid (BCAA) supplementation, have been proposed to mitigate muscle loss; however, evidence on their combined effects remains heterogeneous. This review aimed to map the existing evidence on the effects of physical activity combined with BCAA supplementa-tion on muscle mass, muscle strength, and physical performance in patients with liver cirrhosis. A scoping review was conducted to map the available evidence on structured exercise interventions combined with BCAA supplementation in adults with liver cirrho-sis. Electronic searches were performed in PubMed, Cochrane Library, and Web of Science to identify relevant studies reporting muscle related or functional outcomes. Data were charted and synthesized narratively to describe intervention characteristics, outcome measures, and overall trends in the literature. Five studies met the inclusion criteria. Inter-ventions consisted mainly of walking-based exercise or combined aerobic and resistance training programs lasting 8–12 weeks, along with oral BCAA supplementation. Physical activity was consistently associated with improvements in muscle strength, physical performance, or frailty-related outcomes, while effects on muscle mass were more variable. Exercise based rehabilitation appears to be a central component in the management of sarcopenia in liver cirrhosis. BCAA supplementation may provide supportive benefits when combined with physical activity; however, its independent effects remain incon-sistent.

Keywords: exercise, liver cirrhosis, sarcopenia, branched chain amino acids

1. Introduction

Chronic liver disease and its advanced stages represent a growing public health concern worldwide. Population-based data indicate that liver fibrosis is highly prevalent even in the general population, underscoring the silent and progressive nature of chronic liver injury and the substantial number of individuals at risk of developing cirrhosis (1). Advanced liver disease represents a major global health burden, affecting more than 1.5 billion individuals worldwide (2). Liver cirrhosis accounts for approximately 13.7–14.7% of age-standardized mortality globally (3). As a progressive condition, liver cirrhosis is characterized by extensive hepatic fibrosis leading to impaired liver function and reduced physiological reserve. According to the World Health Organization, liver cirrhosis was responsible for approximately 1.34 million deaths worldwide in 2022, although this figure is likely underestimated (4). Once cirrhosis develops, patients are at increased risk of death due to hepatic decompensation or hepatocellular carcinoma (5).

During disease progression, multiple aspects of health deteriorate, including nutritional status and musculoskeletal integrity, resulting in an increased risk of malnutrition and muscle mass loss (6). In recent years, sarcopenia has been increasingly recognized as a clinically relevant complication in patients with liver cirrhosis. Sarcopenia is characterized by a progressive decline in muscle mass, muscle strength, and physical performance and is associated with poor clinical outcomes (7,8). The development of sarcopenia in cirrhosis is multifactorial and involves malnutrition, malabsorption, altered lipid and protein metabolism, reduced hepatic clearance of ammonia, chronic inflammation, elevated cytokine and myostatin levels, hormonal dysregulation, and insufficient physical activity (9,10).

BCAA supplementation has been explored as a potential strategy to counteract sarcopenia in patients with liver cirrhosis by supporting protein metabolism, muscle strength, and physical function. Evidence from clinical trials, observational studies, and systematic reviews suggests that BCAA supplementation may improve muscle related outcomes, frailty indices, and QOL, in selected patient populations; however, results remain heterogeneous and highly context-dependent (11–13). For example, a recent randomized controlled trial demonstrated that BCAA supplementation significantly improved the Liver Frailty Index (LFI) in frail patients with compensated cirrhosis, supporting a potential benefit in carefully selected individuals (14). Several studies have shown that amino acids, particularly leucine, can enhance muscle protein synthesis and attenuate metabolic disturbances associated with hyperammonemia in cirrhosis (15,16). From another perspective, BCAAs including leucine, isoleucine, and valine play a central role in protein synthesis and ammonia detoxification and serve as important energy substrates for skeletal muscle in patients with cirrhosis, especially in the context of impaired liver metabolism (16).

Despite this rationale, current clinical practice guidelines do not support routine BCAA supplementation for all patients with cirrhosis, as clinical trials evaluating the use of BCAAs for cirrhosis-related complications have yielded inconsistent results (17,18). However, selected studies and guidelines recognize that oral BCAA supplementation may improve QOL, and nutritional status, emphasizing the need for individualized application rather than a universal recommendation (19).

2. Sarcopenia

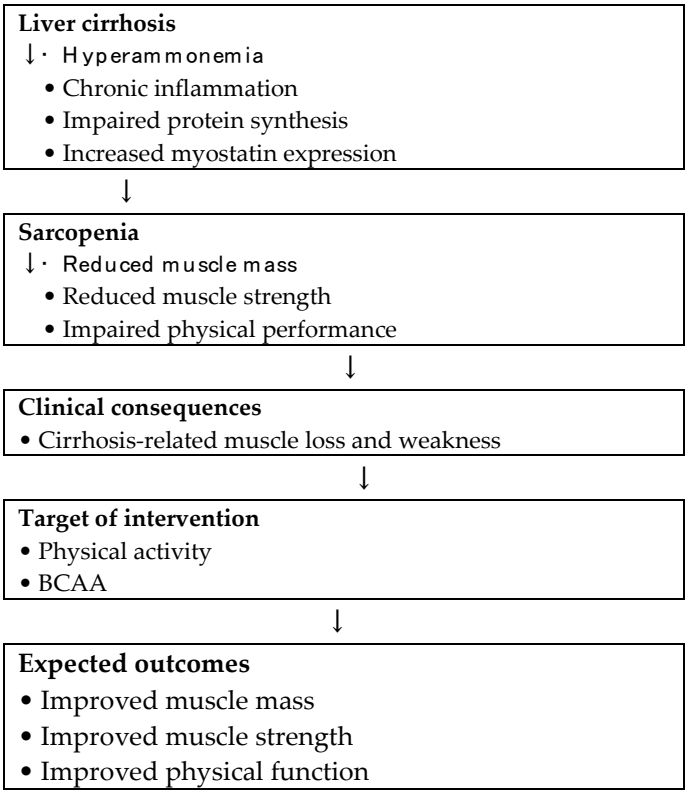
Sarcopenia is a well recognized complication that adversely affects clinical outcomes in patients with liver cirrhosis, leading to impairments in physical function and capacity, reduced and an increased incidence of complications and mortality (20,21). In recent years, QOL exercise therapy has been increasingly recommended as

an effective intervention for sarcopenia associated with liver cirrhosis (22). The beneficial effects of exercise therapy include improvements in muscle mass, muscle strength, endurance, and balance, as well as positive effects on psychological wellbeing and overall QOL (23–26). Consequently, the effectiveness of exercise therapy in patients with liver cirrhosis is supported by a growing body of scientific evidence.

Recent studies have identified resistance training and aerobic exercise, particularly walking, as effective exercise modalities for patients with liver cirrhosis (20,27–30). In individuals with reduced hepatic reserve, cirrhosis is frequently accompanied by sarcopenia, driven by increased skeletal muscle catabolism, impaired protein synthesis, chronic inflammation, decreased testosterone levels, and elevated myostatin concentrations, all of which contribute to progressive muscle loss (31). Previous research has demonstrated favorable effects of exercise based interventions in patients with liver cirrhosis, including increases in muscle mass, improvements in maximal oxygen uptake, and reductions in the hepatic venous pressure gradient (32).

Exercise therapy for chronic diseases should be initiated at low intensity and progressed gradually, with careful monitoring of patient symptoms (19,20). Importantly, exercise prescription should be individualized and guided by the FITT principles (Frequency, Intensity, Time, and Type of exercise) (33), which are unfortunately not consistently applied in clinical practice. Adherence to these principles helps ensure both the quality and safety of exercise therapy in patients with liver cirrhosis, a population in which careful assessment and appropriate adjustment of exercise intensity are essential (22,25). It is important to note that the primary therapeutic goal in sarcopenia is to maintain or increase skeletal muscle mass, attenuate or reverse declines in muscle strength, and preserve functional independence and QOL. These objectives are particularly relevant in patients with liver cirrhosis, in whom sarcopenia is strongly associated with frailty, reduced physical performance, increased complications, and mortality (20,27) (Table1).

Table 1. Characteristics and outcomes of exercise based interventions combined with branched-chain amino acid supplementation in patients with liver cirrhosis.

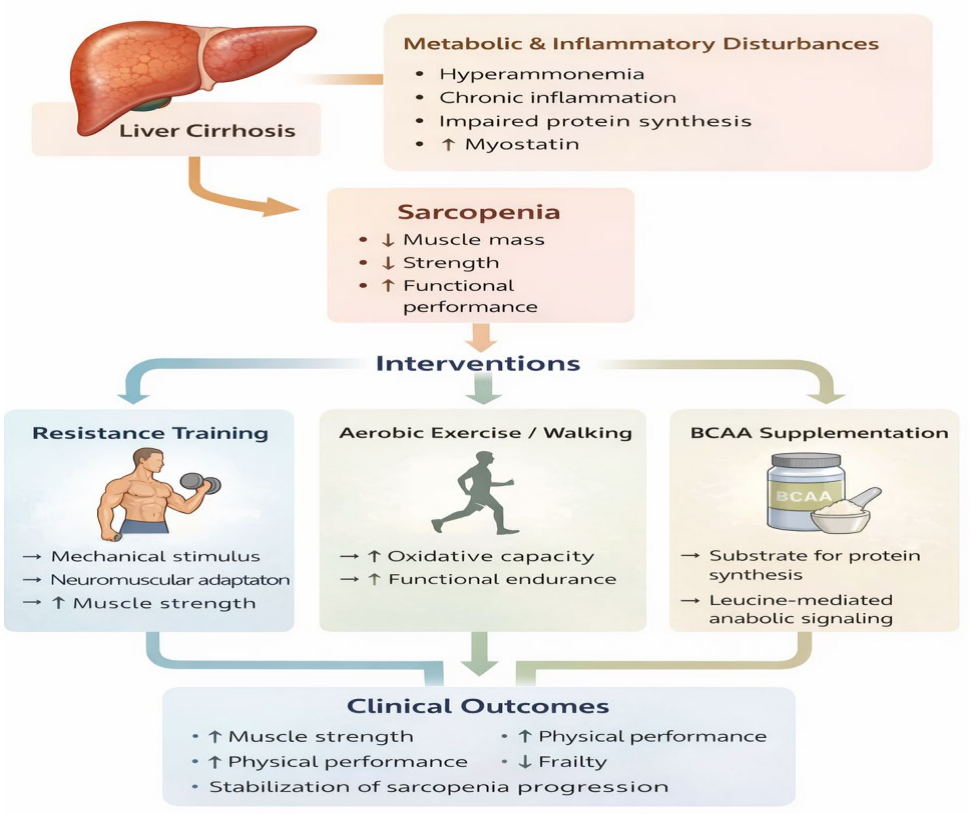


The pathophysiology of sarcopenia is complex and multifactorial, involving chronic inflammation, impaired protein synthesis, metabolic dysregulation, physical inactivity, and disease-specific mechanisms such as hyperammonemia and hormonal alterations in cirrhosis (10,21,34). Consequently, isolated interventions are unlikely to achieve clinically meaningful and sustained improvements, particularly in populations with advanced chronic disease. International clinical practice guidelines therefore emphasize the need for multimodal strategies that integrate exercise-based interventions with appropriate nutritional support (17,18). Evidence from previous studies (26,35) suggests that combining physical exercise with nutritional supplementation may yield superior improvements in muscle strength, muscle mass, and physical function compared with either intervention alone (Figure 1).

Systematic reviews and meta-analyses have demonstrated that resistance exercise combined with protein supplementation enhances muscle-related outcomes in sarcopenic individuals (36,37), while comparative analyses indicate that exercise remains the primary driver of functional improvement, with nutritional strategies acting as supportive adjuncts (35). In the context of liver cirrhosis, where protein metabolism and muscle energy utilization are profoundly altered, this combined approach may be particularly relevant (20,22).

To address these gaps and the heterogeneity of the existing evidence, the present scoping review aimed to map and synthesize available studies investigating the effects of exercise-based interventions, branched-chain amino acid supplementation, and their combination on muscle strength, muscle mass, and physical performance in patients with liver cirrhosis, with the goal of informing more effective strategies for the clinical management of sarcopenia.

Figure 1. Mechanistic Interaction Between Exercise Modalities and BCAA Supplementation in osis Associated Sarcopenia.



3. Methodology

3.1. Study design

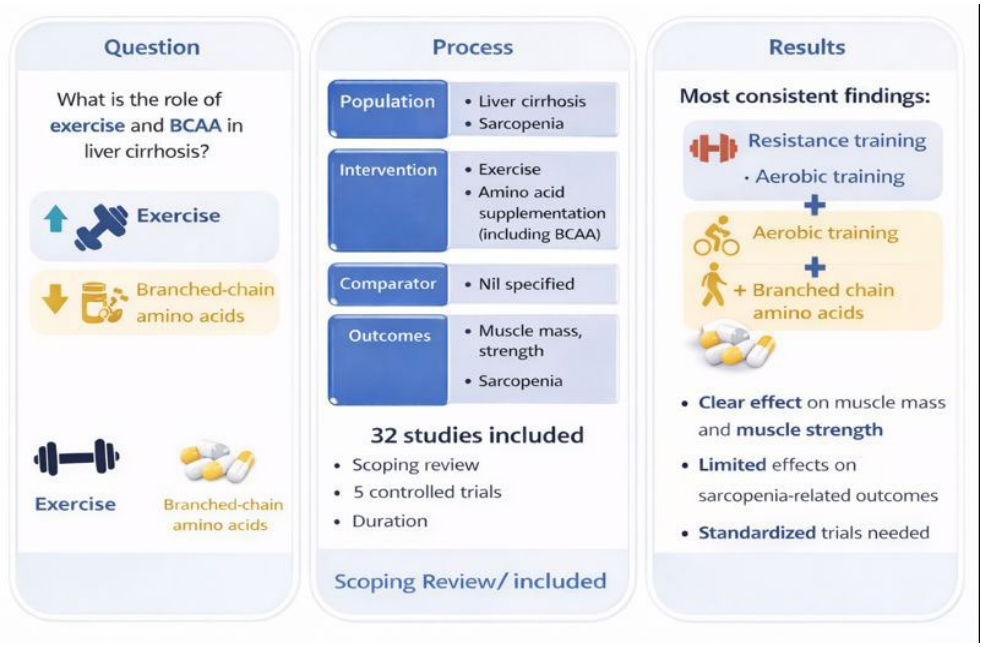
This scoping review design was selected to comprehensively map the characteristics of exercise-based interventions combined with amino acid supplementation in patients with liver cirrhosis and to identify research gaps in this field.

3.2. Eligibility criteria

Eligibility criteria were defined using the Population, Concept, and Context (PCC) framework. The population of interest included adult patients diagnosed with liver cirrhosis, regardless of etiology or disease severity. The concept focused on interventions combining exercise with nutritional supplementation of branched-chain amino acids. The context included clinical or community rehabilitation settings (Figure 2).

Studies were included if they met the following criteria: (1) involved patients with liver cirrhosis; (2) included physical activity (aerobic exercise, resistance training, or a combination thereof); (3) included amino acid supplementation as part of the intervention; and (4) reported outcomes related to muscle mass, muscle strength, physical performance, or sarcopenia. Reviews, meta-analyses, case reports, study protocols, animal studies, and non english publications were excluded, as were studies that did not include both an exercise component and an amino acid intervention.

Figure 2. Conceptual overview of exercise and BCAA-based interventions for sarcopenia in liver cirrhosis.



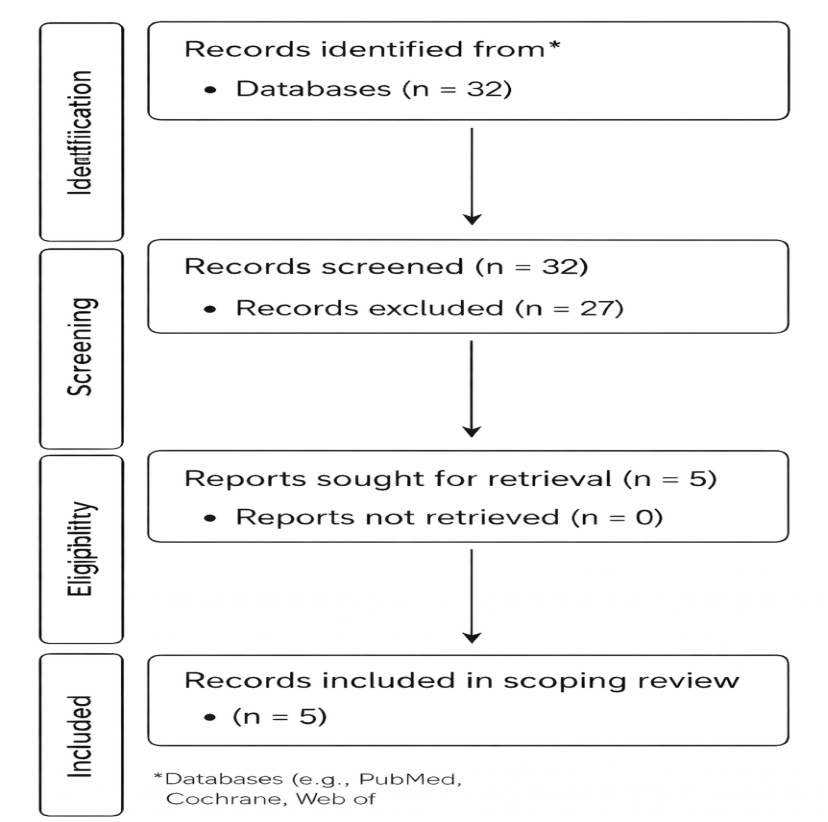
3.3. Information sources and search strategy

A comprehensive literature search was conducted in PubMed, Cochrane Library, and Web of Science. The search strategy combined terms related to exercise, sarcopenia, liver cirrhosis, and amino acids. Keywords included combinations of "exercise," "liver cirrhosis," "sarcopenia," and "branched-chain amino acids." Only studies published in english were considered. The final search yielded 32 records.

3.4. Study selection and data charting and extraction

After the selection process, duplicates were removed using the Rayyan software, and abstracts were screened for relevance. Full-text articles were then assessed for eligibility based on predefined inclusion criteria. Disagreements during the selection process were resolved through discussion. Finally, five studies met the inclusion criteria and were included in the final analysis (Figure 3).

Figure 3. PRISMAC-ScR Flowchart



Data extracted included the author and year of publication, study design, intervention duration, exercise frequency, type of exercise (aerobic, resistance, or combined), details of nutritional supplementation, outcome measures, and main findings. No attempts were made to contact study authors to obtain missing or unpublished data.

4. Intervention characteristics

Exercise interventions varied across studies and included walking based aerobic exercise, resistance training, or combined aerobic and resistance programs. Intervention duration ranged from 8 to 12 weeks, with exercise frequency varying between 3 and 7 sessions per week. Nutritional strategies consisted primarily of BCAAs, although some studies included additional nutrients such as protein, carbohydrates, and vitamins. Details regarding exercise intensity and supplement dosage were not reported consistently across studies.

Table 2. Exercise based interventions combined with BCAA supplementation in patients with liver cirrhosis

Type of diagnosis	Duration	Exercise modality + BCAA	Aim of intervention	Outcomes assessed	Main results	Key limitations	References
Compensated cirrhosis	7 days/ 12 weeks	Walking exercise + oral BCAA	Prevention of muscle decline	Grip strength, skeletal muscle mass index, serological tests	Improvement in grip strength and skeletal muscle mass index, no significant between-group differences	Lack of resistance training limited functional outcomes	(38)
Compensated cirrhosis	7 days/ 4 weeks	Walking and resistance exercise + oral BCAA	Improvement of muscle quantity and quality	Quadriceps thickness, grip strength, SPPB, MELD, blood tests	Significant improvements in quadriceps thickness and physical performance; no significant differences between groups	Short intervention duration heterogeneous intervention arms	(39)
Mixed cirrhosis severity	7 days/ 24 weeks	Walking and resistance exercise + oral BCAA	Improvement of physical performance and muscle mass	6MD, gait speed, lower limb strength, MELD, CLDQ	No significant improvements in motor, liver, or CLDQ outcomes	Possible insufficient intensity/progressionadherence not fully reported	(40)
Frail cirrhosis patients	3 days/12 weeks	Walking and resistance exercise + oral BCAA	Reduction of frailty	LFI, body composition	Significant improvement in LFI; no significant liver function changes	Small sample size; short follow-up	(41)
Compensated cirrhosis	7 days/12 weeks	Walking exercise + oral BCAA	Prevention of sarcopenia progression	Skeletal muscle mass index, grip strength, sarcopenia prevalence	Prevention of sarcopenia progression and improvement in muscle-related parameters	Absence of structured resistance training	(42)

Abbreviations: LFI, Liver Frailty Index; SPPB, Short physical performance battery test, 6MD, 6-minute walking distance; MELD, Model for End-Stage Liver Disease score; CLDQ, Chronic Liver Disease Questionnaire;

5. Outcome measures

Outcome measures were grouped into three main domains: muscle related, functional, and clinical outcomes. Muscle related data included muscle mass, muscle thickness, skeletal muscle mass index, and grip strength. Functional outcomes included physical performance tests, walking speed, and frailty indices, such as the LFI. Clinical outcomes included liver related parameters and QOL measures, when available.

6. Data synthesis and methodological considerations

Due to the heterogeneity of study designs, interventions, and outcome measures, the data were synthesized narratively. The results were summarized descriptively and organized according to physical activity, nutritional strategy, and outcome assessment domain. As this review aimed to map current studies rather than assess intervention effectiveness, no formal assessment of risk of bias was performed. The methodological diversity of the included studies was considered a key finding and contributed to the identification of gaps in the current literature.

7. Discussion

7.1. Exercise modality and training structure

Across the included studies, substantial heterogeneity was observed in exercise modality and training structure. Walking-based interventions were predominantly implemented by Xiang et al. (38) and Hiraoka et al. (42), either alone or in combination with BCAA supplementation. These interventions were mainly associated with modest improvements in certain muscle parameters or attenuation of sarcopenia progression; however, whole body effects were limited. A controlled trial using a smartphone app guided walking program combined with BCAA supplementation demonstrated improvements in skeletal muscle mass and muscle strength, highlighting the potential role of technology-assisted interventions in increasing adherence to low-intensity exercise programs (38).

In contrast, studies incorporating combined aerobic and resistance training, such as those by Sobhy et al. (39) and Hernández-Conde et al. (41), reported more consistent and clinically meaningful improvements in muscle thickness, strength, and frailty-related outcomes. These findings are consistent with current pathophysiological models of sarcopenia in cirrhosis, which emphasize impaired protein synthesis, chronic inflammation, and altered skeletal muscle metabolism as key contributors to muscle loss (27,34). Trifan et al. (43) proposed a systemic perspective on cirrhosis, highlighting clinical hepatology studies addressing liver stiffness, cholestatic disorders, and disease severity, and supporting the need for interventions that target functional decline in addition to biochemical outcomes. From this perspective, exercise modalities that provide sufficient mechanical and metabolic stimuli particularly resistance training appear better suited to counteract these mechanisms than aerobic exercise alone.

7.2. Role of resistance training in sarcopenia management

Mohta et al. (40), despite implementing a 7-day-per-week, 4-week intervention consisting of walking and resistance training combined with BCAA supplementation, did not observe significant improvements in muscle mass or physical function. This finding suggests that intervention duration alone may not be sufficient and highlights the importance of exercise intensity, progression, supervision, and adherence. These observations indicate that resistance training is essential for stimulating muscle protein synthesis and neuromuscular adaptation processes, which are profoundly impaired in cirrhosis-associated sarcopenia (34). Larger clinical studies support the notion that advanced liver disease is frequently associated with reduced functional reserve and increased physical vulnerability, even in compensated stages (44).

7.3. Preventive versus therapeutic effects of exercise interventions

The preventive and therapeutic exercise strategies used by Hiraoka et al. (42) focused on preventing sarcopenia through daily walking combined with BCAA supplementation and reported favorable preventive effects, particularly in patients with early-stage disease. Similarly, Xiang et al. (38) observed improvements in grip strength and skeletal muscle mass index following gait-based interventions delivered through digital tools. However, walking-based approaches appeared less effective in improving pre-existing sarcopenia.

In contrast, interventions that included resistance training were more effective in improving muscle mass, strength, and functional performance, suggesting that preventive strategies differ from therapeutic exercise approaches. These findings are supported by evidence that sarcopenia and frailty in decompensated cirrhosis are associated with metabolic disturbances that may require higher intensity or multimodal interventions to achieve clinically meaningful improvements (27). It is important to emphasize the need to adapt exercise interventions according to disease stage and functional status, as variability in liver stiffness and disease severity can significantly influence functional reserve and therapeutic response in patients with chronic liver disease (44).

7.4. Interaction between exercise and nutritional supplementation

All included studies incorporated nutritional strategies based on amino acid supplementation; however, substantial heterogeneity was observed in supplementation type, dosage, and composition. While BCAA supplementation was a common feature, additional nutrients such as protein, carbohydrates, and vitamins were variably included. This variability complicates the interpretation of the independent and additive effects of amino acid supplementation beyond exercise alone.

Current evidence supports the rationale for amino acid supplementation in liver cirrhosis, as branched-chain amino acids function not only as substrates for protein synthesis but also as alternative energy sources for skeletal muscle in the context of impaired liver metabolism (45). Clinical and nutritional studies have shown that nocturnal nutritional supplementation improves whole body protein balance (11), while international consensus guidelines emphasize optimizing protein and BCAA intake to counteract ammonia related metabolic disturbances in cirrhosis (46). In addition, evidence from systematic reviews and meta-analyses indicates that BCAA supplementation may improve certain parameters related to sarcopenia, however, the effects on functional and clinical outcomes remain heterogeneous (12,13).

Studies indicate that leucine can enhance muscle protein synthesis by activating anabolic signaling pathways and attenuating hyperammonemia induced muscle dysfunction (15). These mechanisms may help explain the results observed in combined exercise and BCAA studies, such as those conducted by Sobhy et al. (39), Hernández-Conde et al. (41), and the smartphone-assisted walking intervention (38), compared with studies in which the exercise stimulus or progression was insufficient or poorly defined (40). Experimental research in the field of gastrointestinal diseases has further suggested that oxidative stress may act as a systemic mechanism influencing metabolic and functional outcomes, indicating that the anabolic response to exercise may be modulated by the inflammatory and redox environment (47,48).

7.5. Outcome measures and clinical relevance

Another limitation of the included studies was the heterogeneity of outcome measures used to assess intervention effectiveness. While muscle mass and strength were frequently evaluated, fewer studies included functional outcomes or measures related to sarcopenia progression. Hernández-Conde et al. (41) uniquely used the LFI, providing a more comprehensive assessment of functional vulnerability. Given the strong association between sarcopenia, frailty, physical function, and adverse clinical outcomes in cirrhosis (27), future studies should prioritize standardized, clinically meaningful functional outcomes alongside body composition measures to enhance clinical relevance and comparability. The importance of integrating functional outcomes alongside clinical assessment criteria has been previously emphasized in hepatology research, underscoring the need for interdisciplinary approaches that capture both disease severity and patient-centered functional decline (44). This perspective is also consistent with rehabilitation-focused literature, which highlights structured exercise and functional evaluation as central components in sarcopenia management(49).

This scoping review highlights exercise based rehabilitation as a central component in the management of sarcopenia among patients with liver cirrhosis. Across the included studies, structured physical exercise particularly interventions incorporating resistance training was consistently associated with improvements in muscle strength, physical performance, and frailty related outcomes. In contrast, walking based interventions alone were primarily associated with preventive effects or modest improvements in selected muscle parameters, with limited efficacy in reversing established sarcopenia. Branched-chain amino acid supplementation has demonstrated heterogeneous effects and appears to provide adjunctive benefits when combined with appropriate exercise, however, it does not act as a stand alone intervention. In particular, recent evidence from technology assisted interventions, such as smartphone app guided walking programs combined with BCAA supplementation, suggests that digital tools can improve adherence and contribute to improvements in skeletal muscle mass and strength, particularly in the early stages of the disease. These findings highlight the potential value of integrating exercise, nutrition, and digital health strategies into multimodal rehabilitation approaches.

7.6 Strengths and Limitations of the Available Evidence

The mapped evidence highlights a growing interest in combined exercise and BCAA-based interventions for sarcopenia in liver cirrhosis, with most studies employing structured exercise protocols and clinically relevant muscle related outcomes. However, the available literature remains limited in scope and is characterized by substantial heterogeneity in intervention design, supplementation regimens, and outcome assessment. Variability in exercise intensity, progression, and reporting standards restricts comparability across studies.

As a scoping review, this work aimed to map the existing evidence rather than appraise methodological quality, thereby underscoring the need for more standardized and rigorously designed trials in this field.

Table. 3 Domain-based mapping of evidence

Domain	Consistent Findings	Inconsistent Findings	Evidence Gap
Exercise Modality	Resistance training improves strength	Walking alone less effective in established sarcopenia	Optimal intensity unclear
BCAA Supplementation	May enhance anabolic response	Effects heterogeneous	Dose response not standardized
Disease Stage	Early stage responds to preventive walking	Decompensated disease under studied	Stage stratified trials lacking
Outcome Measures	Muscle mass frequently assessed	Frailty rarely standardized	Need unified functional endpoints
Digital Tools	Improve adherence	Limited evidence base	Long term impact unknown

8. Conclusions

Overall, the available evidence supports a hierarchical model in which exercise, particularly resistance training, is the primary therapeutic factor for sarcopenia in liver cirrhosis, while nutritional supplementation and digital support tools serve as complementary strategies. Substantial heterogeneity in intervention design, supplementation protocols, and outcome measures underscores the need for future studies that utilize standardized exercise prescriptions, clearly defined nutritional regimens, and clinically meaningful assessment criteria to better inform evidence-based practice.

This scoping review highlights exercise based rehabilitation as a clinically relevant strategy for mitigating sarcopenia in patients with liver cirrhosis. Clinically, these results support the use of structured, individualized exercise programs that adhere to the FITT principles and emphasize progressive neuromuscular loading, while amino acid supplementation may be considered an adjunctive strategy rather than a stand alone intervention. However, substantial heterogeneity in outcome measures and the limited use of standardized functional and frailty related endpoints restrict the interpretability and comparability of the current evidence. Future studies should focus on clearly defined exercise intensity and progression parameters, as well as standardized amino acid supplementation protocols with well defined methodologies across different stages of liver disease.

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