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NARRATIVE REVIEW

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The role of rehabilitation across the continuum of liver disease from cirrhosis to transplantation and beyond: A narrative review

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Abstract

Objective: The authors' objective with this narrative review is to explore the impact of rehabilitative interventions at each stage of liver disease.
Type: Narrative review.
Literature Survey: Literature search conducted in Medline, Embase, and Google Scholar databases.
Methodology: Articles were included if they were identified in one of the three database, written in English, peer-reviewed, and involved human participants without any restrictions on the publication date. Reference lists of these publications were also scrutinized for other articles that might be relevant. Elibigle articles were reviewed to determine whether they met inclusion crtieria.
Synthesis: Authors synthesized findings in the eligible articles to create a narrative summary.
Conclusions: Chronic liver disease is a major cause of morbidity and mortality across the globe. Cirrhosis causes alterations in metabolic and circulatory functions that negatively affect nutritional status and exercise capacity. Frailty is identified in nearly half of patients with advanced liver disease and bears a poor prognosis. Exercise and nutritional interventions improve key components of physical frailty and quality of life in chronic liver disease and after liver transplantation. Early mobility is generally recommended following liver transplantation and deemed to be safe and feasible. Inpatient rehabilitation may be considered in patients who require ongoing daily medical management by a physician, demonstrate a significant functional decline from their baseline, tolerate intensive rehabilitation, and have functional goals that can be addressed by at least two skilled therapies. Rehabilitation is safe and improves outcomes

at every stage of liver disease from cirrhosis to following transplantation. This literature review explores the impact of rehabilitative interventions at each stage of liver disease from cirrhosis to transplantation and beyond.

INTRODUCTION

Chronic liver disease (CLD) is a major cause of morbidity and mortality around the globe. According to 2015 Global Health Estimates, cirrhosis is the 11th leading cause of death and 15th leading cause of morbidity worldwide.[1]

Cirrhosis represents a late stage of progressive liver fibrosis. The predominant causes of cirrhosis are metabolic dysfunction associated fatty liver disease (59%), followed by hepatitis B virus (29%), hepatitis C virus (9%), and alcoholic liver disease (2%).[1] The prevalence of hepatitis C seems to be decreasing in Western countries with the development of new antiviral regimens. In contrast, nonalcoholic fatty liver disease is increasing with the incidence of metabolic risk factors, including obesity and type 2 diabetes.[2] Alcohol-associated liver disease became the leading diagnosis among adult liver transplant candidates following the surge in unhealthy alcohol use during the COVID-19 pandemic. In 2021, alcohol-associated liver disease accounted for 36.3% of waitlist registrations, with the greatest increase in alcohol-associated liver disease listings occurring in young adults and patients with severe alcohol-associated hepatitis.[3,4]

Although early stages of cirrhosis are typically asymptomatic, decompensated cirrhosis is characterized by jaundice and the presence of potentially life-threatening complications, such as ascites, variceal bleeding, hepatorenal syndrome, and hepatic encephalopathy. Once decompensation occurs, the morbidity and mortality resulting from cirrhosis increase sharply. Patients require frequent and increasing amounts of medical attention as the disease progresses. In advanced stages, the only treatment option may be liver transplantation, which is a high-burden option for patients and medical systems with high health care expenditures.[5]

The economic impact of CLD is high and growing. In the United States, the rate of CLD-related hospitalizations per 100,000 hospitalizations increased from 3056 (95% confidence interval [CI], 3042–3069) in 2012 to 3757 (95% CI, 3742–3772) in 2016. Associated inpatient health care costs during that time frame increased from $14.9 billion (95% CI, $13.9–15.9 billion) to $18.8 billion (95% CI, $17.6–20.0 billion).[6] A study that analyzed data collected between 2004 and 2013 found that individuals with CLD are more likely to be unemployed (55% vs. 30%), have higher rates of disability-related unemployment (30.5% vs. 6.6%), and have higher annual health care expenditures ($19,390 vs. $5567) than those without CLD.[7,8]

Adults with CLD report lower quality of life (QOL) and more health-related functional limitations.[8] They are also more likely to require caregiver support to complete activities of daily living (ADLs), such as dressing and bathing, and instrumental ADLs (iADLs), such as grocery shopping and housework.[9] One study found that individuals with cirrhosis received more than twice the number of informal caregiving hours per week compared to age-matched adults without cirrhosis.[9]

There is a need for systematic efforts to improve patient outcomes and simultaneously reduce the health care and economic burden associated with CLD.[10] The role of rehabilitation in management of chronic diseases is well investigated. Rehabilitative interventions have shown positive effects on many patient-related outcomes including morbidity, mortality, physical function, and QOL.[11] This literature review explores the impact of rehabilitative interventions at each stage of liver disease from cirrhosis to transplantation and beyond.

LITERATURE SEARCH STRATEGY

A literature search was conducted in Medline, Embase, and Google Scholar databases using keywords and phrases including (“liver transplant” OR “liver disease” OR cirrhosis OR “liver failure”) AND (rehabilitation OR exercise OR “physical function” OR physiology OR outcomes OR frailty). Articles were included if they were identified in one of the three databases, written in English, peer-reviewed, and involved human participants without any restrictions on the publication date. Exclusion criteria were commentaries, editorials, case reports, not full texts, and not relevant to liver disease or rehabilitation. Authors independently screened titles and abstracts then reviewed relevant full-text articles. Published abstracts were considered if the content was relevant and not available elsewhere. Reference lists of these publications were scrutinized for other articles that might be relevant. Eligible articles were reviewed by first and last authors to determine whether they met inclusion criteria, and any differences were resolved by consensus. This search strategy resulted in 76 total articles, which included original research and review articles. Textbook chapters were referenced where appropriate to include relevant background knowledge on the topic.

DISCUSSION

End-stage liver disease

Physiology

Cirrhosis causes alterations in metabolic and circulatory functions that negatively affect nutritional status and exercise capacity. Sarcopenia develops as a result of malnutrition and hepatic synthetic dysfunction.[12] Malnutrition is estimated to occur in up to 65%–95% of individuals with end-stage liver disease.[13] Malnutrition occurs due to malaise from chronic inflammation, impaired nutrient absorption, and early satiety from ascites. Cirrhosis is associated with an accelerated state of starvation and insulin resistance.[13] Decreased hepatic glycogen causes the body to inappropriately consume protein stores for gluconeogenesis. Excess ammonia beyond what the liver can process is diverted to the muscles for conversion to glutamine. Ammonia is toxic to muscles and contributes to muscle degradation.[14] The presence of sarcopenia in CLD is estimated at approximately 25%–70%. Rates are higher in individuals with end-stage liver disease and in males.[14]

Portal hypertension and hypoalbuminemia cause a redistribution of blood volume and intravascular hypovolemia. Baseline heart rate and cardiac output increase and systemic vascular resistance and arterial blood pressure decrease. Fluid shifts and ascites contribute to decreased lung expansion and impaired pulmonary gas exchange. Systemic inflammation leads to anemia of chronic disease. Together, these physiologic changes lead to reduced muscle function, physical inactivity, and aerobic impairment in liver disease.[12]

The Model for End-Stage Liver Disease (MELD) is a numerical scoring system that uses lab values for serum bilirubin, serum creatinine, and the international normalized ratio for prothrombin time to indicate disease severity and predict outcomes in patients with CLD. The original scale ranges from 6 to 40, with higher scores indicating more severe liver disease and a higher risk of mortality.[15] As a result of its accuracy in predicting short-term survival in patients with liver disease, MELD was adopted by the United Network for Organ Sharing in 2002 for transplant allocation and prioritization in the United States. Newer iterations of the MELD score that include variables such as patient gender, sodium, and albumin have been found to improve prognostic accuracy and continue to be used by the United Network for Organ Sharing for waitlist prioritization.[16]

The Organ Procurement and Transplantation Network replaced the original MELD score with the MELD-Na score in 2016 as emerging research found sodium to be an independent predictor of mortality in cirrhosis. One limitation of these scoring systems was the use of serum creatinine, which may be lower in women and in individuals with lower muscle mass. This may underestimate the degree of renal impairment and subsequently affect the overall MELD/MELD-Na score and waitlist prioritization.[16] The newest iteration currently recommended by the Organ Procurement and Transplantation Network, the MELD 3.0 developed by Kim et al. in 2021, includes variables for female gender and serum albumin to address disparities associated with the MELD/MELD-Na.[16] Markers of nutritional status and physical function, such as frailty and sarcopenia, have been found to improve the predictive accuracy of the MELD score. These factors are often considered by individual transplant centers when deciding to list a patient for transplant.[17]

Pretransplant function and rehabilitation

Frailty is a state of decreased physiologic reserve and increased vulnerability to health stressors. It is a critical determinant of health outcomes in liver disease. Frailty is characterized by skeletal muscle mass depletion (sarcopenia), progressive immobility, decreased energy expenditure, and malnutrition. Cirrhosis accelerates the cycle of frailty through systemic inflammation, decreased protein synthesis, muscle wasting, malnutrition, fatigue, and immobility. This combines with other factors such as aging and comorbidities that all contribute to frailty.[17]

The two most common indices used in liver disease are the Fried Frailty Index and the Liver Frailty Index.[18,19] The Fried Frailty Index was first proposed in 2001 and assesses physical frailty based on five items: unintentional weight loss, weakness, exhaustion, slow gait, and low physical activity.[19] The Fried Frailty Index uses a combination of reported and objective measures to arrive at a score. It has been found to have good evidence for reliably and validity.[20] The Liver Frailty Index was developed more recently by a group of physicians and researchers at University of California-San Francisco and published in 2017. It was originally intended for use in adult patients with cirrhosis awaiting liver transplantation in the outpatient setting. The Liver Frailty Index consists of three performance-based measures, including gender adjusted grip strength, number of chair stands per second, and balance time.[18] This scale has been found to have good reliability and validity.[20] For both the Fried Frailty Index and the Liver Frailty Index, higher values indicate a higher degree of frailty.[18,19]

Frailty is identified in nearly half of patients with advanced liver disease. Frailty bears a poor prognosis, predicting increased morbidity and mortality both pre- and post-liver transplant, independent of MELD score.[21] Knowing a patient's frailty status can be used to complement the MELD score and other data in guiding clinical decisions and facilitating discussions with patients about treatment options, such as if they want to pursue transplant, whether to pursue transplant centers more aggressively with lower MELD thresholds, or perhaps seek palliative services.[18] There are no data to support a single frailty cutoff at which a patient should not undergo liver transplantation.[17]

TABLE 1 Outcomes in chronic liver disease and before liver transplant.

Study (year)	Study type	Time frame	Participants	Intervention(s)	Outcomes	Findings
Al-Judaibi et al. (2019)[22]	Retrospective chart review	Perioperative period/ prehabilitation	458 LT recipients (258 intervention group, 200 control group)	• Exercise training program (undefined timeline)	• 90-d hospital readmission post-LT • Length of hospital stay post-LT • Postoperative complications	• No difference in 90-d hospital readmission (20% vs. 17.9%, $p = .576$), median LOS (17 vs. 14 d, $p = .690$), or post-op surgical complications (27.5% vs. 27.9%, $p = .923$) • Nonsurgical infection rate higher in intervention group post-LT (17.9% vs. 7%, $p = .001$)
Lin et al. (2021)[23]	Ambispective cohort study	Chronic liver disease/ prehabilitation	517 LT candidates with ESLD	• Individualized exercise prescription	• Liver Frailty Index • 6MWT • Gait speed • Survival	• Exercise improved liver frailty index ($p < .001$) and 6MWT ($p = .07$) but did not improve gait speed ($p = .32$) • Liver frailty index improvement by ≥0.3 associated with improved survival ($p < .001$)
Macshut et al. (2021)[24]	Retrospective cohort study	Perioperative period/ prehabilitation	394 living donor LT recipients (86 intervention group)	• 2 weeks prehab and nutritional intervention	• Visceral adiposity • Intraoperative blood loss	• Increased visceral to subcutaneous adiposity was an independent risk factor for high intraoperative blood loss in the recipient (ratio 1.98, $p = .009$) • Visceral adiposity was not a risk factor for surgical blood loss in the intervention group (OR: 0.89, $p = .86$)
Rossi et al. (2022)[25]	Pilot trial	Chronic liver disease	25 patients with cirrhosis (13 intervention group, 12 control group)	• Structured aerobic exercise program of 30–50 min/week $\times$ 12 weeks	• Fatigue • Muscle strength • Quality of life	• Intervention group showed reduced fatigue ($p < .001$), increased muscle strength ($p < .001$), and improved mental health ($p = .003$) • Control group no improvement
Soto et al. (2021)[26]	Prospective cohort study	Chronic liver disease	126 patients with cirrhosis	• None	• Frailty • Gait speed • Mortality	• Higher mortality observed in patients with frailty (68% vs. 21%, $p < .001$) and decreased gait speed (80% vs. 41%, $p < .001$)
Tapper et al. (2015)[27]	Retrospective cohort study	Chronic liver disease	734 inpatients with decompensated cirrhosis	• None	• 90-d mortality • Discharge to IPR • 30-day readmission • LOS	• 90-d mortality was 18.3% • 14.3% were discharged to IPR • 30-d readmission rate was 26.6% • Median LOS was 4 d
Yoh et al. (2020)[28]	Retrospective observational study	Chronic liver disease	411 patients with cirrhosis	• None	• Grip strength • Skeletal muscle mass index • SF-36 • Hepatic decompensation	• Decreased grip strength (25% vs. 12%, $p = .0057$) and decreased skeletal muscle mass (20% vs. 13%, $p = .098$) were associated with more hepatic decompensation • The SF-36 was not an independent predictor of hepatic decompensation

Abbreviations: 6MWT; 6-minute walk test; ESLD, end-stage liver disease; IPR, inpatient rehabilitation; LOS, length of stay; LT, liver transplant; OR, odds ratio; post-op, postoperative; prehab, prehabilitation; preop, preoperative; SF-36, 36-Item Short-Form Health Survey.

Unlike most risk factors such as age, gender (estrogen protective), or MELD score, frailty and sarcopenia are potentially modifiable with exercise and nutritional interventions (Table 1).[17] Exercise improves key components of physical frailty (functional/aerobic capacity, sarcopenia) and QOL in chronic liver disease and after liver transplantation.[29] Rehabilitation interventions have been associated with a decreased rate of 30- and 90-day readmissions in patients with cirrhosis.[30] When rehabilitation interventions are not indicated or available, there are practical ways to maintain activity such as parking further away in the parking lot or taking the stairs instead of the elevator when able.[31] It is also important to consider barriers that may interfere with activity or rehabilitation. Factors that may affect safety include risk of variceal bleeding, falls, cardiovascular and pulmonary comorbidities, fatigue, and cognitive impairment.[32] Studies reporting on outcomes in chronic liver disease and before liver transplant are reported in Table 1.[22–28]

Post liver transplantation

Physiology

Liver transplantation is a complex, life-saving treatment option for patients with end-stage liver failure. There have been several advancements in surgical techniques over the years that have improved perioperative morbidity and mortality. One such example is the application of microsurgical techniques for hepatic artery reconstruction, which have greatly reduced the risk of hepatic artery thrombosis, a potentially devastating complication that threatens the viability of the transplanted organ with a high rate of mortality.[33] Postoperative management plays a crucial role in ensuring the success of the transplant. Immunosuppressants are administered to prevent rejection. Careful drug monitoring is essential to prevent rejection while minimizing side effects.[34] Prophylactic antimicrobial agents are concomitantly administered to reduce the risk of bacterial, viral, and fungal infections in the immunosuppressed patient. Adherence to medications and lifestyle modifications are essential for long-term success following liver transplantation.[35]

Transplantation restores hepatic synthetic function and normalizes portal hypertension almost immediately for most recipients.[36] Sarcopenia and physical capacity tend to improve slowly but recovery is often incomplete.[36] Immunosuppressants are thought to play a significant role in the persistence or development of metabolic syndrome and sarcopenia after transplantation. Recipients typically gain weight and metabolic syndrome features persist or worsen.[36] It is important to consider that vagus innervation in normal hepatic functioning is lost during transplantation. It has been suggested that isolation of the liver from autonomic regulatory control may influence nutrient absorption and metabolism, glucose and lipid homeostasis, as well as appetite signaling and eating behavior. These factors are thought to contribute to body composition and weight changes observed after liver transplantation.[37] Liver transplant recipients are at high risk for cardiovascular morbidity.[36]

Immediate postoperative rehabilitation

Liver transplant recipients are typically monitored in the intensive care unit for a period of time following surgery. Early mobility is generally recommended following liver transplantation and deemed to be safe and feasible and supported by evidence-based practice guidelines.[38,39] Although there is only a small body of literature reporting on safety and rehabilitation outcomes in the early postoperative period after liver transplantation, there is considerable research to support early mobility and therapy intervention in the critically ill population. Early mobilization strategies are typically progressive, starting with in-bed activities such as passive then active range of motion of major joints, assessing physiologic tolerance of supine to sit, moving to sitting up at edge of bed, sit to stand, transfers, moving from bed to chair, and ultimately walking in the room and then the hallway. A similar progression is followed in the performance of ADLs. Typically, these activities are performed with a physical and/or occupational therapist, or sometimes a nurse, with the goal of progressing toward independent mobilization and ADL performance.[40]

Thorough medical assessment of vital signs, laboratory data, active medical conditions, ventilator settings (if appropriate), and medications should be performed to determine adequate medical stability and safety for rehabilitation.[38] Criteria for safe initiation of physical rehabilitation or mobilization in the intensive care unit are described by Devlin et al.[38] Once rehabilitation is started, care needs to be taken to avoid disruption of the surgical drain and other lines/tubes during mobility, including consideration for gait belt placement.[39] Rare events that have been noted during early mobility include onset of cardiopulmonary changes, unplanned extubation, falls, and one report of Achilles tendon rupture.[38]

Limited research suggests that postoperative liver transplant recipients can safely perform early mobility and exercise during acute care, including within the intensive care unit. Benefits may include improved cardiorespiratory and muscular fitness, reduced duration of mechanical ventilation, and a moderate-sized improvement in health-related QOL.[39] One randomized controlled trial evaluated intensive early rehabilitation on 20 patients in the intensive care unit after liver

TABLE 2 Early outcomes after liver transplantation.

Study (year)	Study type	Time frame	Participants	Intervention(s)	Outcomes	Findings
Beyer et al. (1999)[46]	Prospective cohort study	Surgical ICU immediately postoperative and up to 8–24 weeks post transplant	10–17 LT recipients	• In hospital: daily exercises with increasing intensity, step training and ergometer bicycling. • 3 weeks post transplant: part-supervised aerobic, resistance, balance, flexibility for 60 min twice weekly.	• VO_{2max} • 6MWT • Isokinetic knee muscle strength • Timed transfers • Timed squats • Perceived health	• VO_{2max} (43%, $p < .0001$), 6MWT (27%, $p < .0001$), concentric knee flexion strength (100%, $p = .0003$), timed transfers (25%, $p = .0001$), timed squats (25%, $p < .0005$), and health perceived as good or excellent (488%) improved 6 months after LT
Cortazzo et al. (2005)[47]	Retrospective chart review	Inpatient rehabilitation	55 patients after LT admitted to IRF	• Acute inpatient rehabilitation	• Age • Hospital LOS • IRF LOS • FIM scores • Albumin levels • Discharge disposition	• Low albumin ($p < .01$) and long hospital LOS ($p < .05$) correlated with longer IRF LOS • Longer IRF LOS correlated with FIM gain ($p < .001$) • Significant improvements in FIM scores ($p < .001$) noted in patients who discharged home ($n = 50$) • Age, albumin level, and hospital LOS did not predict discharge disposition ($p \geq .05$)
Demir et al. (2020)[48]	Randomized controlled trial	Surgical ICU immediately postoperative	80 LT recipients (40 intervention group, 40 control group)	• Back massage twice daily	• Visual Analogue Scale • State–Trait Anxiety Inventory	• Pain improved from 4.92 to 3.82 in the intervention group ($p < .001$) but not in the control group ($p = .720$) • Anxiety improved from 50.10 to 46.57 in the intervention group ($p < .001$) but not in the control group ($p = .432$)
Ergene et al. (2019)[49]	Randomized controlled pilot trial	Immediate postoperative period	30 LT recipients (15 intervention group, 15 control group)	• Intervention: 2 sessions per day, 5 d per week, strength training, combination supervised and unsupervised × 8 weeks • Control: routine postoperative care	• Muscle strength (quadriceps, anterior deltoid, and middle deltoid) using a hand-held dynamometer • Respiratory muscle strength (maximal inspiratory pressure and maximal expiratory pressure) • 6MWT • 30-second sit-to-stand test • Turkish version of the Checklist Individual Strength (fatigue perception)	• Treatment group showed 8-week improvements in 6MWT, muscle strength, maximal inspiratory pressure ($p = .001$), and maximal expiratory pressure ($p = .047$), whereas control group remained unchanged ($p > .05$) • Treatment group had improved deltoid strength and fatigue perception compared to control group ($p < .05$)

TABLE 2 (Continued)

Study (year)	Study type	Time frame	Participants	Intervention(s)	Outcomes	Findings
Foroncewicz et al. (2011)[50]	Prospective cohort study	Surgical ICU and acute care starting postoperative day 5	13 LT recipients	• "A rehabilitation program"	• 6MWT • Borg Rating Scale of Perceived Exertion	• Walking distance increased from 327 meters on day 7 to 421 meters on day 14 (35%) • Day 7: 1 participant reached predicted distance • Day 14: 3 participants reached predicted walking distance for age-matched controls • The Borg Scale did not change significantly between days 7 and 14
Kleine et al. (2011)[51]	Prospective observational study	Surgical ICU immediately postoperative	27 LT recipients (12 intervention group, 15 control group)	• "Kinetic therapy"	• Respiratory function (PaO_2/FiO_2) • Liver perfusion	• Intervention group had reduced respiratory function (53% of baseline) at 48-hours postop ($p = .001$) • Respiratory function recovered to 95% of baseline at day 9 with kinetic therapy ($p = .001$) • Control group did not show any changes at 48 hours ($p = .401$) or on day 9 postop ($p = .626$) • No adverse effects on graft perfusion in intervention group
Kothari et al. (2016)[52]	Retrospective cohort study	Inpatient rehabilitation	3072 LT recipients	• Inpatient rehabilitation, home, LTAC, or SNF	• 30-d readmission	• Overall 30-d readmission rate was 29.6% • Discharge to IRF (aOR 0.43, $p = .013$) or LTAC/SNF (aOR 0.63, $p = .014$) was associated with decreased odds of 30-d readmission compared with discharge home • Time to first readmission was longest for patients discharged to IRF (17 vs. 8 d, $p < .001$)
Maffei et al. (2017)[41]	Randomized controlled trial	Surgical ICU immediately postoperative	40 LT recipients (20 intervention group, 20 control group)	• Intervention: 1–2 therapy sessions per day, first ROM, then sit, stand, walk • Control: "usual treatment"	• Sitting • Intestinal transit time • LOS	• Intervention group sat on the edge of bed sooner (2.6 vs. 9.7 d; $p = .048$) and resumed intestinal transit time sooner (3.7 vs. 5.6 d; $p = .015$) than patients usual treatment group • No difference in ICU or hospital LOS between groups
Nguyen et al. (2022)[53]	Retrospective chart review	Perioperative period	79 patients with cirrhosis who underwent LT	• Liver transplantation	• Sarcopenia • Hospital LOS • Infections • Complications	• Sarcopenia present in 46% before LT and 62% after • Posttransplant sarcopenia associated with longer hospital LOS (54 vs. 29 d, $p = .002$), more frequent infections (3 vs.

(Continues)

TABLE 2 (Continued)

Study (year)	Study type	Time frame	Participants	Intervention(s)	Outcomes	Findings
						1, $p = .027$), and greater number of complications (5 vs. 3, $p < .001$)
Rongies et al. (2009)[54]	Retrospective chart review	Surgical ICU immediately postoperative	309 LT recipients	• "Early rehabilitation"	• Time to standing	• Mean time to standing after transplantation was 4 d in liver failure due to virus or alcohol and 8 d in acute/ subacute liver failure
Rongies et al. (2008)[55]	Retrospective chart review	Surgical ICU immediately postoperative	136 LT recipients	• "Early rehabilitation"	• Time to initiation of rehab • Time to standing	• Mean time to begin rehab (1.6 d) and mean time to stand (4 d) were shortest in other causes of liver failure (cancer of the liver, Budd-Chiari syndrome, infection with parasites) • Mean time to begin rehab (3.6 d) and mean time to stand (9.5 d) were longest in acute liver failure • Intermediate results were seen in hepatitis B/C, primary biliary cirrhosis/ primary sclerosing cholangitis, and alcoholic cirrhosis
Roshdy et al. (2019)[56]	Prospective cohort study	Surgical ICU immediately postoperative	30 male LT recipients	• Diaphragmatic, apical, costal breathing, POWERbreathe Plus device, and early ambulation for 14 sessions per week and twice daily × 21 d	• Arterial blood gases analysis • 6MWT	• There was a statistically significant difference in pH ($p = .001$), PCO_2 ($p = .001$), PO_2 ($p = .001$), Lactate ($p = .001$), HCO_3 ($p = .001$) measured in the 1st, 7th, and 21st d postop • 6MWT distance increased between 7th d (176 m) and 21st d (546 m) postop ($p = .001$)
Schaller et al. (2016)[57]	Randomized controlled trial	Surgical ICU immediately postoperative	200 critically ill patients in the surgical ICU (104 intervention, 96 control)	• Intervention: daily targeted mobility goal (passive ROM, sitting, standing, walking) performed throughout the day • Control: "standard of care"	• SOMS • SICU LOS • mmFIM	• Intervention group had improved mobilization (SOMS 2.2 vs. 1.5, $p < .0001$), decreased SICU length of stay (7 vs. 10 d, $p = .0054$), and improved functional mobility at hospital discharge (mmFIM 8 vs. 5, $p = .0002$) • More adverse events reported in intervention group (2.8%) than in control group (0.8%)
Senduran et al. (2010)[58]	Prospective cohort study	Surgical ICU immediately postoperative	13 LT recipients	• Respiratory physiotherapy, active ROM, sitting in bed, sitting edge of bed, standing, sitting out of bed, walking	• Heart rate • Blood pressure • SpO_2 • Respiration rate • Visual Analogue Scale • FIM scores	• No significant difference between pretreatment and 5th min of recovery measurements on vital signs and visual analog scale ($p \geq .05$)

TABLE 2 (Continued)

Study (year)	Study type	Time frame	Participants	Intervention(s)	Outcomes	Findings
Sevarolli et al. (2018)[59]	Retrospective trial	Hospitalized solid organ transplant candidates or recipients	157 solid organ transplant candidates or recipients (47 LT recipients)	• Respiratory kinesiotherapy, muscle strengthening of upper and lower limbs, walking, cycle ergometer		• FIM scores improved from initial FIM post transplant but did not return to premorbid baseline

Abbreviations: 6MWT, 6-minute walk test; aOR, adjusted odds ratio; FIM, Functional Independence Measure; FiO_2, fraction of inspired oxygen; ICU, intensive care unit; IPR, inpatient rehabilitation; IRF, inpatient rehabilitation facility; LOS, length of stay; LT, liver transplant; LTAC, long term acute care; mmFIM, mini modified Functional Independence Measure; PaO_2, partial pressure of oxygen in arterial blood; ROM, range of motion; SICU, surgical intensive care unit; SNF, skilled nursing facility; SOMS, SICU optimal mobilization score; SpO2, oxygen saturation; $\dot{V}O_2$ max, maximum rate of oxygen consumption.

transplantation. The intervention group sat on edge of bed sooner (2.6 days vs. 9.7 days; $p = .048$) and resumed intestinal transit sooner (3.7 days vs. 5.6 days; $p = .015$) than controls.[41] Early mobilization after liver surgery has been associated with improvement in sleep, reduction in postoperative complications, and reduced hospital length of stay.[40,42,43] Additional benefits include pain reduction and less postoperative fatigue.[44] Qualitative patient feedback after abdominal surgery has suggested that early mobility is an important part of care, influences recovery, and improves overall well-being.[45] Studies reporting early outcomes after liver transplantation are listed in Table 2.[41,46–59]

There is significant opportunity for physiatry to be actively engaged in the care of liver transplant recipients during the initial postoperative period. Physiatrists can support optimization of function and QOL during hospitalization and long term.[60] Some focuses include sleep regulation, pain management, delirium prevention and treatment, as well as bladder and bowel management.[38–40]

Inpatient rehabilitation

Medical considerations for inpatient rehabilitation

The inpatient rehabilitation facility (IRF) is an ideal post-acute care setting for liver transplant recipients who require close medical oversight and intensive therapy. Inpatient rehabilitation (IPR) may be considered in patients who require ongoing daily medical management by a physician, demonstrate a significant functional decline from their baseline, tolerate intensive rehabilitation, and have functional goals that can be addressed by at least two skilled therapies (physical therapy, occupational therapy, and speech and language pathology).[61] Acute care inpatients who are at moderate and high risk for pressure ulcer formation are more likely to discharge to an IRF compared to patients who are at low risk.[62]

The IPR team, led by a physical medicine and rehabilitation physician, collaborates with the transplant team on medical optimization, including laboratory monitoring, medication titration, in addition to workup and treatment of any new medical concerns and escalation of care when indicated.[60] If the transplant team cannot follow the patient in IPR, a shared electronic medical record or close regular contact is necessary to provide remote advice accordingly. Reliable laboratory and pharmacy services are crucial for monitoring immunosuppression and any signs of rejection.[60]

Subacute rehabilitation at a skilled nursing facility may alternatively be considered for patients who cannot tolerate the level of rehabilitation intensity provided at IRFs or when IRFs are not close by or available. IRFs are preferred in most cases due to the need for ongoing close physician oversight and timely lab monitoring. Other levels of postacute care, including home health and outpatient therapy, may be preferred after the acute care hospitalization in patients who are functionally able to return home and are stable enough for laboratory monitoring and medication titration on an outpatient basis.[52] A retrospective chart review of 3072 liver transplant recipients found discharge to another inpatient facility (IRF, skilled nursing facility, or long-term acute care) had decreased odds of 30-day readmission compared to discharge home. Patients discharged to IRF had the longest time to readmission.[52] Insurers have invested a large amount of resources into these patients and are often willing to approve IPR after liver transplantation.[52]

Role of the interdisciplinary rehabilitation team

A highly skilled multidisciplinary therapy team is integral to the successful recovery of this population. Rehabilitation programs for transplant recipients typically include aerobic exercises, strength training, functional training, and education.[63] The physical therapist focuses on mobility and endurance during the rehabilitation program. The occupational therapist incorporates the use of adaptive equipment, energy conservation, and pacing strategies to manage tremor, optimize dexterity, and assist with ADLs. The speech and language pathologist can address dysphagia, hypophonia, or dysphonia that may occur with central nervous system pathology or vocal cord injury during intubation.[60] Neurocognitive impairments caused by hepatic encephalopathy can also be treated to maximize cognitive capabilities via compensatory strategies and education. Impaired cognition can affect independence with medication management, independent living, and return to work. At many centers, a caregiver is arranged prior to transplant to provide oversight of iADLs and medication administration. Mood and adjustment disorders are frequently comanaged with a rehabilitation psychologist or psychiatrist consultant.[60]

Inpatient rehabilitation outcomes

Inpatient rehabilitation has been found to be safe, tolerable, feasible and may improve functional outcomes after liver transplant. Outcomes have only been reported in a handful of studies, but the growing number of studies looking at functional improvement in this population is promising. A retrospective chart review of 55 patients after liver transplant admitted to IRF found that low albumin and long length of stay in acute care hospital correlated with longer IPR stay and less efficient rehabilitation. Patients who were discharged home ($n = 50$) had significant improvements in functional scores during IRF admission. There was a positive correlation between length of stay and degree of functional gain.[47] Further research suggests that liver transplant recipients demonstrate meaningful improvement in their functional status with IPR, and a high percentage of patients are able to discharge home. Trojetto found that lack of funding, shortages of health care personnel, and low volume of patients can be barriers to developing transplant rehabilitation programs.[63] Additional outcomes research is needed to justify IPR with regard to use of resources, cost, and value-based care plans. A systematic review by Mina et al. concluded that the overall quality of studies evaluating IPR outcomes after liver transplant is poor.[64]

Long-term functional considerations

Short-term survival in the first year after liver transplantation has markedly improved with advancements in immunosuppression and early perioperative care.[65] However, long-term survival has not appreciably improved in the past 30 years.[65] Late mortality continues to be primarily related to long-term sequelae of immunosuppression. Most frequent causes of late death are cardiovascular disease, de novo malignancies, chronic kidney disease, and recurrence of pre-transplantation disease.[66,67] Cardiovascular disease in liver transplant recipients is related to posttransplantation metabolic syndrome, which is characterized by obesity, high blood pressure, high blood triglycerides, low high-density lipoprotein cholesterol, and insulin resistance. In a study by Kallwitz et al., 63.5% of liver transplant recipients had metabolic syndrome 1 year post transplant.[68] Malignancy screening, treatment of recurrent disease, and adequate management of metabolic disease are critical to improving survival outcomes after transplantation.[69]

Liver transplant improves long-term QOL and function compared to preoperative status. QOL improves to a similar level as the general population, but physical function remains worse. A trial evaluating eight healthy liver transplant recipients found impaired peak oxygen consumption and reduced peak heart rate during exercise compared to predicted values. The results were similar to that observed after other solid organ transplants.[70] Worse QOL is predicted by more postoperative complications. QOL improvements after liver transplantation are similar to that seen after other solid organ transplants (kidney, lung, or heart).[71] Postoperative physical activity is correlated with improved health-related QOL.[36,72]

The U.S. Department of Health and Human Services broadly recommends 150 minutes of moderate intensity aerobic activity per week and muscle-strengthening activities two times per week.[73] Regular exercise has been shown to be effective in the management and prevention of cardiac outcomes in metabolic syndrome in the general population.[74,75] In one study, exercise intensity was shown to be inversely related to metabolic syndrome after transplantation.[68] Rehabilitation and therapy interventions may be useful

TABLE 3 Long-term outcomes after liver transplantation.

Study (year)	Study type	Time frame	Participants	Intervention(ss)	Outcomes	Findings
Garcia et al. (2014)[76]	Randomized controlled trial	Chronic	15 LT recipients (9 intervention group, 6 control group)	• Intervention: 24 sessions of continuous 30-min treadmill exercise • Control: usual care	• 6MWT • Resting energy expenditure	• Exercise group showed increase in distance walked (454 m to 583 m, $p \le .05$) and resting energy expenditure (1060 kcal to 1375 kcal, $p \le .05$) • No differences observed in control group
Krasnoff et al. (2006)[77]	Randomized clinical trial	Chronic	151 LT recipients (65 intervention group, 86 control group)	• Intervention: of individualized counseling and follow-up to home-based exercise and dietary modification • Control: usual care	• Exercise capacity (VO_{2peak}) • Quadricep muscle strength • Body composition (DXA) • Nutritional intake (Block 95) • Health-related quality of life (SF-36)	• Exercise group showed greater increase in VO_{2peak} ($p = .036$) and self-reported general health ($p = .038$) compared to usual care group • Both groups demonstrated increases in muscle strength, body weight, body fat and other SF-36 scale scores
Moya-Najera et al. (2017)[78]	Randomized controlled trial	Chronic	50 LT recipients (22 intervention group, 28 control group)	• Intervention: 6-month exercise training program, exercising 2 d for 24 wk in the hospital facilities • Control: usual care	• VO_2max • Maximal strength • Body composition • Liver function • HRQOL	• Intervention group showed significant improvement compared to control group in aerobic capacity (15% vs. 7%, $p = .04$), hip extension (49% vs. 13%, $p < .001$), elbow flexion (28% vs. −9%, $p = .01$), overall maximal strength (31% vs. 9%, $p = .001$), physical functioning (14% vs. −5%, $p = .03$), and vitality (13% vs. −8%, $p = .03$) of HRQOL. • No changes observed in body composition and liver function tests ($p \ge .05$).
Totti et al. (2019)[79]	Clinical trial	Chronic (>6 months after transplant)	29 LT recipients (17 intervention group, 12 control group)	• Intervention: attended supervised training sessions 3 times per week for 12 months • Control: general recommendations about home-based exercise	• VO_{2peak} • BMI • Muscle strength (handgrip dynamometer) • Metabolic profile • Liver and kidney function • HRQOL	• Intervention group had reduction in fasting glucose (94 vs. 90.0 mg/dL, $p = .037$), increased upper limb muscle strength ($p = .005$), and improved scores in vitality, physical health, and mental health ($p < .05$)
Van den Berg-Emons et al. (2014)[80]	Prospective cohort study	Chronic (>1 year after transplant)	18 fatigued LT recipients	• 12-week rehabilitation program including physical exercise training and counseling on physical activity	• Fatigue • Aerobic capacity • Muscle strength • Body fat • Daily physical activity • Lipid profile	• After the program, participants were significantly less fatigued, and the percentage of individuals with severe fatigue was 22% to 53% lower than before the program

(Continues)

TABLE 3 (Continued)

Study (year)	Study type	Time frame	Participants	Intervention(ss)	Outcomes	Findings
					• Glycemic control	• Aerobic capacity and knee flexion strength were significantly higher, and body fat was significantly lower after the program
Van Ginneken et al. (2010)[80]	Prospective cohort study	Chronic	18 LT recipients	• 12-week rehabilitation program, which included supervised exercise training and daily physical activity counseling	• Health-related daily functioning (SIP-68) • Participation and Autonomy (IPA) Scale • RAND-36 Health Survey • Hospital Anxiety and Depression Scale	• After the program, patients showed improvements in daily functioning (23.6%, $p = .007$), autonomy outdoors (34.1%, $p = .001$), physical functioning (11.5%, $p = .007$) and vitality (21.5%, $p = .022$) • Anxiety and depression were unchanged post program

Abbreviations: 6MWT, 6-minute walk test; BMI, body mass index; DXA, dual-energy X-ray absorptiometry; HRQOL, health-related quality of life; IPA, Impact of Participation and Autonomy Questionnaire; LT, liver transplant; SF-36, 36-Item Short Form Survey; SIP-68, Sickness Impact Profile 68; VO_2 peak, highest amount of oxygen consumed at peak exercise.

to help patients achieve target fitness goals and improve long-term outcomes after liver transplantation.[36,68,69,76] Long-term outcomes after liver transplant are reported in Table 3.[77–82] Several studies have looked at exercise interventions, but the literature is sparse.[82] Authors of a 2023 Cochrane review on this topic were very uncertain of the role of exercise training (aerobic, resistance-based exercises, or both) in affecting mortality, health-related QOL, and physical function (ie, aerobic capacity and muscle strength) in liver transplant recipients.[83]

Other long-term outcomes that have been examined include return to employment and sexual function. The rate of continuous employment among individuals with chronic liver disease and liver transplants is low, with most studies quoting <50%.[84,85] One cohort study looked at employment data of 126 patients, which included patients on the liver transplant waitlist and patients who had undergone transplantation. Patients were largely of working age in the later stages of their careers. Only half of patients waiting for transplant were actively working, and only a small percentage of patients work following transplantation. This number decreases with time following transplantation.[86] Research on sexual health and function in liver transplant recipients is limited and conflicting. One questionnaire completed by 150 liver transplant recipients found sexual dysfunction increased from 24% pretransplant to 47% after transplant and occurred at similar rates between men and women.[87] Another survey study evaluating 64 patients who underwent liver transplantation found significant improvement in reported sexual function in men after transplantation but not in women.[88]

CONCLUSION

Liver disease affects metabolic and circulatory functions that have a negative impact on exercise tolerance. Frailty is modifiable through exercise and nutrition and predicts outcome in cirrhosis and after transplantation. Transplantation improves function but not to the level of the general population. The available research suggests that rehabilitation is safe and improves outcomes at every stage of liver disease from cirrhosis to following transplantation. There are ample data published on frailty and prehabilitation. Additional research is needed to inform outcomes and rehabilitation interventions in the perioperative period, inpatient rehabilitation period, and long term.

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REFERENCES

1. Cheemerla S, Balakrishnan M. Global epidemiology of chronic liver disease. *Clin Liver Dis*. 2021;17(5):365-370. doi:10.1002/cld.1061
2. Younossi ZM, Stepanova M, Younossi Y, et al. Epidemiology of chronic liver diseases in the USA in the past three decades. *Gut*. 2020;69(3):564-568. doi:10.1136/gutjnl-2019-318813
3. Kwong AJ, Ebel NH, Kim WR, et al. OPTN/SRTR 2021 annual data report: liver. *Am J Transplant*. 2023;23(2):S178-S263. doi:10.1016/j.ajt.2023.02.006
4. Cholankeril G, Goli K, Rana A, et al. Impact of COVID-19 pandemic on liver transplantation and alcohol-associated liver disease in the USA. *Hepatology*. 2021;74(6):3316-3329. doi:10.1002/hep.32067
5. GBD 2017 Cirrhosis Collaborators. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990–2017: a systematic analysis for the global burden of disease study 2017. *Lancet Gastroenterol Hepatol*. 2020;5(3):245-266. doi:10.1016/S2468-1253(19)30349-8
6. Hirode G, Saab S, Wong RJ. Trends in the burden of chronic liver disease among hospitalized US adults. *JAMA Netw Open*. 2020;3(4):e201997. doi:10.1001/jamanetworkopen.2020.1997
7. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. *J Hepatol*. 2019;70(1):151-171. doi:10.1016/j.jhep.2018.09.014
8. Stepanova M, De Avila L, Afendy M, et al. Direct and indirect economic burden of chronic liver disease in the United States. *Clin Gastroenterol Hepatol*. 2017;15(5):759-766.e5. doi:10.1016/j.cgh.2016.07.020
9. Rakoski MO, McCammon RJ, Piette JD, et al. Burden of cirrhosis on older Americans and their families. *Hepatology*. 2012;55(1):184-191. doi:10.1002/hep.24616
10. Allen AM, Kim WR, Moriarty JP, Shah ND, Larson JJ, Kamath PS. Time trends in the health care burden and mortality of acute on chronic liver failure in the United States. *Hepatol Baltim Md*. 2016;64(6):2165-2172. doi:10.1002/hep.28812
11. Ambrosino P, Marcuccio G, Formisano R, Marcuccio L, Filosa R, Maniscalco M. Cardiac and pulmonary rehabilitation: two underutilized approaches with some unexpected benefits. *J Clin Med*. 2023;12(8):2847. doi:10.3390/jcm12082847
12. West J, Gow PJ, Testro A, Chapman B, Sinclair M. Exercise physiology in cirrhosis and the potential benefits of exercise interventions: a review. *J Gastroenterol Hepatol*. 2021;36(10):2687-2705. doi:10.1111/jgh.15474
13. Shergill R, Syed W, Rizvi SA, Singh I. Nutritional support in chronic liver disease and cirrhotics. *World J Hepatol*. 2018;10(10):685-694. doi:10.4254/wjh.v10.i10.685
14. Allen SL, Quinlan JI, Dhaliwal A, et al. Sarcopenia in chronic liver disease: mechanisms and countermeasures. *Am J Physiol Gastrointest Liver Physiol*. 2021;320(3):G241-G257. doi:10.1152/ajpgi.00373.2020
15. Kim WR, Mannalithara A, Heimbach JK, et al. MELD 3.0: the model for end-stage liver disease updated for the modern era. *Gastroenterology*. 2021;161(6):1887-1895. doi:10.1053/j.gastro.2021.08.050
16. Trivedi HD. The evolution of the MELD score and its implications in liver transplant allocation: a Beginner's guide for trainees. *ACG Case Rep J*. 2022;9(5):e00763. doi:10.14309/crj.0000000000000763
17. Lai JC, Rahimi RS, Verna EC, et al. Frailty associated with waitlist mortality independent of ascites and hepatic encephalopathy in a multicenter study. *Gastroenterology*. 2019;156(6):1675-1682. doi:10.1053/j.gastro.2019.01.028
18. Lai JC, Covinsky KE, Dodge JL, et al. Development of a novel frailty index to predict mortality in patients with end-stage liver disease. *Hepatology*. 2017;66(2):564-574. doi:10.1002/hep.29219
19. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56(3):M146-M156. doi:10.1093/gerona/56.3.m146
20. Williams FR, Milliken D, Lai JC, Armstrong MJ. Assessment of the frail patient with end-stage liver disease: a practical overview of sarcopenia, physical function, and disability. *Hepatol Commun*. 2021;5(6):923-937. doi:10.1002/hep4.1688
21. Laube R, Wang H, Park L, et al. Frailty in advanced liver disease. *Liver Int*. 2018;38(12):2117-2128. doi:10.1111/liv.13917
22. Al-Judaibi B, Alqalami I, Sey M, et al. Exercise training for liver transplant candidates. *Transplant Proc*. 2019;51(10):3330-3337. doi:10.1016/j.transproceed.2019.08.045
23. Lin FP, Visina JM, Bloomer PM, et al. Prehabilitation-driven changes in frailty metrics predict mortality in patients with advanced liver disease. *Am J Gastroenterol*. 2021;116(10):2105-2117. doi:10.14309/ajg.0000000000001376
24. Macshut M, Kaido T, Yao S, et al. Visceral adiposity is an independent risk factor for high intra-operative blood loss during living-donor liver transplantation; could preoperative rehabilitation and nutritional therapy mitigate that risk? *Clin Nutr*. 2021;40(3):956-965. doi:10.1016/j.clnu.2020.06.023
25. Rossi D, D'avila AF, Galant LH, Marroni CA. Exercise in the physical rehabilitation of CIRROTICS: a randomized PILOT study. *Arq Gastroenterol*. 2022;59(3):408-413. doi:10.1590/S0004-2803.202203000-73
26. Soto R, Díaz LA, Rivas V, et al. Frailty and reduced gait speed are independently related to mortality of cirrhotic patients in long-term follow-up. *Ann Hepatol*. 2021;25:100327. doi:10.1016/j.aohep.2021.100327
27. Tapper EB, Finkelstein D, Mittleman MA, Piatkowski G, Lai M. Standard assessments of frailty are validated predictors of mortality in hospitalized patients with cirrhosis. *Hepatol Baltim Md*. 2015;62(2):584-590. doi:10.1002/hep.27830
28. Yoh K, Nishikawa H, Enomoto H, et al. Grip strength: a useful marker for composite hepatic events in patients with chronic liver diseases. *Diagnostics*. 2020;10(4):238. doi:10.3390/diagnostics10040238
29. Williams FR, Berzigotti A, Lord JM, Lai JC, Armstrong MJ. Review article: impact of exercise on physical frailty in patients with chronic liver disease. *Aliment Pharmacol Ther*. 2019;50(9):988-1000. doi:10.1111/apt.15491
30. Kamo T, Momosaki R, Azami M, et al. Effects of in-hospital rehabilitation on preventing hospital readmissions in patients with cirrhosis: a retrospective cohort study. *Arch Phys Med Rehabil*. 2022;103(9):1730-1737. doi:10.1016/j.apmr.2021.12.009
31. Tandon P, Ismond KP, Riess K, et al. Exercise in cirrhosis: translating evidence and experience to practice. *J Hepatol*. 2018;69(5):1164-1177. doi:10.1016/j.jhep.2018.06.017
32. Locklear CT, Golabi P, Gerber L, Younossi ZM. Exercise as an intervention for patients with end-stage liver disease: systematic review. *Medicine (Baltimore)*. 2018;97(42):e12774. doi:10.1097/MD.0000000000012774
33. Chang MK, Cheah AEJ. The role of reconstructive microsurgeons in liver transplantation—a narrative review. *Ann Transl Med*. 2024;12(1):10. doi:10.21037/atm-23-519
34. Rodríguez-Perálvarez M, Guerrero-Misas M, Thorburn D, Davidson BR, Tsochatzis E, Gurusamy KS. Maintenance immunosuppression for adults undergoing liver transplantation: a network meta-analysis. *Cochrane Database Syst Rev*. 2017;3(3):CD011639. doi:10.1002/14651858.CD011639.pub2

35. Damaskos C, Kaskantamis A, Garmpis N, et al. Intensive care unit outcomes following orthotopic liver transplantation: single-center experience and review of the literature. *Il G Chir*. 2019; 40(6):463-480.
36. Dunn MA, Rogal SS, Duarte-Rojo A, Lai JC. Physical function, physical activity, and quality of life after liver transplantation. *Liver Transpl*. 2020;26(5):702-708. doi:10.1002/lt.25742
37. Dasarathy S. Consilience in sarcopenia of cirrhosis. *J Cachexia Sarcopenia Muscle*. 2012;3(4):225-237. doi:10.1007/s13539-012-0069-3
38. Devlin JW, Skrobik Y, Gélinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. *Crit Care Med*. 2018;46(9):e825-e873. doi:10.1097/CCM.0000000000003299
39. Brustia R, Monsel A, Skurzak S, et al. Guidelines for perioperative care for liver transplantation: enhanced recovery after surgery (ERAS) recommendations. *Transplantation*. 2021;106(3): 552-561. doi:10.1097/TP.0000000000003808
40. Tazreean R, Nelson G, Twomey R. Early mobilization in enhanced recovery after surgery pathways: current evidence and recent advancements. *J Comp Eff Res*. 2022;11(2):121-129. doi:10.2217/cer-2021-0258
41. Maffei P, Wiramus S, Bensoussan L, et al. Intensive early rehabilitation in the intensive care unit for liver transplant recipients: a randomized controlled trial. *Arch Phys Med Rehabil*. 2017;98(8): 1518-1525. doi:10.1016/j.apmr.2017.01.028
42. Brustia R, Slim K, Scatton O. Enhanced recovery after liver surgery. *J Vasc Surg*. 2019;156(2):127-137. doi:10.1016/j.jviscsurg.2018.10.007
43. Ni CY, Wang ZH, Huang ZP, et al. Early enforced mobilization after liver resection: a prospective randomized controlled trial. *Int J Surg*. 2018;54 Pt A:254-258. doi:10.1016/j.ijsu.2018.04.060
44. de Almeida EPM, de Almeida JP, Landoni G, et al. Early mobilization programme improves functional capacity after major abdominal cancer surgery: a randomized controlled trial. *Br J Anaesth*. 2017;119(5):900-907. doi:10.1093/bja/aex250
45. Svensson-Raskh A, Schandl A, Holdar U, Fagevik Olsén M, Nygren-Bonnier M. "I have everything to win and nothing to lose": patient experiences of mobilization out of bed immediately after abdominal surgery. *Phys Ther*. 2020;100(12):2079-2089. doi:10.1093/ptj/pzaa168
46. Beyer N, Aadahl M, Strange B, et al. Improved physical performance after orthotopic liver transplantation. *Liver Transpl Surg*. 1999;5(4):301-309. doi:10.1002/lt.500050406
47. Cortazzo MH, Helkowski W, Pippin B, Boninger ML, Zafonte R. Acute inpatient rehabilitation of 55 patients after liver transplantation. *Am J Phys Med Rehabil*. 2005;84(11):880-884. doi:10.1097/01.phm.0000184093.53032.ed
48. Demir B, Saritas S. Effect of hand massage on pain and anxiety in patients after liver transplantation: a randomised controlled trial. *Complement Ther Clin Pract*. 2020;39:101152. doi:10.1016/j.ctcp.2020.101152
49. Ergene TY, Karadibak D, Dönmez R, Polat KY. Effects of early resistance training after liver transplantation procedures: a randomized controlled Pilot trial. *Turk J Gastroenterol*. 2022;33(10): 852-861. doi:10.5152/tjg.2022.21959
50. Foroncewicz B, Mucha K, Szparaga B, et al. Rehabilitation and 6-minute walk test after liver transplantation. *Transplant Proc*. 2011;43(8):3021-3024. doi:10.1016/j.transproceed.2011.08.007
51. Kleine M, Joahnning K, Kousoulas L, et al. Observations with impact on the indication for kinetic therapy in critically ill liver transplant patients. *Ann Transplant*. 2011;16(4):25-31. doi:10.12659/aot.882215
52. Kothari AN, Yau RM, Blackwell RH, et al. Inpatient rehabilitation after liver transplantation decreases risk and severity of 30-day readmissions. *J Am Coll Surg*. 2016;223(1):164-171. doi:10.1016/j.jamcollsurg.2016.01.061
53. Nguyen M, Mukaneza Y, Tremblay M, et al. Renal dysfunction independently predicts muscle mass loss in patients following liver transplantation. *Can Liver J*. 2022;5(3):411-423. doi:10.3138/canlivj-2021-0042
54. Rongies W, Stepniewska S, Golińska B, et al. Influence of the primary disease on rehabilitation results in the early postoperative period in patients after orthotopic liver transplantation. *Transplant Proc*. 2009;41(8):3119-3122. doi:10.1016/j.transproceed.2009.09.040
55. Rongies W, Stepniewska S, Golińska B, et al. An attempt to assess the influence of primary disease on the results of therapeutic rehabilitation in an early post-operative period in orthotopic liver transplant recipients. *Ann Transplant*. 2008;13(1):40-43.
56. Roshdy SHA, Nahas NGE, el Hady AA e AA, Faizy MWE. Impact of early pulmonary rehabilitation on post liver transplantation. *J Adv Pharm Educ Res*. 2019;9(2–2019):7-12.
57. Schaller SJ, Anstey M, Blobner M, et al. Early, goal-directed mobilisation in the surgical intensive care unit: a randomised controlled trial. *Lancet*. 2016;388(10052):1377-1388. doi:10.1016/S0140-6736(16)31637-3
58. Senduran M, Yurdalan SU, Karadibak D, Gunerli A. Haemodynamic effects of physiotherapy programme in intensive care unit after liver transplantation. *Disabil Rehabil*. 2010;32(17):1461-1466. doi:10.3109/09638280903531212
59. Sevarolli MDL, Loschi TM, Pereira E, Miyaura VTO, Baccan MDTA, Pavão DN. Epidemiologic profile of transplant patients treated by the physiotherapy. *Transplant Proc*. 2018; 50(3):831-834. doi:10.1016/j.transproceed.2018.02.028
60. Cifu DX, ed. Front matter. *Braddom's Physical Medicine and Rehabilitation*. 6th ed. Elsevier; 2021:iii. doi:10.1016/B978-0-323-62539-5.01001-8
61. CMS. Inpatient Rehabilitation Facilities. CMS.gov. Published September 6, 2023. Accessed February 5, 2024. https://www.cms.gov/medicare/health-safety-standards/certification-compliance/inpatient-rehabilitation-facilities
62. Sundaram V, Lim J, Tholey DM, et al. The Braden scale, a standard tool for assessing pressure ulcer risk, predicts early outcomes after liver transplantation. *Liver Transpl*. 2017;23(9): 1153-1160. doi:10.1002/lt.24789
63. Trojetto T, Elliott RJ, Rashid S, et al. Availability, characteristics, and barriers of rehabilitation programs in organ transplant populations across Canada. *Clin Transplant*. 2011;25(6):E571-E578. doi:10.1111/j.1399-0012.2011.01501.x
64. Mina DS, Tandon P, Kow AWC, et al. The role of acute in-patient rehabilitation on short-term outcomes after liver transplantation: a systematic review of the literature and expert panel recommendations. *Clin Transplant*. 2022;36(9) e14706. doi:10.1111/ctr.14706
65. Rana A, Ackah RL, Webb GJ, et al. No gains in long-term survival after liver transplantation over the past three decades. *Ann Surg*. 2019;269(1):20-27. doi:10.1097/SLA.0000000000002650
66. Neuberger J. Long-term care of the adult liver transplant recipient. *J Clin Exp Hepatol*. 2022;12(6):1547-1556. doi:10.1016/j.jceh.2022.03.012
67. Choudhary NS, Saraf N, Saigal S, Soin AS. Long-term management of the adult liver transplantation recipients. *J Clin Exp Hepatol*. 2021;11(2):239-253. doi:10.1016/j.jceh.2020.06.010
68. Kallwitz ER, Loy V, Mettu P, Von Roenn N, Berkes J, Cotler SJ. Physical activity and metabolic syndrome in liver transplant recipients. *Liver Transpl*. 2013;19(10):1125-1131. doi:10.1002/lt.23710
69. Watt KD. Keys to long-term care of the liver transplant recipient. *Nat Rev Gastroenterol Hepatol*. 2015;12(11):639-648. doi:10.1038/nrgastro.2015.172
70. Stephenson AL, Yoshida EM, Abboud RT, Fradet G, Levy RD. Impaired exercise performance after successful liver

transplantation. *Transplantation*. 2001;72(6):1161-1164. doi:10.1097/00007890-200109270-00032
71. Yang LS, Shan LL, Saxena A, Morris DL. Liver transplantation: a systematic review of long-term quality of life. *Liver Int*. 2014;34(9):1298-1313. doi:10.1111/liv.12553
72. Painter P, Krasnoff J, Paul SM, Ascher NL. Physical activity and health-related quality of life in liver transplant recipients. *Liver Transpl*. 2001;7(3):213-219. doi:10.1053/jlts.2001.22184
73. U.S. Department of Health and Human Services, ed. *Physical Activity Guidelines for Americans*. 2nd ed. U.S. Department of Health and Human Services; 2018 Accessed November 12, 2024.
74. Sylow L, Richter EA. Current advances in our understanding of exercise as medicine in metabolic disease. *Curr Opin Physio*. 2019;12:12-19. doi:10.1016/j.cophys.2019.04.008
75. Warburton DER, Nicol CW, Bredin SSD. Health benefits of physical activity: the evidence. *CMAJ*. 2006;174(6):801-809. doi:10.1503/cmaj.051351
76. Krasnoff JB, Vintro AQ, Ascher NL, Bass NM, Dodd MJ, Painter PL. Objective measures of health-related quality of life over 24 months post-liver transplantation. *Clin Transplant*. 2005;19(1):1-9. doi:10.1111/j.1399-0012.2004.00306.x
77. Garcia AMC, Veneroso CE, Soares DD, Lima AS, Correia MITD. Effect of a physical exercise program on the functional capacity of liver transplant patients. *Transplant Proc*. 2014;46(6):1807-1808. doi:10.1016/j.transproceed.2014.05.023
78. Krasnoff JB, Vintro AQ, Ascher NL, et al. A randomized trial of exercise and dietary counseling after liver transplantation. *Am J Transplant*. 2006;6(8):1896-1905. doi:10.1111/j.1600-6143.2006.01391.x
79. Moya-Nájera D, Moya-Herraiz Á, Compte-Torrero L, et al. Combined resistance and endurance training at a moderate-to-high intensity improves physical condition and quality of life in liver transplant patients. *Liver Transpl*. 2017;23(10):1273-1281. doi:10.1002/lt.24827
80. van den Berg-Emons RJG, van Ginneken BTJ, Nooijen CFJ, et al. Fatigue after liver transplantation: effects of a rehabilitation program including exercise training and physical activity counseling. *Phys Ther*. 2014;94(6):857-865. doi:10.2522/ptj.20130402
81. Totti V, Tamè M, Burra P, et al. Physical condition, glycemia, liver function, and quality of life in liver transplant recipients after a 12-month supervised exercise program. *Transplant Proc*. 2019;51(9):2952-2957. doi:10.1016/j.transproceed.2019.03.087
82. van Ginneken BTJ, van den Berg-Emons HJG, Metselaar HJ, Tilanus HW, Kazemier G, Stam HJ. Effects of a rehabilitation programme on daily functioning, participation, health-related quality of life, anxiety and depression in liver transplant recipients. *Disabil Rehabil*. 2010;32(25):2107-2112. doi:10.3109/09638288.2010.482174
83. Pérez-Amate È, Roqué-Figuls M, Fernández-González M, Giné-Garriga M. Exercise interventions for adults after liver transplantation. *Cochrane Database Syst Rev*. 2023;2023(5):CD013204. doi:10.1002/14651858.CD013204.pub2
84. Beal EW, Tumin D, Mumtaz K, et al. Factors contributing to employment patterns after liver transplantation. *Clin Transplant*. 2017;31(6). doi:10.1111/ctr.12967
85. Fazekas C, Kniepeiss D, Arold N, Matzer F, Wagner-Skacel J, Schemmer P. Health-related quality of life, workability, and return to work of patients after liver transplantation. *Langenbecks Arch Surg*. 2021;406(6):1951-1961. doi:10.1007/s00423-021-02183-z
86. Sainz-Barriga M, Baccarani U, Scudeller L, et al. Quality-of-life assessment before and after liver transplantation. *Transplant Proc*. 2005;37(6):2601-2604. doi:10.1016/j.transproceed.2005.06.045
87. Ho JK, Ko HH, Schaeffer DF, et al. Sexual health after orthotopic liver transplantation. *Liver Transpl*. 2006;12(10):1478-1484. doi:10.1002/lt.20831
88. Karabulut N, Koraş K, Gürçayır D. Effects of liver transplantation on sexual function and quality of life. *Psychol Health Med*. 2022;27(7):1532-1543. doi:10.1080/13548506.2021.1898003

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