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Review Article

Prehabilitation in patients awaiting liver transplantation

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ABSTRACT

Background: Frailty, malnutrition and sarcopenia lead to a significant increase in morbidity and mortality before and after liver transplantation (LT). Prehabilitation attempts to optimize physical fitness of individuals before major surgeries. To date, little is known about its impact on patients awaiting LT.
Aims: The aim of our scoping review was to describe whether prehabilitation in patients awaiting LT is feasible and safe, and whether it leads to a change in clinical parameters before or after transplantation.
Methods: We performed a systematic review of the literature from 1946 to November 2023 to identify prospective studies and randomized controlled trials of adult LT candidates who participated in an exercise training program.
Results: Out of 3262 citations initially identified, six studies were included. Studies were heterogeneous in design, patient selection, intervention, duration, and outcomes assessed. All studies were self-described as pilot or feasibility studies and had a sample size ranging from 13 to 33. Two studies were randomized controlled trials. Two study restricted to patients with cirrhosis who were eligible for liver transplantation or on the transplant list. Exercise programs lasted between 6 and 12 weeks. In terms of feasibility, proportion of eligible patients that were recruited was between 54 and 100%. Program completion ranged between 38 and 90%. Interventions appeared safe with 9 (9.2%) adverse events noted. In the intervention group, improvements were generally noted in peak oxygen consumption and workload, 6-min walking distance, and muscle strength. One study suggested a decrease in post-transplant hospital length of stay.
Conclusions: Overall, it appears that prehabilitation with exercise training is feasible, and safe in patients awaiting LT. Higher quality and larger studies are needed to confirm its impact on pre- and post-transplantation-related outcomes.

List of abbreviations

6MWD	6 min walking distance
AE	Adverse event
CLDQ	Chronic liver disease questionnaire
CPET	Cardiopulmonary exercise testing
HADS	Hospital anxiety and depression scale
HBEP	Home-based exercise program
HCC	Hepatocellular carcinoma
HGS	Handgrip strength
HIIT	High intensity interval training
HRQoL	Health-related quality of life
LFI	Liver frailty index
LT	Liver transplantation
MELD	Model for end-stage liver disease
peakVO_2	Oxygen consumption at peak exercise
RCT	Randomized controlled trial
RFH-GA	Royal Free Hospital Global Assessment
SPPB	Short physical performance battery

1. Introduction

Liver transplantation (LT) is a life-saving abdominal surgery for

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patients with decompensated liver disease whose survival is only of a few months [1,2]. Ranking on the waitlist is determined by the model for end-stage liver disease (MELD) score, which prioritizes patients based on medical urgency [3]. Despite this, 10–20% of individuals on the LT waiting list become too sick or die before receiving an organ [4]. Although this can be partly explained by organ shortage, the presence of frailty, sarcopenia, and malnutrition, which are unaccounted for in the MELD score, further contribute to patients falling off the waitlist [5–7]. Recent evidence suggests that for the same MELD score, a frail individual will have a worse survival than one who is robust [8].

Patients with cirrhosis on the LT list wait a few weeks to months before receiving an organ. This time window provides a unique opportunity for interventions targeting frailty and malnutrition. Prehabilitation programs aim to improve the physical fitness of patients awaiting surgery [9]. To achieve its aims, these programs often include a backbone of exercise training. As highlighted in a recent meta-analysis of patients awaiting major surgical procedures, these interventions have shown some benefit, but the quality of the evidence is considered low [10]. In addition, the interventions are highly heterogeneous, which limits meaningful comparisons. In the current context, the American and Canadian transplantation societies have encouraged further studies on prehabilitation in patients awaiting organ transplantation [11,12].

Although preliminary evidence suggests that exercise training is safe in patients with cirrhosis, it is unclear if this is the case in patients active on the LT list [13,14]. Our objective is to assess if prehabilitation programs with exercise training in patients awaiting LT are feasible, safe, and effective in improving clinical outcomes. We aim to synthesize the available literature and highlight existing knowledge gaps. We chose to perform a scoping review as opposed to a systematic review with meta-analysis as our objectives are broad and mostly exploratory. We also expected studies to be heterogeneous in design, intervention, and outcome measures preventing us from performing a formal meta-analysis.

2. Methods

To answer the objectives of this review, we focused on interventional studies where potential candidates or individuals actively listed for LT participated in an exercise training program. We collected any information related to the feasibility, safety, and effectiveness of these programs.

2.1. Search strategy

We searched the following databases: MEDLINE, EMBASE, ISI Web of Science and CENTRAL from 1946 to November 2023. The following systematic search strategy/key words was employed to retrieve potential studies: ((prehabilitation) OR (((exercis*) OR (physic*)) AND ((train*) OR (interven*) OR (prescrip*)))) AND ((liver transplant*) OR (cirrhos*) OR (advanced liver diseas*)) AND adult. All results were compiled using EndNote X9.

2.2. Study selection

We included studies that: i) recruited potential candidates or actively listed individuals for LT; ii) evaluated a structured exercise training program. We excluded pediatric (<18 years old) population, non-English publications, conference abstracts, and studies that evaluated exercise training following LT. We included only prospective studies, and randomized controlled trials (RCT). Although this will restrict the studies included, this decision was meant to support our aims which evaluate the impact of a structured exercise training program.

2.3. Validity assessment, data abstraction and rating of evidence

Studies were independently assessed for inclusion by two authors (AB and MM) with discrepancies resolved after discussion. Studies included in the final review were thoroughly analyzed and key information was retrieved. We extracted information related to study design, sample size, description of the included participants, description of the prehabilitation intervention (including duration), and all endpoints related to feasibility, safety, and effectiveness of the intervention. The absence of information related to feasibility, safety, or effectiveness of the intervention did not lead to study exclusion. Examples of data collected pertaining to feasibility, safety, and effectiveness are summarized in Supplementary Table 1.

Data was entered in a pre-formatted Microsoft Excel sheet. Since we expected a limited number of publications with methodological heterogeneity, we present a detailed description of the included studies. The Cochrane Risk of bias tool for randomized trials or the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool were used to assess the risk of bias when appropriate [15,16]. We followed the PRISMA checklist for the reporting of scoping reviews [17].

3. Results

The search strategy retrieved 3262 citations. In the end, six studies (Debette et al. 2015 [18], Duarte-Rojo et al. 2023 [19], Morkane et al. 2020 [20], Serper et al. 2023 [21], Wallen et al. 2019 [22], Williams et al. 2019 [23]) were included in the present review (Fig. 1). Although of interest, the studies by Lai and by Chen were not included as they did not limit inclusion to patients eligible or actively listed for LT [24,25]. A summary of our findings are presented in Tables 1, 2 and 3.

3.1. Characteristics of sources of evidence and bias assessment

All six studies were self-described as pilot or feasibility studies investigating the impact of an exercise program on patients eligible or actively listed for LT [18–23]. The studies by Serper and Wallen were RCTs comparing an active exercise arm to a control group [21,22]. The study by Morkane was a prospective trial which included a non-randomized control arm [20]. The other 3 studies were single-arm prospective interventional cohort studies [18,19,23]. Overall, 98 individuals were enrolled in an exercise program, while 38 individuals were in a control group. Further details can be found in Table 1.

In the studies by Serper and Wallen, the risk of bias was high for performance bias and detection bias since blinding is not possible for this type of intervention [21,22]. The ROBINS-I showed only a moderate risk of bias due to confounding factors in one study and no information was available for bias in selection of the reported results since no protocol were published or available in two studies. All other domains were at low risk of bias (Supplementary Table 2 and Fig. 1).

3.2. Description of participants' selection criteria

All studies included adult patients eligible or actively listed for LT. Only the studies by Duarte-Rojo and Morkane restricted inclusion to patients who also had cirrhosis. Morkane restricted inclusion to those living near the hospital, and Serper recruited English-speaking individuals with a smartphone. Only the studies by Duarte-Rojo and Serper restricted inclusion to patients more likely to be pre-frail, frail or malnourished. Exclusion criteria were also very different between studies but were meant to maximize safety. Further details can be found in Table 1.

In the exercise groups, the average age of participants was between 49 and 60 years, the proportion of female participants was between 12.5% and 71%, and the average MELD was between 12 and 17. The most common cause of liver disease was related to alcohol or a combination of alcohol and non-alcoholic fatty liver disease. Studies inconsistently described presence of hepatocellular carcinoma (HCC) or previous hepatic decompensation. The prevalence of HCC in the study population was between 15 and 43% in the 3 studies where it was

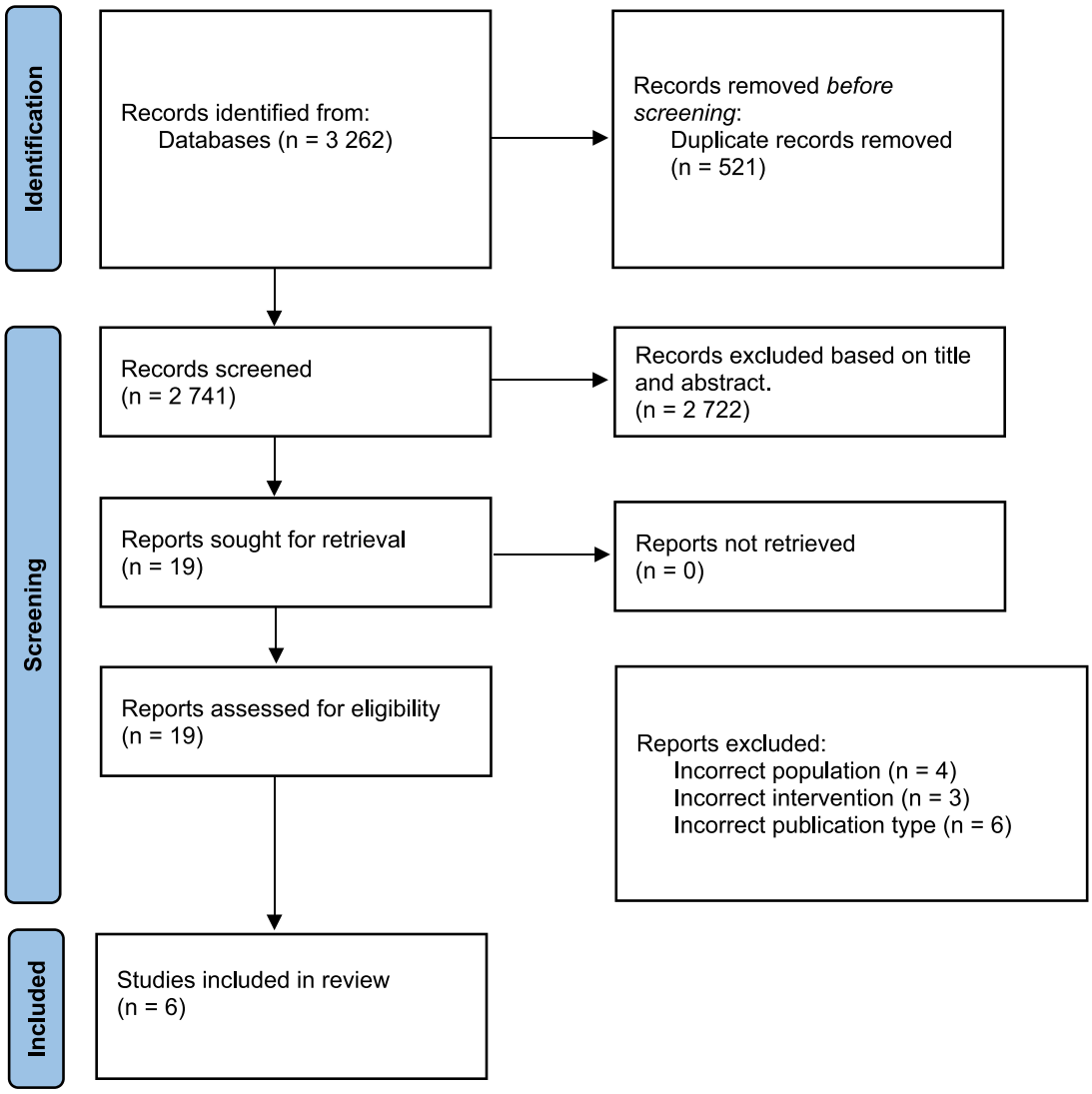

Fig. 1. Flow chart of included studies.

described [18,21,22].

3.3. Description of the prehabilitation programs and their components

Study duration varied between 6 and 12 weeks. All studies planned 2 to 3 exercise sessions per week. Studies by Debette and Morkane offered a hospital-based supervised exercise program, Wallen offered combined hospital- and home-based exercises, while the rest were strictly home-based exercise programs (HBEP). The hospital-based studies included aerobic exercises using a cycle ergometer, while HBEP included increasing step counts. Most studies included a resistance training component as well. Studies by Morkane and Serper included a nutritional assessment and optimization by a dietician, while the study by Williams described nutritional optimization as part of their LT program. The other three (50%) studies did not describe a nutritional intervention.

3.4. Description of motivational intervention

The three HBEP provided incentives to improve adherence [19,21,23]. The study by Duarte-Rojo included a weekly 15–30 min call with a physical activity coach trained in behavioral counseling and motivational interviewing. The study by Serper provided financial incentives to all participants who enrolled and those that completed exit-surveys. They also provided financial incentives to increase step counts. The study by Williams included a supportive health call for the first 6 out of 12 weeks of intervention. The other three studies did not describe any specific incentives [18,20,22].

3.5. Results of the intervention

3.5.1. Feasibility

All studies described the percentage of patients who agreed to participate after being approached, except for the study by Duarte-Rojo. Recruitment was 100% in the study by Debette, while it was closer to 20–56% in the other five studies. Most common reasons for not participating included time commitment, travel commitments, and lack of interest. Proportion of patient who participated in the study after signing consent was between 68%–100%. Once patients agreed to participate, most attrition was due to receiving a LT, being removed from LT waitlist or death. In the study by Duarte-Rojo, 10 (32%) participants did not complete the 2-week run-in phase used to prescribe the HBEP. Study completion was between 38 and 90% depending on the study duration. Details can be found in Table 2.

3.5.2. Adherence

Although adherence was defined differently in each study, it ranged between 51%–100%. Studies which included a supervised hospital

Table 1
Summary of the studies included in the scoping review.

Author, year, Country	Sample size	Study design	Inclusion criteria	Exclusion criteria	Description of intervention (n = number of patients)	Control group, if present (n = number of patients)	Duration of intervention
Debette, 2015, France	13	Prospective cohort study	18–65 years old Eligible for LT Prophylaxis against EVB Negative EST LVEF >45%	Contraindication to exercise	Supervised hospital-based (n = 13) 2 sessions per week, 2 h each Aerobic: cycle ergometer at VT Resistance: weight bench	None	12 weeks
Duarte-Rojo, 2023, USA	31	Prospective cohort study	40–70 years old Decompensated cirrhosis Eligible for LT MELD-Sodium >10	Not described	Home-based using El-Fit app (n = 31) 2 sessions per week Aerobic: increasing daily steps Resistance training	None	12 weeks
Morkane, 2020, UK	33	Prospective cohort study	>18 years old Cirrhosis Listed for LT Living near hospital	LT for Cancer Contraindication to exercise	Supervised hospital-based (n = 16) 3 sessions per week, 40mins each Aerobic: HIIT on cycle ergometer Nutrition advice	SOC with nutrition advice (n = 17)	6 weeks
Serper, 2023, USA	30	RCT	18 years old Eligible for LT English speaking Smartphone owner At-risk patients*	MELD >25 SPPB 0–3 Recent hospitalization High risk of fall	Home-based (n = 20) Aerobic: increasing daily steps Resistance training	Personalized diet and activity recommendations (n = 10)	12 weeks
Wallen, 2019, Australia	21	RCT	18–69 years old Eligible for LT	Prior LT Combined transplant Active smoking AE at CPET Uncontrolled DM Limitation to exercise	Home and hospital-based (n = 10) Home: 1/week; Hospital: 2/week Aerobic: cycle ergometer or walking Resistance training	SOC (n = 11)	8 weeks
Williams, 2019 UK	18	Prospective cohort study**	>18 years old Listed for 1st LT	CV instability Overt HE Inpatient	Home-based (n = 18) 2 sessions per week Aerobic: increasing daily steps Resistance training Nutritional optimization	None	12 weeks

Legend: * = at risk patients as defined by LFI, SPPB, HGS, PG-SGA, ** = CPU random sampling, CPET = cardiopulmonary exercise testing, CPU = central processing unit, CV = cardiovascular, DM = diabetes mellitus, EST = exercise stress test, EVB = esophageal variceal bleeding, HE = hepatic encephalopathy, HIIT = high intensity interval training, LFI = liver frailty index, HGS = handgrip strength, LT = liver transplantation, LVEF = left ventricular ejection fraction, PG-SGA = patient generated subjective global assessment, MELD = model for end-stage liver disease, SOC = standard of care, SPPB = short physical performance battery, VT = ventilator threshold.

based component seemed to have a higher adherence [20,22]. Despite incentives and motivational interventions, the studies by Serper and Duarte-Rojo had the lowest adherence at 51% and 57% respectively [19,21]. Further details about adherence is described in Table 2. Reasons for lack of study completion are detailed in Table 3. The study by Debette did not describe program adherence.

3.5.3. Safety

Overall, 9 (9.2%) adverse events (AE) were reported in 98 individuals who participated in an exercise program. Of the 9 events reported, 7 were musculoskeletal in nature, 2 of which led to discontinuation of the intervention. Of note, in the study by Serper, 33% noted discomfort with exercise. In the study by Duarte-Rojo, 12 (57%) participants were hospitalized due to liver disease and portal hypertension. Although hepatic deteriorations were noted in multiple studies, none appeared related to the intervention. Further details are in Table 2.

3.5.4. Effectiveness

Outcomes measures of effectiveness described in at least 2 studies included cardiopulmonary exercise testing (CPET) in 3 studies [18,20,22], 6 min walking distance (6MWD) in 3 [18,19,22], average daily step counts in 3 [19,21,23], hand grip strength (HGS) in 2 [20,22], Liver Frailty Index (LFI) in 2 [19,21], SPPB in 2 [21,23], gait-speed test in 2 [19,23], and HRQoL in 3 [18,22,23]. Details on effectiveness data can be found in Table 4. In terms of CPET results, there were improvements in within-group peak VO_2 and peak workload by the end of the intervention in the studies by Debette and Morkane. In the RCT by Wallen, peak VO_2 and workload were higher in the intervention arm compared to the control arm, but this was not statistically significant. In terms of 6MWD and the average daily step count, there were significant improvements across all studies both for within-group and between-group comparisons, except for the Duarte-Rojo study which showed no within-group difference in average daily step count at end-of-study. The SPPB improved in the studies by William and Serper, but there were no between group-differences in the latter study. The LFI improved in the studies by Duarte-Rojo and Serper, but there were no between-group differences in the latter study. In terms of HRQoL, although it was reported in 3 studies, they all used different scales. Overall, there was a general trend toward improvement in the physical and mental health domains in the study by Debette, and an improvement in the EQ-VAS score in the study by Williams. Otherwise, there was no improvement in the HADS scale in the study by William, or the CLDQ in the study

Table 2
Summary of feasibility, adherence and safety data.

Author	Feasibility	Adherence	Safety
Debette	13/13 accepted to participate 8 (62%) completed exercise program (2 moved, 2 transplanted, 1 deteriorated)	No data on adherence	1 deteriorated due to hepatorenal syndrome No cardiovascular or hepatic decompensation
Duarte-Rojo	Approached to participate: not mentioned Accepted to participate: 31 Started intervention: 21 (68%) Completed program: 15 (48%) (4 died, 1 transplanted, 1 other surgery)	Adherence to exercising videos: 11 (52%) Adherence to walking goals: 7 (33%) Overall adherence: 12 (57%)	3 AEs 1 fall related to intervention 1 fracture not related to intervention 1 vertigo not related to intervention 12 admitted to hospital for liver diseases
Morkane	Approached to participate: 29 Accepted to participate: 16 (55%) Completed program: 9/16 (56%) (4 health issues, 2 transplant, 1 knee pain)	In those who completed program: Adherence to planned exercise visits: 94%	No AE related to exercise No worsening of liver disease following exercise
Serper	Assessed for eligibility: 284 Contacted to participate: 150 Screening visit: 33 (22%) Randomized: 30 (20%) Completed program: 27 (90%) (2 unenrolled, 1 lost to follow-up)	Adherence to daily step goals: 51%	No serious AE 3 non-injurious falls 33% noted discomfort with exercise No deaths
Wallen	Assessed for eligibility: 38 Randomized: 21 (55%) Completed program: 8 (38%) (8 transplanted, 2 severe medical condition, 1 personal reasons, 1 traveling, 1 delisted)	At 4 weeks, in the 8pts who completed the program Adherence to supervised sessions: 95% Adherence to unsupervised sessions: 75% At 8 weeks, in the 4pts who completed program Adherence to supervised exercise sessions: 100% Adherence to unsupervised sessions: 88%	No serious AE 1 AE from knee injury No worsening of liver disease
Williams	Randomly selected for assessment: 46 Eligible to participate: 32 (70%) Accepted to participate: 18 (56%) Completed 6 weeks of program: 12 (67%) Completed 12 weeks of program: 9 (50%) (5 transplanted, 1 palliated, 1 unable to attend, 1 did not attend, 1 withdrew due to tibial fracture)	At 6 weeks (included motivational calls) Adherence to daily steps: 82% Adherence to exercise: 90% At 12 weeks (no more motivational calls) Adherence to daily steps: 53% Adherence to exercise: 78%	No AE related to program 1 tibial fracture (unrelated)

Legend: AE = adverse events.

Table 3
Reasons for not completing the intervention.

	Number of patients ($N = 98$)
Number of participants not completing the intervention	42 (43%)
Receiving a liver transplant	18 (18%)
Clinical deterioration / Death / Palliation	12 (12%)
Issues with follow-up (including non-compliance, unenrolled, delisted)	10 (10%)
Musculoskeletal injuries	2 (2%)

Table 4
Summary of effectiveness data.

	Peak VO_2, in mL/kg/min		
Author	Pre-intervention	Post-intervention	*p*-value
Debette	21.5 ± 5.9	23.2 ± 5.9	**0.008**
Morkane	16.2 ± 2.4	18.5 ± 4.6	**0.02**
Wallen	EMD = 3.2 (95% CI -2.3 - 8.7)		0.10
	Peak workload, in watts		
Debette	106 ± 42	119 ± 45	**0.02**
Morkane	117 ± 26	134 ± 26	**<0.05**
Wallen	EMD = 41.6 (95% CI 5.9–77.4)		0.12
	6 min walking distance, in meters		
Debette	481 ± 69	521 ± 64	**0.02**
Duarte-Rojo	318 ± 73	358 ± 64	**0.005**
Wallen	EMD = 103.8 (95% CI 22.3–185.2)		0.054
	Average daily steps		
Duarte-Rojo	1260 (639–3081)	958 (656–4169)	0.55
Serper	Exercise: 1925 ± 757 Control: 2632 ± 1599	Exercise: 2539 ± 1650 Control: 2150 ± 1213	**0.03**
Williams	4000 (range 700–10,000)	6700 (IQR 3000–14,000)	**≤0.01**
	Liver Frailty Index		
Duarte-Rojo	3.84 ± 0.71	3.47 ± 0.90	**0.03**
Serper	Exercise: 4.0 ± 0.3 Control: 4.2 ± 0.5	Exercise: 3.7 ± 0.4 Control: 4.0 ± 0.5	0.96
	Muscle strength, in kg		
Morkane (HGS)	26.4 ± 7.5	29.4 ± 6.4	**0.05**
Wallen (HGS)	EMD = 6.3 (95% CI -2.3–14.8)		**0.04**
Debette (IQS)	30 ± 10	37 ± 13	**<0.008**
	Short Physical Performance Battery		
Serper	Exercise: 9.5 ± 1.3 Control: 9.4 ± 1.8	Exercise: 10.5 ± 1.5 Control: 10.1 ± 1.7	0.76
Williams	9.5 (IQR 6–12)	11.5 (IQR 9–12)	**0.02**
	Health Related Quality of Life		
Debette (SF-36)	36% ± 4%	39% ± 3%	0.46
Wallen (CLDQ)	EMD = −0.3 (95% -1.3–0.8)		0.18
Williams (HADS)	10 (IQR 1–26)	7 (IQR 0–22)	0.13
Williams (EQ-VAS)	63% (IQR 30%–100%)	Median change 18%	**0.04**

Legend: CI = confidence interval, CLDQ = chronic liver disease questionnaire, EMD = estimated median difference (vs control group), EQ-VAS = EuroQoL visual analog scale, HADS = hospital anxiety and depression scale, HGS = handgrip strength, IQR = interquartile range, IQS = isometric quadriceps strength, SF-36 = short form 36 items.

by Wallen.

Post-transplant outcomes were described in the studies by Morkane, Serper, Wallen and Williams. In the study by Morkane, they found a shorter hospital length of stay in those that exercised (13 (IQR6) days vs 30 (IQR13) days, $p = 0.02$). In the study by Wallen, there were no between-group differences for intraoperative, perioperative or post-operative outcomes, including 90-days related mortality in those who underwent LT. In the study by Serper, there were no differences in death or LT between study arms at 3 years of follow-up. In the study by Williams, post-transplantation hospital length of stay is described for those

who were transplaned within 6 weeks of starting HBEP (9 [7–14] days) or after completing at least 6 weeks (10 (5–41) days).

4. Discussion

Prehabilitation is an appealing concept in patients awaiting LT. To date, its feasibility, safety, and effectiveness in this patient population were largely unknown. Although Jetten et al. recently published a systematic review on this topic, it mixed patients awaiting LT and those with advanced liver disease [26]. As patients awaiting LT might be called for a LT at any time, the feasibility and completion of prehabilitation programs are likely different than in those who are not listed. This key difference can have a downstream impact on the effectiveness of the intervention. Our scoping review focused on patients who are candidates or are awaiting LT. We identified six studies with heterogeneous design, population, interventions, and outcome measures. The significant heterogeneity between studies precluded us from conducting a meta-analysis, justifying the choice of a scoping review. We were able to better characterize the feasibility, safety, and effectiveness of this intervention through qualitative assessments and descriptive comparisons between studies.

Although prehabilitation programs varied from one study to another, they appeared safe with a low rate of AEs and the absence of serious complications. Most common AEs related to intervention were musculoskeletal in nature. There did not appear to be any worsening of liver disease although this was not formally addressed, except in the study by Wallen where the MELD score remained stable. The overall safety profile of exercise training in patients awaiting LT and the absence of serious complications is in line with exercise training in non-LT listed patients with advanced liver disease as published in previous systematic reviews [13,26,27]. Other studies have reported stable MELD score or Child Pugh score, while one showed reduction in hepatic venous pressure gradient [13,28]. Identifying patients who are medically unfit to exercise, incorporating a run-in phase, and conducting supervised exercise sessions with a physical therapist are all possible ways to minimizing injuries and maximize safety. Impact of exercise on hepatic decompensations and broadening safety criteria for exercise remain to be addressed in future studies.

Feasibility and adherence to exercise were not uniformly defined, making comparisons difficult. Although half of eligible participants approached seem interested in prehabilitation, the proportion of patients awaiting LT who agree to participate in prehabilitation needs to be characterized further. Although this might fluctuate due to regional variabilities of the transplant list, it would give a more precise estimate of how many patients could potentially benefit from prehabilitation. Adherence also varied between studies but seemed lower in the studies with HBEP. The studies by Serper, which included financial incentives, and by Duarte-Rojo, which included motivational calls, had the lowest adherence at 51% and 57% respectively. These studies seemed to include sicker patients, possibly explaining the lower adherence. The low adherence to HBEP was also reported in the STRIVE study where patients with cirrhosis exercised [24]. In this study, adherence was only 14% despite motivational measures. The study by Morkane only recruited patients living near the hospital favoring high adherence to their hospital-based program. This is consistent with reasons for refusal to participate which included time and travel commitments. For future studies, striking a balance between exercise program and the time and commitment required by patients will hopefully maximize adherence.

In terms of effectiveness, outcome measures varied from study to study. Overall, there were within-group improvements in average daily steps, LFI, 6MWD and CPET after prehabilitation in the non-randomized studies, regardless of program duration. The two randomized controlled trials did not find any improvements [21,22]. The lack of benefit could be due to the small sample size, low adherence to exercise training, participant selection, and short duration of the intervention. The study by Morkane showed that patients who did not exercise, or stopped exercising had a decline in peak VO2. This suggests that for prehabilitation to have a sustained impact on the exercise capacity of individuals awaiting LT, exercise should be maintained until the surgery. There also is an important need to harmonize outcomes measured and reported. As more studies will be conducted on prehabilitation in patients awaiting LT, we suggest that LFI, HGS (included in LFI), the 6MWD, and CPET variables if available should be included. This is in line with a recent systematic review which assessed pre-LT tools able to stratify post-LT outcomes [29]. Authors concluded that LFI, sarcopenia by computed tomography, and CPET are most useful to stratify recovery following LT. In addition, when conducting prehabilitation studies, both within-group and between-group differences should be presented. Whenever possible, post-transplant outcomes including hospital length of stay, complications, and mortality should also be captured. A recent systematic review by attempting to describe post-transplantation impact of prehabilitation identified only 1 study highlighting the paucity of data in this field [30]. Future studies should also evaluate the impact of sex and gender in feasibility, adherence, safety, and effectiveness of prehabilitation.

Lastly, the impact of prehabilitation on HRQoL is also poorly described, with studies using different scales. Though many scales are available, the CLDQ is most specific to patients with liver diseases and it evaluates multiple domains related HRQoL [31,32]. It could constitute the ideal scale for prehabilitation studies in patients awaiting LT. Although exercise itself can reduce psychological distress, adding a mindfulness intervention targeting anxiety and stress might have a beneficial impact on the mind-body [9]. Such an intervention might also improve exercise adherence, but further studies are still needed. In addition, while most studies focused solely on exercise as main intervention, a multipronged approach combining exercise training, nutritional optimization, and psychological support could lead to more significant improvements of the participants exercise capacity, nutritional status, and quality of life.

Our scoping review has many strengths. Firstly, we present important feasibility, safety and effectiveness of prehabilitation in patients awaiting LT, including two very recently published studies. The choice of a scoping review was ideal to conduct a broad assessment of this topic. Based on our review of the included studies, we also highlight key knowledge gaps as well as potential paths to maximize feasibility, adherence, safety, and effectiveness. We hope that our suggestions will help guide future studies on this important topic.

Our scoping also has limitations we wish to acknowledge. We purposefully limited our review to prospective studies or RCTs which might have limited the number of studies retrieved. We believe that these study designs are better suited to assess the impact of an intervention. Similarly restricting to patients evaluated or listed for LT might have limited the number of studies retrieved but this was done to focus on this specific population for reasons explained above. Finally, our results need to be interpreted in the context of the studies included. Only small sized single center feasibility studies have been conducted to date, potentially limiting the generalizability of our observations. Furthermore, the regional variations in LT waiting dynamics and center expertise are additional factors that need to be considered.

In conclusion, data on the impact of prehabilitation in patients awaiting LT is very limited and larger multicenter RCTs are desperately needed to appreciate whether such an intervention would be feasible, safe, and effective at improving pre- and post-transplant outcomes.

Assistance with the study

None.

Presentation

None.

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Declaration of competing interest

Amine Benmassaoud, Myriam Martel, Franco Carli, Amal Bessissow, Olivia Geraci: none. Giada Sebastiani has acted as speaker for Merck, Gilead, Abbvie, Novonordisk, Pfizer, served as an advisory board member for Pfizer, Merck, Novonordisk, Gilead and Intercept and has received unrestricted research funding from Theratec.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.trre.2024.100835.

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