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ORIGINAL ARTICLE

Observational Study

Effects of an active lifestyle on the physical frailty of liver transplant candidates

Ilias Marios Oikonomou, Emmanouil Sinakos, Nikolaos Antoniadis, Ioannis Goulis, Olga Giouleme, Maria Anifanti, Georgios Katsanos, Konstantina-Eleni Karakasi, Georgios Tsoulfas, Evangelia Kouidi

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Abstract

BACKGROUND

Liver transplantation is the most important therapeutic intervention for end-stage liver disease (ELD). The prioritization of these patients is based on the model for end-stage liver disease (MELD), which can successfully predict short-term mortality. However, despite its great validity and value, it cannot fully incorporate several comorbidities of liver disease, such as sarcopenia and physical frailty, variables that can sufficiently influence the survival of such patients. Subsequently, there is growing interest in the importance of physical frailty in regard to mortality in liver transplant candidates and recipients, as well as its role in improving their survival rates.

AIM

To evaluate the effects of an active lifestyle on physical frailty on liver transplant candidates.

METHODS

An observational study was performed within the facilities of the Department of Transplant Surgery of Aristotle University of Thessaloniki. Twenty liver transplant candidate patients from the waiting list of the department were included in

the study. Patients that were bedridden, had recent cardiovascular incidents, or had required inpatient treatment for more than 5 d in the last 6 mo were excluded from the study. The following variables were evaluated: Activity level *via* the International Physical Activity Questionnaire (IPAQ); functional capacity *via* the 6-min walking test (6MWT) and cardiopulmonary exercise testing; and physical frailty *via* the Liver Frailty Index (LFI).

RESULTS

According to their responses in the IPAQ, patients were divided into the following two groups based on their activity level: Active group (A, 10 patients); and sedentary group (S, 10 patients). Comparing mean values of the recorded variables showed the following results: MELD (A: 12.05 ± 5.63 *vs* S: 13.99 ± 3.60; $P > 0.05$); peak oxygen uptake (A: 29.78 ± 6.07 mL/kg/min *vs* S: 18.11 ± 3.39 mL/kg/min; $P < 0.001$); anaerobic threshold (A: 16.71 ± 2.17 mL/kg/min *vs* S: 13.96 ± 1.45 mL/kg/min; $P < 0.01$); 6MWT (A: 458.2 ± 57.5 m *vs* S: 324.7 ± 55.8 m; $P < 0.001$); and LFI (A: 3.75 ± 0.31 *vs* S: 4.42 ± 0.32; $P < 0.001$).

CONCLUSION

An active lifestyle can be associated with better musculoskeletal and functional capacity, while simultaneously preventing the evolution of physical frailty in liver transplant candidates. This effect appears to be independent of the liver disease severity.

Key Words: Liver transplantation; Frailty; Six-minute walk test; Cardiopulmonary exercise testing; Exercise therapy; Observational study

Core Tip: This study highlights the importance of regular physical activity and exercise of low and medium intensities in the routine of liver transplant candidates. As liver transplantation is a highly demanding procedure, imposing a significant amount of stress across every system, physical frailty is steadily proving to be a factor of great importance, not only due to its role in mortality prediction but also due to its potential improvement *via* preoperative interventions.

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INTRODUCTION

Liver transplantation is the greatest tool for the management and treatment of end-stage liver disease (ELD)[1]. Nevertheless, there is a worldwide gap between the demand for liver transplants and the availability of organ donations[2], increasing the need for optimization of candidate prioritization and organ distribution[3]. It is well established in the literature that the model for end-stage liver disease (MELD) score is a unique tool in this direction[4]. Nevertheless, there are further clinical parameters that may play a substantial role in the waiting list mortality, especially in patients with lower MELD scores [5].

Sarcopenia is related to waiting list mortality and survival after liver transplantation[6-9]. Furthermore, sarcopenic candidates require longer inpatient care, not only on the intensive care unit level but also in ward-based care[10,11]. Functional capacity has also been described as a useful predictive tool, as it is related to better postoperative survival rates and required length of stay[12,13]. It is worth noting that cardiopulmonary exercise testing (CPET) is used quite extensively in other transplant candidates; nevertheless, it is not equally popular in the prelisting assessment of a liver transplant candidate[14,15]. One of the main disadvantages of CPET is the need for expensive equipment within a laboratory setting with equally trained healthcare professionals. The 6-min walking test (6MWT) is mentioned as an alternative assessor of functional capacity in the literature[16], the lower values of which are associated with increased mortality both in the waiting list and after transplantation[17,18].

Furthermore, physical frailty has been gaining growing attention due to its correlation with mortality prediction in liver transplantation. Physical frailty is a clinical syndrome that is correlated with both sarcopenia and functional capacity and is characterized by reduced strength and stamina, as well as increased mortality risk and postoperative dependence[19-21]. The Liver Frailty Index™ (LFI™) is an

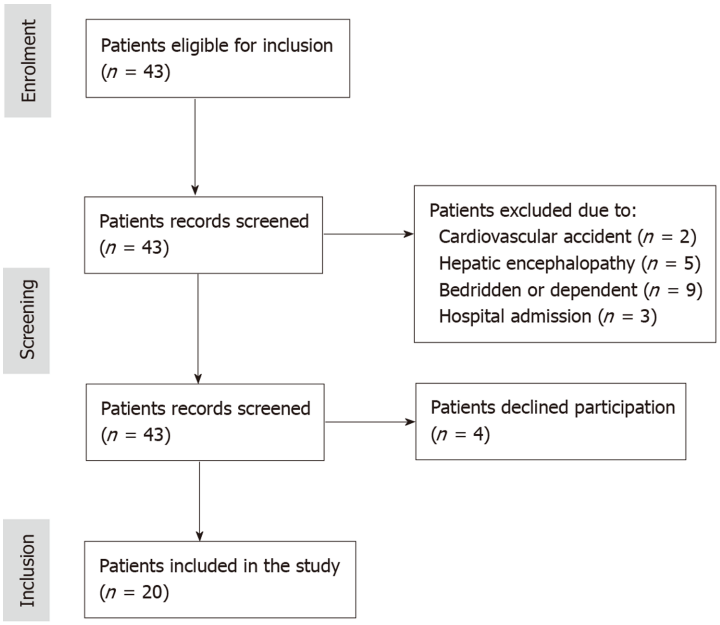

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Figure 1 Recruitment of patients for the observational study.

innovative tool, developed by Lai *et al*[22], which appears to significantly improve mortality prediction when combined with MELD, especially in patients with low MELD scores[22,23].

The course of liver disease is well correlated with a gradual diminishment of both functional capacity and musculoskeletal robustness. Taking the importance of the above clinical tools into consideration, not only on mortality prediction but also on patient prioritization, this observational study evaluated the effects of an active lifestyle on indices of physical functioning, in order to identify the effects of physical activity on physical frailty and cardiovascular capacity on liver transplant candidates.

MATERIALS AND METHODS

Study population

Liver transplant candidates from the Department of Transplant Surgery of the Aristotle University of Thessaloniki in the Hippokration General Hospital of Thessaloniki were recruited for the study. Patients enlisted in the liver transplantation waiting list registry, according to criteria of the Hellenic Transplantation Organization, were deemed eligible for enrollment. The observational study design excluded patients with other comorbidities hindering their activity level or the ones having received instructions from their physicians to limit it, due to a recent acute deterioration of their condition.

Therefore, patients were deemed ineligible if one of the following was true: Recent cardiovascular incident in the preceding 12 mo; grade 2 or higher hepatic encephalopathy; bedridden patients with complete dependence; and recent hospital admission requiring longer than 72 h of inpatient care due to condition deterioration.

A total of 43 patients had their records screened to be included in the observational study. Following the exclusion criteria described above, 19 patients were excluded. In particular, 2 patients were recovering from a recent cardiovascular incident, 5 were classified with hepatic encephalopathy of grade 2 or higher, 9 were completely bedridden and unable to self-accommodate everyday needs, and finally 3 required long inpatient care within the past 3 mo. The remaining 24 patients were contacted and informed about the study; four declined participation. The recruitment process diagram is presented in Figure 1. All patients participating in the study were informed about the purpose and methodology of the study and provided written informed consent. The study protocol was approved by the Department's Ethics Committee of Aristotle University of Thessaloniki (Protocol No. 65/2021). The study was performed from February 16 to June 21, 2021.

Activity level evaluation

The self-administered, short form of the International Physical Activity Questionnaire (IPAQ) was used to evaluate the activity level of the participants. The IPAQ questionnaire was completed by the participants independently, without any guidance from the study investigators. It includes seven questions, collecting self-reported information for the number of days and time spent doing vigorous

Table 1 Study participants' age, sex, and primary cause of end-stage liver disease

No.	Age	Sex	Primary cause
1	32	Female	Primary biliary cholangitis
2	53	Female	Liver hemangioma
3	38	Female	Liver hemangioma
4	53	Male	Hepatitis B virus
5	38	Male	Autoimmune hepatitis
6	51	Female	Hepatocellular carcinoma
7	32	Male	Hepatocellular carcinoma
8	61	Female	Hepatitis B virus
9	63	Male	Non-alcoholic fatty liver disease
10	47	Female	Hepatic cystadenomas
11	62	Female	Primary biliary cholangitis
12	54	Male	Hepatitis C virus
13	52	Male	Alcohol-related liver disease
14	63	Male	Alcohol-related liver disease
15	49	Female	Hepatitis B virus
16	52	Male	Hepatitis B virus
17	50	Male	Hepatitis B virus
18	52	Female	Non-alcoholic fatty liver disease
19	50	Male	Non-alcoholic fatty liver disease
20	50	Female	Primary biliary cholangitis

activity, moderate physical activity, walking, and sitting each day during the course of 1 wk[24,25]. The participants completed the Greek version of the questionnaire[26]. Questions 1 and 2 were about the days and time spent on vigorous activities, questions 3 and 4 referred to activities of moderate intensity, questions 5 and 6 referred to walking, and question 7 asked about the time spent sitting. This tool classifies respondents into three categories of physical activity, namely low, moderate, and high, according to the following criteria[27]: (1) Category 1 - low, consisting of individuals failing to meet any of the criteria detailed below; (2) Category 2 - moderate, consisting of individuals that fulfill any of the following three criteria: At least 3 d of vigorous activity, lasting more than 20 min daily; at least 5 d of moderate activity or walking, lasting more than 30 min daily; and at least 5 d of exercise comprising of a combination of walking, moderate, and vigorous activities, equal to 600 metabolic equivalent of task (MET) minutes or more; and (3) Category 3 - high, consisting of individuals that fulfill either of the following: At least 3 d of vigorous activity, reaching at least 1500 MET minutes weekly; and daily exercise comprising of a combination of walking, moderate, and vigorous activities, reaching at least 3000 MET minutes weekly.

Functional capacity evaluation

Two different methods were used to evaluate the functional capacity of participants, namely CPET and the 6MWT. CPET was performed on the Trackmaster Treadmill (Full Vision Inc., Newton, KS, United States), using the Bruce protocol, whereas gas exchange was measured by the MedGraphics Breeze Suite CPX Ultima (Medical Graphics Corp., St. Paul, MN, United States). The test was performed under the supervision of trained personnel and a cardiologist, within the facilities of the Laboratory of Sports Medicine of the Aristotle University of Thessaloniki. Maximal effort was achieved by all participants, upon reaching a respiratory exchange ratio larger than 1.10. Peak oxygen uptake (VO_{2peak}) and anaerobic threshold (AT) were assessed to evaluate the functional capacity of the participants.

Furthermore, a 6MWT was performed indoors by all participants. The testing design included a 30-m long, flat, and circular track, which was clearly marked for every meter. Patients performed the test twice and the longest distance achieved was recorded as their result. They were also instructed to immediately abandon their attempt if they felt unwell or had uncontrollable fatigue. During the 6MWT, patients received verbal encouragement on the 2nd and 4th min of every attempt and a notification when 60 s were left. Pulse oximetry was used to measure the oxygen saturation and heart rate during the test,

Table 2 International Physical Activity Questionnaire responses

No.	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Result
1	0 d	-	2 d	0 h 15 min	5 d	1 h 0 min	8 h 0 min	Moderate
2	2 d	0 h 15 min	4 d	30 min	5 d	1 h 0 min	4 h 30 min	Moderate
3	0 d	-	2 d	0 h 20 min	7 d	1 h 30 min	6 h 0 min	Moderate
4	0 d	-	0 d	-	3 d	0 h 30 min	8 h 0 min	Low
5	0 d	-	3 d	0 h 30 min	3 d	1 h 0 min	6 h 0 min	Moderate
6	0 d	-	2 d	0 h 20 min	4 d	0 h 45 min	6 h 30 min	Moderate
7	0 d	-	3 d	0 h 45 min	4 d	1 h 15 min	4 h 30 min	Moderate
8	0 d	-	2 d	0 h 15 min	2 d	0 h 30 min	7 h 30 min	Low
9	0 d	-	0 d	-	3 d	0 h 15 min	9 h 30 min	Low
10	0 d	-	3 d	0 h 30 min	3 d	0 h 45 min	6 h 15 min	Moderate
11	0 d	-	0 d	-	3 d	0 h 15 min	9 h 15 min	Low
12	0 d	-	2 d	0 h 20 min	3 d	0 h 30 min	6 h 45 min	Low
13	0 d	-	2 d	0 h 15 min	4 d	0 h 20 min	7 h 0 min	Low
14	0 d	-	0 d	-	5 d	0 h 15 min	8 h 0 min	Low
15	0 d	-	0 d	-	3 d	0 h 40 min	7 h 30 min	Low
16	0 d	-	2 d	0 h 20 min	3 d	0 h 30 min	6 h 0 min	Low
17	0 d	-	3 d	0 h 30 min	4 d	1 h 30 min	4 h 0 min	Moderate
18	0 d	-	3 d	0 h 20 min	4 d	1 h 0 min	6 h 0 min	Moderate
19	0 d	-	0 d	-	7 d	1 h 15 min	5 h 30 min	Moderate
20	0 d	-	0 d	-	3 d	0 h 30 min	8 h 0 min	Low

whereas the Borg scale Rating of Perceived Exertion was used to monitor exercise intensity.

Physical frailty evaluation

The LFI was used to evaluate the physical frailty of the study participants[28]. This clinical tool, developed by Lai *et al*[29], includes three tests that assess balance, neuromuscular coordination, and sarcopenia. The three tests are as follows: (1) Hand grip strength (using a dynamometer in the standard position, the participant squeezes the grip three times while the dynamometer rests on no surface); (2) Sit-to-stand test (from sitting position and keeping both arms folded in front of their chest, the participant is timed while standing up and sitting down five consecutive times); and (3) Balance test (the participant is timed standing up in three different balance positions, with feet side-by-side, semi tandem and tandem, while receiving no further support, for a maximum of 10 s).

Statistical analysis

IBM SPSS Statistics, version 25.0 (IBM Corp., Armonk, NY, United States) was used for the statistical analyses. Continuous parameters were compared using the independent samples *t*-test. The values of the parameters of the sample were tested for normal distribution with the Shapiro-Wilk test. Point biserial correlation analysis was used to determine the relationship between activity level and the frailty and functional capacity variables. Difference between values was considered to be of statistical significance for *P* values less than 0.01. All data are presented as the mean ± standard deviation.

RESULTS

General characteristics of patients

Twenty patients were included in the study, all of whom are listed in the waiting list of the Department of Transplant Surgery in the Hippokration General Hospital of Thessaloniki. The majority of patients came from the city of Thessaloniki (n = 9, 45%), whereas the rest were distributed across the Greek mainland and islands. There were 10 male and 10 female patients included in the study, with a median age of 50.1 years. The primary causes of ELD of the participants were hepatitis B (n = 5, 25%), non-

Table 3 Peak oxygen uptake and anaerobic threshold results

No.	Group	VO_{2peak} in mL/kg/min	AT in mL/kg/min
1	Active	29.9	15.8
2	Active	40.8	21.1
3	Active	27.1	18.0
4	Sedentary	18.9	14.8
5	Active	25.7	14.1
6	Active	24.2	15.0
7	Active	39.6	18.8
8	Sedentary	18.4	14.2
9	Sedentary	13.8	12.8
10	Active	22.2	14.2
11	Sedentary	13.2	11.6
12	Sedentary	25.3	17.0
13	Sedentary	20.0	14.7
14	Sedentary	16.9	12.8
15	Sedentary	17.0	13.8
16	Sedentary	19.5	14.0
17	Active	30.0	16.9
18	Active	28.5	16.5
19	Active	29.8	16.7
20	Sedentary	18.1	13.9

AT: Anaerobic threshold; VO_{2peak}: Peak oxygen uptake.

alcoholic fatty liver disease (n = 3, 15%), primary biliary cholangitis (n = 3, 15%), alcohol-related liver disease (n = 2, 10%), liver hemangioma (n = 2, 10%), hepatocellular carcinoma (n = 2, 10%), hepatitis C (n = 1, 5%), autoimmune hepatitis (n = 1, 5%), and hepatic cystadenomas (n = 1, 5%). The mean MELD score for the patients in the study was 13.02 ± 4.71. Demographic details for each patient are listed in Table 1, including the primary cause of ELD per participant.

Activity level

All responses collected *via* the IPAQ can be seen in Table 2. Ten patients were classified as having a moderate physical activity level (category 2), whereas ten patients were found to be in the low physical activity level category (category 1). Using these responses, the sample was divided into two groups; patients with a moderate activity level were characterized as active (A), and patients with low activity level were allocated in the sedentary group (S). The active and sedentary groups were found to be similar regarding their MELD scores (A: 12.05 ± 5.63 *vs* S: 13.99 ± 3.60, respectively; $P > 0.05$).

Functional capacity

All participants successfully completed their CPET, successfully reaching a respiratory exchange ratio equal to 1.10 or higher. No patient had to abandon their examination due to excess fatigue or the presentation of adverse effects. No patient was instructed to terminate the exercise stress test due to changes to their electrocardiogram.

The mean VO_{2peak} achieved by active participants was higher compared to the mean value recorded by the sedentary group (A: 29.78 ± 6.07 mL/kg/min *vs* S: 18.11 ± 3.39 mL/kg/min, respectively; $P < 0.001$). Similarly, the AT in active subjects was higher than that in their sedentary counterparts (A: 16.71 ± 2.17 mL/kg/min *vs* S: 13.96 ± 1.45 mL/kg/min, respectively; $P < 0.01$). All results for VO_{2peak} and AT are presented in Table 3.

Regarding the 6MWT, all participants successfully completed two attempts, with the longest distance considered the test result. No complication was recorded, and no effort was abandoned due to fatigue or exhaustion. Detailed results per participant are presented in Table 4. The active group covered a larger mean distance on the test compared to the sedentary group (A: 324.7 ± 55.8 m *vs* S: 458.2 ± 57.5 m,

Table 4 Six-minute walking test results

No.	Group	6-min walking test in m
1	Active	396
2	Active	456
3	Active	595
4	Sedentary	250
5	Active	433
6	Active	397
7	Active	429
8	Sedentary	347
9	Sedentary	264
10	Active	502
11	Sedentary	259
12	Sedentary	360
13	Sedentary	431
14	Sedentary	362
15	Sedentary	320
16	Sedentary	330
17	Active	460
18	Active	456
19	Active	458
20	Sedentary	324

respectively; $P < 0.001$).

Physical frailty evaluation

The LFI was used to assess the robustness or frailty of the study participants. Patients successfully completed all exercises after first witnessing a demonstration. The sedentary group was more likely to score a greater LFI score and to be frail, whereas its mean value was above the limit for patient classification as frail compared to the active group, which was more likely to score smaller values (S: 4.42 ± 0.32 *vs* A: 3.75 ± 0.31, respectively; $P < 0.001$). The detailed performance per test is described in Table 5. Patients with a LFI greater than 4.4 were classified as frail[23,29]. No patient from the active group was classified as frail (LFI < 4.4, $n = 10$), whereas 6 patients were found to be frail according to the LFI in the sedentary group (LFI > 4.4, $n = 6$). Mean value comparisons are presented for all variables in Table 6.

Correlation analysis

Pearson correlation analysis was used to determine if disease severity was associated with worse functional capacity or higher frailty scores. Correlation was tested between MELD scores and LFI, VO_{2max}, AT, and 6MWT. No significant correlation was found between MELD and LFI ($r_p = 0.29$, $P > 0.05$), VO_{2max} ($r_p = -0.10$, $P > 0.05$), AT ($r_p = -0.25$, $P > 0.05$) or 6MWT ($r_p = -0.36$, $P > 0.05$).

Point-biserial correlation was run to determine the relationship between the activity level and functional capacity and physical frailty markers. MELD and activity level was not significantly correlated ($r_{pb} = -0.212$, $P > 0.05$), whereas there was significant correlation between activity level and LFI ($r_{pb} = -0.747$, $P < 0.001$), VO_{2peak} ($r_{pb} = 0.781$, $P < 0.001$), AT ($r_{pb} = 0.618$, $P < 0.01$), and 6MWT ($r_{pb} = 0.779$, $P < 0.001$). This relationship is presented in Table 7.

DISCUSSION

According to the results of this observational study, physical activity appears to prevent physical frailty and retain cardiovascular capacity in liver transplant candidates, independent of their MELD score. This can be potentially used as a tool for prehabilitation in listed patients for a liver transplant. Availability of liver transplants has always been well below demand, especially in Greece, with the coronavirus disease

Table 5 Liver Frailty Index test results

No.	Hand grip strength in kg			Sit-to-stand in s	Balance test in s			LFI
	Att. 1	Att. 2	Att. 3		Side-by-side	Semi-tandem	Tandem	
1	18	19	19	12.4	10.0	10.0	10.0	3.95
2	26	26	25	8.5	10.0	10.0	10.0	3.11
3	25	24	24	10.1	10.0	10.0	10.0	3.42
4	19	18	18	16.8	7.9	9.1	8.2	4.76
5	26	27	27	11.0	10.0	10.0	10.0	3.9
6	19	18	19	13.1	9.1	10.0	8.9	4.08
7	30	28	29	10.0	10.0	10.0	10.0	3.71
8	14	14	13	17.2	8.5	9.2	8.1	4.66
9	13	14	14	17.6	8.5	9.4	8.0	4.92
10	18	17	18	13.3	9.0	10.0	9.0	4.15
11	12	11	12	16.1	9.3	10.0	9.0	4.62
12	20	19	19	11.9	10.0	10.0	10.0	4.23
13	26	27	28	12.2	10.0	10.0	10.0	4.00
14	22	21	21	11.8	10.0	10.0	10.0	4.15
15	18	18	17	12.8	10.0	10.0	10.0	4.03
16	18	19	18	13.0	9.5	9.8	8.9	4.42
17	27	27	26	9.4	10.0	10.0	10.0	3.70
18	19	20	20	11.3	10.0	10.0	10.0	3.80
19	27	28	27	9.8	10.0	10.0	10.0	3.74
20	15	14	14	14.2	9.0	9.4	8.4	4.43

Att: Attempt; LFI: Liver Frailty Index.

Table 6 Mean values of peak oxygen uptake, anaerobic threshold, 6-min walking test and, Liver Frailty Index

Value	Active group	Sedentary group
VO_{2peak} in mL/kg/min	29.78 ± 6.07[a]	18.11 ± 3.39[a]
AT in mL/kg/min	16.71 ± 2.17[b]	13.96 ± 1.45[b]
6MWT in m	458.2 ± 57.5[a]	324.7 ± 55.8[a]
LFI	3.75 ± 0.31[a]	4.42 ± 0.32[a]

[a]$P < 0.001$.
[b]$P < 0.01$.
6MWT: 6-min walking test; AT: Anaerobic threshold; LFI: Liver Frailty Index; VO_{2peak}: Peak oxygen uptake.

2019 pandemic posing an even greater challenge. This study was driven by the need to identify possible important and potentially modifiable clinical parameters, which, when used in concordance with the MELD score, would be able to optimize the capacity of a medium-size transplant center[3,6].

According to the LFI, 30% (n = 6) of the study participants are classified as frail (LFI > 4.4)[23,29], a percentage that is concordant with the results of a previous review study[30]. Physical frailty has been associated with increased waiting list mortality, independently of the MELD score, presence of ascites or hepatic encephalopathy[31]. Furthermore, in the postoperative spectrum, frailty has been associated with increased 30-d mortality, extended inpatient and intensive unit care[32], increased rates of acute cellular rejection[33], increased dependency[34,35], and vertebrae fractures[36]. Constructed, the home-based exercise program appears to positively influence frailty indexes and partially restore musculo-skeletal robustness[37-40]. Our study compared each patient's physical activity level with their physical

Table 7 Correlation analysis between activity level and model for end-stage liver disease score peak oxygen uptake, anaerobic threshold, 6-min walking test, and Liver Frailty Index

Value	r_{pb}	*P* value
MELD	-0.212	> 0.05
VO_{2peak} in mL/kg/min	0.781	< 0.001
AT in mL/kg/min	0.618	< 0.01
6MWT in m	0.779	< 0.001
LFI	-0.747	< 0.001

6MWT: 6-min walking test; AT: Anaerobic threshold; LFI: Liver Frailty Index; MELD: Model for end-stage liver disease; r_{pb}: Point-biserial correlation coefficient; VO_{2peak}: Peak oxygen uptake.

frailty. Although patients were not under professional trainer guidance, frequent activity such as walking and gardening, appeared to have a preventive effect on the evolvement of physical frailty. This could potentially provide clinicians with an important tool in the preoperative treatment of candidates, while on the waiting list for a transplant, being a tool that could potentially improve transplantation outcomes.

Functional capacity has also been associated with postoperative dependency and mortality. Epstein *et al*[12] described an increased 100-d mortality in patients with lower peak oxygen uptake, whereas other studies have associated a smaller VO_{2peak} with extended intensive care unit stay and mechanical ventilation dependency[41]. Similarly, smaller distances in the preoperative 6MWT have been associated with increased mortality after liver transplantation[42,43]. In 2021, Henrique *et al*[18] identified a statistically significant increased risk of cirrhosis decompensation in patients with values smaller than 401.8 m in the 6MWT, whereas Bhanji *et al*[44] described a double risk of waiting list mortality in patients with values smaller than 250 m and its statistically significant reduction for every 100 m improvement. In our study, active participants were much more likely to record values above 401.8 m (80% *vs* 10%; $P < 0.01$), consistent with the findings of the effects of exercise in liver patients in other studies[45,46].

The inclusion of indexes of frailty and functional capacity in the clinical practice of liver transplantation appears to be a valuable aid in patient prioritization, especially in candidates with low MELD scores[47]. Furthermore, regular physical activity appears to be a valuable tool to improve these modifiable factors. Physical frailty has been reported as reduced in liver transplant candidates through the adoption of an active lifestyle in several studies[48,49], while functional capacity has been reported as similarly improved[45,50]. This can potentially lead to improved survival rates and reduced hospitalization length and readmission rates[51,52]. Our study shares similar results, further supporting the notion that physical activity can have a significant role in preoperative preparation for candidates, potentially achieving improved outcomes. Furthermore, our data suggests that home-based, patient-controlled exercise can have an adequate impact.

The active participants of our study, although not following an organized and formal exercise protocol, had substantially better musculoskeletal and functional status, appeared to be more robust, and could potentially have great tolerance to stressors. This suggests evidence that exercise interventions could have a positive impact on liver transplant candidates, without the need for formal and difficult exercise regimes that bear a higher risk of lower compliance. However, this study had limitations, namely the small sample size and no prospective results. Further data collection and follow-up could confirm the effects of this lifestyle on pretransplantation and posttransplantation survival, dependency, and complications.

CONCLUSION

In conclusion, an active lifestyle can potentially be a tool of preoperative preparation of liver transplant candidates to reduce mortality, hospitalization, and dependencies. Physical frailty and functional capacity can be improved with exercise training interventions. Clinical tools such as the 6MWT and the LFI could be used for better mortality prediction and patient prioritization, which is of significant importance in smaller and medium-sized transplant centers, where organ donation is unable to meet the existing high demand.

ARTICLE HIGHLIGHTS

Research background

Liver transplantation forces a substantial stress on the human physiology, which is even more significant considered the deconditioning that accompanies end-stage liver disease (ELD). Physical frailty has emerged as an important factor both pre- and postoperatively, aiming to improve results and outcomes.

Research motivation

The limited amount of available organ donations in addition to the high demand in liver transplants, highlight the need for proper planning and prioritization, while at the same time working towards further outcome improvement.

Research objectives

The main objective was to identify if an active lifestyle can significantly improve physical frailty and functional capacity in patients with ELD.

Research methods

An International Physical Activity Questionnaire, a functional capacity assessment, and a physical frailty evaluation were utilized.

Research results

There was a statistically significant difference and statistically significant correlation between the activity level and the Liver Frailty Index, the peak oxygen uptake, the anaerobic threshold, and the 6-min walking distance.

Research conclusions

Physical activity can potentially improve functional capacity and frailty in liver transplant candidates.

Research perspectives

Future research should focus on the regimen of the exercise that would be more suitable, or better quantify the amount of physical exercise needed for these patients. Furthermore, the potential use of these markers in survival and outcomes should be evaluated.

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FOOTNOTES

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