


ORIGINAL ARTICLE

Prospective study of objective physical activity and quality of life in living donor liver transplant recipients

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Abstract

Aim: The aims of this study were to: (a) describe the physical activity (PA) and quality of life (QOL) in living donor liver transplant (LDLT) recipients pre-operatively and at 3 months and 6 months post-operatively; (b) compare PA and QOL at 6 months post-operatively with a healthy control group; and (c) explore pre-operative factors that predict PA changes.

Methods: Patients over 20 years of age who were undergoing LDLT were recruited. PA was measured based on the number of steps/day and time spent performing moderate-to-vigorous PA (MVPA) during 1 week using an accelerometer. QOL was assessed based on a physical (PCS) and mental (MCS) component summary of the eight-item Short-Form Health Survey. The LDLT and healthy control groups were matched for age (± 3 years) and gender. Pre-operative factors predicting a change in PA were calculated using a generalized linear mixed model.

Results: Twenty-four patients completed the study. By 6 months post-LDLT, the MCS and PCS were comparable to those in the control group. The number of steps (3,887 steps/day) and MVPA (29.3 min/week) showed significant improvement by 6 months post-operatively, but remained much lower compared with those in the control group. The multivariate analysis showed that younger age ($p < .01$, $p = .04$) and higher skeletal muscle mass (SMM; $p < .01$, $p = .03$) were predictors of improvement in number of steps and MVPA.

Conclusion: This study suggests the need for pre-operative interventions by healthcare professionals that focus on outcomes such as improving low SMM to facilitate post-operative PA recovery.

KEYWORDS

accelerometer, living donor liver transplantation, physical activity, prospective study, quality of life

1 | INTRODUCTION

The survival rate after liver transplantation (LT) has improved significantly (Kim et al., 2019; Umeshita

et al., 2019). However, LT recipients are at a high risk of developing metabolic syndrome, and more than half of LT recipients develop diabetes, hypertension, and/or dyslipidemia within 1 year after LT (Kallwitz et al., 2013;

Laryea et al., 2007). Side effects of immunosuppressants may play a role in these comorbidities (Singh & Watt, 2012; Hoorn et al., 2011; Heisel, Heisel, Balshaw & Keown, 2004), and physical activity (PA) plays a critical role in prevention along with diet therapy and medication (World Health Organization, 2010).

Moderate-to-vigorous physical activity (MVPA), such as brisk walking, is particularly effective for preventing metabolic syndrome and reducing its severity (World Health Organization, 2010). PA can be measured easily using self-administered questionnaires; however, this has the potential limitation of poor recall. The International Physical Activity Questionnaire (IPAQ) is a commonly used self-administered tool to measure the duration and intensity of PA (Craig et al., 2003), and a study using IPAQ showed that LT recipients ($N = 54$) had lower PA compared with healthy controls (Masala et al., 2012).

PA can be measured objectively using a device such as an accelerometer, which requires high compliance and may have the limitation of a relatively high dropout rate (Pedišić & Bauman, 2015). There was only one small cross-sectional study that measured the PA in LT patients after transplantation (Berg-Emons et al., 2006). Berg-Emons et al. (2006) measured PA in daily life using an accelerometer in eight LT patients from 6 months to 3 years after LT, and they found that five patients had a sedentary lifestyle and that most patients had low-intensity PA.

There are several studies about the predictive factors of PA in transplant patients. In a study of 107 post-LT patients, retirement status and severe obesity were associated with PA, which was measured using the IPAQ and analyzed using a univariate analysis (Kotarska et al. 2014). A study of PA intensity that was measured by accelerometers showed that it was negatively correlated with fatigue in post-LT patients (Berg-Emons et al., 2006).

Among healthy older persons, a prospective study showed that a lower serum albumin level, which is an indicator of nutritional status, was associated with lower muscle mass (Schalk, Deeg, Penninx, Bouter & Visser, 2005), which suggested the importance of nutritional status in PA. PA is also associated with quality of life (QOL). Twenty-six LT patients completed a questionnaire about the PA type and frequency of PA measurement, and the results showed that patients who regularly engaged in physical exercise had a better QOL (Rongies et al., 2011).

Pre-operative biological indicators are reported to be associated with physical function in post-LT patients. Severity of chronic liver diseases as measured using the model for end-stage liver disease score and low skeletal muscle mass (SMM) were predictors of post-operative physical function and recovery (Mizuno et al., 2016; Kaido et al. 2013).

A lack of exercise guidelines is considered to be a major barrier for the promotion of PA in organ transplant recipients (Gustaw et al., 2017). It is more difficult for living donor LT (LDLT) recipients to know the appropriate level of PA compared with deceased donor LT recipients because LDLT recipients receive a partial liver from living donors. The partial liver from a living donor takes more than 3 months to regenerate to the appropriate liver volume (Farkas, Hackl, & Schlitt, 2014; Olthoff et al., 2015). Physical capacity measured by the 6-min walk test in deceased donor LT recipients showed a significant improvement compared with pre-operative results 1 month after surgery (Magalhães et al., 2018), whereas their LDLT counterparts showed no significant improvement (Mizuno et al., 2016). In Asian countries, close to 90% of LTs are LDLTs because of social and cultural factors, such as the unacceptability of cutting into the body and removal of organs from a dead family member and poor donor co-ordination (Farkas, Hackl, & Schlitt, 2014; Yoshimura et al. 2010; LaFleur, 2002).

Our literature search showed there was a paucity of literature on PA among LT recipients, especially among LDLT recipients. Thus, it is necessary to examine the changes in PA from the pre- to early post-LT periods, and to investigate the predictive factors of the changes to promote PA.

The aims of this prospective study were to: (a) describe the PA that was measured using accelerometers and the QOL in LDLT recipients pre-operatively, and at 3 months and 6 months post-surgery; (b) compare PA and QOL at 6 months post-surgery with those of a healthy control group; and (c) explore predictive factors of the changes in PA from pre-surgery to 6 months post-surgery.

2 | METHODS

2.1 | Sampling

The sample population for this prospective study was adult patients who were over 20 years of age and who underwent a LDLT at a university hospital between August 2015 and March 2019. Inclusion criteria were as follows: (a) established LT treatment schedule; (b) living at home before the LT surgery; and (c) able to self-administer the questionnaire in Japanese. The exclusion criteria were as follows: (a) receiving emergency surgery, such as for fulminant hepatitis; or (b) having a gait disorder such as severe arthritis. People without a medical condition who required outpatient treatment in Fukuoka Prefecture were recruited into the healthy control group using the snowball sampling method. Age (± 3 years) and gender were matched to the LDLT participants.

A sample size of 24 patients was sufficient to attain statistically significant differences in PA between LT

recipients. For the sample size calculation, 18 patients would allow the following at a significance level of 5% based on a previous study (Berg-Emons, 2006): a power to detect type 2 errors of 0.8; and an effect size of 0.25 (G*Power, Heinrich-Heine-Universität, Düsseldorf, Germany). To account for potential dropouts, we recruited 24 individuals for each group.

This study was approved by the Ethics Review Board at Kyushu University (ID number 30–491). All participants were informed of the following: (a) participation in the research was voluntary; (b) participation would not affect their treatment; (c) they could withdraw from the study at any time; and (d) their privacy was protected. Written informed consent was obtained from all patients.

2.2 | Study procedures

Eligible patients were selected by examining outpatients' medical records. During pre-operative examination at the hospital, the purpose of this study and the study protocol were explained to the patients. After obtaining informed consent, participants were then given an accelerometer and the questionnaire, and they were instructed on how to use an accelerometer. At 3 months post-LT, when they were hospitalized for external biliary stent tube removal or at an outpatient visit, the patients were given another accelerometer and the questionnaires were re-administered. At 6 months post-LT, questionnaires and accelerometers were distributed during the patients' outpatient visits or by mail. The control group was also given accelerometers and the eight-item Short-Form Health Survey (SF-8) was administered.

2.3 | Physical activity measurements

The amount and intensity of PA were measured based on the number of steps and duration of MVPA (≥ 3 metabolic equivalents); these measurements were recorded using an accelerometer (Lifecorder GS; size: $72.0 \times 42.0 \times 29.1$ mm; weight: 45 g; Suzuken Co. Ltd., Nagoya, Japan). The outcome variables were the mean number of steps/day and the time spent performing MVPA/week. Participants were requested to wear the accelerometer on their waistline, except while sleeping and bathing. The accuracy of the number of steps recorded by the Lifecorder GS and the validity of using metabolic equivalents that were measured by this device have been verified (Kumahara et al., 2004).

The Liferiser Coach 05 (Suzuken Co. Ltd.) was used to analyze the accelerometer data and to calculate the number of steps and the intensity of PA. Based on

previous studies (Tudor-Locke, Johnson, & Katzmarzyk, 2009), subjects wore accelerometers for ≥ 10 hr/day and seven consecutive days of data were used for the analysis.

2.4 | Health-related quality of life

The health-related QOL was measured using the Japanese version of the SF-8, and its reliability and validity were established by Fukuhara (2005). The SF-8 has eight subscales, and it can be aggregated into physical component summary (PCS) scores and mental component summary (MCS) scores. The overall scores for the scales ranged from 0 to 100, with higher scores indicating a better QOL.

2.5 | Patient characteristics

The demographic characteristics of the patients, data related to their operations, and model for end-stage liver disease score were evaluated using serum bilirubin, serum creatinine, and the international normalized ratio for prothrombin time in the patients' medical records. Each patient's height and weight were measured at each outpatient visit to obtain the body mass index (BMI). SMM was measured by InBody 720 (Biospace, Tokyo, Japan), which is a percent of standard SMM, based on age, gender, and height. Two studies reported the accuracy of InBody for SMM measurement, which demonstrated a strong correlation between dual-energy X-ray absorptiometry and computed tomography (Hamaguchi et al., 2016; Yeh et al., 2012). Low SMM, which is a surrogate measure of sarcopenia, of $<90\%$ of the standard skeletal mass was used as a cutoff point (Kaido et al., 2013). The Japanese version of the Brief Fatigue Inventory was used to measure the degree of fatigue (Mendoza et al., 1999), and its reliability and validity were confirmed by Okuyama et al. (2003). The Brief Fatigue Inventory comprises 10 items, and the score ranges from 0 to 10 points. A higher mean score indicates a higher degree of fatigue.

2.6 | Statistical analyses

Pre-operative demographic characteristics were presented as the mean \pm standard deviation (SD) for normal distributions using the Shapiro–Wilk normality test. PA and QOL results that were not normally distributed were displayed as the median (interquartile range [IQR]).

PA data were required for ≥ 4 days for analysis (Togo et al., 2008). If the PA data for ≤ 3 days were missing, the mean of the existing PA data was imputed.

The attrition bias was examined by comparing the pre-operative data between those who completed the follow-up and those who dropped out. The Mann-Whitney *U* test was used for continuous variables and a Chi-square test or Fisher's exact test was used for categorical variables. Comparisons between patients at 6 months post-LT and the control group in terms of PA and QOL were performed using the Mann-Whitney *U* test, Chi-squared test, or Fisher's exact test.

The Wilcoxon signed-rank test was used to detect the median difference between the two time points of PA and QOL. Correlation analysis between the number of steps and MVPA at 6 months post-LT was performed using the Spearman's rank correlation coefficient. A generalized linear mixed model was used to examine predictive factors for the change in PA between the pre-operative and 6-month post-operative period. A generalized linear mixed model provides a flexible framework for the analysis of repeated measures because this model considers that participants can differ from one another in their responses at baseline (intercepts), and each participant differs in their rate of response (slope) over time (Gueorguieva & Krystal, 2004). The independent variables that were selected were the pre-operative variables based on previous studies. The independent variables included pre-operative variables, such as gender, age, model for end-stage liver disease score, albumin level, SMM, QOL, and fatigue. Multicollinearity between the independent variables was screened. All statistical analyses were performed using SPSS Ver. 26 (IBM Corp.,

Armonk, NY, USA). $p < .05$ was considered to indicate statistical significance.

3 | RESULTS

3.1 | Patient recruitment and pre-operative participant characteristics

Among the patients who received LT during the study period, 31 agreed to participate. Among them, seven patients dropped out before 6 months post-LT, and the remaining 24 patients completed the study (Figure 1). A main reason for dropping out was difficulty in continuing to use the device.

The demographic characteristics of the patient and the control groups are shown in Table 1. The mean age was 55 years, and 41.7% were male. The mean BMI was 23.6 kg/m² and 50% of the patients were employed before LT. The mean BMI and employment status for the age and gender-matched control group were comparable to those in the LDLT group. For two patients, SMM was unable to be measured using InBody before surgery, and SMM data were obtained from 22 patients. Additionally, 16% of recipients had low SMM, and the mean model for end-stage liver disease score for LDLT recipients was 14.8. The most common diagnosis was hepatitis C (25%) and pre-operative patients' comorbidities were diabetes (25%) and hypertension (20.8%). The mean fatigue score using the Brief Fatigue Inventory was 3.7 ± 2.8 before LT.

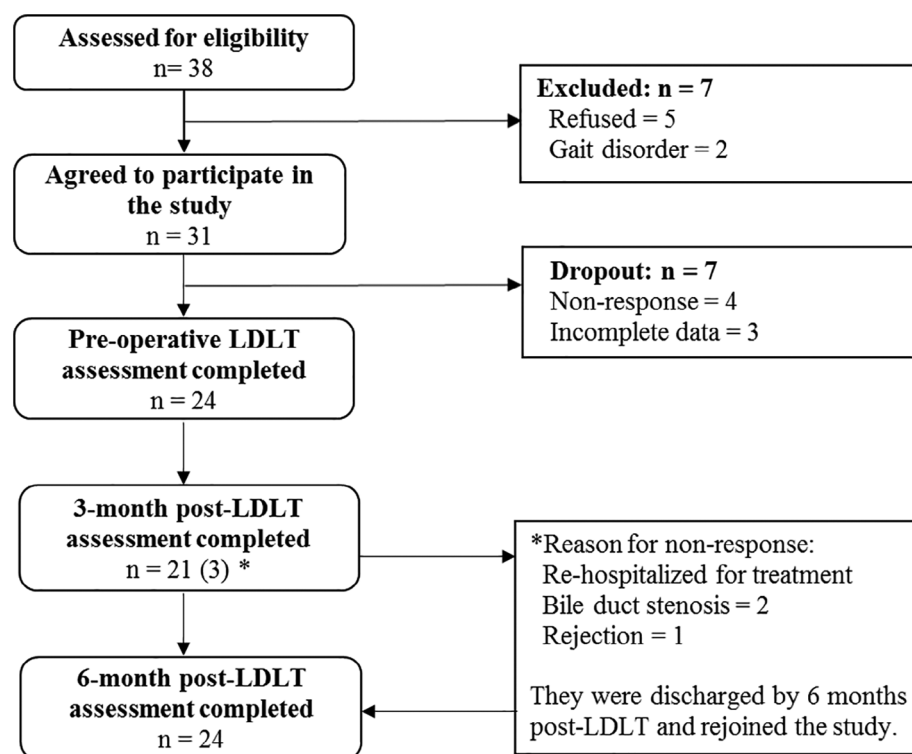


FIGURE 1 Flow chart of study participants. LDLT, living donor liver transplant

3.2 | Difference in the patient characteristics between patients who completed follow-up and those who dropped out

Pre-operative data from dropouts ($n = 7$) were compared with data from the 24 patients who completed the follow-

up. There were no significant differences in mean age (55 ± 11 vs. 53 ± 16 years; $p = .87$), gender (male: 41.7% vs. 71.4%; $p = .17$), mean BMI (23.6 ± 3.3 vs. 24.7 ± 2.7 kg/m²; $p = .39$), mean model for end-stage liver disease score (14.8 ± 5.5 vs. 12.1 ± 4.8 ; $p = .37$), mean operation time (655 ± 130 vs. 756 ± 181 min; $p = .13$), mean graft volume/standard liver volume ratio

TABLE 1 Pre- and post-operative LDLT recipients and control group demographic characteristics

Variables	LDLT recipients $N = 24$	Control participants $N = 24$	p value
Pre-operative			
Gender (male)	10 (41.7%)	10 (41.7%)	1.00 ^a
Age (years)	55 ± 11 (26–68)	57 ± 12 (26–71)	.46 ^c
Body mass index (kg/m ²)	23.6 ± 3.3 (17.0–28.3)	23.2 ± 3.4 (17.5–32.0)	.68 ^c
Employed (yes)	12 (50.0%)	16 (66.7%)	.24 ^a
Physical activity			
Number of steps (steps/day)	2,492 (1849–3,747)		
MVPA (min/week)	13.2 (6.4–69.8)		
Low skeletal muscle mass ($n = 22$)	4 (16.0%)		
Model for end-stage liver disease score	14.8 ± 5.5 (8–29)		
Albumin (g/dL)	2.8 ± 0.4 (2.1–4.0)		
Diagnosis			
Hepatitis C	6 (25.0%)		
Non-alcoholic steatohepatitis	5 (20.8%)		
PBC, PSC	5 (20.8%)		
Alcoholism	4 (16.7%)		
Others	4 (16.7%)		
Comorbidities (yes)			
Diabetes mellitus ^b	6/24 (25.0%)		
Hypertension ^b	5/24 (20.8%)		
Fatigue	3.7 ± 2.8 (0.0–9.4)		
Postoperative			
Physical activity 6 months after LT			
Number of steps (steps/day)	3,887 (2898–6,253)	6,967 (5870–8,469)	<.001 ^c
MVPA (min/week)	29.3 (14.5–102.3)	121 (91.5–170)	<.001 ^c
Operation time (min)	655 ± 130 (472–955)		
Blood loss (mL)	$4,896 \pm 3,474$ (490–13,350)		
GV/SLV (%)	43.6 ± 8.6 (26.8–63.9)		
Length of stay (days)	27 ± 17 (9–84)		
Complications (yes)			
Bile duct stenosis	3/24 (12.5%)		
Rejection, reoperation	3/24 (12.5%)		

Note: Data are presented as n (%) or as the mean \pm SD (range). Physical activity is presented as the median (interquartile range).

Abbreviations: LDLT, living donor liver transplantation; MVPA, moderate-to-vigorous physical activity; PBC, primary biliary cholangitis; PSC, primary sclerosing cholangitis; GV/SLV, graft volume/standard liver volume.

^aChi-square test.

^bDuplicate.

^cMann–Whitney U test.

(43.6 ± 8.6 vs. $47.0 \pm 13.2\%$; $p = .60$), mean length of stay (27 ± 17 vs. 39 ± 30 days; $p = .18$), or post-operative complications (25 vs. 28.6%; $p = .60$) between the group that completed follow-up and the group that dropped out.

3.3 | Physical activity

The mean duration that LDLT patients and control group wore the accelerometer over a 7-day period was 15.3 ± 3.3 hr (range, 10.3–21.2 hr).

The number of steps for the LDLT group showed no significant improvement from the pre-LT period to 3 months post-operatively, and then it increased significantly from 3 months to 6 months post-operatively ($p < .01$; Figure 2). The pattern of changes in MVPA was identical to that of the number of steps (Figure 2). Additionally, the number of steps and MVPA at 6 months post-LT showed a strong positive correlation ($r = 0.72$, $p < .001$).

To investigate the level of improvement in PA in the LDLT group, we compared PA in the LDLT group data with that of the healthy control group. The median

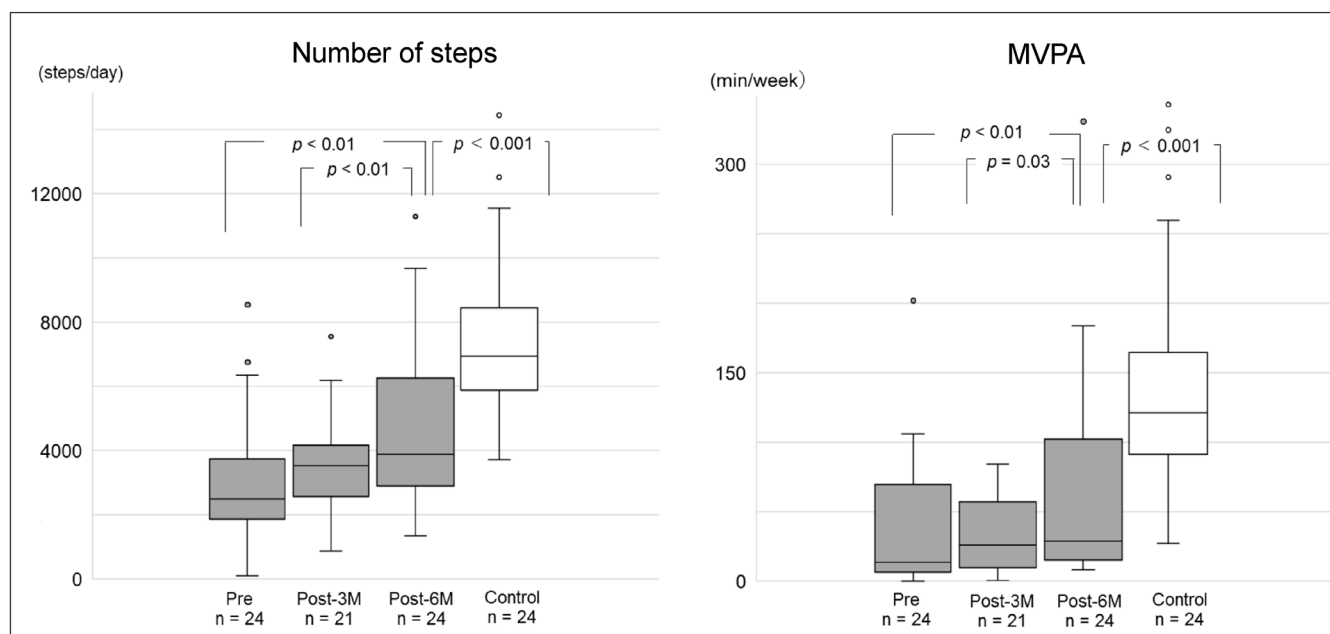


FIGURE 2 Pre- and post-operative changes in the number of steps and moderate-to-vigorous physical activity (MVPA) in the liver transplant (LT) and control groups. The Wilcoxon signed-rank test was used for comparison between LT recipients at two time points. Comparisons between patients at 6 months post-LT and the control group were performed using the Mann–Whitney *U* test

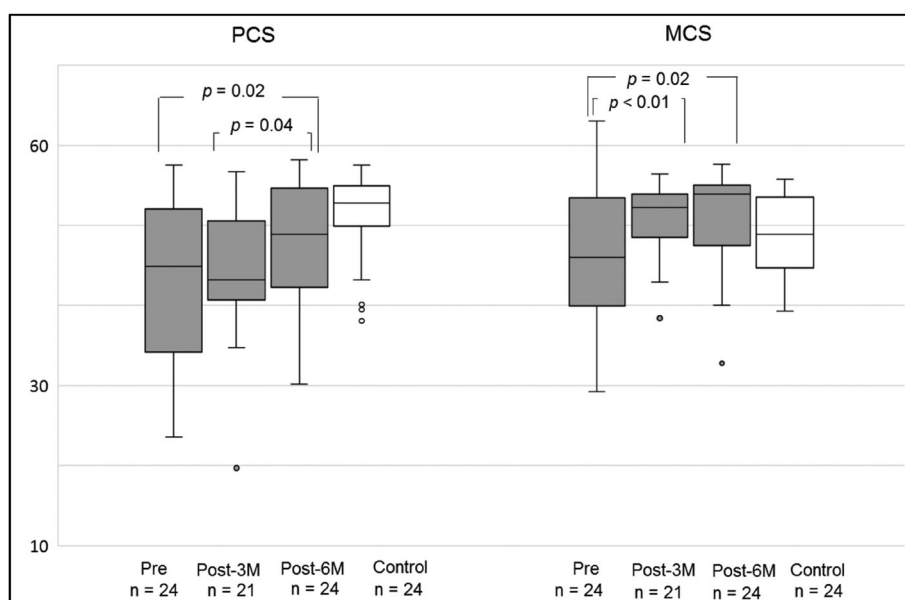


FIGURE 3 Improvement in the physical component summary (PCS) scores and mental component summary (MCS) scores in patients in the pre- and post-operative periods. The Wilcoxon signed-rank test was used for comparison between liver transplant (LT) recipients at two time points. Comparisons between patients at 6 months post-LT and the control group were performed using the Mann–Whitney *U* test

TABLE 2 Predictive factors for changes in physical activity from pre-operative to 6 months post-operative based on pre-operative variables

	Number of steps (steps/day)			MVPA (min/week)		N = 22 p value
	Beta	(95% CI)	p value	Beta	(95% CI)	
Age	-110.5	(-190.7, -30.4)	<.01	-2.9	(-5.6, -0.2)	.04
Gender	—		.36	—		.25
Model for end-stage liver disease score	—		.17	—		.27
SMM	3,202.1	(955.4, 5,448.8)	<.01	71.0	(10.3, 161.7)	.03
Albumin	—		.12	—		.07
PCS	—		.27	—		.46
MCS	—		.93	—		.62
Fatigue	—		.26	—		.18

Note: Generalized linear mixed model. Independent variables are as follows: age, gender (0 = female, 1 = male), Model for end-stage liver disease score, SMM (0 = low SMM, 1 = standard SMM), albumin, SF-8 score, and fatigue.

Abbreviations: CI, confidence interval; MVPA, moderate-to-vigorous physical activity; SMM, skeletal muscle mass; PCS, physical component summary; MCS, mental component summary.

number of steps and MVPA in the LDLT group at 6 months post-LT was significantly less than the healthy control group ($p < .001$). It indicated that the physical activity did not improve to the level of healthy controls (Figure 2). However, individually, five patients (20.8%) reached the median number of steps in the control group by 6 months post-LT, while two patients (8.3%) reached the World Health Organization's recommended level of MVPA by this time.

3.4 | Changes in QOL scores measured by SF-8

The pre-operative PCS scores reached statistical significance at 6 months post-operatively ($p = .02$; Figure 3). However, the pre-operative MCS scores already showed a ceiling effect at 3 months post-LT ($p < .01$; Figure 3). At 6 months post-LT, these two scores did not differ between the LDLT group and the control group (Figure 3).

3.5 | Predictive factors for physical activity

Pre-LT InBody data were not available for two patients, and 22 patients were included in the multivariate analysis. After examining multicollinearity, eight variables were entered into the model. Younger age ($p < .01$, $p = .04$, respectively) and higher SMM ($p < .01$, $p = .03$, respectively) were predictors of the changes in the number of

steps as well as MVPA from pre-operative to 6 months post-LT in the generalized linear mixed model (Table 2).

4 | DISCUSSION

This prospective study of PA and QOL in LDLT recipients revealed that MCS improves by 3 months post-LT and that the number of steps, MVPA, and PCS improved by 6 months post-LT. Additionally, we found that QOL recovered to the level of healthy individuals within 6 months post-LT. Predictors of the changes in these PA indicators are younger age and higher pre-operative SMM in the first 6 months of recovery after LT.

The median number of steps per day for patients waiting for LT in a previous study was 2,436 steps/day (Dunn et al., 2016), which is comparable to that for our study subjects in the pre-LT period. The improvements in the number of steps and MVPA from the pre-LT period to 6 months after LT can be explained below. Liver protein synthesis capacity for the maintenance of SMM normalizes by 6 months after surgery (Urano et al., 2014). Additionally, a lack of improvement in PA during the 3-month post-operative period can be explained by the pain that is caused by the external bile duct stent tube that is inserted to prevent bile duct stenosis, and the tube is generally removed around 3 months after LT.

However, PA at 6 months post-LT was significantly lower in LDLT recipients compared with healthy controls. At 6 months post-LT, more than half of the patients remained at a low MVPA, showing the variability in

post-LT PA among LDLT recipients. A previous prospective study of PA in lung transplant recipients showed a wide range of steps and MVPA among recipients at 6 months post-LT (Wickerson, Mathur, Singer, & Brooks, 2015), with a PA that was as low as that for our study patients. PA was lower in most patients compared with healthy controls, despite normalization of the liver volume and protein synthesis 6 months after LT. This could be because the pre-operative prolonged liver dysfunction and low SMM had not improved at 6 months after LT (Yang, Shan, Saxena & Morris, 2014; Kaido et al., 2017). Recovery of PA in patients with large solid organ transplants such as the liver and lungs may take time. It is necessary to promote PA that is appropriate for the recipient's condition such as rehabilitation or nutrition therapy during the recovery process on a case-by-case basis.

In contrast to the improvement in PA, QOL measured by SF-8 showed faster recovery. Our findings are in agreement with the results from a previous prospective study of Japanese LDLT recipients (Togashi et al., 2013). Additionally, the patients' MCS scores were higher compared with those of the control group, while their PCS scores were lower compared with those of the control group. This is similar to the results of a prospective study that examined LDLT recipients from the pre-LT period to 18 months post-LT using the 36-Item Short-Form Health Survey (Togashi et al., 2013) and also to the findings of a systematic review of the QOL in LT recipients (Yang, Shan, Saxena, & Morris, 2014). While PCS improvement was observed at 6 months after LT, the early recovery of MCS among our patients could be attributed to the psychological effect of a successful transplant; for example, relief from physical symptoms such as ascites and fatigue, a feeling of having survived a life-threatening crisis, and gratitude for surrounding people such as donors and family members (Björk & Nâden, 2008; Jonsen, Athlin, & Suhr, 1998).

For the LDLT recipients, pre-operative factors related to changes in the number of steps and MVPA between the pre-operative and 6-month post-operative time points were age and SMM. Overall, 16% of the subjects in the present study had pre-LT low SMM. Notably, several previous studies have reported that low SMM, known as sarcopenia, is a risk factor for mortality after LDLT (Kaido et al., 2013; Masuda et al., 2014). Ours is the first study to document that low SMM is a predictive factor for changes in PA between the pre- and post-LT periods. Because performing physical activity requires SMM, the pre-LT SMM level can be considered a predictor of PA. Before undergoing LT, patients tended to become undernourished as a result of cirrhosis. Additionally, low levels of PA because of edema and ascites reduced muscle protein synthesis, resulting in sarcopenia (Hayashi et al., 2013).

A review by Duarte-Rojo et al. (2018) of PA in patients with end-stage liver disease showed that sarcopenia improves with exercise- and nutrition-focused interventions. A recent British study showed the importance of pre-LT home rehabilitation interventions (Williams et al., 2019). However, a study in Japan showed that SMM in LDLT recipients does not return to pre-LT levels until 1 year post-LT (Kaido et al., 2017). Studies with a longer follow-up are required to evaluate the effectiveness of pre- and post-LT PA interventions.

We found that age was a predictor of both the number of steps and MVPA. Aging reduces physical function, bone density, and SMM (McPhee et al., 2016). Previous studies of healthy subjects reported a decrease in PA with increasing age (Ayabe et al., 2009), which indicates that LT recipients would experience reductions in PA as they age.

To improve post-operative PA and QOL in LDLT patients, it is important for healthcare professionals to promote light exercise that is suitable for a patient's individual physical condition, so that the pre-operative SMM is not reduced. In addition, PA should be recommended by providing information about post-operative immunosuppressants, which cause lifestyle-related diseases such as hypertension and diabetes.

This study has several limitations. First, our sample size was small, patients were recruited from one hospital, and patients who were hospitalized pre-operatively were excluded. Second, the accelerometer could not measure water-based PA (e.g., swimming). Because of the small sample size, type 2 errors may exist. Further studies with a larger sample size are necessary to evaluate PA and QOL after LT for a longer period and to develop a suitable PA support program.

5 | CONCLUSION

This study prospectively examined the improvement in PA and QOL in LDLT recipients during a 6-months follow-up. MCS in the LDLT group had a ceiling effect by 3 months post-operatively. However, PCS in the LDLT group showed significant improvement at 6 months post-operatively, and the pattern of improvement in the number of steps and MVPA was similar to that of PCS. Although PA did not reach the level of the control group by 6 months post-LT, QOL improved to the levels of the control group by this time. The multivariate analysis showed that pre-LT SMM and age were the predictors for an improvement in PA. Our research suggests the need for a pre-LT care plan to improve low SMM and to facilitate post-LT PA recovery.

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CONFLICTS OF INTERESTS

There are no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

S.T., K.F., M.K., T. I. and T.Y. contributed to the conception and design of this study. S.T., K.F. and M.K. carried out the data collection and analysis. S.T. drafted the manuscript. K.F., M.K., K.M., K.Y., R.T., N.H., T.I. and T.Y. critically reviewed the manuscript. All authors read and approved the final manuscript.

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REFERENCES

- Ayabe, M., Yahiro, T., Yoshioka, M., Higuchi, H., Higaki, Y., & Tanaka, H. (2009). Objectively measured age-related changes in the intensity distribution of daily physical activity in adults. *Journal of Physical Activity and Health*, 6(4), 419–425.
- Björk, I. T., & Nâden, D. (2008). Patients' experiences of waiting for a liver transplantation. *Nursing Inquiry*, 15(4), 289–298.
- Craig, C. L., Marshall, A. L., Sjöström, M., Bauman, A. E., Booth, M. L., Ainsworth, B. E., ... Oja, P. (2003). International physical activity questionnaire: 12-country reliability and validity. *Medicine & Science in Sports & Exercise*, 35(8), 1381–1395.
- Duarte-Rojo, A., Ruiz-Margáin, A., Montaña-Loza, A. J., Macías-Rodríguez, R. U., Ferrando, A., & Kim, W. R. (2018). Exercise and physical activity for patients with end-stage liver disease: Improving functional status and sarcopenia while on the transplant waiting list. *Liver Transplantation*, 24(1), 122–139.
- Dunn, M. A., Josbeno, D. A., Schmotzer, A. R., Tevar, A. D., DiMartini, A. F., Landsittel, D. P., & Delitto, A. (2016). The gap between clinically assessed physical performance and objective physical activity in liver transplant candidates. *Liver Transplantation*, 22(10), 1324–1332.
- Farkas, S., Hackl, C., & Schlitt, H. J. (2014). Overview of the indications and contraindications for liver transplantation. *Cold Spring Harbor Perspectives in Medicine*, 4(5), a015602.
- Fukuhara, S. (2005). Instruments for measuring health-related quality of life: SF-8 and SF-36. *Igaku no Ayumi*, 213, 133–136 in Japanese.
- Gueorguieva, R., & Krystal, J. H. (2004). Move over anova: Progress in analyzing repeated-measures data and its reflection in papers published in the archives of general psychiatry. *Archives of General Psychiatry*, 61(3), 310–317.
- Gustaw, T., Schoo, E., Barbalinardo, C., Rodrigues, N., Zameni, Y., Motta, V. N., ... Janaudis-Ferreira, T. (2017). Physical activity in solid organ transplant recipients: Participation, predictors, barriers, and facilitators. *Clinical Transplantation*, 31(4), e12929.
- Hamaguchi, Y., Kaido, T., Okumura, S., Kobayashi, A., Hammad, A., Tamai, Y., ... Uemoto, S. (2016). Proposal for new diagnostic criteria for low skeletal muscle mass based on computed tomography imaging in Asian adults. *Nutrition*, 32 (11–12), 1200–1205.
- Hayashi, F., Matsumoto, Y., Momoki, C., Yuikawa, M., Okada, G., Hamakawa, E., ... Kobayashi, S. (2013). Physical inactivity and insufficient dietary intake are associated with the frequency of sarcopenia in patients with compensated viral liver cirrhosis. *Hepatology Research*, 43(12), 1264–1275.
- Heisel, O., Heisel, R., Balshaw, R., & Keown, P. (2004). New onset diabetes mellitus in patients receiving calcineurin inhibitors: A systematic review and meta-analysis. *American Journal of Transplantation*, 4(4), 583–595.
- Hoorn, E. J., Walsh, S. B., McCormick, J. A., Fürstenberg, A., Yang, C. L., Roeschel, T., ... Unwin, R. J. (2011). The calcineurin inhibitor tacrolimus activates the renal sodium chloride cotransporter to cause hypertension. *Nature Medicine*, 17(10), 1304.
- Jonsen, E., Athlin, E., & Suhr, O. (1998). Familial amyloidotic patients' experience of the disease and of liver transplantation. *Journal of Advanced Nursing*, 27(1), 52–58.
- Kaido, T., Ogawa, K., Fujimoto, Y., Ogura, Y., Hata, K., Ito, T., ... Uemoto, S. (2013). Impact of sarcopenia on survival in patients undergoing living donor liver transplantation. *American Journal of Transplantation*, 13(6), 1549–1556.
- Kaido, T., Tamai, Y., Hamaguchi, Y., Okumura, S., Kobayashi, A., Shirai, H., ... Uemoto, S. (2017). Effects of pretransplant sarcopenia and sequential changes in sarcopenic parameters after living donor liver transplantation. *Nutrition*, 33, 195–198.
- Kallwitz, E. R., Loy, V., Mettu, P., Von Roenn, N., Berkes, J., & Cotler, S. J. (2013). Physical activity and metabolic syndrome in liver transplant recipients. *Liver Transplantation*, 19(10), 1125–1131.
- Kim, W. R., Lake, J. R., Smith, J. M., Schladt, D. P., Skeans, M. A., Noreen, S. M., ... Kasiske, B. L. (2019). OPTN/SRTR 2017 annual data report: liver. *American Journal of Transplantation*, 19, 184–283.
- Kotarska, K., Wunsch, E., Kempínska-Podhorodecka, A., Raszeja-Wyszomirska, J., Bogdanos, D. P., Wójcicki, M., & Milkiewicz, P. (2014). Factors affecting health-related quality of life and physical activity after liver transplantation for autoimmune and nonautoimmune liver diseases: A prospective, single Centre study. *Journal of Immunology Research*, 2014, 1–9.
- Kumahara, H., Schutz, Y., Ayabe, M., Yoshioka, M., Yoshitake, Y., Shindo, M., ... Tanaka, H. (2004). The use of uniaxial accelerometry for the assessment of physical-activity-related energy expenditure: A validation study against whole-body indirect calorimetry. *British Journal of Nutrition*, 91(2), 235–243.
- LaFleur, W. R. (2002). From agape to organs: religious difference between Japan and America in judging the ethics of the transplant. *Zygon*, 37(3), 623–642.
- Laryea, M., Watt, K. D., Molinari, M., Walsh, M. J., McAlister, V. C., Marotta, P. J., ... Peltekian, K. M. (2007). Metabolic syndrome in liver transplant recipients: Prevalence and association with major vascular events. *Liver Transplantation*, 13(8), 1109–1114.

- Magalhães, C., Garcia, P., Huygens, J., Viana, C. F., Flor, N., José, M., ... Eanes, D. (2018). Exercise capacity and respiratory profile in patients after orthopedic liver transplantation: A follow-up study. *Annals of Hepatology*, 17(1), 98–103.
- Masala, D., Mannocci, A., Unim, B., Del Cimmuto, A., Turchetta, F., Gatto, G., ... La Torre, G. (2012). Quality of life and physical activity in liver transplantation patients: Results of a case-control study in Italy. *Transplantation Proceedings*, 44(5), 1346–1350.
- Masuda, T., Shirabe, K., Ikegami, T., Harimoto, N., Yoshizumi, T., Soejima, Y., ... Maehara, Y. (2014). Sarcopenia is a prognostic factor in living donor liver transplantation. *Liver Transplantation*, 20(4), 401–407.
- McPhee, J. S., French, D. P., Jackson, D., Nazroo, J., Pendleton, N., & Degens, H. (2016). Physical activity in older age: Perspectives for healthy ageing and frailty. *Biogerontology*, 17(3), 567–580.
- Mendoza, T. R., Wang, X. S., Cleeland, C. S., Morrissey, M., Johnson, B. A., Wendt, J. K., & Huber, S. L. (1999). The rapid assessment of fatigue severity in cancer patients: Use of the brief fatigue inventory. *Cancer*, 85(5), 1186–1196.
- Mizuno, Y., Ito, S., Hattori, K., Nagaya, M., Inoue, T., Nishida, Y., ... Ogura, Y. (2016). Changes in muscle strength and six-minute walk distance before and after living donor liver transplantation. *Transplantation Proceedings*, 48(10), 3348–3355.
- Okuyama, T., Wang, X. S., Akechi, T., Mendoza, T. R., Hosaka, T., Cleeland, C. S., & Uchitomi, Y. (2003). Validation study of the Japanese version of the brief fatigue inventory. *Journal of Pain and Symptom Management*, 25(2), 106–117.
- Olthoff, K. M., Emond, J. C., Shearon, T. H., Everson, G., Baker, T. B., Fisher, R. A., ... Everhart, J. E. (2015). Liver regeneration after living donor transplantation: Adult-to-adult living donor liver transplantation cohort study. *Liver Transplantation*, 21(1), 79–88.
- Pedišić, Ž., & Bauman, A. (2015). Accelerometer-based measures in physical activity surveillance: Current practices and issues. *British Journal of Sports Medicine*, 49(4), 219–223.
- Rongies, W., Stepniewska, S., Lewandowska, M., Smolis-Bak, E., Dolecki, W., Sierdzinski, J., ... Stankiewicz, W. (2011). Physical activity long-term after liver transplantation yields better quality of life. *Annals of Transplantation*, 16(3), 126–131.
- Schalk, B. W., Deeg, D. J., Penninx, B. W., Bouter, L. M., & Visser, M. (2005). Serum albumin and muscle strength: A longitudinal study in older men and women. *Journal of the American Geriatrics Society*, 53(8), 1331–1338.
- Singh, S., & Watt, K. D. (2012). Long-term medical management of the liver transplant recipient: What the primary care physician needs to know. *Mayo Clinic Proceedings*, 87(8), 779–790.
- Togashi, J., Sugawara, Y., Akamatsu, N., Tamura, S., Yamashiki, N., Kaneko, J., ... Kokudo, N. (2013). Quality of life after adult living donor liver transplantation: A longitudinal prospective follow-up study. *Hepatology Research*, 43(10), 1052–1063.
- Togo, F., Watanabe, E., Park, H., Yasunaga, A., Park, S., Shephard, R. J., & Aoyagi, Y. (2008). How many days of pedometer use predict the annual activity of the elderly reliably? *Medicine and Science in Sports and Exercise*, 40(6), 1058–1064.
- Tudor-Locke, C., Johnson, W. D., & Katzmarzyk, P. T. (2009). Accelerometer-determined steps per day in adults. *Medicine & Science in Sports & Exercise*, 41(7), 1384–1391.
- Umeshita, K., Eguchi, S., Egawa, H., Haga, H., Kasahara, M., Kokudo, N., ... Uemoto, S. (2019). Liver transplantation in Japan: Registry by the Japanese liver transplantation society. *Hepatology Research*, 49(9), 964–980.
- Urano, E., Yamanaka-Okumura, H., Teramoto, A., Sugihara, K., Morine, Y., Imura, S., ... Takeda, E. (2014). Pre-and postoperative nutritional assessment and health-related quality of life in recipients of living donor liver transplantation. *Hepatology Research*, 44(11), 1102–1109.
- van den Berg-Emons, R., Kazemier, G., van Ginneken, B., Nieuwenhuijsen, C., Tilanus, H., & Stam, H. (2006). Fatigue, level of everyday physical activity and quality of life after liver transplantation. *Journal of Rehabilitation Medicine*, 38(2), 124–129.
- Wickerson, L., Mathur, S., Singer, L. G., & Brooks, D. (2015). Physical activity levels early after lung transplantation. *Physical Therapy*, 95(4), 517–525.
- Williams, F. R., Vallance, A., Faulkner, T., Towey, J., Durman, S., Kyte, D., ... Lord, J. M. (2019). Home-based exercise in patients awaiting liver transplantation: A feasibility study. *Liver Transplantation*, 25(7), 995–1006.
- World Health Organization. (2010). *Global recommendations on physical activity for health*, Switzerland: World Health Organization. Retrieved from <https://www.who.int/dietphysicalactivity/global-PA-recs-2010.pdf>.
- Yang, L. S., Shan, L. L., Saxena, A., & Morris, D. L. (2014). Liver transplantation: A systematic review of long-term quality of life. *Liver International*, 34(9), 1298–1313.
- Yeh, C., Chen, Y. J., Lai, L. Y., Jang, T. R., Chiang, J., Chen, Y. Y., & Hsieh, K. C. (2012). Bioelectrical impedance analysis in a mathematical model for estimating fat-free mass in multiple segments in elderly Taiwanese males. *International Journal of Gerontology*, 6(4), 273–277.
- Yoshimura, N., Okajima, H., Ushigome, H., Sakamoto, S., Fujiki, M., & Okamoto, M. (2010). Current status of organ transplantation in Japan and worldwide. *Surgery Today*, 40(6), 514–525.

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