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Frailty, Mortality, and Healthcare Utilization after Liver Transplantation: From the Multi-Center Functional Assessment in Liver Transplantation (FrAILT) Study

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Abstract

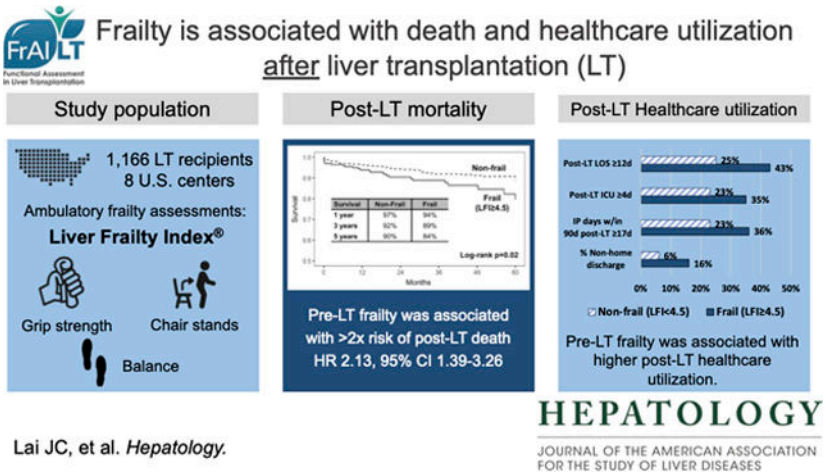
Background: Frailty is a well-established risk factor for poor outcomes in patients with cirrhosis awaiting liver transplantation (LT), but whether it predicts outcomes among those who have undergone LT is unknown.

Methods: Adults LT recipients from 8 U.S. centers (2012–2019) were included. Pre-LT frailty was assessed in the ambulatory clinic using the Liver Frailty Index (LFI). “Frail” was defined by an optimal cut point of LFI≥4.5. We used the 75%ile to define “prolonged” post-LT length of stay (LOS; ≥12d), intensive care unit (ICU; ≥4d) days, and inpatient days within 90 post-LT days (≥17d).

Results: Of 1,166 LT recipients, 21% were frail pre-LT. Cumulative incidence of death at 1- and 5-years was 6% and 16% for frail and 4% and 10% for non-frail patients (overall logrank p=0.02). Pre-LT frailty was associated with an unadjusted 62% increased risk of post-LT mortality (95% CI 1.08–2.44); after adjustment for body mass index, HCC, donor age, and DCD status, the HR was 2.13 (95% CI 1.39–3.26). Patients who were frail versus non-frail experienced a higher adjusted odds of prolonged LT LOS [odds ratio (OR) 2.00, 95% CI 1.47–2.73], ICU stay (OR 1.56, 95% CI 1.12–2.14), inpatient days within 90 post-LT days (OR 1.72, 95% 1.25–2.37), and non-home discharge (OR 2.50, 95% 1.58–3.97).

Conclusions: Compared to non-frail patients, frail LT recipients had a higher risk of post-LT death and greater post-LT healthcare utilization, although overall post-LT survival was acceptable. These data lay the foundation to investigate whether targeting pre-LT frailty will improve post-LT outcomes and reduce resource utilization.

Graphical Abstract



INTRODUCTION

Patients with cirrhosis often experience complications of portal hypertension, including ascites, hepatic encephalopathy, or bleeding gastroesophageal varices for which liver transplantation is an established and effective long-term therapy. But cirrhosis also leads to more insidious—but equally lethal—extra-hepatic effects of muscle wasting and physical deconditioning that have come to be termed “frailty” in the field of hepatology.[1] In contrast to the classic hallmarks of cirrhosis (e.g., jaundice, ascites), which normalize soon after receiving a new liver, these extra-hepatic manifestations may take months to reverse, if at all, potentially compromising both short-term and longer-term outcomes after liver transplantation.[2,3]

Liver transplant clinicians have long acknowledged the potential impact of frailty on outcomes after liver transplantation—1 in 10 transplant candidates are removed from the waitlist for becoming “too sick for transplant”, reflecting a clinician’s perception that the patient is too ill and/or too frail to survive or fully recover after transplant surgery.[4] Yet, despite the contribution of frailty considerations to this decision, there are little data on the actual impact of frailty on post-transplant outcomes. As a result, no objective criteria exist to guide this critical decision of who is too “frail” for transplant surgery—or whether such criteria exist at all. A precise understanding of how pre-transplant frailty impacts post-transplant outcomes is needed to facilitate systematic application of this construct to decision-making in liver transplantation.

In this study, we aimed to evaluate the association between pre-transplant frailty and post-transplant outcomes in a multi-center cohort of liver transplant recipients. We also examined the association between pre-transplant frailty and short-term post-transplant healthcare utilization. Given the association between frailty and adverse outcomes in surgical populations outside of liver transplantation,[5,6] we hypothesized that frailty would be associated with adverse outcomes and high healthcare utilization in patients with cirrhosis who have undergone liver transplantation.

METHODS

Study Population

Data were obtained from the Functional Assessment in Liver Transplantation (FrAILT) Study. Patients were eligible to enroll in the FrAILT Study if: 1) they had cirrhosis and were actively listed for liver transplantation at participating sites and 2) were evaluated in the ambulatory setting (as the frailty tool used in this study was developed for administration in the ambulatory setting), and 3) had a Model for End-Stage Liver Disease (MELD) score ≥12 at the time of enrollment (to enrich the cohort with patients who were more likely to undergo liver transplantation within one year of enrollment). Excluded were those with severe cognitive dysfunction at the time of study screening (given concerns about ability to provide signed informed consent) and those who did not speak English, Spanish, or Chinese (given availability of written consent forms in other languages).

For this specific analysis, data from FrAILT Study participants who underwent liver transplantation between June 2012 through December 2019 were analyzed. The final study cohort included participants from the following sites representing 5 of the 11 United Network for Organ Sharing regions in the United States: University of California, San Francisco (n=727), Johns Hopkins Medical Institute (n=86), Baylor University Medical Center (n=101), Columbia University Medical Center (n=71), University of Pittsburgh (n=51), Duke University (n=69), Northwestern (n=44), and Loma Linda University (n=17).

Study Procedures

All participants underwent the following physical assessments:

1. Grip strength: the average of three trials, measured in the participant's dominant hand using a hand dynamometer;
2. Timed chair stands: measured as the number of seconds it takes to do five chair stands with the participant's arms folded across the chest;
3. Balance testing: measured as the number of seconds that the participant can balance in three positions (feet placed side-to-side, semi-tandem, and tandem) for a maximum of 10 seconds each.

These three tests were administered by trained study personnel. The Liver Frailty Index was calculated from these three tests using the calculator available at: http://liverfrailtyindex.ucsf.edu. Natural differences in grip strength by sex are adjusted for in this calcuation.[7] This index was developed specifically for patients with cirrhosis in the ambulatory setting.[7] The Liver Frailty Index is a continuous metric where a higher number indicates a greater degree of physical functional impairment.

These three tests were administered at enrollment. Because the timing of liver transplantation is unpredictable, patients underwent frailty assessments as part of this study at every clinic visit to capture the ambulatory assessment closest to transplant. The timing of the clinic visit was determined by the patient's hepatologist, independent of study participation.

Demographic, clinical, and laboratory data were extracted from the clinic visit note written on the same day as the frailty assessment. Laboratory tests to calculate the Model for End-Stage Liver Disease-Sodium (MELDNa) score were drawn as part of standard-of-care to maintain active national listing status. The presence of ascites or hepatic encephalopathy were recorded if reported by the hepatologist's clinic visit note and categorized as present or absent. We have previously reported that different definitions/categorizations of ascites and hepatic encephalopathy in our cohort did not change the primary association between frailty and mortality in our cohort.[8] Other transplant [e.g., simultaneous liver-kidney transplantation (SLK)] and donor variables [e.g., living donor (LDLT), age, and donation after cardiac death (DCD)] were also obtained from the electronic health record.

Study outcomes

The primary outcome was death after liver transplantation. Secondary outcomes were the following metrics of healthcare utilization: 1) post-transplant length of stay (LOS) in days, defined as the time from the date of liver transplant to hospital discharge, 2) post-transplant intensive care unit (ICU) days, defined as the number of days spent in the ICU during the post-transplant hospitalizations, 3) number of days housed in an acute care facility within 90 days of liver transplantation, and 4) non-home discharge, inclusive of skilled nursing, long-term care, or acute rehabilitation facilities. To facilitate clinical interpretation, the 75th percentile value for our cohort was selected as cut-points for post-transplant LOS (≥12 days), post-transplant ICU days (≥4 days), and hospitalized days within 90 days of transplant (≥17 days).

Statistical Analysis

The primary predictor was frailty, as measured by the Liver Frailty Index at a study visit closest to liver transplantation. We performed a time-to-event analysis on our study cohort and identified an optimal cut point for predicting the primary outcome within 5 years by maximizing a concordance probability.[9] The primary outcome was the time from liver transplant to death; time to death was censored at the last follow up date for those who were still alive as of March 24, 2020 or on the date of retransplantation for patients who underwent retransplantation.

Baseline characteristics were reported as medians [interquartile ranges (IQR)] or percentages and compared by frailty status using Wilcoxon rank-sum or chi-square tests for continuous and categorical variables, respectively. For the primary outcome of death, we first used univariable Cox proportional hazards regression to evaluate associations between individual variables and post-transplant death. A subset of variables was selected based on clinical judgment and associations from unadjusted analyses with $p<0.10$. These variables were included in a multivariable Cox model, and covariates not attaining significance at the 0.05 level were sequentially eliminated until all covariates were significantly associated with the outcome with $p<0.05$ in the final model. This model was also confirmed using the best subset selection method with Akaike information criterion (AIC). Clinically relevant interactions between frailty and the following co-variables were tested: recipient age, laboratory MELDNa, body mass index (BMI), donor age, DCD, and hepatocellular carcinoma (HCC)—all of which were not significant. For the secondary outcomes, we

used logistic regression. For continuous outcomes, we assessed the odds of reaching the 75th percentile cut-off by frailty status. To quantify the association between pre-transplant frailty and post-transplant healthcare utilization, logistic regression was performed, adjusted for laboratory MELDNa at transplant and DCD status, two factors that are known to be associated with increased healthcare utilization.[10–13]

Several sensitivity analyses were performed. A sensitivity analysis of the primary outcome model was performed, replacing last frailty index closest to the date of liver transplantation with baseline frailty index. A second sensitivity analysis was conducted using center-stratification while controlling for the same set of confounders in the primary multivariable analysis. Lastly, we re-ran the multivariable model stratified by HCC. The stratified-model approach allowed separate baseline hazard functions to be fitted within different strata while including all patients within the analysis to maintain sample size.

Statistical analyses were performed using SAS (v9.4, Cary, NC) and Stata (v16, College Station, TX). The Institutional Review Board at each participating site approved this study.

RESULTS

Patient characteristics

A total of 1,166 liver transplant recipients were included. Baseline characteristics of the entire cohort are displayed in Table 1. Median age was 60 years, 33% were female, and 66% were non-Hispanic white, 36% had chronic hepatitis C as their etiology of cirrhosis, and 43% had hepatocellular carcinoma (HCC). Median laboratory MELDNa at frailty assessment was 18 and at the time of transplant was 22; 37% had ascites and 54% had hepatic encephalopathy. With respect to transplant characteristics, 7% underwent SLK and 18% underwent LDLT. Median donor age was 42 years and 11% received a DCD liver.

Median Liver Frailty Index was 3.87 (IQR 3.34–4.38); 250 (21%) met criteria for “frail” as defined by a Liver Frailty Index ≥4.5. Median Liver Frailty Index was 4.96 (IQR 4.71–5.43) among those who were frail and 3.68 (IQR 3.21–4.02) among those who were non-frail. The median time from frailty assessment to liver transplantation was 1.7 months (IQR 0.8–3.8) in those who were frail and 2.8 months (IQR 1.3–5.7) in those who were non-frail [$p<0.001$]. Baseline characteristics by frailty status are displayed in Table 1. Patients who were frail versus non-frail were similar in age, height, and body mass index, but differed by percentage of women (40 vs. 31%), of Non-Hispanic White (73 vs. 64%), with chronic HCV (28 vs. 38%) or NAFLD (28 vs. 17%), and with HCC (27 vs. 47%). Compared to non-frail patients, patients who were frail differed by laboratory MELDNa (21 vs. 17), serum albumin (2.9 vs. 3.1 g/dL), and the proportion with ascites (60 vs. 30%) and hepatic encephalopathy (68 vs. 50%) at the time of frailty assessment, as well as laboratory MELDNa at transplant (26 vs. 21). A higher proportion of frail versus non-frail patients underwent SLK (12 vs. 6%; $p<0.001$). Median donor age was 44.5 years in the frail group and 41.0 years in the non-frail group and the proportion of DCD transplants was 14% for the frail group and 10% in the non-frail group; both comparisons were not statistically significant between frail and non-frail patients.

Associations between pre-transplant frailty and post-transplant mortality

Patients were followed for a median of 36 months (IQR 22–56). By the end of follow-up, 110 (9%) patients died: 33 / 250 (13%) of frail patients and 77 / 916 (8%) of non-frail patients. The rate of death during transplant hospitalization did not differ significantly between the frail [8/248 (3.2%)] and non-frail [16/901 (1.8%)] patient groups (p=0.16). Overall survival differed between the frail and non-frail groups (log-rank p=0.02) [Figure 1]. Survival rates were lower for frail versus non-frail recipients: 94% versus 97% at 1 year, 89% versus 92% at 3 years, and 84% versus 90% at 5 years.

In univariable analysis, patients who were frail pre-transplant had a 62% increased risk of post-transplant mortality (HR 1.62, 95% CI, 1.08–2.44; p=0.02). The only other variables that were associated with post-transplant mortality in univariable analysis with a p-value <0.10 were: diabetes mellitus, coronary artery disease, BMI, total bilirubin, HCC, donor DCD, and donor age (Table 2). Laboratory MELDNa at transplant was not significantly associated with post-LT mortality (HR 0.98; 95% CI 0.96–1.01) but was evaluated for inclusion in the multi-variable model given its clinical significance. The time from last frailty assessment to transplant was not significantly associated with post-transplant mortality (HR 1.03 per month; 95% CI 1.00–1.06; p=0.05) nor was the term for the interaction between last frailty assessment and LFI (p for the interaction term=0.36). In the final multivariable model, after adjustment for BMI, HCC, donor DCD, and donor age, pre-transplant frailty remained significantly associated with post-transplant mortality (HR 2.13; 95% CI 1.39–3.26; p<0.001) [Table 2]. To control for potential center effects, we performed a sensitivity analysis using center stratification by all 8 sites while adjusting for the same confounders at in the primary multivariable analysis; this yielded similar associations between frailty and post-transplant mortality (HR 2.11, 95% CI 1.36–3.28; p<0.001).

We performed a sensitivity analysis in which the last pre-transplant frailty measurement was replaced with the baseline frailty measurement, which was assessed at a median of 6.9 months (IQR 2.8–13.4) prior to transplant. In this sensitivity analysis adjusted for the same confounders as the primary analysis, baseline frailty remained significantly associated with post-transplant mortality (HR 2.19, 95% CI 1.41–3.42, p<0.001). Again, the interaction term between baseline frailty and the time from baseline frailty assessment was not statistically significant (p=0.62). Lastly, in a sensitivity analysis of the final multivariable model stratified by HCC, frailty remained significantly associated with post-transplant mortality (HR 2.15; 95% CI 1.40–3.30; p<0.001).

Associations between pre-transplant frailty and metrics of healthcare utilization

Patients who were frail experienced higher healthcare utilization than those who were not frail. Specifically, the proportion of patients who had experienced prolonged post-transplant LOS (≥12 days), prolonged ICU stay (≥4 days), high number of hospitalized days within 90 days of transplant (≥17 days), and non-home discharge were significantly higher in those who were frail than those who were not (p<0.001 for each; Table 3). In logistic regression adjusted for laboratory MELDNa and DCD livers, pre-transplant frailty was significantly associated with an increased odds of prolonged post-transplant LOS (OR 2.00, 95% CI

1.47–2.73), prolonged ICU days (OR 1.56, 95% CI 1.12–2.14), hospitalized days within 90 days of transplant (OR 1.72, 95% CI 1.25–2.37), and non-home discharge (OR 2.50, 95% CI 1.58–3.97) [Table 3].

DISCUSSION

Over the last decade, frailty has emerged as a key construct in the evaluation of patients with end-stage liver disease, capturing the combined effects of cirrhosis-related complications and non-hepatic co-morbidities.[8] Multiple studies have demonstrated strong and consistent associations between frailty and adverse health outcomes in patients with cirrhosis both pre- and post-transplant. Tools to assess frailty have been shown to enhance prognostication of mortality above and beyond traditional metrics of mortality risk prediction based on liver disease severity alone.[1] What has been lacking, however, is a precise understanding of how pre-transplant frailty impacts outcomes *after* liver transplantation. Given that the most definitive therapy for end-stage liver disease is liver transplantation, such data are critical to the application of frailty to decision-making for this population.

Using data from the multi-center FrAILT Study, the largest research network dedicated to studying frailty in patients with cirrhosis awaiting liver transplantation, we observed a strong association between pre-transplant frailty and mortality after liver transplantation. Patients who met criteria for “frail” in the ambulatory setting prior to transplant, defined by a Liver Frailty Index ≥4.5, experienced a significantly higher risk of death after transplant compared to patients who were not frail. Pre-transplant frailty was also associated with higher short-term post-transplant healthcare utilization including prolonged length of stay, ICU days, total hospitalized days within 90 days of liver transplantation, and a higher rate of non-home discharge, all of which are known to be associated with higher financial burden of costs on the healthcare system.

We highlight some nuances to the interpretation of our findings. While the magnitude of the association of pre-transplant frailty on post-transplant mortality was two-fold, the aggregate 5-year survival rate among frail patients in our cohort was 84%, above the national average of 79%.[14] This likely reflects the fact that patients were only eligible to enroll in our cohort if they were seen for evaluation in the ambulatory setting and therefore had the benefit of preparation for liver transplantation, as opposed to patients with acute decompensation who must undergo urgent evaluation in the acutely-ill setting (which can often result in a rushed evaluation not capturing the full extent of co-morbid illness). This also explains the relatively high proportion of patients in our cohort who had hepatocellular carcinoma. None of our centers used *standardized or specific* frailty cut-points as part of their criteria for liver transplantation; the fact that the proportion of frail patients who underwent liver transplantation (21%) is similar to the proportion of frail patients awaiting liver transplantation at our centers (25%) is evidence of this.[8] Moreover, transplant clinicians tend to select patients for liver transplantation whom they believe will recover well from transplant, so there is bias against transplanting patients who are determined to be “unsuitable” for transplant surgery, including those who are frail or sarcopenic by the eyeball test.[15] In light of this selection bias, it is all the more remarkable that the frail patients who “made the cut” experienced a 2-fold increased risk of death

compared to non-frail recipients. In addition, while frailty may have been associated with only a relatively modest reduction in post-transplant survival, it was associated with higher healthcare utilization, likely translating into substantially increased costs per liver transplant.

Also worth highlighting are the results from our sensitivity analyses evaluating the association between *baseline* pre-transplant frailty and post-transplant mortality. This analysis yielded a hazard ratio that was similar to the hazard ratio associated with the frailty assessment at the time point closest to transplant. This suggests that meeting the threshold for "frail" at any time point—as opposed to only when one is getting close to the top of the transplant list—may compromise post-transplant outcomes and therefore may have potential implications for transplant decision-making. We did not, however, observe a significant association between the time from frailty assessment to transplant in adjusted analysis. These findings support the original frailty construct developed in the field of geriatrics and defined as a state of decreased physiologic reserve and increased vulnerability to health stressors.[16] The very presence of frailty suggests more chronic and systemic perturbations such as loss of musculoskeletal integrity, systemic inflammation, and immune dysregulation, which may essentially become "imprinted" on patients or take so long to resolve after liver transplantation that they compromise post-transplant outcomes before resolution. This raises the question of whether there might be a threshold along the frailty spectrum—perhaps at a cut-point prior to becoming frail—when a patient should be referred for intensive intervention (e.g., nutritional support, physical therapy) to prevent progression of frailty or, more provocatively, when a patient would benefit from *acceleration of the timing of* liver transplantation—such as through living donor liver transplantation, acceptance of extended criteria donor livers or livers from donors who meet risk criteria for infection transmission—specifically to prevent this phenomenon.

We acknowledge the following limitations to our study. While a strength of our study lies in the inclusion of patients from 8 U.S. liver transplant centers following a standardized protocol for frailty assessment, 68% of the patients were enrolled at a single center that comprised 75% of the primary events. However, a sensitivity analysis that accounted for potential center effects (i.e., center stratification) yielded results that were consistent with the main study findings in magnitude and direction of effect. Enrollment at each site was based on study coordinator availability—not on patient characteristics—so we believe that the risk of selection bias based on non-consecutive enrollment at each site is low. Because the Liver Frailty Index was developed and validated in the ambulatory setting, we only assessed frailty in liver transplant candidates who were seen in the ambulatory setting, as evidenced by their median MELDNa of 15 at the time of assessment. Therefore, our findings are not generalizable to patients evaluated in the inpatient setting and should not be applied to transplant decision-making among those who are acutely ill. Lastly, approximately 40% of our cohort had chronic HCV as their etiology of liver disease, a sub-group that will decrease in the future due to effective HCV eradication. However, we did not observe an interaction between disease etiology and frailty on the association between frailty and mortality, so we believe that our results will remain generalizable to all liver transplant recipients in the future.

Despite these limitations, our multi-center study advances the community's understanding of frailty as a risk factor for adverse outcomes along the spectrum of management options for patients with end-stage liver disease. Frailty is associated with mortality and health care utilization after liver transplantation, a finding that has not yet been described in as large a cohort or with an objective frailty metric that can be feasibly measured in clinical transplant practice. However, given the overall acceptable post-transplant survival in our study, it is important to note that frailty should not be used as the sole criterion to deny a patient liver transplantation. Rather, our results should be viewed as an opportunity for alternative strategies to optimize outcomes for frail patients. Options for early liver transplantation already exist for some—either through living donor liver transplantation, accepting higher risk donor livers, or seeking liver transplantation at a center with a lower transplant MELDNa score. However, the decision to pursue these options is often difficult to accept as compared to standard deceased donor liver transplantation at one's local transplant center. Our findings offer transplant clinicians and patients information to guide discussions regarding the risks and benefits of waiting versus seeking a potentially less optimal transplant option to improve outcomes after liver transplantation. Another consideration for the community to consider is how frailty might be considered within a national liver allocation system, if at all. Whether therapeutics or comprehensive pre-habilitation programs to improve—or even prevent—frailty before liver transplantation will lead to better outcomes in frail liver transplant recipients remains to be seen, but our data lay the foundation for these essential next steps in the field.

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List of abbreviations:

DCD	donation after cardiac death
HR	hazard ratio
IQR	interquartile range
LFI	liver frailty index
LOS	length of stay
LT	liver transplantation
MELD	model for end-stage liver disease

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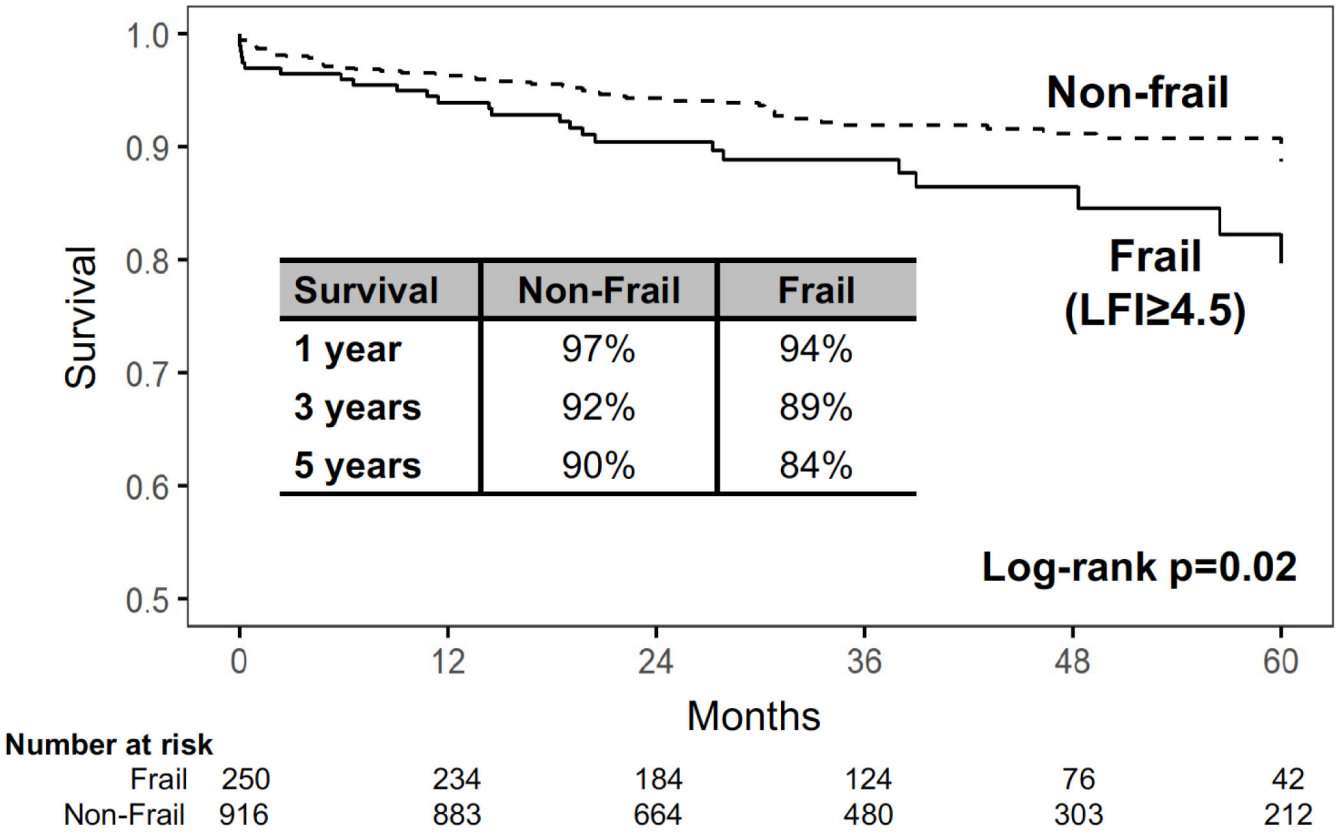

Figure 1.
Kaplan-Meier survival curves of 1,166 liver transplant recipients by frailty.

Table 1.

Characteristics of the 1,166 patients categorized by frailty

Characteristics*		All n=1,166 100%	Frailty Index Categories		p-value
			Frail (≥4.5) n=250 21%	Non-frail (<4.5) n=916 79%	
Age, years		60 (53–64)	59 (53–64)	60 (53–65)	0.505
Female, n (%)		386 (33%)	100 (40%)	286 (31%)	0.009
Race/Ethnicity	**Non-Hispanic White**	66%	73%	64%	0.009
	Black	6%	5%	6%	
	Hispanic White	18%	16%	19%	
	Asian/Pacific Islander	8%	4%	9%	
	Other	2%	2%	2%	
Height, cm		173 (164–180)	172 (162–180)	173 (165–180)	0.178
Body mass index, kg/m^2		28 (25–32)	28 (26–33)	28 (25–32)	0.050
Etiology of liver disease	**Chronic hepatitis C**	36%	28%	38%	<0.001
	Alcohol	20%	22%	19%	
	Non-alcoholic fatty liver disease	19%	28%	17%	
	Cholestatic	12%	10%	13%	
	Other	13%	12%	14%	
Hepatocellular carcinoma		43%	27%	47%	<0.001
Laboratory MELDNa at assessment		18 (12–23)	21 (17–26)	17 (12–21)	<0.001
Laboratory MELDNa at transplant		22 (16–29)	26 (18–31)	21 (15–27)	<0.001
Last LFI (pre-transplant)		3.9 (3.3–4.4)	5.0 (4.7–5.4)	3.7 (3.2–4.0)	<0.001
Albumin, g/dL		3.1 (2.6–3.5)	2.9 (2.6–3.3)	3.1 (2.6–3.6)	<0.001
Ascites		37%	60%	30%	<0.001
Hepatic encephalopathy		54%	68%	50%	<0.001
Donor and transplant characteristics					
SLK		7%	12%	6%	<0.001
LDLT		18%	15%	18%	0.210
Donor age, years		42 (29–54)	45 (30–54)	41 (29–54)	0.297
DCD		11%	14%	10%	0.093

*Median (IQR) or n (%); Mann-Whitney or chi-square tests

Table 2.

Univariable and multivariable associations between variables and post-transplant mortality using Cox regression.

	Hazard ratio (95% Confidence Interval) p-value	
Factor	**Univariable**	**Multivariable**
Frail (LFI ≥4.5)	1.62 (1.08–2.44) p=0.02	2.13 (1.39–3.26) p<0.001
DM	1.48 (1.01–2.18) p=0.05	--
CAD	1.89 (1.04–3.44) p=0.04	--
BMI	0.96 (0.93–1.00) p=0.05	0.95 (0.92–0.99) p=0.02
HCC	1.43 (0.98–2.07) p=0.06	1.55 (1.04–2.31) p=0.03
Donor DCD	1.71 (1.00–2.92) p=0.05	1.98 (1.14–3.43) p=0.01
Donor age, per year	1.01 (1.00–1.03) p=0.05	1.02 (1.00–1.03) p=0.02
Laboratory MELDNa at transplant	0.98 (0.96–1.01) p=0.13	--

Table 3.

Metrics of post-transplant healthcare utilization, by frailty status.

Metric of healthcare utilization*	Frailty Index Categories		p-value	Adjusted† Odds Ratios (95% CI) for frailty p-value
	Frail (≥4.5) n=250 21%	Non-frail (<4.5) n=916 79%		
Total post-transplant LOS ≥ 12 days	105 (42.5)	223 (24.8)	<0.001	2.00 (1.47–2.73) <0.001
Total post-transplant ICU days ≥ 4 days	87 (35.4)	203 (22.8)	<0.001	1.56 (1.12–2.14) 0.01
Hospitalized days within 90 days of transplant ≥ 17 days	88 (35.6)	208 (23.1)	<0.001	1.72 (1.25–2.37) <0.001
Non-home discharge, n (%)	40 (16.1)	53 (5.9)	<0.001	2.50 (1.58–3.97) <0.001

*n (%)

†Adjusted for MELDNa at transplant and DCD status.