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Authors
Carey, Elizabeth J
Lai, Jennifer C
Wang, Connie W
et al.

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A Multicenter Study to Define Sarcopenia in Patients With End-Stage Liver Disease

Elizabeth J. Carey[1,*], **Jennifer C. Lai**[2,*], **Connie W. Wang**[3], **Srinivasan Dasarathy**[5], **Iryna Lobach**[4], **Aldo J. Montano-Loza**[6], **Michael A. Dunn**[7], and **for the Fitness, Life Enhancement, and Exercise in Liver Transplantation Consortium**

[1]Division of Gastroenterology and Hepatology, Mayo Clinic in Arizona, Phoenix, AZ

[2]Division of Gastroenterology and Hepatology, University of California, San Francisco, San Francisco, CA

[3]Division of Internal Medicine, University of California, San Francisco, San Francisco, CA

[4]Division of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA

[5]Division of Gastroenterology and Hepatology, Cleveland Clinic, Cleveland, OH

[6]Division of Gastroenterology, University of Alberta, Edmonton, Alberta, Canada

[7]Center for Liver Diseases, Liver Research Center, Thomas E. Starzl Transplantation Institute, University of Pittsburgh, Pittsburgh, PA

Abstract

Sarcopenia is associated with increased wait-list mortality, but a standard definition is lacking. In this retrospective study, we sought to determine the optimal definition of sarcopenia in end-stage liver disease (ESLD) patients awaiting liver transplantation (LT). Included were 396 patients newly listed for LT in 2012 at 5 North American transplant centers. All computed tomography scans were read by 2 individuals with interobserver correlation of 98%. Using image analysis software, the total cross-sectional area (cm^2) of abdominal skeletal muscle at the third lumbar vertebra was measured. The skeletal muscle index (SMI), which normalizes muscle area to patient height, was then calculated. The primary outcome was wait-list mortality, defined as death on the waiting list or removal from the waiting list for reasons of clinical deterioration. Sex-specific potential cutoff values to define sarcopenia were determined with a grid search guided by log-rank test statistics. Optimal search methods identified potential cutoffs to detect survival differences between groups. The overall median SMI was 47.6 cm^2/m^2: 50.0 in men and 42.0 in women. At a median of 8.8 months follow-up, mortality was 25% in men and 36% in women. Patients who died had lower SMI than those who survived (45.6 versus 48.5 cm^2/m^2; $P < 0.001$), and SMI was associated with wait-list mortality (hazard ratio, 0.95; $P < 0.001$). Optimal search method yielded SMI cutoffs of 50 cm^2/m^2 for men and 39 cm^2/m^2 for women; these cutoff values best combined

Address reprint requests to Elizabeth J. Carey, M.D., Division of Gastroenterology and Hepatology, Mayo Clinic in Arizona, 5779 East Mayo Boulevard, Phoenix, AZ 85054. Telephone: 480-342-2000; FAX: 480-342-1569; carey.elizabeth@mayo.edu.

*These authors contributed equally to the work.

Jennifer C. Lai consults for Third Rock Venturas, LLC.

statistical significance with a sufficient number of events to detect survival differences between groups. In conclusion, we recommend that an SMI < 50 cm^2/m^2 for men and < 39 cm^2/m^2 for women be used to define sarcopenia in patients with ESLD awaiting LT.

Sarcopenia, a term referring to loss of muscle mass, is recognized to be a highly prevalent and life-threatening complication of cirrhosis. Sarcopenia in liver transplantation (LT) candidates is associated with increased wait-list mortality[1–4] and sepsis-related death on the waiting list.[3] Posttransplant outcomes associated with sarcopenia include prolonged hospital and intensive care unit stay, increased risk of infection,[5] and post-LT mortality.[6–11]

Although multiple studies have reported an association between muscle mass and outcomes in LT candidates, no consistent definition of sarcopenia in this population exists. Muscle mass is most often measured on cross-sectional imaging, either by computed tomography (CT) or magnetic resonance imaging (MRI), quantified by body segmentation analysis software (eg, ImageJ, sliceOmatic). Heterogeneity in the literature exists with respect to site of measurements (third or fourth lumbar vertebra) and abdominal muscles measured (psoas versus total abdominal wall). However, most investigators have used the upper level of the third lumbar vertebra (L3) to quantify total abdominal muscle area.[12] Therefore, we sought to determine optimal cutoffs of skeletal muscle index (SMI) to define sarcopenia in patients with end-stage liver disease (ESLD) awaiting LT.

Patients and Methods

PATIENTS

This retrospective multicenter study across 5 academic transplant centers in North America included 396 adult patients with ESLD awaiting LT from 5 transplant centers:

1. University of California, San Francisco (n = 144)
2. University of Pittsburgh (n = 83)
3. University of Alberta (n = 81)
4. Mayo Clinic in Arizona (n = 53)
5. Cleveland Clinic (n = 35)

All adult (≥18 years) patients from each center who were newly listed for LT from January 1 through December 31, 2012 were included, provided they had an abdominal CT scan capturing L3 within 3 months of listing. All centers have a standardized protocol of obtaining a CT scan of the abdomen at the time of evaluation for LT. However, individual imaging decisions are made at the discretion of the clinician. Some patients did not undergo CT scanning for clinical reasons, primarily for concern of kidney injury. The proportion of patients included from each site ranged from 49% to 80%. Each site has comparable acceptance criteria for transplantation but regional differences in access to donor organs exist.

The study protocol was approved a priori by the institutional review board at each center prior to data collection. Deidentified images and clinical data were shared under the terms of a 5-center data use agreement. Each center is a member of the Fitness, Life Enhancement, and Exercise in Transplant Consortium, whose longterm goals are to define the natural course of and relationship between muscle loss, frailty, functional status, and outcomes in LT.

Patient demographic and outcome data were abstracted from the electronic medical record at each site. Variables recorded included age, sex, race, etiology of liver disease, presence of hepatocellular carcinoma (HCC), height, weight, total bilirubin, international normalized ratio (INR), creatinine, and hemodialysis. Patient outcomes were categorized as follows: death on the waiting list or removal from the waiting list for clinical deterioration, deceased donor liver transplant, removal from the waiting list for reasons other than clinical deterioration, or remained on the waiting list at the end of the follow-up period. Ascites and hepatic encephalopathy were ascertained through manual chart review of the progress note at the time of listing.

MEASUREMENT OF MUSCLE MASS

The CT images were read by 2 individuals with an interobserver correlation of 98%. Each reader was blinded to patient outcome. One investigator (A.M.L.) measured muscle mass using the image analysis software application sliceOmatic (TomoVision, Montreal, Canada) and the other (C.W.W.) used Advantage Windows 2.2 Volume Viewer (GE Healthcare, Waukesha, WI). Skeletal muscle area was quantified as follows: first, an individual section on each CT scan was identified at the superior aspect of the L3 vertebral level. In this section, the areas of the psoas, paraspinal, and abdominal wall (including rectus abdominis, transverse abdominis, and internal and external oblique) muscles at L3 were outlined. Houndsfield unit (HU) range included −29 to + 150 HU. The cross-sectional area of these muscles was semiautomatically measured, yielding the total cross-sectional area (cm^2) of the abdominal skeletal muscles at L3. The L3 skeletal muscle area was then normalized to height to calculate the SMI: SMI (cm^2/m^2) = (total abdominal skeletal muscle area in cm^2)/(height in m^2).

This technique was chosen based on previous validation against dual X-ray absorptiometry,[13–15] its use in the oncology literature,[16,17] and its predominance in the transplant literature.[4,18–20]

STATISTICAL ANALYSIS

Statistical analysis was performed with Stata, version 14.1 (StataCorp, College Station, TX). The primary outcome was wait-list mortality, defined as death prior to LT or delisting for clinical deterioration. Patients were censored at the time of transplant or when removed from the waiting list for other reasons (eg, substance abuse, transfer to another center). Patients were observed until censoring, death, or end of the study period.

Measures were described using absolute frequency and percentage or median and interquartile range (IQR). Comparisons between groups were made with chi-square and Kruskal-Wallis tests. Associations between SMI and mortality were assessed using

competing risks regression with liver transplant as the competing risk. Potential predictors of SMI, such as age, sex, race, etiology of liver disease, body mass index (BMI), Model for End-Stage Liver Disease (MELD) score, ascites, and hepatic encephalopathy were included. Variables showing significance in univariate analysis were entered into a stepwise backward regression model. Survival tendency was estimated with the Kaplan-Meier survival method.

A threshold value in SMI was estimated based on a grid search guided by the log-rank test statistics that identified values of SMI that separate patients into 2 groups according to their survival.[21] Given the known baseline differences in SMI between men and women,[4,8,11] the search was stratified by sex. This search yielded several candidate SMI cutoff values for men and women that were associated with significant *P* values, defined as $P < 0.05$. We defined the sex-specific SMI cutoff values as "optimal" based on a combination of maximizing power to detect differences between the groups and a significant *P* value < 0.05. For example, the grid-search method yielded strong associations between SMI and wait-list mortality for men at multiple SMI values > 49 cm^2/m^2. However, with increasing SMI values, there were very few deaths in the nonsarcopenic categories (eg, only 8 total with SMI > 55 cm^2/m^2). The final SMI cutoff value that we selected for men was not only statistically significant with a *P* value of < 0.05 but minimized the risk of type 1 statistical error.

Results

FEATURES OF PATIENTS WITH ESLD

This multicenter study included 396 patients from 5 transplant centers. The median age of the patients was 58 years, 70% of patients were male, and the median calculated MELD score was 15. The majority of patients were non-Hispanic Whites (71%), and significant racial diversity was present with 11% Hispanic, 8% Asian, and 5% black patients. The median BMI was 27.2 kg/m^2 (IQR, 23.9–31.1 kg/m^2) and was similar in men and women. Thirty-nine percent of patients had HCC (Table 1). The most common (68%) reason for removal from the waiting list was that the patient was deemed too sick for transplant (sepsis, multisystem organ failure, too frail). Metastatic HCC accounted for 21% of patients who were removed from the waiting list. Eleven percent were removed for other reasons (cholangiocarcinoma, substance abuse, patient preference, etc).

ASSOCIATION BETWEEN SMI, SEX, ETHNICITY, AND MORTALITY

The overall median (IQR) SMI was 47.6 cm^2/m^2 (41.8–53.6 cm^2/m^2) and was significantly higher in men than in women: 50.0 (44.2–55.2) cm^2/m^2 versus 42.0 (36.1–46.7) cm^2/m^2, respectively ($P < 0.001$). Median (IQR) SMI by race was as follows: 47.6 (41.6–53.5) cm^2/m^2 for non-Hispanic whites, 47.9 (41.3–54.1) cm^2/m^2 for Hispanic whites, 47.6 (43.4–55.9) cm^2/m^2 for blacks, 45.8 (40.5–51.8) cm^2/m^2 for Asians, and 49.0 (44.7–54.3) cm^2/m^2 for all other races ($P = 0.80$). At a median of 8.8 months (3.0–21.7 months) of follow-up, 112 (28%) patients experienced wait-list mortality. Half of the patients received a deceased donor LT, 7% were removed from the waiting list for nonclinical reasons, and 15% were censored.

Patients who died or were delisted had significantly lower SMI than those who survived (45.6 versus 48.5 cm^2/m^2; $P < 0.001$). This relationship held when broken down by sex (Table 2). In univariate analysis, SMI was strongly associated with wait-list mortality (hazard ratio [HR], 0.95; $P < 0.001$). Factors reaching significance in univariate analysis included black race, presence of HCC, and weight. The association of SMI with mortality remained significant (HR, 0.95; $P < 0.001$) in multivariate analysis after adjustment for black race and HCC (Table 3).

OPTIMAL CUTOFF VALUES FOR SARCOPENIA IN ESLD

Our search for optimal SMI cutoffs associated with wait-list mortality started by evaluating the relationship between wait-list mortality and each individual potential SMI cutoff. For men, the SMI range of 49–55 cm^2/m^2 demonstrated high statistical significance, and the tight clustering supports that the optimal SMI is located within this range. For women, a similar clustering was found between SMI values of 33–40 cm^2/m^2 (Fig. 1). Next, each potential SMI cutoff was evaluated with respect to maximizing statistical significance balanced with a sufficient number of events to detect a survival difference between groups. SMI cutoffs of 50 cm^2/m^2 for men and 39 cm^2/m^2 for women emerged as the optimal values (Table 4).

Of 277 men, 139 (50%) were sarcopenic with SMI < 50 cm^2/m^2; this group had a 70% increased risk of wait-list mortality in competing risks analysis (95% confidence interval [CI], 5%–274%; $P = 0.03$). Of 119 women, 39 (33%) were sarcopenic with SMI < 39 cm^2/m^2; these women had 182% increased risk of wait-list mortality (95% CI, 151%–499%; $P = 0.001$). Unadjusted Kaplan-Meier survival curves for both men and women, with sarcopenia as defined by our optimal sex-specific SMI cutoffs, are shown in Fig. 2.

Compared with those without sarcopenia, patients with cirrhosis with sarcopenia (defined as SMI<50 cm^2/m^2 for men and 39 cm^2/m^2 for women) were similar in terms of age, race, etiology of liver disease, serum albumin, and presence of hepatic encephalopathy (Table 5). Compared with the nonsarcopenic group, patients with sarcopenia were more likely to be male, to have ascites, a higher MELD score, higher height, and the need for hemodialysis. Sarcopenic patients had a lower BMI and were less likely than the nonsarcopenic group to have HCC.

SEX DISPARITY IN ESLD

A number of differences were noted between sexes in the population of patients in this study. Compared with men, women were less likely to have hepatitis C virus (HCV) or HCC, had lower creatinine values, and were more likely to have ascites (Table 1). Height and weight were lower in women than in men, but there was no sex difference in BMI. There were no sex differences in MELD score, dialysis, age, or overall outcome at 6 months (Table 1). In univariate competing risks regression, female versus male sex was associated with a 55% increased risk of wait-list mortality (Table 3). Adjustment for SMI completely mitigated this sex disparity (female sex, HR, 1.11; 95% CI, 0.74–1.67; $P = 0.60$), which did not change with adjustment for MELD and black race. Rates of death were significantly higher among sarcopenic women (56%) as compared with nonsarcopenic women (26%).

Discussion

Sarcopenia is recognized as a potentially lethal extrahepatic manifestation of cirrhosis, but significant heterogeneity of the definition of sarcopenia exists. Through our multicenter consortium of 5 North American LT centers, we have developed a standardized definition of sarcopenia in men and women with ESLD awaiting LT. Using optimal search method, we have determined that an SMI of <50 cm^2/m^2 in men and <39 cm^2/m^2 in women correlates best with wait-list mortality.

ESLD patients awaiting LT frequently have CT imaging performed for HCC surveillance or for surgical planning. CT imaging is increasingly used as the gold standard tool to quantify skeletal muscle mass and hence constitutes a good resource for objective identification of sarcopenia.[13] However, the techniques and values to define sarcopenia in patients with ESLD have been heterogeneous, therefore limiting the application of results to clinical practice. All techniques rely on image analysis software (commercial and free versions are readily available) to analyze selected slices of cross-sectional imaging. The software can be used with both CT and MRI scans, although CT is more commonly used as some software enables specific tissue demarcation using previously reported HU thresholds.[14] There is excellent reliability between different software systems, lessening concern that the software package may influence results.[22] In addition to differences in measurement techniques, various definitions of sarcopenia have been used in the existing transplant literature: the lowest sex-specific tertile,[8] < 5th percentile of sex-specific healthy population,[23] or SMI values established for patients with cancer.[4]

To address these limitations in the literature, we sought to determine a scientific multicenter definition of sarcopenia in patients with ESLD awaiting LT. SMI was chosen based on previous validation against dual X-ray absorptiometry,[13–15] its use in the oncology literature,[16,17] and its predominance in the transplant literature.[4,18,19,24] We decided to use SMI at the level of L3 because this area has been shown to have the best correlation with the total muscle mass.[15] There is no evidence confirming that the cross-sectional area of psoas muscles has a good correlation with the whole lumbar or the whole body muscle areas. Moreover, using the umbilicus as a mark for the location of the muscle area evaluated might vary due to ascites or obesity, so that measures may be recorded at different levels in these patients.

Our group represents the most diverse cohort studied to date regarding the effect of sarcopenia on wait-list mortality, supporting the generalizability of our findings to a diverse population of patients at other North American centers. Almost 30% of our cohort reported a race other than Caucasian, with 5% black, 11% Hispanic white, and 8% Asian. Racial differences are known to affect body composition: black race is associated with higher baseline skeletal muscle mass and less propensity to age-related muscle loss, whereas Asian race is associated with lower baseline muscle mass and a higher likelihood of developing sarcopenia.[25–27] Interestingly, however, we did not detect statistically significant differences in SMI by race, although our study was not powered to explore racial differences. It is possible that race-specific cutoff values would provide more accurate prognostic information.

We observed an important impact of sarcopenia on the association between female sex and wait-list mortality. Women were similar to men with respect to age, race, BMI, and listing MELD scores. In univariate analysis, women experienced a 55% increased risk of wait-list mortality, as has previously been described in the literature.[28,29] However, adjustment for SMI mitigated this sex disparity, suggesting that sarcopenia in women may account for the increased wait-list mortality seen in women awaiting LT. Interestingly, using our sex-specific SMI cutoffs for sarcopenia, fewer women (33%) than men (50%) were classified as sarcopenic. Future investigation of the relationship between sex, sarcopenia, and wait-list mortality, using larger cohorts of women, is warranted.

It is difficult to compare these results with the existing literature because prior studies have used a variety of methods to define sarcopenia.[1–3] A recent meta-analysis of 19 studies revealed 7 different methods of measuring muscle mass in patients with cirrhosis.[30] Methodological differences include the location of muscle measurement, type of muscle measured, and adjustment for patient height. In addition to differences in measurement techniques, various definitions of sarcopenia have been used in the existing transplant literature: the lowest sex-specific tertile,[8] < 5th percentile of sex-specific healthy population,[23] or SMI values established for patients with cancer.[4] The absence of a standard approach to measuring muscle mass limits the comparisons that can be made to our proposed definition of sarcopenia. However, studies that measured the SMI at L3, as we did, used SMI cutoff values of <52.4 cm^2/m^2 in men and <38.5 cm^2/m^2 in women to define sarcopenia.[4] These values were determined in patients with solid organ malignancy and are higher than our proposed cutoffs of < 50 cm^2/m^2 in men and < 39 cm^2/m^2 in women. It is possible that the impact of sarcopenia in candidates for LT is even higher than previously reported.

Potential limitations of our study exist. The retrospective study design introduces the potential of selection bias. However, despite this possibility, the prevalence of sarcopenia in our population is similar to that reported in other studies of patients awaiting LT.[4,5,11] Additionally, only patients with a CT scan done within 3 months of listing were included, and this group may have differences from the full candidate list. However, routine pre-LT CT imaging of the abdomen is standard of care at all sites, making this less likely. Optimal stratification is not a perfect statistical method and may be subject to false-positives related to use of medians if the sample is not truly random. Despite these potential limitations, this is the largest in a North American population using standardized and homogeneous inclusion criteria and methods for quantification of muscle area to define sarcopenia in patients with ESLD awaiting LT. Validation of these results in a separate group of patients will be an important step in confirming our values.

In summary, we propose that the definition of sarcopenia in patients with ESLD listed for LT in North American centers should be an SMI of 50 cm^2/m^2 in men and 39 cm^2/m^2 in women. These values best correlate with wait-list mortality and should be used for future research to help identify patients at risk for death on the waiting list. A standard definition is needed to assess response to therapeutic interventions targeting sarcopenia in cirrhosis. A uniform diagnostic criterion will also permit comparison and collation of data from different studies that will help to develop effective therapies for sarcopenia in liver disease.

Abbreviations

AIH	autoimmune hepatitis
BMI	body mass index
CI	confidence interval
CT	computed tomography
ESLD	end-stage liver disease
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HR	hazard ratio
HU	Houndsfield unit
INR	international normalized ratio
IQR	interquartile range
L3	third lumbar vertebra
LT	liver transplantation
MELD	Model for End-Stage Liver Disease
MRI	magnetic resonance imaging
NASH	nonalcoholic steatohepatitis
PBC	primary biliary cirrhosis
PSC	primary sclerosing cholangitis
SMI	skeletal muscle index

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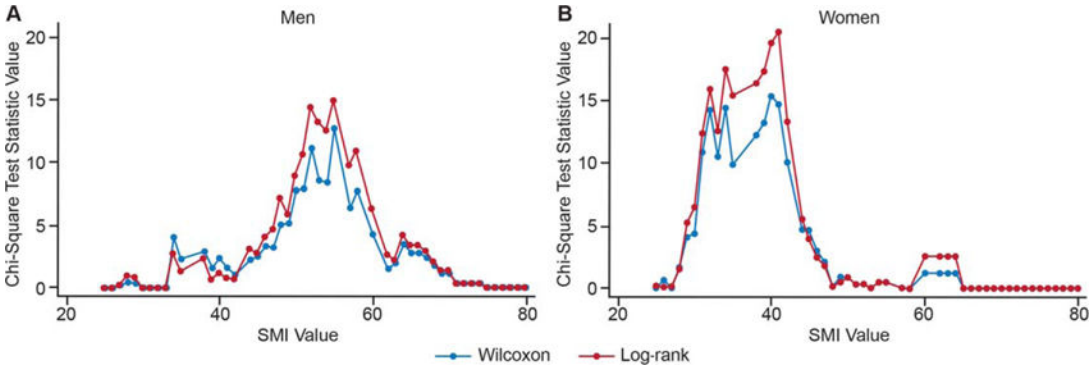

FIG. 1.

Log-rank and Wilcoxon test statistics measuring separation of survival curves at individual SMI cutoff values for (A) men and (B) women.

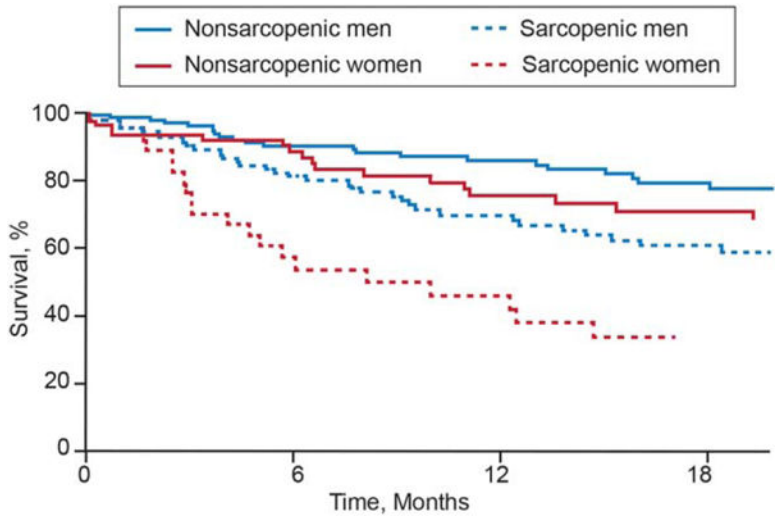

FIG. 2.

Kaplan-Meier survival curves in sarcopenic and nonsarcopenic men and women using our optimal SMI cutoffs of <50 cm^2/m^2 for men and <39 cm^2/m^2 for women to define sarcopenia.

TABLE 1

Characteristics of All Patients at Baseline

Characteristic	All (n = 396)	Men (n = 277; 70%)	Women (n = 119; 30%)	*P* Value
Age, years	58 (51–62)	58 (52–61)	57 (50–62)	0.7
Race				
Non-Hispanic white	280 (71)	198 (71)	82 (69)	0.59
Black	17 (5)	10 (4)	7 (6)	
Hispanic white	42 (11)	32 (12)	10 (8)	
Asian	31 (8)	21 (8)	10 (8)	
Other	26 (7)	16 (6)	10 (8)	
Etiology of liver disease				
HCV	189 (48)	150 (54)	39 (33)	<0.001
Alcohol	67 (17)	50 (18)	17 (14)	
NASH	49 (12)	31 (11)	18 (15)	
AIH/PBC/PSC	41 (10)	13 (5)	28 (24)	
HBV	21 (5)	15 (5)	6 (5)	
Other	29 (7)	18 (7)	11 (9)	
HCC	155 (39)	119 (43)	36 (30)	0.02
Height, cm	172.7 (164.5–178.0)	175.0 (170.2–181.4)	162.0 (157.5–166.0)	<0.001
Weight, kg	81.0 (71.1–95.6)	84.7 (74.8–96.6)	71.0 (57.7–81)	<0.001
BMI, kg/m^2	27.2 (23.9–31.1)	27.0 (24.5–31.1)	27.1 (22.5–31.0)	0.11
MELD score, calculated	15.2 (11.0–20.6)	14.4 (10.7–19.1)	14.7 (11.0–21.8)	0.42
Total bilirubin	2.3 (1.3–4.5)	2.2 (1.3–4.4)	2.4 (1.3–6.1)	0.37
INR	1.4 (1.2–1.7)	1.4 (1.2–1.7)	1.4 (1.2–1.8)	0.36
Creatinine	0.9 (0.7–1.1)	0.9 (0.8–1.1)	0.8 (0.6–1.1)	0.01
Dialysis	23 (6)	16 (6)	7 (6)	0.97
Albumin	3.1 (2.6–3.5)	3.0 (2.6–3.5)	3.1 (2.6–3.5)	0.52
Ascites				0.04
None	142 (39)	104 (41)	38 (35)	
Mild/moderate	144 (40)	90 (36)	54 (50)	
Refractory	76 (21)	59 (23)	17 (16)	
Hepatic encephalopathy				0.86
None	179 (49)	127 (50)	52 (48)	
Well controlled	165 (46)	113 (45)	52 (48)	
Poorly controlled	158 (5)	13 (5)	5 (5)	
Outcome				0.14
Died/delisted	112 (28)	69 (25)	43 (36)	
Deceased donor liver transplant	199 (50)	145 (52)	54 (45)	
Removed for other reasons	27 (7)	21 (8)	6 (5)	
Censored	58 (15)	42 (15)	16 (13)	
Time to outcome, months	8.8 (3.0–21.7)	8.9 (3.7–21.7)	8.0 (2.2–22.0)	0.41
Died/delisted at 6 months	57 (14)	33 (12)	23 (19)	0.05

Characteristic	All (n = 396)	Men (n = 277; 70%)	Women (n = 119; 30%)	*P* Value
Died/delisted at 12 months	79 (20)	46 (17)	32 (27)	0.02

NOTE: Data are given as median (IQR) or n (%).

TABLE 2

Relationship Between SMI and Wait-List Mortality

	Died/Delisted (n = 112)	All Others (n = 284)	*P* Value
SMI, cm^2/m^2	45.6 (38.5–50.8)	48.5 (42.4–54.9)	<0.001
Males			
SMI, cm^2/m^2	48.1 (43.7–51.9)	50.7 (44.6–55.8)	0.02
Females			
SMI, cm^2/m^2	38.8 (32.3–44.2)	43.3 (40.2–47.3)	0.002

NOTE: Data are given as median (IQR).

TABLE 3

Associations Between SMI and Wait-List Mortality

	Univariate		Multivariate	
Variable	**HR (95% CI)**	***P* Value**	**HR (95% CI)**	***P* Value**
SMI, per unit	0.95 (0.94–0.97)	<0.001	0.95 (0.93–0.98)	<0.00
Age, years	1.02 (0.99–1.04)	0.16	—	
Sex, female	1.55 (1.06–2.27)	0.02	—	
Race				
Non-Hispanic white	Reference			
Black	2.33 (1.21–4.47)	0.01	2.60 (1.37–4.92)	0.003
Hispanic white	1.04 (0.55–1.99)	0.90		
Asian	0.69 (0.31–1.57)	0.38		
Other	2.21 (1.20–4.05)	0.01		
Etiology of liver disease				
HCV	1.51 (0.86–2.64)	0.15		
Alcohol	Reference			
NASH	1.33 (0.64–2.79)	0.44		
AIH/PBC/PSC	1.26 (0.57–1.78)	0.56		
HBV	1.30 (0.51–3.30)	0.59		
Other	0.96 (0.37–2.50)	0.93		
HCC	1.46 (1.01–2.11)	0.04	1.87 (1.21–2.91)	0.01
Height, cm	0.98 (0.96–1.00)	0.06		
Weight, kg	0.99 (0.97–1.00)	0.02		
BMI, kg/m^2	0.97 (0.93–1.01)	0.11	—	
MELD score	1.01 (0.99–1.03)	0.28	1.02 (0.99–1.04)	0.14
Dialysis	0.91 (0.40–2.09)	0.83	—	
Albumin	1.02 (0.96–1.09)	0.44	—	
Ascites				
None	Reference			
Mild/moderate	1.53 (1.00–2.36)	0.05		
Refractory	1.15 (0.67–1.97)	0.60		
Hepatic encephalopathy				
None	Reference			
Well controlled	1.06 (0.71–1.56)	0.78		
Poorly controlled	1.32 (0.54–3.20)	0.54		

TABLE 4

Evaluation of Potential SMI Cutoff Values for Men and for Women

Cutoff SMI	Patients With SMI < Cutoff	HR (95% CI)	*P* Value
Men, n (%)			
49	126 (45)	1.48 (0.92–2.37)	0.10
50	139 (50)	1.70 (1.05–2.74)	0.03
51	153 (55)	1.68 (1.03–2.75)	0.04
52	169 (61)	2.25 (1.30–3.89)	0.004
53	180 (65)	2.39 (1.32–4.32)	0.004
55	205 (75)	3.16 (1.52–6.56)	0.002
Women, n (%)			
33	15 (13)	3.62 (1.84–7.11)	<0.001
34	18 (15)	3.75 (1.95–7.21)	<0.001
35	25 (21)	2.94 (1.60–5.40)	0.001
36	29 (24)	2.56 (1.40–4.69)	0.002
37	32 (27)	2.46 (1.34–4.49)	0.003
38	37 (31)	2.74 (1.51–4.99)	0.001
39	39 (33)	2.82 (1.55–5.13)	0.001
40	42 (35)	3.10 (1.70–5.65)	<0.001

TABLE 5

Baseline Characteristics in Sarcopenic Versus Nonsarcopenic Patients With Cirrhosis Using SMI < 50 cm^2/m^2 for Men and < 39 cm^2/m^2 for Women to Define Sarcopenia

Characteristic	Sarcopenic (n = 178; 45%)	Nonsarcopenic (n = 218; 55%)	*P* Value
Age, years	58 (51–62)	58 (52–61)	0.83
Sex, female	39 (22)	80 (37)	0.001
Race			
Non-Hispanic white	130 (73)	150 (69)	
Black	7 (4)	10 (5)	0.65
Hispanic white	19 (11)	23 (11)	
Asian	14 (8)	17 (8)	
Other	8 (5)	18 (8)	
Etiology of liver disease			
HCV	81 (46)	108 (50)	
Alcohol	29 (16)	38 (17)	
NASH	20 (11)	29 (13)	
AIH/PBC/PSC	22 (12)	19 (9)	0.32
HBV	8 (4)	13 (6)	
Other	18 (10)	11 (5)	
HCC	59 (33)	96 (44)	0.03
Height, cm	173 (163–180)	165 (152–175)	<0.001
Weight, kg	79 (68–88)	84 (72–97)	<0.001
BMI, kg/m^2	26.1 (23.4–32.2)	31.4 (27.2–41.6)	<0.001
MELD score, calculated	16 (12–22)	13 (10–18)	<0.001
Creatinine	0.9 (0.7–1.2)	0.9 (0.7–1.1)	0.13
Dialysis	16 (9)	7 (3)	0.01
Albumin	3.0 (2.6–3.4)	3.1 (2.7–3.6)	0.10
Ascites			
None	54 (32)	88 (46)	
Mild/moderate	71 (42)	73 (38)	0.01
Refractory	44 (26)	32 (17)	
Hepatic encephalopathy			
None	82 (49)	97 (50)	
Well controlled	79 (47)	86 (45)	0.91
Poorly controlled	8 (5)	10 (5)	

NOTE: Results reported as median (IQR) or n (%).