A Pilot Study of Racial Differences in the Current Definition of Sarcopenia among Liver Transplant Candidates

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Abstract

Sarcopenia has been shown to have prognostic value in patients awaiting liver transplant. However, the presence of sarcopenia as a prognostic factor among patients awaiting liver transplantation might vary by race. This study aims to assess racial differences of sarcopenia in liver transplant candidates. This retrospective study assessed 102 patients on a liver transplantation list from 2012 to 2016 and used demographic and clinical variables to predict sarcopenia as measured by skeletal muscle index (SMI) and death or removal from the transplant list. Three racial groups were compared in the study: whites (n=34), Asians (n=50), and Native Hawaiians and Other Pacific Islanders (NHOPIs; n=18). NHOPI were more likely to have a body mass index (BMI) ≥ 30 and hepatitis B, and less likely to have alcoholic cirrhosis and sarcopenia than whites. Asians were more likely to have hepatitis B and less likely to have alcoholic cirrhosis and encephalopathy than other races. Using logistic regression, a BMI ≥ 30, multiple waiting list events, alcoholic cirrhosis, and sarcopenia were predictive of death or removal from the list. Although NHOPI had a higher BMI, they had less sarcopenia and similar frequency of ascites, encephalopathy, multiple waiting list events, and death or removal from the list compared to other races. Racial variations in muscle mass might have resulted in fewer NHOPI having sarcopenia as defined by the US criteria. Larger studies of patients with varying ethnicity are needed to develop a universally applicable definition of sarcopenia before we use this for liver transplant listing or allocation.

Keywords

Sarcopenia, Liver transplantation, Racial difference, Pacific Islanders, Chronic liver disease

Abbreviations

BMI = Body mass index
CT = Computed tomography
HCC = Hepatocellular carcinoma
HE = Hepatic encephalopathy
MELD = Model for End-Stage Liver Disease
MRI = Magnetic resonance imaging
NHOPIs = Native Hawaiians and Other Pacific Islanders
PMI = Psoas muscle index
SBP = Spontaneous bacterial peritonitis
SMI = Skeletal muscle index
UNOS = United Network for Organ Sharing

Introduction

Sarcopenia is a state of low muscle mass and has been increasingly been reported to have prognostic value in oncology treatments, aging, malnutrition, and many surgical procedures, especially liver transplantation.[1-5] Initially, sarcopenia was reported descriptively, but more recently, attempts have been made to quantify sarcopenia in order to monitor patient improvement or deterioration, and to standardize reporting between treatment centers and in medical literature. Two commonly-used sarcopenia metrics, skeletal muscle index (SMI) and psoas muscle index (PMI), are cross-sectional imaging measurements from computed tomography (CT) or magnetic resonance imaging (MRI). The indexes represent imaging measurements that have been normalized to patient height as baseline muscle mass differs by height.[6-11]

The use of sarcopenia metrics in liver transplant initially started with evaluation of patients with cirrhosis. Psoas muscle area and thickness were evaluated as predictors of mortality in cirrhosis in several studies.[12,13] Early reports suggested that the presence of sarcopenia had prognostic value for patients while on the liver transplant waiting list and on negative outcomes such as post-transplant complications and mortality, but specific measurements and cutoff values were not determined.[9,14] Two studies suggested that PMI was predictive of outcome after living donor liver transplantation,[8,15] and psoas muscle transversal diameter has been shown to be a predictor of mortality while on the waiting list.[16] A Model for End-Stage Liver Disease (MELD) score is calculated based on laboratory values (bilirubin, prothrombin time and creatinine) to predict 3-month mortality in patients with end-stage liver disease. Currently, the MELD-based score is used to allocate allograft for liver transplantations. The aforementioned studies prompted the addition of sarcopenia to the traditional MELD score creating a MELD-Sarcopenia score which has been shown to be a better predictor of mortality than MELD score alone as sarcopenia status is a non-laboratory assessment of patients' clinical status.[10]

Despite accumulating evidence supporting the importance of sarcopenia in liver transplant candidates, the majority of studies have been conducted with predominantly white populations. Studies that have quantified sarcopenia with cutoff values have only included a small proportion of Asian and Pacific Islander patients.[17] While studies have reported sarcopenia and mortality in Japanese patients, these were done in the setting of living donor liver transplant where lengthy times on a transplant waiting list were not a factor.[18] Consequently, data on deceased-donor liver transplantation in Asians and Native Hawaiians and Other Pacific Islanders (NHOPIs) are limited. As sarcopenia becomes increasingly important as a prognostic factor and allocation tool in liver transplantation, appropriate definition of sarcopenia in different races is crucial. Our hypothesis is that definition of sarcopenia among patients awaiting liver transplantation may

differ by race. This study aims to address potential differences in accepted sarcopenia metrics in liver transplant candidates from a racially-diverse population.

Methods

Study Design

This is a retrospective cohort study conducted at The Queen's Medical Center (QMC) in Honolulu, Hawai'i. QMC is the only transplant and dedicated liver center in the state of Hawai'i, and is the tertiary referral center for liver disease for US territories in the Pacific Rim including American Samoa, Guam, and Micronesia, and for foreign nationals from Asia seeking medical care in the US. This study was approved by the QMC's Research and Institutional Review Committee (RA-2019-029) and was conducted according to the international standards of Good Clinical Practice, applicable government regulations, and institutional research policies and procedures.

Patients

The study identified all patients who successfully completed a liver transplant evaluation and were placed on the United Network of Organ Sharing (UNOS) for liver transplantation during the time period between January 2012 and December 2016. This study included both patients with chronic liver disease and those with fulminant liver failure who required urgent transplant listing. This study collected data on demographics (age and sex), self-reported race (white, Asian, NHOPI, and other), anthropometrics (height, weight, and body mass index [BMI]), etiology of liver disease (hepatitis B, hepatitis C, alcoholic cirrhosis, and nonalcoholic steatohepatitis [NASH]), presence of hepatocellular carcinoma (HCC), MELD score, and dialysis status. Patients who reported being mixed race and had $\geq$50% Asian heritage were classified as Asian. NHOPIs who reported being mixed race, but had $<$50% of another race or ethnicity, were classified as NHOPIs. Whites did not include mixed race. A "significant waiting list event" was defined as having a variceal bleeding episode, ascites, spontaneous bacterial peritonitis (SBP), or hepatic encephalopathy. "Multiple waiting list events" were defined as having 5 or more hospital admission or emergency department visits for liver-related problems. Ascites included documented ascites on medical record, and those patients who required diuretic or paracenteses for management. Hepatic encephalopathy included only those patients receiving treatment for overt encephalopathy as no specific testing was done to identify minimal hepatic encephalopathy.

The team then selected those patients that had cross-sectional images either by CT or MRI done at our institution. Patients who had imaging only done at centers outside our institution were excluded from the analysis. A single investigator analyzed cross-sectional images after receiving training from a radiologist at QMC. Psoas muscle area at the umbilicus and total skeletal muscle area at L3 including paraspinal, psoas, rectus abdominis, transverse abdominis, and external and internal oblique muscles were manually measured by using Vitrea® Enterprise Suite (Vital, a Canon Group Company, Minnetonka, Minnesota).[8,17]

Definition of Sarcopenia

For this study, SMI (cm^2/m^2) was defined by area of total abdominal skeletal muscle (cm^2) divided by patients' height (m^2),[9-11,17,19] and PMI (cm^2/m^2) was defined by area of total psoas muscle (cm^2) divided by patients' height (m^2).[8] Cutoff values for sarcopenia were based upon previously reported studies. A multicenter study done by Carey, et al, (2017) defined sarcopenia by the SMI at L3 with cutoffs of 50 cm^2/m^2 for men and 39 cm^2/m^2 for women while on waiting list for liver transplantation.[17] This study utilized PMI at umbilicus with cutoffs of 6.87 cm^2/m^2 for men and 4.12 cm^2/m^2 for women.[8] The team then divided the cohort into 3 groups by race. This study included only whites, Asians, and NHOPIs as there were too few Hispanics and blacks for adequate comparison. Demographic information, etiology of disease, wait list events, and sarcopenia were compared by race. The primary outcome measures were liver transplant and death or removal from the waiting list; these outcomes were also compared by race. This study included only those patients who were removed from the list for a medical reason. Those patients who were removed because of non-compliance (eg, return to alcohol, drug use) were excluded from the study.

Statistical Analysis

The team performed statistical analysis with R version 3.4.1 (The R Foundation for Statistical Computing, Vienna, Austria) as well as EZR version 1.36 (Division of Hematology, Saitama Medical Center, Jichi Medical University, Japan).[20] Pearson's Chi-squared test was utilized to compare categorical variables among whites, Asians, and NHOPIs. Comparison for age and MELD score at the time of listing for waiting list were made using Kruskal-Wallis test. Odds ratios (OR) with 95% confidence interval (95% CI) for binary variables were obtained using Fisher's Exact Test for Count Data, using whites as the reference group.

Logistic regression was performed to identify the following predictors: (1) sarcopenia by SMI at L3, and (2) death or removal from the waiting list. To predict sarcopenia, we examined baseline characteristics (age, sex, and race), etiologies of chronic liver disease, waiting list complications, and presence of HCC. To predict death or removal from waiting list, we excluded patients who were removed for nonmedical reasons (eg, return to alcohol or other substance abuse, inadequate caregiver support or other evidence of noncompliance) as these did not necessarily represent a deterioration in their medical condition that would warrant removal from the list. Baseline characteristics, etiologies for chronic liver disease, waiting list complications, and sarcopenia defined by SMI at L3 were included as variables in the model. $P < .05$ was considered as statistically significant for both analyses.

Results

During the period between January 2012 to December 2016, 137 patients underwent formal liver transplant evaluation in anticipation of being placed on the transplant waiting list. Many more patients with end-stage liver disease were seen by the hepatologists and surgeons, but were determined to be unsuitable for formal evaluation for various reasons including active substance abuse, extensive hepatocellular cancer or severe cardiovascular disease. Among these 137 patients, 35 (26%) of patients were excluded from analysis for following reasons: 30 (21.9%) of patients did not have cross-sectional images at our medical center, and 5 (4%) had a race other than Asian, white, or NHOPI. In this cohort of 102 patients, the mean age was 55.9 years (standard deviation: 8.83). Fifty-six percent of patients were men, and the race distribution was whites (n=34, 33%), Asians (n=50, 49%), and NHOPIs (n=18, 18%). Etiology of disease was distributed as follows: 16 (16%) of patients had hepatitis B, 36 (36%) had hepatitis C, 28 (28%) had alcoholic cirrhosis, and 15 (15%) had NASH. Other etiologies included autoimmune hepatitis, Budd-Chiari syndrome, polycystic liver disease, primary biliary cholangitis, drug-induced liver injury, and cryptogenic cirrhosis. It is important to note that some patients had more than one etiology of chronic liver disease. HCC was present in 35 (34%) of patients. In terms of outcome, 19 (19%) of patients had multiple waiting list events, 35 (34%) died or were removed from the transplant waiting list, and 57 (56%) underwent liver transplantation. Sarcopenia was identified in 56 (55%) of patients when measured by SMI at L3, and in 10 (13%) of patients when measured by PMI at the umbilicus.

Characteristics by race are summarized in the Tables 1 and 2. We did not observe differences among the 3 races in terms of sex, age, and mean listing MELD score. NHOPIs were much more likely to be obese (78%) compared to whites (27%) and Asians (28%). Asians and NHOPIs (22%, respectively) were more likely to have hepatitis B than whites (3%). Whites were more likely to have alcoholic liver disease (47%) than Asians (18%) and NHOPIs (17%).

A lower proportion of Asians had hepatic encephalopathy compared to whites (OR: 0.31, 95% CI: 0.10-0.88). However, there was no difference between NHOPIs and whites (OR: 0.49, 95% CI: 0.12-2.02).

With respect to sarcopenia, PMI at umbilicus in 76 patients showed no significant difference by race. In analysis of 101 patients for whom for sarcopenia by SMI at L3 was available, NHOPIs (17%) were less likely to have sarcopenia than both whites (70%) and Asians (60%; $P < .001$); however, there was no difference between whites and Asians ($P = .49$). Table 3 summarizes the detailed results of logistic regression regarding predictors of sarcopenia analysis by SMI at L3. Importantly, HCC was a statistically significant positive predictor of sarcopenia, and BMI ≥30, hepatitis C, NASH, and NHOPI were negative predictors. However, age ≥60, sex, ascites, variceal bleeding, significant waiting list events, hepatic encephalopathy, SBP, hemodialysis status, alcoholic liver disease, hepatitis B, and being Asian did not show significant differences compared to whites.

Among the 92 patients in the predictors of death or removal from waiting list analysis, BMI ≥30 (OR: 27.9, 95% CI: 1.05-739) and sarcopenia by SMI at L3 (OR: 84.6, 95% CI: 2.12-3380) were positively associated with death or removal from the waiting list (Table 4). Multiple waiting list events (OR: 0.139, 95% CI: 0.02-0.93) and alcoholic liver disease (OR: 0.05, 95% CI: 0.005-0.48) were negatively associated with death or removal from the waiting list. There was no difference for death or removal from the waiting list among 3 races by Chi-square test (whites: 33%, Asians: 28%, NHOPIs: 13%, $P = .36$, *data not shown*). Age, sex, MELD score at listing, ascites, variceal bleeding, hepatic encephalopathy, SBP, fulminant liver failure, hemodialysis status, HCC, hepatitis B and C, and NASH were not associated with death or removal from the waiting list.

Table 1. Patient Characteristics, Chronic Liver Disease Etiologies, Waiting List Complications, Death or Removal from Waiting List, Transplant Status, and Sarcopenia Status by Race

	White n=34 n (%)[a]	Asian n=50 n (%)	NHOPI n=18 n (%)	*P*-value
Female	14 (41)	23 (46)	8 (44)	.91
Mean Age (SD)[a]	56.1 (8)	56.8 (9)	53.2 (11)	.50
Obesity, BMI≥30	9 (27)	14 (28)	14 (78)	<.001
Ascites	26 (77)	34 (68)	13 (72)	.70
Hepatic encephalopathy	26 (77)	25 (50)	11 (61)	.051
Variceal bleeding	11 (32)	13 (26)	3 (17)	.47
Mean MELD (SD)[a]	18.9 (8)	17.5 (8)	16.9 (8)	.70
Hepatitis B	1 (3)	11 (22)	4 (22)	.044
Hepatitis C	15 (44)	15 (30)	6 (33)	.41
Alcoholic liver disease	16 (47)	9 (18)	3 (17)	.007
NASH	2 (6)	10 (20)	3 (17)	.188
Liver cancer	9 (27)	18 (36)	8 (44)	.40
Significant waiting list event	9 (27)	6 (12)	4 (22)	.23
Death or removal on waiting list	14 (41)	16 (32)	5 (28)	.56
Transplanted	14 (41)	31 (62)	12 (67)	.101
Sarcopenia by SMI at L3	23 (70), n=33[c]	30 (60)	3 (17)	<.001[b]
Sarcopenia by PMI at umbilicus	2 (8), n=24[c]	6 (15), n=39[c]	2 (15), n=13[c]	.70

Abbreviations: NHOPI, Native Hawaiian and Other Pacific Islander; SD, Standard deviation; BMI, Body mass index; MELD, Model for End-Stage Liver Disease; NASH, Non-alcoholic steatohepatitis; SMI, Skeletal muscle index; PMI, Psoas muscle index.
[a] Count and percent presented except where denoted by the asterisk.
[b] Subgroup analysis showed there was no difference between whites and Asians (*P*=.49).
[c] n is number of patients. These differences are based on the availability of cross-sectional images.

Table 2. Odds Ratios for Patient Characteristics, Chronic Liver Disease Etiologies, and Waiting List Complications among Asians and Native Hawaiians and Other Pacific Islanders Compared to Whites

	Asian OR (95% CI)	NHOPI OR (95% CI)
Female	1.21 (0.46-3.23)	1.14 (0.31-4.19)
Obesity, BMI ≥30	1.08 (0.37-3.30)	9.23 (2.18-49.23)[a]
Ascites	0.66 (0.21-1.93)	0.80 (0.19-3.78)
Hepatic encephalopathy	0.31 (0.10-0.88)[a]	0.49 (0.12-2.02)
Variceal bleeding	0.74 (0.26-2.15)	0.43 (0.07-1.99)
Hepatitis B	9.13 (1.21-411.71)[a]	9.43 (0.97-92.07)
Hepatitis C	0.55 (0.20-1.49)	0.64 (0.16-2.39)
Alcoholic liver disease	0.25 (0.81-0.74)[a]	0.23 (0.05-0.92)[a]
NASH	3.94 (0.76-39.51)	3.12 (0.32-41.04)
Liver cancer	1.55 (0.55-4.64)	2.19 (0.56-8.67)
Multiple waiting list events	0.38 (0.01-1.37)	0.80 (0.15-3.55)
Death or removal on waiting list	0.68 (0.25-1.84)	0.56 (0.13-2.17)
Transplanted	2.31 (0.88-6.25)	0.36 (0.09-1.33)
Sarcopenia by SMI at L3	0.66 (0.23-1.81)	0.09 (0.01-0.42)[a]
Sarcopenia by PMI at umbilicus	1.98 (0.32-21.80)	0.51 (0.03-7.92)

Abbreviations: NHOPI, Native Hawaiian and Other Pacific Islander; OR, Odds ratio; 95% CI, 95% confidence interval; BMI, Body mass index; NASH, Non-alcoholic steatohepatitis; SMI, Skeletal muscle index; PMI, Psoas muscle index.
[a] P<.05

Table 3. Logistic Regression for Sarcopenia by SMI at L3 by Patient Characteristics, Chronic Liver Disease Etiologies, and Waiting List Complications

	OR	95% CI	*P*-value
Overall	12.0	1.22-118	.033
Age ≥ 60	2.02	0.42-9.61	.38
Sex	0.25	0.05-1.28	.096
BMI ≥ 30	0.01	0.002-0.09	<.001
Ascites	0.975	0.16-5.90	.98
Variceal bleeding	0.87	0.16-4.50	.86
Multiple waiting list events	1.69	0.19-15.3	.64
Hepatic encephalopathy	5.83	0.98-34.9	.053
SBP	0.63	0.11-3.72	.61
Hemodialysis status	2.50	0.10-63.8	.58
HCC	13.9	1.33-145	.028
Alcoholic liver disease	0.89	0.16-5.06	.90
Hepatitis B	1.02	0.11-9.35	.98
Hepatitis C	0.08	0.009-0.76	.027
NASH	0.04	0.003-0.540	.016
Asian	0.46	0.10-2.19	.33
NHOPI	0.08	0.009-0.81	.032

Abbreviations: OR, Odds ratio; 95% CI, 95% confidence interval; BMI, Body mass index; SBP, Spontaneous bacterial peritonitis; HCC, Hepatocellular carcinoma; NASH, Non-alcoholic steatohepatitis; NHOPI, Native Hawaiian and Other Pacific Islander.
Area under the curve of a receiver operating characteristics curve for this model was 0.937 (95% CI: 0.885-0.989).

Table 4. Logistic Regression for Death or Removal on Liver Transplant Waiting List for Patient Characteristics, Chronic Liver Disease Etiologies, and Waiting List Complications

	OR	95% CI	*P*-value
Overall	0.00002	0.00000001-0.05	<.01
Age≥60	1.08	0.97-1.20	.168
Sex	0.216	0.04-1.21	.081
BMI≥30	27.9	1.05-739	.047
MELD score at wait listing	1.07	0.95-1.20	.27
Ascites	5.55	0.76-40.7	.092
Variceal bleeding	0.834	0.16-4.36	.83
Multiple waiting list events	0.139	0.02-0.93	.042
Hepatic encephalopathy	3.83	0.81-18.1	.090
SBP	0.456	0.08-2.75	.39
Hemodialysis status	2.99	0.15-61.5	.48
Fulminant liver failure	674000	0-infinite	.99
HCC	1.49	0.18-12.7	.72
Alcoholic liver disease	0.05	0.005-0.48	.010
Hepatitis B	0.701	0.10-4.93	.72
Hepatitis C	0.558	0.05-6.21	.64
NASH	0.453	0.05-4.41	.50
Sarcopenia by SMI at L3	84.6	2.12-3380	.018

Abbreviations: OR, Odds ratio; 95% CI, 95% confidence interval; BMI, Body mass index; MELD; Model for End-Stage Liver Disease; SBP, Spontaneous bacterial peritonitis; HCC, Hepatocellular carcinoma; NASH, Non-alcoholic steatohepatitis; SMI, Skeletal muscle index.
The area under the curve of a receiver operating characteristics curve for this model was 0.873 (95% CI: 0.793-0.953).

Discussion

Although the term "sarcopenia" has been used with increasing frequency in the literature, there is no universally accepted metric with well-tested cutoff values for sarcopenia. While groups have attempted to define sarcopenia by sex,[8,17] there is a paucity of data on whether various cutoff values will be applicable to all races. Rush, et al, (2009) in an analysis of 933 Europeans, Asian Indians, and Pacific Islanders showed that racial differences in fat distribution, muscularity, bone mass, and leg length suggest universal BMI cutoffs may not be appropriate.[21] This conclusion also suggests that racial differences in muscle mass could affect the definition of sarcopenia. Studies done in Asia have delineated different cutoffs for SMI than the US-based studies.[17,22,23] A UK-based study of 600 hemodialysis patients consisting of 281 whites, 167 Asians, 149 blacks, and 3 others noted Asians to have a greater prevalence of sarcopenia than whites, though this study utilized appendicular skeletal muscle mass rather than SMI.[24] There may even be regional differences in baseline muscle mass as suggested by a group who described this phenomenon in various parts of Mexico.[25] In our study with a large proportion of Asians and NHOPIs, there was no difference in the incidence of sarcopenia between Asians and

whites, but NHOPIs were less likely to be sarcopenic with the cutoffs for SMI as defined by Carey, et al, (2017).[17] Although we attempted to define cutoffs for sarcopenia using the receiver operating curve, small sample size limited the accuracy of area under the curve. Further, the definition of sarcopenia by race is important, especially if sarcopenia will be used as a tool for determining candidacy or allocation for liver transplantation in the future. Interestingly, a lower proportion of whites received a liver transplant (whites: 41%, Asians: 62%, and NHOPIs: 66%), yet this was not statistically significant (*P*=.10).

While BMI is commonly used to define obesity, it is not reliable for estimating muscle mass. Increasing numbers of patients are found to have "sarcopenic obesity" or the presence of low muscle mass and high fat mass. This finding has clinical significance in multiple disease conditions as sarcopenic obesity is associated with an increased the risk of falls in women[26] and poor outcomes in cardiovascular conditions,[27,28] pancreatic cancer surgery,[29] and gastric cancer surgery.[30] With respect to liver disease, sarcopenic obesity was associated with worse survival in those with cirrhosis,[31] and obesity was a predictor of sarcopenia in pretransplant NASH patients.[32] NHOPIs are known to have a high prevalence of obesity, as 8 of the top 10 most obese countries in the world are Pacific Islands where more than 90% of the population has a BMI above 30.[33] However, it is important to note that BMI definitions for being overweight and obesity may differ by race.[21] In this study, NHOPIs had a much higher prevalence of obesity, but were less likely to be sarcopenic according to the current definition which was calculated in a Caucasian-dominant population.[17] Consequently, it is unclear if NHOPIs truly have less sarcopenia or if racial variations in muscle mass simply result in fewer NHOPIs having sarcopenia as defined by US standards.

Sarcopenia has been shown to be intimately associated with complications of cirrhosis, especially hepatic encephalopathy due to the role of muscle in ammonia detoxification.[34] A recent meta-analysis of 1795 patients with cirrhosis in 6 studies showed a significant association between sarcopenia and hepatic encephalopathy. However, the 6 studies that were analyzed had variable definitions of sarcopenia, 3 different ways of assessing hepatic encephalopathy and were done in different cohorts of patients with cirrhosis (inpatients, liver transplant candidates, and patients awaiting transjugular intrahepatic portasystemic shunts). They did not find any association between ammonia level and sarcopenia.[35] In this study, NHOPIs were less likely to have sarcopenia than Asians or whites but had a similar incidence of hepatic encephalopathy. As a result, there was a higher proportion of NHOPIs without sarcopenia who developed hepatic encephalopathy. It is unclear if NHOPIs inherently have more encephalopathy or if higher baseline muscle mass potentially misclassifies them non-sarcopenic with the current definition. Perhaps the loss of muscle mass over time may be a more relevant indicator of sarcopenia and disability.

Differences in sarcopenia by disease etiology may potentially contribute to ethnic variations. Although this has not been explored definitively, in a study of 265 patients with cirrhosis being evaluated for liver transplant, 47% of those with alcoholic liver disease had sarcopenia compared to 22% of those with NASH.[36] In addition, patients with cirrhosis and lower skeletal muscle attenuation due to fat deposition have been shown to have increased the risk of developing HCC.[37] Hawai'i has a high burden of HCC and 34% of state transplant candidates carry this diagnosis. While there were differences in disease etiology by race with more alcoholic liver disease seen in whites and more hepatitis B present in Asians and NHOPIs, there was no difference in the incidence of hepatitis C or HCC between the races. Despite differences in disease etiology, the presence of HCC was the strongest predictor of sarcopenia (OR: 13.9, 95% CI: 1.33-145); meanwhile, NHOPIs, and those with obesity, NASH, and hepatitis C were independently associated with decreased risk of sarcopenia.

The presence of sarcopenia has been associated with complications in cirrhosis, waiting list mortality, and poor outcome after liver transplant. However, this is controversial as some have reported that sarcopenia did not increase mortality[38,39] and that frailty may be more important than sarcopenia.[36] Furthermore, the definitions for sarcopenia have varied in these studies. Ebadi, et al, (2018) suggested that PMI had poor performance in predicting waitlist mortality in comparison to SMI.[40] This may be because the psoas muscle represents only a portion of the total muscle mass at the level of evaluation and may be susceptible for change in non-hepatic disease conditions.[40,41] Even the use of a MELD-Sarcopenia score has been debated as some have purported that this is superior to MELD score at predicting waitlist and post-operative mortality,[10] while others suggest that it had limited value in predicting waiting list mortality.[40] This study showed that while alcoholic liver disease (OR: 0.05, 95% CI: 0.005-0.48), obesity (OR: 27.9, 95% CI: 1.05-739) and multiple waiting list events (OR: 0.139, 95% CI: 0.02-0.93) were important risk factors, sarcopenia (OR: 84.6, 95% CI: 2.12-3380) was the strongest predictor of death or removal from the waiting list.

This study is limited in that it occurred in a single facility study and was performed retrospectively at a relatively low-volume transplant center. The sample size was also limited because we excluded patients without cross-sectional imaging at our center in order to minimize differences in imaging equipment and technique and to keep the measurements as uniform as possible. We also excluded patients who were of black race or Hispanic ethnicity as these groups were too small for adequate comparison. Finally, sarcopenia was measured manually by a single investigator instead of a computer-based algorithm with multiple investigators. Although training in measuring skeletal muscle area was provided by a radiologist, the investigator did not have formal clinical radiology training. These factors may have potentially overestimated the presence of sarcopenia.

In conclusion, this study is similar to many studies in that we show that HCC is associated with sarcopenia and sarcopenia is associated with death and removal from the transplant waiting list. However, there are distinct differences in the prevalence of sarcopenia by race using conventional definitions. NHOPIs had much less sarcopenia and yet had similar frequency of complications of ascites, hepatic encephalopathy, hospital admissions, multiple waiting list events and removal/death on the waiting list compared to whites and Asians. Perhaps a higher baseline muscle mass in NHOPIs accounts for this difference. Larger studies of patients with varying ethnicities are needed to develop a universally applicable definition of sarcopenia before we use this for liver transplant listing and allocation.

Conflict of Interest

None of the authors identify a conflict of interest.

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