Myosteatosis, the More Significant Predictor of Outcome: An Analysis of the Impact of Myosteatosis, Sarcopenia, and Sarcopenic Obesity on Liver Transplant Outcomes in Johannesburg, South Africa

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Abstract

Objectives: **In high-income countries, myosteatosis, sarcopenia, and obesity with sarcopenia (sarcopenic obesity) are associated with adverse outcomes after liver transplantation. In South Africa, an upper-middle-income country, we investigated the prevalence and impact of these muscle abnormalities on posttransplant outcomes in adult liver transplant recipients.**

Materials and Methods: **We reviewed 106 liver transplant recipients and measured muscle abnormalities on computed tomography using segmentation software. The parameters evaluated were myosteatosis by mean muscle attenuation, sarcopenia by skeletal muscle index at the third lumbar vertebra using validated cutoffs, and sarcopenic obesity as sarcopenia and a body mass index of ≥25 kg/m^2. The effects of these abnormalities on 1-year patient and graft survival (primary endpoint) and length of hospital and intensive care unit stay, costs, and 90-day and overall postoperative complications (secondary endpoints) were assessed.**

Results: **Most liver transplant recipients were male (n = 64, 60%). Alcoholic and/or nonalcoholic steatohepatitis were the most frequent indications for transplant (n = 38, 36%). Myosteatosis occurred in 76 patients (72%), 69 patients (65%) had sarcopenia, and 36 patients (34%) had sarcopenic obesity. One year after transplant, myosteatosis was associated with higher mortality (hazard ratio of 3.3; 95% confidence interval, 1.00-11.13; *P* = .049), greater risk of allograft failure (hazard ratio of 4.1; 95% confidence interval, 1.2-13.5; *P* = .021), and longer hospital and intensive care unit stays compared with those without myosteatosis. All patients with no body composition abnormalities were alive at 1 year compared with 69% with coexisting myosteatosis and sarcopenia.**

Conclusions: **In our setting, liver transplant recipients with myosteatosis had a higher risk of death and allograft failure at 1 year compared with patients without body composition abnormalities.**

Key words: *End-stage liver disease, Muscle abnormality, Skeletal muscle wasting*

Introduction

Liver transplantation (LT) is the definitive treatment of choice for patients with end-stage chronic liver disease.[1] Considerable clinical advances in surgical technique, organ preservation, immunosuppression, and postoperative care have improved survival outcomes of this life-saving surgery.[2,3] However, the procedure is costly. In South Africa, added barriers to the more widespread implementation of LT are small living donor LT programs and low deceased donor rates.[4,5] In this era of organ shortages, further studies on long-term predictors of outcomes after LT may guide difficult clinical decisions on organ utility.

Skeletal muscle wasting, termed sarcopenia, is an important predictor of survival in LT recipients.[6] As cirrhosis is frequently associated with malnutrition and muscle wasting, the European Association for the Study of the Liver offers guidance on nutritional assessment and management.[7,8] Analysis of muscle quantity on cross-sectional computed tomography (CT) or magnetic resonance imaging is a validated and widely available measure of nutritional status in

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these patients.[9] Currently the best internationally studied measure of sarcopenia in patients with cirrhosis is the skeletal muscle index at the third lumbar vertebra (L3) on CT.[10] It has been shown to be an independent predictor of mortality, longer length of stay in an intensive care unit (ICU), and longer total length of stay in the hospital.[6,11]

The term sarcopenic obesity is used to describe patients who are both overweight (body mass index [BMI, calculated as weight in kilograms divided by height in meters squared] of ≥25) and who meet CT skeletal muscle index criteria for sarcopenia.[11,12] Sarcopenic obesity has been described in up to 40% of LT recipients and is significantly associated with higher perioperative morbidity, as patients are at risk of the complications associated with both obesity and sarcopenia.[9,13]

Recent evidence has suggested that both low quantity and low quality of skeletal muscle are associated with poor outcomes. Myosteatosis, characterized by inter- and intramyocellular fat deposition, has emerged as a risk factor for mortality in patients with cancer.[14] Low mean muscle radio attenuation, measured in Hounsfield units on cross-sectional CT imaging at L3, reflects the high fat content of muscle. In many studies, the incidence of myosteatosis in patients with cirrhosis is higher than that of sarcopenia.[11,15,16] Limited data in patients with cirrhosis point toward higher postoperative complication rates, including a higher risk of hepatic encephalopathy, longer hospital and ICU stays, and higher associated costs in patients with myosteatosis compared with those without.[16,17]

The capacity of CT muscle measurements of nutritional status to predict outcomes after LT has not yet been tested in South Africa. In the present study, we described the prevalence of sarcopenia, sarcopenic obesity, and myosteatosis in adult patients undergoing deceased donor LT, using cross-sectional CT imaging analysis, and evaluated the impact of these body composition parameters on length of hospital and ICU stay, cost of hospital stay, posttransplant complications at 90 days and overall, and patient and graft survival at 1 year.

Materials and Methods

Patients

Deceased donor adult (age ≥18 years) LTs performed at Wits Donald Gordon Medical Centre Liver Transplant Unit between January 1, 2011, and January 31, 2019, were assessed. First time LT recipients were included in this retrospective study if they had end-stage liver disease of any etiology and had a plain abdominal CT scan performed at the discretion of the treating clinician in the 6 months before or in the 1 month after surgery. During this period, 293 patients underwent LT. Patients with acute liver failure (n = 29), previous LT (n = 5), and without suitable imaging (n = 153) were excluded. One hundred and six patients were included in the study.

Clinical and biochemical data were extracted from the existing Wits Donald Gordon Medical Centre Adult Liver Transplant Research Electronic Data Capture (REDCap) database.[18] Pretransplant variables analyzed included demographics (age at time of transplant, sex, population group), BMI, etiology of chronic liver disease, Model for End-Stage Liver Disease (MELD) score, and presence of diabetes. Posttransplant outcomes included length of stay in hospital and length of stay in ICU (defined as the number of days admitted from transplant to discharge from hospital or ICU, respectively, or death), total cost of hospital stay, postoperative complications (defined as surgical re-exploration, vascular complications, and/or biliary complications) overall and occurring within 90 days, and recipient and graft survival at 1 year.

Image analysis and analyzed parameters

All CT imaging was obtained with a multidetector CT scanner (Brilliance 64, Philips Medical Systems). Unenhanced cross-sectional images were analyzed using OsiriX MD segmentation software (Version 10.0.0, Pixmeo SARL). The total cross-sectional areas of the psoas, erector spinae, quadratus lumborum, transversus abdominus, external and internal oblique, and rectus abdominus muscles were quantified at the L3 level at -29 to 150 Hounsfield units. This area was normalized for height to compute the skeletal muscle index (in cm^2/m^2). Sarcopenia was defined using published cutoff values of skeletal muscle index of <39 cm^2/m^2 for women and <50 cm^2/m^2 for men.[10] Sarcopenic obesity was defined as the coexistence of sarcopenia and BMI ≥25.[11] Myosteatosis was determined by measuring the mean muscle attenuation for the same muscle area at the L3 level in Hounsfield units, defined according to published cutoff values of mean

muscle attenuation of <41 Hounsfield units for BMI <24.9 and <33 Hounsfield units for BMI ≥25.[19]

A radiologist (L.L.) and a trained observer (N.I.), both blinded to outcome, performed all measurements.

Sample size

Sample size estimation was based on our key research question: the determination of risk factors for patient and allograft survival at 1 year. Based on a 1-year patient and allograft survival of 80%, and a 50% prevalence of a risk factor, our sample size and survival rate would allow the estimation of relative risks of 1.67 or greater with 80% power at the 5% significance level, which is adequate for a study of this nature.[20]

Statistical analyses

The association between skeletal muscle measures and pretransplant variables was determined by the chi-square test (Fisher exact test was used for 2 × 2 tables or where the assumptions of the chi-square test were not met). The relative risk of each study variable on each complication outcome was determined, together with its 95% confidence interval (95% CI), using binomial regression. The effect of each study variable on hospital and ICU length of stay (censored for death), as well as on patient and graft survival, was assessed by Cox proportional hazards regression. The effect of each study variable on cost was assessed by a generalized linear model with a log link. Death in hospital was included as an additional predictor variable. Published annual tariff increases were considered and the total costs of hospital stay were evaluated at 2018 levels.[21] Data were analyzed using SAS version 9.4 (SAS Institute). A 5% significance level was used.

This study was approved by the University of the Witwatersrand Human Research Ethics Committee (M180560) and conducted in accordance with the principles of the Declaration of Helsinki of 1996. Patient records were anonymized prior to analysis.

Results

Demographics and clinical characteristics of evaluated patients

Pretransplant characteristics of patients are summarized in Table 1. Of the 106 patients studied, 64 were men (60%) and 59 patients (56%) were ≥50 years old (range, 20-73 y). By population group, most were White (72; 68%). Alcoholic and/or nonalcoholic steatohepatitis (ASH/NASH) were the most common underlying etiologies of liver disease (n = 38; 36%), followed by autoimmune liver disease (n = 34; 32%). Of total patients, 61% were overweight based on their BMI (>25) and the mean (SD) MELD score was 17 (6).

Table 1. Characteristics of Liver Transplant Recipients at Time of Transplant

	Number of Patients (%)			
	All Patients (n = 106)	Myosteatosis (n = 76)	Sarcopenia (n = 69)	Obesity (n = 36)
Age group				
18-34 years	17 (16.0)	12 (15.8)	14 (20.3)	1 (2.8)
35-49 years	30 (28.3)	19 (25.0)	19 (27.5)	8 (22.2)
50-64 years	47 (44.3)	36 (47.4)	28 (40.6)	20 (55.6)
≥65 years	12 (11.3)	9 (11.8)	8 (11.6)	7 (19.4)
Sex				
Male	64 (60.4)	38 (50.0)	46 (66.7)	28 (77.8)
Female	42 (39.6)	38 (50.0)	23 (33.3)	8 (22.2)
Population group				
White	72 (67.9)	54 (71.1)	48 (69.6)	29 (80.5)
Black-African	20 (18.9)	13 (17.1)	11 (15.9)	2 (5.6)
Indian	12 (11.3)	8 (10.5)	8 (11.6)	3 (8.3)
Asian	1 (0.9)	1 (1.3)	1 (1.4)	1 (2.8)
Mixed	1 (0.9)	0	1 (1.4)	1 (2.8)
Indication for transplant				
ASH/NASH	38 (35.8)	29 (38.2)	25 (36.2)	18 (50.0)
AILD[a]	34 (32.1)	19 (25.0)	16 (23.2)	5 (13.9)
Malignancy[b]	10 (9.4)	5 (6.5)	7 (10.1)	3 (8.3)
Metabolic[c]	6 (5.7)	5 (6.5)	5 (7.2)	1 (2.8)
Hepatitis B	4 (3.8)	1 (1.3)	2 (2.9)	1 (2.8)
Hepatitis C	2 (1.9)	1 (1.3)	1 (1.4)	1 (2.8)
Other[d]	12 (11.3)	16 (21.1)	13 (18.8)	7 (19.4)
BMI				
≤24.9	41 (38.7)	34 (44.7)	33 (47.8)	
25.0-29.9	37 (34.9)	22 (28.9)	24 (34.8)	24 (66.7)
≥30	28 (26.4)	20 (26.3)	12 (17.4)	12 (33.3)
Diabetes mellitus				
Yes	19 (17.9)	15 (19.7)	11 (15.9)	7 (19.4)
No	87 (82.1)	61 (80.3)	58 (84.1)	29(80.6)
MELD score				
<15	40 (37.7)	26 (34.2)	22 (31.9)	9 (25.0)
≥15	66 (62.3)	50 (65.8)	47 (68.1)	27 (75.0)

Abbreviations: AILD, autoimmune liver disease; ASH/NASH, alcoholic/nonalcoholic steatohepatitis; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); MELD, Model for End-Stage Liver Disease

[a]Includes primary sclerosing cholangitis, primary biliary cirrhosis, and autoimmune hepatitis. [b]Includes hepatocellular carcinoma, cholangiocarcinoma, and neuroendocrine tumor. [c]Includes hemochromatosis, oxalosis, and α1 antitrypsin deficiency. [d]Includes hepatic venous outflow obstruction, cryptogenic cirrhosis, sarcoidosis, polycystic liver disease, and portal vein thrombosis.

As shown in Table 2, 76 patients (72%) had myosteatosis, 69 patients (65%) had sarcopenia, and 36 patients (34%) had sarcopenic obesity. Sarcopenia with comorbid myosteatosis was diagnosed in 52 patients (49%). The mean (SD) skeletal muscle index at L3 was 42 (9) cm^2/m^2, and the mean (SD) muscle attenuation was 32 (8) Hounsfield units. Sixty-six patients (62%) had CT scans pretransplant (median of 58 days prior; interquartile range [IQR], 114 to

26 days) and 40 patients (38%) had scans done posttransplant (median of 11 days after; IQR, 7-19 days).

Table 2. Muscular Characteristics of Liver Transplant Recipients

	All Patients (n = 106)	Myosteatosis (n = 76)	Sarcopenia (n = 69)	Sarcopenic obesity (n = 36)
Myosteatosis, No. (%)	76 (72)		52 (75)	25 (69)
Sarcopenia, No. (%)	69 (65)	52 (68)		
Sarcopenic obesity, No. (%)	36 (34)	25 (33)	36 (52)	
Mean (SD) L3 SMI, cm^2/m^2	42 (9)	40 (8)	38 (7)	40 (6)
Mean (SD) muscle attenuation, HU	32 (8)	28 (6)	31 (9)	29 (8)

Abbreviations: HU, Hounsfield units; L3 SMI, skeletal muscle index at the level of the third lumbar vertebra

Survival after liver transplant

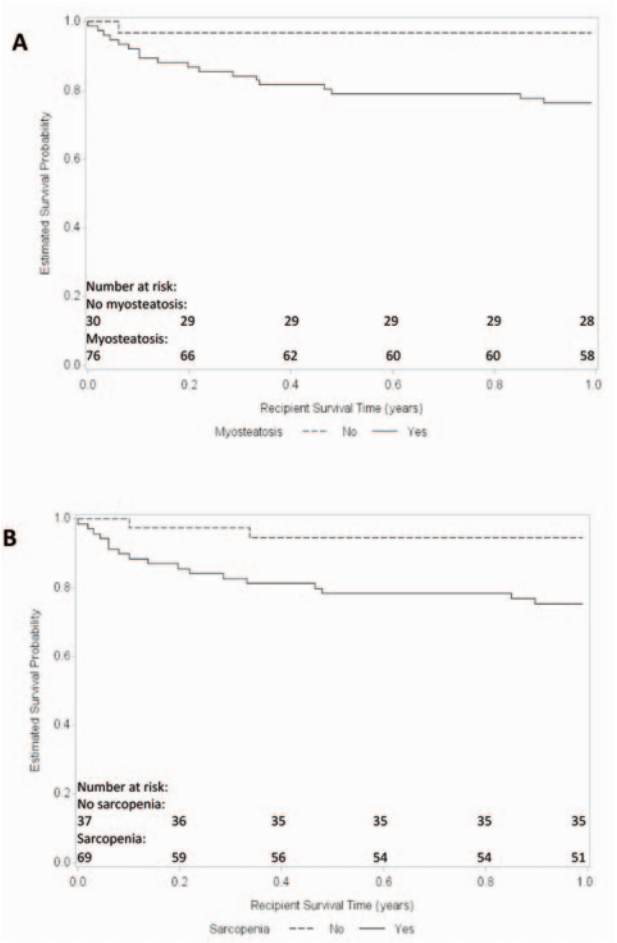
Patients with myosteatosis had significantly worse survival at 1 year than patients without myosteatosis (hazard ratio [HR] of 3.3; 95% CI, 1.003-11.1; $P = .049$) (Figure 1A). In this study, the risk of death at 1 year was increased in patients with sarcopenia compared with those without; the finding was of marginal significance (HR of 2.64; 95% CI, 0.99-7.00; $P = .051$) (Figure 1B). Overall recipient survival at 1 year after LT was 82% (95% CI, 73-88%). Sarcopenic obesity was not associated with a significantly increased risk of death at 1 year (HR of 1.23; 95% CI, 0.56-2.71; $P = .61$). For patients with myosteatosis, sarcopenia, and sarcopenic obesity, survival rates at 1 year were 76%, 75%, and 81%, respectively. All patients without body composition abnormalities were alive at 1 year after LT compared with 69% of those with coexisting myosteatosis and sarcopenia. On univariate analysis, detailed in Table 3, age, sex, BMI, etiology, MELD score, and presence of diabetes also did not influence 1-year survival.

Myosteatosis significantly increased the risk of allograft failure at 1 year (HR of 4.08; 95% CI, 1.24-13.45; $P = .021$), but neither sarcopenia nor sarcopenic obesity impacted the risk (HR of 1.63; 95% CI, 0.73-3.67; $P = .24$ and HR of 1.12; 95% CI, 0.53-2.36; $P = .76$).

Association of skeletal muscle abnormalities with demographic and pretransplant clinical variables

Muscularity varied significantly by sex. Ninety-one percent of female recipients and 59% of male recipients had myosteatosis ($P < .001$). Comparatively, 19% of female and 44% of male recipients had sarcopenic obesity ($P = .012$). Sarcopenic obesity was significantly associated with White ethnicity compared with those with Black-African ethnicity (40% vs 10%; $P = .040$). Categorized MELD score (<15 or ≥15) did not significantly differ in patients with and without muscle abnormalities ($P = .27$ for myosteatosis, $P = .098$ for sarcopenia, $P = .060$ for sarcopenic obesity).

Figure 1. Recipient Survival in Patients With Myosteatosis and Sarcopenia



(A) Myosteatosis group. **(B)** Sarcopenia group. Survival at 1 year was significantly lower in patients with myosteatosis ($P = .049$). Patients with sarcopenia had marginally worse survival than patients without sarcopenia ($P = .051$).

A large percentage of patients with sarcopenia (43% [30/69]), myosteatosis (41% [31/76]), or both (46% [24/52]) had normal nutritional BMI status (BMI of 18.5-24.9).[12] Three patients were underweight (BMI <18.5), with all 3 having both myosteatosis and sarcopenia. The prevalence of sarcopenia decreased with increasing BMI (prevalence of 81% in patients with BMI ≤24.9 vs prevalence of 43% in patients with BMI ≥30; $P < .006$). There were no significant associations between myosteatosis and obesity based on BMI values (72% vs 83%; $P = .071$),

underlying ASH/NASH etiology (76% vs 69%; P = .50), or comorbid diabetes (79% vs 71%; P = .58).

Clinical significance of skeletal muscle abnormalities

Table 4 details the clinical significance of skeletal muscle abnormalities. Of 89 patients, the median length of stay in hospital censored for death was 18 days (95% CI, 14-21 days). Patients with myosteatosis were hospitalized for 20 days (95% CI, 14-25 days) versus only 14 days in patients without myosteatosis (95% CI, 9-20 days; P = .034). Patients with myosteatosis also spent longer in the ICU (8 days; 95% CI, 7-12) than patients without myosteatosis (7 days; 95%, CI, 6-9 days; P = .041). Neither sarcopenia nor sarcopenic obesity was associated with longer median lengths of hospital or ICU stay. The cost of hospital stay did not vary significantly in those with myosteatosis (P = .29), sarcopenia (P = .86), or sarcopenic obesity (P = .42) compared with patients without the corresponding body composition abnormalities.

Table 3. Univariate Analysis of Variables Affecting 1-Year Patient and Graft Survival in Liver Transplant Recipients

	HR for Death at 1 Year	95% CI	*P* Value	HR for Graft Failure at 1 Year	95% CI	*P* Value
No myosteatosis	1.00			1.00		
Myosteatosis	3.34	1.00-11.13	.049	4.08	1.24-13.45	.021
No sarcopenia	1.00			1.00		
Sarcopenia	2.64	0.99-7.00	.051	1.63	0.73-3.67	.24
No sarcopenic obesity	1.00			1.00		
Sarcopenic obesity	1.23	0.56-2.71	.61	1.12	0.53-2.36	.76
Age group						
18-34 years	1.00			1.00		
35-49 years	0.40	0.12-1.30	.13	0.71	0.25-2.04	.52
50-64 years	0.63	0.24-1.69	.36	0.69	0.26-1.82	.45
≥65 years	0.67	0.17-2.70	.58	0.67	0.17-2.70	.58
Sex						
Male	1.00			1.00		
Female	1.30	0.60-2.82	.50	1.11	0.54-2.29	.77
Population group						
White	1.00			1.00		
Black-African	2.22	0.93-5.29	.072	1.99	0.89-4.46	.10
Indian/Asian/Mixed	1.70	0.56-5.19	.35	1.33	0.45-3.97	.61
Indication for transplant						
Other	1.00			1.00		
ASH/NASH	0.49	0.20-1.21	.12	0.48	0.21-1.13	.092
BMI						
<25	1.00			1.00		
25.0-29.9	1.15	0.51-2.61	.74	1.11	0.51-2.44	.79
≥30	0.35	0.10-1.26	.11	0.56	0.20-1.58	.27
Diabetes mellitus						
No	1.00			1.00		
Yes	1.69	0.71-4.02	0.24	1.34	0.58-3.14	.49
MELD score						
>15	1.00			1.00		
≥15	1.16	0.52-2.60	0.72	0.88	0.42-1.83	0.73

Abbreviations: ASH/NASH, alcoholic/nonalcoholic steatohepatitis; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HR, hazard ratio; MELD, Model for End-Stage Liver Disease

Table 4. Outcomes of Liver Transplant Recipients: Length of Stay in Hospital and Intensive Care Unit and Overall Cost of Hospital Stay

	Length of Stay in Hospital. d			Length of Stay in ICU, d			Cost, 1000 Rands*		
	Median Stay	95% CI	*P* Value	Median Stay	95% CI	*P* Value	Mean Cost	95% CI	*P* Value
Myosteatosis									
Yes (n = 76)	20	14-25	.034	8	7-12	.041	787	632-979	.29
No (n = 30)	14	9-20		7	6-9		571	326-1000	
Sarcopenia									
Yes (n = 69)	18	13-23	.40	8	3-13	.13	749	586-957	.86
No (n = 37)	16	12-20		8	6-10		716	461-1111	
Sarcopenic obesity									
Yes (n = 36)	15	10-20	.64	7	2-12	.82	633	395-1016	.42
No (n = 70)	18	14-22		8	4-12		789	612-1017	

Abbreviations: ICU, intensive care unit

*Evaluated at 2018 levels.

Of the total 106 patients, 45 (42%) experienced at least 1 surgical postoperative complication. Most of these (36/45, 80%) occurred within 90 days of transplant. Morbidity overall included 24 patients with a biliary stricture or leak (23%), 21 patients requiring re-exploratory laparotomy (20%), and 19 patients with a vascular complication (18%, most commonly hepatic artery thrombosis in 9/19 patients). As described in Table 5, no significant associations between myosteatosis (P = .083), sarcopenia (P = .51), or sarcopenic obesity (P = .088) and complications occurring within 90 days of LT were found. Similarly, no significant associations between myosteatosis (P = .13), sarcopenia (P = .77), or sarcopenic obesity (P = .10) and overall complications were found.

Table 5. Complications Within 90 Days and Overall in Liver Transplant Recipients

	Yes	No	*P* Value	RR	95% CI for RR
		Myosteatosis			
Complications* at 90 days, No. (%)					
Yes	30 (39)	6 (20)	.083	1.97	0.92-4.25
No	46 (61)	24 (80)		1.00	
Complications overall, No. (%)					
Yes	36 (47)	9 (30)	.13	1.58	0.87-2.86
No	40 (53)	21 (70)		1.00	
		Sarcopenia			
Complications at 90 days, No. (%)					
Yes	25 (36)	11 (30)	.51	1.22	0.68-2.19
No	44 (64)	26 (70)		1.00	
Complications overall, No. (%)					
Yes	30 (43)	15 (41)	.77	1.07	0.67-1.72
No	39 (57)	22 (59)		1.00	
		Sarcopenic obesity			
Complications at 90 days, No. (%)					
Yes	8 (22)	28 (40)	.088	0.56	0.28-1.09
No	28 (78)	42 (60)		1.00	
Complications overall, No. (%)					
Yes	11 (31)	34 (49)	.10	0.63	0.36-1.09
No	25 (69)	36 (51)		1.00	

Abbreviations: RR, relative risk

*Include surgical re-exploration, vascular complications, and/or biliary complications.

Discussion

Patients requiring LT are often severely ill, and the elucidation of objective criteria that can assist in optimizing utilization of this scarce resource may assist clinicians. Sarcopenia is a well-studied risk factor for poor outcomes after LT, but the prevalence and consequences of myosteatosis and sarcopenic obesity in the transplant setting have not been well elucidated. To our knowledge, this is the first study describing these muscle abnormalities and their associations in a South African LT recipient population.

In the present study, muscle abnormalities were frequent, with myosteatosis seen in over 70% of our patients, sarcopenia seen in 65%, and sarcopenic obesity seen in 34%. Myosteatosis is emerging as a significant, and possibly better, correlate of outcome than sarcopenia in LT recipients. In many studies, as well as our own, its incidence is higher than that of sarcopenia.[11,15] There were proportionately more women with myosteatosis in our study group, an association that has been previously described.[15] The presence of myosteatosis appears to increase length of both hospital and ICU stay; however, further studies are needed as the published literature on this is contradictory. Some authors have reported a significant association with prolonged and consequent increased cost of stay, whereas others have only reported an association with longer length of ICU stay.[11,16] We observed that patients with myosteatosis spent an average of 6 days longer in the hospital and 1 day longer in the ICU than those without myosteatosis. Similar associations between sarcopenia and length of hospital or ICU stay were not noted. In addition, no significant associations between body composition abnormalities and cost of hospital stay were observed.

This study described, using univariate modeling only, that both low-quantity muscle mass (sarcopenia) and low-quality fat-infiltrated muscle (myosteatosis) were factors influencing mortality in patients with end-stage liver disease 1 year after LT. The risk of death was 2.5 to 3 times higher in those with sarcopenia or myosteatosis than in those without muscle abnormalities. Importantly, the prognostic value of myosteatosis was better than that of sarcopenia in predicting patient survival as well as length of hospital and ICU stay and allograft survival. In our study, none of the 3 muscle measures were predictive of complications or costs; we also found that sarcopenic obesity was not significantly associated with poor survival outcomes.

Our findings concurred with prior publications identifying myosteatosis as a risk factor for allograft dysfunction and mortality.[11,22] Notably, in our study, myosteatosis was a more significant risk factor for mortality than sarcopenia. Our results are consistent with those of Czigany and colleagues who measured

myosteatosis by the same technique and described its superiority over sarcopenia in predicting poor perioperative outcomes, including mortality.[16] It is postulated that intramuscular fat accumulation disrupts the architecture and alignment of muscle fibrils weakening their mechanical action. In addition, immunity is impaired and oxidative stress is worsened by local proinflammatory cytokines and adipokines, which together all seem to predispose to increased complications and mortality.[23,24] The reasons why myosteatosis might predispose to a worse outcome over sarcopenia have not yet been established. Interorgan crosstalk between muscle and the liver via myokines, such as myostatin, promotes liver inflammation and worsens muscle atrophy in patients with body composition abnormalities.[23] Further studies on these crosstalk mechanisms may help to explain the differing effects of myosteatosis and sarcopenia.

There are limitations to our study. Although many patients received LT at Wits Donald Gordon Medical Centre, only a small subset had suitable CT imaging available for review. It is possible that only those with an adverse clinical course were referred for imaging, leading to a selection bias for only the most ill patients. The consequent small sample size, from a single center, may not represent the entire LT recipient population. The prevalence of muscle abnormalities may be lower in a more representative sample. Furthermore, there is growing recognition that muscle wasting is one part of a multidimensional frailty syndrome, requiring functional assessment of muscle strength and physical performance in addition to measures of muscle quantity or quality.[25,26] Because of the retrospective nature of this study, data on measures such as grip strength or gait speed were not available. Lastly, the conclusions are based on univariate analysis only.

This study however serves as a primary analysis of muscle abnormalities in a diverse South African LT recipient population. The findings highlighted the clinical relevance of identifying both myosteatosis and sarcopenia in pre-LT assessment. Nutritional, pharmacological, and exercise interventions, such as branch chain amino acid supplementation, testosterone supplementation, minimization of immunosuppression, and physical resistance training, aim to prevent fatty infiltration and wasting of muscle and so may delay functional decline and mortality in these patients.[27-29]

Conclusions

Our study results suggested that both myosteatosis and sarcopenia infer a disproportionately higher risk for mortality at 1 year after LT; however, myosteatosis appears to be the more significant predictor of patient and allograft survival and length of hospital and ICU stay. Further studies are needed to determine the underlying pathological mechanisms accountable for this observation.

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