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Visceral adiposity in cirrhosis: Association with disease severity and impact of liver transplantation

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Abstract

Background: Changes in adipose tissue distribution in liver cirrhosis are poorly characterized and may affect clinical outcomes.

Methods: Adult liver transplant (LT) January 2008–August 2017 recipients with abdominal MRI within 6 months pre-LT were retrospectively assessed. Visceral adipose tissue, subcutaneous adipose tissue, and skeletal muscle area (cm^2) were determined at L3. Visceral-to-subcutaneous adipose tissue ratio (VSR) was used to define relative adipose distribution, stratified by sex. Correlation was tested with Pearson. Body composition measures were compared by Child-Turcotte-Pugh (CTP) class, before and after LT, and evaluated as predictors of clinical outcomes.

Results: A total of 318 patients were studied. Mean age was 56 years, 33.64% were female, and 47.80% had CTP C cirrhosis. CTP C was associated with a 0.42-point increase in VSR compared with CTP A (95% CI = 0.13–0.71, $p < 0.01$), adjusting for age, sex, diabetes, and HCC. Among the 79 (24.84%) patients with repeat MRI 1–2 years after LT, VSR significantly improved from before LT (1.31 vs. 0.95, $p < 0.01$). In adjusted analysis, CTP C was associated with a 0.86-point decrease in post-LT VSR compared with pre-LT VSR (95% CI = −1.27 to −0.44, $p < 0.01$). Body mass index poorly correlated with VSR before and after LT. Elevated pre-LT VSR trended toward an association with a 7.17-point decrease in pre-LT glomerular filtration rate (95% CI = −14.35 to −0.02, $p = 0.05$), adjusting for CTP C, age, sex, diabetes, hypertension, pre-LT sarcopenia, and hepatocellular carcinoma. Elevated pre-LT VSR did not affect 3-year post-LT mortality (log-rank $p = 0.24$).

Conclusions: Poorly represented by body mass index, visceral adiposity is increased in cirrhosis and is associated with CTP class. However, this adipose redistribution may be modifiable by LT.

Abbreviations: AASLD, American Association for the Study of Liver Diseases; BMI, body mass index, CUIMC, Columbia University Irving Medical Center; CTP, Child-Turcotte-Pugh; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; GFR, glomerular filtration rate; IQR, interquartile range; LT, liver transplant; MDRD, Modification of Diet in Renal Disease; MELD, Model for End-stage Liver Disease; Ref, reference; SAT, subcutaneous adipose tissue; SATI, subcutaneous adipose tissue index; SM, skeletal muscle; SMI, skeletal muscle index; VAT, visceral adipose tissue, VATI, visceral adipose tissue index; VSR, visceral-to-subcutaneous adipose tissue ratio.

INTRODUCTION

Obesity and its complications are increasingly common among patients with cirrhosis.[1] Although the epidemic of obesity has had a profound impact on human health, the risks associated with obesity are increasingly thought to be driven by specific adipose compartments, with higher risks associated with increased visceral adiposity specifically.[2] However, we do not currently understand how adipose tissue distribution changes in liver cirrhosis and how visceral adiposity impacts clinical outcomes in this population.

Visceral adipose tissue (VAT), which surrounds the intra-abdominal organs, is distinct from other adipose tissue in its participation in hormonal and immunologic processes.[3] In advanced chronic diseases, such as the human immunodeficiency virus (HIV), chronic obstructive pulmonary disease (COPD), cancer, and congestive heart failure (CHF), VAT is increased despite a catabolic state and is associated with mortality.[4–7] In the general population, increased VAT is also associated with chronic kidney disease.[8] Conversely, subcutaneous adipose tissue (SAT), which is located between the dermis and the muscle fascia, is thought to be more protective.[9]

In patients with cirrhosis, body mass index (BMI) has been widely used to measure obesity,[1,10,11] but BMI poorly reflects total adipose tissue amount and distribution in patients with cirrhosis with portal hypertension, ascites, and sarcopenia.[12] Although some recent studies have sought to more meticulously investigate body composition in cirrhosis using novel imaging techniques,[13–17] several of these failed to adjust measurements for total body size, severity of liver disease, or metabolic factors known to affect body composition. Others used BMI to estimate visceral adiposity when imaging data were not available, leading to inconsistent results.

We performed the largest study to date evaluating body composition in patients with cirrhosis, including both outpatient and inpatients with diverse liver disease etiologies and stages of cirrhosis. We aimed to better characterize how adipose tissue distribution changes at different severities of cirrhosis in relation to other body composition measures and whether liver transplantation (LT) changes or "restores" adipose tissue distribution. We also aimed to evaluate the relationship between BMI and adipose tissue distribution at different severities of cirrhosis and post-LT. Finally, we aimed to determine whether increased visceral adiposity is associated with adverse clinical outcomes.

EXPERIMENTAL PROCEDURES

Adults 18 years of age and older with cirrhosis who underwent LT at Columbia University Irving Medical Center (CUIMC) from 2008 to 2017 were assessed in a retrospective cohort study. Those with abdominal MRIs available for review in the CUIMC picture archiving and communication system within 6 months before LT were included. Patients with dual organ transplant, re-LT, non-hepatocellular carcinoma malignancy, and HIV were excluded. We excluded patients with HIV because the presence of HIV can change body composition regardless of CD4 count or viral load.[18] Although severe stages of COPD and CHF are associated with body composition changes in non–liver disease populations,[4,19] we did not exclude patients with COPD or CHF because all patients underwent LT and did not have severe stages of COPD or CHF that would preclude transplant surgery. All individuals in the final cohort were documented to have cirrhosis based on chart review of explant histopathology reports, clinic notes, or imaging.

Body composition measurements

One MRI within 6 months before LT was reviewed per patient. If multiple MRIs were available before LT, the one closest to transplant was selected. For the subset of patients who also had an MRI within 1–2 years after LT, post-LT imaging was also analyzed. If multiple post-LT MRIs were available, the one closest to 1 year after LT was selected. To minimize the impact of immediate post-LT complications on body composition findings, post-LT MRIs before 1 year were not included.

From the MRI sequences obtained during routine abdominal imaging, we chose the Gradient Recall Echo T1-weighted imaging with opposed-phase/out-of-phase technique given the optimal differentiation between fat and water-containing tissues (ie, bowel, solid abdominal organs, and blood vessels) (Figure 1A).[20,21] The optimal differentiation between adipose and nonadipose tissue in this sequence are due to type 2 MRI chemical shift artifact, which occurs due to difference in proton precession rate in water and fat molecules, resulting in the creation of dark lines (also known as India ink artifact) drawn at the boundary of every vessel bowel muscle and abdominal organ. This artifact optimizes the subcutaneous and visceral fat quantification on axial images.

VAT, SAT, and skeletal muscle (SM) cross-sectional areas were quantified at the L3 vertebral level using semi-automated software adapted for MRI developed by the CUIMC Computational Imaging Analysis Laboratory.[22–24] The segmentation algorithm on MRIs was motivated by the similar algorithm of quantification of body composition on volumetric CT.[23] The algorithm automatically delineates the outer boundary of the body and an inner boundary that separates VAT from SAT on a given slice using a

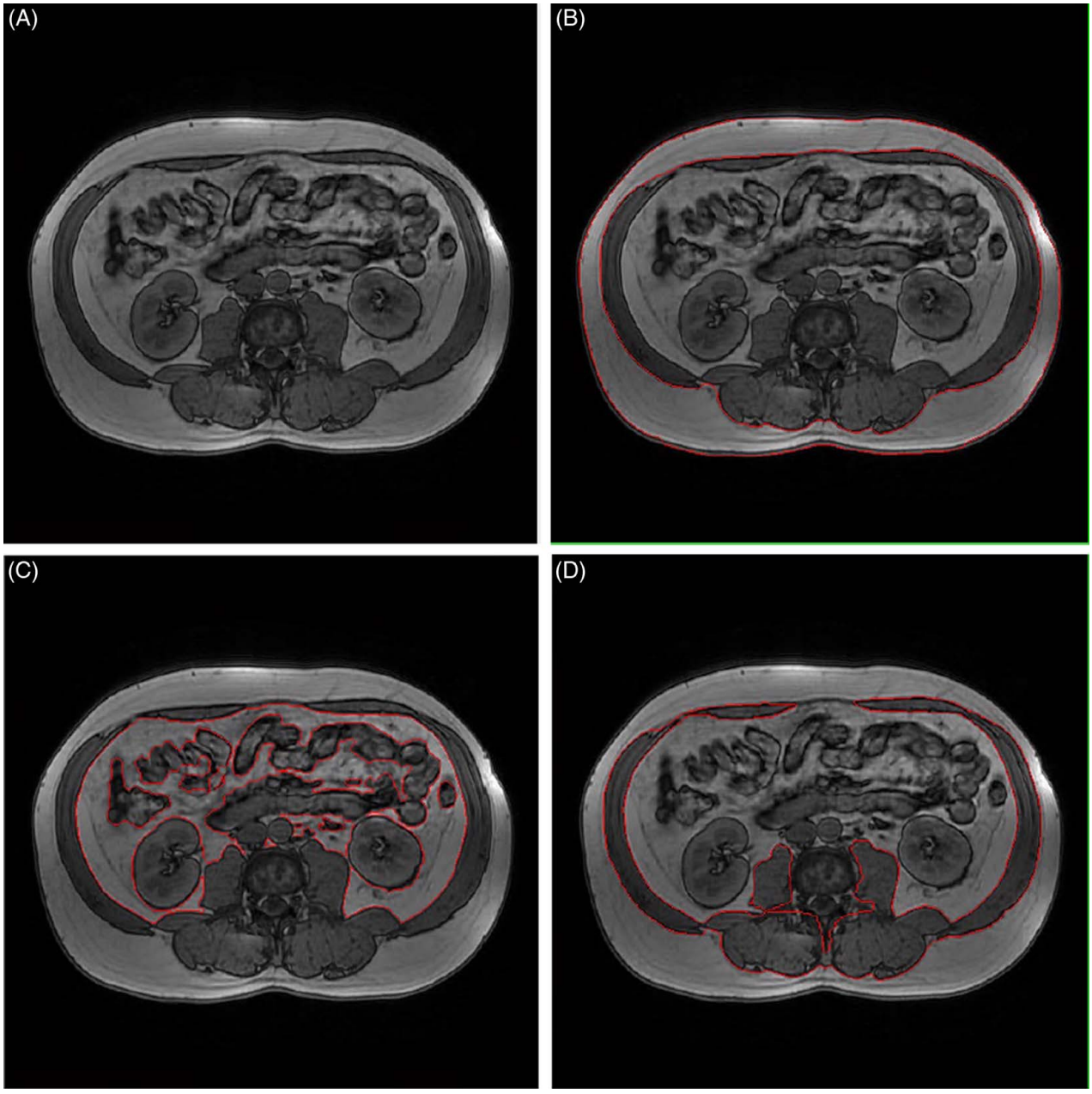

FIGURE 1 (A) MRI without contour. (B) Contour of subcutaneous adipose tissue. (C) Contour of visceral adipose tissue. (D) Contour of skeletal muscle.

combination of global and local region-based active contours.[25,26] Each region of interest is further separated into adipose tissue and nonadipose tissue parts using an adapting thresholding technique supervised by the operator. Each body composition contour was then manually edited by the operator by removing and/or adding sections of contours or adjusting the contour line itself to ensure that each contour properly outlines the body composition compartment of interest. For SAT, the layer between the dermis and aponeurosis and fascia of muscles was outlined (Figure 1B), and for VAT, all adipose tissue within the fascia of the inner boundary of muscles was outlined while removing bowel, bone, and other organs (Figure 1C).[27] For SM, the psoas, paraspinal, and abdominal wall muscles were outlined (Figure 1D).[28] Using this method, the intraclass correlation coefficient was 0.99 (95% CI = 0.989–0.998) for SAT, 0.99 (95% CI = 0.992–0.998) for VAT, and 0.99 (95% CI = 0.985–0.997) for SM cross-sectional areas when comparing different operators including a trained radiologist.

Cross-sectional areas (cm^2) of VAT, SAT, and SM were adjusted for body size by dividing by height^2 (m^2) to generate the visceral adipose tissue index (VATI), subcutaneous adipose tissue index (SATI), and the skeletal muscle index (SMI), respectively. Sarcopenia

was defined as an SMI <39 cm^2/m^2 in women and <50 cm^2/m^2 in men.[28] The visceral-to-subcutaneous adipose tissue ratio (VSR) was used to represent relative adipose tissue distribution, that is, the propensity to store adipose tissue in the visceral compared with the subcutaneous compartment. VSR has been shown to be more strongly predictive of poor outcomes compared with VAT or SAT alone in several studies of both non–liver disease and liver disease groups.[29–33] Elevated pre-LT VSR was defined as a VSR > 0.96 for women and > 1.06 for men, the median VSR for women and men, respectively.

Clinical characteristics

Child-Turcotte-Pugh (CTP) class

Using American Association for the Study of Liver Diseases (AASLD) definitions, we determined the grade of HE (none, 1 point; mild-moderate or grade 1–2, 2 points; and severe or grade 3–4, 3 points) from retrospective chart review of clinical documentation written closest in time before LT.[34] We categorized ascites as none (1 point), mild-moderate or responsive to diuretics (2 points), and severe or diuretic refractory (3 points) based on retrospective chart review of imaging (provided no large-volume paracentesis or dialysis in the week before image) and clinical documentation of diuretic dose and response to diuretic use.[35] We collected bilirubin (< 2 mg/dL, 1 point; 2–3 mg/dL, 2 points; and > 3 mg/dL, 3 points), albumin (> 3.5 g/dL, 1 point; 2.8–3.5 g/dL, 2 points; and <2.8 g/dL, 3 points), and international normalized ratio (< 1.7, 1 point; 1.7–2.2, 2 points; and > 2.2, 3 points) at the time of LT. For each patient, points assigned to each component above were tallied manually to calculate the CTP score.[36]

Other variables

Cardiovascular disease was either the first coronary artery disease event or CHF event after LT. Coronary artery disease events included requiring a left heart catheterization (with or without percutaneous coronary intervention) or coronary artery bypass graft surgery. CHF events included an ejection fraction ≤ 40% on echocardiogram, right heart catheterization confirming CHF, or the requirement of an assist device. Smoking was defined as ever having smoked, including active smoking versus never having smoked, which was obtained from chart review.

Immunosuppression

Our center's immunosuppression protocol includes a calcineurin inhibitor (usually tacrolimus, and cyclosporine if intolerant of tacrolimus), mycophenolate mofetil, and a 6-month steroid taper. In this cohort, all patients were discharged home after LT on tacrolimus except 1 patient who was on cyclosporine. All but 14 individuals were discharged home on mycophenolate mofetil, and all patients were on prednisone in the first 6 months after LT. At 1 year after LT, 46 individuals were still reported to be on prednisone. Therefore, we chose to examine MRI within 1–2 years after LT to avoid influence of high levels of immunosuppression, particularly steroids, in the first 6 months after LT.

Clinical outcomes

The primary outcomes assessed were pre-LT VSR (entire cohort, ie, patients with pre-LT MRI) and change in VSR between pre-LT and post-LT periods (patients with both pre-LT and post-LT MRI) to determine which clinical factors are associated with increased visceral adiposity pre-LT and associated with an improvement in visceral adiposity after transplant, respectively. Secondary clinical outcomes included pre-LT glomerular filtration rate (GFR) calculated with the Modification of Diet in Renal Disease (MDRD) equation[37] and post-LT mortality. Pre-LT GFR, hypertension, and diabetes were determined from data at the time of the pre-LT MRI used for body composition quantification (within 6 mo of LT). Post-LT clinical outcomes were analyzed for all patients with pre-LT MRI. There was no wait-list mortality in this cohort, as all patients underwent LT as a study inclusion criterion.

Statistical approach

Continuous variables that were normally distributed were reported as mean ± SD and compared using the one-way ANOVA test to determine any difference between CTP A, B, and C group means. The Tukey post hoc test was used to identify which pairs of the CTP A, B, and C group means are significantly different. Continuous variables that were skewed were reported as median with interquartile range (IQR). Categorical variables were reported as percentages and were compared with the χ^2 test. Continuous pre-LT and post-LT body composition measures were compared using the paired *t* test or Wilcoxon signed-rank test.

Scatter plots and Pearson correlation were performed comparing BMI and body composition measures. Linear regression was performed to determine predictors of pre-LT VSR, change in VSR defined as post-LT VSR minus pre-LT VSR, and also for pre-LT GFR. Interactions between elevated pre-LT VSR and pre-LT diabetes and between elevated pre-LT VSR and pre-LT sarcopenia were tested for the outcome of pre-LT GFR, but they were not significant. Kaplan-Meier

failure curves with post-LT death as the failure event were compared between patients with elevated pre-LT VSR and those without elevated pre-LT VSR using the log-rank test. Multivariable models were constructed using clinically relevant variables decided a priori for inclusion and also a backward elimination approach with prespecified elimination criteria that was based on level of significance threshold of 0.20. The variables that were a priori selected for inclusion in multivariable models included age, sex, pre-LT diabetes, and HCC for clinical factors associated with increases in pre-LT VSR; age, sex, pre-LT diabetes, pre-LT hypertension, and HCC for clinical factors associated with a decrease in pre-LT GFR; and age and sex for clinical factors associated with a decrease in VSR between pre and post-LT (variables were limited due to lower power). All analyses were performed using Stata 15.1 (StataCorp). This study has been approved by the CUIMC IRB Committee. CUIMC IRB protocol number AAAR5638, initially approved on 9/6/2017. Given the retrospective nature of this study, we received a waiver of informed consent. All authors had access to the study data and reviewed and approved the final manuscript.

RESULTS

Overall, 912 transplants were performed in the study period. Of these, 318 adult LT candidates met inclusion criteria and had a local MRI available for quantification within 6 months of LT. The mean age was 56 years, 33.64% were female, 60.55% had viral hepatitis, and 43.56% had HCC. Overall, 47.80% had CTP class C cirrhosis, and the mean calculated Model for End-stage Liver Disease (MELD) score at LT was 20. The median time from MRI to LT was 1.70 months (IQR: 0.90 mo). The median follow-up time was 4.62 years (IQR: 3.54 y). The range of follow-up was from 95 to 4055 days with only 7 individuals with <365-day follow-up.

Visceral adiposity and liver disease severity

Body composition measures compared by CTP class are summarized in Table 1. VSR was significantly higher in CTP C compared with CTP A (1.47 vs. 1.09, $p < 0.01$) and with CTP B cirrhosis (1.47 vs. 1.03, $p < 0.01$). Similarly, VATI was significantly higher in CTP C compared with CTP B (63.77 vs. 55.32, $p = 0.03$) but not with CTP A (63.77 vs. 59.20, $p = 0.45$). SMI was lower in CTP C compared with CTP A (47.12 vs. 51.82, $p < 0.01$) and with CTP B cirrhosis (47.12 vs. 53.77, $p = 0.03$) (Table 1). There were no significant differences in SATI or BMI among the 3 CTP class groups.

In univariable linear regression analysis, SMI (β coefficient: −0.01, 95% CI −0.02 to −0.006, $p < 0.01$), MELD (β: 0.02, 95% CI = 0.01–0.03, $p < 0.01$), HDL (β: −0.01, 95% CI = 0.013 to −0.002, $p < 0.01$), and CTP C class cirrhosis (β: 0.43, 95% CI 0.17–0.70, $p < 0.01$) were significantly associated with VSR (Table 2). In multivariable linear regression, CTP C cirrhosis was associated with a 0.42-point increase in VSR compared with CTP A cirrhosis (CTP C vs. A: $\beta = 0.42$, 95% CI = 0.13–0.71, $p < 0.01$; CTP B vs. A: $\beta = 0.07$, 95% CI = −0.23 to 0.37, $p = 0.66$), when adjusting for age, female sex, pre-LT diabetes, and HCC (Table 2). SMI did not reach significance in multivariable models adjusting for factors that are known to affect body composition.

Post-LT changes in visceral adiposity

Seventy-nine (24.84%) patients had MRIs available 1–2 years after LT. The mean age was 56 years, 19.28% were female, 61.40% had viral hepatitis, and 59.04% had HCC. The median time from LT to post-LT MRI was 14.97 months (IQR: 2.04 mo). Compared with patients without a post-LT MRI, patients with a post-LT MRI were more likely to be male (79.82 vs. 59.35%, $p < 0.01$), have HCC (61.40% vs. 33.80%, $P < 0.01$), have CTP A cirrhosis (CTP A: 32.73 vs. 13.40%, CTP B: 26.36% vs. 34.93%, CTP C 40.91% vs. 51.67%, $p < 0.01$), and a lower average MELD score at LT (17.50 vs. 20, $p < 0.01$).

Mean VSR significantly improved from pre-LT to post-LT (1.31 ± 0.11 vs. 0.95 ± 0.05, $p < 0.01$). In addition, pre-LT VATI was higher than post-LT VATI (62.52 ± 25.64 vs. 56.98 ± 25.85, $p = 0.03$). However, there were no significant differences between pre-LT and post-LT BMI, SMI, or SATI.

These body composition changes from pre-LT to post-LT periods were most striking among patients with CTP C cirrhosis at LT (n = 31). In patients with CTP C cirrhosis, VSR significantly decreased (1.78 ± 0.26 vs. 0.99 ± 0.09, $p < 0.01$), VATI decreased (71.55 ± 21.84 vs. 56.86 ± 26.74, $p < 0.01$), and SATI increased (59.24 ± 37.78 vs. 72.49 ± 35.05, $p = 0.04$) from pre-LT to post-LT (Figure 2). On the contrary, VSR did not significantly change before and after LT in CTP A (1.06 ± 0.12 vs. 0.98 ± 0.10, $p = 0.13$) or B cirrhosis (0.96 ± 0.07 vs. 0.99 ± 0.09, $p = 0.78$), nor did VATI or SATI. In univariable linear regression analysis, MELD score (β = −0.03, 95% CI = −0.06 to −0.01, $p < 0.01$) and CTP C (CTP C vs. A: $\beta = -0.81$, 95% CI = −1.22 to −0.41, $p < 0.01$; CTP B vs. A: β = 0.11, 95% CI = −0.34 to 0.56, $p = 0.62$) were associated with a decrease in post-LT VSR from pre-LT VSR. When adjusting for age ($\beta = 0.004$, 95% CI = −0.01–0.02, $p = 0.67$) and female sex ($\beta = 0.35$, 95% CI

TABLE 1 Patient characteristics by CTP class

Variables	n (%) CTP class A (N = 64)	CTP class B (N = 102)	CTP class C (N = 152)	*p*
Demographic characteristics				
Age (mean ± SD) (y)	59.45 ± 9.52	56.30 ± 12.53	55.72 ± 11.22	0.06
Female sex	14 (21.88)	37 (36.27)	56 (36.84)	0.08
Race				0.24
White	33 (51.56)	54 (52.94)	88 (57.89)	
Black	5 (7.81)	10 (9.80)	14 (9.21)	
Asian/Pacific Islander	11 (17.19)	11 (10.78)	8 (5.26)	
Other/multiracial	15 (23.44)	27 (26.47)	8 (27.63)	
Hispanic ethnicity	13 (20.31)	22 (21.78)	35 (23.33)	0.90
Liver disease etiology				
Alcohol-associated liver disease	3 (4.69)	13 (12.75)	25 (16.45)	
Viral hepatitis	51 (79.69)	56 (54.90)	87 (57.24)	
NAFLD or cryptogenic	4 (6.25)	7 (6.86)	15 (9.87)	0.021
Autoimmune liver disease	4 (6.25)	22 (21.57)	23 (15.13)	
Other	2 (3.12)	4 (3.92)	2 (1.32)	
MELD [median (IQR)]	10 (5)	17 (3)[c]	23 (4)[ab]	< 0.01
HCC	43 (67.19)	48 (47.06)[c]	48 (31.79)[a,b]	< 0.01
Ascites	4 (6.25)	42 (41.18)[c]	126 (82.98)[a,b]	< 0.01
Encephalopathy	3 (4.69)	48 (47.06)[c]	118 (77.63)[a,b]	< 0.01
Varices	23 (46.00)	67 (72.83)[c]	113 (85.61)[a,b]	< 0.01
Pre-LT metabolic factors				
Diabetes	13 (22.03)	27 (28.42)	37 (25.87)	0.68
Hypertension	28 (44.44)	39 (38.61)	54 (35.76)	0.49
Triglycerides (mean ± SD) (mg/dL)	114.72 ± 65.00	123.73 ± 113.14	106.49 ± 64.73	0.38
HDL (mean ± SD) (mg/dL)	45.13 ± 14.11	42.89 ± 24.89	29.38 ± 22.55[a,b]	< 0.01
GFR ≤ 60 (mL/min/1.73 m^2)	5 (7.81)	16 (15.84)	54 (35.76)[a,b]	< 0.01
Cardiovascular disease	4 (6.25)	5 (4.90)	18 (11.84)	0.12
Smoking	36 (56.25)	46 (45.10)	75 (49.34)	0.38
Pre-LT body composition				
Visceral adipose tissue cross-sectional area/height^2 (mean ± SD) (cm^2/m^2)	59.20 ± 28.23	55.32 ± 24.21	63.77 ± 25.22[b]	0.03
Subcutaneous adipose tissue cross-sectional area/height^2 (mean ± SD) (cm^2/m^2)	63.89 ± 34.55	55.87 ± 26.04	59.48 ± 35.10	0.30
VSR (mean ± SD)	1.03 ± 0.52	1.09 ± 0.52	1.47 ± 1.19[a,b]	< 0.01
Elevated VSR	21 (13.29)	48 (30.38)	89 (56.33)	< 0.01
Skeletal muscle/height^2 (mean ± SD) (cm^2/m^2)	53.77 ± 10.35	51.82 ± 19.25	47.12 ± 10.93[a,b]	< 0.01
Body mass index (mean ± SD) (kg/m^2)	27.67 ± 5.34	27.85 ± 5.83	27.84 ± 5.89	0.98

[a]Comparison between CTP C and A class cirrhosis was significant ($p < 0.05$).
[b]Comparison between CTP C and B class cirrhosis was significant ($p < 0.05$).
[c]Comparison between CTP B and A class cirrhosis was significant ($p < 0.05$).
Abbreviations: CTP, Child-Turcotte-Pugh; GFR, glomerular filtration rate; IQR, interquartile range; LT, liver transplant; MELD, Model for End-stage Liver Disease; VSR, visceral-to-subcutaneous adipose tissue ratio.

= −0.09 to 0.79, $p = 0.12$), patients with CTP C cirrhosis compared with CTP A cirrhosis had a 0.86-point decrease in post-LT VSR from pre-LT VSR (CTP C vs. A: $\beta = -0.86$,95% CI = −1.27 to −0.44, $p < 0.01$; CTP B vs. A: $\beta = 0.09$, 95% CI = −0.37 to 0.56, $p = 0.69$).

Lack of correlation between BMI and VSR before or after LT

There were no significant differences in pre-LT BMI among the 3 CTP groups. There was a poor correlation between BMI and pre-LT VSR in CTP class A

TABLE 2 Clinical factors associated with elevated pre-LT visceral-to-subcutaneous adipose tissue ratio—linear regression

	Univariable linear regression			Multivariable linear regression		
Variables	**β coefficient**	**95% CI**	***p***	**β coefficient**	**95% CI**	***p***
CTP class						
A	Ref	Ref	Ref	Ref	Ref	Ref
B	0.05	−0.23 to 0.34	0.72	0.07	−0.23 to 0.37	0.66
C	0.43	0.17–0.70	< 0.01	0.42	0.13–0.71	< 0.01
Age (y)	0.01	−0.01 to 0.01	0.56	0.01	−0.004 to 0.02	0.23
Female sex	−0.18	−0.39 to 0.02	0.08	−0.32	−0.56 to −0.09	< 0.01
Pre-LT diabetes	−0.06	−0.30 to 0.18	0.62	−0.12	−0.37 to 0.12	0.33
HCC	−0.17	−0.37 to 0.03	0.10	−0.22	−0.47 to 0.02	0.08

Abbreviations: CTP, Child-Turcotte-Pugh; LT, liver transplant; Ref, reference.

(r = −0.07, p = 0.58), CTP class B (r = −0.01, p = 0.95), and CTP class C (r = −0.14, p = 0.08) cirrhosis (Figure 3A). Similarly, there was a poor correlation between BMI and post-LT VSR (r = −1.13, p = 0.24) (Figure 3B).

Association between pre-LT visceral adiposity and clinical outcomes

We then analyzed the association between pre-LT VSR and clinical outcomes before and after LT. As all patients in this cohort successfully underwent transplant, and given associations in the literature between VSR and CKD,[8] the pre-LT clinical analysis focused on kidney function. In multivariable linear regression, elevated pre-LT VSR trended toward a significant association with a 7.17-point decrease in pre-LT GFR (β = −7.17, 95% CI = −14.35 to −0.02, p = 0.05), adjusting for CTP class, age at LT, female sex, pre-LT diabetes, pre-LT hypertension, sarcopenia, and HCC (Table 3).

We also evaluated the impact of pre-LT VSR on post-LT mortality. There were 18 (5.7%) deaths after LT during the study follow-up. There was 1 death in the first year after LT and 7 deaths within 3 years after LT. In Kaplan-Meier analysis, there was no difference in 3-year post-LT mortality between patients with elevated pre-LT VSR and those without (log-rank p = 0.24). There was also no association between pre-LT sarcopenia and 3-year post-LT mortality (log-rank p = 0.41) and for pre-LT sarcopenic obesity (log-rank p = 0.48) when combining our definition of elevated VSR and sarcopenia. In additional Kaplan-Meier analysis, there was also no difference for post-LT mortality during the total study follow-up (log-rank p = 0.28). Of the patients who had a repeat MRI at 1–2 years after LT, there were 2 deaths, and therefore, we were not able to perform Kaplan-Meier analysis. We additionally did not see significant differences when comparing those with elevated pre-LT VSR and those without for additional post-LT outcomes including acute cellular rejection (11.39% vs. 20.38%), post-LT infection (39.24% vs. 44.38%), any cardiac events after LT (8.23% vs. 8.75%), need for re-operation after LT (27.85% vs. 28.75%), and HCC recurrence after LT (4.71% vs. 3.00%).

DISCUSSION

In this study, we demonstrate that adipose tissue redistribution to the visceral compartment, as measured by an increase in VAT relative to SAT, occurs in patients with advanced cirrhosis. This elevation in VSR is strongly associated with CTP class C cirrhosis and improves after LT in those who had CTP class C cirrhosis. Importantly, BMI does not correlate with these changes in body composition both before and after LT. We did not see a relationship between elevated VSR on post-LT mortality, possibly due to the small number of deaths.

CTP C cirrhosis was associated with a 0.42-point increase in pre-LT VSR compared with CTP class A, after adjusting for age, sex, pre-LT diabetes, and HCC, which are factors known to be associated with body composition changes. Although we saw an increase in visceral adiposity in CTP C versus A, we did not see a difference between CTP B and A, suggesting that advanced cirrhosis has a predisposition to accumulating visceral adiposity compared with milder forms. Our results support prior literature in which adipose tissue accumulates preferentially in the visceral compartment in the end stages of several severe chronic diseases, including cancer, HIV (not only severe stages), COPD, and CHF.[4,6,7,38] One prior study of patients with cirrhosis showed that visceral fat area was increased in CTP B/C compared with CTP A, but fat area was not adjusted for body size, leading to risk for misclassification.[39] A possible mechanism to explain increased VSR in advanced cirrhosis could be that systemic inflammation leads to the selective hypertrophy of VAT,[40] and in turn, the preferential accumulation of VAT relative to SAT may contribute further to systemic inflammation through the

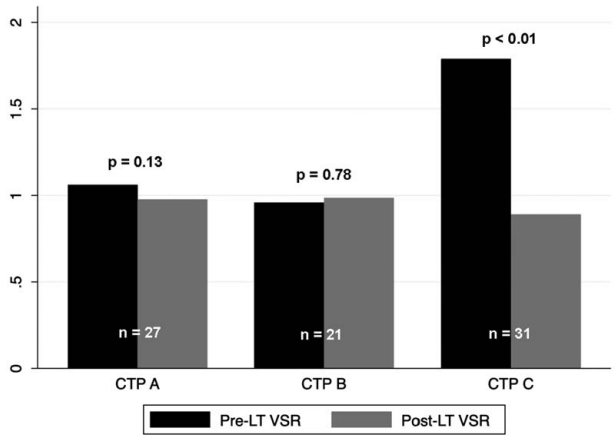

FIGURE 2 Improvement in VSR from pre-LT to post-LT by CTP class. Abbreviations: CTP, Child-Turcotte-Pugh; LT, liver transplant; VSR, visceral-to-subcutaneous adipose tissue ratio.

secretion of inflammatory cytokines and adipokines.[3] In addition, increased intestinal permeability and changes in fecal microbiome in severe illness have also been associated with the accumulation of visceral adiposity.[41]

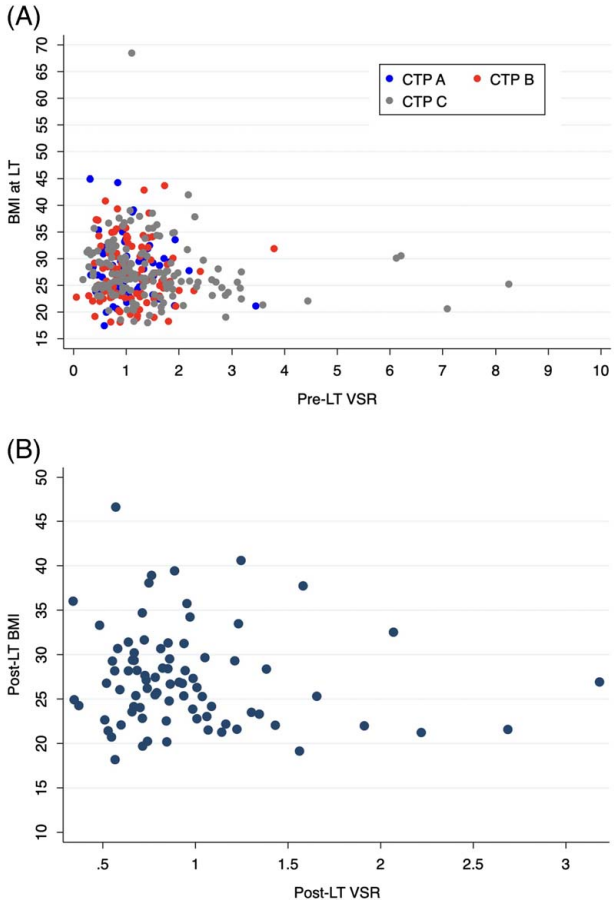

FIGURE 3 (A) Scatter plots comparing pre-LT BMI and pre-LT VSR by CTP class. (B) Scatter plot comparing post-LT BMI and post-LT VSR. Abbreviations: BMI, body mass index; CTP, Child-Turcotte-Pugh; LT, liver transplant; VSR, visceral-to-subcutaneous adipose tissue ratio.

Prospective studies are needed to elucidate whether increased visceral adiposity is a risk for or a consequence of advanced cirrhosis.

We also show that VSR improves within 1–2 years after LT in those with CTP class C cirrhosis, who have the most severe pre-LT elevations in visceral adiposity. We did not see improvements in SMI after LT. To our knowledge, ours is the first study to characterize changes in visceral adiposity after LT. Despite significant exposure to steroids and other immunosuppressive agents with known metabolic adverse effects, significant improvements in visceral adiposity are seen 1–2 years after transplant with restoration of liver function even among those with the most severely decompensated disease. This suggests that severe hepatic dysfunction may play a role in the tendency to accumulate VAT. Our results are consistent with findings of improved visceral adiposity as early as 6 months after TIPS placement, suggesting that adipose tissue distribution is dynamic and could change more quickly than muscle.[14] Future studies are needed to confirm our findings and determine whether an improvement of visceral adiposity after LT shown in this study improves risk of death and other adverse outcomes.

Prior studies in liver disease have examined VAT and SAT areas as absolute values alone.[14,15,32,39,42–44] However, absolute quantities of any given adipose tissue depot such as VAT or SAT alone do not reflect relative distributions in the body, making it difficult to tell whether the observed associations between absolute quantities and adverse liver disease outcomes in these studies are due to a certain pattern of adipose tissue distribution or due to changes in total body adipose tissue. For example, increased VAT alone could reflect either increased total body adipose tissue or increased distribution to the visceral compartment relative to other compartments. In addition, several prior studies did not adjust VAT area for individual body size (ie, dividing by height-squared),[14,15,39,42] resulting in a risk for misclassification of visceral obesity. In our study, we used VSR, which is able to distinguish between the two by representing the propensity to accumulate adipose tissue in the harmful visceral compartment relative to the protective subcutaneous compartment.[29] Moreover, VSR has been more strongly associated with poor outcomes compared with VAT or SAT alone in the general adult population[29–31] and in patients with liver disease.[17,29–33]

Another important finding in this study is the lack of association between BMI and VSR or other body composition measures. While limited prior work has demonstrated that there is a weak correlation between VATI and BMI in patients with cirrhosis,[1] we are able to demonstrate that BMI also poorly correlates with VSR in each CTP class separately, even in compensated patients with CTP A cirrhosis, and also poorly correlates

TABLE 3 Clinical factors associated with pre-LT estimated GFR—linear regression

	Univariable linear regression			Multivariable linear regression		
Variables	**β coefficient**	**95% CI**	***p***	**β coefficient**	**95% CI**	***p***
Elevated VSR	−13.06	−21.47 to −4.65	<0.01	−7.17	−14.35 to −0.02	0.05
CTP class						
A	Ref	Ref	Ref	Ref	Ref	Ref
B	13.15	1.50–24.81	0.03	9.72	−0.44 to 19.88	0.06
C	−9.87	−20.75 to 1.01	0.08	−8.79	−18.61 to 1.03	0.08
Age at LT	−1.40	−1.74 to −1.06	<0.01	−1.28	−1.63 to −0.93	<0.01
Female sex	−7.71	−16.71 to 1.28	0.09	−4.19	−12.22 to 3.84	0.31
Pre-LT diabetes	−0.78	−9.89 to 8.34	0.87	4.95	−3.26 to 13.16	0.24
Pre-LT hypertension	−2.72	−10.70 to 5.25	0.50	0.96	−6.47 to 8.38	0.80
Sarcopenia	5.26	−3.30 to 13.82	0.23	2.10	−5.31 to 9.52	0.58
HCC	0.79	−7.82 to 9.40	0.86	9.27	1.09–17.46	0.03

Abbreviations: CTP, Child-Turcotte-Pugh; GFR, glomerular filtration rate; LT, liver transplant; Ref, reference; VSR visceral-to-subcutaneous adipose tissue ratio.

with VSR even 1–2 years after LT. Given that BMI does not represent adipose tissue distribution before or after LT, prior studies that have used BMI may have misclassified elevated adipose tissue.[1,10,11,15] Some studies have used bioelectrical impedance analysis to approximate adipose tissue; however, this assumes a fixed water mass derived from healthy adults, which is violated in populations with volume overload, including those with cirrhosis, leading to inaccurate measurements.[12,16] Instead, cross-sectional imaging using CT or MRI is the gold standard to more accurately measure abdominal adipose tissue distribution and is not affected by volume overload, sarcopenia, and osteopenia, which are common in patients with cirrhosis. We propose that BMI should no longer be used to estimate adipose tissue in patients with cirrhosis and post-LT patients, and efforts should be made to develop accurate and cost-effective tools that are able to approximate adipose tissue distribution in these patients.

In Kaplan-Meier analysis, pre-LT elevated VSR was not associated with 3-year post-LT mortality, though there were few deaths even at this long-term time point (n = 7). Prior evidence is conflicting regarding the impact of pre-LT body composition on post-LT mortality.[13,15,17]. Our study differs from the study by Ha and colleagues in that their cohort was sicker hospitalized patients needing urgent LT largely with CTP C cirrhosis and high MELD, whereas our cohort included a proportion of CTP A cirrhosis and outpatients. The study by Engelmann et al[13] included a larger cohort (n = 612), comprising mostly CTP B/C individuals, suggesting that visceral adiposity could be significant in more advanced cirrhosis. The study by Kamo et al[15] was limited to living donor transplants but did not adjust VAT area for body size, resulting in a risk for misclassification. As a result, a larger multicenter cohort is needed that includes enough power to better understand the effects of pre-LT visceral adiposity on post-LT mortality at varying stages of cirrhosis, and whether improvement in visceral adiposity post-LT can modify risk of post-LT death. In exploratory analyses, we also found no association between pre-LT sarcopenia or sarcopenic obesity and 3-year post-LT mortality. Ha et al[17] also did not find an association for pre-LT sarcopenia alone but did show an association between pre-LT sarcopenic obesity and post-LT mortality in its acutely ill hospitalized cohort. These differences suggest that there could be differences in effects of visceral obesity and sarcopenia at varying severity of cirrhosis, but larger studies are needed as the relationship between sarcopenia and visceral obesity is still unknown. Finally, in the pre-LT setting, elevated VSR trended toward a significant association ($p = 0.50$) with decrease in GFR. Increased inflammation, kidney structural changes, and increased capillary pressures related to visceral adiposity could help explain this observed association.[45,46]

There are several limitations in this study. Pre-LT body composition measurements were taken at 1 time point, and thus, change in body composition over time before LT was not available. The retrospective, single-center design of this study and limitation to only on-campus MRIs introduce potential selection bias, but our VSR,[17] VATI,[43] SATI,[32] and SMI[28] values are similar to other studies of patients with cirrhosis. For patients listed for LT, our center requires cross-sectional imaging, preferably MRI; however, patients may obtain MRIs locally, require CT scans instead of MRI due to intolerance or contraindications, have insurance barriers to MRI, or had their MRI before 6 months of LT. For this study, it was out of scope to obtain the images of locally performed MRIs, but future directions will be to study a larger cohort to try to minimize selection bias. We did not have enough patients in this cohort to allow for stratification by sex when comparing by CTP class, but to address this issue, we controlled for sex in all

regression models and created sex-specific cutoffs for elevated VSR. Even after adjusting for sex, CTP class C cirrhosis remained associated with increased visceral adiposity before LT and improvement in VSR after LT. We did not collect immunosuppression doses and reasons for deviations from our post-LT immunosuppression protocol. We did not have enough power in our post-LT analyses to adjust for immunosuppression (particularly prolonged steroid use beyond 6 mo); however, we aim to conduct a larger future study to understand how changes in immunosuppression could affect body composition. In addition, given our study design, we were unable to determine causality, whether liver decompensation causes increased visceral adiposity or vice versa. Finally, this study lacks power to determine the effect of increased pre-LT and post-LT visceral adiposity on post-LT mortality, as there were only 18 deaths in the entire cohort.

In conclusion, we demonstrate that visceral adiposity is increased in severe cirrhosis independent of known risk factors for VAT accumulation, highlighting a potential link between the severity of liver disease and the redistribution of adipose tissue to the visceral compartment. Visceral adiposity improves after LT in those with CTP class C cirrhosis, further suggesting that restoration of liver function with LT could modify the deleterious body composition changes that occur in advanced cirrhosis. In addition, BMI does not accurately represent adipose tissue distribution even in those with compensated cirrhosis (CTP A) and after LT. We are also able to show that increased visceral adiposity in the pre-LT setting trends toward an association with decreased GFR, controlling for liver disease severity. These data highlight the ongoing need to refine our metrics of obesity when studying and caring for patients with cirrhosis, with a more specific focus on the pathogenesis of visceral fat accumulation in those with advanced disease. These findings are especially important as obesity becomes more common and NAFLD is among the most common indications for LT.

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CONFLICTS OF INTEREST

Rajani Sharma is on the advisory board for Takeda and has consulted for Takeda. Elizabeth C. Verna is on the Gilead advisory board and receives Salix research support. This study did not receive any support from these organizations, and these organizations did not have a role in the design and conduct of the study. The remaining authors have no conflicts to report.

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REFERENCES

1. Nair S, Verma S, Thuluvath PJ. Obesity and its effect on survival in patients undergoing orthotopic liver transplantation in the United States. Hepatology. 2002;35:105–9.
2. Pou KM, Massaro JM, Hoffmann U, Lieb K, Vasan RS, O'Donnell CJ, et al. Patterns of abdominal fat distribution: the Framingham Heart Study. Diabetes Care. 2009;32:481–5.
3. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. J Clin Endocrinol Metab. 2004;89:2548–56.
4. Furutate R, Ishii T, Wakabayashi R, Motegi T, Yamada K, Gemma A, et al. Excessive visceral fat accumulation in advanced chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2011;6:423–30.
5. Koutkia P, Meininger G, Canavan B, Breu J, Grinspoon S. Metabolic regulation of growth hormone by free fatty acids, somatostatin, and ghrelin in HIV-lipodystrophy. Am J Physiol Endocrinol Metab. 2004;286:E296–303.
6. Cicoira M, Kalra PR, Anker SD. Growth hormone resistance in chronic heart failure and its therapeutic implications. J Card Fail. 2003;9:219–26.
7. Cohn SH, Gartenhaus W, Sawitsky A, Rai K, Zanzi I, Vaswani A, et al. Compartmental body composition of cancer patients by measurement of total body nitrogen, potassium, and water. Metab Clin Exp. 1981;30:222–9.
8. Madero M, Katz R, Murphy R, Newman A, Patel K, Ix J, et al. Comparison between different measures of body fat with kidney function decline and incident CKD. Clin J Am Soc Nephrol. 2017;12:893–903.
9. Porter SA, Massaro JM, Hoffmann U, Vasan RS, O'Donnel CJ, Fox CS. Abdominal subcutaneous adipose tissue: a protective fat depot ? . Diabetes Care. 2009;32:1068–75.
10. Leonard J, Heimbach JK, Malinchoc M, Watt K, Charlton M. The impact of obesity on long-term outcomes in liver transplant recipients—results of the NIDDK liver transplant database. Am J Transplant. 2008;8:667–72.
11. Ortiz V, Berenguer M, Rayón JM, Carrasco D, Berenguer J. Contribution of obesity to hepatitis C-related fibrosis progression. Am J Gastroenterol. 2002;97:2408–14.
12. Burkhauser RV, Cawley J. Beyond BMI: the value of more accurate measures of fatness and obesity in social science research. J Health Econ. 2008;27:519–29.
13. Engelmann C, Aehling NF, Schob S, Nonnenmacher I, Handmann L, Macnaughtan J, et al. Body fat composition determines outcomes before and after liver transplantation in patients with cirrhosis. Hepatol Commun. 2022;6:2198–209.
14. Artru F, Miquet X, Azahaf M, Labreuche J, Ntandja Wandji LC, Sergent G, et al. Consequences of TIPSS placement on the body composition of patients with cirrhosis and severe portal hypertension: a large retrospective CT-based surveillance. Aliment Pharmacol Ther. 2020;52:1516–26.
15. Kamo N, Kaido T, Hamaguchi Y, Okumura S, Kobayashi A, Shirai H, et al. Impact of sarcopenic obesity on outcomes in patients undergoing living donor liver transplantation. Clin Nutr. 2019;38:2202–9.
16. Shida T, Akiyama K, Oh S, Sawai A, Isobe T, Okamoto Y, et al. Skeletal muscle mass to visceral fat area ratio is an important determinant affecting hepatic conditions of non-alcoholic fatty liver disease. J Gastroenterol. 2018;53:535–47.
17. Ha NB, Montano-Loza AJ, Carey EJ, Lin S, Shui AM, Huang C-Y, et al. Sarcopenic visceral obesity is associated with increased post-liver transplant mortality in acutely ill patients with cirrhosis. Am J Transplant. 2022;22:2195–202.
18. Engelson ES, Kotler DP, Tan Y, Agin D, Wang J, Pierson RN, et al. Fat distribution in HIV-infected patients reporting truncal enlargement quantified by whole-body magnetic resonance imaging. Am J Clin Nutr. 1999;69:1162–9.

19. Christensen HM, Kistorp C, Schou M, Keller N, Zerahn B, Frystyk J, et al. Cross-talk between the heart and adipose tissue in cachectic heart failure patients with respect to alterations in body composition: a prospective study. Metab Clin Exp. 2014;63:141–9.
20. Chang JS, Taouli B, Salibi N, Hecht EM, Chin DG, Lee VS. Opposed-phase MRI for fat quantification in fat-water phantoms with 1H MR spectroscopy to resolve ambiguity of fat or water dominance. AJR Am J Roentgenol. 2006;187:W103–6.
21. Shetty AS, Sipe AL, Zulfiqar M, Tsai R, Raptis DA, Raptis CA, et al. In-phase and opposed-phase imaging: applications of chemical shift and magnetic susceptibility in the chest and abdomen. Radiographics. 2019;39:115–35.
22. Shen W, Punyanitya M, Wang Z, Gallagher D, St-Onge M-P, Albu J, et al. Visceral adipose tissue: relations between single-slice areas and total volume. Am J Clin Nutr. 2004;80:271–8.
23. Zhao B, Colville J, Kalaigian J, Curran S, Jiang L, Kijewski P, et al. Automated quantification of body fat distribution on volumetric computed tomography. J Comput Assist Tomogr. 2006;30:777–83.
24. Shen W, Punyanitya M, Wang Z, Gallagher D, St-Onge M-P, Albu J, et al. Total body skeletal muscle and adipose tissue volumes: estimation from a single abdominal cross-sectional image. J Appl Physiol. 2004;97:2333–8.
25. Lankton S, Tannenbaum A. Localizing region-based active contours. IEEE Trans Image Process. 2008;17:2029–39.
26. Chan TF, Vese LA. Active contours without edges. IEEE Trans Image Process. 2001;10:266–77.
27. Shen W, Wang Z, Punyanita M, Lei J, Sinav A, Kral JG, et al. Adipose tissue quantification by imaging methods: a proposed classification. Obes Res. 2003;11:5–16.
28. Carey EJ, Lai JC, Wang CW, Dasarathy S, Lobach I, Montano-Loza AJ, et al. A multicenter study to define sarcopenia in patients with end-stage liver disease. Liver Transpl. 2017;23:625–33.
29. Kaess BM, Pedley A, Massaro JM, Murabito J, Hoffmann U, Fox CS. The ratio of visceral to subcutaneous fat, a metric of body fat distribution, is a unique correlate of cardiometabolic risk. Diabetologia. 2012;55:2622–30.
30. Fujioka S, Matsuzawa Y, Tokunaga K, Tarui S. Contribution of intra-abdominal fat accumulation to the impairment of glucose and lipid metabolism in human obesity. Metab Clin Exp. 1987;36:54–9.
31. Wang Y, Chen F, Wang J, Wang T, Zhang J, Han Q, et al. The relationship between increased ratio of visceral-to-subcutaneous fat area and renal outcome in chinese adults with type 2 diabetes and diabetic kidney disease. Can J Diabetes. 2019;43:415–20.
32. Ebadi M, Tandon P, Moctezuma-Velazquez C, Ghosh S, Baracos VE, Mazurak VC, et al. Low subcutaneous adiposity associates with higher mortality in female patients with cirrhosis. J Hepatol. 2018;69:608–16.
33. Bhanji RA, Narayanan P, Allen AM, Malhi H, Watt KD. Sarcopenia in hiding: the risk and consequence of under-estimating muscle dysfunction in nonalcoholic steatohepatitis. Hepatology. 2017;66:2055–65.
34. Vilstrup H, Amodio P, Bajaj J, Cordoba J, Ferenci P, Mullen KD, et al. Hepatic encephalopathy in chronic liver disease: 2014 Practice Guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. Hepatology. 2014;60:715–35.
35. Biggins SW, Angeli P, Garcia-Tsao G, Ginès P, Ling S, Nadim M, et al. Diagnosis, evaluation, and management of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology. 2021;74:1014–58.
36. Tsoris A, Marlar CA. Use of the Child Pugh score in liver disease. https://www.statpearls.com/ArticleLibrary/viewarticle/19534. StatPearls, Treasure Island (FL): StatPearls Publishing; 2022.
37. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med. 2006;145:247–54.
38. Grinspoon S, Carr A. Cardiovascular risk and body-fat abnormalities in HIV-infected adults. N Engl J Med. 2005;352:48–62.
39. Tapper EB, Zhang P, Garg R, Nault T, Leary K, Krishnamurthy V, et al. Body composition predicts mortality and decompensation in compensated cirrhosis patients: a prospective cohort study. JHEP Rep. 2020;2:100061.
40. Montague CT, O'Rahilly S. The perils of portliness: causes and consequences of visceral adiposity. Diabetes. 2000;49:883–8.
41. Gummesson A, Carlsson LMS, Storlien LH, Bäckhed F, Lundin P, Löfgren L, et al. Intestinal permeability is associated with visceral adiposity in healthy women. Obesity (Silver Spring). 2011;19:2280–2.
42. Feng H, Wang X, Zhao T, Mao L, Hui Y, Fan X, et al. Myopenic obesity determined by visceral fat area strongly predicts long-term mortality in cirrhosis. Clin Nutr. 2021;40:1983–9.
43. Montano-Loza AJ, Mazurak VC, Ebadi M, Meza-Junco J, Sawyer MB, Baracos VE, et al. Visceral adiposity increases risk for hepatocellular carcinoma in male patients with cirrhosis and recurrence after liver transplant. Hepatology. 2018;67:914–23.
44. Montano-Loza AJ, Ebadi M, Tandon P, Mazurak VC. Loss of subcutaneous adipose tissue associates with higher mortality risk in patients with cirrhosis. J Hepatol. 2018;68:S699.
45. França AKTdC, Dos Santos AM, Salgado JV, Hortegal EV, da Silva AAM, Filho NS. Estimated visceral adipose tissue, but not body mass index, is associated with reductions in glomerular filtration rate based on cystatin C in the early stages of chronic kidney disease. Int J Nephrol. 2014;2014:574267.
46. Young JA, Hwang S-J, Sarnak MJ, Hoffmann U, Massaro JM, Levy D, et al. Association of visceral and subcutaneous adiposity with kidney function. Clin J Am Soc Nephrol. 2008;3:1786–91.

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