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Sarcopenia and Fat Mass in Children With Chronic Liver Disease and Its Impact on Liver Transplantation

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ABSTRACT

Background: In adults, weight loss and sarcopenia are prognostic indicators of poor outcomes for patients awaiting liver transplant (LT). We tested the hypothesis that sarcopenia in children awaiting LT was related to poor outcomes.

Methods: Children with end-stage chronic liver disease undergoing assessment for LT were recruited into an observational longitudinal study. Anthropometry and body composition (BC; whole-body dual-energy x-ray absorptiometry scan) were assessed before and, on average, 1 year after LT.

Results: Eleven children (6 females:5 males) were assessed (4.7 to 17.2 years; median, 9.9) at baseline. Nine children went on to have an LT. The aspartate aminotransferase-to-platelet ratio index had a significant positive correlation with trunk lean mass and trunk lean mass index (LMI) SD score (SDS). At baseline, 4 patients were sarcopenic with appendicular LMI SDS less than −1.96. All fat mass and fat mass index (FMI) SDSs were within the normal range (above −1.96). There was a strong negative correlation between FMI SDS and height SDS. After transplant, there was a significant reduction in trunk LMI from 1.20 to −0.51 (95% CI, 1.03-2.4; $P < 0.01$). Body mass index SDS had a negative correlation with days to discharge after transplant. The majority of patients discharged after 16 days were sarcopenic. One year after transplantation, all patients were alive with normal graft function regardless of BC before LT.

Conclusion: FMIs were normal regardless of LMIs and correlated negatively with height. BC was related to days to discharge after LT but not to outcomes a year after LT.

Key Words: muscle wasting, adiposity, DXA, body composition

What Is Known

- Children with end-stage chronic liver disease can be underweight and stunted.
- Weight loss and loss of lean mass (sarcopenia) is a prognosticator of poor outcomes for patients requiring liver transplantation.

What Is New

- Fat mass in children with end-stage chronic liver disease is normal at the cost of reduced lean mass.
- Fat mass in children with end-stage chronic liver disease is preserved at a cost of reduced growth; the shorter children had the higher fat mass indices.
- Body composition was related to days in hospital post-liver transplant but not to their outcomes a year after liver transplant.

INTRODUCTION

Sarcopenia (loss of muscle mass) is a defining feature of cachexia—a metabolic syndrome associated with weight loss frequently described in patients with chronic diseases like cancer, heart failure, chronic obstructive pulmonary disease, and cirrhosis (1–4). Children with end-stage chronic liver disease (ESCLD) can be underweight and stunted. They tend to have thin limbs but also hepatosplenomegaly and water retention. Therefore, measurement of body weight provides a misleading indication of their nutritional status. Increasingly, the adult literature has shown that weight loss, in particular, loss of lean mass (LM) and muscle wasting, is a prognostic indicator of poor outcomes for patients on the liver transplant (LT) list and for those undergoing LT (5–7).

Data from pediatric patients with chronic liver disease (CLD) undergoing LT are showing a similar importance of sarcopenia for the outcomes of these patients (8–12). We tested the hypothesis that the presence of sarcopenia in children was related to poor outcomes and investigated whether changes in indices of fat tissue occurred in tandem to those in lean tissue. We looked at surrogate markers of portal hypertension and of systemic inflammation and how they correlate with body composition (BC) parameters and in particular, LM indices (LMIs).

METHODS

Children 4 to 18 years old with ESCLD undergoing assessment for LT or who were already listed for LT were eligible for recruitment to this observational longitudinal study. Children undergoing LT for acute liver failure, liver tumors, or for inborn errors of metabolism were excluded. All participants had their weight, height, mid-upper arm circumference (MUAC), and body mass index (BMI) measured. Measurements were converted to SD scores (SDS) using UK World Health Organization reference data in ImsGrowth program© (13–15).

The participants had a whole-body dual-energy x-ray absorptiometry (DXA) scan (Lunar Prodigy Advance PA+ 303999 whole-body scanner, with software Encore 2002; GE Medical Systems, Madison, WI). We used the age of 4 years as a cutoff because the published UK reference data we used for comparison are for children

Received December 24, 2021;accepted January 14, 2022.
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The authors report no conflicts of interest.
This work was funded by a joint BSPGHAN/CORE Charity grant and the King's College Hospital Charity Starfish Appeal and MowatLabs.
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JPGN Reports (2022) 3:2(e200)
ISSN: 2691-171X
DOI: 10.1097/PG9.0000000000000200

over 4 years old (16,17). DXA provides data on total and regional BC, including values of total fat mass (FM) and LM. Data on FM and LM were expressed as SDSs to allow comparison between the patients (16,17). FM and LM were also expressed as FM index (FMI) and LMI and converted to SDS (13–15). This adjusts BC for height, which is of relevance as pediatric patients with chronic diseases, particularly CLD, often have short stature (18,19). SDSs for regional BC measures were also generated for the trunk, arms, and legs. Patients were categorized as at risk for sarcopenia if either arm or leg LMI SDS was below −1.645 (fifth centile) and as sarcopenic if arm or leg LMI SDS was below −1.96 (2.5th centile).

Basic laboratory blood results like full blood count, kidney function, liver function, bone profile, and international normalized ratio (INR) were recorded. The aspartate aminotransferase-to-platelet ratio index (APRI) and the neutrophil-to-lymphocyte ratio were calculated. The first has been used as a noninvasive marker of portal hypertension (20) and the second as a surrogate marker for systemic inflammation (21–23).

The participants who went on to have an LT had repeat anthropometry and whole-body DXA scan approximately 1 year after their transplant. The days to discharge after the transplant and the complications related to the transplant in the first year of follow-up were recorded. The participants who were not transplanted also had a repeat BC assessment approximately 1 year after their first review.

Data were assessed for normal distribution, and parametric or nonparametric tests were used accordingly. Means between groups were compared using the Mann-Whitney *U* test or independent samples t-tests, while changes within individuals over time were assessed using paired t-tests. Correlations between BC and biochemical markers were assessed with the Pearson correlation or Spearman's Rho, whereas correlation between BC and outcomes was estimated with linear regression. Statistical significance was at a *P* value below 0.05. Statistical calculations were done using IBM SPSS Statistics 27. Informed consent in writing was obtained for each patient, and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the appropriate institutional review committee. The study received ethical approval from the London-Central Research Ethics Committee Research Ethics Committee (11/LO/1146).

RESULTS

Eleven children (6 females:5 males) undergoing assessment for LT had their BC assessed. Nine (5 females:4 males) had an LT and had BC studies after their transplant. Two of the children did not go on the transplant list and also had a second BC assessment.

Age ranged from 4.7 to 17.2 (median, 9.9) years. The diagnoses were biliary atresia (n = 3), Alagille syndrome (n = 2), neonatal sclerosing cholangitis (n = 1), biliary cirrhosis of unknown etiology (n = 1), primary sclerosing cholangitis (n = 1), hepatitis C (HCV) related cirrhosis (n = 1), and redo LT (n = 2). The basic laboratory parameters on the day of the first BC assessment were as follows: mean bilirubin, 53 (range, 20 to 99; median, 29) umol/L; mean albumin, 36 (range, 23 to 51; median, 36) g/L; mean hemoglobin, 117 (range, 81 to 152; median, 116) g/L; mean platelets, 87 (range, 32 to 187; median, 67) 10^9/L; average INR, 1.4 (range, 1 to 1.9; median, 1.4); and aspartate aminotransferase, 87 (range, 36 to 294; median, 67) IU/L.

Basic Anthropometry at Baseline

Mean weight SDS before LT was −0.67 (range, −2.16 to 1.06; median, −0.77), mean height SDS was −1.00 (range, −3.88 to 2.67; median, −1.55), and mean BMI SDS was −0.04 (range, −2.21 to 1.18; median, 0.28). Mean MUAC SDS was −0.96 (range, −2.4 to 1.9; median, −1.29). FM, FMI SDS, LM, and LMI SDS indices before and after LT are described in Table 1. All FM and FMI SDS indices were more than −1.96. The relationship at baseline between total FMI and leg LMI SDS is shown in Figure 1.

TABLE 1. FMIs and LMIs at baseline and 1 year after liver transplant

Body composition indices for all patients at baseline				
n = 11	tFMI SDS	aFMI SDS	lFMI SDS	trFMI SDS
Mean	−0.24	−0.58	−0.31	−0.11
Median	−0.11	−0.54	−0.23	0.02
SD	0.63	0.76	0.68	0.56
n = 11	tLMI SDS	aLMI SDS	lLMI SDS	trLMI SDS
Mean	−0.40	−1.69	−1.49	0.99
Median	−0.42	−0.98	−1.42	0.93
SD	1.26	1.53	1.06	1.55
Body composition indices of patients post-liver transplant				
n = 9	tFMI SDS	aFMI SDS	lFMI SDS	trFMI SDS
Mean	0.10	0.09	−0.01	0.16
Median	−0.17	−0.18	−0.27	−0.15
SD	1.02	1.04	1.03	0.95
n = 9	tLMI SDS	aLMI SDS	lLMI SDS	trLMI SDS
Mean	−1.19	−0.93	−1.27	−0.51
Median	−1.62	−0.39	−1.09	−0.62
SD	1.37	1.52	1.15	1.36

All patients at baseline had total FMI SDS and arm, leg, and trunk FMI SDS that were above −1.96. When corrected by height, only 4 of the patients had at least one LMI SDS score below −1.96 and could be classified as sarcopenic. After liver transplantation, there was a statistically significant reduction in trunk LMIs. aFMI = arm fat mass index; aLMI = arm lean mass index; FMI = fat mass index; lFMI = leg fat mass index; lLMI = leg lean mass index; LMI = lean mass index; SDS = SD score; tFMI = total fat mass index; tLMI = trunk lean mass index; trFMI = trunk fat mass index; trLMI = trunk lean mass index.

Correlations Between BC Parameters and Laboratory Parameters

MUAC SDS correlated with arm LM SDS (0.61; 95% CI, −0.01 to 0.89; $P < 0.05$) and arm LMI SDS (0.64; 95% CI, 0.04-0.90; $P < 0.05$). There was a negligible correlation between LMI SDS and height SDS, whereas FMI SDS was strongly negatively associated with height SDS at baseline (Fig. 2).

Low albumin and prolonged INR—characteristics of liver synthetic failure—correlated with a higher weight and total LM SDS, while albumin had a negative correlation with trunk LM SDS. The APRI (platelets are low in hypersplenism due to splenomegaly of portal hypertension and would increase the ratio in portal hypertension) had a significant positive correlation with trunk LM and LMI SDS (Table 2). The neutrophil-to-lymphocyte ratio had a significant negative correlation with arm FMI SDS (Table 2).

We found no significant differences between the sexes.

Differences Between Sarcopenic and Nonsarcopenic Patients

When at risk for sarcopenia was defined as arm or leg LMI SDS below −1.645 (fifth centile), then 6 patients classified for this diagnosis. When this group of 6 patients was compared to the remaining 5, we found no statistically significant differences with age, weight, height, BMI and MUAC SDS, and no differences in laboratory parameters. The only significant difference in BC was in leg LMI SDS as expected.

When sarcopenia was defined as arm or leg LMI SDS below −1.96 (2.5th centile), then 4 patients classified as sarcopenic. When

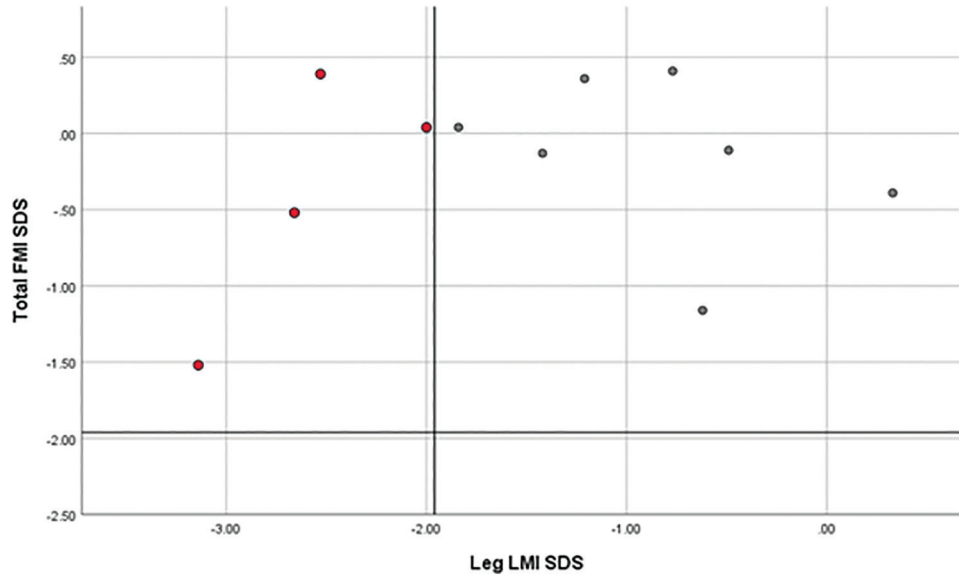

FIGURE 1. Leg LMI SDS vs total FMI SDS. The blue dots represent the children with a leg LMI SDS above −1.96 who are, therefore, not sarcopenic, whereas the red dots represent the children with a leg LMI SDS below −1.96 who are sarcopenic. Total FMI SDS remains above −1.96 for all children, even for the ones with sarcopenia. The correlation between leg LMI SDS and total FMI SDS was weak (equation: y = 0.07 + 0.11x; correlation, 0.11; 95% CI, −0.62 to +0.60) and not statistically significant. FMI = fat mass index; LMI = lean mass index; SDS = SD score.

we compared these 4 patients to the remaining 7, we found no statistically significant differences with age, weight, height, BMI and MUAC SDS, or laboratory parameters. There were no differences between the two groups in FM and FMI SDS or LM SDS. There were significant differences between the two groups in total LMI, arm LMI, and leg LMI but not trunk LMI SDS.

BC and Outcomes

Nine children had LT. The days to discharge from the day of LT were on average 25 (range, 10 to 80; median, 16) days. Three patients stayed in hospital for more than 16 (29 to 80) days. Two of them (66.7%) were sarcopenic, and one had the lowest FMIs of the whole cohort. Of the ones discharged within 16 days, 22.2% were sarcopenic. BMI SDS correlated negatively with days to discharge, and 53% of the variance in days to discharge could be explained by BMI SDS (linear regression: $R = 0.73$; $R^2 = 0.53$; $P < 0.05$). There was a similar correlation with trunk FMI SDS and a positive one with height SDS but did not quite reach significance.

All patients at follow-up were doing well and had normal graft function. In terms of complications post-LT, the four who were

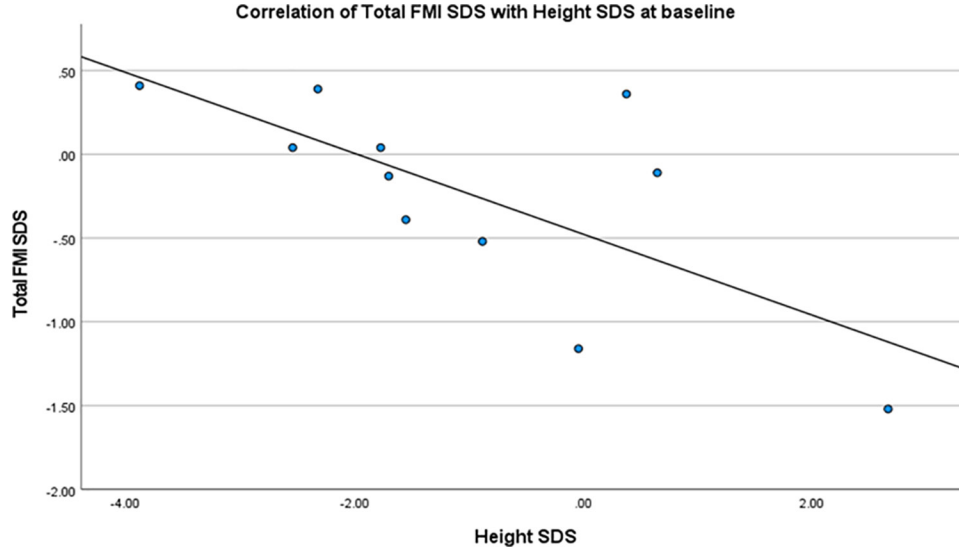

FIGURE 2. Correlation of total FMI SDS with height SDS at baseline. There was a strong inverse correlation between FMI SDS and height SDS at baseline (equation: y = 0.48 − 0.24x; correlation, −0.75; $P < 0.05$). There was no significant correlation between LMI SDS and height SDS at baseline (at follow-up, the correlation for FMI and height was significant but weaker, while the correlation for LMI and height remained nonsignificant but became positive). FMI = fat mass index; LMI = lean mass index; SDS = SD score.

TABLE 2. Correlations between laboratory parameters and body composition indices at baseline

	Bilirubin	Albumin	INR	AST	PLT	APRI	Ne:Ly ratio
Wt SDS	−0.19 (−0.72 to +0.48), $P = 0.57$	−0.75* (−1.25 to −0.25), $P = 0.008$	0.64† (0.05 to +1.22), $P = 0.04$	0.09 (−0.55 to +0.67), $P = 0.79$	−0.35 (−0.79 to +0.34), $P = 0.3$	0.60 (−0.03 to +0.89), $P = 0.05$	−0.03 (−0.63 to +0.60), $P = 0.94$
Ht SDS	−0.11 (−0.68 to +0.54), $P = 0.74$	−0.50 (−0.90 to −0.07), $P = 0.12$	0.53 (−0.17 to +0.85), $P = 0.09$	−0.04 (−0.64 to +0.59), $P = 0.92$	−0.19 (−0.72 to +0.48), $P = 0.57$	0.34 (−0.35 to 0.79), $P = 0.31$	0.14 (−0.52 to +0.69), $P = 0.69$
BMI SDS	−0.20 (−0.65 to +0.57), $P = 0.56$	−0.25 (−0.73 to +0.46), $P = 0.31$	0.06 (−0.45 to +0.74), $P = 0.06$	−0.26 (−0.75 to +0.42), $P = 0.35$	−0.24 (−0.77 to +0.38), $P = 0.48$	0.47 (−0.41 to +0.76), $P = 0.15$	−0.30 (−0.82 to 0.25), $P = 0.76$
tFMI SDS	0.18 (−0.48 to +0.72), $P = 0.59$	0.07 (−0.53 to +0.69), $P = 0.85$	−0.20 (−0.75 to +0.43), $P = 0.27$	0.23 (−0.44 to +0.74), $P = 0.49$	0.25 (−0.43 to +0.75), $P = 0.46$	−0.02 (−0.63 to +0.6), $P = 0.95$	−0.32 (−0.78 to +0.36), $P = 0.33$
aFMI SDS	0.28 (−0.40 to +0.76), $P = 0.4$	0.21 (−0.50 to +0.70), $P = 0.53$	−0.21 (−0.71 to +0.50), $P = 0.09$	0.23 (−0.45 to +0.74), $P = 0.23$	0.14 (−0.52 to +0.69), $P = 0.69$	0.04 (−0.59 to +0.64), $P = 0.92$	−0.63† (−0.9 to −0.02), $P = 0.04$
lFMI SDS	0.23 (−0.44 to +0.74), $P = 0.49$	0.13 (−0.67 to +0.55), $P = 0.71$	−0.18 (−0.68 to +0.54), $P = 0.41$	0.26 (−0.42 to +0.75), $P = 0.45$	0.19 (−0.48 to +0.72), $P = 0.29$	0.04 (−0.59 to +0.64), $P = 0.92$	−0.27 (−0.76 to +0.41), $P = 0.42$
trFMI SDS	−0.19 (−0.72 to +0.48), $P = 0.58$	−0.10 (−0.72 to +0.48), $P = 0.76$	−0.14 (−0.78 to +0.43), $P = 0.67$	0.17 (−0.5 to +0.71), $P = 0.62$	0.27 (−0.41 to +0.76), $P = 0.26$	0.01 (−0.61 to +0.62), $P = 0.99$	−0.06 (−0.65 to +0.58), $P = 0.87$
tLMI SDS	−0.43 (−0.83 to +0.25), $P = 0.18$	−0.41 (−0.79 to +0.34), $P = 0.21$	0.19 (−0.56 to +0.66), $P = 0.64$	0.06 (−0.57 to +0.65), $P = 0.86$	−0.18 (−0.72 to +0.49), $P = 0.59$	0.35 (−0.34 to +0.79), $P = 0.3$	−0.17 (−0.71 to +0.49), $P = 0.61$
aLMI SDS	−0.21 (−0.73 to +0.46), $P = 0.53$	0.11 (−0.51 to +0.70), $P = 0.76$	−0.14 (−0.69 to +0.53), $P = 0.67$	−0.23 (−0.74 to +0.45), $P = 0.5$	0.66† (0.07 to +0.91), $P = 0.03$	−0.64† (−0.9 to +0.05), $P = 0.03$	−0.33 (−0.78 to +0.36), $P = 0.33$
lLMI SDS	−0.29 (−0.77 to +0.39), $P = 0.38$	−0.20 (−0.67 to +0.55), $P = 0.57$	0.05 (−0.64 to +0.59), $P = 0.31$	−0.06 (−0.65 to +0.57), $P = 0.86$	0.13 (−0.53 to +0.69), $P = 0.71$	0.03 (−0.60 to +0.63), $P = 0.94$	−0.46 (−0.84 to +0.22), $P = 0.16$
trLMI SDS	−0.36 (−0.80 to +0.32), $P = 0.27$	−0.53 (−0.86 to +0.12), $P = 0.1$	0.26 (−0.40 to +0.76), $P = 0.93$	0.20 (−0.47 to +0.72), $P = 0.08$	−0.55 (−0.87 to +0.10), $P = 0.08$	0.66† (0.07 to +0.91), $P = 0.03$	0.06 (−0.58 to +0.65), $P = 0.06$

In brackets, confidence intervals at 95%. aFMI = arm fat mass index; aLMI = arm lean mass index; APRI = aspartate aminotransferase-to-platelet ratio index; AST: aspartate aminotransferase; BMI = body mass index; Ht = height; lFMI = leg fat mass index; lLMI = leg lean mass index; INR = international normalized ratio; Ly = lymphocyte; Ne = neutrophil; PLT = platelet; SDS = SD score; tFMI = total fat mass index; tLMI = trunk lean mass index; trFMI = trunk fat mass index; trLMI = trunk lean mass index; Wt = weight.

*Statistical significance <0.01.

†Statistical significance <0.05.

sarcopenic experienced the following complications: one had bilateral pneumothoraces, one had 2 admissions for fever and for diarrhea, one had stress cardiomyopathy, and one had CMV reactivation. If we include the 2 patients at risk of sarcopenia, then one had PTLD and the other was not listed but experienced 2 bone fractures in the year of follow-up.

The remaining 5 patients who were not sarcopenic had the following complications post-transplant: two of them had none; one had a hepatic artery thrombosis, acute cellular rejection, and ventricular bigeminy; one had hepatic artery thrombosis; and one was treated successfully and removed from the list.

Changes in BC After LT

The 9 transplanted children had a repeat whole-body DXA scan on average 1.8 years from their first DXA scan and 1.12 years after their transplant. Their age range was 6.9 to 18.4 (median, 12.2) years.

After transplant, there was a statistically significant reduction in trunk LMIs. Mean trunk LM SDS decreased from −0.00 to −0.90 (Δ = 0.9; 95% CI, 0.4-1.4) and mean trunk LMI SDS from 1.20 to −0.51 (Δ = 1.7; 95% CI, 1.03-2.4; $P < 0.01$). Appendicular LM and LMIs increased, but the change did not achieve statistical significance. Two of the patients with appendicular LMI SDS less than −1.96 continued to have low appendicular LMI SDS post-transplant, two improved, but two more now had LMI SDS below −1.96; for one, the total LMI and for the other, leg LMI SDS.

FMIs remained in the normal range without significant change from baseline, except for arm FM, which significantly increased. There was an increase in total FMI SDS over the time period, especially if they had high FMI at baseline, but it did not reach statistical significance. Equivalent changes for arm FM (Δ = −0.65; 95% CI, −1.04 to −0.27) and FMI SDS (Δ = −0.69; 95% CI, −1.10 to −0.31) did reach significance ($P < 0.01$).

Two patients were removed from the LT list. One was a male already transplanted for biliary atresia, who was considered for a second LT, but after the assessment, it was felt he could wait. The second was a female with HCV related liver disease, who had successful HCV treatment and was removed from the list. Both had repeat whole-body DXA scan on average 14 months after their first assessment. The boy had an increase in all the FM and FMI SDS, but his LM and particularly LMI SDS decreased. The girl showed an overall increase in FM, FMI, LM, and LMI SDS.

DISCUSSION

In this study of 11 patients with ESCLD, we have shown that 36% of the children were sarcopenic. This is within the reported prevalence of 24% to 46% (8,11,12). There are no clear definitions for sarcopenia in pediatrics. Traditionally, values below an SDS of −1.96 would be considered pathologically low. It is important in patients with CLD that we choose a method that assesses appendicular BC. Methods assessing overall BC will overestimate LM because of the organomegaly seen in these patients. From this point of view, DXA is a safe and viable option.

Children with ESCLD tend to have enlarged liver and spleens, which the DXA scan reads as lean mass. Therefore, trunk LM as measured by DXA is more likely to be in the normal range, as it not only reflects the trunk muscle mass but also the tissue of the enlarged liver and spleen. Interestingly, markers of more advanced liver disease and portal hypertension like INR, APRI, and low albumin correlated with higher trunk LM and weight, as would be reflected with more organomegaly. In line with this explanation, there was a statistically significant reduction in trunk LM and LMI SDS after LT, as now the children had smaller livers and spleen size was likely to reduce. In this particular cohort, the children did not have ascites. Regional BC, at least as far as LM is concerned, is more appropriate for these patients.

A striking observation is the preservation of FM, despite significant deficits in LM for some of the patients. DXA scans tend to overestimate fat tissue, but we have used SDS, which is a relative measure. The scores were derived from measurements of the reference population on the same equipment; therefore, the differences we are seeing are likely to be typical of the true FM difference.

The process of fat tissue preservation may be part of the metabolic response of the body to CLD as it aims to minimize anabolic activities and to conserve energy. Peripheral insulin resistance has been clearly described in adults with cirrhosis (24) as has growth hormone resistance in children with CLD (25). These processes could result in a reduction of LM and a preservation of FM. This study did not explore the presence of anabolic resistance in the children, but it did find that the more stunted children had a higher FMI. The trade-off of the riskier strategy of linear growth in favor of other metabolic tasks like immune-related functions has been previously described in children (26,27), and it is possible that the preservation of body fat has a role in mitigating the energy shortfall in these situations (28). Mangus et al (29) using computed tomography have shown a significant higher visceral FMI for children with CLD in comparison to healthy controls. Normal data for visceral fat in children based on computed tomography do not exist, so it is not clear if this increase is still within the normal range. Nevertheless, this study also points toward the preservation of FM in these patients.

In adults, differences between the sexes have frequently been described in relation to sarcopenia and CLD. In adults, loss of LM is more relevant to male patients, and loss of FM is more relevant to female patients (7,30,31). In children, these differences may not be as relevant or prevalent (12). Teenagers with CLD are likely to have delayed puberty, and, therefore, most children with ESCLD biologically are prepubertal, and we are seeing a more female phenotype.

For the albeit small number of patients in this study, BC was associated to stay in hospital after the LT but did not seem to be related with outcomes a year after their transplant as all children were doing well at that point. This is similar to studies in adults (31). One study of 89 children showed a tendency for lower 1-year survival in sarcopenic children with biliary atresia post-LT, but this did not quite reach statistical significance (10). These children had more postoperative complications, but their stay in hospital was not longer than their nonsarcopenic counterparts. They were a lot younger than the children of this study.

A year after LT, there was a tendency for an improvement in appendicular LMIs, but significant deviations continue to exist, as also shown by Mager et al (9). Arm FMIs increased significantly within that first year, but the rest of the FMIs did not change significantly. A longer period of observation post-LT would be helpful to show if there was a further increase in weight gain and particularly an increase in FM post-transplant. Obesity and metabolic syndrome have been described in longer term outcomes of solid organ recipients (32–34).

The advantages of this study are that it was prospective with paired before and after LT BC data. To our knowledge, this is the first time this has been reported. The weakness of the study is the small number of patients, which can affect the generalizability of the results.

Patients with a higher BMI SDS had a shorter stay in hospital post-LT regardless of sarcopenia. If this was confirmed in larger cohorts, it may mean that for children increasing FM via improving nutrition (eg, with nasogastric feeding or parenteral nutrition) may be helpful for improving outcomes. The metabolic signature of CLD with anabolic resistance, loss of LM, and preservation of fat with the ultimate reduction of FM being the hallmark of significant deterioration deserves closer study in larger prospective studies. A better

understanding of this process may provide significant insights into how to best manage this spiral of metabolic changes that can influence the long-term metabolism of these patients long after they have had their LT and are well into adulthood.

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