Pre-transplant Psoas Muscle Density as a Ready-to-Use and Low-cost Predictor of Patient Survival After Liver Transplant

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Abstract

Background: Sarcopenia, defined as low muscle mass with reduced function, is frequently encountered in cirrhotic patients and is a major predictor of adverse events, including post-liver transplant (LT) outcome.

Objectives: This study assessed the impact of sarcopenia using computed tomography (CT)-based measurements on post-LT mortality and complications.

Methods: From January 2008 to June 2016, 646 adult patients underwent 613 LTs at our institution. We analyzed the postoperative outcome of 287 patients who had pathologically proven cirrhosis on the explanted liver and who had performed a CT examination three months before LT. Psoas muscle density (PMD) was detected for every patient using standard instruments present in the radiological workstation and was related to postoperative survival rates and complications. Statistical analysis was carried out using the appropriate tests.

Results: Postoperative mortality was 6.3%. At least one grade III-IV postoperative complication was experienced by 121 patients. Respiratory and infective complications occurred in 30 and 32 patients, respectively. Also, PMD was an independent predictor of postoperative mortality (P = 0.021), respiratory complications (P = 0.015), and infections (P = 0.010). The ROC analysis identified a PMD ≤ 43.72 HU as the best cutoff value for predicting 90-day mortality after LT.

Conclusions: Psoas muscle density accurately predicted post-LT mortality and complications. Its ease and low-cost determination can allow widespread use of this parameter to improve clinical care and help with the decision to give these patients some priority on the transplant waiting list.

Keywords: Sarcopenia, Malnutrition, Liver Transplant, Muscle Density, Complications, Infection, MELD

1. Background

Liver transplant (LT) is the only curative option for patients with end-stage liver disease (ESLD).

Unfortunately, severe graft shortage prolongs the time on the waiting list, leading to advanced liver disease and worse patient clinical conditions at the same rate (¹). Efforts to increase the donor pool have included adding donation after cardiac death to standard donation after brain death (²). Moreover, older donors and donors with fatty livers have been utilized in recent years (³). At the same time, the predicted decline in organ availability in the future, due to graft quality deterioration (⁴), confirms the strict selection of transplant candidates being of paramount importance.

Sarcopenia can be defined as low muscle mass associated with a lower muscle function (⁵). It is frequent in pa-
tients with ESLD, with a reported incidence up to 70% (6-9), and is a major predictor of adverse clinical outcome measures, including survival, quality of life, development of other complications of cirrhosis, and post-transplant outcomes (9-13). In particular, a recent study demonstrated that both short- and long-term post-LT survival were considerably poorer in the sarcopenic group than in the non-sarcopenic group (82% versus 98% and 53.6% versus 79.8%; \( P < 0.001 \)) (14). In the study by Valero et al. (15), sarcopenia was an independent predictor of postoperative complications in multivariable analysis (Odds Ratio 3.06, 95%CI = 1.07 - 8.72, \( P = 0.03 \)).

Sarcopenia is an objective measure of malnutrition in cirrhotic patients instead of serum (pre-) albumin, body mass index (BMI), and weight, which may be conditioned by liver impaired function or ascites. In the literature, computed tomography (CT) measurements of skeletal muscle mass include a wide variety of tools, such as Psoas muscle area (PMA) (16), PMA normalized for height (14), psoas thickness normalized for height (17), and third lumbar vertebra (L3) muscle index standardized by the squared height (8, 17). Due to many clinical definitions, the European Working Group on Sarcopenia in 2010 stated that “more research is urgently needed to obtain good reference values” (5). In particular, no precise cut-off value is available to diagnose sarcopenia in patients affected by ESLD. Moreover, this definition recommends the use of a practical clinical definition and a consensus diagnostic criterion.

The main limit in finding a cut-off agreed upon by the scientific community is that many authors use different measurements, some of which requiring expensive software that is not readily available in every center (8, 14, 16, 17).

2. Objectives

In the present study, we assessed the impact of sarcopenia on post-LT mortality and complications, using single-slice CT-based measurements of Psoas muscle density (PMD).

3. Methods

3.1. Study Design

From January 1, 2008, to June 15, 2016, 646 adult patients underwent 613 LTs from AB0-identical or AB0-compatible brain-death-deceased donors at our institution. From the 646 transplanted patients, we designated 287 patients with pathologically proven cirrhosis on the explanted liver, for whom a CT examination was available (three months before LT). The availability of recent imaging depended on the oncologic follow-up in patients with HCC (18) and modifications of patient clinical conditions, which needed a CT scan evaluation (i.e., sudden liver decompensation, acute abdominal pain, etc.).

The clinical features of both donors and recipients, including biochemical and surgical parameters, were stored in the institutional database. Since 2004, a two-center regional allocation based on the model for end-stage liver disease (MELD) score has been used, with additional points assigned for different indications (hepatocellular carcinoma (HCC), metabolic diseases, etc.), with periodical re-evaluation between the two centers involved (18, 19). At present, malnutrition determines an assignation of extra points only in patients affected by the polycystic hepatic disease, for whom the loss of weight was exclusively related to the mass effect imposed by massive hepatomegaly (20). The results were assessed considering post-transplant survival rates and complications. Since sarcopenic patients are at higher risk of developing respiratory or infective postoperative complications (15, 21), we performed an additional analysis of these issues.

This single-center study, carried out at our tertiary care center, was approved by the institutional review board and written informed consent was obtained from each patient.

3.2. Definitions

The postoperative course was designated as the period comprising 90 days after LT, as previously done (19, 22). Postoperative complications were graded according to the Dindo-Clavien classification (23). Only were grade III-IV complications analyzed, as previously performed (19). Acute-on-chronic Liver Failure (ACLF) was defined as a rapid decompensation in a chronic setting of liver disease, with a potential organ failure(s) predefined by the CLIF-SOFA score (24). Hepatorenal syndrome (HRS) was diagnosed as per the International Club of Ascites definition (25). Prolonged post-LT mechanical ventilation (MV) was defined as MV for at least 72 h postoperatively (26). Postoperative respiratory complications included pneumonia, pulmonary edema, and respiratory failure (defined as prolonged MV, the need for re-intubation for respiratory failure, and the need for tracheotomy) (27). Infections were defined following the standard criteria recommended by the centers for disease control and prevention (28).
3.3. Imaging Analysis

The CT examinations were performed in all patients, following a previously described protocol (29). A more than 10-year experienced radiologist in the abdominal imaging field, blinded to all of the information, including clinical history, assessed the images. All the images were retrieved from and evaluated on our institutional picture archiving and communication system (Carestream PACS®, version 1.4; Kodak, Rochester, NY). All the measurements (size, area, or density evaluation) were performed using standard instruments present in all the imaging workstations without the use of dedicated software. We decided to perform three different evaluations: (1) transversal psoas muscle thickness (TPMT) measurement; (2) cross-sectional PMA measurement; and (3) PMD measurement. All the measurements were performed on both the right and the left psoas muscles, and their means were calculated by halving the sum of right and left assessments (Figure 1).

Measurements of TPMT on CT were performed, according to the previously described method by Durand et al. (17). Besides, TPMT was normalized for stature divided by height (TPMTh). Measurements of PMA and PMD were performed on a single axial image of basal CT scan at the level of L3. The radiologist traced the contour of the muscle using the freehand instrument for density measurement, automatically obtaining the following values: -area (mm²) and-density (Hounsfield Unit, HU). Then, PMA was normalized for Body Surface Area (BSA) (14). Normal density for skeletal muscle is defined as 30 - 100 HU (30); a lower density is related to “fatty replacement” of muscle tissue due to patient age, obesity, and concomitant diseases, such as neurological chronic conditions, type 2 diabetes, malignancy, or cirrhosis (30-32).

3.4. Statistical Analysis

Continuous variables were expressed as median and range and compared using a two-tailed unpaired Student’s t test. Categorical variables were compared using χ² or Fisher analysis. Patient survival was calculated from the date of LT to the last date of follow-up or death. Actuarial survivals were computed with the Kaplan-Meier method, and the differences between the groups were compared by the log-rank test.

To identify the predictors of 90-day mortality and 90-day postoperative complications, a univariable analysis was performed. A multilinear regression was also performed, including those variables significantly correlated to the outcome at univariable analysis. In this way, it evaluated the correlation between some of these identified predictors. In particular, since ACLF definition, according to the CLIF-SOFA score, already included the MELD-score, and HRS was diagnosed based on the serum creatinine level, which is one factor used to calculate the MELD-score, only was the variable with the higher chi-square value included in the multivariable analysis. In this way, the rule of thumb of one variable for 10 events was fulfilled.

Since our principal goal was to better understand which recipient characteristics will most impact post-LT survival and considering that we have already demonstrated comparable post-transplant outcomes regardless of donor characteristics (19), the latter were not analyzed as possible predictors of postoperative survival and complications.

The prognostic value of PMD measurement in predicting 90-day postoperative mortality was assessed using receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC), sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios for the cut-off point obtained were reported. A P-value less than 0.05 was considered statistically significant. Statistical analysis was performed with SPSS version 17.0 software (SPSS, Inc., Chicago, IL). The ROC analysis was performed with MedCalc version 12.5.0 (MedCalc Software, Ostend, Vlaanderen, Belgium). The statistical review of the study was performed by a biomedical statistician.

4. Results

4.1. Recipient Characteristics and Postoperative Course

The baseline characteristics of the study population are summarized in Table 1. After a median follow-up of 40 months (0 - 109 months), 58 (20.2%) patients died. The one- and five-year overall survival rates were 87.1% and 78.9%, respectively.

Men made up 74.2% of the cohort. Notable characteristics included a median BMI of 24.7 kg/m² (range: 11.8 - 37.2) and post-necrotic cirrhosis as the cause of liver dysfunction in 61.7% of the cases. Respecting the markers of liver disease severity, the median pre-LT MELD score was 20 (6 - 49), and HRS and ACLF were diagnosed in 29.3% and 20.9% of the cases, respectively. Postoperative mortality was 6.3% (18 patients). The main cause of postoperative death was infection/multi-organ failure (MOF) (61.1%, 11 patients), followed by hemorrhagic shock (22.2%, four patients). At least one grade III-IV postoperative complication was observed in 121 (42.2%) patients. Respiratory and infective complica-
4.2. Psoas Muscle Density and 90-day Mortality and Complications

The ROC analysis identified a PMD $\leq 43.72$ HU as the best cut-off value for predicting 90-day mortality after LT (AUC = 0.746, 95% CI = 0.691–0.795; sensitivity = 94.4%; specificity = 57.3%; positive predictive value [PPV] = 12.4%; negative predictive value [NPV] = 99.4%; positive likelihood ratio [PLR] = 2.21; negative likelihood ratio [NLR] = 0.097; P < 0.001) (Figure 2A). Seventeen (94.4%) of the 18 patients who died in the postoperative period had PMD $\leq 43.72$ HU, while only one (5.6%) had higher PMD (P < 0.001).

We used the ROC analysis to find the PMD cut-off value also for grade III-IV complications, respiratory complications, and infections. According to this statistical analysis, the three cut-off values respectively were:

- PMD $\leq 46.11$ HU (AUC = 0.569, 95% CI = 0.510–0.628; sensitivity = 66.1%; specificity = 46.4%; PPV = 12.1%; NPV = 92.5%; PLR = 1.23; NLR = 0.73; P = 0.043) (Figure 2B);

- PMD $\leq 42.41$ HU (AUC = 0.722, 95% CI = 0.666–0.773; sensitivity = 73.3%; specificity = 64.6%; PPV = 18.7%; NPV = 95.6%; PLR = 2.07; NLR = 0.41; P < 0.001) (Figure 2C);

- PMD $\leq 40.39$ HU (AUC = 0.664, 95% CI = 0.606–0.719; sensitivity = 53.1%; specificity = 74.5%; PPV = 18.7%; NPV = 93.5%; PLR = 2.08; NLR = 0.63; P = 0.002) (Figure 2D).

4.3. Analysis of Factors Affecting 90-day Mortality and Complications

The following factors were analyzed for their impact on postoperative mortality and complications: Recipient age, gender, BMI, and BSA; type of liver disease, presence of HCC, hepatitis C virus (HCV) or hepatitis B virus (HBV) infection; MELD score, the onset of ACLF or HRS; pre-LT in-hospital stay, the need for continuous venovenous hemofiltration (CVVH), MV or norepinephrine; TPMTh, PMA normalized for BSA, and PMD.

A higher MELD score, onset of ACLF, and lower PMD were correlated with higher 90-day mortality in univariable analysis (Table 2). The only independent predictor of 90-day mortality was PMD (Exp(B) = 0.929, 95% CI = 0.872
Grade III-IV complications were significantly related to the MELD score, onset of ACLF, diagnosis of HRS, and hospitalization at the time of LT (Table 3). In multivariable analysis, only could the MELD score independently predict postoperative complications (Exp(B) = 1.051, 95% CI = 1.015 - 1.087; P = 0.004).

Postoperative respiratory complications occurred more frequently in older patients, with higher MELD score, pre-LT diagnosis of HRS and ACLF, and lower PMD (Table 4). In multivariable analysis, recipient age (Exp(B) = 1.060, 95% CI = 1.005 - 1.119; P = 0.032), MELD score (Exp(B) = 1.088, 95% CI = 1.034 - 1.145; P = 0.001), and PMD (Exp(B) = 0.930, 95% CI = 0.878 - 0.986; P = 0.015) independently predicted the occurrence of post-LT respiratory complications.

Post-LT infections arose more frequently in patients

Figure 2. ROC analysis of psoas muscle density for predicting: A, 90-day postoperative mortality; B, Grade III-IV postoperative complications; C, Postoperative respiratory complications; D, Postoperative infections.
with higher MELD scores, pre-LT diagnosis of HRS, and lower PMD (Table 5). Multivariable analysis found HRS and PMD as independent predictors of postoperative infections (Exp(B) = 3.688, 95% CI = 1.698 - 8.013; P = 0.001 and Exp(B) = 0.934, 95% CI = 0.887 - 0.984; P = 0.010, respectively).

4.4. Analysis of Factors Affecting 90-day Mortality of Sarcopenic Patients

To better understand the impact of sarcopenia on post-LT mortality, we performed a further sub-analysis, considering only the patients with PMD value ≤ 43.72 HU (n = 132, 46.0% of the cases), searching for possible differences between survivors (115 patients, 87.1%) and deceased patients (17 patients, 12.9%) in this sarcopenic subgroup. By analyzing the same variables reported above, a higher median MELD score (22 versus 27; P = 0.012) and age (55 versus 61 years; P = 0.041) were associated with 90-day mortality in univariable analysis. In multivariable analysis, both MELD score and recipient age independently predicted 90-day postoperative mortality (Exp(B) = 1.095, 95% CI = 1.022 - 1.174; P = 0.010 and Exp(B) = 1.098, 95% CI = 1.010 - 1.193; P = 0.028, respectively).

5. Discussion

The identification of patients listed for LT with an increased risk of postoperative morbidity and mortality is crucial to improve candidate selection, organ allocation, and optimal graft-to-recipient matching. Malnutrition and sarcopenia have been correlated with mortality in cirrhotic patients, waiting-list mortality, post-transplant severe infections, and longer hospital stay (9-16). Considering that prolonged MV, bacterial infections, intensive care, and hospital long stay are well-known negative predictors of post-LT survival (19, 33, 34), the impact of malnutrition and muscle reduction on these variables is fundamental.

At present, different methods are available to evaluate body composition and estimate muscle mass in patients with cirrhosis; however, most of these modalities present some limitations, primarily owing to limited reproducibility. In this setting, the muscle thickness assessment based on cross-sectional CT imaging has been proposed as a quantitative index of nutritional status in patients with cirrhosis, particularly owing to its objective nature (8, 13-17, 32).

Englesbe et al. (16) first introduced the concept of sarcopenia to LT using an objective and recordable value, namely PMA at level L4. In fact, one-year post-LT survival ranged from 49.7% for the quartile with the smallest PMA to 87.0% for the quartile with the largest PMA, with a hazard ratio of 3.7/1,000 mm² decrease in PMA (P < 0.001). Subsequently, many other authors used PMA or TPMT to find a relationship between these values and post-LT survival or complications (14, 15, 17). The principal limitation of these studies is that PMA and TPMT, even if normalized for height.
or BSA, could vary significantly due to gender, ethnicity, age, height, weight, and other clinical conditions, leading to potential confounding results (30-32). In addition, the location of the umbilicus, as proposed by Durand et al. for TPMT (17), may change owing to ascites or obesity. Thus, some measurements may be recorded at different levels.

Montano-Loza et al. (8) demonstrated a correlation between sarcopenia, defined using abdominal muscle density, and mortality in cirrhotic patients (HR = 2.21, P = 0.008). As previously reported, muscle density is independent of gender, height, weight, or ethnicity, and thus appears to be more objective than muscle area or thickness (31). Interestingly, the frequency of sepsis-related death was significantly higher in sarcopenic patients than in non-sarcopenic patients (22% versus 8%; P = 0.02), supporting the hypothesis of impaired immunity in these patients (34-36). Moreover, the same authors more recently demonstrated that sarcopenia predicted post-LT outcomes independently of MELD score; in fact, if present, sarcopenia was equivalent to adding 10 points to the MELD score (37). The principal limitations of these studies were the need for specifically dedicated software and the use of cut-off values taken from a population of non-cirrhotic patients (38). In this sense, the measurement of PMD seemed to be a more rapid and low-cost method. Regarding the cut-off value for PMD, interestingly, Kalafateli et al. (32) reported a 43.14 HU of psoas muscle density as the best predictor of 12-month mortality in a population of 98 cirrhotic patients, which is similar to ours. Our study demonstrated that PMD was the best predictor of postoperative mortality after LT (P = 0.021); in fact, 94% of the patients who died within 90 days after LT had a PMD lower than 43.72 HU, which is the cut-off we applied to define sarcopenic patients. Among 132 sarcopenic patients, the variables that independently in-

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Table 2. Comparison of Preoperative Characteristics of Patients Deceased 90-day post-LT with Those of Patients Who Survived

| Variables                      | 90-Day Survivors (N = 269) | 90-Day Deceased Patients (N = 18) | P    | Exp(B) | C.I.     | P    |
|--------------------------------|-----------------------------|-----------------------------------|------|--------|----------|------|
| Age                            | 54 (14 - 71)                | 53 (21 - 65)                      | 0.377| -      | -        | -    |
| Male gender                    | 202 (75.1)                  | 11 (61.1)                         | 0.189| -      | -        | -    |
| BMI, kg/m²                     | 24.7 (11.8 - 37.2)          | 24.5 (21.2 - 36.7)                | 0.071| -      | -        | -    |
| BSA, m²                        | 1.86 (1.37 - 2.40)          | 1.84 (1.57 - 2.12)                | 0.590| -      | -        | -    |
| Liver disease                  |                             |                                   |      |        |          |      |
| Post-necrotic cirrhosis        | 167 (62.1)                  | 10 (55.6)                         | 0.581| -      | -        | -    |
| Alcoholic cirrhosis            | 43 (16.0)                   | 3 (16.7)                          | 0.575| -      | -        | -    |
| Cholestatic disease            | 19 (7.1)                    | 2 (11.1)                          | 0.386| -      | -        | -    |
| Other                          | 41 (15.2)                   | 2 (11.1)                          | 0.476| -      | -        | -    |
| Hepatocellular carcinoma       | 122 (45.4)                  | 5 (27.8)                          | 0.146| -      | -        | -    |
| HCV infection                  | 121 (45)                    | 9 (50.0)                          | 0.679| -      | -        | -    |
| HBV infection                  | 79 (29.4)                   | 3 (16.7)                          | 0.190| -      | -        | -    |
| MELD score at LT               | 19 (6 - 49)                 | 25 (7 - 42)                       | 0.017| -      | -        | -    |
| Pre-LT ACLF                    | 52 (19.3)                   | 8 (44.4)                          | 0.011| 2.712  | 0.994-7.398 | 0.051|
| Pre-LT in hospital stay        | 93 (34.6)                   | 9 (50.0)                          | 0.186| -      | -        | -    |
| Pre-LT hepatorenal syndrome    | 77 (28.6)                   | 7 (38.9)                          | 0.354| -      | -        | -    |
| Pre-LT CVVH/HD                 | 6 (2.2)                     | 2 (11.1)                          | 0.083| -      | -        | -    |
| Pre-LT MV                      | 8 (3.0)                     | 2 (11.1)                          | 0.124| -      | -        | -    |
| Pre-LT use of norepinephrine   | 6 (2.2)                     | 1 (5.6)                           | 0.368| -      | -        | -    |
| Transversal psoas muscle       | 18.01 (4.98 - 26.99)        | 18.55 (9.26 - 22.72)              | 0.927| -      | -        | -    |
| thickness/height               | 342.17 (253.4 - 432.08)     | 351.90 (181.92 - 139.27)          | 0.815| -      | -        | -    |
| Psoas muscle area/BSA, mm²/m²  |                            |                                   |      |        |          |      |
|                                | 45.28 (12.99 - 59.78)       | 39.52 (31.21 - 45.91)             | 0.005| 0.929  | 0.872-0.989 | 0.021|
| Psoas muscle density (HU)      |                            |                                   |      |        |          |      |
|                                | 43.72 HU                    |                                   |      |        |          |      |

Values are expressed as median (range) or No. (%).
Table 3. Comparison of Preoperative Characteristics of Patients Who Experienced Postoperative Grade III-IV Complications with Those of Patients Without Postoperative Complicationsa

| Variables                  | No Grade III-IV Complications (N = 166) | Grade III-IV Complications (N = 121) | P    | Exp(B) | C.I.     | P    |
|---------------------------|----------------------------------------|--------------------------------------|------|--------|----------|------|
| Age                       | 54 (18 - 71)                           | 54 (18 - 69)                         | 0.691| -      | -        | -    |
| Male gender               | 118 (71.1)                             | 95 (78.5)                            | 0.355| -      | -        | -    |
| BMI, kg/m²                | 24.6 (17.7 - 37.2)                     | 25.0 (15.3 - 36.7)                   | 0.529| -      | -        | -    |
| BSA, m²                   | 1.86 (1.37 - 2.40)                     | 1.87 (1.47 - 2.30)                   | 0.500| -      | -        | -    |
| Liver disease             |                                        |                                      |      |        |          |      |
| Post-necrotic cirrhosis   | 103 (62.0)                             | 74 (61.2)                            | 0.878| -      | -        | -    |
| Alcoholic cirrhosis       | 21 (12.7)                              | 25 (20.7)                            | 0.068| -      | -        | -    |
| Cholestatic disease       | 16 (9.6)                               | 5 (4.1)                              | 0.077| -      | -        | -    |
| Other                     | 27 (16.3)                              | 16 (13.2)                            | 0.476| -      | -        | -    |
| Hepatocellular carcinoma  | 81 (48.8)                              | 46 (38.0)                            | 0.069| -      | -        | -    |
| HCV infection             | 74 (44.6)                              | 56 (46.3)                            | 0.775| -      | -        | -    |
| HBV infection             | 50 (30.1)                              | 32 (26.4)                            | 0.496| -      | -        | -    |
| MELD score at LT          | 18 (6 - 39)                            | 22 (6 - 49)                          | < 0.001| 1.051| 1.015 - 1.087| 0.004|
| Pre-LT ACLF               | 28 (16.9)                              | 32 (26.4)                            | 0.049| -      | -        | -    |
| Pre-LT in-hospital stay   | 48 (28.9)                              | 54 (44.6)                            | 0.006| 1.277| 1.077 - 2.277| 0.046|
| Pre-LT hepatorenal syndrome | 31 (18.7)                           | 53 (41.8)                            | < 0.001|        |          |      |
| Pre-LT CVVH/HD            | 2 (1.2)                                | 6 (5.0)                              | 0.062| -      | -        | -    |
| Pre-LT MV                 | 6 (3.6)                                | 4 (3.3)                              | 0.579| -      | -        | -    |
| Pre-LT use of norepinephrine | 3 (1.8)                     | 4 (3.3)                              | 0.331| -      | -        | -    |
| Transversal psoas muscle thickness/height | 18.04 (14.98 - 25.87) | 18.06 (14.98 - 25.87) | 0.849| -      | -        | -    |
| Psoas muscle area/BSA, mm²/m² | 343.94 (68.49 - 617.64) | 341.01 (253.14 - 832.08) | 0.867| -      | -        | -    |
| Psoas muscle density, HU   | 45.37 (32.99 - 59.78)                 | 43.23 (22.61 - 59.78)                | 0.071| -      | -        | -    |
| Psoas muscle density ≤ 46.11 HU | 89 (53.6)                      | 89 (56.1)                            | 0.022| -      | -        | -    |

Values are expressed as median (range) or No. (%).

The present study must be considered within the context of its limitations. One limitation is the small sample size, which restricted the type of analyses that we were able to perform. The principal limitation is the retrospective design of the study, which determined a potential selection bias. In particular, the sample may have been biased toward sicker patients, as these patients are more likely to undergo abdominal CT scans. Since sarcopenia was associated with cirrhosis severity (7-10, 37), our results are probably exaggerated by focusing on sicker patients.

Nevertheless, this study was innovative in its approach by using a simple and rapid way to check sarcopenia. Actually, the strength of this method is that every radiologist could measure PMD, with no need for specifically dedicated software. Another advantage of using PMD to assess sarcopenia is that muscle density is independent of...
Table 4. Comparison of Preoperative Characteristics of Patients Who Experienced Postoperative Respiratory Complications with Those of Patients Without Postoperative Respiratory Complications

| Variables                              | No Respiratory Complications (N = 257) | Respiratory Complications (N = 30) | P     | Exp(B)   | CI          | P     |
|----------------------------------------|---------------------------------------|-----------------------------------|-------|----------|-------------|-------|
| Age                                    | 53 (14 - 70)                          | 59 (39 - 69)                      | 0.011 | 1.060    | 1.005 - 1.119 | 0.032 |
| Male gender                            | 192 (74.7)                            | 21 (70.0)                         | 0.577 | -        | -           | -     |
| BMI, kg/m²                              | 24.7 (11.7 - 37.2)                    | 25.0 (15.8 - 32.5)                | 0.855 | -        | -           | -     |
| BSA, m²                                | 1.86 (1.37 - 2.40)                    | 1.84 (1.48 - 2.24)                | 0.365 | -        | -           | -     |

Liver disease

- Post-necrotic cirrhosis: 162 (63.0) vs 15 (50.0); P = 0.165
- Alcoholic cirrhosis: 38 (14.8) vs 8 (26.7); P = 0.093
- Cholestatic disease: 21 (8.2) vs 0 (0); P = 0.090
- Other: 37 (14.4) vs 6 (20.0); P = 0.416

Hepatocellular carcinoma

- 117 (45.5) vs 10 (33.3); P = 0.203

HCV infection

- 118 (45.9) vs 12 (40.0); P = 0.538

HBV infection

- 76 (29.6) vs 6 (20.0); P = 0.272

MELD score at LT

- 19 (6 - 39) vs 25 (10 - 49); P < 0.001

Pre-LT ACLF

- 47 (18.3) vs 13 (43.3); P = 0.001

Pre-LT in-hospital stay

- 87 (33.8) vs 15 (50.0); P = 0.080

Pre-LT hepatorenal syndrome

- 67 (26.1) vs 17 (56.7); P = 0.001

Pre-LT CVVH/HD

- 6 (2.3) vs 2 (6.7); P = 0.199

Pre-LT MV

- 9 (3.5) vs 1 (3.3); P = 0.719

Pre-LT use of norepinephrine

- 6 (2.3) vs 1 (3.3); P = 0.542

Transversal psoas muscle thickness/height

- 18.26 (4.98 - 26.99) vs 16.32 (9.26 - 24.51); P = 0.058

Psoas muscle area/BSA, mm²/m²

- 345.72 (68.49 - 832.08) vs 335.47 (25.34 - 626.72); P = 0.326

Psoas muscle density (HU)

- 45.28 (12.99 - 59.78) vs 39.05 (22.61 - 57.44); P < 0.001

Psoas muscle density ≤ 42.41 HU

- 91 (35.4) vs 22 (73.3); P < 0.001

Footnotes

Values are expressed as median (range) or No. (%).

gender, height, weight, or ethnicity compared to muscle area or thickness and thus appears more objective. In this sense, PMD should better contextualize the nutritional status of patients affected by nonalcoholic steatohepatitis, who are often malnourished (40); in these patients, a low PMD should guide clinicians to prescribe specific nutritional programs.

5.1. Conclusions

Further prospective studies on the utility of using PMD in prognostication and care of high-risk LT patients are needed. A better diagnosis of sarcopenia in cirrhotic patients should improve clinical care and help with the decision to give these patients some priority on the transplant waiting list.

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Table 5. Comparison of Preoperative Characteristics of Patients Who Experienced Postoperative Infections with Those of Patients Without Postoperative Infections

| Variables                        | No Infections (N = 255) | Postoperative Infections (N = 32) | P     | Exp(B) | C.I.  | P    |
|----------------------------------|-------------------------|-----------------------------------|-------|--------|-------|------|
| Age                              | 54 (14.7)               | 56 (35.6)                         | 0.370 | -      | -     | -    |
| Male gender                      | 190 (74.5)              | 21 (71.9)                         | 0.748 | -      | -     | -    |
| BMI, kg/m²                       | 24.5 (11.7 – 37.2)      | 26.6 (18.0 – 34.4)                | 0.052 | -      | -     | -    |
| BSA, m²                          | 1.86 (1.37 – 2.40)      | 1.83 (1.52 – 2.26)                | 0.899 | -      | -     | -    |
| Liver disease                    |                         |                                   |       |        |       |      |
| Post-necrotic cirrhosis          | 160 (62.7)              | 17 (53.1)                         | 0.291 | -      | -     | -    |
| Alcoholic cirrhosis              | 41 (16.1)               | 5 (15.6)                          | 0.947 | -      | -     | -    |
| Cholestatic disease              | 20 (7.8)                | 1 (3.1)                           | 0.293 | -      | -     | -    |
| Other                            | 35 (13.7)               | 8 (25.0)                          | 0.092 | -      | -     | -    |
| Hepatocellular carcinoma         | 118 (46.2)              | 9 (28.1)                          | 0.051 | -      | -     | -    |
| HCV infection                    | 116 (45.5)              | 14 (43.8)                         | 0.852 | -      | -     | -    |
| HBV infection                    | 75 (29.4)               | 7 (21.9)                          | 0.374 | -      | -     | -    |
| MELD score at LT                 | 19 (6 – 49)             | 24 (8 – 39)                       | 0.038 | -      | -     | -    |
| Pre-LT ACLF                      | 51 (20.0)               | 9 (28.1)                          | 0.287 | -      | -     | -    |
| Pre-LT in hospital stay          | 88 (34.5)               | 14 (43.8)                         | 0.303 | -      | -     | -    |
| Pre-LT hepatorenal syndrome      | 65 (25.5)               | 19 (59.4)                         | < 0.001 | 3.688 | 1.698 - 8.013 | 0.001 |
| Pre-LT CVVH/HD                   | 6 (2.4)                 | 2 (6.2)                           | 0.220 | -      | -     | -    |
| Pre-LT MV                        | 9 (3.5)                 | 1 (3.1)                           | 0.691 | -      | -     | -    |
| Pre-LT use of norepinephrine     | 5 (2.0)                 | 2 (6.2)                           | 0.177 | -      | -     | -    |
| Transversal psoas muscle thickness/height | 18.01 (4.98 – 25.87) | 18.48 (9.45 – 26.99) | 0.302 | -      | -     | -    |
| Psoas muscle area/BSA, mm²/m²    | 340.92 (25.34 – 832.08) | 361.87 (169.08 – 639.27)          | 0.489 | -      | -     | -    |
| Psoas muscle density, HU         | 44.99 (12.99 – 59.78)   | 40.25 (22.61 – 55.47)             | 0.001 | 0.934  | 0.887 - 0.984 | 0.010 |
| Psoas muscle density ≤ 40.39 HU  | 65 (25.5)               | 17 (53.1)                         | 0.002 | -      | -     | -    |

Values are expressed as median (range) or No. (%).

References

1. Yi Z, Mayorga ME, Orman ES, Wheeler SB, Hayashi PH, Barritt A. Trends in Characteristics of Patients Listed for Liver Transplantation Will Lead to Higher Rates of Waitlist Removal Due to Clinical Deterioration. Transplantation. 2017;101(10):2368–74. doi: 10.1097/TP.0000000000001851. [PubMed: 28858174]. [PubMed Central: PMC5667556].
2. Morrissey PE, Monaco AP. Donation after circulatory death: current practices, ongoing challenges, and potential improvements. Transplantation. 2014;97(3):258–64. doi: 10.1097/TP.00000000000001851. [PubMed: 24492420].
3. Wong TC, Fung JY, Cheung TT, Chan AC, Sharr WW, et al. Excellent outcomes of liver transplantation using severely steatotic grafts from brain-dead donors. Liver Transpl. 2016;22(2):226–36. doi: 10.1002/lt.24160. [PubMed: 25939934].
4. Orman ES, Mayorga ME, Wheeler SB, Townsley RM, Toro-Diaz HH, Hayashi PH, et al. Declining liver graft quality threatens the future of liver transplantation in the United States. Liver Transpl. 2015;21(6):1040–50. doi: 10.1002/lt.24060. [PubMed: 25939947]. [PubMed Central: PMC4566853].
5. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010;39(4):412-23. doi: 10.1093/ageing/afq034. [PubMed: 20392703]. [PubMed Central: PMC886201].
6. Dasarathy S, Merli M. Sarcopenia from mechanism to diagnosis and treatment in liver disease. J Hepatol. 2016;65(6):1232–44. doi: 10.1016/j.jhep.2016.07.040. [PubMed: 27515775]. [PubMed Central: PMC516259].
7. Marasco G, Serenari M, Renzulli M, Alemanni LV, Rossini B, Pettinari I, et al. Clinical impact of sarcopenia assessment in patients with hepatocellular carcinoma undergoing treatments. J Gastroenterol. 2020;55(10):927–43. doi: 10.1007/s00535-020-01711-w. [PubMed: 32748172]. [PubMed Central: PMC7510899].
8. Montano-Loza AJ, Meza-Junco J, Prado CM, Lieffers JR, Baracos VE, Bain VG, et al. Muscle wasting is associated with mortality in patients with cirrhosis. Clin Gastroenterol Hepatol. 2012;10(2):166–73. 173 e1. doi: 10.1016/j.cgh.2011.08.028. [PubMed: 21893129].
9. Alberino F, Gatta A, Amadio P, Merkel C, Di Pascoli L, Boffo G, et al. Nutrition and survival in patients with liver cirrhosis. Nutrition. 2009;25(6):445-50. doi: 10.1016/j.nut.2009.03.017.e1. [PubMed: 1999401].
10. Periyalwar P, Dasarathy S. Malnutrition in cirrhosis: contribution and consequences of sarcopenia on metabolic and clinical responses.
20. Drenth JP, Chrispijn M, Nagorney DM, Kamath PS, Torres VE. Medical nutrition status and quality of life in current patients with liver cirrhosis as assessed in 2007-2011. Hepatol Res. 2013;43(2):106-12. doi: 10.1111/hepr.12004. [PubMed: 23409849].

21. Underwood PW, Cron DC, Terjimanian MN, Wang SC, Englesbe MJ, et al. Sarcopenia adversely impacts postoperative complications following resection or transplantation in patients with primary liver tumors. J Gastrointest Surg. 2016;20(8):1625-32. doi: 10.1007/s11605-016-3046-0. [PubMed: 26803743].

22. Mayo SC, Shore AD, Nathan H, Edil BH, Hirose K, Anders RA, et al. Refining the definition of perioperative mortality following hepatectomy using death within 90 days as the standard criterion. HPB (Oxford). 2018;10(7):747-58. doi: 10.1177/1477257918813201. [PubMed: 30895961].

23. Bertoletto VR, Giannella M, Cucchetti A, Pinna AD, Grossi A, Ravaioli M, et al. Actual Risk of Using Very Aged Donors for Unselected Liver Transplant Candidates: A European Single-center Experience in the MELD Era. Ann Surg. 2017;265(2):388-96. doi: 10.1097/SLA.0000000000001608. [PubMed: 28009967].

24. Brellenthin JA, Chrispignin M, Nagorney DM, Kambath PS, Torres VE, Medical and surgical treatment options for polycystic liver disease. Hepatology. 2010;52(2):2223-30. doi: 10.1002/hep.23066. [PubMed: 21051114].

25. Moreau R, Jalain R, Gines P, Pavesi M, Angeli P, Cordoba J, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. Gastroenterology. 2013;144(7):1342-37. 1347 et al. [PubMed: 23742484].
39. Alwarawrah Y, Kiernan K, Maciver NJ. Changes in Nutritional Status Impact Immune Cell Metabolism and Function. *Front Immunol*. 2018;9:1055. doi: 10.3389/fimmu.2018.01055. [PubMed: 29868016]. [PubMed Central: PMC5968375].

40. Carias S, Castellanos AL, Vilchez V, Nair R, Dela Cruz AC, Watkins J, et al. Nonalcoholic steatohepatitis is strongly associated with sarcopenic obesity in patients with cirrhosis undergoing liver transplant evaluation. *J Gastroenterol Hepatol*. 2016;31(3):628-33. doi: 10.1111/jgh.13166. [PubMed: 26399838]. [PubMed Central: PMC6615558].