AI-based body composition score predicts survival after liver transplantation

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Article

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**Abstract**

**Importance**: Recent studies have shown that the body composition can significantly predict survival in patients with malignant diseases. This study aims to evaluate the importance of body composition for predicting short- and long-term survival after liver transplantation.

**Design, Setting, and Participants**: Body composition of all patients who underwent liver transplantation between January 2010 and December 2022 was assessed fully automated with artificial intelligence (AI) based technique. Clinical data such as demographic data and pre-, intra- and postoperative data were retrospectively reported. Uni- and multivariate regression analyses were performed to identify independent prognostic factors for survival.

**Results**: There were 346 patients with a mean age of 52.2 years (SD 10.8) and a mean BMI of 26.4 kg/m² (SD 4.8) included in this study. The univariate and multivariate cox regression analyses identified the ratio of the subcutaneous fat volume to muscle volume (FSM-ratio) as well as the ratio of the visceral fat volume to muscle volume (FVM-ratio) as significant prognostic parameter for the overall survival.

**Conclusion**: Based on the results of our study we can conclude that the FVM-ratio has an essential impact on overall survival after liver transplantation. The fully automated AI based assessment is fast, accurate and investigator independent.

**Introduction**

Organ shortage is a well-known problem in transplantation medicine worldwide, especially in Germany. Consequently, optimal patient selection is becoming increasingly important to maximize short- and long-term survival. Organ allocation is based on the MELD score, which has been developed to reflect the urgency of liver transplantation. However, its prognostic predictive value for the outcome after liver transplantation is limited. Besides many other well-known parameters, several recent studies have clearly shown a significant impact of psoas muscle volume as a parameter of sarcopenia, as well as visceral adipose tissue volume on the outcome after liver transplantation (1). While the independent influence of each factor is evident, the role of the relation of muscle and adipose tissue and related pathologies such as ‘Sarcopenic Obesity,’ for survival after liver transplantation has not been adequately studied up to now. An accurate assessment of psoas and adipose tissue volume is essential to address this question. Precise and objective manual assessment of these factors is time-consuming and extremely difficult. The need for new tools to implement these factors easily in the process of patient selection and organ allocation is therefore widely accepted. We developed a fully automated body composition analysis for routine CT imaging using convolutional neural networks in a previous study. We assessed the exact volume of the total muscle and subcutaneous and intra-abdominal adipose tissue (SAT and VAT). The fully automated volume assessment is examiner-independent, reproducible, and fast (2). This study aims to evaluate automatically assessed body composition, which contains subcutaneous and visceral
adipose tissue volume, muscle volume, and the relation of adipose tissue to muscle volume, as a prognostic factor for the outcome after liver transplantation in adult patients.

Patients and Methods

All patients who underwent deceased donor LT between January 2009 and December 2020 in our center were retrospectively reviewed. Due to the retrospective nature of this study, informed consent was waived. The study protocol was approved by our ethics’ committee (vote # 23-11226-BO).

Pediatric patients, patients with acute liver failure, and re-transplantations and patients with insufficient imaging data or a time span of more than three months between imaging data and LT were excluded. Preoperative, intraoperative, and postoperative data were retrospectively reported from our hospital's electronic database and access to patients’ medical records.

Computed tomography of the abdomen was defined from the diaphragm to the thigh. It was performed as triple-phase, contrast-enhanced, multidetector abdominal computed tomography (CT) with a slice thickness of 5 mm. All CT scans were performed using multidetector-row systems, mainly with 16 or higher detector-row systems. Venous phase imaging was performed 70–80 s after intravenous administration of a contrast agent, with a median tube voltage of 115 kVp ranging from 90 to 150 kVp. The total muscle, SAT, and VAT volume on these CT examinations were assessed using a neuronal network, as described in our previous study (Figure 1) (2). In addition, the ratio of subcutaneous adipose tissue volume to muscle volume and visceral adipose tissue volume to muscle volume (Figure 2+3), and total adipose tissue volume to muscle volume was calculated.

All patients underwent orthotopic deceased donor liver transplant in standard technique with caval interposition. Intraoperative and postoperative data such as the duration of surgery, blood transfusion, cold ischemic time, warm ischemic time, duration of intensive care unit (ICU) stay, postoperative complications, duration of hospital stay, and survival rates were assessed retrospectively. Perioperative mortality was defined as mortality within 30 days—immunosuppressant therapy after LT was based on calcineurin inhibitors and prednisone supplemented with mycophenolate mofetil. Modifications in dose or compounds were performed individually, depending on the clinical course. All patients were followed after LT according to the standard follow-up protocol. Morbidity was defined according to the Clavien–Dindo classification of surgical complications, with severe postoperative complications defined as grades IIIb and IV. (3).

This study was conducted in accordance with the principles of the World Medical Association, as defined in the Declaration of Helsinki, and the national regulations for the conduct of clinical trials. Institutional ethical board approval was obtained.

Statistical analyses
Values are reported as median values and interquartile range (IQR, in parentheses) or as mean values and standard deviation. We used the Mann–Whitney test to compare continuous variables and Fisher's exact test or the chi-square test for comparisons of proportions. Univariate and multivariate regression and linear multivariate analyses were performed to identify independent prognostic factors for overall survival after LT. They were tested in different models because BMI, SAT, VAT, and muscle volume are integrative variables. Statistical significance was defined as $p < 0.05$. A professional biostatistician used the SPSS 23.0 statistical package for Windows to perform all statistical analyses.

**Results**

Between January 2010 and December 2022, 1091 patients with end-stage liver disease underwent liver transplantation (LT) at our center. Of these, 346 patients with adequate imaging data (CT studies in our hospital's electronic system less than three months before LT) were included in the study. There were 268 male (60.1%) and 178 female (39.9%) patients with a mean age of 52.2 years (SD 10.8). The mean BMI was 26.4 kg/m$^2$ (SD 4.8). The main etiologies of cirrhosis were hepatitis C virus infection in 105 patients (30.3%) and alcoholic liver cirrhosis in 99 patients (28.6%). Comorbidities were observed in 287 patients (82.9%), cardiovascular disease in 141 patients (31.6%), diabetes mellitus in 112 patients (25.1%), and renal disease in 98 patients (21.9%). The mean MELD score at the time of LT was 24.3 (SD 5.0). The mean volume of the subcutaneous and visceral adipose tissue and muscle tissue assessed were fully automated by AI, and the calculated FSM and FVM-ratios are shown in Table 1.

The mean cold ischemic time was 448 min (SD 139.5), and the mean warm ischemic time was 33 min (SD 17.6). Blood transfusion was necessary in 177 patients (51.1%). The mean number of blood transfusions was 2.5 units (SD 1.7). The mean time of surgery was 306 min (SD 108). All patients were monitored postoperatively in the ICU. Major postoperative complications were observed in 86 patients (24.8%). These were biliary complications with interventional or surgical treatment in 32 patients (9.2%), postoperative bleeding in 36 patients (10%), arterial complications with surgical treatment in 9 patients (2.6%), and other complications in 9 patients (2.6%). Perioperative mortality (30 days mortality) was observed in 46 patients (18.4%). The mean ICU stay was 11.0 days (SD 6.0). The mean hospital stay was 30 days (SD 18). The median overall survival was 146 months. The 1-, 3- and 5-year survival rates were 87%, 83%, and 74%, respectively.

The results of the univariate and multivariate Cox regression analyses are shown in Table 2+3. The ratio of the subcutaneous fat volume to muscle volume and the ratio of the visceral fat volume to muscle volume were identified as significant prognostic factors for overall survival. Parameters such as subcutaneous fat volume, visceral fat volume, muscle volume, and BMI were not significant in predicting overall survival. Of all the significant factors, the ratio of visceral fat volume to muscle volume (FVM-ratio) has the most significant impact on overall survival.

**Discussion**
Several retrospective studies have clearly shown that sarcopenia as well as subcutaneous- and visceral adipose tissue volume have a significant impact on the mortality rate of patients on the waitlist for liver transplantation (LT) and on the posttransplant period (4–7). According to more recent studies, it is likely that the relationship between these compartments plays a more critical role than the absolute value of each compartment (8,9). Engelmann et al. retrospectively assessed the body composition of patients with liver cirrhosis listed for LT and patients after liver transplantation. A total of 612 patients who received an abdominal CT scan at the time of transplantation were included in the study. Cox regression analyses showed that decreasing subcutaneous fat was associated with an increased risk of cirrhosis-related complications and death on the waitlist. Increased paraspinal and visceral fat was positively correlated with metabolic comorbidities before transplantation and was predictive of 1-year survival after transplantation.

Consequently, the distribution of body fat is a significant determinant of outcome (10). Similar results were observed in our previous retrospective and prospective studies to evaluate the role of sarcopenia and frailty (1).

The impact of body composition on posttransplant mortality after LT is addressed in another recently published study with 116 patients. The results showed significantly lower survival in patients with sarcopenia and visceral obesity (sarcopenic obesity), while sarcopenia and visceral obesity independently had no impact on survival. Therefore the relative distribution of adipose tissue appears to be more important than the absolute value (11). The results of our study confirm these findings. Our study showed that the FVM-ratio is the strongest prognostic factor for survival after liver transplantation. The FVM-ratio increases if the visceral fat volume is higher in relation to the skeletal muscle volume, which leads to decreased survival.

Consequently, patients with normal BMI have inferior survival rates if their weight is mainly based on visceral fat volume rather than muscle volume. Accurate assessment of visceral fat and muscle volume is essential for predicting survival after LT.

Several methods have been described in the literature to assess body composition. The gold standard is the use of cross-sectional CT-derived assessment (1,8,12). All these methods of body composition assessments have limitations. There is a lack of recommendations for technical standards, such as contrast agents, tube voltage, and slide thickness. A further problem is the discriminating ability between muscle/soft tissue compartments in patients with end-stage liver disease, which leads to strong investigator dependency. Another major problem is that all manual and semiautomated segmentation tools are time-consuming and labor-intensive (13). The fully automated AI-based body composition assessment method used here is investigator-independent, requires technical standards, and can be done in seconds, as we have proven before (2). This study shows that this method can also be used in patients with end-stage liver disease to predict survival after LT.

Recent studies describe myosteatosis as a significant factor for survival after major liver resections for malignant disease and for survival prediction after LT (14,15). The assessment of myosteatosis is
performed using HU thresholds on CT scans. The discrimination of normal muscles and muscles with signs of myomatosis with this method is even more difficult than that with regular body composition. The fully automated AI-based assessment method can also describe and define standards for muscle quality, which can be correlated with muscle strength measured by handgrip strength.

The main limitation of our study is its retrospective character with all its drawbacks. However, with 612 patients included we present solid data that can be used as a starting point for further prospective studies. Another limitation is the selection bias due to the inclusion criteria. Only patients with CT scans 30 days before transplantation were included in the study. This might present a patient selection bias that leads to a study population in reduced physical condition. However, because we did not compare groups, the selection bias did not impact the significance of our results for this study population.

Notwithstanding the results are of high clinical importance and future automated assessment of FVM-ratio can help in clinical decisions regarding perioperative care.

Conclusion

Based on the results of our study, we can conclude that the relationship between subcutaneous and visceral fat volume and muscle volume is an independent prognostic factor for overall survival after LT. An accurate manual assessment of volumes is challenging because it is time-consuming and investigator-dependent. The completely automated AI-based assessment is fast and investigator-independent and yields important patient characteristics that might support perioperative care.

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>Hz</td>
<td>Hertz</td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
</tr>
<tr>
<td>INR</td>
<td>International Normalized Ratio</td>
</tr>
<tr>
<td>IQR</td>
<td>Interquartile range</td>
</tr>
<tr>
<td>Kg</td>
<td>Kilogram</td>
</tr>
<tr>
<td>LT</td>
<td>Liver Transplantation</td>
</tr>
<tr>
<td>MELD</td>
<td>Model for End-stage Liver Disease</td>
</tr>
<tr>
<td>nl</td>
<td>Nanoliter</td>
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</table>

Declarations
Authorship:


Funding Source: There was no funding for the study

Conflict of interest: There is no conflict of interest for any of the authors

Data availability: The datasets analysed during the current study available from the corresponding author on reasonable request.

Author Contribution Statement


References


**Table**

**Table1**: Mean values of body composition

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous adipose tissue volume (SAT)</td>
<td>83.6 ml</td>
<td>47.9 ml</td>
</tr>
<tr>
<td>Visceral adipose tissue volume (VAT)</td>
<td>52.0 ml</td>
<td>29.9 ml</td>
</tr>
<tr>
<td>Muscle Volume</td>
<td>68.1 ml</td>
<td>14.7 ml</td>
</tr>
<tr>
<td>FSM-ratio</td>
<td>1.23</td>
<td>0.71</td>
</tr>
<tr>
<td>FVM-ratio</td>
<td>0.76</td>
<td>0.41</td>
</tr>
</tbody>
</table>

Abb.: FSM=Ratio of subcutaneous fat volume to muscle volume, FVM=Ratio of visceral fat volume to muscle volume

**Table2**: Univariate analyses for survival
<table>
<thead>
<tr>
<th>Variables</th>
<th>HR</th>
<th>p-value</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>1.02</td>
<td>0.895</td>
<td>0.74-1.4</td>
</tr>
<tr>
<td>BMI</td>
<td>1.02</td>
<td>0.09</td>
<td>1.00-1.05</td>
</tr>
<tr>
<td>MELD-Score</td>
<td>1.04</td>
<td>0.001</td>
<td>1.01-1.06</td>
</tr>
<tr>
<td>Cold ischemic time</td>
<td>1.0</td>
<td>0.355</td>
<td>1.00-1.01</td>
</tr>
<tr>
<td>Time of Surgery</td>
<td>1.0</td>
<td>&lt;0.001</td>
<td>1.00-1.02</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>1.10</td>
<td>0.001</td>
<td>1.05-1.15</td>
</tr>
<tr>
<td>Subcutaneous adipose tissue volume (SAT)</td>
<td>1.0</td>
<td>0.277</td>
<td>1.00-1.01</td>
</tr>
<tr>
<td>Visceral adipose tissue volume (VAT)</td>
<td>1.01</td>
<td>0.210</td>
<td>1.00-1.02</td>
</tr>
<tr>
<td>Muscle Volume</td>
<td>1.00</td>
<td>0.564</td>
<td>0.98-1.01</td>
</tr>
<tr>
<td>FSM-ratio</td>
<td>1.45</td>
<td>0.016</td>
<td>1.07-1.96</td>
</tr>
<tr>
<td>FVM-ratio</td>
<td>2.31</td>
<td>0.023</td>
<td>1.12-4.73</td>
</tr>
</tbody>
</table>

Abb.: FSM=Ratio of subcutaneous fat volume to muscle volume, FVM=Ratio of visceral fat volume to muscle volume

**Table 3:** Multivariate Cox regression model for survival

<table>
<thead>
<tr>
<th>Variables</th>
<th>HR</th>
<th>p-value</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>1.02</td>
<td>0.09</td>
<td>1.00-1.05</td>
</tr>
<tr>
<td>MELD-Score</td>
<td>1.02</td>
<td>0.08</td>
<td>1.00-1.04</td>
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<tr>
<td>Cold ischemic time</td>
<td>1.00</td>
<td>0.45</td>
<td>1.00-1.00</td>
</tr>
<tr>
<td>Time of Surgery</td>
<td>1.00</td>
<td>&lt;0.001</td>
<td>1.00-1.00</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>1.07</td>
<td>&lt;0.001</td>
<td>1.03-1.10</td>
</tr>
<tr>
<td>Subcutaneous adipose tissue volume (SAT)</td>
<td>1.00</td>
<td>0.16</td>
<td>1.00-1.00</td>
</tr>
<tr>
<td>Visceral adipose tissue volume (VAT)</td>
<td>1.01</td>
<td>0.35</td>
<td>1.00-1.01</td>
</tr>
<tr>
<td>Muscle Volume</td>
<td>1.00</td>
<td>0.96</td>
<td>0.99-1.01</td>
</tr>
<tr>
<td>FSM-ratio</td>
<td>1.12</td>
<td>0.04</td>
<td>0.88-1.41</td>
</tr>
<tr>
<td>FVM-ratio</td>
<td>1.96</td>
<td>0.03</td>
<td>1.05-3.64</td>
</tr>
</tbody>
</table>

Abb.: FSM=Ratio of subcutaneous fat volume to muscle volume, FVM=Ratio of visceral fat volume to muscle volume
Figures

Figure 1

CT-Abdomen for the assessment of the total volume of subcutaneous- and visceral adipose tissue and muscle tissue using convolutional neuronal network

\[ \text{FSM-Ratio} = \frac{\text{SAT}_{\text{mean}}}{\text{Muscle}_{\text{mean}}} \]

Figure 2

FSM-Ratio= Ratio of the mean subcutaneous fat volume to the mean muscle volume, SAT=subcutaneous adipose tissue

\[ \text{FVM-Ratio} = \frac{\text{VAT}_{\text{mean}}}{\text{Muscle}_{\text{mean}}} \]

Figure 3
**Figure 2:** FVM-Ratio= Ratio of the mean visceral fat volume to the mean muscle volume, VAT=Visceral adipose tissue