

## Original Article

# Association of Imaging-based Skeletal Muscle Metrics, Biochemical Markers, and MELD Score with Liver Transplant Complications and Survival: Insights from a Single-Center Cross-sectional Study

Pooneh Dehghan<sup>1</sup>, Fatemeh Ghiasi<sup>1</sup>, Seyedhassan Langari<sup>1</sup>, Amirhassan Rabbani<sup>2</sup>, Hesameddin Eghlimi<sup>3</sup>, Mahmoud Amiri<sup>4</sup>, Javad Khoshrou<sup>1\*</sup>

<sup>1</sup>Radiology Department, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>2</sup>Department of Transplant & Hepatobiliary Surgery, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>3</sup>Department of General Surgery, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>4</sup>Department of Medical-Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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## Abstract

**Background:** Identifying pre-transplant predictors of postoperative complications and survival following liver transplantation can improve patient outcomes and resource allocation. This study aimed to assess the predictive role of laboratory biomarkers and imaging-based parameters in post-transplant complications and patient survival.

**Materials and Methods:** In this cross-sectional study, data from patients aged 17–75 years undergoing liver transplantation from deceased donors between October 2019 and December 2023 were retrospectively analyzed. Patients with malignancy, cardiovascular diseases, living donor transplants, or incomplete data were excluded. Preoperative clinical variables included demographics, MELD score, vascular features, biochemical laboratory parameters, and imaging-based muscle metrics (Skeletal Muscle Area, Skeletal Muscle Index, Skeletal Muscle Radiodensity Assessment, myosteatorsis). Postoperative complications, survival status, and associated predictors were evaluated using appropriate statistical tests.

**Results:** Of 79 patients (mean age  $49.4 \pm 12.2$  years, 58.2% male), complications occurred in 39 (49.4%). Male sex ( $p=0.015$ ) and lower SMRA ( $p=0.008$ ) were significantly associated with postoperative complications. Patients who died had substantially higher MELD scores ( $23.3 \pm 10.6$ ) than survivors ( $17.3 \pm 7.7$ ;  $p=0.037$ ). Portosystemic collaterals were significantly less frequent among patients with complications (23% vs. 50%,  $p=0.019$ ). Routine biochemical laboratory parameters, SMA, SMI, myosteatorsis, and vascular diameters were not significantly associated with outcomes. Kaplan-Meier survival analysis demonstrated an 85% survival rate at one year, with mortality primarily occurring within the first three months post-transplant.

**Conclusion:** Pre-transplant MELD score tends to predict survival, whereas lower SMRA, male sex, and the absence of portosystemic collaterals may predict postoperative complications. Identifying these factors can enhance risk stratification and perioperative management in liver transplant recipients.

**Keywords:** Deceased donor liver transplantation, Overall survival, Liver transplant complications, SMRA, Skeletal Muscle Metrics

\*Corresponding Author: Javad Khoshrou, Radiology Department, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran. ORCID ID: 0000-0002-1425-2028 Email: drjkh234@gmail.com

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## Introduction

Liver transplantation (LT) rates have significantly increased worldwide as the definitive therapeutic option for end-stage liver disease (ESLD) and acute liver failure<sup>1</sup>. In recent years, overall survival following LT has notably improved. For example, in Europe, the one- and five-year survival rates have reached 86% and 74%, respectively, while global patient survival rates have reached 91.8% and 76.1%, respectively<sup>2,3</sup>. Despite these improvements, there remains an essential need to more accurately predict postoperative complications to enhance LT outcomes further and optimize resource allocation.

Predicting complications following LT presents several challenges. Complex interactions between donor and recipient characteristics, such as organ quality and recipient comorbidities, complicate effective risk stratification<sup>4,5</sup>. Additionally, current predictive models are predominantly based on clinical assessments, such as the Model for End-Stage Liver Disease (MELD) scoring system, which primarily predicts pre-transplant mortality but does not adequately address post-transplant outcomes<sup>6</sup>. Moreover, geographical disparities and differences in patient demographics hinder the development of universally applicable prediction models, underscoring the need for region-specific studies<sup>6,7</sup>.

Beyond MELD, end-stage liver disease is characterized by systemic catabolism, chronic inflammation, hyperammonemia, and malnutrition, which drive loss of muscle mass (sarcopenia) and intramuscular fat infiltration (myosteatosis)<sup>8-11</sup>. These alterations impair immune competence, wound healing, and ventilatory mechanics, thereby plausibly increasing perioperative complications and mortality after LT<sup>10,11</sup>. Various imaging techniques, including ultrasound and MRI, performed pre- and post-transplantation, have shown promising results in diagnosing vascular, biliary, parenchymal, and surgical complications, thereby improving patient survival<sup>12</sup>. Computed tomography (CT)-derived measures obtained during routine pre-LT assessment—skeletal muscle index (SMI), skeletal

muscle area (SMA), and skeletal muscle radiodensity attenuation (SMRA)—offer objective quantification of muscle quantity (SMI/SMA) and muscle quality (SMRA/myosteatosis). Importantly, reduced muscle quality can occur despite preserved mass and has been associated with adverse outcomes in several cohorts<sup>13-18</sup>. These metrics provide insights into muscle quantity and quality, which seem to be linked to survival, complications, and graft outcomes.

While these tools individually have shown promising results in predicting post-transplant mortality, prior studies differ in endpoints, cutoffs, and populations, and evidence from Iranian LT recipients is limited, underscoring the need for context-specific evaluation of these metrics alongside clinical and laboratory factors. In addition, evidence suggests that combining pre-transplant clinical, laboratory, and imaging assessments could enhance predictive accuracy<sup>19</sup>. Therefore, in this retrospective cross-sectional study, we aimed to investigate the predictive roles of SMA, SMI, SMRA, myosteatosis, and biochemical markers for LT outcomes, including postoperative complication status and patient survival, in a cohort of Iranian deceased-donor LT patients with diverse underlying liver diseases.

## Methods

This cross-sectional study was conducted from October 2019 to December 2023 at Taleghani Hospital, Tehran, Iran. Patients who underwent liver transplantation from deceased donors at our center within this period were screened for eligibility. Patients aged 17 to 75 years with no history of malignancy or cardiovascular disease and a compatible blood group with the donor were included. Availability of complete pre-transplant imaging data (CT scan) and detailed records of post-transplant complications was also mandatory for inclusion. Exclusion criteria encompassed patients who received liver transplants from living donors, those with incomplete medical records, and those outside the specified age range or with known cancer or cardiovascular diseases.

Data were retrospectively extracted from electronic

medical records and hospital archives. Pre-transplant parameters included patient demographics (age, sex), underlying liver disease, presence of vascular variations and portosystemic collaterals, diameters of the splenic artery and common bile duct (CBD), Model for End-stage Liver Disease (MELD) score, imaging-based muscle parameters (Skeletal Muscle Area [SMA], Skeletal Muscle Index [SMI], Skeletal Muscle Radiodensity Attenuation [SMRA], and Myosteatorsis), as well as comprehensive laboratory parameters (Aspartate aminotransferase [AST], Alanine aminotransferase [ALT], Albumin, Total Bilirubin, Hemoglobin, Creatinine, Prothrombin Time [PT], Partial Thromboplastin Time [PTT], International Normalized Ratio [INR], Platelet count, Sodium [Na], Potassium [K], and Blood Urea Nitrogen [BUN]).

Post-transplant parameters recorded included the presence or absence of complications such as hepatic vein or artery thrombosis, portal vein thrombosis, infections, bile leaks, strictures of the portal vein or artery, hemorrhage, rejection, delirium, seizures, disorders of consciousness, encephalopathy, pulmonary or renal dysfunctions, and hepatorenal syndrome. Survival status was documented through December 21, 2023, including the date of patient death, if applicable.

The primary outcomes were the presence of post-transplant complications and patient survival status. Differences in age, sex distribution, MELD score, pre-transplant laboratory values, and imaging characteristics were analyzed between patients with and without post-transplant complications and between survivors and non-survivors.

All abdominal CT studies were performed on Siemens multidetector CT scanners (SOMATOM series; Siemens Healthineers, Germany). Scans were acquired at 120 kVp with automatic tube-current modulation. Body composition was quantified on a single axial slice at the L3 vertebral level. Skeletal muscle was identified using Hounsfield unit (HU) thresholds of  $-29$  to  $+150$  HU. For each patient, we recorded skeletal muscle area (SMA,  $\text{cm}^2$ ) and skeletal muscle radiodensity attenuation (SMRA, HU) as the mean attenuation across the segmented muscles. Skeletal muscle index (SMI,  $\text{cm}^2/\text{m}^2$ ) was calculated as SMA normalized to height squared. Myosteatorsis

was defined as SMRA  $<33$  HU in men and  $<29$  HU in women.

All statistical analyses were performed using Python version 3.11, employing the following open-source libraries: pandas for data management, SciPy for statistical testing, and matplotlib for visualization. Continuous variables were summarized as means and standard deviations. The Welch's unequal-variance t-test was used to compare continuous variables between two independent groups, given potential heteroscedasticity and unequal sample sizes. Categorical variables were expressed as counts and percentages. Comparisons between categorical variables were performed using the Fisher's exact test for  $2 \times 2$  contingency tables, and the Chi-square test for larger tables, as appropriate. The threshold for statistical significance was set at  $p < 0.05$ . Kaplan–Meier survival analysis was conducted to estimate overall survival probabilities. Survival time was defined as the interval (in days) from the date of transplantation to either death or the last known follow-up. For postoperative complications, we used logistic regression including age (per 10 years), sex, MELD (per 5 points), and skeletal muscle radiodensity attenuation (SMRA; per 5 Hounsfield units); a sensitivity model substituted skeletal muscle index (SMI; per  $5 \text{ cm}^2/\text{m}^2$ ) for SMRA. Model calibration and discrimination were assessed using the Hosmer–Lemeshow test and AUC. For survival, we fit Cox proportional hazards models including MELD (per 5) and SMRA (per 5), with age (per 10 years) added in a secondary model. Proportional hazards were evaluated, and results are reported as adjusted hazard ratios (HRs) with 95% confidence intervals. A log-rank test was used to compare survival curves across underlying disease groups.

## Results

A total of 79 patients were included in this study. The mean age of the cohort was  $49.4 \pm 12.2$  years. When comparing patients by complication status, there was no significant difference in age between those who developed postoperative complications ( $50.2 \pm 11.9$  years) and those who did not ( $48.6 \pm 12.6$  years;  $p = 0.648$ ). Similarly, there was no significant difference in mean age between survivors ( $48.7 \pm 12.4$  years) and

**Table 1.** Patient Demographic Characteristics.

Characteristic	Overall (n=79)	No Complications (n=40)	Complications (n=39)	p-value	Alive (n=62)	Expired (n=17)	p-value
Age (years)	49.4 ± 12.2	48.6 ± 12.6	50.2 ± 11.9	0.648	48.7 ± 12.4	51.2 ± 11.3	0.505
<b>Sex, n (%)</b>							
Male	46 (58.2%)	18 (45%)	28 (72%)		34 (55%)	12 (71%)	
Female	33 (41.8%)	22 (55%)	11 (28%)	0.015	28 (45%)	5 (29%)	0.264

patients who expired following transplantation (51.2 ± 11.3 years; p = 0.505).

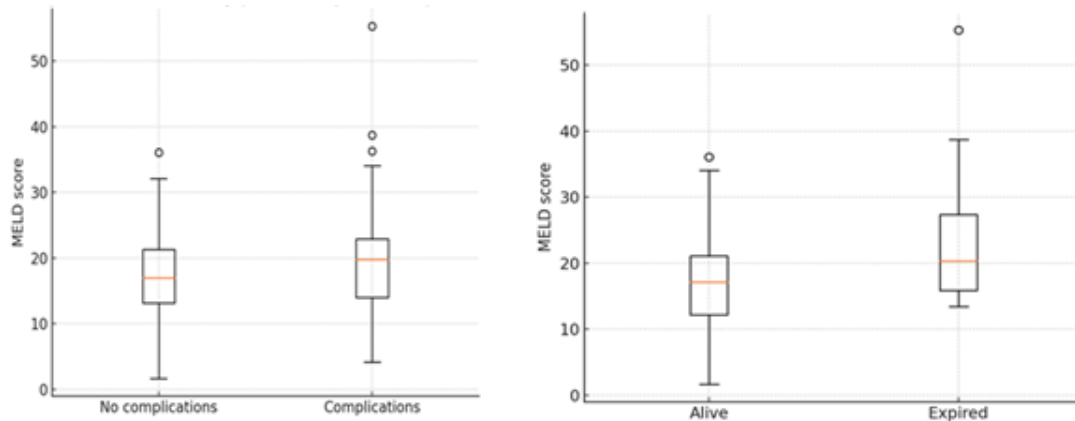
The overall sex distribution showed a higher representation of male patients (58.2%, n=46) compared to females (41.8%, n=33). However, male sex was significantly associated with postoperative complications, with males constituting 72% (n=28) of the complication group compared to 45% (n=18) in the group with no postoperative complications (p = 0.015). In contrast, sex distribution did not significantly differ between survivors (55% male, 45% female) and expired patients (71% male, 29% female; p = 0.264). Detailed patient demographic characteristics are summarized in Table 1.

Routine pre-transplant biochemical markers,

including ALT, AST, total bilirubin, albumin, creatinine, hemoglobin, PT, PTT, INR, thrombocytes, sodium, potassium, and BUN, were evaluated for potential associations with postoperative complications and patient survival. No statistically significant differences were observed for these parameters between patients who developed postoperative complications and those who did not (p-values > 0.05). Similarly, no significant associations were identified between these laboratory values and survival status. Although total bilirubin and PT showed some numerical differences between groups, these differences did not reach statistical significance (bilirubin, p = 0.176; PT, p = 0.097). These findings suggest only a potential trend and warrant further investigation with larger sample

**Table 2.** Clinical and Laboratory Parameters by Complications and Survival Status.

Parameter	No Complications (n=40)	Complications (n=39)	p-value	Alive (n=62)	Expired (n=17)	p-value
ALT (U/L)	242.98 ± 352.88	300.79 ± 432.50	0.518	265.40 ± 415.83	293.82 ± 303.29	0.756
AST (U/L)	350.48 ± 561.64	455.97 ± 590.02	0.418	371.71 ± 575.99	515.06 ± 572.21	0.369
Total Bilirubin (mg/dL)	7.42 ± 7.45	8.93 ± 9.73	0.442	7.34 ± 7.94	11.18 ± 10.52	0.176
Albumin (g/dL)	3.17 ± 0.71	3.13 ± 0.97	0.863	3.12 ± 0.68	3.27 ± 1.31	0.645
Creatinine (mg/dL)	1.09 ± 0.78	1.43 ± 1.43	0.189	1.17 ± 1.01	1.57 ± 1.56	0.329
Hemoglobin (g/dL)	10.52 ± 1.99	10.93 ± 1.99	0.368	10.69 ± 2.01	10.86 ± 1.97	0.756
PT (seconds)	17.28 ± 4.67	17.15 ± 4.38	0.903	16.70 ± 4.18	19.17 ± 5.26	0.097
PTT (seconds)	37.15 ± 9.06	40.92 ± 10.93	0.106	38.58 ± 8.97	40.75 ± 13.95	0.562
INR	1.75 ± 0.69	2.85 ± 6.82	0.336	1.68 ± 0.63	4.58 ± 10.28	0.277
Thrombocytes (×10 <sup>3</sup> /μL)	116.02 ± 105.71	159.05 ± 141.54	0.131	141.15 ± 125.76	123.12 ± 128.62	0.611
Sodium (mmol/L)	138.28 ± 4.56	137.56 ± 3.95	0.460	138.02 ± 4.16	137.59 ± 4.70	0.737
Potassium (mmol/L)	4.06 ± 0.55	4.03 ± 0.59	0.843	4.03 ± 0.57	4.08 ± 0.56	0.750
BUN (mg/dL)	22.60 ± 33.72	22.05 ± 18.05	0.929	21.77 ± 27.79	24.35 ± 24.39	0.711



**Figure 1.** MELD in patients without complications (n = 40) vs with complications (n = 39); group difference p = 0.22. MELD in survivors (n = 62) vs expired patients (n = 17) at last follow-up; group difference p = 0.037. Boxplots display median, interquartile range (IQR), and whiskers to 1.5×IQR; points denote outliers. Abbreviation: MELD, Model for End-Stage Liver Disease.

**Table 3.** Imaging Parameters by Complication and Survival Status.

Parameter	No Complications	Complications	p-value	Alive	Expired	p-value
SMA	114.65 ± 29.97	116.45 ± 31.79	0.796	112 ± 28	128.25 ± 37.24	0.110
SMI	40.1 ± 8.6	42.5 ± 10.0	0.277	40.3 ± 8.61	45.28 ± 11.3	0.137
SMRA	34.1 ± 6.6	29.7 ± 7.9	<b>0.008</b>	32.6 ± 7.5	29.5 ± 7.38	0.140

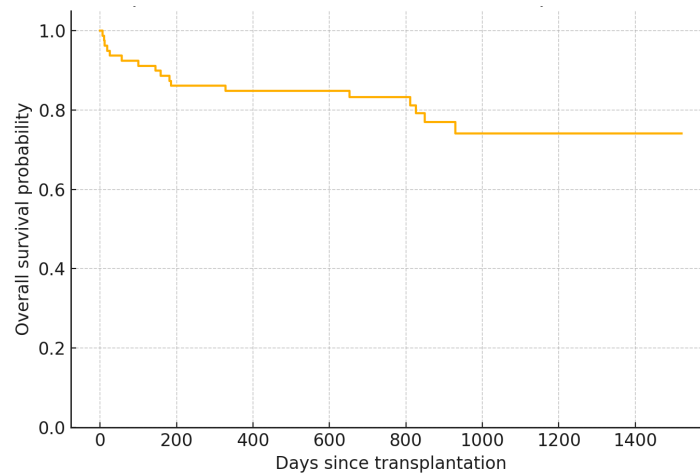
sizes. Detailed laboratory results are summarized in Table 2.

The MELD score was slightly higher among patients who developed postoperative complications (20.0 ± 10.1) compared to those without complications (17.5 ± 7.7); however, this difference was not statistically significant (p = 0.22, Cohen's d = -0.28). Patients who expired had significantly higher MELD scores (23.3 ± 10.6) compared to survivors (17.25 ± 7.67), demonstrating a significant association with survival status (p = 0.037, Cohen's d = -0.73) (Figure 1).

Skeletal Muscle Area (SMA) did not differ significantly between patients based on complication status (p = 0.796) or survival status (p = 0.110), though numerically higher values were noted in the expired group (128.25 ± 37.24 vs. 112 ± 28 for survivors). Skeletal Muscle Index (SMI) showed no significant differences for complication status (p = 0.277) or survival (p = 0.137), despite a trend toward higher values among expired patients (45.28 ± 11.3 vs. 40.3 ± 8.61). Skeletal Muscle Radiodensity Attenuation (SMRA) was significantly lower in patients with complications (29.7 ± 7.9) compared to those without (34.1 ± 6.6, p = 0.008, Cohen's d = 0.61). No significant association with survival was observed (p

= 0.140). The presence of Myosteatosi s did not differ significantly across complication or survival groups (p-values > 0.999), indicating limited predictive relevance in this cohort. Imaging-based parameters are summarized in Table 3.

The presence of portosystemic collaterals was significantly lower among patients who developed complications (23%) than among those without complications (50%; p = 0.019). The diameters of the splenic artery and common bile duct (CBD) showed no significant differences based on complications or survival status (p-values > 0.05). In multivariable logistic regression (n=77), lower pre-transplant SMRA showed a borderline association with higher odds of postoperative complications (adjusted OR 0.67, 95% CI 0.45–1.00; p=0.052; AUC 0.70; HL p=0.35), whereas MELD was not significant (aOR 1.22, 95% CI 0.91–1.63; p=0.18). In a sensitivity model substituting SMI for SMRA (n=67), SMI (per 5 cm<sup>2</sup>/m<sup>2</sup>) was not associated with complications (aOR 1.22, 95% CI 0.89–1.66; p=0.22; AUC 0.65; HL p=0.63).



**Figure 2.** Kaplan–Meier survival after liver transplantation. Time zero is the transplantation date; follow-up was administratively censored on 21 December 2023.

### Survival Analysis

Kaplan–Meier analysis indicated that survival dropped rapidly during the first 2–3 months following transplantation, stabilizing thereafter. The 1-year survival rate was approximately 85%. Median survival was not reached during the study period, highlighting favorable long-term outcomes for most patients (Figure 2). The global log-rank test showed no significant difference in survival across underlying disease categories ( $p = 0.50$ ). MELD was independently associated with higher mortality in the Cox model (HR 1.41, 95% CI 1.13–1.76;  $p=0.0026$ ). SMRA showed a non-significant trend toward lower mortality (HR 0.76, 95% CI 0.57–1.02;  $p=0.068$ ). Adding age yielded similar results (MELD HR 1.33, 95% CI 1.06–1.67;  $p=0.013$ ; SMRA HR 0.83, 95% CI 0.61–1.13;  $p=0.234$ ).

## Discussion

Our findings identify pre-transplant MELD and muscle quality as complementary predictors of post-liver transplant (LT) outcomes. Higher MELD was significantly associated with increased post-transplant mortality, and lower SMRA was significantly associated with postoperative complications (directionally consistent after adjustment). In addition, male sex was significantly associated with complications. In contrast, the presence of portosystemic collaterals was inversely associated with complications, highlighting recipient phenotype

and portal decompression as potential modifiers of perioperative risk.

The MELD score is widely used in LT to prioritize organ allocation because it effectively identifies patients at the highest risk of pre-transplant mortality<sup>20</sup>. Prior studies have shown that both preoperative and early postoperative MELD scores predict complications and mortality<sup>21,22</sup>. Consistent with these reports, our cohort showed a significant association between higher pre-transplant MELD scores and mortality. In contrast, MELD did not discriminate complication risk, underscoring that mortality and complication risks are not fully overlapping constructs. Some reports suggest long-term survival may not differ markedly across MELD strata<sup>23</sup>. Collectively, these points illustrate the limits of relying solely on MELD and motivate the use of additional or combined metrics to improve prediction (e.g., APACHE IV)<sup>24</sup>. In this context, body-composition metrics have attracted increasing attention. Among CT-derived parameters, SMRA (muscle quality) showed the clearest clinical signal in our data, as it was associated with postoperative complications. This aligns with reports that myosteotosis (low SMRA) relates to adverse outcomes after LT<sup>14,17</sup>. For example, Kyselova et al. linked lower SMRA with higher revision surgery and transfusion needs and with increased long-term mortality risk<sup>18</sup>. Bot et al. found higher muscle attenuation associated with lower 1-year mortality<sup>16</sup>. Czigan et al. further demonstrated worse 5-year graft and patient survival in recipients with myosteotosis<sup>17</sup>. While our mortality analysis did not

show a significant association with SMRA, the direction of effect was consistent with these data, and differences in cohort size, follow-up duration, or cutoffs may explain discrepancies.

By contrast, muscle quantity metrics (SMA/SMI) did not significantly predict complications or mortality in our cohort. This is consistent with studies reporting the limited prognostic value of SMI alone<sup>16,18</sup> and with Czigany et al., who showed that low muscle mass without myosteatosis was not associated with graft or patient survival<sup>17</sup>. However, heterogeneity exists: Shafaat et al. observed that continuous decreases in SMI and in muscle attenuation are each associated with higher mortality risk, emphasizing that continuous modeling may capture risk gradients better than binary cutoffs<sup>25</sup>. Overall, these data support the primacy of muscle quality over quantity for perioperative risk and suggest that how these metrics are modeled (continuous vs dichotomized) matters.

The discrepancy in association between SMI and post-transplant outcomes may reflect the limitations of using muscle mass alone as a surrogate for physiologic reserve or functional status. SMI, while quantitative, does not account for intramuscular fat infiltration or muscle strength, which are increasingly recognized as more relevant indicators of sarcopenia's clinical impact. Additionally, cutoff thresholds for defining low SMI vary across studies, potentially contributing to heterogeneity in results. It is also possible that the pathophysiological burden of muscle wasting becomes more pronounced only when combined with reduced muscle quality (i.e., myosteatosis), a hypothesis supported by studies showing synergistic effects of low SMI and SMRA on mortality risk<sup>13,18</sup>.

Emerging evidence also indicates that muscle quality and quantity interact: Lu et al. showed myosteatosis most adversely affected survival within the sarcopenic subgroup, not in non-sarcopenic patients<sup>13</sup>, a synergistic pattern echoed by Kyselova et al.<sup>18</sup>. Together with our findings (SMRA signal and SMI null), this supports composite muscle health assessment over single-metric approaches. In line with this, Huang et al. reported that combining SMI with the albumin-globulin score (AGS) improved prediction of short- and long-term LT outcomes<sup>26</sup>.

Non-significant findings in our cohort—including routine laboratory markers and SMA/SMI when

analyzed as primary predictors—emphasize that MELD (mortality) and SMRA (complications) carry the main prognostic signal in our setting.

This study has some strengths, including the comprehensive evaluation of multiple muscle-related metrics (SMI, SMRA, SMA, and myosteatosis) alongside clinical parameters (MELD score and vascular factors). However, some limitations must be acknowledged. Firstly, the retrospective nature of the study limits causative interpretations. Additionally, the single-center design and relatively small sample size may limit the generalizability of our findings. Our sample size and event count were insufficient to adequately power subgroup or interaction analyses by sex and disease etiology; therefore, we did not perform these post hoc stratifications. Given 39 complication events and 17 deaths, adjusted models were intentionally restricted to key confounders. Thus, estimates should be interpreted cautiously due to the limited number of events per variable. Lastly, potential selection bias and the absence of longitudinal data regarding post-transplant interventions may influence the observed associations.

## Conclusion

In conclusion, this study underscores the prognostic value of pre-transplant muscle quality, particularly skeletal muscle radiodensity attenuation (SMRA), in predicting postoperative outcomes among liver transplant recipients in an Iranian cohort. Our findings support the integration of detailed muscle health assessments into pre-transplant evaluation protocols, as they may enable more accurate risk stratification and guide individualized perioperative management strategies. To strengthen the generalizability and clinical utility of these results, future research should prioritize prospective, multicenter studies with larger and more diverse populations.

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## Ethical Approval

The study protocol was approved by the Research Ethics Committee of the Shahid Beheshti University of Medical Sciences (Ref. No.: IR.SBMU.MSP.REC.1403.580), and the study adhered to the ethical standards outlined in the Declaration of Helsinki. Given the retrospective nature of the research and the anonymized data handling, the ethics committee waived informed consent.

## Funding

None.

## Conflict of interest

The authors further declare that they have no conflict of interest.

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