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Impact of sarcopenia on the survival of patients undergoing liver transplantation for decompensated liver cirrhosis

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Abstract

Background Patients with decompensated cirrhosis (DC) are prone to skeletal muscle loss, namely, sarcopenia, before liver transplantation (LT). While sarcopenia is reportedly associated with adverse outcomes after LT, these findings are limited owing to mixed diseases and retrospective data. We investigated the association between sarcopenia and 1-year overall survival (OS) in patients with DC after LT and established and validated a prediction model for postoperative OS based on sarcopenia.

Methods Overall, 222 consecutive patients who underwent LT at our centre were registered between September 2020 and June 2022. Third lumbar spine skeletal muscle mass index was measured using computed tomography. Patients were divided into sarcopenia and non-sarcopenia groups according to the skeletal muscle mass index, and baseline data and postoperative outcomes were collected, compared and analysed. The primary outcome was the 1-year OS after LT. We established a dynamic nomogram of the OS predictive model.

Results We included 177 DC patients [mean (standard deviation) age, 50.2 ± 9.3 years; 52 women (29.4%)]; 73 (41.2%) had sarcopenia. The mean (standard deviation) body mass index was 22.6 ± 4.5 kg/m^2, 28 (15.8%) patients had weight loss ≥5% within 6 months before admission, and the mean (standard deviation) model for end-stage liver disease (MELD) score was 18.4 ± 7.9. Patients with sarcopenia had a longer duration of intensive care unit stay (4.1 ± 2.2 vs. 3.1 ± 1.1 days, $P = 0.008$), higher rate of major complications (45.2% vs. 22.1%, $P = 0.001$) and higher postoperative mortality (15.1% vs. 2.9%, $P = 0.003$) than those without sarcopenia. The median 1-year OS after surgery was shorter in patients with sarcopenia than in those without ($P < 0.001$). Sarcopenia [hazard ratio (HR), 2.54; 95% confidence interval (CI), 1.54–5.63; $P = 0.022$], weight loss ≥5% (HR, 2.46; 95% CI, 1.39–5.09; $P = 0.015$) and MELD score (HR, 1.05; 95% CI, 1.01–1.09; $P = 0.009$) were independent risk factors associated with 1-year OS. The area under the curve of the established dynamic nomogram was 0.774, the calibration curve showed good consistency, and analysis of the decision curve showed more clinical benefits than the MELD score alone. High-risk patients (>102.9 points calculated using the nomogram) had a significantly reduced survival rate.

Conclusions Sarcopenia is associated with adverse outcomes after LT in patients with DC. High-risk patients should be classified by dynamic nomogram upon admission.

Keywords Dynamic nomogram; Liver transplantation; MELD; Sarcopenia; Survival

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Introduction

The liver is the largest organ involved in metabolizing various nutrients and is closely related to nutritional status. Patients with decompensated cirrhosis of various aetiologies have severely impaired liver function, for which liver transplantation (LT) is the only curative treatment.[1] Sarcopenia (an important feature of malnutrition due to liver failure) is a syndrome characterized by the progressive and systemic loss of skeletal muscle mass, strength and function,[2] which is most likely to occur during the waiting period for LT. The prevalence of sarcopenia ranges between 30% and 70% in cirrhotic patients and LT candidates according to a previous study.[3] Recently, different guidelines and expert consensus have recommended increased awareness of sarcopenia and assessment consideration in all patients with decompensated cirrhosis waiting for LT.[4–6]

Multiple definitions of sarcopenia in patients with decompensated cirrhosis have been reported, including low muscle mass (the main diagnostic indicator of sarcopenia). Regardless of its measurement, sarcopenia is the main indicator of adverse outcomes in patients with decompensated cirrhosis undergoing LT. These include poor quality of life,[7] hepatic dysfunction,[8] longer intensive care unit (ICU) and hospital stay,[9,10] and higher incidence of infection and mortality.[11] Early nutritional support can extend life expectancy, improve quality of life, reduce complications and help prepare for more successful LT.[12] This suggests that if nutritional status is assessed immediately before LT, it may be possible to take preoperative interventions to improve patient outcomes. Simultaneously, pre-transplant risk assessment is of utmost clinical importance in the face of critical organ shortage. Although LT allocation is now based on the model for end-stage liver disease (MELD) score,[13] this score is a poor predictor of perioperative LT mortality because it does not take into account the many factors that influence postoperative complications. Existing literature has reported that sarcopenia strongly correlates with waiting-list mortality in LT candidates with liver cirrhosis, particularly in those with MELD scores $\leq$15.[14] Therefore, it is more practical to augment the MELD score by determining the effect of sarcopenia on the survival after LT. Most studies investigating the association between sarcopenia and survival post-LT have been performed in North American populations, which may differ significantly from Chinese populations. Additionally, there is a lack of easy-to-use predictive models. A dynamic nomogram can be used online to help clinicians identify patients who are likely to benefit more from surgery.

Therefore, this study assessed the effect of sarcopenia on relevant post-LT outcomes, including complications and 1-year overall survival (OS), in a consecutive Chinese cohort of patients with decompensated cirrhosis undergoing LT. It further aimed to establish and verify a dynamic nomogram model of 1-year OS post-LT based on independent risk factors, including sarcopenia.

Methods

Study population

A total of 222 patients receiving LT at our centre were prospectively enrolled between September 2020 and June 2022. The flowchart of this study is shown in *Figure* 1. The inclusion criteria were as follows: (1) consecutive adult patients ($\geq$18 years) with decompensated cirrhosis; (2) integrity of the required data and (3) abdominal computed tomography (CT) examination performed at the study centre 3 months before LT. The exclusion criteria were as follows: (1) non-cirrhotic decompensation; (2) incomplete data; (3) retransplantation; and (4) serious medical conditions such as heart failure, persistent infection, and renal insufficiency. We excluded 45 patients for incomplete data (n = 5), inconsistency with decompensated cirrhosis (n = 30), or loss to follow-up (n = 10). Written informed consent was obtained from patients prior to research. This study conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Ethics Committee of Jinling Hospital (2020-0918).

Data collection and follow-up

Data related to patient clinical characteristics, including age, sex, body mass index (BMI), unintentional dry weight loss within 6 months before admission, hepatic encephalopathy (HE), ascites, comorbidities (presence or absence of diabetes) and aetiology of cirrhosis before LT were collected prospectively based on their medical records. Weight was measured using a weighing scale and dry weight was estimated if the patient had ascites or peripheral oedema. Specifically, dry weight was calculated by subtracting 5% of the patient's weight for mild ascites, 10% for moderate ascites, 15% for massive ascites and another 5% for peripheral oedema.[15] BMI was calculated based on the measured weight or dry weight. Preoperative haematological tests included albumin, creatinine and sodium levels and liver function (bilirubin and international standardized ratio). The MELD and MELD-Na score[16] were calculated using the above indicators. Simultaneously, the degree of liver cirrhosis was scored and graded using the Child–Pugh score (Child–Pugh grades B and C indicate decompensation of liver function). Furthermore, intraoperative and postoperative features such as operative time, operative blood, length of hospital stay, duration of ICU stay, severe postoperative morbidity (defined as Dindo–Clavien $\geq$ III) and mortality [defined as death during

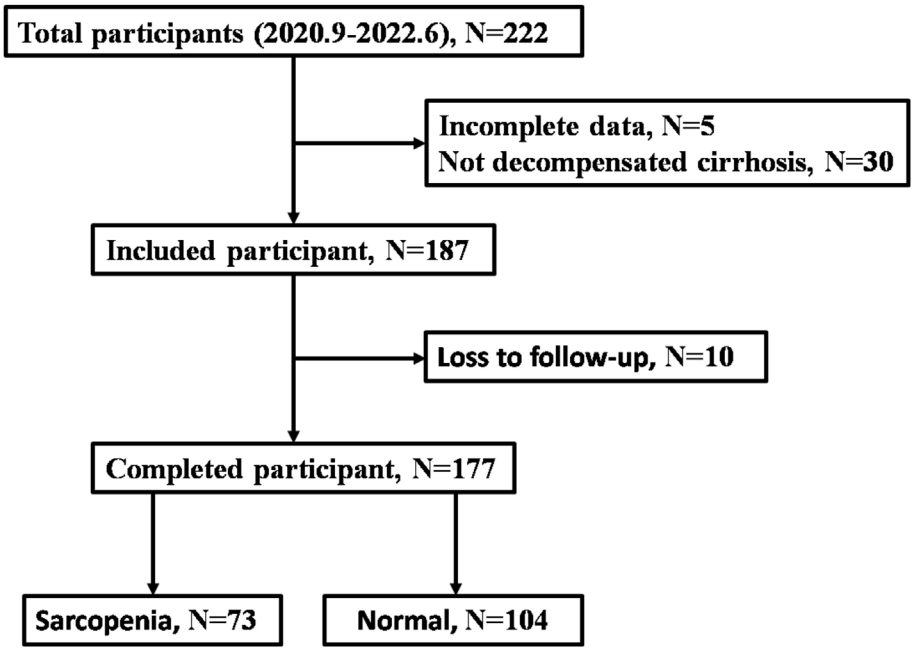

Figure 1 Flow-chart of participant selection.

initial hospitalization or before the postoperative day (POD) 90] were also recorded in detail. Deceased and living donor LT was performed using orthotopic or piggyback techniques. On POD 1, all patients received a routine immunosuppressive regimen of glucocorticoids, tacrolimus and mycophenolate mofetil. After discharge, glucocorticoids were administered for 3 months, while the other two drugs were administered for lifelong maintenance. After excluding contraindications, the abdominal CT was performed between POD 7 and POD 14.

The primary outcome of this study was 1-year OS after LT. All patients were followed-up via telephone or at the outpatient department of our hospital every 6 months after surgery. The last follow-up was completed in March 2023. If patients died, the date and time of death were recorded.

Skeletal muscle assessment

A single trained investigator analysed all CT images preoperatively using SliceOmatic software version 5.0.9 (TomoVision, Montreal, Canada). –29 CT Hounsfield unit (HU) values to 150 HU corresponded to skeletal muscle tissue (*Figure* S1). The area of skeletal muscle tissue (cm^2) in the paralumbar section of the third lumbar spine (L3) was calculated within this range. The L3 SMI (cm^2/m^2) was calculated by normalizing skeletal muscle tissue to the height. L3 SMI < 42 cm^2/m^2 for men and L3 SMI < 38 cm^2/m^2 for women was defined as sarcopenia, according to the Japan Society of Hepatology guidelines.[6]

Statistical analysis

A systematic review and meta-analysis reported an overall sarcopenia prevalence of 37.9–46.7% among patients with decompensated cirrhosis.[17] We assumed that the prevalence of sarcopenia at our centre was 40%. Considering a two-tailed type I error rate of 5% and a statistical power level of 80%, a sample size of at least 171 patients was required [calculated by PASS version 15.0.5 (Power Analysis and Sample Size, NCSS, USA)]. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA) and R version 4.0.5 (R Project for Statistical Computing, Vienna, Austria). Continuous variables were tested for normality, and quantitative data were described as means with standard deviations (normal distribution) or medians with quartile spacing (non-normal distribution). Categorical variables were described as numbers and proportions. To compare the baseline characteristics of patients with and without sarcopenia, independent *t*-tests were used to analyse continuous variables with a normal distribution. Mann–Whitney *U* tests were used to analyse continuous non-normally distributed or ranked data. Chi-squared tests were used to analyse classification variables. The Kaplan–Meier method and log-rank tests were used to estimate and compare the 1-year OS between the two groups. Prognostic factors for survival were identified using Cox proportional hazards models and were displayed in a forest plot. Multivariate analysis was performed to identify the predictive factors of the 1-year OS using forward- and backward-likelihood ratio methods. The dynamic nomogram

for survival prediction was formulated using predictive factors and internally validated using 1000 bootstraps. The performance of the nomogram was assessed using the C-index, the area under the time-dependent receiver opeArating characteristic (ROC) curve (time ROC-AUC), calibration curve and decision curve analysis (DCA) for the entire study cohort. The total points for each patient were calculated according to the established nomogram, and three groups of patients with different risks of prognosis (based on the total points) were delineated using the X-tile program.[18] Survival curves among the three groups were plotted using the Kaplan–Meier method. Statistical significance was set using a two-sided p-value of $P \leq 0.05$.

Results

After applying strict exclusions, a total of 177 patients with decompensated cirrhosis were included in the study. *Table* 1 shows the baseline demographic characteristics of the population in the study cohort. The mean (standard deviation, SD) age was 50.2 (9.3) years, and the majority of patients were men (70.6%). Although 27 (15.3%) patients had a BMI $\leq$ 18.5 kg/m^2, the average BMI was in the normal range. Among them, 28 patients experienced weight loss ≥5% before admission, and 26 patients (14.7%) were diagnosed with hepatocellular carcinoma (HCC). In this cohort, 45 patients (25.4%) had Child–Pugh Stage C disease. The mean (SD) MELD score was 18.4 (7.9), and the mean (SD) MELD-Na score was 19.3 (9.6). The main cause of cirrhosis was hepatitis B virus infection (75.7%). Ascites was present in 102 (57.6%) patients, and 26 patients (14.7%) had HE.

The included patients were divided into two groups according to the L3SMI. The incidence of sarcopenia was 41.2% in the study cohort (*Table* 1). Among clinical characteristics, the sarcopenia group had a lower proportion of male patients (58.9% vs. 78.8%, P = 0.004), lower BMI (20.4 ± 3.5 kg/m^2 vs. 24.1 ± 4.5 kg/m^2, $P < 0.001$), a higher proportion of BMI $\leq$ 18.5 kg/m^2 (35.6% vs. 1%, $P < 0.001$), a higher proportion of weight loss $\geq$ 5% (34.2% vs. 2.9%, $P < 0.001$), and a higher proportion of HE (24.7% vs. 7.7%) than the non-sarcopenia group. Regarding preoperative hematologic tests, compared with nonsarcopenic patients, the bilirubin levels were higher [136.2 (IQR, 33.55–288.5) vs. 50.15 (IQR, 28.76–97.3), P = 0.007], and sodium levels were lower (137.7 ± 3.8 vs. 139.4 ± 4.9, P = 0.013) in sarcopenic patients. Further, sarcopenic patients had higher MELD scores (20.3 ± 8.3 vs. 17.1 ± 7.4, P = 0.007), higher MELD-Na scores (21.1 ± 9.3 vs. 18.0 ± 9.6, P = 0.036), and higher Child–Pugh scores (8.7 ± 1.8 vs. 8.15 ± 1.3, P = 0.013) than nonsarcopenic patients. No differences in age were observed. The proportion of patients who were additionally diagnosed with diabetes, abnormal serum albumin level, or other cirrhosis aetiology was the same between the two groups.

Table 1 Baseline characteristics

Characteristic	Total patients (N = 177)	Sarcopenia patients (N = 73)	Non-sarcopenia patients (N = 104)	P value*
Age, year	50.2 ± 9.3	50.5 ± 9.8	49.9 ± 9.1	0.711
Sex, female/male	52/125	30/43	22/82	0.004
BMI, kg/m^2	22.6 ± 4.5	20.4 ± 3.5	24.1 ± 4.5	<0.001
BMI $\leq$ 18.5 kg/m^2, *n* (%)	27 (15.3)	26 (35.6)	1 (1)	<0.001
Weight loss $\geq$ 5%, *n* (%)	28 (15.8)	25 (34.2)	3 (2.9)	<0.001
Combined diabetes, *n* (%)	28 (15.8)	12 (16.4)	16 (15.4)	0.872
Albumin, g/L	36.8 ± 5.9	36.4 ± 6.2	37.4 ± 5.5	0.298
Albumin≤ 30 g/L, *n* (%)	25 (14.4)	11 (15.1)	14 (13.5)	0.763
Bilirubin, μmol/L	57.7 (29.9–223.6)	136.2 (33.55–288.5)	50.15 (28.76–97.3)	0.007
Creatinine, μmol/L	64 (51–78)	63 (49.5–82)	64.5 (53–74)	0.758
INR	1.49 (1.25–1.90)	1.57 (1.22–2.27)	1.43 (1.27–1.71)	0.132
Sodium, mmol/L	138.7 ± 4.6	137.7 ± 3.8	139.4 ± 4.9	0.013
MELD score	18.4 ± 7.9	20.3 ± 8.3	17.1 ± 7.4	0.007
MELD-Na score	19.3 ± 9.6	21.1 ± 9.3	18.0 ± 9.6	0.036
Child–Pugh score	8.4 ± 1.6	8.7 ± 1.8	8.15 ± 1.3	0.013
Child–Pugh grade, B/C	132/45	50/23	82/22	0.119
Cirrhosis aetiology, *n* (%)				
HBV	134 (75.7)	50 (68.5)	84 (80.8)	0.061
Alcohol	12 (6.8)	5 (6.8)	7 (6.7)	0.975
HCV	2 (1.1)	0 (0)	2 (1.9)	0.513
Autoimmune	14 (7.9)	9 (12.3)	5 (4.8)	0.068
Biliary	12 (6.8)	8 (11.0)	4 (3.8)	0.075
Other	3 (1.7)	1 (1.4)	2 (1.9)	0.779
HCC indication, *n* (%)	26 (14.7)	11 (15.1)	15 (14.4)	0.905
HE, *n* (%)	26 (14.7)	18 (24.7)	8 (7.7)	0.002
Ascites, *n* (%)	102 (57.6)	46 (63)	56 (53.8)	0.224

BMI, body mass index; MELD, model for end-stage liver disease; INR, international normalized ratio; HCC, hepatocellular Carcinoma; HE, hepatic encephalopathy.
*Comparison of patients with sarcopenia vs. without sarcopenia.

In total, 105 patients (59.3%) received orthotopic LT, with an operative time of 382.5 ± 97.9 minutes. Regarding the intraoperative and postoperative results (*Table* 2), the surgical method, operative time, operative blood loss and the duration of hospital stay did not differ significantly between the two groups. Specifically, patients with sarcopenia showed significant differences in the duration of ICU stay (4.1 ± 2.2 vs. 3.1 ± 1.1 days, P = 0.008), severe morbidity [Dindo–Clavien ≥ III (45.2% vs. 22.1%, P = 0.001)], and 90-day postoperative mortality (15.1% vs. 2.9%, P = 0.003) compared with patients without sarcopenia. The median follow-up time was 621 [IQR, 453–752] days, and 36 patients (20.3%) died postoperatively. More importantly, the 1-year postoperative OS in the sarcopenia group was significantly shorter (log-rank $P < 0.001$) than that in the non-sarcopenia group (*Figure* 2).

The univariate Cox proportional hazards results showed that weight loss ≥ 5% pre-admission, sarcopenia, MELD score, Child–Pugh score, HE, and operative blood loss were significantly associated with reduced survival after LT (*Table* 3). In the multivariable analysis, weight loss ≥ 5% (hazard ratio, 2.46; 95% CI, 1.39–5.09; P = 0.015), sarcopenia (hazard ratio, 2.54; 95% CI, 1.54–5.63; P = 0.022), and MELD score (hazard ratio, 1.05; 95% CI, 1.01–1.09; P = 0.009) were independent predictors of 1-year OS postoperatively when both forward-LR and backward-LR methods were used, as shown in the forest plot (*Figure* 3).

We created a simple-to-use predictive dynamic nomogram for OS using the independent predictors shown in *Figure* 4A, which is now available online (https://livertransplantationdynamicnomogram.shinyapps.io/LiverTransplantationSurvivalrediction/; *Figure* 4B). In the time-ROC analysis, the nomogram showed a good ability to identify the 1-year OS after LT, with an AUC of 0.774 (95% CI, 0.50–0.76; *Figure* 5A). Internal validation and calibration of the nomogram were performed using 1000 bootstrap analyses. The model showed that the C-index was 0.754, and the C-index was 0.737 after bootstrapping. The calibration plot of the nomogram (*Figure* 5B) demonstrated a good correlation between the observed and predicted 1-year OS rates. The DCA of the nomogram is shown in *Figure* 5C. The decision curve showed that if the threshold probability of 1-year mortality was between 20% and 50%, using the nomogram to predict 1-year OS provided more benefit than the MELD score.

We further divided patients with decompensated cirrhosis into three risk groups: low (<68.6 points), middle (68.6 ≤ total point ≥ 102.9 points) and high (>102.9 points) to evaluate the subgroups of patients that were positively influenced by the nomogram. The Kaplan–Meier curves for the study cohort (*Figure* 5D) indicated that the nomogram showed a good prognostic classification for the probability of 1-year OS (log-rank $P < 0.001$) in patients with decompensated cirrhosis post-LT.

Discussion

To the best of our knowledge, this is the first prospective study to investigate the relationship between sarcopenia and survival outcomes after LT in patients with decompensated cirrhosis in China. Most retrospective studies have focused on the impact of pretransplant sarcopenia on post-transplant outcomes in adult patients with liver cirrhosis.[19] Two previously published prospective studies were limited because one of the studies included patients with different cirrhosis grades and liver diseases, thus including non-decompensated cirrhosis (Child–Pugh A), simple HCC, biliary atresia, Budd–Chiari syndrome and polycystic liver.[20] The other study mostly included patients (99.13%) with DC but compared only short-term outcomes (90-day mortality) after LT.[21] Generally, differences in the pathological features of these diseases imply that there would be different postoperative outcomes in patients with Child–Pugh A, and thus, they would be less likely to develop sarcopenia. In contrast, patients with simple HCC undergo anti-tumour therapy after surgery, which may obscure the effect of sarcopenia on OS after LT in patients with decompensated cirrhosis. Therefore, it would be beneficial to include specific populations for obtaining reliable data. This study found that preoperative sarcopenia, weight loss ≥ 5% within 6 months before admission, and MELD score was independent risk factors for

Table 2 Intraoperative and postoperative features

Outcomes	Total patients (N = 177)	Sarcopenia patients (N = 73)	Non-sarcopenia patients (N = 104)	P value
Orthotopic LT/piggyback LT	105/72	46/27	59/45	0.402
Operative time, min	382.5 ± 97.9	393.4 ± 103.0	367.0 ± 88.6	0.078
Operative blood loss, mL	1800 (1100–2850)	1800 (1115–2838)	1800 (1000–2850)	0.742
Duration of hospital stay, day	26.9 ± 9.6	26.9 ± 9.4	26.8 ± 9.9	0.911
Duration of ICU stay, day	3.4 ± 1.7	4.1 ± 2.2	3.1 ± 1.1	0.008
Severe morbidity Dindo–Clavien ≥ III, n (%)	56 (31.6)	33 (45.2)	23 (22.1)	0.001
Postoperative mortality,* n (%)	14 (7.9)	11 (15.1)	3 (2.9)	0.003

LT, liver transplantation.
*Postoperative mortality = death in hospital or before POD 90.

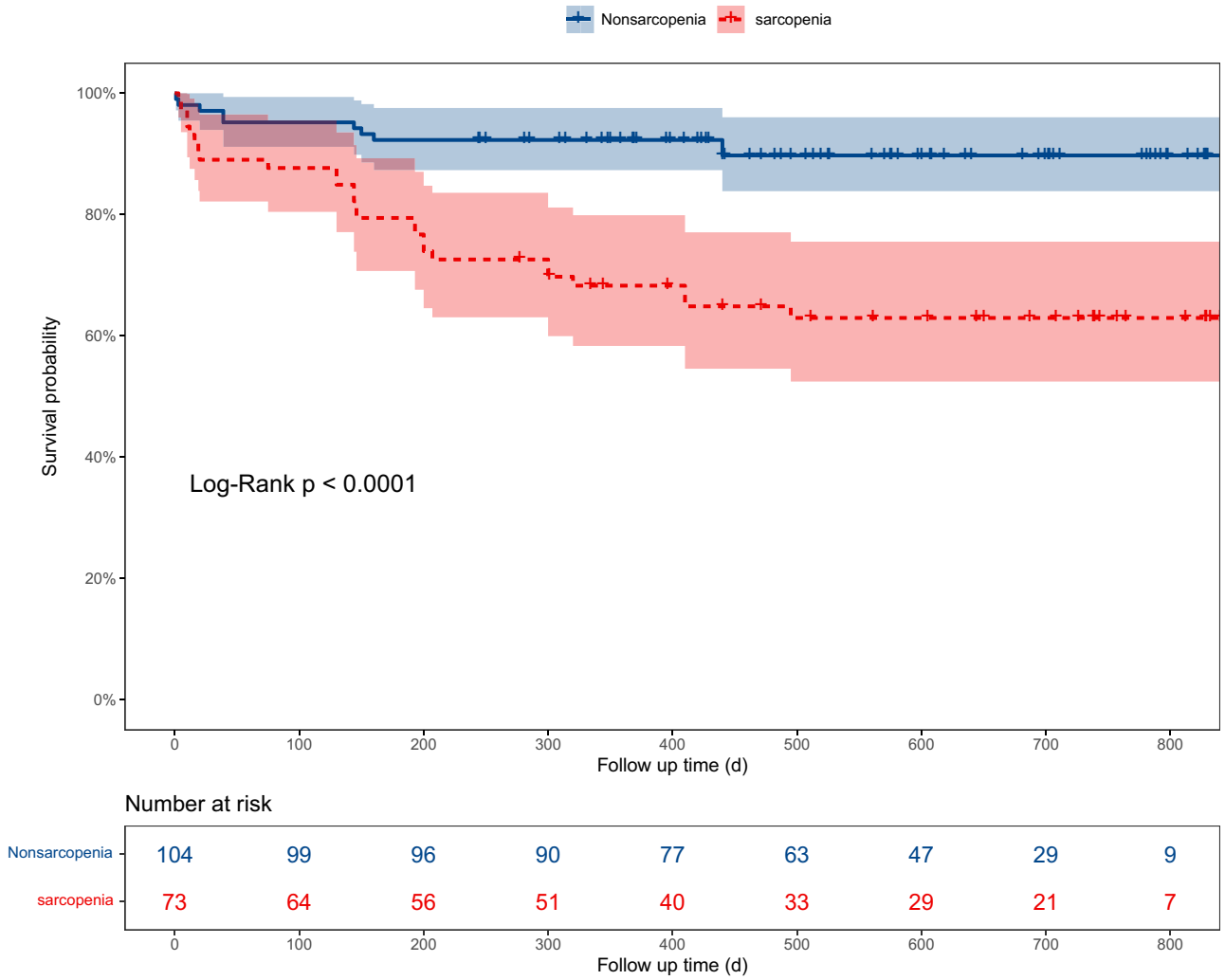

Figure 2 Kaplan–Meier curves for patients with sarcopenia and without sarcopenia.

Table 3 Univariate analysis of risk factors for 1-year mortality in the whole cohort

	P value	HR (95% CI)
Age	0.62	1.01 (0.97–1.05)
Sex	0.79	1.81 (0.93–3.52)
BMI	0.78	1.01 (0.94–1.08)
BMI ≤ 18.5 kg/m^2	0.81	1.12 (0.44–2.89)
Weight loss ≥ 5%	<0.001	3.40 (1.72–6.72)
Sarcopenia	<0.001	4.23 (2.04–8.77)
Combined diabetes	0.83	0.90 (0.35–2.32)
Albumin level	0.16	0.96 (0.91–1.02)
Albumin ≤ 30 g/L	0.94	1.04 (0.40–2.68)
MELD score	<0.001	1.07 (1.04–1.12)
Child–Pugh score	0.001	1.36 (1.13–1.64)
HBV	0.71	0.86 (0.39–1.89)
HCC indication	0.26	1.97 (0.60–6.41)
HE	0.002	3.15 (1.55–6.41)
Ascites	0.83	0.93 (0.48–1.80)
Operative time	0.977	1.01 (0.98–1.01)
Operative blood loss	0.029	1.01 (1.01–1.02)

1-year OS in a cohort receiving LT for decompensated cirrhosis. Furthermore, a simple and practical dynamic nomogram was established using the above independent risk factors, which better predicted postoperative OS than the MELD score and properly identified the high-risk population (>102.9 points).

Sarcopenia was initially defined as an age-related loss of skeletal muscle but has since been expanded to reflect the negative effects of low muscle mass on physical performance and clinical outcomes in a wide range of disease states, beyond the older population. In various associations of liver disease, sarcopenia is defined as low L3SMI measured by abdominal CT in patients undergoing LT.[4,5,22] Although sarcopenia should not be the sole criterion for declining or delisting candidates for LT,[5] screening for sarcopenia in liver cirrhotic patients waiting for transplantation is recommended as a routine medical procedure.[4] Sarcopenia is common in

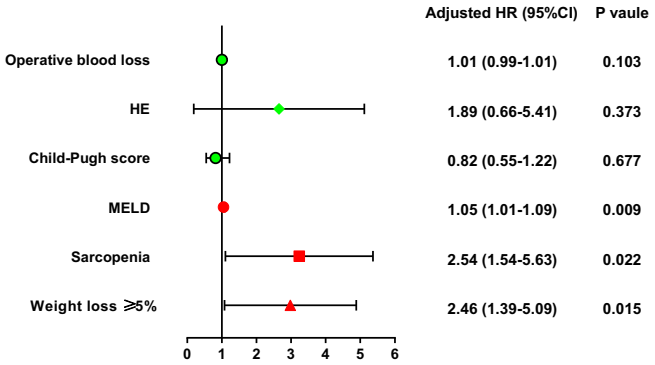

Figure 3 Independent risk factors for 1-year overall survival after liver transplantation for decompensated cirrhosis. HE, hepatic encephalopathy; MELD model for end-stage liver disease.

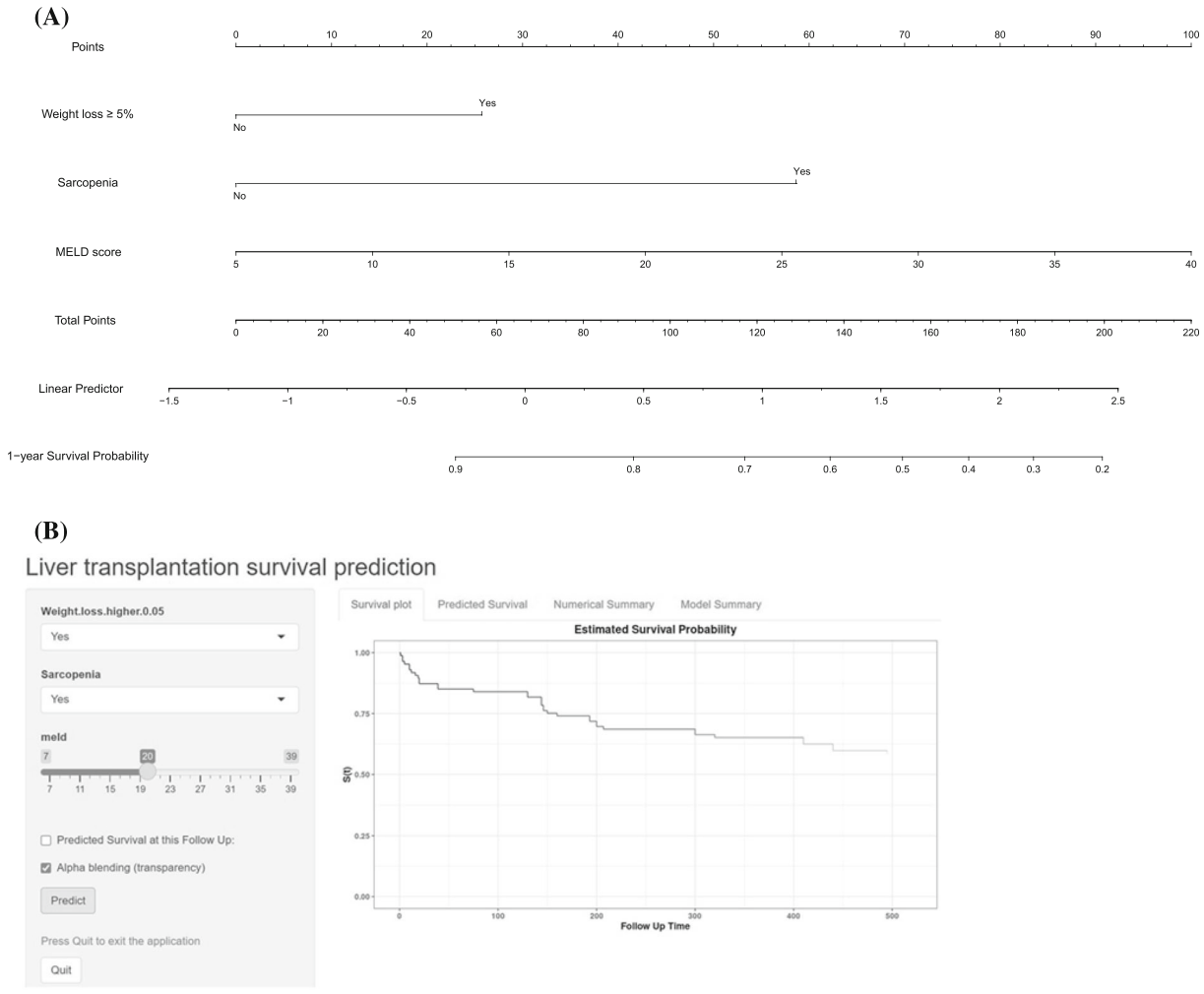

Figure 4 Nomogram to predict the probability of 1-year overall survival. (A) Nomogram for predicting 1-year overall survival for decompensated cirrhosis patients in the study cohort. (B) An example diagram on the dynamic nomogram.

adults with liver cirrhosis undergoing LT; the prevalence of sarcopenia in one large multicentre study was 45%,[23] which is similar to our results (41.2%). Previous studies demonstrated that sarcopenia is a powerful predictor of clinically relevant adverse outcomes. We observed a significantly higher rate (23.1%) of severe complications after LT in patients with sarcopenia than in those without. However, 1-year OS was chosen as the primary endpoint in this study

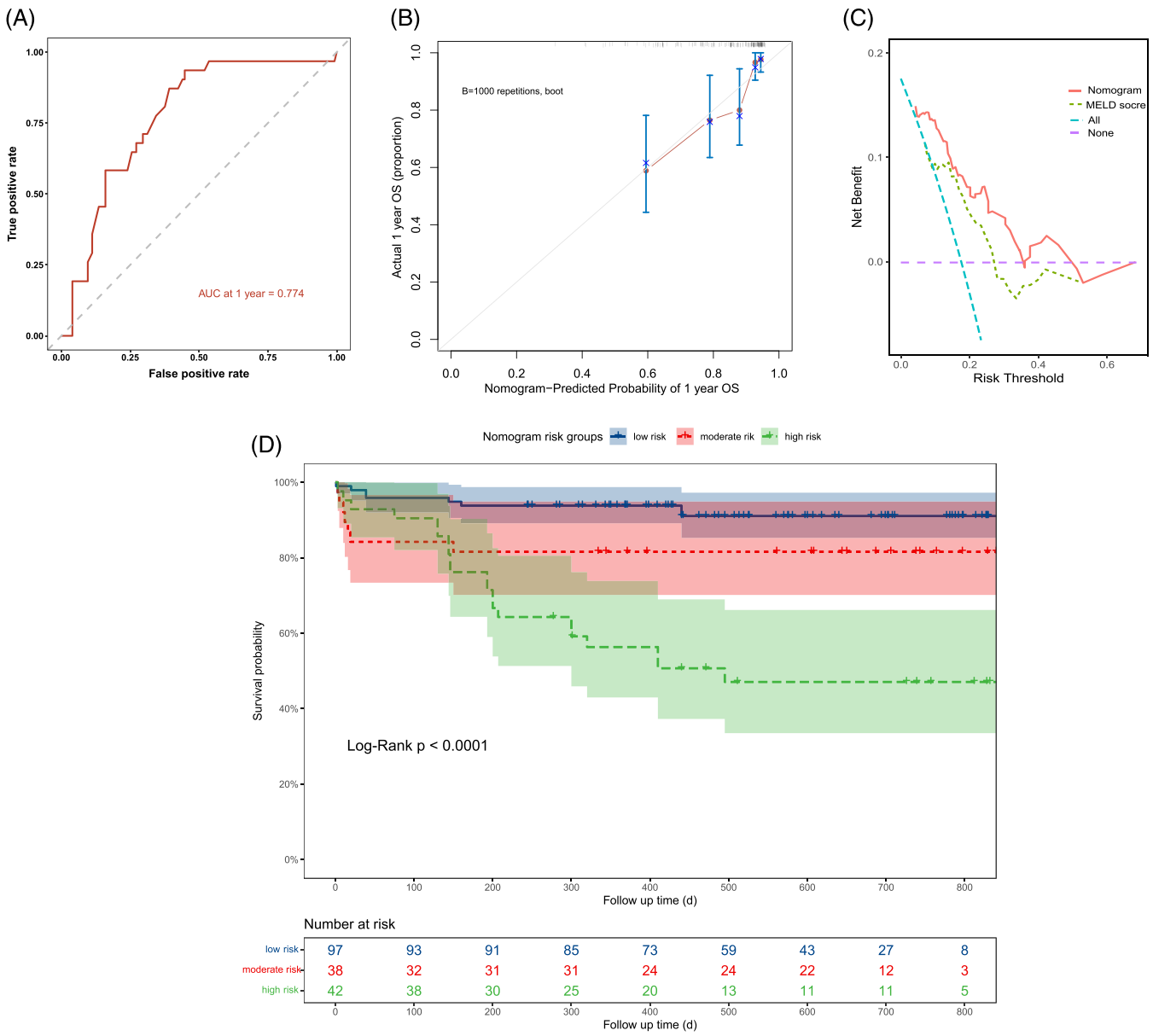

Figure 5 Evaluation of the predictive ability of the nomogram. (A) Time-dependent ROC curve of the nomogram at 1-year in the study cohort. (B) Calibration curve of the nomogram at 1-year in the study cohort. (C) Decision curve analysis for 1-year overall survival in the study cohort. (D) Kaplan–Meier curve of the nomogram model.

because peak mortality in sarcopenic patients occurred during the first post-LT year.[24] In the presence of sarcopenia, patients with decompensated cirrhosis had a 26% reduced survival time after LT, independently associated with poor survival in this study cohort. The possible reasons include the following: Rahima et al. suggested that these important negative effects may be related to the systemic nature of sarcopenia, which involves vital organs including the cardiac and respiratory muscles,[25] which further adversely affect patients undergoing LT. Animal studies have shown that sarcopenia leads to left ventricular dysfunction in the absence of cardiovascular disease.[26] This view is supported by human studies, in which patients with cirrhosis and left ventricular dysfunction are more likely to develop sarcopenia.[27] Respiratory muscles are composed of skeletal muscles, and sarcopenia involves the respiratory muscles, resulting in difficulty with breathing, fatigue and weakness. Furthermore, sarcopenia can reduce graft survival rate. In a retrospective study, preoperative sarcopenia was an independent predictor of liver survival after LT (OR = 7.38, 95% CI, 1.51–35.97, P = 0.01).[28] More importantly, preoperative sarcopenia was not effectively improved after LT. Among patients with preoperative sarcopenia followed up for approximately 1 year after LT, only five (6.4%) had resolution of sarcopenia following

transplantation, and approximately one-quarter were diagnosed with de novo sarcopenia.[29] This may be owing to higher postoperative skeletal muscle expression of myostatin.[30]

Ascites is a common clinical feature of decompensated liver cirrhosis, usually leading to weight gain. The presence of weight loss indicates a poor nutritional status. An international consensus classified patients with a >5% loss of stable body weight over the past 6 months as having cachexia.[31] Cachexia occurs in the late stages of liver cirrhosis, with an incidence of 15.8% in this study cohort. Cachexia is the ongoing loss of body composition (skeletal muscle or fat mass), leading to progressive functional impairment. Muscle wasting is a well-known phenomenon associated with decompensated cirrhosis,[32] and body fat distribution is also a marker of outcome in patients with liver cirrhosis after LT. An observational study found that lower visceral fat mass (HR: 1.403, 95% CI, 1.057–1.862, P = 0.019) significantly reduced the 1-year OS after LT in patients with liver cirrhosis.[33] Unintentional weight loss is one of five domains of the Fried frailty phenotype.[34] Previous research showed that each 1-unit increase in the Fried frailty score was independently associated with a 45% increased risk of waitlist mortality for LT.[35] Involuntary weight loss is usually reported by patients and is easily mistaken for true body weight, which is why it can be subjective and may lead to inaccurate data collection. For this reason, for patients with decompensated cirrhosis, calculating dry weight can exclude the effect of ascites on true body weight, which is more accurate for evaluation ahead of LT. However, few studies have reported its association with 1-year survival in patients with decompensated cirrhosis after LT. In this study, body weight was measured using a standardized weighing scale, and changes in dry weight could be more accurately assessed. We found that involuntary dry weight loss ≥5% within 6 months before admission was an independent risk factor for 1-year OS after LT, even after adjusting for MELD. This result in the present study provides a basis for the clinical nutrition management of patients with decompensated cirrhosis undergoing assessment ahead of LT.

The possible causes of pre-LT sarcopenia and weight loss are a low-calorie and low-protein diet, hypermetabolic status, imbalance of plasma amino acid profile, endotoxaemia and decreased serum testosterone concentrations.[3] The identified liver-muscle axis mediator (hyperammonaemia) can cause a significant increase in the breakdown of skeletal muscle protein.[36] The high incidence of HE in patients with sarcopenia than in those without sarcopenia (24.7% vs. 7.7%) can be explained by their decreased ability to undergo ammonolysis due to ongoing skeletal muscle depletion.

Malinchoc et al. originally developed the MELD score to predict the survival of patients who underwent transjugular intrahepatic portal shunt placement.[37] The MELD score is a reliable indicator of short-term survival in patients with end-stage liver disease.[38] In a large cohort study, pre-LT MELD scores were independently associated with poor patient survival, with the impact of a MELD score of >25 being maximum during the first year post transplantation.[39] However, the ability of the MELD score to discriminate patient survival was poor[40]; therefore, better prognostic models are needed to provide an overall assessment of the transplant benefit relative to decompensated cirrhosis. In this study, we established a dynamic nomogram combining the MELD score, sarcopenia and weight loss ≥5% with a higher clinical survival benefit than the MELD score alone through DCA. Simultaneously, the nomogram can be operated easily online and has higher stability and consistency after evaluation.

This study has some limitations that should be addressed in future research. First, although we prospectively collected data on preoperative skeletal muscle mass, we did not collect data on grip strength or physical activity. According to the latest European Working Group on Sarcopenia in Older People, these measures are key diagnostic factors for sarcopenia.[2] Moreover, although our results were internally verified in this prospective cohort, external validation is warranted. Overall, the dynamic nomogram only estimated survival in China and may not be applicable in other settings. In addition, the causes of DC in this study included both alcoholic cirrhosis and non-alcoholic steatohepatitis (7.3%). It is well known that these factors can affect the metabolism and function of skeletal muscle through different mechanisms and may amplify the effects of sarcopenia, which may also limit the generalizability of this work to a wider range of populations. Finally, we recorded only the time and not the cause of death during the follow-up period. Death from other unexpected causes may amplify the effect of sarcopenia on 1-year OS, which can be adjusted through competing risk analysis in future longer follow-ups.[41]

In conclusion, sarcopenia was strongly associated with the 1-year OS after LT in patients with decompensated cirrhosis. Our prediction model can be easily used online to identify patients at risk of poor postoperative survival based on MELD score, sarcopenia and weight loss ≥5% within 6 months before admission. These patients may benefit from drug or nutritional interventions to improve their postoperative survival within an effective time window.

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Conflict of interest

The authors report no conflicts of interest related to this work.

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Online supplementary material

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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