Liver Cancer

Research Article

Liver Cancer
DOI: 10.1159/000529676

Received: March 24, 2022
Accepted: January 29, 2023
Published online: February 23, 2023

Computed Tomography-Defined Sarcopenia in Outcomes of Patients with Unresectable Hepatocellular Carcinoma Undergoing Radioembolization: Assessment with Total Abdominal, Psoas, and Paraspinal Muscles

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Keywords
Computed tomography · Sarcopenia · Carcinoma · Hepatocellular · Prognosis · Radioembolization

Abstract

Introduction: Sarcopenia is an adverse prognostic factor in patients with liver cirrhosis and hepatocellular carcinoma (HCC). Image-based sarcopenia assessment allows a standardized method to assess abdominal skeletal muscle. However, which is an index muscle for sarcopenia remains unclear. Therefore, we investigated whether sarcopenia defined according to different muscle groups with computed tomography (CT) scans can predict the prognosis of HCC after radioembolization. ***Methods:*** In this retrospective study, we analyzed patients who underwent radioembolization for unresectable HCC between January 2010 and December 2019. Before treatment, the total abdominal muscle (TAM), psoas muscle (PM), and paraspinal muscle (PS) areas were evaluated using a single CT slice at the third lumbar vertebra. In previous studies, sarcopenia was determined using the TAM, PM, and PS after stratifying by sex. Finally, we investigated each muscle-defined sarcopenia to decide whether or not it can serve as a prognostic factor for overall survival (OS). ***Results:*** We included 92 patients (74 men and 18 women). TAM, PM, and PS areas were significantly higher in the men than in the women (all $p < 0.05$). The patients with sarcopenia defined using PM, but not TAM

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and PS, exhibited significantly poorer OS than those without sarcopenia (median 15.3 vs. 23.8 months, $p = 0.034$, 0.821, and 0.341, respectively). After adjustment for clinical variables, such as body mass index, liver function, alpha-fetoprotein level, clinical staging, treatment response, and posttreatment curative therapy, PM-defined sarcopenia (hazard ratio: 1.899, 95% confidence interval: 1.087–3.315) remained an independent predictor for the poor OS. ***Conclusion:*** CT-assessed sarcopenia defined using PM was an independent prognostic factor for the poorer prognosis of unresectable HCC after radioembolization.

Introduction

Hepatocellular carcinoma (HCC) is the sixth most commonly diagnosed cancer and the fourth leading cause of cancer deaths worldwide [1]. The Barcelona Clinic Liver Cancer (BCLC) staging system stratifies patients with HCC into very early, early, intermediate, advanced, and terminal stages, with the 5-year survival rates of 40–70%, 14–45%, 6–14%, and 10%, respectively [2]. Because of the limitation of treatment options, transarterial chemoembolization and systemic therapy have served as first-line treatment for intermediate to advanced HCC for more than a decade [3]. However, recent advancements in intra-arterial treatments, such as drug-eluting beads, radioembolization, and hepatic arterial infusion chemotherapy, have provided interventional radiologists with more tools to treat unresectable HCCs [4]. Radioembolization has demonstrated promising results in randomized controlled trials [5] and was recommended by recent practice guidelines for patients with multiple tumors or vascular invasion [6].

Patients with a large tumor burden or vascular invasion commonly exhibit sarcopenia and cachexia [7]. In contrast to the complicated and multifactorial criteria of cachexia, sarcopenia is defined as low muscle mass, decreased muscle strength, or poor performance [8]. Sarcopenia diagnosed based on low muscle mass can be easily accessed through computed tomography (CT), which is a standard diagnostic tool for HCC and routinely used for cancer staging. The total abdominal muscle (TAM) area of a single CT slice at the third lumbar vertebra (L3) strongly predicted fat-free mass [9]. Prado et al. [10] reported that TAM-defined sarcopenia, <52.4 cm^2/m^2 in men and <38.5 cm^2/m^2 in women after adjustment for body height (BH), independently predicted outcomes for patients with solid tumors of the respiratory and gastrointestinal tracts and was widely accepted by many studies.

Hamaguchi et al. [11] used BH-adjusted psoas muscle (PM) mass of <6.36 cm^2/m^2 for men and <3.92 cm^2/m^2 for women based on liver donors as criteria for healthy controls. A study demonstrated that sarcopenia defined using PM mass with cross-sectional imaging might be an independent prognostic factor for hepatic malignancy after intra-arterial therapy [12]. However, this study enrolled patients with various hepatic malignancies, including HCC; intrahepatic cholangiocarcinoma; and colorectal, neuroendocrine, and other liver metastases. Other studies conducted in Western countries have indicated that magnetic resonance imaging (MRI)-derived, paraspinal muscle (PS)-defined sarcopenia (<31.97 cm^2 for men and <28.95 cm^2 for women) might be associated with mortality and outcomes in patients with HCC receiving radioembolization [13, 14]. However, the definition of sarcopenia should be sex and ethnic specific. The analyses of TAM- and PS-defined sarcopenia are mainly based on the Western population and the survey of PM-defined sarcopenia consists of the Eastern people. Meanwhile, they used different cutoffs for diagnosing sarcopenia between men and women and various protocols for measuring muscle mass.

In summary, which muscle group can serve as a sentinel indicator for sarcopenia remains controversial [15, 16]. Furthermore, the difference in prognostic prediction among TAM, PM, and PS remains unclear. Whether the Western criteria can be transferred to the Eastern population and sarcopenia has a similar effect on the outcomes between male and female patients are also unknown. Therefore, we explored whether CT-based sarcopenia can be used as a prognostic factor for patients with unresectable HCC after radioembolization and determined an index for abdominal muscle mass to assess sarcopenia.

Materials and Methods

Study Population

This study was based on a retrospective and observational cohort. We enrolled patients who underwent resin-based yttrium-90 radioembolization for intermediate to advanced HCCs between January 2010 and December 2019 at National Taiwan University Hospital (NTUH), a tertiary referral center in northern Taiwan. We analyzed abdominal CT images within 2 months before radioembolization. Those who had decompensated cirrhosis (Child-Pugh score >7), a high lung shunt fraction (>20%), an estimated tumor burden of >50% of the liver,

or had no adequate CT images for analysis were excluded. Because of the retrospective nature of the study, the requirement of informed consent was waived. The study protocol followed the Declaration of Helsinki and was approved by the Institutional Review Board of NTUH (No. 201805070RIND).

Study Variables

In this study, individuals aged ≥70 years were termed elderly. Patients aged <70 years with a body mass index (BMI) of <20 kg/m^2 and those aged ≥70 years with a BMI of <22 kg/m^2 were categorized as reduced BMI according to the European Society of Clinical Nutrition and Metabolism consensus [17]. Patients who were positive for hepatitis B surface antigen or hepatitis C antibody were considered to have hepatitis B virus (HBV)-related HCC and hepatitis C virus (HCV)-related HCC, respectively. The liver function was evaluated using the albumin-bilirubin (ALBI) and Model for End-Stage Liver Disease (MELD) score as follows: log10 total bilirubin [in μmol/L] × 0.66) + (serum albumin [in g/L] × −0.085 and 9.57 × ln(creatinine) + 3.78 × ln(total bilirubin) + 11.2 × ln(INR) + 6.43 [18]. The ALBI grades were determined according to the ALBI scores (1 [−2.60 or lower], 2 [greater than −2.60 to −1.39, and 3 [greater than −1.39]); only objective parameters were collected for better evaluation of liver function than the Child-Pugh score [19]. The tumor burden was assessed using the maximal tumor size, tumor number, distribution, and volume. The demographic data of the study population are presented in Table 1.

Yttrium-90 Radioembolization and Follow-Up

In our hospital, the weekly multidisciplinary meeting, which included hepatologists, surgeons, medical/radiation oncologists, and intervention/nuclear medicine radiologists, reviewed the diagnosis of HCC and determined the indication for radioembolization, following the recommendations of the European Society for Medical Oncology and Taiwan Liver Cancer Association (TLCA) [6, 20]. According to the TLCA guideline, the diagnostic criteria of HCC include arterial phase hyperenhancement and washout in the portal venous phase under dynamic CT/MRI or tumor biopsy if the imaging pattern was nontypical [6]. Before radioembolization, mapping angiography was performed to explore possible extrahepatic blood supply to the tumor and nontarget organs. If necessary, vascular redistribution was achieved through coil embolization. Then, the intra-arterial administration of technetium 99m-labeled macroaggregated albumin and subsequent planar and single-photon emission CT was performed to evaluate lung shunt, detect extrahepatic perfusion, and calculate the fraction between the tumor and normal liver. After evaluation, SIR-spheres (Sirtex Medical, Sydney, Australia) were applied, and the radiation dose was determined using the body surface area or partition model. Finally, Bremsstrahlung subsequent planar and single-photon emission CT was performed to verify target embolization on the second day after radioembolization. Dynamic CT was routinely arranged 1 month after radioembolization to evaluate the efficacy of the technique. The patients then underwent serum biochemistry testing, alpha-fetoprotein (AFP) level measurement, and CT every 3 months. The treatment response at 1-month, 4-month, and 7-month follow-up CT was evaluated according to the modified Response Evaluation Criteria in Solid Tumors and stratified as complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD) [21]. Overall survival (OS) was calculated from the date of yttrium-90 administration to death or final follow-up (June 30, 2021). Progression-free survival (PFS) was determined from the treatment date to the date of disease progression, death, or final follow-up. Only the 4-month treatment response was included in survival analysis because the 1-month evaluation may be too early for radioembolization, and we usually shift further therapy at the sixth month.

Imaging Study and Processing

Abdominal CT was performed using a multidetector CT scanner (Brilliance iCT and Ingenuity CT; Philips Healthcare, Amsterdam, The Netherlands). Nonenhanced CT images at the L3 level were analyzed to determine TAM, PM, and PS areas and were processed on a compatible computer using open-source software (ImageJ version 1.51; National Institutes of Health, Bethesda, MD, USA). Muscle tissues were differentiated by setting Hounsfield units from unenhanced images based on specific attenuation values (−29, 150), and contours were obtained using a manual tracing method. A radiologist (C.-H.W.) with 10 years of experience in abdominal imaging processed the images based on the method described previously [22]. TAM, PM, and PS areas were obtained from CT images (Fig. 1), and TAM and PM indices were calculated as follows: TAM and PM area/(BH [m])^2 [10, 11]. Sarcopenia based on TAM (<52.4 cm^2/m^2 for men and <38.5 cm^2/m^2 for women after BH adjustment), PM (<6.36 cm^2/m^2 for men and <3.92 cm^2/m^2 for women after BH adjustment), and PS (<31.97 cm^2 for men and <28.95 cm^2 for women without BH adjustment) was determined by following the protocols proposed by Prado, Hamaguchi, and Guichet, respectively [10, 11, 13].

Statistical Analysis

Data were analyzed using Excel 2013 (Microsoft, Redmond, WA, USA) and R 3.4.3. A p value <0.05 was considered statistically significant in all statistical analyses. The χ^2 test was used to compare categorical variables, and the Student's t test was used to compare continuous variables. If continuous variables do not conform to normal distribution, these values were described as median and interquartile range. The Wilcoxon-Mann-Whitney test was used to compare the difference between groups, and Fisher's exact test was used for an estimated sample size of less than 5. The paired t test was used to compare muscle areas before and after radioembolization. The Kaplan-Meier method and the log-rank test were used to estimate OS and PFS. Finally, the Cox proportional hazards model was used to analyze survival outcomes in univariate and multivariate analyses.

Results

Patient Characteristics

A total of 94 patients were enrolled. Two patients were excluded because they had no adequate CT images for analysis. Finally, we analyzed 92 patients whose nonenhanced abdominal CT images were successfully processed (Fig. 2). Of them, 60 (65.2%) had HBV-related HCC, 18 (19.6%) had HCV-related HCC, 2 (2.2%) had HBV/HCV coinfection, and 16 (17.4%) had no evidence

Table 1. Baseline characteristics of the study population (N = 92)

Variable		Value (mean±SD, median [IQR], or number [%])
Age, years		65.6±10.9
Sex	Male	74 (80.4)
	Female	18 (19.6)
Body weight, kg		64.5±10.6
BH, cm		164.4±7.5
BMI, kg/m^2		23.8±3.3
HBV related		60 (65.2)
HCV related		18 (19.6)
Alanine aminotransferase, U/L		49±44
Albumin, g/dL		4.3±0.5
Total bilirubin, mg/dL		0.95±0.55
ALBI grade	1	55 (59.8)
	>1	37 (40.2)
MELD sore		8±2
Maximal tumor size, cm		7.5±4.2
Tumor size, cm	≤5	30 (32.6)
	>5	62 (67.4)
Tumor number	1	29 (31.5)
	2–5	39 (42.4)
	>5	24 (26.1)
Tumor distribution	Unilobar	47 (51.1)
	Bilobar	45 (48.9)
Total tumor volume, mL		252 (405)
Non-tumor liver volume, mL		1,151±359
AFP, ng/mL	≤400	52 (56.5)
	>400	40 (43.5)
BCLC stage	B	52 (56.5)
	C	40 (43.5)
ECOG performance status	0	81 (88.0)
	1	11 (12.0)
Administered activity (GBq)		1.47±0.74
Prior therapy		64 (69.6)
1-month objective response		43 (46.7)
4-month objective response		43 (46.7)
7-month objective response		28 (30.4)
Posttreatment curative therapy		19 (20.7)

SD, standard deviation; IQR, interquartile range; HBV, hepatitis B virus; HCV, hepatitis C virus; MELD, Model for End-Stage Liver Disease; BCLC, Barcelona Clinic Liver Cancer; ECOG, Eastern Cooperative Oncology Group.

of HBV or HCV infection. Moreover, 87 (94.6%) patients had Child-Pugh A and 5 (5.4%) had Child-Pugh B liver cirrhosis, 7 (9.5%) patients had extrahepatic metastasis, and 38 (41.3%) had vascular invasion. The mean MELD score was 8. Furthermore, 33 (35.9%) patients underwent operation, 60 (65.2%) underwent locoregional therapy, and 11 (12.0%) underwent systemic therapy before radioembolization. Among 33 patients who underwent operation, 26 and 7 received open hepatectomy and laparoscopic approach, respectively. Four patients underwent liver transplantation, 3 underwent liver resection, and 14 underwent radiofrequency ablation after radioembolization. There was a wide range of total tumor volumes (median: 252 mL, interquartile range: 405 mL) and the non-tumor liver volume was 1,151 ± 359 mL. The administrated activity was 1.47 ± 0.74 GBq with 45 and 47 patients using body surface area and partition models, respectively (Table 1).

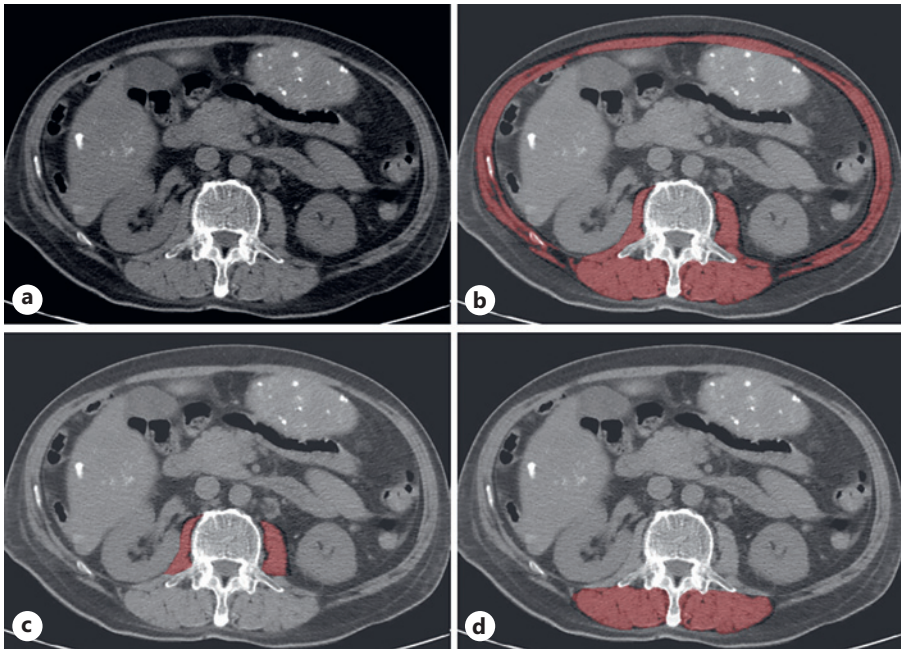

Fig. 1. CT image reading demonstration of a 64-year-old man. Unenhanced CT (**a**) at the L3 level shows lipiodol retention at both hepatic lobes, which was analyzed to determine the (**b**) TAM, (**c**) PM, and (**d**) PS after image processing. TAM, PM, and PS areas were 105.85, 54.43, and 15.91 cm^2, respectively. CT, computed tomography; L3, the third lumbar level; TAM, total abdominal muscle; PM, psoas muscle; PS, paraspinal muscle.

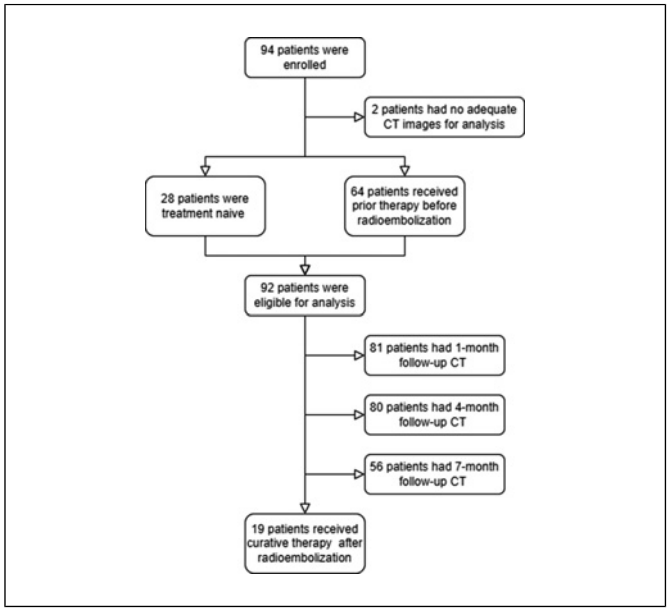

Fig. 2. Flowchart of patient enrollment.

Abdominal Muscle Analysis and Sarcopenia Assessment

Compared with the men, the women had a significantly lower TAM area ($p < 0.001$), lower PM area ($p = 0.020$), lower PS area ($p < 0.001$), lower TAM index ($p < 0.001$), and lower PS index ($p = 0.002$). By contrast, no significant difference was observed in the PM index (mean: 6.29 ± 3.49 vs. 4.95 ± 3.19 cm^2/m^2, $p = 0.140$) between the men and women. Similarly, TAM- and PS-defined sarcopenia exhibited significant sex differences ($p = 0.034$ and 0.001) but not PM-defined sarcopenia ($p = 0.293$; Table 2). Furthermore, PM-defined sarcopenia was associated only with performance status but not with age, sex, BMI, albumin, tumor size, number, distribution, volume, non-tumor liver volume, administrated activity, and response (Table 3). In contrast, TSM- and PS-defined sarcopenia were associated with age and sex. The PS-defined sarcopenia was also associated with weight, BH, BMI, and albumin.

During follow-up, significant increases were observed in PM index 1 month after radioembolization (6.14–7.17 cm^2/m^2, $p = 0.040$), but TSM and PS areas and indices were not. No significant difference in all imaging-based muscle measurements was noted at 4-month and 7-month follow-up images (online supplement 2; for all online suppl. material, see www.karger.com/doi/10.1159/000529676).

Treatment Response and Survival Analysis

During follow-up, 43, 21, and 17 patients had PR, SD, and PD on 1-month CT. 6, 37, 15, and 22 patients had PR, SD, and PD on 4-month CT. 7, 21, 6, and 22 patients had PR, SD, and PD on 7-month CT. The objective response rates (CR + PR) were 46.7% (43/92), 46.7% (43/92), and 30.4% (28/92) at the 1-month, 4-month, and 7-month follow-up CT. The disease control rates (CR + PR + SD)

Table 2. Areas and indices of the TAM, PM and PS and percentage of patients with sarcopenia among men and women

Measurement	Men (n = 74)	Women (n = 18)	p value
TAM area, cm^2	131.43±27.90	88.64±18.34	<0.001*
PM area, cm^2	17.56±9.75	11.75±7.19	0.020*
PS area, cm^2	54.88±16.71	36.12±13.23	<0.001*
TAM index, cm^2/m^2	47.08±9.16	37.02±6.53	<0.001*
PM index, cm^2/m^2	6.29±3.49	4.95±3.19	0.140
PS index, cm^2/m^2	19.62±5.57	14.96±4.90	0.002*
TAM-defined sarcopenia (%)	59 (79.7)	10 (55.6)	0.034*
PM-defined sarcopenia (%)	39 (52.7)	7 (38.9)	0.293
PS-defined sarcopenia (%)	3 (4.1)	5 (27.8)	0.001*

TAM, total abdominal muscle; PM, psoas muscle. PS, paraspinal muscle. *$p < 0.05$.

were 69.6% (64/92), 63.0% (58/92), and 37.0% (34/92) at the 1-month, 4-month, and 7-month follow-up CT.

The median OS rates of the entire cohort, men, and women were 16.2, 15.2, and 23.8 months, respectively. Reduced BMI, ALBI grade >1, MELD score, AFP level >400 ng/mL, BCLC stage C, 4-month objective response, and curative therapy after radioembolization were significant prognostic factors, but prior therapy before radioembolization was not. After applying optimal sex-specific cutoff points for TAM, PM, and PS, only the patients with PM-defined sarcopenia exhibited significantly poorer OS than did those without (median 15.3 vs. 23.8 months, p = 0.034; Fig. 3c), and PM-defined sarcopenia remained an independent predictor of poor OS (hazard ratio: 1.899, 95% confidence interval: 1.087–3.315, p = 0.024; Table 4), after adjustment for other clinical variables. TAM- and PS-defined sarcopenia were not significant prognostic factors in univariate and multivariate analyses (Fig. 3; Table 4).

The median PFS rates of the entire cohort, men, and women were 7.2, 6.8, and 9.2 months, respectively. AFP level >400 ng/mL, 4-month objective response, and curative therapy after radioembolization were significant prognostic factors, but TAM-, PM-, or PS-defined sarcopenia was not (online supplement 1).

Subgroup Analysis Stratified by Sex and Presence of Posttreatment Curative Therapy

In the women, the mean OS rates were 55.1 and 35.2 months for the nonsarcopenic and sarcopenic groups, respectively, for TAM-defined sarcopenia; 55.1 and 19.8 months, respectively, for PM-defined sarcopenia; and 36.7 and 52.3 months, respectively, for PS-defined sarcopenia. PM-defined sarcopenia was a prognostic factor in the women (p = 0.043, Fig. 4c). In the men, the mean OS rates were 19.0 and 23.2 months for the nonsarcopenic and sarcopenic groups, respectively, for TAM-defined sarcopenia; 26.6 and 17.5 months, respectively, for PM-defined sarcopenia; and 22.7 and 7.0 months, respectively, for PS-defined sarcopenia. PM-defined sarcopenia was not a significant factor for poor prognosis in the men (p = 0.168, Fig. 4d).

In 19 patients who received curative therapy after radioembolization, the mean OS rates were 48.1 and 43.7 months for the TAM-defined nonsarcopenic and sarcopenic groups; 55.2 and 34.6 months for PM-defined nonsarcopenic and sarcopenic groups; and 47.3 months for PS-defined nonsarcopenic group. PM-defined sarcopenia was a nonsignificant prognostic factor in patients who received curative therapy (p = 0.251, Fig. 5d). In 73 patients without curative therapy, the mean OS rates were 20.8 and 18.0 months for the TAM-defined nonsarcopenic and sarcopenic groups; 23.9 and 13.0 months for PM-defined nonsarcopenic and sarcopenic groups; and 16.4 and 38.1 months for PS-defined nonsarcopenic and sarcopenic groups. PM-defined sarcopenia was a significant poorer prognostic factor in patients without curative therapy (p = 0.032, Fig. 5c).

Discussion

In this retrospective study, CT-assessed, PM-defined sarcopenia was a prognostic factor for OS after adjustment for reduced BMI, ALBI grade >1, AFP level >400 ng/mL, BCLC stage C, and posttreatment curative therapy in the patients with intermediate to advanced HCC receiving radioembolization. After stratification by sex, PM-defined sarcopenia was determined to be a poorer prognostic factor for OS in women but not in men. But the survival curves in females and males diverged in the same direction of proportional hazard between patients with and without PM-defined sarcopenia (Fig. 4c, d). Therefore, after combining two

Table 3. Comparison of clinical characteristics between sarcopenic and nonsarcopenic groups

Variable	TAM-defined sarcopenia (n = 69)	TSM-defined nonsarcopenia (n = 23)	p value	PM-defined sarcopenia (n = 46)	PM-defined nonsarcopenia (n = 46)	p value	PS-defined sarcopenia (n = 8)	PS-defined nonsarcopenia (n = 84)	p value[a]
Age, year	67.46±10.72	61.70±10.64	0.028*	66.60±10.75	65.44±11.22	0.614	73.50±8.04	65.31±10.94	0.042*
Sex (male)	59 (85.5%)	15 (65.2%)	0.034*	39 (84.8%)	35 (76.1%)	0.293	3 (37.5%)	71 (84.5%)	0.007*
Body weight, kg	64.2±10.3	65.5±11.8	0.621	63.5±9.9	65.4±11.3	0.396	52.5±5.6	65.7±10.3	0.001*
BH, cm	165.0±6.9	162.7±9.0	0.191	164.6±7.7	164.3±7.3	0.829	152.4±7.3	165.6±6.4	<0.001*
BMI, kg/m^2	23.6±3.4	24.6±2.9	0.204	23.5±3.2	24.2±3.3	0.294	22.6±3.8	23.9±3.3	0.293
TAM area, cm^2	116.14±26.56	143.82±35.58	<0.001*	118.04±30.50	128.09±31.58	0.124	87.58±34.25	126.44±29.00	0.001*
PM area, cm^2	15.19±9.28	20.16±9.59	0.030*	9.02±4.96	23.84±6.92	<0.001*	15.87±10.85	16.48±9.49	0.864
PS area, cm^2	49.20±15.83	57.22±21.65	0.112	54.68±17.80	47.73±17.05	0.059	19.44±10.76	54.23±15.05	<0.001*
HBV related	46 (66.7%)	14 (60.9%)	0.613	34 (73.9%)	26 (56.5%)	0.080	3 (37.5%)	57 (67.9%)	0.121
HCV related	12 (17.4%)	6 (26.1%)	0.363	6 (13.0%)	12 (26.1%)	0.115	4 (50.0%)	14 (16.7%)	0.044*
Alanine aminotransferase, U/L	48±43	52±45	0.700	47±33	51±52	0.641	61±39	48±44	0.417
Albumin, g/dL	3.9±0.4	3.8±0.7	0.607	3.8±0.5	3.9±0.5	0.505	3.4±0.6	3.9±0.5	0.006*
Total bilirubin, mg/dL	0.91±0.41	1.09±0.81	0.163	0.97±0.47	0.93±0.62	0.776	0.89±0.50	0.96±0.55	0.725
ALBI grade >1	28 (40.6%)	9 (39.1%)	0.902	20 (43.5%)	17 (37.0%)	0.524	6 (75.0%)	31 (36.9%)	0.057
MELD score	8±2	9±3	0.195	8±2	8±3	0.667	8±2	8±3	0.526
Maximal tumor size, cm	7.6±4.4	7.3±3.3	0.730	7.8±4.6	7.3±3.7	0.588	7.8±4.8	7.5±4.1	0.836
Tumor size > 5 cm	47 (68.1%)	15 (65.2%)	0.797	31 (67.4%)	31 (67.4%)	0.999	6 (75.0%)	56 (66.7%)	>0.999
Tumor number >5	17 (24.6%)	7 (30.4%)	0.583	16 (34.8%)	8 (17.4%)	0.058	1 (12.5%)	23 (27.4%)	0.675
Bilobar	32 (46.4%)	13 (56.5%)	0.399	18 (39.1%)	27 (58.7%)	0.061	5 (62.5%)	40 (47.6%)	0.481
Total tumor volume, mL[b]	254 (411)	249 (400)	0.885	300 (659)	242 (293)	0.417	140 (191)	261 (437)	0.178
Non-tumor liver volume, mL	1,133±372	1,205±316	0.405	1,191±357	1,111±360	0.285	1,103±240	1,156±369	0.691
AFP > 400, ng/mL	30 (43.5%)	10 (43.5%)	>0.999	24 (52.2%)	16 (34.8%)	0.092	5 (62.5%)	35 (41.7%)	0.288
BCLC stage C	32 (46.4%)	8 (34.8%)	0.331	23 (50.0%)	17 (37.0%)	0.207	2 (25.0%)	38 (45.2%)	0.458
ECOG performance status 1	10 (14.5%)	1 (4.3%)	0.194	9 (19.6%)	2 (4.3%)	0.024*	3 (37.5%)	8 (9.5%)	0.052
Administered activity (GBq)	1.42±0.67	1.63±0.90	0.229	1.51±0.71	1.44±0.77	0.639	1.09±0.47	1.51±0.08	0.123
Prior therapy	50 (72.5%)	14 (60.9%)	0.295	32 (69.6%)	32 (69.6%)	0.999	4 (50.0%)	60 (71.4%)	0.240
1-month objective response	32 (46.4%)	11 (47.8%)	0.904	23 (50.0%)	20 (43.5%)	0.531	4 (50.0%)	39 (46.4%)	>0.999
4-month objective response	29 (42.0%)	14 (60.9%)	0.117	22 (47.8%)	21 (45.7%)	0.834	4 (50.0%)	39 (46.4%)	>0.999

Table 3 (continued)

Variable	TAM-defined sarcopenia (n = 69)	TSM-defined nonsarcopenia (n = 23)	p value	PM-defined sarcopenia (n = 46)	PM-defined nonsarcopenia (n = 46)	p value	PS-defined sarcopenia (n = 8)	PS-defined nonsarcopenia (n = 84)	p value[a]
7-month objective response	21 (30.4%)	7 (30.4%)	>0.999	13 (28.3%)	15 (32.6%)	0.650	2 (25.0%)	26 (31.0%)	>0.999
Posttreatment curative therapy	15 (21.7%)	4 (17.4%)	0.656	10 (21.7%)	9 (19.6%)	0.797	0 (0.0%)	19 (22.6%)	0.198

PM, psoas muscle; TAM, total abdominal muscle; PS, paraspinal muscle; HBV, hepatitis B virus; HCV, hepatitis C virus; MELD, Model for End-Stage Liver Disease; BCLC, Barcelona Clinic Liver Cancer; ECOG, Eastern Cooperative Oncology Group. *$p < 0.05$. [a]Fisher's exact test used for estimated number <5. [b]Presented as median (interquartile range) and Wilcoxon-Mann-Whitney test used for to comparison.

subgroups, the entire cohort demonstrated that PM-defined sarcopenia has poorer OS. In contrast, the survival curves of TAM- and PS-defined sarcopenia crossed each other in females (Fig. 4a, e), males (Fig. 4b, f), and entire cohort (Fig. 3). Therefore, TAM- and PS-defined sarcopenia are not prognostic factors in our study. PM-defined sarcopenia was associated with performance status but not with age, sex, BMI, albumin levels, tumor factors, prescribed activity, and response. By contrast, significant differences were observed in TAM- and PS-defined sarcopenia in age and sex. PS-defined sarcopenia was also associated with body weight, BH, and albumin level. Furthermore, the TAM area, PM area, PS area, TAM index, and PS index were significantly higher in the men than in the women. Only the PM index showed no significant difference after stratification by sex. Therefore, the PM index may be a more robust and independent indicator for muscle mass as previous articles demonstrated in patients with advanced HCC [7].

Currently, CT remains the gold standard for measuring muscle mass [23]. In contrast to the BMI and albumin level, CT provides cross-sectional images and allows accurate muscle mass evaluation through the analysis of cross-sectional areas without bias from tissue edema, ascites, or tumor mass in the abdominal cavity [23]. Moreover, a single CT slice at the L3 level is often included in the HCC survey and serves as a good indicator for sarcopenia [24]. MRI can obtain cross-sectional images to derive fat or fat-free mass with several MRI sequences [25]. However, such sequences are time-consuming and susceptible to respiratory/motion artifacts. Although some techniques have been developed to reduce scanning time, they involve high costs and labor-intensive image analysis [26]. Therefore, only few studies have used manually feasible techniques to evaluate the fat-free muscle area of PS after radioembolization through MRI [13, 14]. However, the results and conclusion cannot be applied to our population with CT-based muscle assessment. Furthermore, the diagnosis of TAM- and PS-defined sarcopenia based on the Western population was significantly associated with gender. In contrast, the diagnosis of PM-defined sarcopenia by the Eastern population was only associated with PM area and ECOG performance status. These findings demonstrated that the Eastern PM-based criteria might be more appropriate for defining sarcopenia in Eastern countries, including Taiwan. Meanwhile, the CT-based PM-defined sarcopenia seemed reproducible in previous studies for patients with advanced HCC and those who underwent liver operation [7, 27].

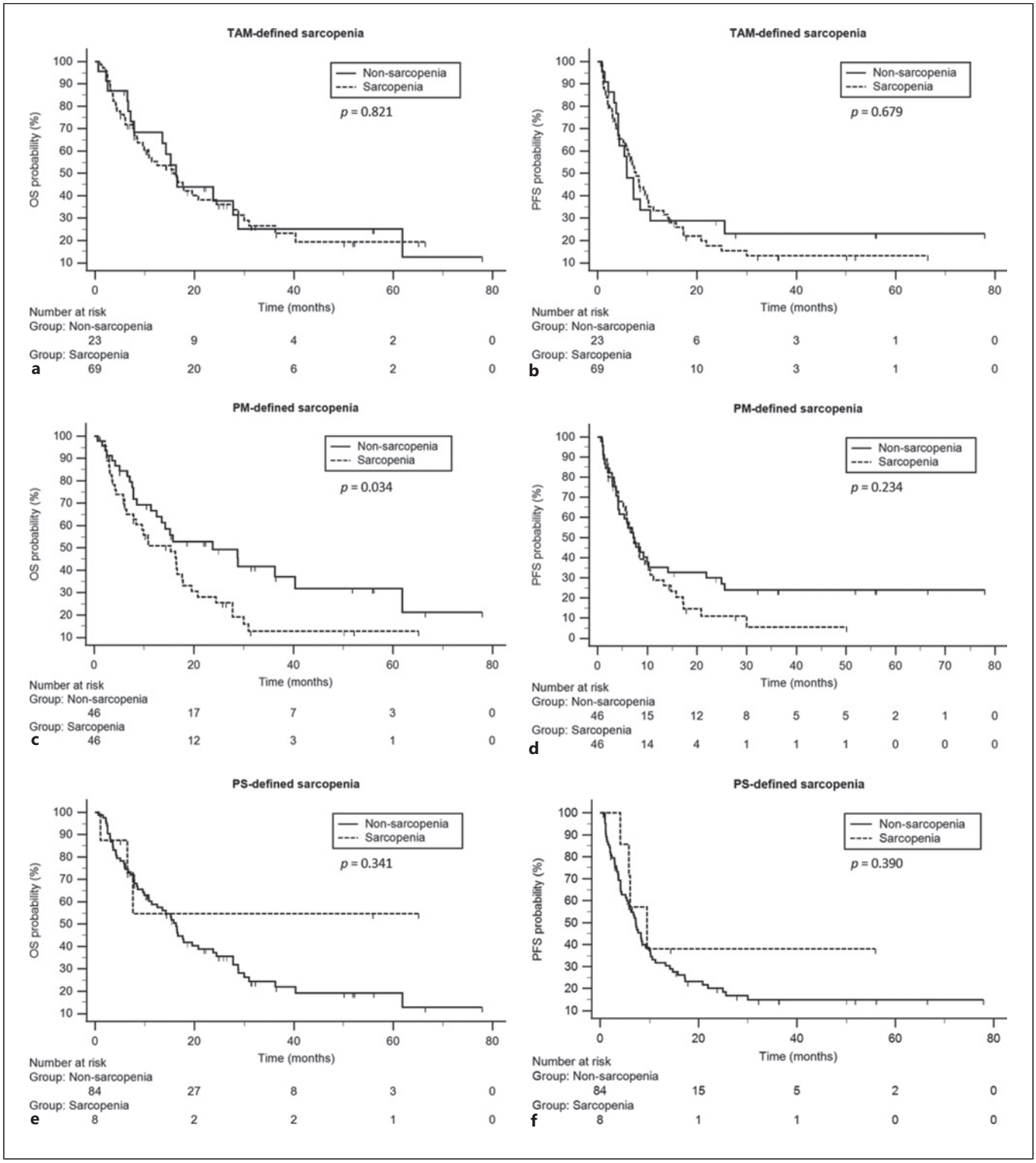

Fig. 3. Comparison of survival rates. OS was significantly different when using the PM criteria (**c**, $p = 0.034$) but did not significantly differ when using TAM and PS criteria (**a**, **e**, $p = 0.821$ and 0.341). PFS was not significantly different when using the TAM, PM, and PS criteria (**b**, **d**, and **f**, $p = 0.679$, 0.234, and 0.390). OS, overall survival; PM, psoas muscle; TAM, total abdominal muscle; PS, paraspinal muscle; PFS: progression-free survival.

Table 4. Univariate and multivariate OS analyses

	Univariate analysis				Multivariate analysis		
	HR	95% CI	*p* value		HR	95% CI	*p* value
Elderly	0.932	0.536–1.621	0.803				
Male	1.922	0.910–4.060	0.130				
Reduced BMI	2.064	1.084–3.931	0.028*	Reduced BMI	1.982	0.995–3.950	0.052
HBV related	1.461	0.848–2.516	0.172				
HCV related	0.804	0.417–1.550	0.515				
ALBI grade >1	3.262	1.931–5.509	<0.001*	ALBI grade >1	2.711	1.565–4.695	<0.001*
MELD score	1.108	1.018–1.207	0.017*	MELD score	1.131	1.020–1.254	0.019*
Size >5 cm	1.363	0.792–2.346	0.263				
Number >5	1.349	0.790–2.305	0.273				
Bilobar	0.774	0.466–1.287	0.323				
AFP >400 ng/mL	2.603	1.551–4.371	<0.001*	AFP >400 ng/mL	1.525	0.834–2.789	0.170
BCLC stage C	1.978	1.184–3.305	0.009*	BCLC stage C	0.860	0.639–1.158	0.320
ECOG performance status 1	1.946	0.954–3.969	0.067				
Prior therapy	0.666	0.392–1.132	0.133				
4-month objective response	0.431	0.257–0.724	<0.001*	4-month objective response	0.464	0.265–0.812	0.007*
Posttreatment curative therapy	0.283	0.141–0.568	<0.001*	Posttreatment curative therapy	0.405	0.187–0.877	0.022*
TAM-defined sarcopenia	1.070	0.603–1.897	0.817				
PM-defined sarcopenia	1.735	1.036–2.903	0.036*	PM-defined sarcopenia	1.899	1.087–3.315	0.024*
PS-defined sarcopenia	0.574	0.179–1.842	0.351				

HR, hazard ratio; CI, confidence interval; BMI, body mass index; HBV, hepatitis B virus; HCV, hepatitis C virus; ALBI, albumin-bilirubin; MELD, Model for End-Stage Liver Disease; BCLC, Barcelona Clinic Liver Cancer; ECOG, Eastern Cooperative Oncology Group; TAM, total abdominal muscle; PM, psoas muscle; PS, paraspinal muscle. *$p < 0.05$.

Although performance status is included in the BCLC staging system for HCC and has been associated with poor prognosis [28], its clinical diagnosis is subjective with interobserver variability [29]. By contrast, we observed that PM-defined sarcopenia remained an independent predictor of OS even after adjustment for tumor size, extent, and liver function, whereas performance status did not. These results are similar to the previous study in patients receiving sorafenib treatment [7]. Like patients receiving sorafenib treatment, the inclusion criteria of our study were unresectable HCCs. Therefore, the percentage of downstaging to curative therapy was around 20%. The downstaging rate will increase if we include patients with borderline resectable HCC. After stratification by the presence of posttreatment curative therapy, PM-defined sarcopenia was still a poorer prognostic factor in patients without posttreatment curative therapy. But PM-defined sarcopenia was a non-significant poorer prognostic factor in patients receiving posttreatment curative therapy. Our results showed that patients who underwent curative treatment after radioembolization had a more favorable prognosis. In previous studies, sarcopenia was associated with postoperative complications, longer hospital stays, and poorer prognosis for liver transplantation and resection [30, 31]. Therefore, identifying patients with further curative treatment potential or sarcopenia before radioembolization is crucial. Further studies should investigate whether perioperative nutritional therapy can increase survival in patients undergoing radioembolization for downstaging.

Liver function is also an essential factor associated with HCC prognosis [32]. Our study demonstrated this concept in patients who underwent radioembolization. Furthermore, ALBI grade is a more objective and accurate indicator than the Child-Pugh score to predict the prognosis of liver cirrhosis and advanced HCCs [33, 34]. ALBI grading requires objective laboratory data, obviating the subjectivity in the judgment of ascites amount and hepatic encephalopathy, which is required for Child-Pugh staging. However, the albumin level may fluctuate after intravenous supplement. The PS-defined sarcopenia was associated with albumin level in our study and might be biased by liver function. Therefore, CT-assessed TAM- and PM-defined sarcopenia may be a potential adjustment and serve as a poorer prognostic factor in patients with liver cirrhosis in many studies [35–37]. Recently, a study indicated that the composite model with sarcopenia

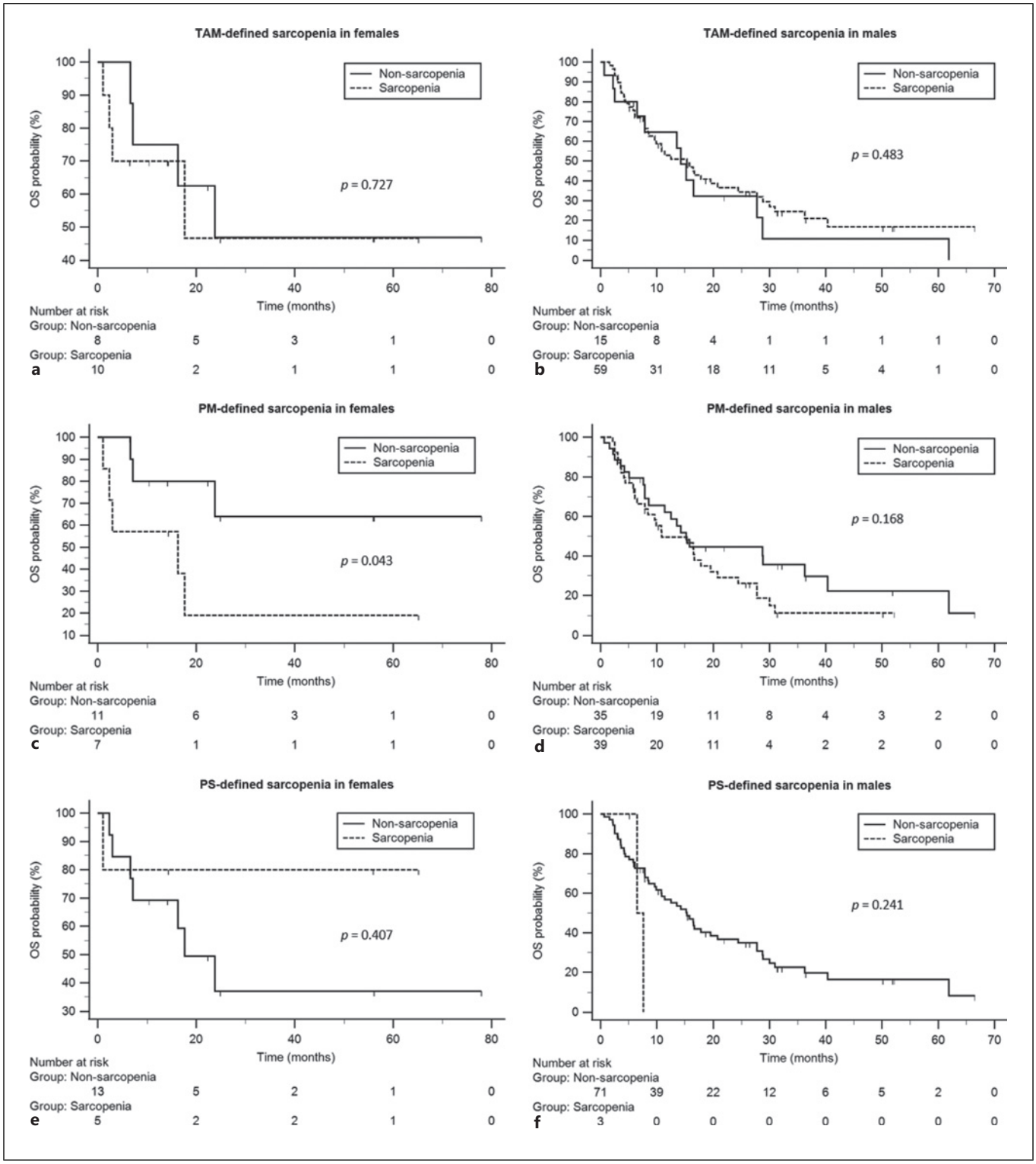

Fig. 4. Comparison of survival rates stratified by sex. OS was significantly different when using PM-defined sarcopenia (**c**, $p = 0.043$) in women but not in men (**d**, $p = 0.168$). OS did not significantly differ when using TAM (**a**, **b**) or PS (**e**, **f**) criteria in either sex. OS, overall survival; PM, psoas muscle; TAM, total abdominal muscle; PS, paraspinal muscle.

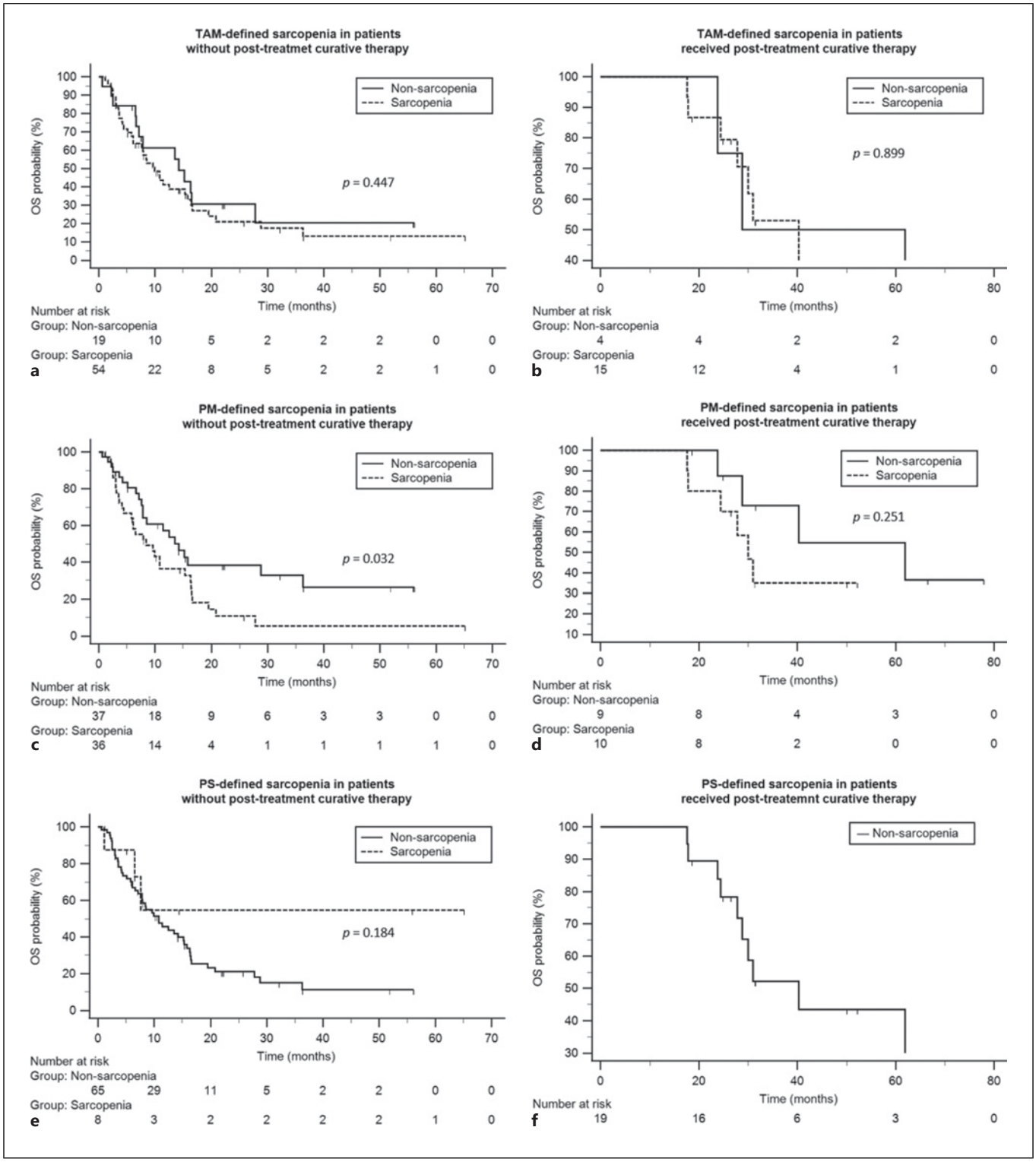

Fig. 5. Comparison of survival rates stratified by the presence of posttreatment curative therapy. OS was significantly different in patients without posttreatment curative therapy (**c**, $p = 0.032$) but not in patients received posttreatment curative therapy (**d**, $p = 0.251$). OS did not significantly differ when using TAM (**a**, **b**) or PS (**e**, **f**) criteria. OS, overall survival; PM, psoas muscle; TAM, total abdominal muscle; PS, paraspinal muscle.

and the MELD are better prognostic models than ALBI and MELD scores in patients with HCC awaiting liver transplantation [38]. Finally, a large tumor burden may compress the gastrointestinal tract and reduce patients' appetite. However, in our study, no significant difference was reported in the maximal tumor size, the percentage of tumor size >5 cm, total tumor volume and non-tumor liver volume between patients with and without sarcopenia, and the percentage of patients with >5 tumors was nonsignificantly higher in the sarcopenia group than in the nonsarcopenia group.

In our study, only PM served as a prognostic factor in the patients receiving radioembolization rather than TAM or PS. The debate regarding which abdominal muscle can serve as an indicator for sarcopenia has been outlined in previous studies [15, 16]. However, an internationally accepted standard for assessing sarcopenia based on CT is unavailable. In an earlier study, TAM correlated well with whole-body muscle mass in DXA-based validation [39]; however, a recent study concluded that PM was more correlated than TAM with lean soft tissue [40]. TAM contains diverse muscles, including the PM, PS, abdominal wall muscles, and rectus abdominis. By contrast, PM represents a minority of the total trunk mass, but the measurement of PM alone is much easier and time-saving. PS is also relatively easy to measure in abdominal MRI, so previous MRI-based studies showed PS had a survival impact in patients who received radioembolization [13, 14]. Different results may indicate different muscles with a specific function [41]. For example, PM is the main flexor of the hip, and PS is the primary extensor of the trunk [42–44]. So we can hypothesize that PM may be a better indicator if the disease affects dynamic muscle function. In contrast, if the disease mainly affects static muscle function, PS may be a better indicator. Identifying the index muscle can help plan physical activity for muscle training and improve outcomes. Furthermore, the purpose of the adjustment for PM and TAM areas is to enable unbiased comparisons across the range of BH, such as BMI. Similar to BMI, the PM and TAM indices – defined as PM and TAM areas divided by squared BH in meters – have been widely used in most studies [10, 12, 45] and systematic reviews [46, 47]. Only a few have used the unadjusted muscle area [13, 14] or another adjusted method with BH only [48].

Our study has some limitations. First, this retrospective review study included a modest sample size with more than 1-year follow-up. After stratification by sex, PM-defined sarcopenia was a significant factor in the women and a nonsignificant factor in the men for poorer prognosis. TAM- or PS-defined sarcopenia had inconsistent results for prognosis between the men and women. But the potential role of PM-defined sarcopenia can be identified. However, after combining the data of the men and women, PM-defined sarcopenia was still an independent prognostic factor. Further large-scale studies with long-term and serial follow-up should be conducted to confirm the role of sarcopenia in both sexes. Second, additional interventional studies, such as nutritional support, muscle training, or hormone-related agents, may be considered to extend our findings and observe changes in muscle mass after interventions. Third, we used the manual tracing method to measure TAM, PM, and PS areas. Some observational bias may be present, but we followed the semiautomatic method to reduce observer variability. The measurement error during manual tracking may be solved soon using automated processes to mitigate interobserver and intraobserver variabilities [49, 50]. Finally, our data were only involved in a single tertiary-referred medical center, and all the patients had intermediate to advanced HCCs and underwent resin-based radioembolization for locoregional control. Additional studies should evaluate whether our findings can be applied to patients who underwent glass-based radioembolization or combined with immunotherapy, such as PD1 blockade. In conclusion, CT-assessed, PM-defined sarcopenia was a prognostic factor for OS in the patients with intermediate to advanced HCC receiving radioembolization after adjustment for reduced BMI, ALBI grade >1, MELD score, AFP level >400 ng/mL, BCLC stage C, 4-month objective response, and posttreatment curative therapy.

Acknowledgments

The study was partially presented at the 2022 APASL-STC (Asia Pacific Association of the Study of the Liver – Single Topic Conference) on HCC in Taiwan and awarded the Outstanding Abstract Award.

Statement of Ethics

This study protocol was reviewed and approved by the Institutional Review Board of National Taiwan University Hospital, approval number, 201805070RIND. The need for informed consent was waived by the Institutional Review Board of National Taiwan University Hospital, approval number, 201805070RIND.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

The study was financially supported by National Taiwan University Hospital (106-23).

Author Contributions

All authors are aware of and agree to the submission and that they have all contributed to the work described sufficiently to be named as authors. Chih-Horng Wu was responsible for radioembolization procedure, manuscript writing, and statistical analysis. Ming-Chih Ho, Chien-Hung Chen, Ja-Der Liang, and Kai-Wen Huang contributed to clinical data collection. Mei-Fang Cheng helped for the dosimetry of radioembolization. Chih-Kai Chang and Chia-Hung Chang helped in image collection and radioembolization technique. Po-Chin Liang performed the radioembolization procedure, designed the study, and revised the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

References

1 Rawla P, Sunkara T, Muralidharan P, Raj JP. Update in global trends and aetiology of hepatocellular carcinoma. Contemp Oncol. 2018;22(3):141–50.
2 European Association For The Study Of The Liver; European Organisation For Research And Treatment Of Cancer. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. J Hepatol. 2012 Apr;56(4):908–43.
3 Bruix J, Sherman M, American Association for the Study of Liver Diseases. Management of hepatocellular carcinoma: an update. Hepatology. 2011 Mar;53(3):1020–2.
4 Liapi E, Geschwind J-FH. Intra-arterial therapies for hepatocellular carcinoma: where do we stand? Ann Surg Oncol. 2010 May;17(5):1234–46.
5 Chow PKH, Gandhi M, Tan S-B, Khin MW, Khasbazar A, Ong J, et al. SIRveNIB: selective internal radiation therapy versus sorafenib in asia-pacific patients with hepatocellular carcinoma. J Clin Oncol. 2018 Jul;36(19):1913–21.
6 Shao Y-Y, Wang S-Y, Lin S-M; Diagnosis GroupSystemic Therapy Group, Ho M-C, et al. Management consensus guideline for hepatocellular carcinoma: 2020 update on surveillance, diagnosis, and systemic treatment by the Taiwan Liver Cancer Association and the Gastroenterological Society of Taiwan. J Formos Med Assoc. 2021 Apr;120(4):1051–60.
7 Wu C-H, Liang P-C, Hsu C-H, Chang F-T, Shao Y-Y, Ting-Fang Shih T. Total skeletal, psoas and rectus abdominis muscle mass as prognostic factors for patients with advanced hepatocellular carcinoma. J Formos Med Assoc. 2021;120(1):559–66.
8 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 Jul;39(4):412–23.
9 Mourtzakis M, Prado CMM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Appl Physiol Nutr Metab. 2008 Oct;33(5):997–1006.
10 Prado CMM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. Lancet Oncol. 2008 Jul;9(7):629–35.
11 Hamaguchi Y, Kaido T, Okumura S, Kobayashi A, Hammad A, Tamai Y, et al. Proposal for new diagnostic criteria for low skeletal muscle mass based on computed tomography imaging in Asian adults. Nutrition. 2016 Dec;32(11–12):1200–5.
12 Dodson RM, Firoozmand A, Hyder O, Tacher V, Cosgrove DP, Bhagat N, et al. Impact of sarcopenia on outcomes following intra-arterial therapy of hepatic malignancies. J Gastrointest Surg. 2013 Dec;17(12):2123–32.
13 Guichet PL, Taslakian B, Zhan C, Aaltonen E, Farquharson S, Hickey R, et al. MRI-derived sarcopenia associated with increased mortality following yttrium-90 radioembolization of hepatocellular carcinoma. Cardiovasc Intervent Radiol. 2021 Oct;44(10):1561–9.
14 Faron A, Sprinkart AM, Pieper CC, Kuetting DLR, Fimmers R, Block W, et al. Yttrium-90 radioembolization for hepatocellular carcinoma: outcome prediction with MRI derived fat-free muscle area. Eur J Radiol. 2020 Feb;125:108889.
15 Ebadi M, Wang CW, Lai JC, Dasarathy S, Kappus MR, Dunn MA, et al. Poor performance of psoas muscle index for identification of patients with higher waitlist mortality risk in cirrhosis. J Cachexia Sarcopenia Muscle. 2018;9(6):1053–62.
16 Baracos VE. Psoas as a sentinel muscle for sarcopenia: a flawed premise. J Cachexia Sarcopenia Muscle. 2017 Aug;8(4):527–8.
17 Cederholm T, Bosaeus I, Barazzoni R, Bauer J, Van Gossum A, Klek S, et al. Diagnostic criteria for malnutrition - an ESPEN consensus statement. Clin Nutr. 2015 Jun;34(3):335–40.
18 Kamath PS, Wiesner RH, Malinchoc M, Kremers W, Therneau TM, Kosberg CL, et al. A model to predict survival in patients with end-stage liver disease. Hepatology. 2001 Feb;33(2):464–70.
19 Johnson PJ, Berhane S, Kagebayashi C, Satomura S, Teng M, Reeves HL, et al. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. J Clin Oncol. 2015 Feb;33(6):550–8.
20 Chen L-T, Martinelli E, Cheng A-L, Pentheroudakis G, Qin S, Bhattacharyya GS, et al. Pan-Asian adapted ESMO Clinical Practice Guidelines for the management of patients with intermediate and advanced/relapsed hepatocellular carcinoma: a TOS–ESMO initiative endorsed by CSCO, ISMPO, JSMO, KSMO, MOS and SSO. Ann Oncol. 2020 Mar;31(3):334–51.
21 Lencioni R, Llovet JM, Modified RECIST. Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. Semin Liver Dis. 2010 Feb;30(1):52–60.
22 Gomez-Perez SL, Haus JM, Sheean P, Patel B, Mar W, Chaudhry V, et al. Measuring abdominal circumference and skeletal muscle from a single cross-sectional computed tomography image A step-by-step guide for clinicians using national Institutes of Health ImageJ. JPEN J Parenter Enteral Nutr. 2015;40(3):308–18.
23 Mitsiopoulos N, Baumgartner RN, Heymsfield SB, Lyons W, Gallagher D, Ross R. Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. J Appl Physiol. 1998 Jul;85(1):115–22.

24 Kim TY, Kim MY, Sohn JH, Kim SM, Ryu JA, Lim S, et al. Sarcopenia as a useful predictor for long-term mortality in cirrhotic patients with ascites. J Korean Med Sci. 2014 Sep; 29(9):1253–9.
25 Fujiwara N, Nakagawa H, Kudo Y, Tateishi R, Taguri M, Watadani T, et al. Sarcopenia, intramuscular fat deposition, and visceral adiposity independently predict the outcomes of hepatocellular carcinoma. J Hepatol. 2015 Jul;63(1):131–40.
26 Guerri S, Mercatelli D, Aparisi Gómez MP, Napoli A, Battista G, Guglielmi G, et al. Quantitative imaging techniques for the assessment of osteoporosis and sarcopenia. Quant Imaging Med Surg. 2018 Feb;8(1): 60–85.
27 Thomas EL, Fitzpatrick JA, Malik SJ, Taylor-Robinson SD, Bell JD. Whole body fat: content and distribution. Prog Nucl Magn Reson Spectrosc. 2013 Aug;73:56–80.
28 Valero V, Amini N, Spolverato G, Weiss MJ, Hirose K, Dagher NN, et al. Sarcopenia adversely impacts postoperative complications following resection or transplantation in patients with primary liver tumors. J Gastrointest Surg. 2015 Feb;19(2):272–81.
29 Hsu C-Y, Lee Y-H, Hsia C-Y, Huang Y-H, Su C-W, Lin H-C, et al. Performance status in patients with hepatocellular carcinoma: determinants, prognostic impact, and ability to improve the Barcelona Clinic Liver Cancer system. Hepatology. 2013;57(1):112–9.
30 Blagden SP, Charman SC, Sharples LD, Magee LRA, Gilligan D. Performance status score: do patients and their oncologists agree? Br J Cancer. 2003 Sep;89(6):1022–7.
31 Berardi G, Antonelli G, Colasanti M, Meniconi R, Guglielmo N, Laurenzi A, et al. Association of sarcopenia and body composition with short-term outcomes after liver resection for malignant tumors. JAMA Surg. 2020 Nov;155(11):e203336.
32 Kaido T, Hamaguchi Y, Uemoto S. Significance of preoperative sarcopenia to liver surgery. Hepatobiliary Surg Nutr. 2019 Feb; 8(1):59–62.
33 Llovet JM, Bru C, Bruix J. Prognosis of hepatocellular carcinoma: the BCLC staging classification. Semin Liver Dis. 1999;19(3): 329–38.
34 Wang J, Zhang Z, Yan X, Li M, Xia J, Liu Y, et al. Albumin-Bilirubin (ALBI) as an accurate and simple prognostic score for chronic hepatitis B-related liver cirrhosis. Dig Liver Dis. 2019;51(8):1172–8.
35 Kuo Y-H, Wang J-H, Hung C-H, Rau K-M, Wu I-P, Chen C-H, et al. Albumin-Bilirubin grade predicts prognosis of HCC patients with sorafenib use. J Gastroenterol Hepatol. 2017 Dec;32(12):1975–81.
36 Hanai T, Shiraki M, Nishimura K, Ohnishi S, Imai K, Suetsugu A, et al. Sarcopenia impairs prognosis of patients with liver cirrhosis. Nutrition. 2015 Jan;31(1):193–9.
37 Golse N, Bucur PO, Ciacio O, Pittau G, Sa Cunha A, Adam R, et al. A new definition of sarcopenia in patients with cirrhosis undergoing liver transplantation. Liver Transpl. 2017 Feb;23(2):143–54.
38 Giusto M, Lattanzi B, Albanese C, Galtieri A, Farcomeni A, Giannelli V, et al. Sarcopenia in liver cirrhosis: the role of computed tomography scan for the assessment of muscle mass compared with dual-energy X-ray absorptiometry and anthropometry. Eur J Gastroenterol Hepatol. 2015 Mar; 27(3):328–34.
39 Alsebaey A, Sabry A, Rashed HS, Elsabaawy MM, Ragab A, Aly RA, et al. MELD-sarcopenia is better than ALBI and MELD score in patients with hepatocellular carcinoma awaiting liver transplantation. Asian Pac J Cancer Prev. 2021 Jul;22(7):2005–9.
40 Georgiou A, Papatheodoridis GV, Alexopoulou A, Deutsch M, Vlachogiannakos I, Ioannidou P, et al. Validation of cutoffs for skeletal muscle mass index based on computed tomography analysis against dual energy X-ray absorptiometry in patients with cirrhosis: the KIRRHOS study. Ann Gastroenterol. 2020;33(1):80–6.
41 Wu CH, Chao CT, Liang PC, Shih TTF, Huang JW. Computed tomography-based sarcopenia in patients receiving peritoneal dialysis: correlation with lean soft tissue and survival. J Formos Med Assoc. 2022 Feb; 121(2):500–9.
42 Arbanas J, Klasan GS, Nikolic M, Jerkovic R, Miljanovic I, Malnar D. Fibre type composition of the human psoas major muscle with regard to the level of its origin. J Anat. 2009 Dec;215(6):636–41.
43 Wakabayashi H, Watanabe N, Anraku M, Oritsu H, Shimizu Y. Pre-operative psoas muscle mass and post-operative gait speed following total hip arthroplasty for osteoarthritis. J Cachexia Sarcopenia Muscle. 2016 Mar;7(1):95–6.
44 Kim JC, Lee SU, Jung SH, Lim JY, Kim DH, Lee SY. Natural aging course of paraspinal muscle and back extensor strength in community-dwelling older adults (sarcopenia of spine, SarcoSpine): a prospective cohort study protocol. BMJ Open. 2019 Sep 1; 9(9):e032443.
45 Harimoto N, Shirabe K, Yamashita Y-I, Ikegami T, Yoshizumi T, Soejima Y, et al. Sarcopenia as a predictor of prognosis in patients following hepatectomy for hepatocellular carcinoma. Br J Surg. 2013 Oct; 100(11):1523–30.
46 Chang K-V, Chen J-D, Wu W-T, Huang K-C, Lin H-Y, Han D-S. Is sarcopenia associated with hepatic encephalopathy in liver cirrhosis? A systematic review and meta-analysis. J Formos Med Assoc. 2019 Apr; 118(4):833–42.
47 Chang K-V, Chen J-D, Wu W-T, Huang K-C, Hsu C-T, Han D-S. Association between loss of skeletal muscle mass and mortality and tumor recurrence in hepatocellular carcinoma: a systematic review and meta-analysis. Liver Cancer. 2018 Mar;7(1):90–103.
48 Derstine BA, Holcombe SA, Ross BE, Wang NC, Su GL, Wang SC. Optimal body size adjustment of L3 CT skeletal muscle area for sarcopenia assessment. Sci Rep. 2021 Jan; 11(1):279.
49 Popuri K, Cobzas D, Esfandiari N, Baracos V, Jägersand M. Body composition assessment in axial CT images using FEM-based automatic segmentation of skeletal muscle. IEEE Trans Med Imaging. 2016 Feb;35(2):512–20.
50 Cespedes Feliciano EM, Popuri K, Cobzas D, Baracos VE, Beg MF, Khan AD, et al. Evaluation of automated computed tomography segmentation to assess body composition and mortality associations in cancer patients. J Cachexia Sarcopenia Muscle. 2020 Apr; 11(5):1258–69.