

# Sarcopenia is Associated with Poor Performance Status in Indonesian Patients with Hepatocellular Carcinoma

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## ABSTRACT

**Background:** Sarcopenia has a notable impact on the prognosis of hepatocellular carcinoma (HCC). The prevalence of sarcopenia in patients with HCC is relatively high, with studies reporting rates between 39% and 41.7%. A substantial proportion of individuals diagnosed with HCC also exhibit muscle wasting and reduced muscle function. This study aims to determine the prevalence of sarcopenia in Indonesian patients with HCC (based on the Japanese Society of Hepatology (JSH) JSH criteria) and to examine its correlation with poor performance status.

**Methods:** We performed a cross-sectional study of 85 HCC patients between January and October 2021. The skeletal muscle index at L3 (L3 SMI) was measured on CT scans (applying JSH cut-offs for sarcopenia). Clinical data, including Eastern Cooperative Oncology Group (ECOG) performance status, were collected. Bivariate analyses and logistic regression were performed to identify factors associated with sarcopenia.

**Results:** A total of 85 HCC patients (median age: 52 years) were included in the analysis. Sarcopenia was observed in 49.4% of the cohort. Bivariate analysis revealed a statistically significant association between sarcopenia and an ECOG performance status of 2+ ( $p = 0.003$ ), as well as a MELD-Na score of  $\geq 15$  ( $p = 0.023$ ). In multivariate analysis, poor ECOG-PS remained independently associated with sarcopenia (adjusted OR 4.17; 95% CI 1.50–11.56,  $p = 0.006$ ).

**Conclusion:** Sarcopenia is highly prevalent among Indonesian HCC patients, and it is strongly associated with poor ECOG performance status.

**Keywords:** ECOG, hepatocellular carcinoma, Indonesia, L3-SMI, sarcopenia

## ABSTRAK

**Latar Belakang:** Sarkopenia mempengaruhi prognosis karsinoma sel hati (KSH). Prevalensi sarkopenia pada pasien KSH cukup tinggi, penelitian melaporkan berkisar antara 39% hingga 41,7% individu yang didiagnosis dengan KSH juga mengalami kehilangan otot dan penurunan fungsi otot. Studi ini bertujuan untuk menggambarkan proporsi sarkopenia pada dewasa, dengan menggunakan kriteria Japan Society of Hepatology dan menilai hubungan antara sarkopenia dan status performa yang buruk.

**Metode:** Studi ini dilakukan di Rumah Sakit Tersier selama bulan Januari – Oktober 2021. IMOS dievaluasi dengan menggunakan gambaran CT setinggi L3 pada 85 pasien KSH. Data klinis, laboratorium dan komposisi tubuh dianalisis dengan menggunakan analisis bivariat. Regresi logistic dilakukan untuk memperoleh hubungan independent antara status performa ECOG dan status sarkopenia pada pasien KSH.

**Hasil:** Delapan puluh lima pasien KSH (usia median: 52 tahun) dilakukan analisis. Sarkopenia diamati pada 49,4% pasien KSH. Analisis bivariat menunjukkan bahwa KSH secara statistik signifikan berhubungan dengan ECOG-PS 2+ ( $p = 0,003$ ) dan skor MELD-Na  $\geq 15$  ( $p = 0,023$ ). Hasil analisis regresi multivariate menunjukkan status performa ECOG buruk berhubungan secara independent dengan sarkopenia pada KSH (adjusted OR = 4,169 (95% CI: 1,504-11,555),  $p = 0,006$ ).

**Kesimpulan:** Proporsi sarkopenia dijumpai tinggi pada pasien KSH. Terdapat hubungan yang kuat antara status performa ECOG dan sarkopenia pada KSH.

**Kata kunci:** ECOG, karsinoma hepatoseluler, Indonesia, L3-SMI, sarkopenia

## INTRODUCTION

Hepatocellular carcinoma (HCC) accounts for approximately 90% of primary liver cancer (90%), with an estimated 906,000 new diagnoses and 830,000 deaths globally.<sup>1</sup> In Indonesia, as in many other Asian countries, chronic infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) remains the leading risk factor for HCC.<sup>1</sup> This disease is associated with high mortality, morbidity, and significant healthcare costs.<sup>1-3</sup> In addition to clinical complications arising from hepatocellular failure and portal hypertension, sarcopenia is another important health problem that is commonly found in HCC. Previously known as an age-associated muscle disease characterised by the progressive loss of muscle mass, it is also known to occur in chronic diseases. In Asian countries, guidelines regarding sarcopenia are still limited, and only a small number of countries have established a definite cutoff for the assessment of sarcopenia. Japan Society of Hepatology (JSH) defines sarcopenia as a decrease in skeletal muscle mass shown by low lumbar 3 skeletal muscle index (L3SMI).<sup>4</sup> Sarcopenia is associated with poor outcomes in HCC. In Indonesia, only one study has reported sarcopenia prevalence using retrospective data.<sup>5</sup>

Sarcopenia evaluation in HCC involves measuring muscle mass. Muscle mass can be quantified using several modalities, such as computed tomography (CT), magnetic resonance imaging (MRI), dual X-ray absorptiometry (DXA), and bioelectrical impedance analysis (BIA). Cross-sectional imaging, such as CT, has allowed for

direct assessment of skeletal muscle mass. According to JSH, the muscle mass evaluation reference standard for L3SMI is CT-scan.<sup>4,6</sup>

Currently, clinicians still depend on the Eastern Cooperative Oncology Group performance status (ECOG-PS) assessment to determine therapy for HCC. Evidence suggests that PS assessment can help determine survival.<sup>7</sup> Furthermore, PS assessment is subjective and has inter-observer variability. Physical inactivity, one of the parameters in ECOG-PS, is known to reduce muscle mass. In addition, Cortellini et al.<sup>8</sup> also reported an association between poor ECOG-PS and sarcopenia in patients diagnosed with cancer. Early detection of low muscle mass or sarcopenia and the factors associated with this condition may aid in improving its treatment and, therefore, increase the prognosis of HCC. The aims of the present study were (1) to estimate sarcopenia prevalence using the JSH guidelines, and (2) to identify the association between ECOG-PS and sarcopenia.

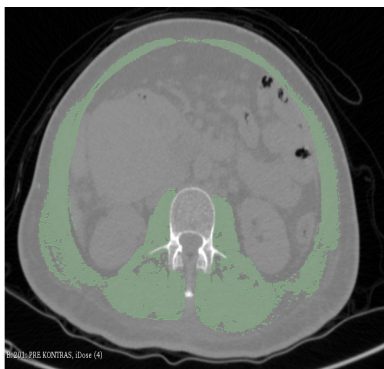
## METHODS

This cross-sectional study was approved by the Ethical Committee of the Faculty of Medicine Universitas Indonesia/Cipto Mangunkusumo Hospital (No. KET-1509/UN2.F1/ETIK/PPM.00.02/2020) and conducted from January to October 2021 at the Hepatology Clinic and Medical Ward of Cipto Mangunkusumo Hospital, Jakarta, Indonesia. We recruited patients aged 18–60 years who underwent a multiphase abdominal CT scan with contrast and could comply with study procedures,

including thigh muscle thickness examination (performed on the day consent was obtained). Those with active non-HCC malignancies, HIV infection, and chronic obstructive pulmonary disease were excluded.

The patients' characteristics included in this study included age, sex, aetiology of HCC, Child-Pugh score, Barcelona Clinic Liver Cancer (BCLC) stage, Model for End-Stage Liver Disease (MELD) score, MELD-sodium (MELD-Na) score, albumin, and ECOG-PS. Nutritional status was evaluated based on body weight, body status, and body mass index (BMI). Patients were categorized according to their BMI ( $< 18,5 \text{ kg/m}^2$  and  $\geq 18,5 \text{ kg/m}^2$ ), Child-Pugh score ( $< 8$  and  $\geq 8$ ), albumin level ( $< 3 \text{ g/dL}$  and  $\geq 3 \text{ g/dL}$ ), MELD-Na score ( $< 15$  and  $\geq 15$ ), and ECOG-PS (good: 0 and 1; poor: 2+).

CT scans were performed as a standard procedure for the diagnosis of HCC. Skeletal muscle area was segmented at the center plane of the third lumbar vertebra (L3) using axial CT scans.<sup>4</sup> The total skeletal muscle area was assessed using 3D slicer, a software platform for medical image segmentation.<sup>9</sup> The analysis included several muscle groups: rectus abdominis, transversus abdominis, internal and external obliques, quadratus lumborum, psoas major, and erector spinae. All muscle areas were measured using a Hounsfield Unit (HU) range of -29 to 150. The skeletal muscle index at L3 (L3SMI) was calculated using the formula:  $\text{mL3SMI (cm}^2/\text{m}^2) = \text{total skeletal muscle area at L3 (cm}^2) \text{ divided by the square of body height (m}^2\text{)}$ . A representative case is presented in **Figure 1**.



**Figure 1.** CT scan of a representative case. Cross-sectional areas ( $\text{cm}^2$ ) of the skeletal muscles at the third lumbar level were measured by manual tracing on the CT images, and their sum was calculated. The green area shows skeletal muscle at the third lumbar level. CT, computed tomography.

According to the JSH, the cutoff values for diagnosing sarcopenia are less than  $38 \text{ cm}^2/\text{m}^2$  for females and less than  $42 \text{ cm}^2/\text{m}^2$  for males. When using the psoas muscle index (PMI), the thresholds are  $< 3.92 \text{ cm}^2/\text{m}^2$  for females and  $< 6.36 \text{ cm}^2/\text{m}^2$  for males. Sarcopenia is defined by

the presence of low muscle mass. Data from additional laboratory and radiological (CT scan) examinations were obtained by the main researcher and research assistants. The participants also underwent body weight and height measurements.

Statistical analyses were conducted using SPSS version 23.0. The study was designed with the statistical power of 80% and a significance level ( $\alpha$ ) of 5%. Based on these parameters, the minimum sample size was 74 subjects. The baseline and clinical characteristics of the research subjects are presented in tabular form. Categorical data are presented as numbers and percentages. Numerical data are presented as mean and standard deviation if the data distribution is normal, and median, minimum, and maximum values if the data distribution is not normal.

To assess the association between ECOG-PS and sarcopenia in HCC patients, bivariate analysis was initially conducted on variables potentially linked to sarcopenia. Each variable was analyzed using the chi-square test or Fisher-exact test as an alternative if the conditions for the Chi-square test were not met. The odds ratio (OR) of each variable associated with sarcopenia was determined. Significant variables with a p-value  $< 0.25$  in bivariate analysis were included in the logistic regression model. Logistic regression analysis was performed to determine the correlation of the ECOG-PS and sarcopenia in patients with HCC after adjusting for other significant variables.

## RESULTS

There were 95 subjects who met the inclusion criteria and 10 subjects who did not, resulting in 85 subjects being included in the final analysis. The complete characteristics of the research subjects are presented in **Table 1**.

Bivariate analyses were carried out to determine the association between sarcopenia (based on L3SMI criteria) and body mass index, sex, Child-Pugh score, ECOG-PS, albumin level, MELD-Na score, and BCLC stage (**Table 2 and 3**). Statistically significant associations were found between sarcopenia in patients with HCC and an ECOG-PS score of 2+ ( $p = 0.003$ ), an MELD-Na score  $\geq 15$  ( $p = 0.023$ ), and BCLC staging ( $p = 0.012$ ). BMI, sex, Child-Pugh score, and albumin level were not associated with sarcopenia in HCC based on the L3SMI criteria.

**Table 3** shows that variables with a p value  $< 0.25$  included MELD-Na, BMI and BCLC stage. These three variables were subsequently entered into the logistic regression analysis one at a time, following the Hierarchically Well Formulated (HWF) principle.

**Table 1. Research Subjects Characteristics**

Variables	n = 85
Age in years, median (min-max)	52 (35-60)
BMI in kg/ m <sup>2</sup> , median (min-max)	22.68 (15.63-37.95)
Sex, n (%)	
Male	63 (74.1)
Female	22 (25.90)
Sarcopenia based on L3SMI criteria, n (%)	
Yes	42 (4.40)
No	43 (50.6)
Sarcopenia based on PMI criteria, n (%)	
Yes	68 (80.0)
No	17 (20.0)
Child-Pugh class, n (%)	
Class A	46 (54.10)
Class B	31 (36.50)
Class C	8 (9.40)
HCC aetiology, n (%)	
Hepatitis B	51 (60.00)
Hepatitis C	20 (23.50)
Hepatitis Non-B Non-C	13 (15.30)
Hepatitis B and C	1 (1.20)
BCLC criteria, n (%)	
Stage 0	1 (1.20)
Stage A	18 (21.20)
Stage B	29 (34.10)
Stage C	30 (35.30)
Stage D	7 (8.20)
ECOG performance status, n (%)	
ECOG 0-1	56 (65.90)
ECOG 2+	29 (34.10)
Albumin in g/ dL, mean (SD)	3,42 (0.67)
Bilirubin in mg/ dL, median (min-max)	1.03 (0.28-36.85)
INR, median (min-max)	1.11 (0.85-2.78)
Creatinine in mg/ dL, median (min-max)	0.8 (0.40-2.60)
Sodium in mEq/ L, median (min-max)	135 (120-143)
MELD score, median (min-max)	9 (6-32)
MELD-Na score, median (min-max)	13 (6-33)
PMI in cm <sup>2</sup> / m <sup>2</sup> , mean (SD)	4.35 (1,76)
L3 skeletal muscle index in cm <sup>2</sup> / m <sup>2</sup> , mean (SD)	41.13 (9.31)

Note: min-max: minimal – maximal, n: number, BMI: body mass index, SD: standard deviation, kg: kilograms, mm: millimeter, cm: centimeter, m: meter, PMI: psoas muscle index

**Table 2. Association Between ECOG Performance Status and Sarcopenic HCC Patient**

Variables	Sarcopenia	Non-Sarcopenia	p value	Odds Ratio (95% CI)
ECOG Performance Status, n (%)				
ECOG 2+	21 (72.41)	8 (27.59)	<b>0.003</b>	<b>4.375 (1.646-11.630)</b>
ECOG 0-1	21 (37.50)	35 (83.93)		

**Table 3. Association between confounding and sarcopenic HCC patient**

Variables	Sarcopenia	Non-Sarcopenia	P value	Odds Ratio (95% CI)
BMI, n (%)				
< 18.5 kg/ m <sup>2</sup>	6 (75.00)	2 (25.00)	0.147	3.417 (0.649-18.001)
≥ 18.5 kg/ m <sup>2</sup>	36 (46.75)	41 (53.25)		
Sex, n (%)				
Male	29 (46.03)	34 (53.97)	0.294	0.590 (0.221-1.579)
Female	13 (59.10)	9 (40.90)		
Child-Pugh score, n (%)				
≥ 8	11 (52.38)	10 (47.62)	0.754	1.171 (0.437-3.141)
< 8	31 (43.48)	33 (56.52)		
Albumin, n (%)				
< 3 g/ dL	15 (55.56)	12 (44.44)	0.440	1.435 (0.573-3.593)
≥ 3 g/ dL	27 (46.55)	31 (53.45)		
MELD-Na, n (%)				
≥ 15	22 (64.71)	12 (35.29)	<b>0.023</b>	<b>2.842 (1.155-6.992)</b>
< 15	20 (39.22)	31 (60.78)		
BCLC stage, n (%)				
C – D	24 (64.86)	13 (35.14)	<b>0.012</b>	<b>3.077 (1.260-7.513)</b>
0 – A – B	18 (37.50)	30 (62.50)		

**Table 4. Association Between ECOG Performance Status and Sarcopenic HCC Patient Based on the PMI Criteria**

Variables	Sarcopenia	Non-Sarcopenia	p value	Odds Ratio (95% CI)
ECOG Performance Status, n (%)				
ECOG 2+	27 (93.10)	2 (6.90)	<b>0.030</b>	<b>4.939 (1.045-23.347)</b>
ECOG 0-1	41 (73.21)	15 (26.79)		

**Table 5. Association Between Confounding and Sarcopenic HCC Patient Patient Based on the PMI Criteria**

Variables	Sarcopenia	Non-Sarcopenia	P value	Odds Ratio (95% CI)
BMI, n (%)				
< 18.5 kg/ m <sup>2</sup>	8 (100.00)	0 (00.00)	0.348	1.283 (1.139-1.445)
≥ 18.5 kg/ m <sup>2</sup>	60 (77.92)	17 (22.08)		
Sex, n (%)				
Male	53 (84.13)	10 (15.87)	0.128	2.473 (0.804-7.604)
Female	15 (68.18)	7 (31.82)		
Child-Pugh score, n (%)				
≥ 8	18 (85.71)	3 (14.29)	0.545	1.680 (0.432-6.535)
< 8	50 (78.13)	14 (21.88)		
Albumin, n (%)				
< 3 g/ dL	25 (92.59)	2 (7.41)	0.048	4.360 (0.920-20.659)
≥ 3 g/ dL	43 (74.14)	15 (25.86)		
MELD-Na, n (%)				
≥ 15	29 (85.29)	5 (14.71)	0.319	1.785 (0.566-5.629)
< 15	39 (76.47)	12 (23.53)		
BCLC stage, n (%)				
C - D	34 (91.89)	3 (8.11)	0.016	4.667 (1.229-17.724)
0 - A - B	34 (70.38)	14 (29.17)		

Bivariate analyses were also conducted to determine the association between sarcopenia based on the PMI criteria and variables including body mass index, sex, Child-Pugh score, ECOG-PS, albumin level, and MELD-Na score (**Table 4 and 5**). Statistically significant associations were found between sarcopenia in patients with HCC and an ECOG-PS score of 2+ ( $p = 0.030$ ), an albumin level  $< 3$  ( $p = 0.048$ ), and BCLC stage ( $p = 0.016$ ). BMI, sex, Child-Pugh score, and MELD-Na were not associated with sarcopenia in HCC based on PMI criteria.

**Table 5** shows variables with a  $p$  value less than 0.25, specifically BCLC staging, albumin and sex. Each variable was sequentially included in the logistic regression analysis and analysed according to the hierarchically well formulated (HWF) principle.

Based on L3SMI criteria, crude analysis revealed that an ECOG performance status  $\geq 2$  was associated with higher odds of sarcopenia (OR = 4.375, 95% CI = 1.646–11.630). Sequential adjustments for MELD-

Na  $\geq 15$ , BMI  $< 18.5$  kg/m<sup>2</sup>, and BCLC stage C–D reduced the OR to 3.807, 4.169, and 3.452, respectively, corresponding to relative changes of –12.98%, –4.71%, and –21.10%, respectively, as shown in **Table 6**.

Using the PMI criteria, crude analysis indicated that patients with an ECOG performance status  $\geq 2$  had significantly higher odds of sarcopenia (OR = 4.939, 95% CI = 1.045–23.347). After adjusting for male sex, the OR increased slightly to 5.006 (95% CI = 1.043–24.031), reflecting a modest change of 1.36%. Subsequent adjustment for albumin  $< 3$  g/dL reduced the OR to 4.068 (95% CI = 0.823–20.108), corresponding to a 17.63% decrease. When BCLC stage C–D was included in the model, the OR further decreased to 2.915 (95% CI = 0.549–15.475), showing the largest attenuation of 23.34%. These findings suggest that albumin level and BCLC stage may partially confound the association between ECOG performance status and sarcopenia, while sex had minimal impact as shown in **Table 7**.

**Table 6. Multivariate Logistic Regression Analysis Sarcopenia in HCC Based on L3SMI Criteria**

Variables	OR (95% CI)	Delta OR	% Change in OR
Crude: ECOG performance status 2+	4.375 (1.646-11.630)		
Adjusted:			
(+) MELD-Na $\geq 15$	3.807 (1.400-10.353)	-0.568	-12.98%
(+) BMI $< 18.5$ kg/ m <sup>2</sup>	4.169 (1.504-11.555)	-0.206	- 4.71%
(+) BCLC Stage C-D	3.452 (1.193-9.994)	-0.923	-21.10%

**Table 7. Multivariate Logistic Regression Analysis Sarcopenia in HCC Based on PMI Criteria**

Variables	OR (95% CI)	Delta OR	% Change in OR
Crude : ECOG performance status 2+	4.939 (1.045-23.347)		
Adjusted :			
(+) Male Sex	5.006 (1.043-24.031)	0.067	1.36%
(+) Albumin < 3 g/dL	4.068 (0.823-20.108)	-0.871	-17.63%
(+) BCLC Stage C-D	2.915 (0.549-15.475)	-1.153	-23.34%

## DISCUSSION

In Asian countries, such as Indonesia, which have a high prevalence of Hepatitis B Virus (HBV) infection, HCC typically presents in individuals under 60 years old.<sup>12</sup> Previous studies reported that the median age of patients with HCC was 54 years and 55 years consecutively.<sup>10,11</sup> A study conducted in Egypt showed that 72% of HCC cases occurred in men, with the remaining 28% in women, and the mean age of participants was approximately 53.4 years.<sup>13</sup> The higher incidence of hepatocellular carcinoma (HCC) among men may be partially attributed to the presence of androgen receptors, which are more prevalent in males. These receptors may contribute to HCC progression by inhibiting the role of p-53 and DNA repair and producing oxidative stress.<sup>14</sup>

Various research stated that sarcopenia is found in 30-70% of patients with liver cirrhosis. This is due to malnutrition, impaired protein and myostatin synthesis.<sup>15</sup> A study conducted in Africa showed that in African countries other than Egypt, the number of subjects with ECOG-PS 0-1 was 42%, while 58% had ECOG-PS  $\geq 2$ , indicating that patients had already shown poor liver performance status at the initial presentation of the disease.<sup>16</sup> The high prevalence of ECOG-PS 2+ suggests that HCC with poor performance status is still underdiagnosed, possibly due to the lack of comprehensive surveillance program.

This contrasts with findings from Japan, where the prevalences of sarcopenia were reported at 65.1% and 63%, respectively.<sup>15,17</sup> In those studies, most HCC patients had undergone multiple treatment protocols prior to initiating systemic therapy such as sorafenib. These prior therapies for HCC may impair liver function, reduce quality of life, and contribute to a higher incidence of sarcopenia. In contrast, the majority of patients in our study were treatment-naïve and referred from type B hospitals.

In this study, the most common aetiology of HCC was HBV infection, accounting for 60% of cases, followed by HCV infection, non-B and non-C infection, and coinfection with HBV and HCV. Globally, HBV is implicated in approximately 50–80% of HCC cases, with particularly high prevalence in countries such

as Indonesia.<sup>18</sup> Hepatitis viruses contribute to HCC development through several indirect mechanisms affecting infected liver cells. These include chronic inflammation with immune-mediated oxidative stress, intracellular damage from viral proteins, and deregulation of cell-signaling pathways by viral proteins. Additionally, HBV has a unique ability to integrate its DNA into the host genome, leading to genomic instability, whereas HCV contributes to cancer progression by inducing metabolic alterations, such as steatosis, which accelerates the development of fibrosis and HCC.

To evaluate the association between ECOG-PS and sarcopenia based on L3SMI in patients with HCC, firstly associations between confounding variables and sarcopenia in HCC need to be assessed. Confounding variables in this study were MELD-Na, BMI, and BCLC staging. MELD-Na score, known as the best modality for predicting mortality in patients with liver cirrhosis, was also related to sarcopenia in some studies. In liver cirrhosis, where there is liver synthesis dysfunction, loss of muscle mass can occur rapidly.<sup>14</sup> Under normal conditions, muscle mass will decrease 1% annually from 30 until 70 years, increasing to 1,5% per year thereafter. However, another study found that muscle mass decrement per year in liver cirrhosis patients was 2.2%, suggesting that liver cirrhosis complication will accelerate skeletal muscle depletion. Skeletal muscle depletion in liver cirrhosis has been reported to decrease liver function severity based on the Child-Pugh score. Muscle mass decrement per year was correlated with Child-Pugh and MELD score.<sup>17</sup> Another study showed that there was a negative correlation between MELD-Na score and ratio between psoas muscle thickness, a muscle mass indicator in liver cirrhosis patients with ascites.<sup>19</sup> In this study, MELD-Na score is considered a confounding variable to the association between ECOG-PS and sarcopenia. This condition is understandable considering that a high MELD-Na score, as a sign of liver function severity, is usually accompanied by a decrease in muscle mass.

Sarcopenia is more prevalent in late BCLC stage patients due to a combination of factors related to cancer progression and treatment. Advanced liver cancer often leads to malnutrition, inflammation, and hormonal

imbalances, all of which contribute to muscle wasting. Additionally, cancer treatments, especially in later stages, can have catabolic effects and further exacerbate muscle loss. Advanced HCC is associated with a greater tumor burden and more extensive liver damage. This can lead to malnutrition, inflammation, and hormonal changes lead to interference of nutrient absorption and metabolism, chronic inflammation linked to muscle breakdown, and hormone balance disruption leading to increase muscle protein breakdown.

This study demonstrated that ECOG performance status (ECOG-PS) was independently associated with sarcopenia in patients with HCC, even after adjusting for several body composition and prognostic factors, including body mass index (BMI), albumin level, MELD-Na score, and Child-Pugh score. Multivariate analysis identified that ECOG-PS was associated with sarcopenia in patients with HCC. This study was consistent with the previous one.<sup>20</sup>

Decrease of muscle mass and strength often occur in chronic diseases. Therefore, it is not unusual to see a significant difference between ECOG-PS 2+ and sarcopenia. Performance status is a modality to measure the physical status and activity of daily living, which is related to muscle mass and strength.

A study reported the presence of sarcopenia in 34.4% of subjects with ECOG-PS 0–1 and 38.1% of those with ECOG-PS  $\geq 2$ .<sup>21</sup> Another study revealed sarcopenia in 64.8% of subjects with ECOG-PS 0-1 and 80% of subjects with ECOG-PS 2+.<sup>19</sup> Whereas other study found sarcopenia in 51.4% of subjects with ECOG-PS 0-1 and 71.4% of subjects with ECOG-PS 2+. The increasing prevalence of sarcopenia among individuals with ECOG-PS  $\geq 2$  suggests the presence of cancer cachexia, a state of loss of muscle mass and body fat in patients with more advanced stages of cancer.<sup>22</sup>

A systematic review about the association between sarcopenia and physical activity in the elderly showed that physical activities reduced the incidence of sarcopenia with OR = 0.45. Physical activities enhance muscle strength and muscle mass in adulthood. Resistance training is specifically the best way to prevent sarcopenia.<sup>23</sup> A study showed that sarcopenia was more commonly found in patients with sedentary lifestyle with less physical activities. A decrease in skeletal muscle mass could occur in early stages of the disease due to impaired protein synthesis. Physical exercises and nutritional therapy would improve physical function and increase muscle mass in patients with chronic liver disease. However, daily physical activities are disrupted in patients with ECOG-PS 2+, which will affect the incidence of sarcopenia.<sup>24</sup>

This is the first prospective study in Indonesia to examine sarcopenia in HCC patients. This study also used primary data; therefore, it did not experience a recording bias. This study defines sarcopenia by using measurements of muscle mass according to the gold standard in chronic liver disease. Patients aged over 60 years old were excluded to show the true disease entity, rather than as part of aging. However, this exclusion limits the generalisability of the findings to older HCC patients. Another limitation of the study was the small sample size of women in this study.

## CONCLUSION

In summary, the measurement of patient performance and muscle mass using validated and easily replicated tools may aid clinicians in improving the treatment of HCC patients. These assessments enable more accurate prediction of successful therapeutic goals for patients at potential risk from planned treatments, thereby allowing intervention to be targeted for each HCC patient.

## Conflict of Interest

The authors have no competing interests to disclose.

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## Author contribution

All authors contributed significantly to the work and approved the final manuscript.

## Data Availability

All data have been provided within the manuscript.

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